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ISOM posters and poster pitches

Case report

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Pubic Symphysis Osteomyelitis: A Case report
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Introduction
Pubic symphysis osteomyelitis following vaginal delivery is a rare and painful infection involving the symphysis and parasymphyseal parts of the pubic bones. It accounts for 2% of haematogenous osteomyelitis. Pubic symphysis osteomyelitis usually presents with pubic and generalized pelvic pain and low-grade fever, and may be associated with pelvic instability and a waddling gate.

Case
A 34 year old woman was brought in by ambulance after the very sudden onset of excruciating pubic pain four days postnatally following a vaginal delivery, where forceps extraction was required. She later developed pyrexia with a temperature of 38.4 degrees, elevated inflammatory markers (CRP 65.5 mg/L, white cell count 13.84 10^9/L). Blood cultures revealed a persistent Staphylococcus aureus bacteraemia, for which no other source was identified. She underwent CT of her abdomen and pelvis, and was treated with a prolonged course of intravenous then oral antibiotics.

Discussion
This condition is described infrequently in pregnancy. The main differential diagnosis is osteitis pubis, a non-infectious inflammatory disorder of the symphysis pubis that usually occurs following shearing trauma of pelvis in young athletes but can occur after delivery. Furthermore, the diagnosis of pubic symphysis osteomyelitis can be challenging with other similarly presenting conditions involving the pelvis in postnatal women, such as postpartum endomyometritis, urinary infection, persistent pelvic girdle pain and diastasis of the pubic symphysis joint. The diagnosis of pubic symphysis osteomyelitis is usually made on clinical grounds supported by investigations including inflammatory markers, blood cultures and imaging findings supportive of pubic bone infection. A biopsy from the symphysis pubis and positive bacterial culture establishes a definitive diagnosis but this is not always required to make the diagnosis. Conservative treatment based on long term antibiotics is usually sufficient in most cases; however, failure to respond properly to antibiotics would require surgical debridement.

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Squamous cell carcinoma of the tongue in pregnancy - an emerging management dilemma.
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Introduction
Increasing incidence of head and neck squamous cell carcinoma (SCC) in females is reported. There is concern this emerging trend will see increasing numbers in pregnancy with no consensus on management. In the literature, when treatment has been limited by fetal concerns, there is a trend towards early recurrence and poor prognosis. This is usually delay in treatment or restricting extent of surgery in contrast to typical management outside of pregnancy.

Case
A 33-year-old woman reported an ulcer on the lateral aspect of her tongue from the first trimester. At 29 weeks a biopsy demonstrated aggressive SCC of the tongue with lymph node metastasis (T2 N1). She had a history of type-2 diabetes mellitus. She had never smoked or drunk alcohol. An urgent multidisciplinary discussion resulted in a plan for elective pre-term caesarean section to facilitate early surgery. She was delivered at 31+2 weeks following corticosteroids and magnesium sulphate for fetal lung maturation and neuroprotection respectively. She was transferred to a tertiary maxillofacial unit and a partial glossectomy, unilateral neck dissection and lymph node excision performed on day 4 postpartum. She made an uneventful recovery and is coping well with speech therapy.
Now 9 months postpartum there is no evidence of recurrence. Her baby was discharged at 4-weeks-old and to date has no ill effects of prematurity.

Discussion
There is increasing understanding of the benefits of managing women with cancer in pregnancy in accordance with non-pregnant standards, avoiding under-treatment and poor prognosis. Rarely is premature delivery necessary. Head and neck SCC presents unique challenges, surgery can be complex with difficult airway management and unpredictable, long operating times. Limiting extent of surgery because of fetal concerns is reported with grave consequences. Multidisciplinary planning with patient involvement is key to make a balanced risk assessment for the mother and fetus.

Exceedingly rare presentation of gestational trophoblastic disease: Molar pregnancy implantation in Caesarean scar
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Introduction: Gestational trophoblast disease (GTD) forms a spectrum of illnesses that are rare, almost always highly curable, but not always well understood by non-specialists. The types of trophoblast disease range from the usually benign partial molar pregnancy through complete molar pregnancy and invasive mole to the malignant choriocarcinoma and placental site trophoblast tumours. All of these illnesses share the characteristic that they arise from a pregnancy. While ectopic pregnancy may occur in 1:1000 pregnancies (mortality 1.7 per 10,000 cases caesarean scar ectopic is an extremely rare condition with an incidence of between 1:1800–2216 pregnancies. The coexistence of these two conditions have not been reported in Australia with only a handful described internationally. Methods: Case report Results: I present the case of a 34 year old multiparous lady presented with the unfortunate diagnosis of a molar pregnancy implanted in her caesarean scar. She was initially treated at a metropolitan centre before requiring transfer to a specialist unit. Discussion: I discuss the clinical manifestations, appropriate diagnostic tools and management of this extremely unusual and unexpected clinical case.

Pregnant with Marfan syndrome and aortic root aneurism: dissection case report for the third quarter
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INTRODUCTION
The main cardiovascular complications of Marfan Syndrome (MS) are valvar disease, heart failure and aortic dissection. Pregnancy in a patient with MS presents greater risk of aortic complications. Aortic root diameter greater than 45 mm is a class IV of modified World Health Organization classification of maternal pregnancy risk (high risk of maternal death or severe morbidity). We discuss a case of aortic dissection in the third trimester in a MS patient with aortic dilation previous to pregnancy.

METHOD
Review of medical charts.

CASE DESCRIPTION
Patient 40 years old, with MS, previous echocardiogram with aortic root of 54mm, ascending aorta of 56mm, and normal aortic arch. She refused therapeutic abortion. During prenatal she remained asymptomatic, under use of metoprolol for 75mg. A new echocardiogram was made in the second trimester, without alterations. At 30 weeks of gestation, she presented with aortic dissection type Stanford A. A cesarean section was performed under general anesthesia, followed by subtotal hysterectomy, during which the patient remained stable. Subsequently, correction of dissection of the ascending aorta was initiated, with a Benton procedure and right coronary artery bypass. An intraoperative myocardial infarction caused cardiorespiratory arrest reversed during surgery, but a new episode during anesthetic lead to death. The 1370g live neonate had a good outcome.

DISCUSSION
Aortic dissection is a severe condition with high rates of mortality. Pregnancy in a patient with aortic dilation is a
reason to pregnancy termination, refused by this patient. Even with medical treatment with beta-blocker, she presented a type A aortic dissection, with immediate indication of premature therapeutic cesarean section followed by surgery. Despite prompt diagnosis and treatment, an intraoperative myocardial infarction was the cause of maternal death. This case shows that in spite of optimal care, pregnancy in Marfan syndrome patient with aortic dilation may have a fatal outcome.

**Maternal and Neonatal Seizures Secondary to Severe Hyponatraemia from Acute Intrapartum Water Intoxication**  
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**Introduction**  
We wish to highlight how unregulated intrapartum water ingestion can result in significant maternal and neonatal morbidity. Early symptoms can be non-specific or confused with common pregnancy complications such as pre-eclampsia.  
We present a case of maternal and neonatal seizures secondary to severe hyponatraemia following water intoxication. We will discuss the challenges in identifying high risk patients and their subsequent management.

**Case Presentation**  
A healthy primiparous women presented at term in spontaneous labour. She developed a generalized seizure followed a short period of acute confusion and disorientation intrapartum. She was mildly hypertensive without proteinuria. Magnesium sulphate was given and an emergency caesarean section performed. Following delivery the neonate developed seizures. Cord blood gases were normal. Maternal and fetal bloods showed severe hyponatraemia. Their biochemical and hormonal profile was otherwise normal. Brain and renal imaging were normal. Both required intensive care treatment. Fluid excess was calculated and they were fluid restricted accordingly. Supplementary hypertonic saline was given. Both made a full neurological recovery.

**Discussion**  
Identifying antenatal risk factors for hyponatraemia, strict fluid balance monitoring and renal function testing in labour may identify at risk women and reduce the incidence of seizures and associated morbidity secondary to water intoxication.

**Transient Ischemic attacks from Moya Moya disease associated with Graves disease during Pregnancy: A case report**  
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**Background:**  
Moya moya disease (MMD) is a rare idiopathic progressive vasculopathy characterised by stenosis of the terminal portion of the internal carotid arteries and proximal portions of its major branches with the development of a thin collateral network of small vessels.It presents in young Asians with transient Ischemic attacks (TIAs), headaches, seizures, cognitive changes, ischemic or haemorrhagic strokes and is associated with many conditions including Graves disease.

**Case Description:**  
31 year old female with Graves disease (poorly controlled due to non-compliance) and previous 2 normal pregnancies presented during the third trimester of her 3rd pregnancy with intermittent headaches associated with right sided numbness of face and extremities lasting for few seconds without any features of Preeclampsia that were treated symptomatically. She had fluctuant thyroid function during her pregnancy and normal vaginal delivery at 40 weeks. She presented 2 months postpartum with severe headache and right sided numbness lasting for an hour without any features of Preeclampsia. She was thyrotoxic (FT4:51pmol/L, FT3:16.6pmol/L, TSH < 0.005mIU/L, TSH receptor antibody: 5.2IU/L) due to noncompliance to medications postpartum, ESR 15 and normal autoimmune workup. Although the Magnetic resonance imaging of the brain showed no infarcts and revealed features of MMD, the CT-Angiography of the Brain reported features suspicious of Takayasu’s arteritis with no evidence of it on Aortogram.
She was treated with Aspirin, atorvastatin, carbimazole and a short course of Steroids.

**Discussion:**
Awareness of the association between Graves’ disease and MMD in younger patients presenting with stroke like symptoms is important as early diagnosis and treatment of MMD in the setting of Graves Disease may prevent severe neurologic sequelae and eliminate the need for surgical intervention. Fluctuations in baseline thyroid function for patients with known Graves’ disease may be a potentiating factor in exacerbating Moyamoya vasculopathy. Most centres prefer caesarean delivery for patients with MMD to avoid haemodynamic instability.

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**Folate deficiency in pregnancy presenting with severe anaemia and thrombocytopenia: a case series**
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**Introduction**
Pancytopenia in pregnancy presents a diagnostic dilemma. Folate or B₁₂ deficiency are reversible and easily treated while more sinister causes such as malignancy and aplastic anaemia are important to consider. Severe folate deficiency causing a megaloblastic anaemia and pancytopenia is also seen secondary to haemolysis (including HELLP syndrome and thrombotic thrombocytopenic purpura) or poor nutritional intake.

**Objective**
We present two cases of severe anaemia in pregnancy secondary to severe folate deficiency with subsequent management and pregnancy outcomes.

**Case 1**
A 31-year-old multiparous woman with a poor diet presented with lethargy at 35 weeks’ gestation. Notable abnormalities on admission blood tests were Hb 58g/L (MCV 93fL), platelets 45x10⁹/L and LDH 4500 IU/L. A blood film showed hypersegmented neutrophils, oval macrocytes and fragmented cells.

**Case 2**
A 25-year-old multiparous woman presented with shortness of breath and lethargy at 25 weeks’ gestation. Blood tests showed Hb 58g/L (MCV 106fL), platelets 110x10⁹/L, LDH 2801 IU/L and typical appearances on blood film of folate deficiency.
In both cases, the women were proteinuric, but systemically well and normotensive. TTP and HELLP were both considered, but the identification of very abnormal folate levels of <3mg/L in both made this the likely diagnosis. They each received folic acid 15mg daily, parenteral vitamin B₁₂, thiamine and oral iron and made good haematological recoveries. Case 1 received 2 units of blood on her initial presentation but case 2 did not.

**Discussion**
Anaemia in pregnancy is very common and most often due to iron deficiency, which is frequently treated without excluding other causes. Folate requirement increases in pregnancy and deficiency is easily and rapidly treated, and does not necessarily require the administration of blood products. Adequate antenatal correction of vitamin deficiency like this avoids bone marrow suppression and helps minimise poor obstetric outcomes associated with pre-existing anaemia should haemorrhage ensue.

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**Pyrexia in the puerperium as first manifestation of systemic lupus erythematosus**
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We report the case of a 29 year-old Asian woman who presented 13 days post-normal vaginal delivery with pyrexia, tachycardia and feeling generally unwell referred to hospital by her general practitioner (GP). She had a background of recurrent urinary tract infections and recently had an uncomplicated vaginal delivery with normal observations immediately post-partum and an uneventful short hospital stay. She was a non-smoker. She was started on oral antibiotics by her GP. She had a septic screen and was commenced on intravenous antibiotics. She developed a cough with clear sputum. Her broad-spectrum antibiotics were changed on microbiology advice and Tamiflu was commenced. She had a multitude of investigations performed including blood tests, blood cultures and swabs, echocardiogram, electrocardiography (ECG), pelvic ultrasound scan, Computed tomography (CT) abdomen/pelvis scan and infectious diseases screen. Despite the antibiotics, her pyrexia persisted. Following review by the respiratory team, an auto-immune screen was performed. This was positive for ANA, SSA-60, chromatin and DsDNA. A diagnosis was made for systemic lupus erythematosus with nephritis as she also developed proteinuria and haematuria. She was then reviewed by a rheumatologist and commenced on corticosteroid treatment.
Recurrent hepatocellular carcinoma in pregnancy: a case report and literature review
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The incidence of hepatocellular carcinoma (HCC) in pregnancy is rare, with less than 50 cases reported in the past sixty years. We describe the case of a 39-year old woman in her second pregnancy, with a diagnosis of HCC, and provide a review of relevant literature. We delineate the management challenges, highlighting the importance of multi-disciplinary care in women with complex medical conditions.

A diagnosis of HCC was made incidentally following hepato-splenectomy for a presumed hepatic adenoma in the context of multiple arterio-venous malformations (AVMs) in 2013 on a background of Hereditary Haemorrhagic Telangiectasia (HHT; Osler-Weber-Rendu syndrome). Despite surgical resection and chemoradiotherapy, recurrent inoperable HCC persisted in conjunction with pulmonary hypertension. An unplanned pregnancy was assessed in the first trimester in the Perinatal Medicine clinic with multi-disciplinary involvement from surgery, hepatology, radiology, cardiology and anaesthetics throughout the pregnancy. This included antenatal serial multi-disciplinary assessment, surveillance Magnetic Resonance Imaging (demonstrating continued tumour growth at 17 and 33 weeks), surveillance echocardiographies and a right cardiac catheterisation. Following spontaneous onset of labour at 33 weeks gestation under epidural anaesthesia, a live female infant delivered spontaneously, with maternal and neonatal survival six months following delivery.

The incidence of HCC worldwide is 5.5/10000 and is associated with liver cirrhosis and hepatitis. In previous cases affecting pregnancy, increased oestrogen and liver vascularity have expedited progression of HCC and deterioration in pregnancy, which was not ultimately evident in our case. It is also implicated with poorer obstetric outcomes, an increased risk of hepatic rupture and shorter median survival than non-pregnant counterparts. Associated conditions such as pulmonary hypertension and HHT have an additional impact on maternal and fetal morbidity and mortality. We outline the first case report of recurrent, inoperable HCC in pregnancy that with dedicated MDT involvement, maternal and fetal outcome can be optimised, with favourable outcomes possible.

Choriocarcinoma in a 27 week pregnancy
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Introduction:
We present a 41 year old female, HIV positive, on antiretroviral therapy with a CD4 count of 387 and a suppressed viral load. She was diagnosed and treated for tuberculosis in 2008. She presented with hemoptysis and chest pain at 27+4 weeks in her fourth pregnancy. She had an early first trimester miscarriage in 2016, documented with a B-HCG of 364. She was hypoxic and in respiratory failure. A chest Xray revealed multiple, bilateral round lesions. A CT scan confirmed cannon ball lesions in the lung fields. An obstetric ultrasound done ten days prior to presentation showed a normal intrauterine pregnancy with a smooth normal placenta. Three days after presentation the patient passed away after a failed resuscitation attempt.

Results:
On post mortem examination her cause of death was found to be a massive hemorrhage secondary to a ruptured metastatic choriocarcinoma lesion lying adjacent to her spleen. The patient had several hemorrhagic lesions in both lungs. The placenta and uterus showed no evidence of tumor. All other organ structures were normal.

Discussion:
Choriocarcinoma is a malignancy of the syncytiotrophoblast or cytotrophoblast and can arise during or after any gestation. It is usually preceded by a molar pregnancy or miscarriage. Choriocarcinoma coexisting with a normal viable pregnancy is extremely rare, with an estimated occurrence of 1 per 160 000 pregnancies. There are case reports in the literature of choriocarcinoma presenting with metastasis that responded well to chemotherapy. Unfortunately a delay in diagnosis lead to this woman’s death. It is important that choriocarcinoma be recognised as a rare yet dangerous cause of breathlessness and chest pain in otherwise healthy pregnant women. It is also important to consider choriocarcinoma as a differential diagnosis of multiple round lesions on a chest Xray in the HIV community.
Novel Influenza A/H1N1/2009 Viral infection in pregnancy: A case report from Singapore
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Seasonal Influenza is common in Singapore, a tropical country, with two peaks a year (April-June and year end). The novel influenza A virus is easily transmissible via respiratory droplets. High-risk population include the elderly, children, and pregnant mothers.

The patient was a 40-year-old Malay lady, G5P4, a chronic hypertensive not compliant with medications. She presented at 37-weeks gestation to the emergency room with a 2-day history of hyperpyrexia, breathlessness, flu-like symptoms, and decreased fetal movement. Her vital signs were pulse rate 110, respiratory rate 20, blood pressure 190/110, temperature 39.8°C and oxygen saturation 94-96%. On examination, her throat was injected and she had bilateral lung crepitations. Her white cell count was 14.67, CRP 64. Chest X-Ray revealed patchy alveolar shadowing in the right lower zone suggestive of pneumonia. Uric acid was 594, aspartate transaminase was 84 and urine PCR was 0.3. CTG showed fetal tachycardia of 170 with poor variability. She was admitted to the high dependency labour ward for severe pre-eclampsia and possible chest infection. High flow oxygen was given together with Ceftriaxone, Azithromycin for possible chest infection and Labetalol for blood pressure control. Respiratory throat swabs were sent for Influenza A PCR and tested positive for Novel Influenza A/H1N1/2009. She was referred to Infectious Disease physicians and started on Oseltamivir. IV Magnesium Sulphate was started for her severe pre-eclampsia and she underwent induction of labour. She delivered vaginally and the newborn was admitted to high dependency neonatal ward. The patient was admitted for a total of 6 days.

Pregnant women, especially those with comorbidities, are at higher risk of influenza infections, resulting in increased morbidity and mortality to mother and her newborn. Despite convincing evidence of both safety and benefit of influenza vaccination, vaccination rates among pregnant women remain low. Education of pregnant mothers and healthcare workers are essential.

Catastrophic rectus sheath haematoma in pregnancy
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Introduction:
We present a case of rectus sheath haematoma (RSH) resulting in intra-uterine fetal demise, in a woman who was therapeutically anti-coagulated for a massive pulmonary embolism.

Objectives:
This relatively rare complication of anticoagulation therapy is easily misdiagnosed in the pregnant population and the publication of this case seeks to highlight the diagnostic and management challenges faced by obstetricians.

Case:
A woman receiving anti-coagulant treatment for a large saddle pulmonary embolus diagnosed at 34 weeks gestation, complained of increasing abdominal pain and swelling at 37 weeks gestation. The pain was associated with a fall in haemoglobin concentration and ultrasonography was consistent with a large rectus sheath haematoma (10x10x2cm). Despite initial conservative management her condition deteriorated and she collapsed as a result of hypovolaemia. Intra-uterine fetal demise was diagnosed and a caesarean section was performed with evacuation of a 2000ml RSH and ligation of the inferior epigastric artery.

Methods:
A pubmed literature search and review of results.

Results:
There are few reported cases of RSH in pregnancy; the key discussion points are addressed below.

Discussion:
RSH is a rare presentation, more commonly found in patients who are anticoagulated. Risk factors for the development of RSH include conditions which increase the intra-abdominal pressure, such as coughing. The patient presented above had been complaining of a cough, and subsequent imaging confirmed a lobar pneumonia. These features, in combination with her anticoagulation predisposed her to the development of a RSH. In the context of a haemodynamically stable patient the management of RSH should be conservative, hence the importance of accurate diagnosis and early management to avoid unnecessary laparotomy which could result in further bleeding. In unstable patients surgical and/or radiological intervention is indicated.

Conclusion:
We present a rare case of antepartum rectus sheath haematoma requiring surgical intervention.
A unique case of pregnancy-induced parathyroid hyperplasia with severe hypercalcemia

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CASE REPORT: A G1P0 30-year-old woman presented with new onset vomiting and hypertension (160/100) at 24 weeks of gestation. Lab showed a calcium at 4.79 mmol/L. A diagnosis of primary hyperparathyroidism was made (PTH of 31 pmol/L). She was treated with IV hydration, s/c calcitonine and nifedipine. Neck ultrasound, MRI and 4D CT-scan found hypervascular micronodules behind the right thyroid lobe and below the right mainstem bronchus. Parathyroid exploration was performed; 2 ½ glands were removed (hyperplasia), half of a gland was left in place, but the right inferior gland was not found. PTH dropped to 13.6 pmol/L immediately after surgery but started increasing again after. Parathyroid scintigraphy did not allow identification of ectopic/extra glands. The ½ gland was excised and implanted in the forearm and cinacalcet was added. This failed to significantly reduce calcium and PTH levels. Extended right neck and upper mediastinal exploration including right hemithyroidectomy was performed; no parathyroid tissue was found. PTH decreased initially (8 pmol/L) but increased again later (17.5 pmol/L). Implanted parathyroid tissue of the forearm was removed. Despite maximum treatment, PTH (29.5 pmol/L) and calcium (3.7 mmol/L) increased. After multidisciplinary consultation, delivery was performed (31 weeks). The PTH decreased monoexponentially (half-life of 9.9 hours) to a nadir of 0.5 pmol/L over days, with ensuing hypocalcemia that required calcitrol and calcium supplements. The baby did not have hypocalcemia.

REVIEW OF LITERATURE AND CONCLUSION: Severe hypercalcemia is rare in pregnancy. Pregnancy outcomes are generally similar to the general population, but intrauterine fetal deaths have been reported. Treatment is challenging since little is known about cinacalcet and bisphosphonates during pregnancy. This is the first description of pregnancy-induced parathyroid hyperplasia with severe hypercalcemia. Although the cause is unknown, aberrant receptors on the parathyroid glands responding to hormones produced by the placenta is suspected.

Caesarean Section in a Labouring Parturient with Stress Induced Anaphylaxis

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A 32-year-old primigravida presented to the Maternal Assessment Unit in spontaneous labour contracting regularly with a 36 hour history of prolonged rupture of membranes. The patient had a 7 year medical history of Stress Induced Anaphylaxis (SIA). This was triggered by particular foods followed by exercise. The patient had been taking regular antihistamines prior to pregnancy and carries an epi-pen. Unfortunately the patient presented to the Maternal Assessment Unit in established labour in the early hours of the morning. The patient had no anaphylactic symptoms on presentation. 150mg IV hydrocortisone and IV antihistamine were given prophylactically. A decision was made to proceed to caesarean section. We collectively felt that a spinal anaesthetic was the most effective way of blunting any evolving stress response to labour. An uncomplicated caesarean section was performed under spinal anaesthetic and the patient was discharged home well on Day 3 postoperatively.

Stress or Exercise Induced Anaphylaxis was first described in 1980 by Sheffer and Austen. To date there are only five cases of SIA in pregnancy in the literature. Given the fact that this patient presented in labour and was at higher risk of potentially developing stress induced anaphylaxis we felt that a spinal anaesthetic would be the most efficient and safest method of blunting the stress response and thus preventing anaphylaxis. Although it is reported that morphine and other histamine releasing drugs should be avoided in this patient cohort, it is important to note the our patient received intra-thecal morphine prior to caesarean section without complication. This case also highlights the importance of thorough multidisciplinary antenatal care in order to plan for such complex patients should they present out of hours in labour. From the evidence to date, if these women do proceed to labour IV hydrocortisone, IV antihistamine and early epidural is recommended.
Inflammatory myositis in pregnancy. The value of early diagnosis and aggressive treatment: A case series
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Introduction:
‘Inflammatory myositis’ (IM) encompasses multi-systemic autoimmune conditions including dermatomyositis (DM), polymyositis (PM) and myositis-overlaps. Diagnostic delays reflect the rarity of IM (1-6 per 1,000,000), the varying presentations associated and a dismissal of symptoms as ‘normal for pregnancy’. Immunosuppression is often withheld unduly.

Objectives:
We aim to increase the awareness of this aggressive yet treatable condition.

Methods:
We describe 4 cases of IM treated in pregnancy.

31yr multigravida: Known autoimmune disease (hypothyroidism and type-1-diabetes) presents with varying symptoms throughout pregnancy: fatigue and proximal myopathy (12/40), shawl rash (22/40), pneumonia requiring intubation (25/40) and pre-eclampsia (PET) necessitating caesarean section (CS) (26/40). Post-partum, ECMO was required for a progressive organising pneumonia. The unifying diagnosis was DM, treated with IV methylprednisolone (IVMP), rituximab and cyclosporine.

35yr multigravida: Complicated by gestational diabetes, unexplained transaminitis and proteinuria presented 38/40 with an intraterine death. Post-partum a photosensitive rash (2/52), inflammatory arthritis (4/52) and organising pneumonia (11/52) developed. CK was normal. MDA-5 (amyopathic) DM was diagnosed and treated with IVMP, cyclophosphamide and methotrexate.

39yr primip: Known RNA-polymerase diffuse systemic sclerosis (SSc) presented with dyspnoea and orthopnoea, requiring intubation (7/40). CK, troponin and BNP were elevated and myositis-overlap SSc with cardiac, proximal muscle and gastrointestinal involvement diagnosed. Treatment included IVMP and intravenous immunoglobulin. Steroid-sparing agents (azathioprine and rituximab) were instituted to avoid a renal-crisis. She remains pregnant.

30yr primip: Known anti-SRP (necrotising) myositis, presented with proximal myopathy, respiratory muscle weakness and CK rise (12/40) following discontinuation of maintenance therapy. Re-treated with IVMP and rituximab at 16/40. Emergency CS (32+4/40) was performed for placenta praevia.

Results:
Despite extreme presentations of IM peri-partum, all 4 patients were treated aggressively with complete resolution of symptoms. Obstetric outcomes were less favourable.

Discussion:
Rituximab is effective and safe in early pregnancy. Pregnancy should not be a barrier to early diagnosis or treatment.
**Results:**
The patient presented with epigastric pain, nausea and vomiting. On examination she was haemodynamically stable and both foetal heartbeats were heard. Initial management was medical, with intravenous fluids, anti-emetics and analgesia. Both pain and nausea worsened over 3 days. Abdominal ultrasound found prominent static bowel consistent with obstruction and the patient was referred urgently to the general surgeons. Further MRI confirmed the diagnosis. She underwent an emergency laparotomy, resection of small bowel (30cm) and primary anastomosis. Recovery was complicated by post-operative ileus managed conservatively. She was discharged to complete a course of dalteparin during pregnancy and 6 weeks post-partum. The pregnancy continued to full term, delivering via elective C-section without issue at 37 weeks.

**Discussion:**
Abdominal pain within pregnancy can offer a wide breadth of differentials and obstruction can be difficult to recognise. A low threshold for alternative diagnoses must therefore be kept for these examples. Equally, urgent imaging is key. Although contemporary management favours magnetic resonance (MR) imaging in order to minimise the effects of radiation on the foetus, organisation of this should not delay diagnosis and treatment. Ultrasound can be a useful alternative. Close partnership between surgical teams is also paramount.

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**A case report of Maternal Sweet’s syndrome: a rare complication of pregnancy**

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A 31-year-old multiparous woman from Pakistan presented at 29 weeks gestation with arthralgia, a generalized rash and a painful breast swelling. She had high-grade pyrexia, erythema nodosum, inflammed MCP joints, conjunctivitis and a tender immobile 10 cm lesion in the left breast. The remainder of the examination including the obstetric assessment was unremarkable.

Specialists in rheumatology, dermatology, microbiology, ophthalmology, breast surgery, and obstetrics reviewed the patient. Differential diagnoses included atypical tuberculosis, systemic staphylococcal infection, inflammatory arthritis, panniculitis, and paraneoplastic phenomenon. Investigations revealed a neutrophilia and a raised CRP. Screening and culture for infection and an autoimmune screen was negative. She was commenced on IV antibiotics, but with no clinical response.

Skin biopsy showed neutrophilic lobular panniculitis. Breast biopsy showed prominent chronic and acute inflammation of the breast lobules with no evidence of malignancy. Following review of all histopathological results, the diagnosis of subcutaneous Sweet’s syndrome was made.

The patient’s clinical condition stabilized on oral steroid therapy. However, serial fetal growth scans revealed a fall off in growth at 37 weeks gestation. An elective Caesarean section was performed and a vigorous male infant was born in good condition, weighing 2.7 kgs. Interestingly, placental histology was normal, indicating that the placenta was spared the effect of systemic inflammation.

Sweet’s syndrome, also known as acute febrile neutrophilic dermatosis, is a rare inflammatory disorder characterized by acute skin changes, neutrophilia, fever and malaise. There are three subtypes: classical, malignancy-related and drug-induced. Pregnancy-associated Sweet’s syndrome is defined as classical Sweet’s syndrome with its initial presentation during pregnancy. This is another case to add to the four previously reported (1).

Reference

Hypertension

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THE ECLAMPSIA MATERNAL MORTALITY IN DR SOETOMO GENERAL HOSPITAL JANUARY 2015 - DECEMBER 2017: EVIDENCE FROM DR SOETOMO GENERAL HOSPITAL
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Introduction
The incidence of Eclampsia in developed country is 1.5-10 cases per 10,000 delivery. The incidence of Eclampsia in developing country is 6-157 cases per 10,000 delivery. More than 50,000 women annually because of Eclampsia. Maternal Mortality Ratio more than 1-2% in developed country. Maternal Mortality Ratio more than 10% in developing country.

Objective
To know the incidence of Eclampsia and Case Fatality Rate of Eclampsia in dr. Soetomo General Hospital from January 2015 – December 2017.

Methods
This research was Case Control Study.

Results
There was 134 Eclampsia cases with 35 maternal death cases. The highest percentage of Eclampsia was maternal age 20-35 year old (62.7%). Place of delivery at Soetomo Hospital 84.18%, hospitalized 1-5 days 49.3%, gestational age ≥ 36 weeks 81.7%; Multigravida 84.3%, performed Caesarean Section (74.6%). Case fatality rate from maternal age ≤ 20 year old 34.6%, the address out of Surabaya 66.46%, place of delivery out of Soetomo General Hospital has highest case fatality rate (31.8%), the highest case fatality rate from duration of hospitalization was 6-10 days (50%), the gestational age ≤ 34 weeks gestation (58.3%), the highest case fatality rate was primigravida 57.1% and the case fatality rate of vaginal delivery 14.28%.

Conclusion
Eclampsia was highest in age 20-35 years old, the case fatality rate was highest in age ≤ 20 years old. The duration of hospitalization was highest was 1-6 days hospitalization, the highest case fatality rate was 6-10 days hospitalization, the highest incidence was age > 36 weeks gestation, the highest case fatality rate was ≤ 34 weeks gestation. The incidence of Eclampsia was highest in Multigravida, the highest case fatality rate was primigravida. The highest mode of delivery was Caesarean Section, case fatality no different between caesarean and vaginaly.

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* Poster pitch

Risk factors of pulmonary edema among patients with pre-eclampsia: A case control study.
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Introduction: Pulmonary edema (PE), an uncommon event in preeclampsia, is associated with an increased risk of maternal and fetal morbidity and mortality. Patho-physiological changes associated with preeclampsia such as endothelial dysfunction and increased capillary permeability predispose them to PE. Due to the effect of anti-angiogenic mediators which is found to be increased in nulliparous women, the risk of development of PE is increased in these women compared to those with multiparity. We aimed to assesses the association of parity and other risk factors with development of pulmonary edema in preeclamptic women.

Methods
A matched case control study was conducted using data extracted from the hospital records matched for age during the time period January 2012 and December 2018 in a tertiary care and regional centre in South India. We used matched analysis using conditional logistic regression to assess the association of parity and other risk factors with pulmonary edema.

Results
PE developed in 2.67% of the preeclamptic women in this time period. More women were nulliparous among those who developed PE compared with the matched controls (76.7% vs. 50.0%, p = 0.032). Bivariate analysis adjusted for age showed nulliparous women to be at higher risk of development of PE (OR 5.0, 95% CI 1.06 – 23.41, p = 0.041). After adjusting for other variables (BMI, platelet counts, Systolic & diastolic blood pressure, presence of anaemia, serum albumin levels, and presence of help syndrome), analyses revealed matched OR of 5.44 (95% CI 1.36 – 21.33) indicating that nulliparous women are at higher risk to develop PE compared with multiparous women.

Conclusion
Nulliparous preeclamptic women were found to be at increased risk of development of pulmonary edema. Being an uncommon complication, a prospective study, also taking in to consideration of the stress on cardiac function, is needed to stratify the risk of PE.

*Poster pitch*

Retrospective Review of Hypertensive Disorders of Pregnancy in Multiple Pregnancy
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**Objective:** To investigate the impact of Hypertensive Disorders of Pregnancy (HDP) on perinatal outcomes in multiple pregnancy.

**Methods:** Retrospective cohort study of all multiple pregnancies delivered between 1st January 2013 and 31st December 2016 in Cork University Maternity Hospital. Birth registers, ultrasound reports, laboratory data & patient charts were reviewed. The cohort was dichotomised into those that did or did not develop a HDP. Differences between the groups were examined using Chi square and t-tests where appropriate.

**Results:** Over the 4 year period, 876 women had a multiple pregnancy where 18.3% (n=161) developed HDP. Those who developed a HDP were more likely to be nulliparous (39.8%, n=64 v 28.7%, n=204; p=0.008) and have conceived using assisted reproductive therapy (ART) (45%, n=67 v 32%, n=208; p=0.007). From these multiple pregnancies, 1756 neonates were delivered. Those born to a women with a HDP were more likely to be; delivered <37 weeks gestation (74.4%, n=238 v 57.1%, n=812; p<0.001), have an Apgar score < 7 at 1 minute of life (16.6%, n=52 v 11%, n=150; p=0.009) and to be admitted to the Neonatal Intensive Care Unit (NICU) (52.8%, n=169 v 43.9%, n=822; p=0.005). No differences were noted in rates of fetal anomaly, stillbirth or neonatal death between the groups.

**Discussion:** HDP is more common in multiple than singleton pregnancy especially in nulliparous women conceiving using ART. Our findings highlight that although multiple pregnancies complicated by a HDP are more likely to require pre-term delivery and neonatal NICU admission, these neonates do not have increased mortality. This information is useful when counselling patients antenatally.

*Poster pitch*

Postnatal Hypertension - What do women want?
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**Introduction**
Hypertensive disorders often persist or arise de novo in the postpartum period and there is a lack of robust evidence to guide therapy. Current first line antihypertensives used antenatally require multiple daily doses, which may cause issues with compliance postnatally. This in part, explain the increase in the complications such as eclampsia and intracerebral haemorrhage occurring after delivery.

**Objectives**
Understand prescribing habits, adherence and patient views on antihypertensive use in women with postpartum hypertension.

**Methods**
We undertook a prospective cross sectional study at Whipp's Cross Hospital between January and April 2018. Women with postpartum hypertension, requiring medication, were included and questioned at discharge and then again at 2 weeks postpartum. Demographics, obstetric and medication history were all recorded, along with self-reported adherence.

**Results**
Thirty six women with a mean age of 32 (±4.6) years were included in the study. The commonest cause of postpartum hypertension was pre-eclampsia (64%) and on discharge labetolol was the most commonly prescribed therapy (50%) with one third of patients requiring combination therapy. At discharge only 5 patients (14%) correctly reported their prescription and dosage regime, despite this half of the
cohort predicted they would be “likely” or “very likely” to remember to take medication regularly. At two weeks postpartum 57% admitted to forgetting their medication on up to 3 occasions, with only 40% reporting no missed doses. Ninety-five percent of patients now stated a preference for once daily medication, compared to 69% when questioned at discharge.

Conclusion
The majority of mothers prior to discharge do not have a clear idea of their antihypertensive regime, which is often combination therapy, but predict that they will not have any issues. The reality at two weeks postpartum is the majority have missed doses and now would almost all favour a more simpler once daily dosing regimen.

Nephrology

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Perspectives of Pregnancy in Women with Chronic Kidney Disease: A National Registry Survey Study.
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Background
Women with chronic kidney disease (CKD) are at risk of complications in pregnancy. Understanding of the experience of pregnancy for women with chronic kidney disease is limited. Currently, care for many pregnant women with CKD is provided by nephrologists and obstetricians in tertiary centres. This survey will seek to determine care received.

The aim of this questionnaire study is to describe variability in care received by women with CKD during and after pregnancy, and explore the impact of model of care delivery on their experiences of care.

Methods
An online questionnaire was developed and sent to women with CKD who had had at least one pregnancy and who had consented to be contacted for research from the UK Rare Renal Diseases Registry (RaDaR), Pre-eclampsia Chronic Hypertension rEnal and SLE study (PEACHES) and Pregnancy Adaptation In Renal disease Study (PAIRS).

Results
There was a 10% response rate.
Most women (90%) were of white ethnicity. Most women had successful pregnancies, however, approximately one in seven women had previously had a fetal or perinatal loss.

There were no differences in model of care (joined up or fragmented) according to disease severity. Anxiety for health was similar between women with ‘mild’ and ‘severe’ disease. Fewer women in the fragmented care group found the care by their midwife reassuring.

Conclusion
Findings suggest variability in care is not necessarily based on disease severity but geography or hospital resource. Women are more satisfied with ‘joined up’ care, supporting a move to MDT care for women with high-risk pregnancies as suggest by NICE. The trend toward lower satisfaction levels with midwives when fragmented care is experienced highlights an area of further research needed, with possibly more training for midwives into CKD pregnancies and more integration of midwives into care for these women.

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* Poster pitch

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Introduction: Early identification of Acute Kidney Injury during pregnancy (P-AKI) is critical to reduce adverse maternal and fetal outcomes. The StatSensor Xpress (Nova Biomedical) is a handheld device that may improve feasibility of rapid, serial creatinine concentration measurement, especially in low resource settings with a high incidence of P-AKI. Prior to implementation the device requires validation in a pregnant population.
Objective: To evaluate the performance of the StatSensor Xpress creatinine analyser in capillary blood compared to an enzymatic serum assay, in a pregnant population.

Methods: Serum and capillary blood samples were obtained prospectively from pregnant participants at antenatal obstetric clinics, and non-pregnant controls. Repeatability was assessed in quality control lots and venous blood from three participants at low (50 µmol/L), mid (90 µmol/L) and high (200 µmol/L) concentrations. Creatinine concentration was determined using an enzymatic reference method in serum samples and StatSensor in capillary blood, as per manufacturer's specifications. Agreement was assessed by concordance and construction of Bland-Altman plots. A retrospective adjustment factor was separately applied to evaluate the inbuilt offset function.

Results: Coefficients of variation (CV) from repeatability analysis, ranged from 2.1-3.0%CV in aqueous solution and 4.0%CV, 3.0%CV and 4.1%CV in whole blood samples of low, mid and high creatinine concentrations respectively. Lin’s concordance correlation coefficients between the methods were 0.95 (n=15), and 0.96 (n=11) when non-pregnant participants were excluded. The median difference between methods was +12 µmol/L.

Discussion: The StatSensor met desirable criteria for precision and accuracy. 95% limits of agreement were adequate once systematic bias was corrected for by retrospective application of an adjustment factor, which can be used for future analysis. Device performance may be superior in pregnancy due to the lower serum creatinine concentration observed secondary to glomerular hyperfiltration. Findings require replication in a larger population with prospective evaluation of the offset function.

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Improving screening for bacteriuria in pregnancy: a quality improvement project
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Introduction
Screening for asymptomatic bacteriuria is an essential aspect of antenatal care. Urinalysis using dipsticks is most commonly performed for the identification of proteinuria and is cheap and easy to do. However, often too much weight is put on other components of the dipstick testing for the identification or exclusion of infection. National guidelines do not advocate the use of urine dipstick in screening for infection.

Objective
We constructed a project to assess the current pathway in our high-risk Obstetrics clinics, the impact of collection methods on contamination rates as well as the usefulness of urine dipstick results for identification of bacteriuria.

Methods
We analysed patient encounters in two specific clinics from January to June 2017. We looked at urine dipsticks and cultures if they were performed. The association between dipstick data and positive cultures was then assessed.

Results
Of 883 patient encounters with full data available, 486 cultures were sent. There was a 18.9% contamination rate and 1.85% had significant growth of a pathogenic organism identified. The presence of protein or leucocytes did not correlate with bacteriuria, however the presence of nitrates did predict a positive culture result (PPV 0.71).

Discussion
There was a high contamination rate in the culture samples that were analysed. Our data support national guidelines that state that dipsticks are a poor indicator for bacteriuria. We therefore implemented some significant changes:

- Changed our default container for urine collection
- Production of a standard operating procedure for urine sample collection
- Production of a patient information leaflet for urine collection
- Construction of new Trust guidelines about the investigation and treatment of bacteriuria in pregnancy
- Education sessions for all staff

These above interventions and a post-implementation survey will be presented.
Diabetes

Early Gestational Diabetes
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Introduction
In 2010 the International Association of Pregnancy Study groups (IADPSG) first published its recommendations for the diagnosis of gestational diabetes in wake of the HAPO study results. They introduced a new definition of Gestational Diabetes by including those women with a fasting Glucose of equal to or more than 5.1 to 6.9 mmol/l as being diagnosed as Gestational Diabetics.

Objectives
Determine how many patients in our hospital population were diagnosed at < 20 weeks of gestation with Gestational Diabetes.
Follow their further progress antenatally and observe the pregnancy outcome.
Ascertain whether this is a valid method of testing for Gestational Diabetes

Method
Prospective Observational Study from 1st January 2016 till 31st December 2016.
Electronic medical records of all those patients who were diagnosed as GDM by means of their fasting glucose prior to 20 weeks gestation were scrutinized.
The blood glucose profiles of these women were studied and level of glycaemic control established.

Results
During the study period 6,970 women registered their pregnancies in Corniche Hospital. 546 women i.e. 8% had pre-existing diabetes. The remainder (6,244) were requested to do a Fasting Glucose Screen. Of these only 1,781 did have the test done of which 355 were abnormal. Thus 20% of these pregnant women were diagnosed as having gestational diabetes in the first trimester.
They were channelled into dietary intervention and self-monitoring of blood glucose.

Discussion
Testing for Gestational Diabetes in the first trimester does not have a large evidence base. However researchers have published inconsistent results. We believe that in our population where there is a high incidence of type 2 Diabetes, there is also an increased risk of pre diabetes which would manifest in pregnancy as Gestational Diabetes.

Impact of Diagnostic Criteria Change for Gestational Diabetes: Increased complications rates in women with untreated milder level of hyperglycemia
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Background and Purpose
Screening for gestational diabetes (GDM) at the CHUM was previously based on stricter criteria than those proposed by the WHO in 2013. In March 2015, the CHUM harmonized its criteria.
We assessed whether pregnancy complication rates increased at the CHUM using less-stringent criteria.

Methods
We performed a retrospective cohort study in women with singleton pregnancy who were screened for GDM between March 2015 and February 2016 with one-step 75g oral glucose tolerance test (OGTT).
Three groups were analyzed: Group 1, normal OGTT with both old and new criteria; Group 2, normal OGTT with the new criteria only; and Group 3, GDM with the new criteria.
Composite primary outcome included birth weight ≥ 90th percentile, caesarean in labor, pre-eclampsia (PE) and gestational hypertension. Secondary outcomes included excessive weight gain (EWG), induction rate, shoulder dystocia, 3rd-4th degree laceration, macrosomia, respiratory distress, neonatal hypoglycemia, prematurity and NICU admission.
Univariate analyses were used to describe the population. Differences between groups were assessed with an X²-test.

Results
To date, 505/1500 pregnancies were analyzed. Group 2 had a higher complication rate (31.5%) than women with GDM (21.3%) or the control group (18.3%). We did not have the power to detect differences in secondary outcome, although Group 2 had a tendency toward increased rates of EWG, PE, LGA, 3rd-4th degree laceration, respiratory
distress, prematurity and NICU admission.

Conclusion
Preliminary results show higher complication rates among women who are no longer considered GDM under the WHO criteria, which raises concerns. Refined antenatal predictors are required to identify these women and implement strategies to improve outcomes.

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Medication use in Gestational Diabetes
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Introduction
In the United Arab Emirates, the prevalence of Gestational Diabetes is reported as 28-37% using the IADPSG criteria for diagnosis. In our hospital the population has a 39% occurrence of Gestational Diabetes. Those diagnosed with Gestational Diabetes are commenced on a Diabetic Diet and advised to increase their physical activity as the first step in their management. If glycaemic control is not achieved medication is prescribed. A choice of Insulin versus Metformin is given.

Objectives
Determining the proportion of women requiring medication for Gestational Diabetes.
Documenting the medication used in the majority of cases and the dosage required.

Methods
Retrospective case note analysis using the electronic medical records of all women with Gestational Diabetes delivered in Corniche Hospital from 1st January 2014-31st December 2015.

Results
A total of 1,481 women were identified as having Gestational Diabetes during the study period. The proportion of women managed with a Diabetic Diet was 45%, while those who required medication to optimize glycaemic control was 55%. Of which 87% commenced Metformin, and 14% required additional insulin. Also, 13% were on Insulin alone as they declined Metformin or could not tolerate it due to side effects. Characteristics of this population were an average age of 33 years, multiparity and a BMI more than 30. The average gestation at which medication was offered was 28 weeks. Pregnancy outcomes of all these groups were similar.

Conclusions
As the demographics of our pregnant population change to incorporate an increasing maternal age, increased parity and a higher BMI. The requirement for medication use in Gestational Diabetes will continue to increase.

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* Poster pitch

The impact of implementing the new diagnostic criteria of gestational diabetes mellitus on prevalence and pregnancy outcomes
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Introduction: In 2013 the World Health Organization (WHO) adopted new diagnostic criteria for gestational diabetes mellitus (GDM).

Objective: To determine the impact of implementing the new WHO-2013 criteria on prevalence of GDM and pregnancy outcomes compared to the WHO-1999 thresholds.

Methods: A retrospective study was conducted in pregnant women who were referred to the Erasmus MC for an oral glucose tolerance test (OGTT) between 2010 and 2015.

Results: Of 3089 women, 11.6% (n=359) were diagnosed with GDM regarding the WHO-1999 criteria and 17.2% (n=532) using the revised 2013-criteria, with 102 (3.3%) reclassified to non-GDM and 275 (8.9%) reclassified to GDM when shifting from 1999 to 2013-criteria. In contrast to 59.5% of those in the WHO-2013 group, none of the women in the WHO-1999 group were diagnosed because of a fasting glucose only. Cases reclassified to GDM by WHO-2013 had a higher BMI and were more often multiparous and smokers. Interestingly, 30 women in WHO-2013 only were diagnosed with GDM according to WHO-1999 thresholds after a second OGTT. The latter group, who had a delayed diagnosis of seven weeks, delivered a significantly higher rate of large for gestational age (LGA) babies.

Discussion: The fasting glucose of the WHO-1999 group does not have an added value for diagnosing GDM, which advocates for lowering the fasting glucose threshold. The 30 women with a delay in diagnosis, which could have been prevented by using the revised criteria, showed the highest rate of LGA babies. However, 102 women will be
missed by the new criteria. It is unknown whether this group could have been safely left untreated and whether the women reclassified with GDM according to the WHO-2013 thresholds would benefit from treatment. Further studies are needed to answer those questions.

**Remaining**

***Poster pitch***

**Relationship between early pregnancy nutrition and abdominal subcutaneous fat**
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**Introduction:** Objective clinical measures of metabolic health during pregnancy would be desirable. As recent work suggests dietary macronutrient balance is important in regulating energy intake and metabolic health the aim of this study was to assess the associations between dietary macronutrient composition and US measures of SAT layers.

**Method:** 200 women recruited at 11-14 weeks gestation completed a food frequency questionnaire and measurements were performed on abdominal SAT, dividing it into the two anatomical layers superficial SAT (SSAT) and deep SAT (DSAT), assessing SAT density with US strain elastography. Plausible diets of 185 women were used. Generalised additive models using thin plate regression splines were used to associate intake of dietary protein, carbohydrate and fat (kJ/day) with these measures of SAT.

**Result:** Dietary intake did not differ between the body mass index (BMI) categories, except when macronutrients intakes were adjusted for weight. In early pregnancy, there was an association between a high protein, low fat intake diet with increased SSAT thickness. There was no significant association of macronutrient intake with DSAT. When assessing the relationship of SAT density with macronutrient intake there was an association between decreased density of SSAT with low fat intake. There was no association of macronutrients and SAT density in the DSAT.

**Conclusion:** Although it is difficult to make assumptions from human studies using dietary recollection and considering a life-time of dietary pattern has contributed to the current body AT, macronutrient balance may have a prominent place in metabolic health, deposition and density of AT and long-term AT distribution. Prospective studies are warranted to investigate whether SAT measures meaningfully reflect macronutrient composition and metabolic health in pregnancy.

***Poster pitch***

**Elastography: a novel evaluation of abdominal subcutaneous fat in pregnancy**
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**Introduction:** Chronic inflammation leads to adipose tissue (AT) fibrosis through excessive accumulation of extracellular matrix proteins. An increasing degree of fibrosis in AT is associated with increasing body mass index (BMI) and insulin resistance. Anecdotally AT has been observed to vary with ease of ultrasound penetration on medical examinations. Ultrasound strain elastography (SE) is a useful tool in assessing fibrosis in liver disease but has not previously been used to assess AT fibrosis. This study assesses the variance in density of the two anatomical layers of subcutaneous AT, superficial subcutaneous adipose tissue (SSAT) and deep subcutaneous adipose tissue (DSAT) in pregnancy using SE.

**Method:** Women (n=210) recruited in early pregnancy. Density of SSAT and DSAT were assessed using SE at five-time points throughout pregnancy and post-partum. Semi-quantitative density measures were achieved using two methods, strain values (SV) of the two layers calculated by the ultrasound machine and ImageJ software to calculate the percentage colour pixels in the elastography image these were correlated with the SSAT/DSAT thickness and BMI.
**Results:** Adipose tissue demonstrated a difference in density with the SSAT layer being denser than DSAT. Correlation of tissue density measures with BMI was poor. There was slight change of AT density during pregnancy with a tendency towards harder SSAT and softer DSAT in the third trimester. Post-partum SSAT became softer associated with an increase in SSAT thickness.

**Conclusion:** Elastography demonstrated density differences in adipose tissue. SE is a new method of assessing the AT demonstrating density differences in adipose tissue. Information on AT density in future work may determine AT fibrosis and be valuable for metabolic disease risk.

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Internet use by pregnant French-speaking women with chronic diseases.
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Objectives: 1) To study the use of the Internet as a source of information on chronic diseases and pregnancy by French-speaking women from Canada and France and 2) To list their expectations and satisfaction regarding the information provided.

Methodology: Women with a pregnancy < 15 weeks presenting chronic hypertension, diabetes, inflammatory intestinal disease or epilepsy were asked to answer a questionnaire on 1) sociodemographic data 2) use of different sources (websites, family, nurse, pharmacist, physician) to get information about the preparation of pregnancy, health habits before and during pregnancy, the impact of their disease and medications on the pregnancy and breastfeeding, and the effect of the pregnancy on their disease 3) their topics of interest regarding their disease and pregnancy and 4) their satisfaction regarding the quality of the information received.

Results: 29 women answered the questionnaire, 19 in Canada and 10 in France. 68% browsed francophone websites only. 47% considered the Internet as their main source of information for their disease, 100% evaluated that their physician was a good source of information, 82% confirmed the information gathered online with a physician while 24% checked the information given by a doctor with Internet sources.

Women were equally satisfied by the information provided by physicians and the Internet on general information about pregnancy. However specific questions about their disease, maternal, fetal and neonatal possible complications and use of medications were best provided by physicians. 40 to 60% of women considered that information provided by any source about exercise, risks of miscarriage, fetal demise, malformation, prematurity and breastfeeding was unsatisfactory.

Conclusion: French-speaking women do not consider francophone websites as satisfactory sources of information on chronic medical diseases and pregnancy, mainly because they do not provide specific and personal information.

Study funded by the Réseau mère enfant de la Francophonie

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Counselling and consenting for diagnostic imaging in pregnancy
Sandra Lowe
Australia

Diagnostic imaging in pregnancy requires a detailed understanding of the risks and benefits of the imaging options. This will ensure the most appropriate and safest imaging modality is performed to provide maximal information for diagnosis and management. Counselling and obtaining informed consent for imaging that involves radiation requires the clinician to communicate with the woman and her family a realistic estimate of the potential radiation dose to herself and her fetus, to describe and quantitate the risks of this estimated dose, to outline the benefits of the imaging procedure and to respond to any questions or concerns.

Although the “as low as reasonably achievable” (ALARA) should be applied, pregnant women should be imaged using the standard imaging protocols used for any other patients. If dose reduction strategies do not compromise image quality, then they should be used for all patients. The American College of Radiology particularly note that “It is best to create written protocols for all imaging of pregnant patients to avoid reactive, non-optimal protocol
adjustments by physicians attempting to reduce radiation exposures. All allied staff must also be well informed to ensure the patient receives a consistent message about the risks and benefits of the proposed test(s). In almost all diagnostic imaging, with or without contrast or nuclear isotopes, maternal and fetal risks are negligible and therefore the most sensitive and specific imaging should be performed at the most appropriate time whether during or after pregnancy. With adequate information and knowledge, the reflex "no radiation" approach to selection of diagnostic imaging modalities in pregnancy should be replaced with principle of ensuring that non-ionising radiation options are considered first, whether during or after pregnancy; but when X ray, CT, nuclear scan or PET are the most suitable modality; these should be applied with appropriate care and counselling.

**Hematology**

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* Poster pitch

**Adherence to a selective antenatal haemaglobinopathy screening policy within a tertiary level obstetric unit in Australia**

Ailsa Borbolla Foster
Australia

**Introduction**

There is no national Australian antenatal haemoglobinopathy screening policy and a previous Australian study of antenatal haemoglobin electrophoresis requests highlighted poor patient selection. Whilst benefits of screening have been well demonstrated, adherence to selective screening protocols in low prevalence populations has not been well described.

**Objectives**

This study aims to assess adherence to an established selective antenatal screening policy within a low prevalence Australian population.

**Methods**

This single-centre retrospective cohort study identifies all women attending for routine public antenatal care with estimated due date between 1st January 2014 and 31st December 2016 who meet criteria for selective screening on the basis of established guidelines. The primary outcome was the proportion of eligible women who were appropriately screened. Secondary outcomes included rates of partner testing and rates of specialist referral where fetal risk was identified.

**Results**

A total of 11,709 births were recorded during the study period. Eligibility for screening was identified on the basis of ethnicity in 1076 (9.1%), abnormal red cell indices in 427 (3.6%) and known personal or family history in 77 (0.6%). 158 (10%) had haemoglobin electrophoresis results documented during the antenatal course with 64 (4%) initiated by obstetric staff during the index pregnancy at a median gestation of 22 weeks. Partner testing was documented in 140 (88.6%) of “at risk” pregnancies and of these, appropriate specialist referral was indicated in 28 (20%) but occurred in only 17.

**Discussion**

This is the first Australian study to describe the rate of pregnancies meeting established criteria for selective screening in a low prevalence population. This data demonstrates poor identification of “at risk” patients leading to limitation of informed choice for affected families. The demonstration of poor adherence within the clinical setting supports arguments for universal screening which becomes increasingly cost effective as the selective screen failure rate rises.

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**Thrombolysis for intermediate risk pulmonary embolism in pregnancy**

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**Introduction**

Pulmonary embolism (PE) in pregnancy is a leading cause of maternal death. Due to inherent hemorrhage risk, thrombolysis is reserved as a life-saving intervention for massive PE. There is current controversy about using
thrombolysis in those with intermediate risk (submassive) PE. We present two cases of intermediate risk PE who failed to respond to IV unfractionated heparin (UFH).

Case 1
A 34-year-old para 2 without risk factors for venous thromboembolism (VTE), presented at 22 weeks gestation with hypoxia and breathlessness that confined her to bed for over a week. She had multiple bilateral PEs, right ventricular strain on echocardiogram and elevated troponin and BNP. She did not improve with 24hrs IV UFH and so was treated with systemic thrombolysis according to the MOPPETT regime and then converted to low molecular weight heparin (LMWH). She had an uncomplicated vaginal delivery at 36 weeks with no haemorrhage.

Case 2
A 28-year-old para 1, low risk for VTE, presented at 31 weeks with dyspnoea worsening over two weeks. She had bilateral main pulmonary artery PEs, echocardiographic right-sided heart strain and increased levels of troponin and BNP. She was admitted for IV UFH, but within 24 hours suffered an acute hypotensive episode. She was not delivered; instead she was treated with ultrasound-enhanced catheter-directed thrombolysis (EKOS, BTG Int'l) via catheters placed in the right and left pulmonary arteries. A total dose of 22mg alteplase was administered over 24hrs. Fibrinogen was monitored and supplemented if <2g/l. Her symptoms, vital signs and echocardiogram improved and she was switched to IV UFH, then full dose LMWH. She is now in her 39th week of gestation.

Discussion
These cases illustrate that thrombolysis for poorly responding intermediate risk and massive PE need not be withheld in pregnancy, delivery need not be expedited, and pregnancy can continue successfully after treatment.

* Poster pitch

Nitinol venous stent outcomes in peripartum women following treatment for acute ilio-femoral deep vein thrombosis
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Introduction
Deep vein thrombosis (DVT) is the leading cause of morbidity and mortality within pregnant and post-partum women. Contemporary management of acute ilio-femoral DVT includes catheter-directed thrombolysis and stenting of an obstructive lesion.

Objective
This study examines venous stent related outcomes of peripartum women (pregnant or within 6wks post-partum) with acute ilio-femoral DVT.

Methods
Peripartum women (2012-2017) treated for acute ilio-femoral DVT were included for analysis. Primary patency was defined as a patent stent with <50% diameter reduction; primary-assisted patency included those requiring re-intervention to maintain patency, and; secondary patency defined as stents that were blocked and successfully re-opened.

Results
Of 190 patients treated for acute ilio-femoral DVT, 81 (43%) were women. Cumulative patency was 88% (median follow-up 2.3yrs; range 30-328wks). From this group, 9 women were peripartum (11%). Onset of DVT was post-partum for all (mean 4wks after birth; range 3-6wks). Two women were treated with catheter-directed thrombolysis alone, and 7 women were also stented. Median age at the time of stent placement was 29yrs (range 22-41yrs). Primary, primary-assisted, and secondary patency rates were 14%, 43%, and 43%, respectively. Re-intervention was required in 6/7 (86%) peripartum women, with mean time to re-intervention of 9wks (range 1-33wks). Venous stenting in peripartum women was associated with a higher risk of re-intervention (HR 6.58; p=0.0001, 95% CI [2.46, 17.60]), and was a strong predictor of cumulative patency loss (HR 10.71; p=0.002, 95% CI [2.37, 48.51]).

Discussion
Peripartum women are significantly more likely to require re-intervention and experience patency loss compared with their non-peripartum counterpart. Thresholds for intervention may need to be higher and periprocedural anticoagulation strategies require more investigation if treatment is to be offered in the peripartum period.
**Poster pitch**

### The impact of a tailored checklist on the quality of peripartum care delivered to women with inherited bleeding disorders.

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#### Introduction

Women with inherited bleeding disorders (IBD) can be at increased risk of bleeding peripartum and/or their babies are at risk of fetal or neonatal haemorrhage. The care they require is specific to the type of bleeding disorder they have and the plan for delivery requires multidisciplinary input.

The World Health Organisation (WHO) has recommended new safety checklists as part of a drive to reduce medical errors and make healthcare safer. Communication is essential for optimal care. Developing an easy to follow bleeding disorder checklist draws the specialists information together and enables all healthcare professionals to quickly identify the care they must provide.

#### Objectives

The aim of the study was to identify any errors in care, to develop and implement a tailored bleeding disorder checklist, and to assess the impact of this on quality of care.

#### Methods

Fifty women with (or carriers of) an IBD were identified from a Maternal medicine service database and charts were reviewed. Quality of care indicators were assessed by chart review before and after the introduction of the checklist into clinical practice.

#### Results

When standards of care were compared before and after the introduction of the checklist: Haemostatic support was recommended for 19% of the group peripartum and given to 100%, compared to 29% and 100%.Maternal precautions were recommended in 42% and adopted in 78% compared to 43% and 100%. Fetal precautions were recommended in 86% and implemented in 94% compared to 89% and 100%. Cord bloods were advised in 58% and taken in 55% compared to 54% and 93%.

#### Discussion

Deficiencies in care were identified in this high risk group of women despite multidisciplinary peripartum planning of care. The development of a simple checklist that could be modified to meet the specific individuals needs resulted in improved quality and safety of care.

### Treatment/Outcome

**UDCA Treatment Partially Reverses Placental Dyslipidemia in Intrahepatic Cholestasis of Pregnancy**

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#### Introduction

Intrahepatic cholestasis of pregnancy (ICP) presents with maternal elevated serum bile acids together with deranged liver function tests. No global molecular profiling has yet been performed to characterise the associated placental phenotype.

#### Objective

Ultra-performance liquid chromatography - mass spectrometry (UPLC-MS) is a powerful tool for metabolic profiling, offering excellent separation and detection capabilities. We have developed a robust method for the extraction of lipid metabolites from placenta and subsequent profiling and applied this to samples from ICP cases +/- UDCA treatment and controls.

#### Methods

Placental samples (n=120) were collected at delivery, snap-frozen and stored at -80°C until analysis. Placental lipids were extracted and profiled using an Acquity UPLC system coupled to a XEVO Synapt G2-S mass spectrometer.
Quality control samples were utilised to assess analytical reproducibility. Data were processed using XCMS and multivariate analysis performed using SIMCA-P software.

**Results**

60 placental fatty acids, phospholipids and triglycerides were identified. Fatty acid and phospholipid species were shown to be altered in cases, whereas there was no major effect on triglycerides. ICP placentas showed different lipid profiles to controls, and there were alterations between those patients treated with UDCA and those who were not. Importantly, levels of some lipids were restored to control levels after treatment. Specifically, levels of six phosphatidylcholines and seven phosphatidylethanolamines were similar to control levels in UDCA treated patients. This accounted for ~25% of all phospholipids identified. Of these 13 restored lipids, half had 16:0 fatty acid chains and half had 18:0 fatty acid chains. Interestingly, no individual fatty acids were observed to be restored to control levels after UDCA treatment.

**Discussion**

We have developed a lipid profiling method for placental analysis and applied it to identify considerable alterations in lipid profiles from placentas from women with ICP that are partially restored by UDCA treatment.

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**Poster pitch**

**The Use of Biologics in Pregnant Women with Chronic Conditions and Adverse Maternal Outcome: A Systematic Review and Meta-Analysis**

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**Introduction:**

The increased availability and awareness of biologics safety has led to an increase in their use over the past decade. Previous concern regarding adverse pregnancy outcome resulted in the discontinuation of biologics before carefully planned conception. With the greater appreciation of the safety of a number of these agents, in addition to the need to control the underlying disease activity, many physicians now maintain patients on treatment for at least a portion of their pregnancy. However, conflicting opinions remain and there is little data to the safety of certain biologics in pregnancy. There are multiple systematic reviews that have studied foetal/infant outcomes but not maternal outcomes.

**Objectives:**

Primary; to study the effect of biologics during pregnancy on the rate of miscarriage. Secondary outcomes include the rate of maternal infections, C-sections and hypertensive disorders in pregnancy.

**Methods:**

We performed a comprehensive search to identify potentially relevant published studies on the use of biologics 3-months before or during pregnancy and their effect on maternal outcomes from 1998 to December 2017 in all languages. Databases including PubMed, EMBASE and Cochrane were searched using a detailed strategy. We potentially selected studies and retrieved their full-text. We performed data extraction and currently in the process of quality and risk of bias appraisal and heterogeneity assessment. Incidence data will be combined where feasible in a meta-analysis using Stata software and fixed-effects or random-effects models as appropriate. This systematic review will be reported according to the PRISMA guidelines.

**Results:**

The search resulted in 1244 studies. 16 studies included (11 TNF-inhibitors, 3 tocilizumab, 1 tofacitinib and 1 abatacept) for the qualitative analysis after excluding other studies from title and abstract and after removing duplicates. We are currently in the process of quality assessment and risk of bias appraisal. In the symposium we will present the final results.

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**Prenatal bed rest in developed and undeveloped countries: A meta-analysis**

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**Background:** Bed rest is prescribed by many obstetric care providers for high-risk pregnancy complications. There is strong evidence that prolonged bed rest negatively impacts maternal health, but is justified in order to try and improve fetal health outcomes.

**Objective:** To quantify the influence of maternal bed rest on fetal health outcomes in developed and undeveloped countries.
countries.

**Search Strategy:** A structured search was conducted through MEDLINE, EMBASE, CINAHL, Web of Science, Ovid’s Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews and ClinicalTrials.gov up to December 16, 2016. The search combined keywords and MeSH-like terms such as “bed rest,” “pregnancy” and “randomized controlled trial (RCT)”

**Selection Criteria:** RCTs comparing standard care to standard care plus bed rest after 20 weeks gestation were assessed.

**Data Collection and Analysis:** Our search identified 694 publications of which 61 were assessed for eligibility. Sixteen publications reporting on fourteen unique studies (2608 women, 3328 fetuses’) were included in the analysis.

**Main Results:** Overall newborn outcomes were similar between groups; however, there was a 50g greater birth weight with bedrest (Weighted Mean Difference [WMD]: 50g, 95% confidence interval [CI]:0g, 100g, I²=31%). Studies conducted in undeveloped countries took place solely in Zimbabwe. In subgroup analyses between developed and undeveloped countries, divergent effects were observed. Gestational length was shorter with bedrest in developed countries (WMD: -0.77 weeks, 95% CI: -1.26, -0.27, I²=0%). The odds of a very premature birth (Odds Ratio [OR]: 2.72, 95%CI: 1.22, 6.07, I²=0%) and having a newborn weighing less than 1500g (OR: 1.96, 95% CI: 1.04, 3.67, I²=0%) were also increased in developed countries.

**Conclusions:** In developed countries, treatment of complicated pregnancies with prolonged bedrest results in worse newborn outcomes.

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**Poster pitch**

Obese primiparous women undergoing induction of labour have a higher caesarean section rate: An analysis using the Robson 10-group classification system

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Singapore

**Introduction**

Obesity in pregnant women is rising rapidly, and is associated with increased rates both elective and emergency caesarean sections, the most frequently performed surgical procedure globally, and this has implications on short and long term maternal and perinatal health.

**Aim**

To evaluate the effect of maternal obesity on CS rates and identify the key patient categories according to the Robson Ten-Group Classification System (TGCS) contributing to the high CS rates.

**Methods**

Retrospective analysis of obese gravidas (BMI >30kg/m2) who delivered in our unit from 1 January 2010 to 31 December 2017. Parameters of parity, number of fetuses, fetal presentation, gestational age, type of onset of labour and mode of delivery were collected to form the 10 patient groups. Non-obese gravidas who delivered during the same period were controls.

**Results**

There were 6115 deliveries, with 740 (12.1%) obese. Overall CS rate in the obese group was 42%, compared to 32% in the control group (P<0.05). The largest contributor to the overall CS rate was Group 5 (term multiparous singleton pregnancies with at least a previous uterine scar). Among the obese with unscarred uteri, Group 2a (term nulliparous singleton cephalic, induced labour) and Group 10 (all singleton women with preterm deliveries) were the top contributors to the overall CS rate. Induced obese primigravida had a higher CS rate (43.5%) compared to induced obese multigravida (6.9%) (p<0.05).

**Conclusion**

Maternal obesity is a significant risk factor for CS, with almost 1 in two obese women having a CS. Parity has an important influence on the success of induction of labour in obesity, with primparity conferring a 6 fold increased risk for CS. The high contribution of preterm CS delivery reflects the association of maternal obesity with high risk obstetric complications such as pre-eclampsia, gestational diabetes and fetal growth disorders.
**Poster pitch**

**Characteristics and Outcomes of Prospectively Reported Pregnancies Exposed to Certolizumab Pegol from a Safety Database**

Megan E. B. Clowse, Angela E. Scheuerle, Christina Chambers, Anita Afzali, Alexa B. Kimball, John J. Cush, Maureen Cooney, Laura Shaughnessy, Mark Vanderkelen, Frauke Förger

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**Introduction:** Anti-tumour necrosis factor (anti-TNF) medications are effective in controlling chronic inflammatory diseases, but information about their use and safety in pregnancy is limited. Consequently, anti-TNFs are often discontinued early in gestation. Certolizumab pegol (CZP), a PEGylated, Fc-free anti-TNF approved for treatment of rheumatic diseases and/or Crohn’s disease, has no active placental transfer.

**Objective/Hypothesis:** To provide information on pregnancy outcomes in women receiving CZP, especially those with early pregnancy exposure.

**Methods:** Prospective and retrospective data on maternal CZP exposure, including timing and duration, outcomes, comorbidities, and major malformations were extracted from the UCB Pharma safety database through 6 March 2017. This analysis was limited to prospective reports to avoid bias associated with retrospective submissions. Numbers of live births, miscarriages, elective abortions, stillbirths, and major congenital malformations were ascertained.

**Results:** From a total of 1541 maternal CZP-exposed pregnancies, 1137 were reported prospectively, of which 528 pregnancies (including 10 twins) had 538 known outcomes: 459 live births (85%), 47 miscarriages (9%), 27 elective abortions (5%), and 5 stillbirths (1%). Of the 459 live births, 8 (2%) cases of major congenital malformations were reported. Of the 528 prospective pregnancies with known outcomes, 436 (83%) were exposed to CZP during the 1st trimester, when most organogenesis occurs; 201 (45%) pregnancies were exposed during all 3 trimesters.

**Discussion:** This analysis represents the largest published cohort of pregnant women exposed to an anti-TNF for management of chronic inflammatory diseases. Analysis of pregnancy outcomes does not indicate a malformative effect of CZP compared to the EU general population (2–3%), nor an increased risk of foetal death. These data are reassuring for women of childbearing age considering treatment with CZP, however, the ongoing collection of post-marketing surveillance data, including the ongoing MotherToBaby study from the Organization of Teratology Information Specialists, will provide further important information.

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**Poster pitch**

**Anti-TNF Treatments for Women with Chronic Inflammatory Diseases: Comparing Attitudes and Perceptions of Physicians in Europe and the US**

Angela Tincani, Peter Taylor, Rebecca Fischer-Betz, Cécile Ecoffet, Eliza Chakravarty

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3 University Hospital of Düsseldorf
4 UCB Pharma
5 Oklahoma Medical Research Foundation

**Introduction:** Chronic inflammatory disease (CID) activity in Women of Childbearing Age (WoCBA) is associated with higher risk of pregnancy complications and adverse outcomes. Tumour necrosis factor antagonists (anti-TNFs) are effective, but data on utilisation for these patients (pts) are limited.

**Objective/Hypothesis:** To understand physicians’ attitudes towards anti-TNF use around pregnancy, and differences between Europe- and US-based physicians.

**Methods:** The online survey was conducted in the US (Jul-17) and EU5 (France, Italy, Spain, UK, Germany; Nov/Dec-17). WoCBA were female pts aged 18–45. Participants included rheumatologists (RH) and obstetrician/gynaecologists (OB) among other healthcare professionals (HCPs).

**Results:** 203 US HCPs participated (50 RH, 50 OB) and 401 EU5 (152 RH, 114 OB). EU5 HCPs were less inclined to prescribe anti-TNFs for WoCBA; US RH (43%) had the highest proportion prescribed anti-TNFs (EU5 RH: 33%).
Both US and EU5 HCPs’ comfort with prescribing anti-TNFs declined with onset of family planning. EU5 RH (61%) and OB (67%) were more likely to recommend stopping anti-TNFs pre-conception than US HCPs (RH: 46%; OB: 62%); similarly, >50% EU5 RH and OB agreed women should stop anti-TNFs post-conception (US RH: 34%; OB: 54%). These findings may be due to more US RH strongly agreeing on making disease control during pregnancy a priority (42% vs EU5 RH: 25%) and that controlled disease reduces risk of pregnancy complications (US RH: 42%; EU5 RH: 28%), as well as more EU5 (34%) than US RH (12%) being very concerned about adverse events in pregnant pts on anti-TNFs. More EU5 (16%) than US RH (6%) strongly believed breastfeeding pts should not take anti-TNFs; uncertainty was high.

Discussion: Confidence in clinical management of WoCBA with CID varies, highlighting differences in physicians’ attitudes. Uncertainty and concerns about anti-TNFs for WoCBA are common, emphasising a need for better information/education of HCPs on anti-TNF use before/during/after pregnancy.

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* Poster pitch

‘Nadolol use in pregnancy and Small for Gestational Age (SGA) newborns at term: a case series’.
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Background: Nadolol, a hydrophilic, long-acting, non-selective beta-blocker, is commonly used to treat congenital long QT-syndrome (LQTS) in non-pregnant adults. Nadolol is efficacious in both primary and secondary prevention of cardiac events in non-pregnant adults with LQTS.1 Recent evidences suggests Nadolol may be superior to other beta-blockers at preventing cardiac events in these patients and hence more women are continuing Nadolol during pregnancy. The current published data regarding Nadolol in pregnancy is limited to a single case and suggests that use during pregnancy may be associated with SGA of the fetus.2 This case series will contribute to the literate on the possible effects of Nadolol on the fetus and assist with counselling women.

Case series: This case series describes three pregnancies in two mothers treated with Nadolol for LQTS during pregnancy. In all three cases, the newborns were SGA with birth weights below the 10th percentile at term using Fenton growth charts. The mothers were non-smokers and had no other significant medical history. Informed consent from both women was obtained prior to publication.

Discussion: This case series suggests a possible association between Nadolol use in pregnancy and SGA at term. Adding Nadolol to a cardiac registry may be helpful to further define its implications on pregnancy outcome.

References:

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A retrospective audit of the socio-demographic characteristics and pregnancy outcomes for all women with multiple medical problems giving birth at a tertiary hospital in the UK in 2016
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3Oxford University Hospitals NHS Trust, Oxford, United Kingdom

Introduction: Surveillance data from Confidential Enquiries shows that women who become pregnant with pre-existing health conditions are at risk of poor outcomes, and those that have multiple medical problems are at greatest risk. Our understanding of the socio-demographic characteristics, associated medical and obstetric morbidity and pregnancy
outcomes for this group is limited at present.

Objective:
To describe the socio-demographic, medical and pregnancy characteristics of all women with multiple medical problems giving birth at a tertiary hospital in 2016, and to compare their outcomes with all women giving birth in the same period.

Methods:
A comprehensive search of the Electronic Patient Record system was conducted to identify all women giving birth in 2016 at a tertiary hospital. The prevalence of multiple medical problems in pregnant women, defined as two or more known pre-existing conditions, was estimated with 95% confidence intervals, and, their sociodemographic, medical and pregnancy characteristics and outcomes compared with all other women in the cohort. Factors associated with poor outcomes were explored using logistic regression.

Results:
2004 women with multiple medical problems were identified amongst a cohort of 8121 women giving birth (prevalence of 25%, 95% CI 24–26%). Women with multiple medical problems had a median age of 35 years (IQR = 27 – 35 years) and nearly three quarters were multiparous (73%). Women with multiple medical problems gave birth at a median gestation of 39+5 weeks (IQR = 38+5 – 40+5 weeks). Data collection is ongoing, but will be complete by the time of presentation.

Discussion:
These data from a tertiary obstetric unit highlight the high prevalence of multiple medical problems amongst women giving birth. Further research is needed to understand how maternity care can be best structured and delivered, taking into account the varying severity and impact of these conditions, to optimise maternal and neonatal outcomes.

Cardiology

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* Poster pitch

Percutaneous closure of interatrial septal defects in pregnancy: experience at John Radcliffe Hospital (UK)
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Introduction
Patent foramen ovale (PFO) and atrial septal defects (ASD) are common congenital cardiac defects in adults, which may cause complications in pregnancy such as paradoxical embolism. Closure of PFO/ASDs in pregnancy is rarely necessary, but has been suggested as a safe option in selected patients under expert hands.

Objective
To review the outcomes and follow-up of patients who underwent percutaneous device closure of PFO/ASD during pregnancy at John Radcliffe Hospital since 2005.

Methods
Retrospective review of all medical and obstetric notes of patients that fulfilled inclusion criteria. Helex® device was used in all patients. Procedures were performed with local anaesthesia under intracardiac echocardiography guidance (ICEG) and low frame rate fluoroscopy with a highly collimated beam.

Results
Twelve women were included, 3 (25%) with ASD, 9 (75%) with PFO. Average age was 31 [24-41]. None of the patients had clinical deep vein thrombosis (DVT) at diagnosis. Half of patients had a negative thrombophilia screen, and one resulted lupus anticoagulant positive. Indications for the procedure were: TIA (33.3%), stroke (33.3%), severe migraine (25%), myocardial infarction (8%). Successful PFO/ASD closure was achieved in all patients. Average radiation dose was 39 cGy/cm² [2.3-260], with estimated uterine/fetal dose of less than 0.001 mGy. Median gestation age was 19 weeks [10-31]. All women received aspirin 75mg daily for 6 months after procedure. Of those, 25% had aspirin+ dipyridamol/clopidogrel, 17% aspirin+ prophylactic low molecular weight heparin (LMWH), 8% aspirin+ therapeutic LMWH. Follow up period was 6 years [1-10]. Eleven women (92%) had no recurrent symptoms; one patient had migraine. No medical nor obstetric complications were observed except preeclampsia in one patient.

Discussion
Overall, high rate of successful procedures and low rate of complications were seen. In conclusion, closure of PFO/ASDs in selected pregnant patients can be performed safely, if these women develop complications secondary to them.
Objectives: Cardiovascular diseases are the leading cause of death worldwide. The most interesting feature of cardiovascular diseases is that they can be prevented. Majority of the risk factors are controllable including hypertension, dyslipidemia, obesity, diabetes, smoking, stress and sedentary lifestyle etc. We aim to assess knowledge, awareness, perception of cardiovascular diseases and risk factors among pregnant women living in rural areas of Pakistan. We also aim to evaluate the level of prevention of cardiovascular diseases as a result of awareness and knowledge.

Methods: The study was conducted in peripheral areas of Lahore, Pakistan during the year 2016. A structured questionnaire was established that targeted 350 female population >20 years during their 1st and 2nd trimester. Informed consent was obtained and questionnaire were filled. The data was analysed using SPSS 16.0.

Results: Only 26% of the participating pregnant women agreed that cardiovascular diseases are the most leading causes of mortality. Knowledge regarding cause, risk factors and complications was found inadequate. There was identified lack of health promoting behaviours and practices among the subjects. Practices regarding diet and lifestyle were also found unsatisfactory. Awareness of risk factors was present in 110(31%) of targeted population. On risk assessment scale, 62% were found at high risk and 38% at low risk of developing cardiovascular diseases.

Conclusion: It has been concluded that a significant number of people had little or now awareness regarding the cardiovascular diseases and its complications. We can surely lessen the morbidity and mortality of both mother and fetus by primary prevention followed by early detection of the diseases and early interventions. The proportion of individuals found high risk and low risk should be screened regularly. We should prevent CVD though outreach programs and mass media.

Poster pitch

Pregnancy in Cardiac disease - an audit on outcomes in the Joint Cardiac Pregnancy Clinic , Singapore General Hospital.
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Singapore

Introduction: Cardiac disease is an increasingly important cause of maternal morbidity and mortality. Joint multidisciplinary care of these pregnancies is strongly advocated.

Aim: Pregnancy outcomes in cardiac patients seen at the cardiac joint clinic.

Method and results: All pregnant mothers with acquired or congenital heart diseases are referred to CJC, which is jointly run by consultant obstetricians and cardiologists., with easy access to anaesthesia and neonatal referrals. Delivery was in a tertiary level teaching hospital. 60 new cases were seen from 2009 to 2013. Median maternal age was 29 (19 - 40). Most had WHO class 1 disease (66.6%) with NYHA status 1 (90%). 10% of the population had WHO class 4 disease but none had a NYHA score worse than 2. Two thirds had congenital heart disease, which 55% were valvular. Acquired heart conditions made up the remaining third of which only 15 % were valvular. The most common cardiac diagnoses include MVP (21.7%), AS/VSD (16.7%) and cardiomyopathy (16.7%).

Caesarian sections rate was 59.3% (40% emergency sections) with a median hospital stay of 3 days. Vaginal delivery rates were 40.7% with 16% being assisted. There were no neonatal or maternal mortalities. Patients who developed cardiomyopathy postpartum or have a history of previous or existing cardiomyopathy had longer hospitalisation stays. Median gestational age was 38+2 days (32 - 41 weeks) and median birth weight was 3072.5g. Median APGAR scores were 8, 9 at 1 and 5 minutes respectively. Median length of stay for the baby was 4 days with average length of stay being 5.58 days.

Conclusion: Congenital heart disease remains an important contributing aetiology to cardiac disease in pregnancy. The majority of our patients achieved good maternal and neonatal outcomes, underpinning the importance of providing a seamless joint service providing multi-disciplinary pre-pregnancy, antepartum , intrapartum and postpartum care.
"Care of pregnant women with Prosthetic heart valves: Still a formidable challenge in low to middle income countries?"

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Introduction

Patients with mechanical heart valves require lifelong anticoagulation and pregnancy being a pro-thrombotic state poses additional risk of thromboembolic complications. In pregnancy, anticoagulation regimes using Coumadin derivatives or various heparins offers advantage over each other remains inconclusive. Especially in low to middle income countries cost of medication/monitoring and compliance remains a major challenge. We report a single center experience of managing pregnancy in women with prosthetic heart valve from South India.

Methods

We collected demographic, medical and obstetric details of pregnant women with prosthetic heart valve admitted to a regional tertiary center catering to rural population of South-eastern India from Jan 2011 to March 2018. Outcomes assessed were maternal complications such as maternal mortality, prosthetic valve thrombosis, and perinatal complications such as miscarriages or rates of congenital malformation. Data was expressed as mean with standard deviation or frequency with percentages as appropriate.

Results

We collected data of 73 pregnancies in 59 women with prosthetic heart valve during the time period. Majority of the women (84%) had valve replacement in mitral position and were replaced with ttk Chitra (titling disc) valve (80%). Five women developed thrombotic complication; three while on unfractionated heparin and two on warfarin therapy. Among three women with prosthetic valve thrombosis, two underwent thrombolysis while one succumbed to the disease. Two third of women were on warfarin therapy in first trimester. One fetus was diagnosed with warfarin-embryopathy and 4 had miscarriages. Cesarean section rates were 16.4%. Hemorrhagic complications occurred in six women in the postpartum period; four of them were on heparin.

Conclusion:

Pregnancy in women with prosthetic mechanical heart valves can lead to life-threatening complications. Anticoagulation regimes should take into consideration fetal risk concerns, cost or treatment/monitoring which will ensure a better compliance especially in low to middle income countries.

Management of cardiomyopathy in pregnancy in a tertiary hospital: Case series of 7 cases of cardiomyopathy managed in Singapore General Hospital.

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Peri-partum cardiomyopathy is a type of dilated cardiomyopathy of unknown aetiology affecting a small but significant proportion of mothers. It occurs in previously healthy mothers and has an incidence of about 1 in 2000 live births. Peripartum cardiomyopathy accounts for 17% of maternal cardiac deaths in the UK. The presentation and course of disease progression in peripartum cardiomyopathy is highly variable and can progress quickly into cardiac failure.

We present 7 cases of peripartum cardiomyopathy managed in Singapore General Hospital between 2009 and 2013, of which 2 cases consist of patients with pre-existing cardiomyopathy and 5 cases of patients with a history of peripartum cardiomyopathy in a previous pregnancy. Their presentations varied in severity and time, each representing challenges in both diagnosis and subsequent management of the pregnancies. The 7 cases discussed highlighted the prevalence of peripartum cardiomyopathy in previously well woman and its propensity to occur in woman at the extreme of ages. A history of cardiomyopathy in a previous pregnancy pre-disposes one to peripartum cardiomyopathy in future pregnancies. Early identification of at risk mothers or mothers in deterioration can put in place management plans that can help safeguard maternal and fetal outcomes. Planned elective deliveries can alleviate a lot of the risk as opposed to an emergency delivery and it is important for such plans to be in place in the pregnancy. Even in the events of an emergency delivery or acute deterioration, good outcomes can still be achieved with multidisciplinary support.

Separating mothers with peripartum cardiomyopathy post-delivery based on recovery of their cardiac functions would help risk stratify them allowing better counselling and management of future pregnancies. With close monitoring and careful management of deterioration along with planned elective deliveries, woman with cardiomyopathy in their current or previous pregnancies can achieve favourable maternal and fetal outcomes.
Role of non-specialized tertiary perinatal center for the care of pregnancy complicated with adult congenital heart disease
Hironobu Hyodo, Takeshi Nagao, Satoshi Nitta, Saho Fujino, Norihiko Nakazato, Etsuko Saito, Atsushi Wakasaya, Sorahiro Sunagawa, Takahiro Kasamatsu, Koji Kugu
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Prognosis of congenital heart disease has been improved remarkably and many women with the disease have become able to reach to the reproductive age. The pregnant women of adult congenital heart disease (ACHD) has been therefore increasing and most of them have uneventful pregnancy. However, cardiac function and condition are diverse even in the same disease and the care for them are therefore different from case by case. Specialized care for them should be important but the number of specialized institute has not reached to sufficient to take care of the women. Experience of the care of many cases should be accumulated and shared in order to provide high-quality management.

The medical records of pregnancy in the ACHD women that managed at our hospital from 2010 to 2017 were reviewed. The situation of the management, the evaluation, the medication, and the strategy during and after pregnancy were investigated. Forty-four cases and fifty-three pregnancies were identified. VSD was the most major disease. All of them were in NYHA 1 at the first visit and none of them had cardiac events during and after pregnancy. A severe AS case was referred to the specialized institute for the care and the therapeutic approach based on more experience of ACHD. It is possible that a pregnant woman with ACHD in NYHA 1 with no remarkable symptom may get worse in heart condition as the pregnancy progress. As ACHD has diverse condition even in the same disease, individual evaluation is very important and the most appropriate management should be provided. Most of them are mild and may be taken care at a non-specialized hospital.

Abnormalities in cardiac structure or function after hypertensive disorders of pregnancy: a systematic review and meta-analysis
Marie-Pier Arsenault, Maria Agustina Lopez-Laporte, Tara Landry, Veronique Cyr, Natalie Bottega, Natalie Dayan, Sophie Grand’Maison
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Hypertensive disorders of pregnancy (HDP) are a significant cause of maternal morbidity and mortality worldwide. Pre-eclampsia has recently emerged as an independent risk factor for future cardiovascular diseases. Modifications of cardiac structure and function have been described during normal and hypertensive pregnancies. Cardiovascular changes in pregnant women with HDP include increased peripheral resistance, left ventricular remodelling, diastolic dysfunction and, for some of them but still debated, a decreased in left ventricular systolic function. The aim of this systematic review and meta-analysis is to summarize evidence of sustained modifications of cardiac structure and function at least 3 months after delivery. Studies included were observational, with HDP as the main exposure and outcome measured by echocardiography (TTE) or cardiac magnetic resonance. We pooled results of modalities reported in >3 studies using a random effects model. Of 2733 potentially relevant studies, 22 were included in the meta-analysis and all of them used TTE. Women with prior HDP had a tendency to have lower LV ejection fraction, larger left atria, a higher E/A ratio and, interestingly, a higher 2D strain when compared with women with prior normal pregnancy. In conclusion, preliminary pooled data from studies evaluating post-partum cardiac structure and function by TTE suggest that echocardiographic indices of early diastolic dysfunction persist after HDP as compared with women with prior normal pregnancy.
The investigation of cardiac-sounding chest pain in pregnant women
Melanie Nana, Holly Morgan, Anita Banerjee
United Kingdom

Introduction
Cardiac disease remains the leading cause of maternal mortality. 21% of cardiac deaths during pregnancy are attributed to ischaemic heart disease. Despite the presence of NICE guidance on the management of cardiac-sounding chest pain, the UK Obstetric Surveillance System demonstrated large variability in the investigation of such symptoms in pregnant women. This may reflect concerns clinicians have regarding safety of investigations in pregnancy.

Objectives
Determine clarity with regards the appropriate investigation of cardiac-sounding chest pain in pregnancy.

Methods
Review the case of a patient with a myocardial infarction (MI) postpartum and undertake a literature review.

Results
A 38-year-old female with type 1 diabetes mellitus reported exertion chest pain prior to and during pregnancy. She underwent routine blood tests, troponin, BNP, ECG and an echocardiogram all of which were normal. She was reassured and advised to seek urgent medical attention if she developed red flag features. During the postpartum period she suffered an acute MI with an occlusion in her left anterior descending artery. Following percutaneous coronary stent insertion she recovered well.

Discussion
NICE guidelines recommend CT coronary angiogram (CTCA) in patients describing stable angina. If CTCA is unavailable or non-diagnostic a number of functional tests can be considered. If patients remain symptomatic of angina despite optimal medical management, revascularisation should be considered. The literature reveals that the radiation from CTCA to the mother ranges from 4-15mSv with no fetal data available, compared to standard CTPA which is 5-10 mSv to mother and 0.01-0.1 mGy to fetus. Stress agents are considered category B, gadolinium and tectnetium-99 are avoided if possible.

In light of increasing prevalence and mortality from cardiac disease in pregnancy, work to develop guidance to provide clarity regarding the appropriate diagnostic tests may be warranted. The importance of multidisciplinary team involvement in obstetric patient management remains paramount.

* Poster pitch

Simulation-based education at the heart of the matter...
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Introduction:
Cardiac disease in pregnancy remains the leading cause of mortality and morbidity worldwide. Recognition and management can be challenging. In response, we developed a multi-disciplinary simulation-based training programme; 50% practical/technical skills and 50% human-factors/non-technical skills (communication, leadership and teamwork).

Objectives:
Utilising a systematic ABCDE approach, knowing & understanding the symptoms, signs & management of cardiac disease in pregnancy and be aware of the important human factors to improve patient safety.

Methods:
Each scenario involved a simulated-patient, played by the Maternal Simulator (Noelle®), an embedded practitioner and course participants (3-5) comprising of midwives, obstetricians, physicians and anaesthetists. Scenarios included acute coronary syndrome, pulmonary oedema, aortic dissection and cardiac arrest.

Results:
This study evaluated the educational impact of six one-day courses with healthcare staff (n = 84). There was an improvement in both participants’ knowledge, clinical management of cardiac disease in pregnancy and an improvement in a validated and reliable self-efficacy human-factors toolkit; I am confident in my knowledge of the physiological changes of the heart in pregnancy. The chi-square statistic was 15.4189. The p-value was <0.0001.
I am confident in managing pregnant women with cardiac disease. The chi-square statistic was 15.4756. The p-value was <0.0001.
Using the Human Factor Skills for Healthcare Instrument 0-10 score. The paired two-tailed T-test of 42 sets of paired pre and post data had a mean change 0.96. The value of t was 6.854051. The p-value was <0.00001.

Discussion:
This course provided technical knowledge and confidence in managing cardiac disease, whilst allowing for a greater understanding of others’ professional roles. Simulation-based education is a promising avenue for reducing the mortality and morbidity of cardiac disease in pregnancy. It is responsive to the changing needs of the team whilst managing a pregnant woman.
Angiogenic markers \((sflt-1, \text{plgf})\) in patients with suspected und confirmed placental dysfunction (preeclampsia, iugr, placental abruption) - continuous values according to biochemical, clinical symptoms and particular perinatal results

Sebastian Kwiatkowski\(^1\), Magdalena Bednarek-Jedrzejek\(^1\), Joanna Ksel\(^2\), Piotr Tousty\(^1\), Ewa Kwiatkowska\(^3\), Rafał Rzepka\(^3\), Barbara Michalczyk\(^3\), Wioletta Mikołajek-Bedner\(^3\), Aneta Cymbałuk\(^3\), Andrzej Torbê\(^8\)

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Aims: to assess value of the serum level of soluble Fms-like tyrosine kinase 1 \((sFlt-1)\), placental growth factor \((\text{PlGF})\) and \(sFlt-1/\text{PlGF}\) ratio according to clinical, ultrasound, biochemical symptoms and particular perinatal results in pregnant women with suspected/confirmed placental dysfunction (preeclampsja, IUGR, HELLP, placental abruption)

Material i methods: 927 pregnant women between 18 and 41 weeks of pregnancy with suspected/confirmed placental dysfunction. Everyone woman included to cohort had introduced monolithe clinical, biochemical, ultrasound management and \(sFlt-1, \text{PLGF, sFlt-1/PIGF}\) ratio was assessed.

Results: In patients with confirmed placental dysfunction \(sFlt-1/\text{PIGF}\) ratio was higher independent from clinical symptoms compare to patients who didn't develop clinical placental dysfunction. Trial occurs statistical correlation angiogenic markers with parameters doppler ultrasound (i.e umbilical artery, uterine artery) traditional biochemical predictors (i.e. uric acid, AST,ALT, LDH, prothrombin time), clinical symptoms (systolic and diastolic pressure) and perinatal results (prematurity, days to delivery, birth weight, pH umbilical blood)

Conclusions: Angiogenic markers \(sFlt-1 \text{ and PlGF}\) and \(sFlt-1/\text{PlGF}\) ratio increase in placental dysfunction independent from clinical presentation. The values angiogenic markers correlate with traditional clinical, ultrasound, biochemical parameters and there are independent predictors perinatal results. \(sFlt-1/\text{PIGF}\) is helpful in diagnosis and monitoring women with suspected/confirmed placental dysfunction and can be useful in making therapeutic decisions in the future.

Angiogenic factors and preeclampsia with severe features among a primarily african american cohort with hypertensive disorders of pregnancy

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Preeclampsia related morbidity and mortality is rising predominantly due to delayed identification of patients at risk for severe features (preE-SF). This study explored the association between angiogenic markers (soluble fms-like tyrosine kinase-1 \([sFlt]\) and placental growth factor \([\text{PIGF}]\) and preE-SF.

Women with hypertensive disorders of pregnancy \((\text{HDP})\) were enrolled upon admission. Blood samples were collected within 96 hours prior to delivery. Angiogenic markers were measured on an automated platform. Severe disease was defined by ACOG criteria as BP ≥160/110, thrombocytopenia, right upper quadrant pain/epigastric pain/transaminases, renal insufficiency, pulmonary edema, or cerebral/visual disturbances. Descriptive statistics were generated and assessed with a Wilcoxon Rank Sum, chi-square or Fisher's exact test, as appropriate.

Univariate and multivariable logistic regression was used to assess for differences in outcomes and angiogenic markers were assessed in tertiles.

Our study included 375 women with HDP, of which 127 (33.9%) had preE-SF, 115 (30.7%) had gestational
hypertension, and 66 (17.6%) had chronic hypertension. Our cohort was predominantly African American (74.4%). Figure 1 outlines the prevalence of severe features among those with severe disease. Levels of sFlt1 (pg/ml) were significantly higher in women with severe features compared to those without (9372.5 vs. 3607.0; p<0.0001), while levels of PIGF (pg/ml) were lower (51.0 vs. 122.0; p<0.0001) and the ratio of sFlt1/PIGF was significantly higher (212.0 vs. 32.0, p<0.0001). The highest tertile of sFlt1/PIGF was strongly associated with preE-SF (OR 9.05, 95% CI: 4.25-19.24; p<0.0001) in multivariable analysis.

This study demonstrates a significant association between an abnormal angiogenic profile and preE-SF in a primarily African American cohort. Additional evaluation of the role of angiogenic markers during assessment for HDP and disease severity is needed.

The role of VEGF as prognostic marker of Preeclampsia.
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Background: Preeclampsia is one of the most frequent and severe pregnancy complications, which reaches 15-25% women in our country. It was found that the formation of hypertensive states in pregnancy due to endothelial dysfunction and the associated imbalance of angiogenic factors. The danger lies in the development of complications such as preeclampsia or eclampsia, fetoplacental insufficiency, fetal growth retardation, fetal hypoxia and fetal death. The aim of the work was to study role of VEGF as prognostic marker of preeclampsia.

Methods: We studied 84 pregnant women in different weeks of gestation, with various type of preeclampsia and 40 healthy pregnant women, which was the control group. All pregnant women were treated in Tashkent Maternal Complex â‘-6. All women underwent standard lab tests according to modern protocols. We investigated vascular endothelial growth factor (VEGF) determined by enzyme immunoassay.

Results: In control group the level of VEGF has averaged 5,4±0,3pg/ml. In women with preeclampsia in II trimester 11,6±0,6pg/ml, III trimester 22,2±1,4pg/ml. Emphasis is placed on the following most significant changes in the content of VEGF in serum. Two times increasing in VEGF in the serum of women with preeclampsia. During pregnancy level of VEGF in II and III trimester increasing remains stable. The level of VEGF in physiological pregnancy is increasing only in the first 10 weeks. In the subsequent curve, reflecting the content of VEGF accepts plateau-like character and does not change until the end of pregnancy.

Conclusions: Increased production of growth factor is nonspecific and is likely to reflect the disturbance of angiogenesis and vasculogenesis. Increased VEGF is already in I trimester of pregnancy can be understood as an early sign of predicting the formation of obstetric pathology at a later stage of pregnancy. Increased level of VEGF in the II and III trimester could be a predicted factor of preeclampsia.
TLR9-transfected cells. And then we evaluated the effect of si-TLR9 on human trophoblast migration/invasion through transwell assay and wound healing assay.

**Results**
1. Placental TLR9 and sFLT1 levels were upregulated while VEGFA levels were downregulated in women with PE.
2. ODN1826 could induce PE-like symptoms in pregnant mice. And ODN1826 could activate TLR9 signalling and induce upregulated sFLT1 levels, downregulated VEGFA levels in the placentas of PE-like mouse model.
3. ODN2006 could activate TLR9 signalling and induce increased sFLT1 levels, decreased VEGFA levels in the HTR-8/SVneo cells. And TLR9 siRNA could upregulate VEGFA levels and downregulate sFLT1 levels in the HTR-8/SVneo cells. Silencing TLR9 promotes the migration and invasion of HTR-8/SVneo cells.

**Discussion**
TLR9 is profoundly capable of suppressing angiogenesis by differentially regulating the expression of VEGFA and sFLT1 at the feto-maternal interface, potentially contributing to the development of PE.

**Aldosterone as independent predictor of placental and birth weights: Odense Child Cohort Study**
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**Introduction:**
Aldosterone is involved in plasma volume expansion and its levels, along with the levels of other members of the renin-angiotensin-aldosterone system (RAAS), are increased in healthy pregnancy. Aldosterone appears to contribute to an optimal fetal development by enhancing placental growth factor (PlGF) expression and trophoblast cell proliferation. In contrast to normal pregnancy, aldosterone is suppressed in preeclampsia.

**Hypothesis:**
Aldosterone independently contributes to placental and fetal growth.

**Methods:**
The project is based on data from the Odense Child Cohort, a prospective population-based study from the Municipality of Odense, Denmark, currently with 2500 active families. The participants were recruited between 2010 and 2012. To analyze plasma aldosterone levels and urinary aldosterone excretion (UAldoV), we used a subsample of 637 urine samples (24-h collections) from gestational week 28. Plasma aldosterone and UAldoV were determined by a commercially available ELISA. Predictive values of aldosterone were assessed by multiple regression analysis. Primary outcomes were placental weight (PW) and gestational age-adjusted birth weight Z-score (BW sds).

**Results:**
UAldoV, but not plasma aldosterone concentration, independently contributed to PW and BW sds (adjusted β coefficients ± SEM: 3.21 ± 1.51, p < 0.05 and 0.04 ± 0.01, p < 0.001, respectively). No significant differences in aldosterone excretion were found between women who later developed preeclampsia and the control group.

**Discussion:**
At 28 weeks of gestation, 24-h urinary aldosterone excretion was an independent predictor of placental and birth weights. In perspective, aldosterone could be a candidate biomarker for future screening and monitoring programs of high-risk pregnancies. Our findings support the physiological role for aldosterone and likely NaCl conservation for normal pregnancy. Mineralocorticoid supplementation could be considered for pregnancies with high risk for IUGR in order to achieve elevated levels of mineralocorticoids and thus benefit placental and fetal development.
The development of pre-eclampsia in oocyte donation pregnancies is related to the number of HLA class II mismatches
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Introduction (286 of 300 words)
Oocyte donation pregnancies are associated with a higher incidence of pregnancy complications, such as pre-eclampsia. In OD pregnancies the fetus may be completely allogeneic to the mother, since the fetus carries paternal and donor derived Human Leukocyte Antigen (HLA) genes. The higher incidence of pregnancy complications might be related to the high level of immunogenetic dissimilarity, reflected by the number of HLA mismatches.

Objective/Hypothesis
We studied the number of HLA mismatches in OD pregnancies in relation to pre-eclampsia.

Methods
In this retrospective study, HLA typing was performed in 99 women pregnant after OD and 118 children between 2004 and 2017. The HLA-genotype was determined for HLA-A, HLA-B, HLA-C (HLA class I), HLA-DR and HLA-DQ (HLA class II). The number of HLA mismatches of the child was calculated at the national reference laboratory for histocompatibility testing (LUMC).

Results
Twenty-two women developed preeclampsia in our group of 99 oocyte donation pregnancies. Maternal age and the frequency of twin pregnancies was significantly higher in the pre-eclampsia group, whereas gestational age was significantly lower in OD pregnancies complicated by pre-eclampsia.

The number of HLA class II mismatches of the child was significantly higher in the cases with pre-eclampsia (n=2.35 vs 3.15; p=0.014; OR=1.964 (95% CI=1.149-3.355)), even after correction by logistic regression for maternal age and twin pregnancies. No significant effect of HLA class I mismatches was observed.

Discussion
This study showed that OD pregnancies with a higher level of HLA class II mismatches have a significantly higher chance to develop pre-eclampsia. Hence, HLA class II matching could be considered in OD pregnancies to decrease the risk of developing pre-eclampsia, and preventive pre-eclampsia treatment (aspirin) could be considered in OD pregnancies with a higher level of HLA class II mismatches.

Baseline characteristics and angiogenic markers in women diagnosed with preeclampsia according to the new ISSHP and ACOG criteria
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Introduction
Preeclampsia is characterized by new onset of hypertension and proteinuria after 20 weeks of gestation. The inaccuracies in the measurement of proteinuria combined with the occurrence of complications in women with de novo hypertension without proteinuria led both the ACOG and ISSHP to revise their definition of preeclampsia.

Objective: To evaluate the baseline characteristics of women diagnosed with preeclampsia according to the new ISSHP 2014 and ACOG 2013 criteria.

Methods: In a cohort of 616 women with hypertensive pregnancy disorders we determined the baseline characteristics of women diagnosed with preeclampsia according to the ISSHP 2014 and ACOG 2013 criteria.

Results: On grounds of the old criteria 143 (23%) out of 616 patients were diagnosed with preeclampsia. According to the new criteria, the prevalence of (de novo) preeclampsia increased to 178 (28%) (ISSHP 2014) and 156 (25%) (ACOG 2013). The rise according to the ISSHP 2014 criteria was partially because HELLP is no longer considered an isolated disorder. Patients merely diagnosed according to the new criteria (ISSHP 2014 and ACOG 2013) were mainly characterized by new-onset hypertension without proteinuria in the presence of intrauterine growth restriction (ISSHP 2014), hematological complications and liver involvement. As expected, this group displayed lower protein-to-creatinine ratio than the old criteria (p<0.05). Preeclampsia based on new-onset hypertension with either renal insufficiency or neurological abnormalities was diagnosed in 3 patients, while no diagnosis was made based on pulmonary edema (ACOG 2013). No differences were found in median sFlt-1 or PI GF levels or the number of patients with sFlt-1/PIGF ratio <38 and >85.

Discussion: The use of the revised (ISSHP 2014) and (ACOG 2013) criteria increases the prevalence of
Risk factors for early and late severe preeclampsia
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Introduction. PE complicates 5-8% of pregnancies and is the leading cause of maternal death—about 60,000 women die from it every year around the world. It should be noted that to date, early (up to 34 weeks) and late (after 34 weeks) PE are seen as two completely separate units, rather than as different clinical forms of the same disease.

Keywords: chronic arterial hypertension, early and late preeclampsia, maternal mortality. Objective. To study risk factors in women, whose pregnancy was complicated by severe preeclampsia with early and late debut. Methods. A retrospective cohort study of 254 histories of pregnant women operated on for severe PE. Results and its discussion. The early onset of preeclampsia was in women with multiple pregnancies (4.5%), with genetic thrombophilia (6.4%). Heavy PE with late onset was observed in obese women (23.2%). Primiparity, chronic arterial hypertension, kidney disease are the most common risk factors for severe PE, but do not have significant differences in women with early and late PE. In both early and late PE, the leading position was occupied by chronic arterial hypertension (33%). In contrast to early PE in obese women with late PE, 13.5% occurred. At early PE—disturbances of system of a hemostasis (genetic trombophilia) it is marked in 6.4% of observations. In 24.1% of cases, the somatic history was not burdened. The frequency of occurrence of PE in previous pregnancies did not have significant differences between the groups with early and late PE (11.2% and 12.6%, respectively). In the group of pregnant women due to IVF—the frequency of severe PE was 8.3%. Of these, 6.7% fell to early PE, 1.6% to late PE. In case of multiple pregnancies, the rate of development of severe PE reached 12.2%. Early debut up to 34 weeks is marked in 8.7%, late-3.5%.

Risk Factors for Superimposed Preeclampsia in Women with Chronic Hypertension
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Introduction
Chronic maternal hypertension is associated with a 3 to 5-fold increased risk of preeclampsia. The compounding effect of additional risk factors on both preeclampsia risk and pregnancy outcome in such patients is uncertain.

Objectives/hypothesis
We hypothesised there may be additional risk factors identifiable in early pregnancy within this cohort which are associated with an increased risk of preeclampsia. If so, early risk stratification may help guide management and intervention to attenuate this risk.

Methods
Risk factors for preeclampsia identified at the pregnancy booking visit in women with known chronic hypertension were obtained from two centres in Melbourne, Australia in a retrospective analysis of 42,500 singleton deliveries(2008-2018). Risk factors included age, parity, previous preeclampsia, ethnicity, smoking, secondary hypertension, renal disease/proteinuria, hypertension duration, diabetes, antihypertensive use at conception and/or first trimester, aspirin use before 16 weeks, blood pressure(BP) at booking and body mass index(BMI). Associations were evaluated by univariate and multivariate logistic regression analysis, with significance p<0.05.

Results
233 births occurred in women with chronic hypertension(0.55% prevalence). Preeclampsia occurred in 36(15.5%) of these births, of which 19(8.2%) were severe preeclampsia. On univariate analysis, previous preeclampsia [OR 5.45(1.89-12.71)] and hypertension duration [OR 2.4(1.76-4.92)] were most strongly associated with any severity of preeclampsia. Adjusting for age, parity, previous preeclampsia, BMI, BP and renal disease, hypertension duration >5 years remained an independent risk factor [OR 1.23(1.03-1.48)]. For severe preeclampsia, strongest associations were maternal age >35, renal disease, BMI <30 and previous preeclampsia, the last remaining significant after adjustment [OR 13.2(1.47-119.6)].
Discussion
Risk of preeclampsia of any severity and severe preeclampsia were most strongly associated with a duration of hypertension >5 years and previous preeclampsia respectively. This highlights the importance of careful clinical appraisal in early pregnancy in women with chronic hypertension as early interventions (eg. aspirin) may mitigate risk of preeclampsia in this group.

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Is small placental biometry independent of increased uterine artery Doppler resistance for the prediction of fetal growth restriction?
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Introduction:
Fetal growth restriction (FGR) is associated with significant perinatal morbidity and mortality. Therefore, early prediction of FGR remains an important research question. 2-dimensional placental biometry offers an affordable and readily available adjunct to uterine artery (UtA) Doppler and fetal biometry measurement in the prediction of FGR.

Objective:
To determine if there is an association between placental biometry and birthweight and explore its relationship with UtA Doppler.

Methods:
This was a retrospective study of 820 pregnant women presenting to the high-risk research clinics at a tertiary centre. Women underwent a “placental screen” at 22-24 weeks’ gestation, during which UtA Dopplers, fetal and placental biometry were measured. FGR was defined as birthweight <3rd centile. Mean UtA PI distribution was normalised by logarithmic transformation. Interaction terms were included in regression analyses to assess potential effects of FGR outcome on the relationship between the UtA PI, placental biometry and birthweight centile. Continuous variables were compared between the FGR and non-FGR pregnancies using t-test.

Results:
74/820 pregnancies were complicated by FGR. Placental size was significantly smaller in FGR pregnancies and correlated with birthweight centile (p<0.001). Placental size significantly predicted FGR, even after adjusting for UtA PI (OR 0.72 per 2 cm increase in diameter [0.55-0.93], p=0.01). There was a modest association between placental biometry and log(UtA PI), with a significant interaction with FGR outcome.

Discussion:
Smaller placental biometry independently predicts FGR although there is a relationship with increased UtA PI. This suggests that an alternate pathological process causing reduced placental growth aside from reduced placental perfusion might be present in some cases of FGR. Research exploring the relationship between placental size and fetal and neonatal growth is required to investigate this further.

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Prediction of preeclampsia-related complications in women with suspected/confirmed preeclampsia: development and validation of a clinical prediction score
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Introduction: A simple clinical prediction model that could reliably predict the risk of preeclampsia (PE)-related pregnancy complications does not exist.”

Objective: To develop and to validate a clinical score for predicting the risk of women presenting with suspected/confirmed PE for developing pregnancy complications in the subsequent 7, 14 and 30 days.

Methods: Data from our previous study, a prospective, multicenter, observational cohort study of 384 women with suspected/confirmed PE were used to develop and to internally validate a clinical score to predict PE-related maternal and fetal complications in subsequent days. For the development of the risk score the possible contribution of clinical and standard laboratory variables as well as the biomarkers soluble FMS like tyrosine kinase-1 (sFlt-1), placenta growth factor (PIGF) and their ratio were explored using multivariate regression analysis. We assessed the discriminative ability of the model with the concordance (c-) statistic. Bootstrapping procedure with 500 replications
were used to correct the estimate of the risk score performance for optimism and to compute a shrinkage factor for the regression coefficients to correct for overfitting.

**Results:** 96 women with suspected/confirmed PE had PE-related adverse outcomes at any time after hospital admission. Remaining significant predictors of PE-related outcomes included sFlt-1/PIGF ratio (continuous), gestational age at time of biomarker measurement (continuous) and protein-to-creatinine ratio (continuous). The c-statistic (corrected for optimism) for developing a PE-related complication within 7, 14 and 30 days was respectively 0.888, 0.881 and 0.870. There was no significant overfitting. Internal validation by means of bootstrap resampling resulted in a shrinkage factor of 0.908.

**Conclusions:** We successfully developed an internally validated clinical prediction score with an excellent discriminative performance to predict short-term and longer term PE-related complications. Its usefulness in clinical practice awaits further investigation.

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**The additional value of fetal growth velocity parameters and maternal biochemical biomarkers for the detection of small-for-gestational-age neonates?**

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**Introduction**
Small-for-gestational age (SGA) neonates are a major cause of perinatal morbidity. The detection of SGA needs to be improved.

**Objective/hypothesis**
To evaluate the value of adding fetal growth velocity parameters to maternal biochemical biomarkers for the detection of SGA neonates.

**Methods**
A retrospective cohort study of 1094 singleton pregnancies (SGA and AGA), in the Maastricht University Medical Centre (MUMC) between 2011 and 2016. All women had ultrasound data of fetal growth from two periods: 18-22 and 30-34 weeks. In a subgroup the PAPP-A, β-hCG, PI GF and sFlt-1 at 11-13 weeks were measured. Differences in maternal biochemical biomarkers and fetal growth velocities (mm/week) of the abdominal circumference (AC), biparietal diameter (BPD), head circumference (HC) and femur length (FL) were compared between the AGA (birth weight percentiles 10-90), and SGA (birth weight percentiles <10), using one-way ANOVA and post-hoc.

**Results**
Compared to AGA (n=1049) as reference group, SGA (n=45) had significant lower growth velocities ACv (10.08±0.98 vs. 11.26±1.00, p<.0001) BPDv (2.78±0.29 vs.3.08±0.27, p<.0001), HCv (9.98±0.83 vs 10.67±0.82, p<.0001) and FLv (2.34±0.252 vs. 2.52±0.20, p<.0001).

SGA compared with optimal AGA had lower PAPP-a MoM (0.87±0.48 vs 1.13±0.70, p=0.015), higher Sfnt-1 (1283.96±699.36 vs. 1088.21±480.80, p=0.048), and a higher PIGF/ sFlt-1 ratio (50.16±41.56 vs. 35.67±19.68, 0.002). Combining all maternal biomarkers resulted in an AUC of 0.762 (0.655-0.869) for prediction of SGA. The combination of growth velocities resulted in an AUC of 0.729 (0.631-0.828). However, the addition of fetal growth velocities to the maternal biomarkers, improves the prediction of SGA with an AUC of 0.823(0.741-0.906) sensitivity 92.3%(95%CI 79.4-97.7%); specificity 50.0% (95%CI 43.7-56.3%); and NPV 97.3% (95%CI 92.3-99.2%).

**Discussion**
Detection of small-for-gestational neonates can be improved using the combination of fetal growth velocity parameters and maternal biochemical markers. A larger prospective study including serial maternal biochemical markers is needed.

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**Relation of plasma kisspeptin-10 to altered reproductive hormones in preeclamptic pregnant women**

Maysoun al-Kaabi, Farqad Hamdan, Hisham al-Matubsi
Iraq

Introduction: Hypertension and proteinuria associated with the diagnosis of preeclampsia (PE) following 20 weeks of gestation influences affects 5-10 % of all pregnancies. More importantly, however, PE is the main cause of maternal and perinatal morbidity and mortality.

**Objective/hypothesis:** To evaluate plasma kisspeptin-10 and assess its relation to altered reproductive hormones in
Methods: First time pregnant women (N=120) at 20 weeks of gestation participated in this study and divided into preeclamptics (N=60) and normotensives (N=60). The preeclamptics group were further subdivided into PE without severe features (N=39) who were beforehand normotensive, or severe PE (N=21). Kisspeptin-10, luteinizing hormone, follicle stimulating hormone, beta-human chorionic gonadotropin (β-HCG), estradiol, and progesterone were evaluated during second and third trimesters of pregnancy for all women.

Results: Kisspeptin-10 levels were reduced in severely preeclamptic women compared with uncomplicated pregnancies. During the second trimester, Kisspeptin-10 levels inversely correlated with severity of disease, whereas levels directly correlating with β-human chorionic gonadotropin, estradiol, and progesterone concentrations. Additionally, Kisspeptin-10 directly correlated with levels of follicle stimulating hormone during the third trimester in preeclamptic pregnant women. In contrast, Kisspeptin-10 inversely correlated with progesterone during the second trimester in preeclamptic patients without severe features, and during third trimester in patients with severe preeclampsia.

Conclusion: Testing for maternal Kisspeptin-10 plasma levels may be useful as an effective screening tool to predict preeclampsia when used as a biomarker in association with another tests such as hormonal profiling.

Is there any biomarker(s) for predicting immediate delivery or expectant management in preeclampsia?

Introduction: Preeclampsia is a pregnancy specific disorder and currently the only effective treatment is delivery of placenta. To control maternal and fetal complications, immediate delivery is well recommended, although studies have suggested that expectant management is possible for both severe and mild preeclampsia. A recent study also suggested that the most trigger for delivery in preeclampsia was difficult to control blood pressure. The indications for delivery within or after 48 hours were largely dependent on obstetricians’ experiences. Objectives: In this study we investigated whether there is any biomarker(s) or clinical parameter(s) that may affect the decision for either immediate delivery or expectant management.

Methods: Data from 157 women with preeclampsia were collected from a referral university teaching hospital and data included clinical parameters and laboratory biomarkers. A retrospective analysis was performed.

Results: There were 122 cases (77%) who delivered within 48 hours because of either maternal or fetal conditions. Of 157 cases, 110 cases (70%) were early onset preeclampsia. In early onset preeclampsia, 79 cases (72%) delivered within 48 hours. There was no difference in clinical parameters between cases who delivered within 48 hours and who did not. There were no differences in ALT or ASL or ALP or Uric acid or Blood urea nitrogen or creatinine or cystatin C or platelet counts between cases who delivered within 48 hours and who did not. In late onset preeclampsia (n=47), 43 cases (91%) delivered within 48 hours. There were also no differences in both clinical parameters and liver or renal biomarkers between cases who delivered within 48 hours and who did not. Similar findings were also observed in severe and mild preeclampsia.

Conclusions: Our study demonstrated that there is currently no biomarker(s) for predicting immediate delivery or expectant management. These results were regardless of the severity or the time of onset of preeclampsia.

Implementation and effects of risk-dependent obstetric care in the netherlands: a clinical impact study (expect study ii)

Introduction: This study evaluates former obstetric care as usual (Expect I) with risk-dependent care using a prediction tool (Expect II). The Expect I study externally validated 39 prediction models using data of 2,614 women prospectively included from 2013 to 2015. Clinically useful models were embedded in a web-based prediction tool. Additionally, risk-dependent care paths were developed, resulting in antenatal care tailored to the outcomes of individual risk assessments. Risk-dependent care was embraced by a consortium of obstetric healthcare
professionals in the Dutch province of Limburg.

**Objective:** This part focuses on adherence of healthcare professionals and compliance of women to key recommendations; e.g. adequate calcium intake in all women and low-dose aspirin treatment in women at increased risk of preeclampsia.

**Methods:** Women receiving risk-dependent care are being enrolled in a prospective multicenter cohort (Expect II) and receive four questionnaires at intervals.

**Preliminary results:** Ten months after introduction our prediction tool is being used in an estimated 24-40% of pregnant women in our region. Currently, 435 women have been enrolled. Recommendations regarding calcium intake were discussed with 351 women (81%), of which 285 (81%) reported the intention to comply (Expect I, adequate calcium intake in 34% of women). In case of an elevated preeclampsia risk (n=223) aspirin treatment was discussed with 180 women (76%), of which 52 (29%) intended to comply (Expect I, actual use in the high-risk group: 1.5%).

**Discussion:** The preliminary results indicate risk-dependent care has been implemented by a reasonable proportion of healthcare professionals. Furthermore, usage of the prediction tool increases recommendation of preventive interventions. Implementing new guidelines asks an additional effort of healthcare professionals, especially if it includes novel strategies such as a prediction tool. Future research should focus on barriers that hamper the adherence of healthcare professionals to risk-dependent care and on reasons for non-compliance of women.

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**Immunohistochemical and molecular study of placental bed in preeclampsia and iugr**

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Objectives: to study placental bed (PB) and microRNA expression in women with PE and PE, complicated by IUGR.

200 women 18-43 yrs old were divided into 3 groups: I–50 with early onset PE: Ia with IUGR (34), Ib without IUGR (16); II–50 with late PE: Ila with IUGR (11); Ib without IUGR (39) and 100 - as control. Samples of PB were obtained during CS after prior patient’s informed consent.

44% primigravida in group_Ia and 18,1% in group_Ila conceived within 6 months after marriage. BMI was higher and cardiovascular disorders occurred more often in group_Ila than in group_Ia (p<0.05). Family history of PE had 23,5% in Ia, Re-PE - 18% in Ila. Bleeding in early pregnancy had 30,0%; 25,0%; 9,0% and 7,0% respectively in all study groups. Delivery terms - 33,69±2,63; 33,5±1,06; 38,1±0,98 and 38,1±1,13 wks (p<0.01). CKW+ cell’s in PB tissue, Vimentin+ in endometrium, CD34+ in vessels, % of nonremodeled spiral aa, expression of SMA, HIF-1, VEGF, VEGFR, miR-34A were prevalent in group_I (p<0.05). In Ia and Ib, expression of CKW+ in the endometrium was low and completely absent in myometrium, level of mRNA 34a in the vascular endothelial tissue was high, especially in group_Ia. High expression of SMA+ and the appearance of immature fibroblastic Vimentin+cells, a low amount of CD34+ in the vessels and angiogenesis factors (VEGF, VEGFR, IGF, IGFR, HIF-1) was seen in these groups (p<0.05). In group_Ila and Ib higher expression of CKW+ in endometrium and myometrium, partial loss of microRNAs 34a, SMA+, Vimentin+cells, the mean expression of VEGF, VEGFR, IGF, IGFR, HIF-1 (p<0.05) were noticed.

A key role of placental site and mechanisms of placenta in early onset PE especially in combination with IUGR was suggested. Further research will help to create a basis for prediction, early diagnosis, and adequate management of those great obstetrical syndromes.

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**Association of levels of antepartum angiogenic factors with severe postpartum hypertension**

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Postpartum hypertension (PPHTN) often arises from an existing hypertensive disorder of pregnancy (HDP). Limited data exists about antecedent presentation and risk factors of PPHTN, especially among high risk groups such as African American (AA) women. We studied the association between levels of antepartum angiogenic biomarkers (soluble fms-like tyrosine kinase-1 [sFlt1] and placental growth factor [PIGF]) and risk of severe PPHTN among predominantly AA women.

Women with HDP were enrolled upon admission and blood was collected within 96 hours of delivery. sFlt1 and PIGF
were measured on an automated platform. PPHTN was defined as severe if systolic blood pressures (SBP) was ≥160 or diastolic blood pressure (DBP) ≥ 110 and mild if SBP ≥ 140 or DBP ≥ 90. Descriptive statistics are reported and assessed with a Wilcoxon Rank Sum or chi-square test, as appropriate. Univariate and multivariable logistic regression was used to assess the association between PPHTN and angiogenic factors, reporting the area under the receiver operating curve (AUC).

A total of 375 women were enrolled, with 279 (74.4%) AA and 151 (40.3%) who met criteria for severe PPHTN. About half (52.9%) of women with severe PPHTN also had pre-eclampsia with severe features prior to delivery. The sFlt1/PlGF ratio was significantly higher for both severe and mild PPHTN compared to women with normal postpartum BPs (73.5, 46.0 and 13.0 respectively, p-values<0.0001). Furthermore, the highest tertile of antepartum sFlt1/PlGF ratio was associated with severe PPHTN [OR 2.52, 95% CI: 1.49-4.27; p=0.001] which persisted after adjustment of confounders [OR 2.83; p=0.001]. When predicting severe PPHTN, the adjusted AUC for sFlt1/PlGF was 0.71.

Severe PPHTN is frequent in women presenting with antepartum HDP in this patient population. There is a significant association between antepartum angiogenic biomarkers and severe PPHTN. Further studies need to evaluate the mechanisms of such association.

Efficacy of a novel non-invasive indicator of arteriosclerosis for the prediction of hypertensive disorder of pregnancy
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Prediction of the onset of hypertensive disorder of pregnancy (HDP) has been burden for the obstetrician. Arterial velocity pulse Index (AVI) which reflects systemic hemodynamic status and arterial pressure volume Index (API) which reflects brachial artery stiffness are effective for accessing risks of adult cardiovascular disease because they are simply evaluated by an arm-cuff monitor and indicate a future risk for arteriosclerosis. However, the efficacy of AVI and API for pregnant woman remains unknown. The aim of the present study is to preliminarily examine distributions of AVI and API during pregnancy and assess the involvement of AVI and API in HDP.

AVI and API of pregnant women who visit to the outpatient unit of Kumamoto University Hospital between 2015 and 2017 were examined using PASESA® AVE-1500 (Shisei Datum, Tokyo, Japan). All pregnant outcomes were prospectively reviewed after the measurement of AVI and API and were thereafter classified into HDP group and non-HDP group with or without a diagnosis of HDP. Spearman tests and Student t tests were used for statistical analysis.

Outcomes of a total of 144 pregnant women were identified. The mean age of the women was 32.9±5.0 years old (20-42 years old). AVI and API were assessed at 32±8weeks of gestation (ranges; 10-42 weeks). There was negative correlation between API and weeks of gestation, whereas AVI was not correlated with the gestational weeks. Twelve women (8.3%) developed HDP. The mean AVI in HDP group was not different with that in non-HDP group (15.2±3.2 vs 14.4±2.8, P=0.49). The mean API in HDP group was significantly higher than that in non-HDP group (29.0±8.0 vs 23.5±5.7, P<0.05).

This is a first report to examine the range of AVI and API in pregnant women. Evaluation of API during pregnancy may worth to predict of the onset of HDP.

The usefulness of sFlt-1/PlGF on late onset preeclampsia
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Introduction
Endothelial cell dysfunction is thought to be the main pathophysiological condition of preeclampsia(PE). Increased production of soluble Fms-like tyrosinekinase-1(sFlt-1) and decrease on placental growth factor(PIGF) in PE patients lead to be an established biomarker for early onset PE at 1st trimester. Other hand, the utility of this angiogenic
Biomarker for predicting late onset PE has not been clarified.

**Objectives**
We performed this study to assess the usefulness of sFlt-1/PlGF at late weeks of gestation as a predictive biomarker for late-onset PE.

**Methods**
This is a single-center, retrospective cohort study conducted between April 2016 and June 2017 using the records of the Department of Obstetrics at Perinatal Medical Center of TOYOTA Memorial Hospital, Japan. We examined this biomarker for patients who had or were expected to develop PE. We defined sFlt-1/PlGF<38 as low-risk, 38<sFlt-1/PlGF<85 as intermediate risk and 85<sFlt-1/PlGF as high-risk respectively. Age at delivery, rate of PE, duration of pregnancy from blood sampling to termination, rate of Cesarean section, gestational age at delivery and fetal birth weight were collected.

**Results**
36 patients were included in the study and the mean age was 31.5 years old and median gestational weeks at blood sampling were 35 weeks of gestation. High risk group included 23 patients, middle risk group included 7 patients and low risk group included 6 patients. The rates of PE in each group were 73.9%, 28.5% and 16.7%. The rate of Cesarean section was significantly higher in high risk group compared with low risk group (70.0% vs 16.7%, p=0.018). Gestational age at delivery was much shorter in high risk group than intermediate (35w vs 37w p=0.003) and low risk group (35w vs 39w p=0.002).

**Discussion**
sFlt-1/PlGF at late weeks of gestation can be useful on predicting late onset PE. Further clinical research is needed to make this biomarker established.

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**Microfluidic platform to restore the angiogenic balance in preeclampsia**
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**Introduction** Preeclampsia is a hypertensive disorder of pregnancy linked to placenta insufficiency. Clinical studies have shown that the severity of preeclampsia is associated with the excess or the lack of angiogenic factors such as the sFlt-1/PlGF ratio (soluble Fms-like tyrosine kinase 1 and placental growth factor).

**Objectives** Our objective is to readjust the angiogenic balance of factors that play a causative role in preeclampsia by a competitive bioassay. A specific ligand, here VEGF (Vascular Endothelial Growth Factor), is used to both capture the protein sFlt-1 in excess and release its ligand PlGF in default.

**Method** A microfluidic extra corporal technology of micro-fluidized bed was developed to be used as a platform to screen strategies of competitive bioassay. This fluidic configuration enhances transfer between a fluid and the surface of the beads, with low back pressure and reduced risks of clogging. By grafting specific ligands on the surface of the beads, we can use this asset to capture a target present in the sample.

**Results** This device was able to capture sFlt-1 (up to 46% ± 1 of capture) in culture supernatant and maternal plasma. We demonstrate more importantly that compared to classical apheresis columns the nonspecific absorption is completely controlled (<3%). Using our competitive biomimetic binding approach, the ligation of sFlt-1 increases the bioavailability of PlGF. We were able to show a decrease of 83% of the ratio sFlt-1/PlGF from original samples at preeclamptic growth factors concentrations, leading to a final sample with a healthy ratio.

**Discussion** Continuous flow analysis enables to reach a good capture efficiency of sFlt-1. This dynamic platform mimics an extracorporeal circulation device at high flow rate, low cost and needs small volumes of sample. This last property enables us to work with precious samples such as maternal pathologic plasma.
Model: Pelvic muscle pressure is the missing link in pregnancy hypertension
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Hypothesis
Placental ischemia/hypoxia is NOT the major initiating event in the pathogenesis of preeclampsia. It is pelvic muscle pressure.

Methods
During my Winston Churchill Memorial Trust traveling fellowship to explore how to prevent trauma to pelvic floor muscles during birth, I conducted a review of the literature published between 1990 and 2017 investigating classification, assessment, and (physiotherapeutic) treatment of pelvic dysfunction and muscle physiology and biomechanics during pregnancy and postpartum. Expert opinions with biomedical engineers and muscle physiologists were also sought via interviews.

Findings
Studies revealed a conceptual model where muscles in the pelvic area become chronically tense (a high tone pelvis) because of multifactorial insults antepartum and postpartum. Pressurizing the pelvis and culminating in raised blood pressure. A triad of interrelated insults were identified which are mothers being encouraged to do Kegels with no relaxation component. The growing number of mothers with emotional stress disorders which manifest physically as tense muscles especially those in the pelvic region. And thirdly postural adaptations of pregnancy such as lumbar lordosis and anterior pelvic tilt being amplified by mothers poor lifestyle practices such as prolonged sitting, wearing heels and inadequate breathing causing shortened piriformis, quadriceps and other pelvic region muscles. Creating an unstable pelvis and compensatory spasm of antagonist muscles such as the pelvic floor to try and balance the pelvis. These tight or spasmed pelvic muscles are not just dysfunctional, but theoretically left unused their blood vessels become stiff resisting blood flow and causing volume overload at the heart, with a compensatory heart rate and blood pressure increase.

Conclusion
We are dealing with a pelvic pressure issue, not just a blood pressure one. A silent epidemic of tight pelvic muscles should be considered as a major initiating event in the pathogenesis of pregnancy hypertension in a significant number of mothers. Further studies are needed in this exciting area.

The role of PIGF in the prediction of preeclampsia
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Background: Simple, accurate and non-invasive biomarker testing is needed to predict preeclampsia and stratify its risk to enable and appropriate management. Various biomarkers have been tested for their role. One of the commonly used biomarker is PIGF which is found to be decreased in patients with preeclampsia and on average heralds the onset of disease and antedates the appearance of clinical symptoms.

Objective and study design: The purpose of this meta-analysis was to test this concept using the available evidence in the literature. We explored the predictive accuracy of PIGF in pre-eclampsia. 18 studies with following criteria were included:
• Using serum PIGF to predict preeclampsia
• Analysing after 18 weeks of gestation
• Excluding multiple and non-viable pregnancies
• Sufficient data to construct a 2 x 2 diagnostic table

What we found: • PIGF has high sensitivity and low negative likelihood ratio in predictive screening of preeclampsia. But, the sensitivity is not enough for it to be recommended as a screening test for preeclampsia. • It may help in making decision regarding hospitalization and follow-up in women at a high risk of preeclampsia.
• The use of PIGF may also decrease the anxiety and health care costs in managing patients with a negative test.

Looking Forward:
• This points to the need for larger cohort studies with uniformity in study criteria and involving diverse patient population.
• Studies disagree about cut-off, gestational age for screening, single or multiple testing, type of preeclampsia tested (early/ late onset) and the eligible patient population.
This is the first meta-analysis studying the potential of PIGF as a biomarker in predicting preeclampsia.
Differences in longitudinal sFlt-1, PlGF and sFlt-1/PlGF ratio measurements in predicting the development of maternal placental syndrome in a high risk population

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Introduction
Preeclampsia and related complication known as placental syndrome (PS), are most likely caused by abnormal placentation. Longitudinal measurements of these markers are suggested to be better predictors of PS than measurements at a single time.

Objective
To investigate the predictive value of longitudinal sFlt-1, PlGF and sFlt-1/PlGF ratio measurements in predicting PS.

Methods
This was a retrospective longitudinal cohort study in women with singleton pregnancies, identified as high risk patients between January 2015 and December 2017. All patients had serial measurements of PlGF and sFlt-1 at different intervals (12, 16, 20 and 30 weeks). We evaluated the absolute and relative differences (delta) in serum concentrations. The AUC of ROC curve analysis were compared to assess the performance in the prediction of PS.

Results
A total of 556 samples were analyzed in 139 patients of which 26 developed PS (18.7%). Women who developed PS had a lower increase in PlGF in the 12-30 interval: absolute difference: 258.5 (±211.7) versus 364.4 (±215.0), (p=0.025) and relative 9.4 (±7.3) versus 13.6 (±7.1), (p= 0.007), respectively. Similar differences were found in the delta PlGF in the 16-30 weeks interval: absolute 211.3 (±192.7) versus 319.2 (±203.0), (p=0.015) and relative: 3.5 (±1.7) versus 5.4 (±2.9) (p=0.001).

Patients who developed PS had a higher absolute sFlt-1 in the 16-30 weeks interval: 610.8 (±849.2) versus 299.8 (±672.4), (p=0.045). There were no significant differences found in absolute or relative sFlt-1 or in absolute or relative sFlt-1/PlGF ratio between women who developed PS versus those who did not at other time intervals. The AUC of PlGF at the 4 different intervals combined was: 0.75 (CI95%-0.65-0.86, p=0.00) the AUC of delta PlGF between 12-30 weeks was 0.67 (CI95%-0.54-0.80, p=0.01), for the prediction of PS.

Conclusion
In our population, longitudinal measurements could play a role in better prediction of PS than measurements at a single time point during pregnancy.

Cardiology/Nephrology

Poster pitches

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Adaptation of Cardiac Output and Systemic Vascular Resistance during Pregnancy: Systematic Review and Meta-analysis

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Introduction: Insights in the adaptation of cardiac output (CO) and peripheral systemic vascular resistance in normal pregnancy may aid in identifying women with deviant adaptation. These women are thought to be at risk for hypertensive related complications during pregnancy.

Objectives: First, to describe the pattern of CO and peripheral resistance changes in normotensive singleton pregnancies. Second, to explore the adaptation of these variables in pregnancies complicated by hypertension, pre-eclampsia and/or foetal growth restriction.

Methods: We performed a meta-analysis of systematically reviewed literature on CO and peripheral resistance throughout normotensive and complicated pregnancies, using PubMed (NCBI) and Embase (Ovid) databases. Only studies reporting measurements during pregnancy and non-pregnant reference values were included. Pooled mean differences between pregnant and non-pregnant women were calculated for predefined intervals of gestational age.
using a random-effects model.

**Results:** In total, 92 studies were included in this meta-analysis. In uncomplicated pregnancies, CO progressively increased from the first weeks on. After peaking in the early third trimester (+1.47L/min, over 30% increase as compared to the non-pregnant reference group), CO declined slightly until term. Next to that, peripheral resistance decreased progressively until early third trimester (-316 dyn·sec·cm⁻⁵, -24% as compared to the non-pregnant group), after which it increased a little. In the first trimester of complicated pregnancies, an augmented increase in CO was observed (+1.36L/min versus +0.73L/min in the uncomplicated pregnancies, p<0.001), that diminished quickly in the course of the pregnancy. In the second half of complicated pregnancies, CO values were similar to non-pregnant women.

**Discussion:** During normal pregnancy, CO increases and peripheral resistance decreases by 30% and 24% respectively, reaching their maximum measure in the second half of pregnancy. Deviant hemodynamic adaptations showing an initial augmented increase with a cross-over to a low cardiac output might identify pregnancies that will be complicated by hypertension and/or growth restriction.

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**Cardiovascular health in early pregnancy and hypertensive disorders of pregnancy**

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**Background:** Women with a hypertensive disorder of pregnancy (HDP) have an increased risk for cardiovascular disease (CVD). It remains unknown whether this results from the HDP itself or suboptimal cardiovascular health (CVH) before the onset of a HDP.

**Objective:** To determine the association between early pregnancy CVH and the risk for a HDP. Secondly, whether early pregnancy CVH is associated with CVH and carotid intima-media thickness (CIMT) after pregnancy, irrespective of a HDP.

**Methods:** Women (normotensive [n=7008]/HDP [n=240]) participated in the Generation R Study. We determined CVH in early pregnancy and nine years after according to the American Heart Association criteria. CVH comprised of seven metrics (blood pressure, BMI, smoking, physical activity, diet, total-cholesterol and glucose concentrations), which were categorized and weighted as poor, intermediate or ideal (zero, one or two points). All seven metrics combined created the CVH score, ranging from 0-14 points. CIMT nine years after pregnancy was used as a preclinical CVD marker.

**Results:** Women with higher CVH in early pregnancy had a 22% lower risk of developing a HDP than women with lower CVH. Higher blood pressure, BMI and glucose in early pregnancy were the strongest risk factors for developing a HDP. Higher CVH in early pregnancy was associated with higher CVH after pregnancy, especially after a HDP. Also, women with higher CVH in early pregnancy had a smaller CIMT, irrespective of having had a HDP.

**Discussion:** Higher CVH in early pregnancy reduces the risk of developing a HDP and CIMT thickening after pregnancy. Also, women with higher CVH in early pregnancy have higher CVH after pregnancy, especially those with a previous HDP. Remarkably, early pregnancy CVH was a better predictor of CIMT thickening than HDP. Early pregnancy CVH could be used to predict the risk of HDP and optimize CVH both in pregnancy and afterwards.

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**Cardiac small vessel imaging by light sheet microscopy and micro CT - discovering the missing link between preeclampsia and higher risk for further cardiovascular disease**

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**Introduction:** In preeclampsia, symptoms such as high blood pressure and albuminuria are caused by a state of anti-angiogenic and immune imbalance resulting in severe endothelial dysfunction. The evaluation of smaller vessels
Objective: We want to examine whether the increased risk for postpartum maternal cardiovascular disease after preeclamptic pregnancy is resultant from microvascular changes in connection with the structural remodeling processes.

Methods: We compared echocardiographic data from a human cohort with data from our transgenic animal model (hAGTxhRen) after preeclamptic pregnancy. In addition, we investigated cardiac changes in gene (qPCR) and protein expression levels (ELISA, IHC staining) in maternal rats, as well as alterations in microvascular 3D remodeling using Light Sheet Microscopy and Micro CT.

Results: We were able to show that the echocardiographic changes in our transgenic rat model are comparable to human data. In our rodent model we found maternal structural remodeling involving ventricular hypertrophy, myocardial fibrosis and inflammation at the end of pregnancy. The microvasculature and entire vascular network has been visualized so far only in cleared mouse brains and lymph nodes and partially in adult mouse hearts. Here, we present the 3D network of lectin-labeled blood vessels in cleared adult rat hearts with the analysis of cardiac small vessels with regard to branching points, vessel length and up to a diameter of 6µm.

Discussion: Preeclampsia leads to a structural remodeling in maternal hearts as a presumed cause for weakened functionality. Studies are underway to quantify coronary microvascular pathology as a possible missing link between preeclampsia and higher risk for further cardiovascular disease.

Early onset preeclamia predicts increased cardiovascular risk 1 year postpartum

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Objective/hypothesis
Cardiovascular follow-up of women with previous hypertensive disorder of pregnancy (HDP) has been suggested, as they are at increased long-term CVD risk. There is however no consensus on when to start follow-up of women who regained normal blood pressure postpartum. We assessed at 1 year postpartum if a previous HDP predicts cardiovascular risk beyond risk factors generally known.

Methods
Gestational hypertension (GH) was defined as de novo hypertension ≥gestational week (GW) 20 and preeclampsia (PE) was defined as GH with new-onset proteinuria. Early-onset PE was defined as PE with delivery <GW 37. Controls (n=102) were normotensive throughout pregnancy and delivered ≥GW 37. Women with gestational/pregestational diabetes were excluded, as were women with a growth restricted offspring (<3% percentile) or currently on antihypertensive therapy. The 30 year Framingham Risk Score (FRS; including age, systolic blood pressure, smoking, total and HDL cholesterol) was measured in 221 women 1 year postpartum.

Linear regression was used to measure associations between the FRS and previous HDP and adjusted for body mass index, age, smoking, premature cardiovascular disease in a 1st degree relative, and blood pressure at beginning of index pregnancy. P <0.05 was considered statistically significant.

Results
Framingham Risk Scores according to pregnancy diagnosis:

Discussion
Early-onset PE independently confers increased cardiovascular risk 1 year postpartum. Women with previous early-onset PE should receive early follow-up for prevention of cardiovascular disease.

Accuracy and precision of USCOM versus transthoracic echocardiography before and during pregnancy

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Introduction: Monitoring hemodynamic status early in pregnancy may be helpful in identifying women with deviant adaptation, who are thought to be at increased risk for hypertensive complications. The Ultrasonic Cardiac Output Monitor (USCOM) is a non-invasive and efficient method to measure cardiac output (CO). This method is not yet compared to transthoracic echocardiography (TTE) longitudinally in pregnant women.

Objectives: To assess agreement between USCOM and TTE for CO in 1) non-pregnant women to correct for possible sources of error; 2) pregnant women over the course of pregnancy.

Methods: High risk women admitted for cardiovascular risk factor evaluation after pregnancy and at 12, 16, 20 and 30 weeks of gestational age were included. CO was measured by TTE directly followed by an USCOM
measurement. Bland-Altman analysis was performed to derive mean bias, limits of agreement and percentage error of the two methods. Analyses were repeated with only high quality USCOM readings and measured instead of estimated aortic diameter. We performed a linear mixed model analysis on the longitudinal data in pregnant women.

**Results:** Percentage error was moderately improved by optimizing the measurements in 132 non-pregnant women (36.7% to 31.5%). During pregnancy, in total 83, 107, 96 and 77 acceptable measurements were obtained at respectively 12, 16, 20 and 30 weeks of gestational age. Mean CO in USCOM was over 0.5L/min higher compared to TTE in all trimesters and percentage error ranged from 35.2% to 45.6%. Linear mixed model analysis showed no association between bias, moment of measurement and subject.

**Discussion:** Due to its safe and feasible use, USCOM could be used to determine CO in pregnant women. However, absolute values of USCOM and TTE cannot be used interchangeably. Future research should focus on the agreement of USCOM and TTE in clinical decision making with the information of measured CO.

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**Uteroplacental acute atherosis, cardiovascular biomarkers and vasoactive hormones in pregnancy**

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**INTRODUCTION:**
Cardiovascular disease (CVD) is the leading cause of death for women. A history of hypertensive disorders of pregnancy increases the risk. Uteroplacental spiral arterial acute atherosis is a pregnancy-specific lesion resembling early atherosclerosis, frequently found in preeclampsia. The renin-angiotensin-system (RAS) plays a role in atherosclerosis and is dysregulated in preeclampsia. RAS and natriuretic peptides are physiological opponents in the regulation of arterial blood pressure and intravascular volume control. We previously reported increased concentrations of the natriuretic hormone precursor midregional proatrial natriuretic peptide (MR-proANP) in preeclampsia and suggested a cardiac origin.

**OBJECTIVE:**
To assess whether uteroplacental acute atherosis correlates with cardiovascular biomarkers and vasoactive hormones in maternal circulation at delivery in preeclamptic and normotensive pregnancies.

**METHODS:**
Third trimester maternal blood samples were analyzed for renin, prorenin and MR-proANP [normotensive pregnancies n=50, preeclampsia (PE) n=71]. Decidua basalis tissue for acute atherosis diagnosis (immunohistochemistry) was available for 53 of these pregnancies (normotensives n= 25 and PE n= 28). Statistical analyses: Skewed data were log-transformed. Linear regression and Fisher's Exact test were applied as appropriate. A p-value <0.05 was considered significant.

**RESULTS:**
A negative correlation between renin and MR-proANP concentrations was confirmed for both study groups. The presence of acute atherosis was not associated with maternal levels of circulating renin, prorenin or MR-proANP. Presence of acute atherosis was neither associated with MR-proANP/renin ratio nor maternal renin in the lower 2 quartiles in combination with MR-proANP in the upper 2 quartiles (normotensives p=1.0 and PE p=0.7)

**DISCUSSION:**
This is the first report on RAS and vasoactive hormones in pregnancy in relation to uteroplacental acute atherosis. We find that maternal circulating biomarkers previously shown to indicate hemodynamic stress in preeclampsia are not increased in pregnancies with acute atherosis. Further studies exploring the longitudinal association between maternal circulating cardiovascular biomarkers and postpartum CVD surrogate markers are underway.
Carotid intima media thickness and diagnostic of preeclampsia
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Objective: Compare the measure of Carotid Intima-Media Thickness (IMT) between patients who developed preeclampsia (PE) and those who did not and test the hypothesis that these measures are different in normal pregnancies compared with PE.

Methods: A prospective observational study using the measures of IMT was performed in 300 pregnant women who came to do the ultrasound routine scan at Hospital Presidente Vargas in Porto Alegre, Brazil, from April/16 until september/17. The outcome was scored as normal or PE. We used high-frequency ultrasound (12 MHz) with semi-automatic method to estimate the individual common carotid artery IMT.

Results: The partial results were obtained from 198 patients. Twelve had diagnostic of PE and 186 were classified as normal. The measures of CIMT were significantly higher in patients who developed PE compared with controls (mean 0.71 mm vs 0.59 mm; p <0.001).

Conclusion: Our findings suggest that the CMID measures in pregnants has the potential to detect women at risk for subsequent development of PE. We stil running the study.

Key-Words: Carotid intima-media thickness;pregnancy Preeclampsia, high frequency ultrasound

Markers of maternal cardiac dysfunction in pre-eclampsia and superimposed pre-eclampsia
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INTRODUCTION: Women who experience hypertensive disorders of pregnancy have an increased risk of developing cardiovascular disease in later life. The mechanism underlying this association unknown.

OBJECTIVES: To determine whether elevated glycogen phosphorylase isoenzyme B (GPBB) and/or brain natriuretic peptide (BNP) concentrations suggestive of cardiac dysfunction are observed in pre-eclampsia and superimposed pre-eclampsia (SPE).

METHOD: Four groups of women were selected from an existing cohort study: healthy controls (n=21), pre-eclampsia (n=19), pre-existing chronic hypertension (CHT) and/or chronic kidney disease (CKD) without (n=20), or with SPE (n=19). Plasma samples taken in the third trimester or at time of disease were assayed using Diagenics Dianeonatal® Glycogen phosphorylase Isoenzyme BB (GP-BB)-ELISA in-vitro diagnostic device kits and Alere Triage © CardioRenal assays (BNP). Log transformed GPBB and BNP concentrations were compared using interval regression as ratios of the geometric means with 95% confidence intervals.

RESULTS: No difference was observed in GPBB plasma concentrations between the control and pre-eclampsia groups (mean [95% C.I.]: 4.72 [2.49-8.94] ng/mL vs 4.98 [2.52-9.84] ng/mL; N=40, p=0.91), or between CHT and/or CKD and SPET groups (mean [95% C.I.]: 9.49 [4.93-18.25] ng/mL vs 10.24 [5.27-19.92] ng/mL; N=39, p=0.87). BNP plasma concentrations were significantly raised in the pre-eclampsia group compared to the control group (mean [95% C.I.]: 31.75 [19.21-52.49] pg/mL vs 11.31 [7.00-18.25] pg/mL; N=40, p=0.004), but did not reach statistical significance between the SPET and CHT and/or CKD groups (GM [95% C.I.]: 20.66 [12.40-34.44] pg/mL vs 16.06 [9.83-26.23] pg/mL; N=39, p=0.486).

DISCUSSION: There was no difference in GPBB concentration between groups. BNP concentrations were elevated in cases of pre-eclampsia compared to controls. This suggests cardiac dysfunction at the time of pre-eclampsia but through a mechanism other than cardiac ischaemia, and little role for the use of GPBB as a biomarker in hypertensive disorders of pregnancy.
Can cardiovascular adaptation in early pregnancy predict later hypertension?
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Introduction
The mechanism behind the increased risk for cardiovascular disease (CVD) after preeclampsia (PE) is unclear, both preexisting cardiovascular dysfunction and harmful effects of the preeclamptic episode have been proposed.

Objective
To compare risk factors for CVD during pregnancy and at a later follow up in women with a history of severe PE and women without such a history. A secondary aim was to evaluate risk factors for prediction of later hypertension (HT).

Methods
Women treated at Danderyd University Hospital, Stockholm, Sweden between 1999 and 2004, for severe PE and controls with normal pregnancies matched for age, year of delivery and parity were contacted between 2013 and 2016. Of 148 with PE, 82 agreed to participate and 84 of 172 invited controls. Data from the index pregnancy were retrieved from medical records. At follow up blood pressure, BMI, waist measurement and level of HbA1c as well as family history of CVD and hypertensive medication were registered.

Results
In the group with PE three had HT before the index pregnancy versus none in the control group. At follow up 24 of 82 (29.3%) in the PE group had HT versus 9 out of 84 (10.7 %) (p=0.003) in the control group. In women with only one episode of PE the rate of HT was 4.5% versus 52.9% (p=0.003) in those with more than one.

All variables were introduced in a logistic regression with stepwise analysis. Three variables were significantly related to HT at follow up: Systolic blood pressure (equal or more than 120) and BMI (equal or more than 25) in early pregnancy as well as family history of CVD. History of PE was not significantly related.

Conclusion
Blood pressure in early pregnancy may indicate impaired cardiovascular adaptation and be an indication of later hypertension.

IMPACT OF HYPERTENSION IN PREGNANCY OUTCOMES AND GRAFT FUNCTION IN KIDNEY TRANSPLANTED WOMEN
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Introduction
Hypertension, elevated serum creatinine and proteinuria are prepregnancy factors described in association with adverse pregnancy outcomes and graft dysfunction. Obstetric and neonatal complications include preeclampsia, gestational diabetes mellitus (GDM), intrauterine growth restriction (IUGR), preterm delivery, cesarean section, low and very low birth weight (LBW/VLBW).

Objective/Hypothesis
To evaluate obstetric, neonatal and graft outcomes in kidney transplanted women with prepregnancy hypertension.

Methods
Retrospective and comparative analyses of 41 pregnancies in 33 renal recipients followed in our department from 1989 to 2017. We considered two groups: women with prepregnancy hypertension (group 1) and women without prepregnancy hypertension (group 2 – control group). Statistical analysis was performed using IBM SPSS® Statistics v22 (p-value<0.05).

Results
There were 13 (31.7%) pregnancies in group 1 and 28 (68.3%) in group 2. The mean maternal age, mean time between transplant and pregnancy and mean prepregnancy serum creatinine were similar in both groups. The incidence of GDM (25.0% vs 4.2%,p=0.07), preeclampsia (16.7% vs 8.3%,p=0.47), anemia (50.0% vs 20.8%,p=0.08), IUGR (41.7% vs 12.5%,p=0.05) and preterm delivery (66.7% vs 54.2%,p=0.47) was higher in group 1. All cases of preeclampsia were diagnosed before 34 weeks in this group. Newborns with LBW (75.0% vs 45.8%,p=0.09) and VLBW (33.3% vs 0.0%,p<0.05), as well as admissions in the neonatal intensive care unit (58.3% vs 39.5%,p=0.09), were also higher in group 1. There were no significant differences between groups in other parameters: cesarean sections (58.3% vs 66.7%,p=0.63), urinary infections (16.7% vs 20.8%,p=0.76), miscarriages (0.0% vs 10.7%,p=0.23), abortions (7.7% vs 3.6%,p=0.57), stillbirths (0.0% vs 8.3%,p=0.20), graft dysfunction (39.5% vs 39.3%,p=0.96) and mean pospregnancy serum creatinine (1.70±1.07 [0.7-4.6] vs 1.16±0.36 [0.6-1.7] mg/dL,p=0.08).
Discussion
According to our results, prepregnancy hypertension is associated with worse obstetric and neonatal outcomes in pregnancies after kidney transplantation, although it seems to have no impact on graft function.

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Ideal interval between renal transplantation and pregnancy regarding obstetric outcomes
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Introduction: The optimal timing for pregnancy after kidney transplant remains uncertain, due to the risk of allograft failure. In the last consensus of American Transplant Society, this interval decreased from 2 years to 1 year, due to advanced maternal age with fewer childbearing years and lower risk of rejection with the more recent and potent immunosuppressive strategies.

Objective/hypothesis: Analyze whether the interval between transplantation and pregnancy (TTPI) influences obstetric outcomes.

Methods: Medical records from a retrospective cohort of pregnancies following kidney transplanted in our department, since 1989 (n=41), were analyzed. Obstetric and neonatal outcomes were compared according to transplantation-to-pregnancy interval (TTPI). Statistical analysis was performed using SPSS® version 22.0 (p=0.05).

Results: The study includes 41 pregnant patients after kidney transplant, 4 (10%) in the first year, 7 (17%) in second year and 30 (73%) after 24 months. Within the first year after transplantation, we observed a higher incidence of fetal growth restriction (66.7% vs 18.2%, p=0.06), preterm labor (100% vs 54.5%, p=0.06) and low and very low birth weight (100% vs 51.5%, p=0.05 and 66.7% vs 6.1%, p=0.013). Mean gestational age (32.3±0.6 [32-33] vs 35.8±2.5 [29-39] week, p=0.04) and weight at delivery (1500±282 [1300-1700] vs 2523±642 [885-3740], p=0.04) were significantly lower 1 year after transplant. In the second year, the incidence of gestational hypertension (57%) is similar to first year (33%), but significantly higher when compared with TTPI > 24 months (15%, p=0.03). With a transplantation-to-pregnancy interval higher than 2 years, the incidence of urinary infections is higher (27% vs 0%, p=0.02).

Discussion: Regarding the obstetric outcomes and according to our results, the ideal time for pregnancy after transplantation is between 12 and 24 months, with a lower risk of urinary infections, restriction of fetal growth, preterm birth and low birth weight.

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Maternal Endothelium and risk of cardiovascular diseases
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Background: In Pakistan, it has been strongly suggested that women with hypertensive disorders of pregnancy are at risk of developing cardiovascular disorders.

Objective: Our objective was to ascertain the persistence of endothelial activation in hypertensive pregnancies compared to women with normal pregnancies.

Methodology: Case control study design was chosen in two matched group. Endothelial activation was determined by the evaluation of adhesion molecules namely P selectin, E-selectin, Intercellular adhesion molecules-1 (ICAM-1) and vascular cellular adhesion molecules-1 (VCAM-1).

Results: In the first study, adhesion molecules were measured in 40 women with hypertensive pregnancies and in a matched control group with an uncomplicated pregnancy one month and three months after delivery. In the second study, adhesion molecules were measured in 40 patients with a history of HELLP syndrome several years after pregnancy and in 40 matched controls. Shortly after the delivery, increased levels of soluble adhesion molecules were found in women with hypertensive complications. However women with uncomplicated pregnancy did not have any increase
level of soluble adhesion molecules. Significant differences were still present, several years after delivery comparing levels of adhesion molecules in women with a history of HELLP syndrome with those found in control patients.

Conclusion:
An abnormal activation of endothelium was seen in hypertensive pregnancies. It has also been concluded that is abnormal activation of endothelium remains increased even after delivery which pre disposes the patient towards cardiovascular disorder. The risk of cardiovascular complications including ischemic heart diseases, chronic hypertension and stroke is more commonly seen in women experiencing HELLP syndrome.

Posters

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The impact of having twins on maternal cardiovascular adaptation during and after pregnancy
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Introduction
The cardiovascular adaptation required for pregnancy is considered a stress test for later life cardiovascular disease (CVD).

Objective
The aim of this study is to assess cardiovascular adaptation in women with a twin pregnancy during and after pregnancy.

Methods
In a population based prospective cohort study we compared 91 women with a twin pregnancy to 8089 women carrying a singleton. To determine cardiovascular adaptation during pregnancy we measured soluble fms-like tyrosine kinase-1 (sFLT-1), placental growth factor (PGF), systolic (SBP) and diastolic blood pressure (DBP), uterine artery resistance index (RI-UtA) and the occurrence of pre-eclampsia (PE). Six years after pregnancy maternal measurements were obtained on SBP, DBP, cardiac function and retinal calibers. Intima media thickness (IMT) and distensibility of the common carotid artery (CCA), SBP and DBP were also obtained nine years after pregnancy.

Results
sFLT-1 and PGF concentrations were higher in early and mid pregnancy in women with twin pregnancies compared to women with singleton pregnancies. Late in pregnancy, women with twin pregnancies showed a lower RI-UtA. Also a different DBP pattern was observed. Women with a twin pregnancy had a higher risk for developing PE (OR 3.15; 95% CI 1.52-6.53). Six and nine years after pregnancy, we did not observe differences in the cardiovascular profile.

Discussion
Women with a twin pregnancy show an altered cardiovascular adaptation during pregnancy compared to women with a singleton pregnancy. This is associated with a substantially increased risk for PE. However, this different cardiovascular stress during pregnancy does not seem to result in altered cardiovascular adaptation years after pregnancy.

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Can Obstructive Sleep Apnea Worsen Hypertension During Gestation? CASE REPORT.
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Introduction: Several studies have demonstrated the association between obstructive sleep apnea syndrome (OSAS), characterized by airflow limitation, chronic intermittent hypoxia and apnea, and hypertensive disorders, but few report such events to gestation Objective: Show the significant improvement of the clinical parameters of an hypertensive pregnant woman with the treatment of OSAS. Case Report: a 26 years old, afro-descendant, obese, G3P2 with chronic arterial hypertension, was hospitalized at 32 weeks of gestation with progressive dyspnea, associated with tachycardia, orthopnea and nocturnal paroxysmal dyspnea. She was medicated with nifedipine 40mg and alfaemildopa 2g (progressively escalated doses since the beggning of pregnancy). At physical exam: BMC 60, HR 125bpm, RR 22irpm, BP 140x100mmHg, O2 Saturation (SatO2)98%, bilateral pulmonary crackling in
the middle third, lower limbs with good perfusion and no edema and fetal heart rate of 150bpm. Chest radiograph showed pulmonary congestion, sinus tachycardia at electrocardiogram, echocardiogram with ejection fraction (EF) 56%. Measures were taken to treat pulmonary congestion, with noninvasive ventilation, furosemide and propranolol, with general clinical improvement. Arterial blood gas analysis without evidence of CO2 retention discarded the hypothesis of hypoexpansibility by obesity (PCO2 31.7). The polysomnography of type IV without the use of CPAP showed a SatO2 mean of 94% and a minimum of 84%, diagnosing moderate OSAS. During CPAP, there was an improvement in SatO2 standards. She underwent CPAP treatment with improved sleep and blood pressure levels, and discontinued the use of antihypertensive drugs, remaining normotensive. Fetal well being has always remained normal. A new echocardiogram after treatment showed increased EF (62%).

**Discussion:** Significant improvement in the clinical parameters of the pregnant woman after the use of CPAP. With the increased incidence of obesity, obstructive sleep apnea may become more frequent, but the literature is still scarce in relation to studies of this comorbidity in pregnancy.

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**Preeclampsia and risk of dementia later in life**

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**Introduction.** Preeclampsia has been linked with later cognitive impairment and brain atrophy, but epidemiologic studies have not confirmed a link with dementia later in life.

**Objective.** To explore associations between preeclampsia and later dementia, by dementia subtype and timing of onset.

**Methods.** Our study cohort included all women in Denmark with ≥1 live birth or stillbirth between 1978 and 2015. Using Danish national registers, we identified women who subsequently developed dementia. We used Cox regression to estimate hazard ratios comparing dementia risk among women with and without a history of preeclampsia.

**Results.** Our cohort consisted of 1,178,005 women with 20,352,695 person-years of follow-up. Women with a history of preeclampsia had a 53% increase in risk of dementia overall (hazard ratio [HR], 1.53; 95% confidence interval [CI], 1.26-1.85) and more than three times the risk of vascular dementia (HR, 3.46; 95% CI, 1.97-6.10) later in life, compared with women with no history of preeclampsia. In contrast, only modest associations were observed for both Alzheimer’s disease (HR 1.45; 95% CI 1.05-1.99) and unspecified dementia (HR, 1.40; 95% CI 1.08-1.83). The association with vascular dementia appeared to be stronger for late-onset disease (age ≥65 years, HR, 6.53; 95% CI, 2.82-15.1) than for early-onset disease (age <65 years, HR, 2.32; 95% CI, 1.06-5.06) (P=0.08). Adjustment for diabetes, hypertension, and cardiovascular disease attenuated the hazard ratios only moderately. Sensitivity analyses estimating the impact of unmeasured confounding by obesity (for which complete information was unavailable) showed that obesity was unlikely to explain the association between preeclampsia and vascular dementia.

**Discussion.** Preeclampsia was associated with an increased risk of dementia, vascular dementia in particular. Cardiovascular disease, hypertension, and diabetes were unlikely to mediate the associations substantially, suggesting that preeclampsia and vascular dementia may share underlying mechanisms or susceptibility pathways.

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**Simultaneous systolic waveform changes in uterine and ophthalmic artery Doppler in severe preeclampsie: a hemodynamic model based on increased pulse wave reflection.**

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**Introduction**

In hemodynamics pulse wave (PW) propagation and reflection is well established and body reflection from the pelvic region contributes an accelerative impulse to systolic flow.

**Objectives**

In progressive preeclampsia (PE) ophthalmic artery (OA) Doppler shows increasing 2nd systolic peak (OA-P2) and peak ratio P2/P1. Simultaneously, in uterine artery (UtA) Doppler a systolic shoulder (UtA-S) may appear. We assume both changes indicate increased PW reflection.
Methods
In PW modelling UtA-S appearance indicates arrival of wave reflection and time to shoulder-onset (ΔT) corresponds to the 2-way travel time (2wTT) of a PW travelling with velocity c between pelvic and cardiac reflection sites with distance L:

\[ 2\text{wTT} = \frac{2L}{c} \] (eq.1); \( L \approx (\text{aorta} + \text{common iliac artery}) \)

To test this model we performed UtA- and OA-Doppler in severe PE. When UtA-S was present, we compared measured ΔT with predicted 2wTT, using published data on distance L and PW velocity in PE.

Seen from UtA, reflected waves travel “back-and-forth”, and visa-versa, as seen from OA. As both additional path lengths agree, both waveform features will coincide.

Results
In 2017, six patients with severe PE finally entailed UtA-S and required delivery < 32wks. GA was 29±3wks and ΔT-measurements yielded 123±9ms (mean±SD). Published data show: distance L= 56cm and PW velocity c in PE: 8m/s - 10m/s. Equation 1 yields: 2wTT between 120ms and 140ms.

This agreement between observed (ΔT) and predicted (2wTT) temporal delay and mid-systolic coincidence of UtA-S and OA-P2, substantiate the validity of the model. Furthermore P2/P1 exceeded 0.8 in all cases.

Discussion
Body reflection to cerebral circulation is well known in adults with cardiovascular dysfunction. But we are not aware of reports focused on PE-associated PW reflection to OA or UtA. Hemodynamic modelling shows evidence that UtA-S appearance and OA-P2 augmentation results from increased PW reflection in severe PE, indicating maternal cardiovascular dysfunction.

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Adaptation of cardiac diastolic function during pregnancy - a systematic review and meta-analysis
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Introduction: During pregnancy, left ventricular (LV) diastolic function is of utmost importance to accommodate the increased preload in order to maintain increased cardiac output without triggering excessive sympathetic-tone-regulated reliance on heart rate. Insight in the physiological adaptation of diastolic function during pregnancy may enable the identification of women with impaired cardiac compliance, maladaptive to the pregnancy associated volume overload.

Objective: To meta-analytically determine the pattern of diastolic function indices during singleton normotensive pregnancies and hypertensive complicated pregnancies.

Methods: We performed a systematic review and meta-analysis on diastolic function during pregnancy using PubMed and Embase. We included studies that reported a non-pregnant reference measurement. Indices of interest were: mitral E-wave velocity, mitral A-wave velocity, E/A ratio, and left atrial volume (LAV). Mean differences between pregnant and reference measurements were calculated for predefined gestational age intervals using a random-effects model.

Results: We included 29 eligible studies. Normotensive pregnancies were characterized by a larger increase in passive LV filling (E-wave, 12%) compared to active LV filling during diastole (A-wave, 5%) resulting in a 17% increase of the E/A ratio in the first trimester. The E/A ratio progressively decreased during advancing gestation with 18%, resulting from normalized E-waves and increased A-waves. Hypertensive complicated pregnancies had a tendency of a larger decrease of the E/A ratio although not statistically significant (31%, p=0.74). LAV increased more in hypertensive pregnancies compared to normotensive pregnancies (30% vs. 112% respectively, p<0.01).

Discussion: Diastolic function in normotensive pregnancy is mainly dominated by passive filling in the first trimester while more by active filling later on in pregnancy. The E/A ratio therefore increases in the first trimester, to eventually progressively decrease in the second half of pregnancy. Stronger decline in E/A ratio along with concomitant increase in LAV in hypertensive pregnancies suggest fortified loss in cardiac diastolic function.
Adaptation of blood pressure during normotensive pregnancies and pregnancies complicated by hypertension - a systematic review and meta-analysis
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Introduction: Data on blood pressure (BP) adaptation in pregnancy show conflicting results on the occurrence of a mid-pregnancy BP drop. These inconsistent findings may contribute to delayed recognition of maladaptation in women at risk for a hypertensive complicated pregnancy.

Objective: To meta-analytically describe the pattern of BP adaptation in singleton normotensive pregnancies and hypertensive pregnancies.

Methods: We performed a systematic review and meta-analysis using PubMed and Embase. Studies included, needed to report a reference non-pregnant measurement. Mean differences between pregnant and reference measurements were calculated for systolic BP (SBP) and diastolic BP (DBP) in predefined gestational intervals using a random-effects model.

Results: In total, 110 studies were included (23079 BP readings). In normotensive pregnancy, both SBP and DBP started to decrease early in pregnancy, reaching their maximum reduction of -3.3% (-3.7 mmHg, (95% CI, -5.1 to -2.3)) and -5.6% (-3.9 mmHg, (95% CI, -4.8 to -3.0)) respectively in the late second trimester. In the third trimester, SBP and DBP gradually increased to reference values. In hypertensive complicated pregnancies, SBP did not decrease, while DBP initially decreased with -7.2% (-5.8 mmHg, (95% CI, -8.3 to -3.4)) in the early second trimester. From the second half of pregnancy onwards, BP increased to values higher than reference. SBP and DBP increased with 35% (38.2 mmHg, (95% CI, 27.3 to 49.2)) and 37% (26.1 mmHg, (95% CI, 18.4 to 33.8)) respectively in the hypertensive group, statistically significantly higher than normotensive pregnancies (p<0.01).

Discussion: This is the first meta-analysis on BP adaptation during pregnancy. In normotensive pregnancy, both SBP and DBP initially decrease, reaching their nadir in the late second trimester showing a clinically moderate, but statistically significant mid-pregnancy drop. Hypertensive complicated pregnancies lack a SBP decrease in early pregnancy which might reflect impaired vascular compliance in these women.

Cardiogenic and Non-cardiogenic Acute Pulmonary Edema in Hypertensive Disorder in Pregnancy
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Introduction
Acute pulmonary edema (APE) in hypertensive disorder in pregnancy (HDP) is one of the serious conditions and may have various origins, which roughly classified into non-cardiogenic (NCPE) and cardiogenic (CPE). Treatment strategy may be different from each other.

Objective
Similarity and difference of symptoms, physical or laboratory findings, and treatment between NCPE and CPE were investigated and appropriate approach may be established.

Methods
The HDP cases which had acute dyspnea and underwent echocardiography in our hospital between January 2014 and March 2018 were recruited to the study. The medical records were retrospectively reviewed.

Results
Twenty HDP cases were reviewed. Sixteen cases were confirmed as NCPE including one beta-adrenergic drug-induced, two transfusions related, which were mainly treated with diuretics. Based on the echocardiography findings, four cases were confirmed as CPE all of which were diagnosed with peripartum cardiomyopathy (PPCM). While only one NCPE case had orthopnea, all of CPE cases did. Furthermore, most of NCPE cases showed systemic edema, but none of CPE cases did not. No significant difference was observed in other clinical or laboratory findings between two groups.

Discussion
Orthopnea is known to be a typical symptom of heart failure. CPE is basically caused by pulmonary congestion followed by left heart dysfunction. From this study, it could be one of the characteristic symptoms of CPE. Severe hypertension may sometimes increase afterload leading to left heart dysfunction. NCPE was the most common cause of dyspnea in HDP, but it may come from various situation Hyperpermeability and hypoosmolality, are
essential features of HDP. Some medical interventions such as steroid for fetal lung maturation, and beta-adrenergic drugs for tocolysis may possibly cause NCPE. Infusion overload or transfusion-related acute lung injury may sometimes accompany with serious conditions of HDP such as placental abruption, HELLP syndrome.

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HELPP-syndrome a stair to atypical hemolytic uremic syndrome (aHUS)
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INTRODUCTION AND AIMS: To assess and compare the severity of hematological, renal and liver manifestation, the blood PLGF and sFlt1 levels in patients with HELLP-syndrome, PE and aHUS, and evaluate the association markers with the severity of clinical manifestations.

METHODS: Women with PE (Gr1), HELLP (Gr2), P-aHUS (Gr3), PE and with normal pregnancies were recruited for the retrospective study from September 1, 2013 to December 31,2017.

RESULTS:
Gr3 had a poor outcome and most severe course.

CONCLUSIONS: Based on clinical findings in P-aHUS, we propose a similar mechanism for a pathogenetic role of complement in HELLP. PE is only trigger or complement-activating condition for development HELLP-syndrome. Depending on the triggering stimuli and vascular bed involved, aHUS or the HELLP syndrome may develop. There were more severe clinical manifestations of renal impairment in all pts with HELLP and PaHUS as compared to women with PE and control gr. The sFlt-1 level was significantly higher in pts with PE as compared with HELLP and HELLP-onset aHUS. Less increased ratio of sFlt-1 / PIGF in gr.1 may confirm that PE is only complement amplifying factor to HELLP-development.

Treatment/Management/Outcome

Poster pitches

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Maternal and neonatal outcome in vaginal delivery versus caesarean section in severe early onset preeclampsia prior to 28 weeks’ gestation, a systematic review
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Introduction
preeclampsia with an onset prior to 28 weeks’ gestation poses a dilemma for the obstetrician with regard to mode of delivery for optimal maternal and neonatal outcome.

Objective
To analyze the success rate of attempted vaginal delivery (VD) in preeclampsia prior to 28 weeks’ gestation and the maternal and neonatal outcome according to mode of delivery (VD versus CS).

Methods
A comprehensive search was performed in the bibliographic databases Pubmed, Embase.com and Wiley Cochrane Library from inception up to June 2017. Main outcome was success rate of attempted vaginal delivery in women with preeclampsia prior to 28 weeks’ gestation. Secondary outcomes were maternal outcomes: maternal death, ICU admission, postpartum hemorrhage >1 liter, placental abruption and manual removal of placenta after VD or CS.
Neonatal outcomes were: neonatal death, neonatal morbidity (composite outcome) and live discharge from NICU after VD versus CS.

**Results**

Eight studies, either retrospective or prospective cohort studies, describing a total of 162 women, were included for this review. No RCT’s were found. Success rates of vaginal delivery varied from 1.8 to 80% and rates for CS after attempted vaginal delivery after induction of labor varied from 13 to 51%. Two studies (n=53) described no statistical significant difference in maternal outcomes according to delivery mode. Two other studies (n=107) described no statistical significant difference in neonatal outcomes according mode of delivery.

**Conclusions**

There are no RCT’s on mode of delivery in women with severe early-onset preeclampsia prior to 28 weeks’ gestation. Studies that do report the primary outcome are small, therefore no firm conclusions can be made. However, giving the available evidence in the reported studies, a trial of labor can be considered in preeclamptic patients prior to 28 weeks’ gestation.

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**The prevalence of chronic hypertension in pregnant women: a systematic review and meta-analysis**

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**Introduction**

Within the construct of Sustainable Development Goal (SDG) target 3.1, improving the measurement of maternal health will be key to addressing negative maternal outcomes. As such there has been a shift in focus from maternal mortality to morbidity, and in particular, pre-existing maternal conditions, such as chronic hypertension. This is associated with a number of poor maternal and perinatal outcomes, but the global prevalence of chronic hypertension among pregnant women is currently unknown.

**Objective**

To determine the global prevalence and regional distribution of chronic hypertension in pregnant women

**Methods**

We completed a comprehensive search using several electronic data bases as well as a grey literature search using Google. Observational studies from 1990-2015 were included regardless of language. To obtain a pooled estimate of the prevalence of chronic hypertension in pregnancy, a random effects model was used. Potential factors that might affect the prevalence of chronic hypertension were defined a priori (study type, quality, period and country income level) and stratified analyses were conducted in STATA 14.1.

**Results**

Of 40 relevant studies, 22 were population-based and 30 were from high-income countries; one study was from a low-income country (Togo) and 9 from middle-income countries. The overall prevalence of chronic hypertension was 1.6%, 95% CI 0.12-0.20, without a difference between hospital-based and population based studies. Chronic hypertension prevalence was lower in middle-income (0.6%, 95% CI 0.004-0.009) than high-income countries (1.7%, 95% CI 0.013-0.022) (p<0.001). Prevalence also increased over time (from 1% to 2%, p<0.001) and was higher in association with lower quality studies.

**Discussion**

This is the first study to provide a global estimate of the prevalence of chronic hypertension in pregnant women. However, there are several limitations including poor quality studies, predominance of studies from high-income countries and variable definitions of chronic hypertension.
Reliability and agreement of auscultatory and oscillometric blood pressure devices used in pregnancy
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Introduction
Accurate blood pressure (BP) measurements are vital in the detection of hypertensive disorders of pregnancy, such as gestational hypertension and preeclampsia. In South Australia, the manual technique remains the gold standard of measuring BP in the antenatal clinic, but may be inferior to sophisticated automated devices.

Objective
The objective of this study was to compare the manual technique with three automated oscillometric BP devices (Microlife Vital Signs Alert (MVSA) [Microlife, Taipei, Taiwan], Arteriograph [Tensiomed, Budapest, Hungary] and Uscom BP+ [USCOM, Sydney, Australia]) in a pregnant population.

Methods
This prospective study recruited 200 pregnant women at any stage of gestation between June and August 2017. Manual BP was measured first to prevent observer bias, followed by two measurements per device in a randomised order. Intra- and inter-technique reliability between repeated measurements was assessed with Intraclass Correlation Coefficients. Bland-Altman analyses evaluated the level of agreement between each variable. Techniques were graded according to British Hypertension Society (BHS) and Association for the Advancement of Medical Instrumentation (AAMI) criteria.

Results
Intra- and inter-technique reliability was excellent for all four techniques (all ICC >0.80). According to our pre-defined levels of agreement for mean systolic BP, MSVA and Uscom BP+ (mean difference <5mmHg), but not Arteriograph (mean difference 8mmHg), demonstrated good agreement with the manual technique. There was acceptable agreement for mean diastolic BP measurements for manual versus the three other techniques. Manual technique, MVSA and Uscom BP+, but not Arteriograph, fulfilled BHS and AAMI criteria.

Conclusion
Although each technique demonstrated excellent intra- and inter-device reliability, only MVSA and Uscom BP+ reached an acceptable clinical level of agreement with manual technique, and also fulfilled the BHS and AAMI criteria. Arteriograph consistently read higher systolic BP readings, indicating it may be unsuitable for use in an antenatal clinic setting.

Views and preferences of medical professionals and pregnant women about a novel primary prevention intervention for hypertensive disorders of pregnancy: a qualitative research.
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Objective
To explore the acceptability, views and preferences of pregnant women and primary healthcare providers for a fixed-dose combined preparation of aspirin and calcium (the polypill) as primary prevention of hypertensive disorders in pregnancy in an unselected pregnant population.

Method
A qualitative study was conducted, consisting of seven focus group discussions with 25 women with low-risk pregnancies and eight in-depth semi-structured interviews with primary care midwives and general practitioners of varying primary care practices in the Netherlands. Topics discussed were: perceptions of preeclampsia; information provision about preeclampsia and the polypill within antenatal care; views on the polypill concept; and preferences and needs regarding implementation of the polypill. MAXQDA computer software was used to carry out thematic analysis of the data transcripts to identify emerging themes.

Results
Two major themes shaped medical professionals’ and women’s views on the polypill: ‘Informed Choice’ and ‘Medicalization’. Both could be divided into subthemes related to information provision, personal choice and discussions with regard to the balance between ‘unnecessary medicalization’ and ‘scientific progress’.

Discussion
In general, women and healthcare practitioners expressed a positive attitude towards the polypill intervention as
primary prevention strategy with aspirin and calcium, providing some conditions are met. The most important conditions for implementation of such a strategy were safety, effectiveness and the possibility to make a well-informed autonomous decision.

Training of trainers of midwives and nurses as a strategy for the reduction of preeclampsia and eclampsia related maternal and perinatal mortality in Nigeria
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Background: Preeclampsia and eclampsia (PE/E) are major contributors to maternal and perinatal mortality in Nigeria. Despite the availability of current curriculum at Nigerian schools of nursing and midwifery, the knowledge on the management of PE/E among the students has remained poor. In order to reduce maternal and perinatal mortality in developing countries, pre service training of nurses and midwives is important.

Methodology: A total of 292 tutors from 171 schools of nursing and midwifery participated in the training of the trainers’ workshops on current management of PE/E across Nigeria. Pre and post test assessments were administered. Six months after the training, 29 schools and 84 tutors were randomly selected for follow-up to evaluate the impact of the training.

Results: Significant knowledge transfer occurred among the participants as the pretest/posttest analysis at the workshop showed knowledge transmission across all the 13 knowledge items assessed. The follow-up evaluation also showed that the trained tutors conducted 19 step-down trainings and trained 157 other tutors in their respective schools. Subsequently, 2382 nursing and midwifery students were trained. However, six of the monitored schools (24.2%) lacked essential kits for teaching PE/E.

Conclusion: Updating the knowledge of tutors leads to improved preservice training of the future generation of nurses and midwives. This will result in higher quality of care to patients and reduced PE/E-related maternal and perinatal mortality. However, there is need to provide essential training kits for teaching of student nurses and midwives.

Recurrence Rates of Preeclampsia over the Past 20 Years in Women Assessed for Non-Pregnant Cardiovascular Risk Factors
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Introduction: Recurrence rates of preeclampsia vary based on severity of disease in the complicated pregnancy together with presence of risk factors consistent with the metabolic syndrome. Several efforts to reduce recurrent disease have been implemented in clinical practice in the past decades.

Objective: To assess whether recurrence rates of preeclampsia and related foetal complications decreased in the past 20 years in women who received tailored preventive advices after an extensive non-pregnant assessment on cardiovascular risk factors.

Methods: In this observational cohort study, we included 752 women who had their first pregnancy complicated by preeclampsia between 1996 and 2012, and who participated in a non-pregnant cardiovascular and metabolic assessment at least 4 months after delivery. A questionnaire was sent to women to follow-up on their next pregnancy outcome. We divided the study population in three groups based on year of their second delivery 1) 1996-2004; 2) 2005-2009; and 3) 2010-2016. We compared recurrence rates of preeclampsia and related foetal complications between the groups with the chi-square test.

Results: In total, 467 (62%) women responded to the questionnaire of which two-thirds had a subsequent ongoing pregnancy. The overall recurrence rate of preeclampsia was 24%. Preeclampsia occurred in 29% (29/99) of women who delivered between 1996 and 2004, compared to recurrence rates of 20% (20/99) in 2005-2009 and 24% (28/119) in 2010-2016 (p-value .319). Related offspring complications, including small for gestational age, decreased significantly over time (p-value .016).

Discussion: Recurrence rates of preeclampsia did not decrease over the past 20 years in women who have been extensively assessed on cardiovascular risk factors. In the same period, foetal and neonatal outcomes improved
substantially. Efforts to extend and improve strategies to reduce recurrence risk of preeclampsia still seem to be necessary.

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Recovery of second trimester preeclampsia in triplet after foetal reduction; a case history and review of the literature
Jeske bij de Weg, Christianne de Groot, Eva Pajkrt, Hanneke de Vries, Marjon de Boer

Abstract
Introduction: Women with a multiple pregnancy are at increased risk of developing hypertensive disorders of pregnancy. Electively reduction in a triplet pregnancy have lower prevalence of preeclampsia compared to ongoing triplets or spontaneously reduced triplets.
Objective/hypothesis: Selective feticide might suggested as an option in early onset preeclampsia in dichorionic multiple pregnancies as alternative for termination the whole pregnancy.
Methods: We described a case of a dichorionic triamniotic triplet complicated by severe preeclampsia at 16 weeks gestational age. Additionally, we performed a review of the literature on selective feticide in multiple pregnancies on maternal indication in PubMed, MEDLINE and EMBASE.
Results: In our case, after reduction of the monochorionic twin, symptoms of preeclampsia clinically resolved, and delivery was postponed for more than 17 weeks at 32 weeks of gestation. In an additional review of the literature, we described 6 papers including 8 cases on multifetal pregnancy reduction on maternal indication. Reduction of multifetal pregnancy resulted in 2 to 21 week extension of time to delivery in women with preeclampsia.
Discussion: Selective feticide might be suggested as an (exceptional) alternative in early onset preeclampsia in dichorionic multiple pregnancies. Unequivocal counselling is essential because of the increased risk of adverse pregnancy outcome by extension of complicated pregnancy.

Clinical trial of metformin to treat preterm preeclampsia: pharmacokinetics and biomarker studies
Stephen Tong, Eric Decloedt, Tu‘Uhevaha Kaitu‘U-Lino, Brownfoot Fiona, David Hall, Sue Walker, Cathy Cluver

INTRODUCTION
Metformin is a potential therapeutic for preeclampsia as it decreases sFlt-1 and soluble endoglin and rescues endothelial dysfunction. Metformin pharmacokinetics in preeclampsia, where there is increased renal clearance and proteinuria, has not been established.
OBJECTIVE/HYPOTHESIS:
To evaluate metformin XR (extended release) pharmacokinetics in preterm preeclampsia, obtain data on pregnancy prolongation and circulating levels of biomarkers associated with endothelial dysfunction.
METHODS
15 women with preterm preeclampsia were treated with 1.5 grams metformin XR twice daily. Pharmacokinetic sampling was performed on day 1 at 2,4,5,6,7,8,24 hours, and concentrations measured using liquid chromatography-tandem mass spectrometry. Given steady state is reached at 24-48 hours, trough concentrations were measured at day 1 and 5 to assess the increase in Cmin over time. Plasma was taken twice weekly and biomarkers of endothelial dysfunction measured.
RESULTS
Gestation at recruitment ranged from 27 to 31 weeks, and median prolongation was 11.5 days [IQR 5.8 – 23.8]. Pharmacokinetic studies confirmed excellent circulating levels at 0-12h exposure, with Cmax [median (IQR)] 1.6 (1.3 – 1.9) mg/l, AUC 0-12 11.7 (8.9 – 13.5) mg.h/l and AUC 0-infinity 17.0 (10.7 – 36.6) mg.h/l.

Day 1 and 5 trough concentrations were 0.55 (0.34 - 1.22)mg/l and 0.01 (0.01 - 0.70) mg/l suggesting steady state exposure is similar to day 1. Umbilical cord blood:plasma ratios taken 4 (3 – 9.5) hours after dosing were 0.67(0.2 – 0.86).
None of the following circulating biomarkers increased across pregnancy among those who remain undelivered:

Delivery or expectant management for the prevention of adverse maternal and neonatal outcomes in hypertensive disorders of pregnancy: an individual patient data meta-analysis.

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Introduction: Hypertensive disorders affect about 10% of pregnancies. Delivery is the definitive treatment. Delay carries maternal risks, but early delivery increases fetal risk so appropriate timing is difficult.

Objective: To compare immediate delivery and expectant management for prevention of adverse maternal and neonatal outcomes in hypertensive disease of pregnancy.

Study Design: A systematic review and meta-analysis of individual patient data of randomized controlled trials including pregnant women from 34 gestational weeks with hypertensive disease allocated to immediate delivery or expectant management. Main outcomes were respiratory distress syndrome (RDS) and a composite of HELLP syndrome and eclampsia. Five datasets (GRIT, HYPITAT I and II, DIGITAT, and “Deliver or Deliberate”) were merged and analyzed using a 2-stage meta-analysis approach. We calculated relative risks (RR) and numbers needed to treat or harm (NNT/NNH) with 95% confidence intervals (CI).

Results: Main outcomes were available for 1,724 eligible women. Immediate delivery reduced overall HELLP syndrome and eclampsia risk (0.8% vs. 2.8%; RR 0.33, CI [0.15-0.73]; I²=0%; NNT 51, CI [31.1-139.3]) as well as in the subgroup with preeclampsia (1.1% vs. 3.5%; RR 0.39, CI [0.15-0.98]; I²=0%). The risk of RDS increased after immediate delivery (3.4% vs. 1.6%; RR 1.9, CI [1.05-3.6]; I²=24%; NNH 58, CI [31.1-363.1]), but this effect was dependent on gestational age. Increased risk was present in the 35th week (5.1% vs. 0.6%; RR 5.5, CI [1.0-29.6]; I²=0%), but this risk was lower in the 36th week, and did not reach statistical significance. (1.5% vs. 0.4%; RR 3.4, 95% CI [0.4-30.3]; I²=0%). We found no evidence of difference in NICU admissions, 5-min Apgar score <7, umbilical cord arterial pH <7.05, severe post-partum hemorrhage and cesarean sections.

Conclusion: In women with hypertension in pregnancy, immediate delivery reduces the risk of maternal complications, while the effect on the baby is dependent on gestational age.

Quantifying adherence to antihypertensive medication for chronic hypertension during pregnancy

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Introduction: The incidence of chronic hypertension in pregnancy is around 3%. Non-adherence to antihypertensive medication is a barrier to effective treatment of chronic hypertension and may impact maternal and perinatal outcomes; there are no robust estimates of adherence in pregnancy. The aim of this study was to evaluate adherence amongst pregnant women with chronic hypertension randomised to antihypertensive treatment.

Method: Spot urine samples were collected from pregnant women (12th to 35th weeks’ gestation) who participated...
in the PANDA trial (labetalol versus nifedipine for control of chronic hypertension in pregnancy) from three maternity units. Liquid chromatography-tandem mass spectrometry instrumentation was used to identify metabolites of labetalol and nifedipine in spot urine samples. Data were analysed using the statistical software Stata/SE version 14.

**Results:** Samples from 75 women randomised to first-line antihypertensive treatment were included in the analysis (n=39 labetalol, n=36 nifedipine). Mean highest blood pressure between randomisation and delivery was comparable in each treatment arm (165/97mmHg labetalol versus 165/99mmHg nifedipine). In 120 of 136 (88%) samples, documented prescribing and urine metabolite detection were concordant. No antihypertensive medication metabolite was detected in the urine of 9 of 136 (6.6%) samples; three (8%) of the women assigned to labetalol had no metabolite detected (dose range 200-1200mg/day) and six (17%) women assigned to nifedipine had no metabolite detected (dose range 10-80mg/day). There were no significant differences in BP (non-adherent mean 134/87mmHg versus adherent 133/84mmHg) or birthweight <10th centile (RR 1.55, 95% CI 0.64 to 3.73) between adherent and non-adherent women, though numbers were small. There was evidence of self-administration of alternative treatment with undocumented antihypertensive metabolites detected in 7 (5%) samples.

**Conclusion:** Assessment of urinary antihypertensive metabolites in women with chronic hypertension in pregnancy provides a novel insight into treatment adherence. Identifying non-adherence could facilitate initiation of interventions to improve blood pressure control.

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**The Sildenafil Therapy In Dismal Prognosis Early-Onset Intrauterine Growth Restriction Randomized Controlled Trials (STRIDER RCTs): A Consortium Approach**

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**Introduction:** The Global Obstetrics Network (GONet) initiative facilitates global collaboration in obstetrics research. The STRIDER Consortium is one such initiative - a consortium of four independently funded and powered trials (Australasia, UK, Netherlands, and Canada) that have a shared protocol (that includes a planned individual participant data meta-analysis) and harmonised data definitions and platform.

**Objective:** To establish a centralised clinical trial and database management infrastructure for the STRIDER consortium.

**Methods:** The STRIDER Coordinating Centre, University of British Columbia, created an electronic case report form (eCRF) database on REDCap for a central repository with role-based access control, and partnered with the BC HIV Trials Network to provide a participant randomisation system. The Coordinating Centre further developed an in-house program (iSTAR), allowing for customizations in participant randomisation, drug management, and improvements in eCRF integration. The randomisation algorithm generated in R software guarantees balanced allocations across treatment groups. The drug management system monitors inventory at each site and provides alerts if inventory falls below pre-determined thresholds, thus creating a continuous flow of supply for participants. To ensure data quality and patient safety, the Coordinating Centre developed online unblinding process, querying programming with validation rules and implemented processes with trial coordinators, allowing timely monitoring of data and trial activities.

**Results:** The Coordinating Centre provided centralised clinical operation and database management support to more than 50 sites in five countries. The SCC successfully supported the completion of STRIDER UK and STRIDER NZAus, recruiting 135 and 122 participants respectively. Currently, Dutch STRIDER and STRIDER Canada have recruited 192/354 and 20/90 participants respectively.

**Discussion:** Conducting trials as a consortium helps streamline clinical research infrastructure and promotes unified data collection and safety monitoring processes, thereby improving trial quality. Running clinical trials as a consortium can benefit patients and funders, increases research collaboration, and is cost-effective.
Policy and system bottlenecks influencing the management of pre-eclampsia in five countries.
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Introduction: While training and mentoring programs have focused on primary healthcare (PHC) level providers to identify, stabilize and refer women with pre-eclampsia, policy and procurement bottlenecks are barriers to provision of care.

Objective: To describe health system factors that affect timely management of preeclampsia at all levels in Bangladesh, Ethiopia, Kenya, Nigeria and Pakistan.

Methods: Qualitative data were collected through in-depth interviews with policy makers and health managers across five countries on the knowledge of existing policies and procurement plans. Assessment of data used NVivo (Version 10) to derive codes for themes.

Results: Most countries have maternal health policies and guidelines covering management and treatment of pre-eclampsia however it is less clear within the different health system levels on specific task shifting to PHC level. Bangladesh, Ethiopia and Nigeria have task-shifting policies allowing PHC providers to administer a loading dose of magnesium sulphate (MgSO₄) and referral, but is less clear on prescription of anti-hypertensives to control blood pressure. MgSO₄ is on each country’s essential medicines list, however, procurement of MgSO₄ (and other MH drugs) continues to be haphazard. The commodity is either not budgeted for, or the budget line is not being implemented, due to over-reliance on donor procurement or poor forecasting, tracking and accountability (Kenya, Pakistan). Widespread practice of patients and their families expected to procure drugs themselves continues; many stakeholders are concerned about quality of these drugs.

Discussion: Procurement of essential maternal health drugs and commodities for effective management of HDPs, have not been prioritized across all countries. Even tertiary hospitals fail to procure essential drugs and keep at point of use. Challenges remain in formalizing task shifting policies to manage pre-eclampsia effectively across the health system. Recommendations include lobbying ministries of finance and health to collaborate and prioritise maternal health care.

Posters

Induction of labor for maternal indications at a periviable gestational age; survey on management, reporting and auditing amongst dutch maternal-fetal medicine specialists and neonatologists
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Background
In exceptional cases of severe and life-threatening maternal conditions in the periviable period, professionals may consider immediate delivery the only option to prevent deterioration of the maternal illness. Fetal demise is then the inevitable consequence of the treatment of the mother. We sought the opinion of involved medical specialists on management, reporting and auditing in these difficult cases.

Methods
All registered fetal-maternal medicine specialists (MFM-specialists) (n=197) and neonatologists (n=282) were invited to participate in an online survey. The survey presented to hypothetical cases of severe early-onset preeclampsia at perivable gestational age. Two management-options were presented: immediate delivery and expectant management directed towards newborn survival. During expectant management two episodes with eclamptic seizures occurred.

Findings
In the case managed by immediate termination, 62% answered that fetal demise resulting from induction of labor for severe maternal illness should be audited within the medical profession only. In the case managed expectantly, 17% agreed with this management. 75% of MFM-specialists answered that an eclamptic seizure is always a reason for
immediate delivery. Some answers revealed a significant difference in opinion between the MFM-specialists and the neonatologists. The first concern of the MFM-specialists is the health of the mother, while the first concern of the neonatologists is, to achieve optimal gestational age for the newborn.

**Conclusion**
Perspective of MFM-specialists and neonatologists differs with regard to counseling prospect parents in case of severe early-onset preeclampsia. The majority of professionals is willing to report late termination of pregnancy (after 24 weeks’ gestation) for severe maternal disease to medical experts for internal audits, but not for legal auditing.

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**Preeclampsia and hELLP syndrome - obstetric prognosis**
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We are selected 185 pregnant women with HELLP syndrome and severe preeclampsia. The physical examination of patients the blood, function of liver, ultrasound. Patient with HELLP syndrome is a microangiopathic hemolytic anemia. Red blood cells become fragmented as they pass through small blood vessels with endothelial damage and fibrin deposits. The peripheral smear may reveal spherocytes, schistocytes, triangular cells and burr cells, increase in Bilirubin and lactic dehydrogenase levels. The elevated liver enzyme levels in the syndrome are thought to be secondary to obstruction of hepatic blood flow by fibrin deposits in the sinusoids. This obstruction leads to periportal necrosis and, in severe cases, intraparenchymal hemorrhage, subcapsular hematoma formation or hepatic rupture. The thrombocytopenia has been attributed to increased consumption and/or destruction of platelets. Our results of clinical presentation: 90% of patients present with generalized malaise, 65% with epigastric pain, 30% with nausea and vomiting, 31% with headache. Because of the variable nature of the clinical presentation, the diagnosis of HELLP syndrome is generally delayed for an average of eight days. Only two of 14 patients entered the hospital with the correct diagnosis. Because early diagnosis of this syndrome is critical, any pregnant woman who presents with malaise or a viral-type illness in the third trimester should be evaluated with a complete blood cell count and liver function tests. However, there is obviously still a lack of consensus on the laboratory parameters and their cutoff values used to diagnose. We are examination laboratory diagnostic criteria for HELLP syndrome. Clinical utility of strict diagnostic criteria for the HELLP the use of strict diagnostic criteria in the definition of the HELLP syndrome allows for greater prediction of complication rates. and define the cases that are Eligible to conservative management.

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**Results of a questionnaire survey on blood pressure management in hypertensive disorders of pregnancy in aomori prefecture, japan**
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Aim: To clarify the appropriate management of hypertensive disorder of pregnancy (HDP) and establish a long-term follow-up system for women with HDP after delivery. We investigated issues with HDP management approaches by evaluating blood pressure measurement on medical examination, home blood pressure measurement (HBPM) penetration rate, time of blood pressure examination during labor, and follow-up procedure after delivery in women with HDP.

Methods: We distributed questionnaires on blood pressure management during pregnancy, at delivery, and after delivery to 53 obstetrics and gynecology departments of professional medical institutions in Aomori prefecture, Japan.

Results: We retrieved completed questionnaires from 52 institutions, and analyzed responses to questionnaires from pregnant women in 39 institutions. Some institutions reported that antihypertensive medication was begun for mild hypertension (140/90 mmHg); these institutions had set a lower target BP. Only 56% of institutions measured blood pressure after labor pain onset. The postpartum follow-up was carried out not only by obstetric and gynecological clinics, but also by many institutions. However, sufficient education on the risk of recurrence in a subsequent pregnancy and lifestyle guidance were not provided.

Conclusions: There is little consensus on the timing of antihypertensive medication initiation or the appropriate level of blood pressure control. Labor onset hypertension may have been overlooked. Short-term follow-up of women with HDP was found to be frequently carried out; however, long-term follow-up was not. We will continue to provide the appropriate follow-up duration and approach to women with a history of HDP and to proactively engage in lifestyle interventions with the aim of improving longevity.
Eclampsia at a Tertiary Facility offering Free Maternity Services in South-western Nigeria - a Five-Year Review
Lawal Oyeneyin
Mother & Child Hospital, Ondo, Nigeria

INTRODUCTION
Eclampsia is a leading cause of maternal mortality in developing countries like Nigeria. The Mother & Child Hospital Akure (MCHA), Ondo State, south-western Nigeria was established in February, 2010 as a State-funded tertiary facility which offered completely free maternal and child (0 - 5 years) care services from inception till December 2014. During this period, it institutionalised protocol management of eclamptics and became one of the busiest maternity centres in Nigeria. The resultant data could assist care providers and policy-makers in eradicating the scourge.

OBJECTIVES
Determine prevalence of eclampsia at the MCHA from 2010 to 2014
Determine its contribution to the facility-based maternal mortality ratios
Determine its case fatality rates (CFR) during period of study

METHODOLOGY
This retrospective study was conducted in the MCHA. Data from February 2010 to December 2014 were retrieved from the medical records register and folders of patients. Analysis was through Microsoft Excel and SPSS.

RESULTS
Total deliveries in the 5-year period of study was 30,031 increasing by 108% from 3,673 in 2010 to 7,634 in 2013 before dipping to 6,234 in 2014. Number of eclamptics treated was 384, from 56 in 2010 to 107 in 2012 (a 91% increase), before dipping to 74 and 58 in 2013 and 2014, respectively. The overall prevalence was 1.3% with a downward trend from 1.5% in 2010 to 0.9% in 2014. Eclampsia contributed 36 out of 115 (31%) maternal deaths while the CFR was 9.4%.

DISCUSSION
This study’s CFR was among the lowest in Nigerian literature. It showed that offering free maternity services premised on protocol management could result in a steady reduction in number and prevalence of eclamptic cases after an initial spike, though the volume of deliveries could increase. It is recommended that the MCHA model be adopted in other tertiary maternity centres.

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The influence of acute respiratory infection in pregnant women on the development of preeclampsia.
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Introduction. In recent years, there has been an increase of the incidence of acute respiratory infections (ARI) in pregnant women, reaching 35.6%. There is conflicting evidence that ARI during gestation may increase the risk of placental dysfunction, preeclampsia and perinatal infections, eclampsia. Research material: the course of pregnancy was analyzed in 232 women who had undergone ARI in different terms of pregnancy. According to the classification ICD-10, pregnant women were divided into two groups: ARI of the upper respiratory tract (URT) (n=124) and acute respiratory infections of the lower respiratory tract (NDP) (n=108).

Results: the study of the course of pregnancy in women who underwent ARI in the first trimester showed the development of placental dysfunction (ED) in 36.4% of women with ORI NDP and 30.6% of women with ARI VDP. Whereas, in women who underwent ARI in the II trimester PD development was observed in 1.9 and 2.5 times less than in women with ARI in the I trimester. The above results showed that the development of PD in women with ARI in 1 and 2 trimester was not dependent on the localization of the infectious process. Pre-eclampsia depended on the period in which he moved, ARI, i.e. from early development of PD. Thus, the most often severe preeclampsia was observed in the group with ARI in the first trimester. In the III trimester of women who have undergone ARI, pregnancy was complicated by the development of preeclampsia (10.8%). The interval between the ARI and the manifestation of symptoms of pre-eclampsia made up 9.46±1.13 weeks.

Conclusions: the most typical gestational complications after ARI are: PD (22.4%), preeclampsia (10.8%). An increase in the frequency of PD in the early stages more than 2 times significantly increased the likelihood of PE in 1.8 times.
Antenatal/intrapartum management of parturient with methamphetamine induced cardiomyopathy in a regional centre

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Introduction: Peripartum cardiomyopathy (PPCM) is an uncommon form of heart failure that happens during the last month of pregnancy or up to five months after giving birth. It typically presents with signs of LV failure in a previously healthy woman and has an incidence of approximately 1:300-1:4000 with most occurring postpartum. Although the aetiology is still controversial, obesity, viral infection and drugs are all associated.

It carries a mortality of up to 28% and symptoms range from shortness of breath and tachypnea to haemptysis, chest pain and right upper quadrant pain.

Methods: Case Report

Results: A multiparous obese woman developed peripartum cardiomyopathy after her first delivery. After investigation, the aetiology was thought to be a combination of super morbid obesity and methamphetamine use. I discuss the antenatal investigations as well as the appropriate intrapartum management associated.

Discussion: I discuss the clinical manifestations, appropriate diagnostic tools and management of this condition.

Superimposed pre-eclampsia is best defined broadly - analyses from the CHIPS Trial (Control of Hypertension In Pregnancy Study)

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Background: Any definition of superimposed pre-eclampsia should identify women at increased risk of adverse outcomes.

Methods: In the CHIPS trial, women at 14+0-33+6 weeks with non-severe chronic or gestational hypertension and a live fetus were randomised to 'less tight' (target diastolic blood pressure [dBP] 100mmHg) or 'tight' control (target dBP 85mmHg). There was no between-group difference in the primary outcome (pregnancy loss or high level neonatal care for >48h in the first 28d), secondary outcome (serious maternal complications before 6 weeks postpartum), or pre-eclampsia defined restrictively (by new proteinuria) or broadly (by maternal symptoms, signs, or abnormal laboratory tests). 'Less tight' (vs. 'tight') control was associated with significantly more severe hypertension, platelets <100x10⁹/L, and elevated liver enzymes with symptoms. We compared restrictive and broad pre-eclampsia definitions regarding identification of women with adverse outcomes.

Results: For 981/987 women in CHIPS with outcomes, 280 (28.6%) developed pre-eclampsia defined restrictively, and 464 (47.4%) pre-eclampsia defined broadly. The broad (vs. restrictive) definition had higher sensitivity but lower specificity and classification accuracy for all outcomes but severe hypertension (Table 1).

Conclusion: Superimposed pre-eclampsia broadly defined can better identify true cases of risk in hypertensive pregnancy, but the potential harm of increasing false positives requires contextualisation.

Table 1

https://www.dropbox.com/s/eqnuo9d0vs0sl1j/CHIPS%20%20superimposed%20PET%203Table%201.docx?dl=0

Correct class (correct classification), sens (sensitivity), spec (specificity)
Strengthening Antenatal Care Services for early detection of Pre-Eclampsia and timely delivery: A Case of Three States in Nigeria
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Introduction
In Nigeria, maternal deaths due to pre-eclampsia/eclampsia (PE/E) are now the leading cause of maternal mortality at referral facilities' level. Lack of proper identification and management coupled with delay arrivals at referral facilities have been identified as contributing factors.

Objectives
This study seeks to understand maternal and newborn outcomes following training and mentoring of primary health care providers in identification and management of women with PE/E in 3 states in Nigeria.

Methods
Health care providers working at antenatal and maternity units in 36 secondary and 144 primary health care (PHC) facilities were trained and mentored on the prevention, detection and management of PE/E. Service data were extracted from monitoring tool that tracks how women with pre-eclampsia were identified and managed and their childbirth outcomes. Data were entered using Epi Info and analyzed through SPSS software.

Results
Ninety-three pregnant women were detected to have PE in one year. Sixty-four (68.8%) registered their pregnancies before developing PE, 32 (34.4%) were aged 15–25 years and most were married (n=74, 79.6%). None of the patients registered before 12-weeks gestational age; 65% (n=60) had proteinuria >2+; and 74.2% (n=69) had hypertension of >160/110mmHg. Seventy percent (n=65), 25.8% and 1.1% were identified with severe PE, PE and eclampsia, respectively. Of women with severe PE, 60% (n=39) received MgSO4 while 40% (n=26) did not. Although most mothers and babies survived, there was three maternal death and thirty perinatal deaths. In ten of the new-borns, death occurs at < 36 weeks of gestation age while most newborns (86.0%) survived at ≥ 36 gestation age.

Discussions
Appropriate training and mentoring of lower cadre service providers has the potential to improve detection and management of PE/E at PHC level, but more focus must be made on saving lives born before 36 weeks gestation.

Maternal, fetal and neonatal outcomes of women diagnosed with preeclampsia according to the new ISSHP and ACOG criteria.
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Introduction
Preeclampsia is characterized by new-onset of hypertension and proteinuria after 20 weeks of gestation. The inaccuracies in the measurement of proteinuria combined with the occurrence of complications in women with de novo hypertension without proteinuria led both the ACOG and ISSHP to revise their definition of preeclampsia.

Objective: To determine the difference in maternal, fetal and neonatal outcomes in women diagnosed with preeclampsia according to the traditional ISSHP 2001 criteria and the new ISSHP 2014 and ACOG 2013 criteria.

Methods: In a cohort of 616 women with hypertensive pregnancy disorders admitted between 2014 - 2016, we determined the maternal, fetal and neonatal outcomes according to the different criteria.

Results: The number of maternal and of fetal/neonatal complications was respectively 127 (21%) and 237 (38%). Median (range) gestational age at time of delivery was 35 (20-41) weeks according to all three criteria. On grounds of the traditional criteria (ISSHP 2001), median (range) birth weight was 2168 (280-4640) and declined to 2107 (170 – 4640) for ISSHP 2014 and 2125 (280 - 4640) for ACOG 2013 (p>0.05). No differences were found in maternal complication rate between the 3 groups. The number of patients with intrauterine growth restriction increased by 16 (80%) (ISSHP 2014) and 5 (25%) (ACOG 2013). Finally, no differences were observed in other fetal or neonatal complications and hospitalization days.

Results: Overall, no differences in maternal, fetal or neonatal outcomes were observed in women diagnosed with preeclampsia according to the new criteria (ISSHP 2014 and ACOG 2013). As the presence of intrauterine growth restriction, in contrast to the diagnosis of preeclampsia, does not necessarily require admission, an important question remains whether to include this in the diagnosis of preeclampsia. Prospective trials are warranted to assess whether application of the new criteria will significantly improve clinical outcomes.
**Introduction.** HELLP syndrome complicates 0.5-1% of all pregnancies, and among pregnant women with PE - 2-20% and is characterized by high maternal and perinatal mortality. **Objective.** To study modern features of the current, maternal and perinatal outcomes in pregnant women with HELLP syndrome. **Methods.** 28 stories of pregnant women with HELLP syndrome were analyzed. **Keywords:** HELLP syndrome, arterial hypertension, maternal mortality. **Results and its discussion.** In 71.4% of cases, the diagnosis of HELLP syndrome was made during pregnancy, and 28.5% after delivery. In women with severe preeclampsia, 11% were observed. HELLP syndrome was observed more often in primiparous women older than 30 years. In HELLP syndrome: chronic arterial hypertension (28.5%), IVF (7.1%), history of PE (10.7%), genetic thrombophilia (14.2%), antiphospholipid syndrome (7.1%), chronic pyelonephritis (21.4%). Only 32.1% of HELLP syndrome was combined with severe AH (BP>160/110 mm Hg). In 25% of patients, mild proteinuria is found, and 10.7% is not detected at all. Clinical symptoms were pain in the right upper quadrant (46.4%), weakness (21.4%), headache (17.8%), vomiting (17.8%), nausea (14.2%), increase in hepatic Enzymes were detected in 53.5% of cases, thrombocytopenia in 64.2%, hemolysis was detected in 7.1% of cases, an increase in LDH more than 600 U/L in 39.2% of cases. Increase in hepatic enzymes – AST more than 70 U/L - in 78.5% of cases, ALT more than 150 U/L - 60.7% The classical manifestation of HELLP syndrome was noted only in 64.2% of cases, monosymptomatic course in 35.7%. Circulation of lupous anticoagulant (BA) in 7.1% of cases. The perinatal complications: preterm labor (85.4%), IUGR (57.1%), placental insufficiency (53.5%) are exceptionally high. Antenatal fetal death is revealed in 21.4% of cases. Maternal complications: hepatic insufficiency (3.5%), acute renal failure (3.5%), cerebral edema (3.5%), pulmonary edema (3.5%), subcapsular hematoma of the liver (3.5%).

**Demographic and clinical profiles of women with Hypertensive Disorders in Pregnancy (HDPs) across tertiary health facilities in Nigeria**

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**Introduction**

HDPs are the leading cause of maternal mortality in referral facilities in Nigeria. Understanding who the women with HDPs are is important for designing a more inclusive and responsive health system intervention.

**Objectives**

To understand the demographic and clinical profiles of pregnant women with hypertensive disorders in Nigeria

**Methods**

A prospective cohort study of women with HDPs. Enrollment occurs within 24 hours of delivery which started in August 2017 with 1-year follow-up to measure maternal and infant outcomes associated with HDPs. The study collects clinical and demographic data at enrollment, 9 weeks, 6 months and 1 year using a pre-tested, interviewer-administered questionnaire across 7 tertiary hospitals in Nigeria with 404 enrolled women as of March 2018. Preliminary data provides a snapshot of who the women with HDPs in Nigeria are, and may provide insight to inform future health system.

**Results**

Seventeen percent of HDPs are occurring in maternal age deemed to be high-risk (13% and 4% are younger than 18 and older than 35 respectively). Twenty percent are first time pregnancies and 24% are para 4. Among those with records of gestational age at booking (239), only 9.2% booked within the first trimester. Thirty five percent were unbooked. 7.9%, 32.5%, 46.8% and 12.7% were admitted with chronic hypertension, gestational hypertension, pre-eclampsia and eclampsia respectively. Seventy percent of HDPs were late-onset.

**Discussion**

HDPs are compounded by other high-risk maternal behaviors and demographics. This calls for risks reduction and care-seeking improvement programs within our communities. This snapshot may provide insight to inform future health system intervention.
Maternal ICU admissions at the McGill University Health Centre and Impact of Advanced Maternal Age on Outcomes: Retrospective Chart Review
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INTRODUCTION Severe maternal morbidity (SMM) necessitating intensive care unit (ICU) admission is rising. Advanced maternal age (≥ 35 years, AMA) is associated with SMM, but its impact on ICU outcomes is not clear.

OBJECTIVES We aimed to describe characteristics of pregnant and postpartum women admitted to the ICU at our institution, and to evaluate the impact of AMA on length of stay, need for invasive intervention, number of SMM indicators, and death.

METHODS We conducted a retrospective chart review of ICU admissions during, or within 42 days, of pregnancy, from January 1, 2006 to December 31, 2016. Impact of AMA on outcomes will be assessed with linear and log-linear regression.

RESULTS 205 women were admitted to the ICU during pregnancy or postpartum. We report descriptive analysis on a subset of patients (n = 97). Mean age was 32.5 ± 6 years; 39 (40.1%) had AMA. Most admissions (70.1%) occurred during postpartum period. High prevalence of hypertensive disorders of pregnancy (19.6%) and gestational diabetes (13.4%) was noted. One third delivered prematurely (<37 weeks), 34% required emergent C-section, and rate of intra-uterine fetal demise was high (4.1%). Reasons for ICU admission were obstetrical (41.2%), medical (20.6%), and surgical (21.1%). Mean length of ICU stay was 2.6 ± 3.5 days, with 43.3% exceeding 1 day. The vast majority (72.2%) of patients required invasive interventions. No deaths recorded.

DISCUSSION The majority of maternal ICU admissions are in the postpartum period in women with at least one maternal or fetal complication. Further analyses will explore outcomes according to maternal age.

Management and pregnancy outcomes in women with hypertensive disorders of pregnancy in University of Calabar Teaching Hospital (UCTH), Calabar, Nigeria: - one year preliminary review.
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University of Calabar, Calabar, Nigeria

Introduction: Hypertensive disorders in pregnancy (HDP) is one of the leading causes of maternal mortality in Nigeria contributing over 23%. There is no locally available guideline that directs care for women with HDPs during the postnatal period. Population Council under the Ending Eclampsia project proposed a study across the six geo-political zones of Nigeria that will recruit women with HDP around the time of delivery and prospectively follow them for up to 1 year afterwards. UCTH Calabar is one of the centers, and this is a one year preliminary review of data before commencement of the study.

Objective: To assess service delivery gaps and pregnancy outcome of women with hypertensive disorders in pregnancy.

Methodology: Case folders of women with HDP who delivered between 1st April 2016 and 31st March 2017 were retrieved from the record department of the hospital. 97 out of 105 had adequate data which was entered into excel and imported to SPSS version 23 for analysis.

Results: The prevalence of HDP was 5.3%. More than half 65(67.0%) were in the 25-34 years age and 40.2% were primigravida. A total of 68(70.1%) were pre-eclamptic with 17(17.5%) eclamptic only 3(3.1%) had chronic hypertension. Majority of the women had caesarean section compared to spontaneous vaginal delivery (80.4% versus 19.6%). A total of 85.6% babies were alive.

Only 26(26.8%) had the required investigations done, while only 18(18.6%) received thromboprophylaxis. At discharge, those with normal systolic BP were more than those with normal diastolic BP (42.3% versus 32.0%). Only 26(26.8%) of the women returned foe postpartum visit.

Conclusion: The rate of eclampsia is still very high in our center. Also the number of women with required investigations, those who received thromboprophylaxis and those returning for postpartum follow up is very low..
Low self esteem amongst preeclampsia population; should we be worried?
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Introduction: preeclampsia is a hypertensive disease in pregnancy that worries both the care giver and the patient. They have a more frequent visit to the clinic compared with low risk pregnancy. Knowing about the complications of pregnancy apart from developing complications may affect the patient emotionally. This is a descriptive, cross sectional study to evaluate self esteem of patients diagnosed with preeclampsia at the antenatal clinic.

Methods: 100 pregnant women diagnosed at various gestational age of pregnancy were examined. The instrument for examination was via questionnaire. Rosenberg self esteem scale was used to evaluate all patients and classified as having low self esteem or not. Effect of Social demographics were also evaluated with descriptive statistical analysis. They were classified into groups based on parity.

Result: 42% had low self esteem. It was higher amongst primigravidas. Patients with lower economic status had a higher incidence of low self esteem. ANC seems to affect the penetration of low self esteem.

Conclusion: Low self esteem is seen among preeclampsia population and prenatal clinic should intensify education to reduce the effect this.

Identifying the severity depression among pregnant women diagnosed with Hypertension. Do we need emotional support groups?
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Background: Pregnancy is a hyper dynamic state and depression plays a devastating role among women diagnosed with hypertension during any trimester of pregnancy. It is believed that hypertensive distress is recognised as major psychological issue among Pakistani pregnant women.

Objectives: Our study aims to identify hypertension associated distress among Pakistani pregnant women diagnosed with hypertension. We also aim to find out the relationship among depression, distress caused by hypertension and cardiovascular diseases.

Methods: A cross sectional study was conducted in Sir GangaRam Hospital Lahore during February 2015 to June 2016. Total 80 pregnant women diagnosed with hypertension during their 2nd trimester were included in the study. Blood pressure and certain laboratory investigations were done including total cholesterol, LDL, VLDL and HDL. A personalized health questionnaire was used to classify depression among women. Hypertensive distress scale was used to identify hypertension distress and other factors such as social distress, interpersonal distress, physician related distress, emotional distress and regimen related distress.

Results: The rate of depression was 39% among women diagnosed with hypertension. 8% were categorised as mild depression, 14% moderate depression and 17% with severe depression. Hypertensive depression was found in 71% of the selected population. Rates of social distress, interpersonal distress, and physician related distress, emotional distress, infant death distress, regimen related distress were 23%, 33.5%, 17.8%, 73.4% and 42.6 respectively. There was no association between depression and low HDL.

Conclusion: Our study concludes that hypertensive distress is very common among pregnant women in Pakistan and this is an alarming condition for Pakistani population. We need to develop and modify our management plans in order to combat this deadly distress. Mass media should be involved in order to raise awareness about
Thrombosis and treatment

Posters

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Trombophilia and pregnancy - a participation of pai 4g/5g
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INTRODUCTION: Pregnancy is hypercoagulable state. The tendency to thrombosis, has been developed rapidly and has been linked to many aspects of pregnancy. It is recently that severe pregnancy complications such as severe preeclampsia, intrauterine growth retardation, abruptio placentae and stillbirth has been shown to be associated with thrombophilia. The obstetrics service of the Federal University of Juiz de Fora has an Ambulatory for the attendance of pregnant women with poor obstetric result and this study was taken.

METHODS: Study was performed when 79 a coort study with poor obstetric results (hypertensive syndromes, intrauterine fetal death, abortium, intrauterine growth retardation, abruptio placenta) were evaluated. All those patients were submitted to trombophilia research (V Leiden factor, mutation of prothrombin, SAAF, MTHFR, protein S, protein C, antithrombin III and PAI 4G/5G mutation).

RESULTS: The mutation PAI 4G / 5G was associated to abortium (p <0.05). Hypertensive syndromes were also frequent and associated with the 4G / 5G mutation, when combined with other trombophilias (p <0.05).

CONCLUSIONS: The authors conclude that this mutation should be searched in the effective effects of the fetal result.

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Hypertensive disorders of pregnancy and trombophilia association
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INTRODUCTION: Hypertensive disorders during pregnancy are classified into 4 categories, as recommended by the national high blood pressure education program working group on high blood pressure in pregnancy: 1) chronic hypertension, 2) preeclampsia-eclampsia, 3) preeclampsia superimposed on chronic hypertension and 4) gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy). The role of thrombophilia in the pathogenesis of preeclampsia is controversial, and it’s possible the thrombophilia increases the risk of preeclampsia or interferes with its clinical course.

METHODS: We study 79 pregnancy patients with a poor obstetrics results. All those patients were submitted to trombophilia research (V Leiden factor, mutation of prothrombin, SAAF, MTHFR, S protein, C protein, antithrombin ) and mutation of PAI (4G/5G).

RESULTS: We identified 38% of patients with preeclampsia, and there was association between SAAF and preeclampsia (p< 0.05). There was association between PAI mutation (4G/5G) and preeclampsia and preeclampsia superimposed on chronic hypertension, when this mutation was associate with other hereditary trombophilia (p<0.05). There was no association between preeclampsia and others hereditary trombophilias.

CONCLUSIONS: SAAF and PAI 4G/5G mutation are important trombophilia for the adverse outcome of pregnancy.
The prognostic role of the plasma antithrombin level in patients with obstetric DIC induced by placental abruption
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Introduction
In patients with disseminated intravascular coagulation (DIC), the processes of coagulation and fibrinolysis continue with consumption of coagulation inhibitors. The plasma antithrombin (AT) level is a powerful prognostic marker of DIC related to sepsis, malignancy, and liver disease. However, no previous studies had addressed the prognostic role of the AT level in patients with obstetric DIC.

Objectives
To investigate whether the plasma AT level has a prognostic role to predict the prognosis of patients with obstetric DIC.

Methods
We conducted a single-center, retrospective cohort study from January 2007 to August 2016. Patients with obstetric DIC induced by placental abruption were eligible for this study. Obstetric DIC was diagnosed as a score of ≥8, based on the obstetric DIC score approved by the Japanese Society of Obstetrics and Gynecology. We collected data pertaining to baseline characteristics, and evaluated data to identify the following outcomes: incidence of organ damage and lowest serum AT activity level within 4 days after an obstetric DIC diagnosis.

Results
29 patients were enrolled in this study and 8 patients developed organ damages. According to the receiver operating characteristic curve analyses, the calculated value of the area under the curves for the lowest AT activity predictive of organ damage was 0.777 (p = 0.023). At an AT activity cutoff point of 60.5%, the sensitivity was 90.5% and specificity was 62.5%. We assessed four possible confounders related to decreasing AT activity by logistic regression analysis: hypertensive disorders of pregnancy (HDP), Cesarean delivery, the volume of transfused FFP, the initial albumin level. Consequently, HDP and the volume of transfused FFP were identified as prognostic variables.

Discussion
As in other DIC, serum AT activity can be a prognostic marker in obstetric DIC: the incidence of organ damage increased when the AT activity was 60.5% or less.

Recombinant human soluble thrombomodulin for obstetric disseminated intravascular coagulation
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Introduction
Disseminated intravascular coagulation (DIC) is a syndrome characterized by systemic activation of coagulation which results in widespread fibrin deposition and excessive consumptions of platelets and clotting factors. Recombinant human soluble thrombomodulin (rhTM) is a novel anticoagulant agent and reduces excessive thrombin generation and regulates imbalanced activation of coagulation systems. Although the efficacy of rhTM for obstetric DIC is still uncertain, it has been reported that rhTM reduces morbidity and mortality in sepsis-induced DIC patients.

Objectives
To examine whether rhTM administration could be effective for DIC patients induced by obstetric underlying disorders.

Methods
This study is a retrospective cohort study in a single perinatal medical center performed between January 2007 and December 2015. Eligibility criteria are obstetric DIC documented on the basis of clinical and laboratory data and association with one or more major underlying obstetric disorders. We evaluated both laboratory findings and clinical conditions at the early phase.

Results
Sixty-five patients (including 17 preeclampsia patients) admitted to our hospital fulfilled the criteria. Thirty-six were categorized as a rhTM group and twenty-nine were categorized as a control group. Age, delivery method and diagnosis were not different between groups. For details, amount of hemorrhage, laboratory parameters, DIC score and therapeutic intervention were not shown statistically meaningful. After adjusting two groups, treatment by rhTM was associated with significant improvements in platelet levels, D-dimer concentration, fibrinogen levels and PT-INR.
The amounts of platelets transfused was significantly lower in a rhTM group (3.02 vs 6.03 units, P=0.016). None of the adjusted group differences were statistically significant for all types of multiple organ failure.

**Discussion**

In DIC patients induced by obstetric underlying disorders, improvements of both clinical conditions and laboratory findings were confirmed in a rhTM group. Further clinical research is expected to clarify the optimal solution for administrating rhTM in obstetric DIC patients.

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**Successfully treated postpartum atypical hemolytic uremic syndrome: A case report in a woman with a gene mutation encoding complement**

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Pregnancy-associated atypical hemolytic uremic syndrome (P-aHUS) and HELLP syndrome are induced by thrombotic microangiopathies in the kidney and in the liver, respectively. Both clinical entities are characterized by microvascular endothelial activation, cellular damage and thrombosis following the complement dysregulation during pregnancy or postpartum. Same complement mutations are identified in women with P-aHUS and in women with HELLP syndrome; however, a risk of women with a complement mutation during the subsequent pregnancy remains unknown.

A 24-year-old pregnant woman underwent caesarean section because of cephalopelvic disproportion at a private clinic. Her prenatal course was uneventful. Progressive anemia, thrombocytopenia, and elevated creatinine value were detected until the postpartum day 5, and she was therefore referred to Kumamoto University Hospital. Blood examination on admission revealed thrombocytopenia, hemolytic anemia and renal failure. ADAMTS-13 was not decreased and Shiga toxin-producing Escherichia coli was not detected on culture of stool. Therefore, she was diagnosed as P-aHUS. Plasma exchange therapy was performed a total of five times and hemolytic anemia, thrombocytopenia and creatinine value were improved gradually. Her serum creatine levels were improved and remained normal levels. Her genetic analysis showed a mutation of the gene encoding C3 (p.Ser562Leu). She was conceived two years after the delivery, and her pregnancy course currently remains uneventful. Prompt diagnosis and the initiation of plasma exchange therapy is required for the treatment of P-aHUS because some P-aHUS patients reached end-stage renal disease. It is also important to manage women with a complement mutation during the subsequent pregnancy with the possibility of P-aHUS or HEELP syndrome.

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**A cohort study utilising a biochemical assessment of aspirin compliance vs resistance in high-risk pregnant women.**

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**Introduction**

The benefit of low-dose aspirin in preventing preeclampsia is well established. Despite prescription of aspirin, 30-40% of women still develop preeclampsia. Aspirin-resistance or non-compliance and their effects on clinical outcomes has not been examined in high-risk pregnant women and could explain the observed lack of clinical response.

**Objective**

We aimed to examine for aspirin non-compliance and resistance through biochemical analysis and compare against self-reported compliance. We also examined clinical outcomes against biochemical compliance.

**Methods**

Sequential recruitment of women in a high-risk pregnancy clinic was undertaken in a metropolitan hospital. Demographic and clinical data, together with a 3-point questionnaire and plasma collection was undertaken at 8 time-points (12, 16, 20, 24, 28, 32, 36, 38 weeks gestation). Blood samples were assessed for PFA100 (platelet function
analyser) and plasma salicylate acid (SA) detection through liquid chromatography, mass-spectrometry (LCMS). Non-compliance was defined as normal PFA100 and non-detectable plasma SA in <90% timepoints. Resistance was defined as a normal PFA100 but detectable plasma SA. Clinical outcomes were compared between compliant and non-compliant women prescribed aspirin <16 weeks of gestation. Statistical analysis utilised chi-squared analysis and linear regression utilising SPSSv24 and significance was set at p<0.05

Results
Seventy-one women completed the protocol. Biochemical non-compliance was identified in 22(31%) women and only 45(63%) of women’s self-reported compliance corresponded biochemically (kappa coefficient=0.65). No women were aspirin resistant. The clinical outcomes of compliance and non-compliance with aspirin were significantly different. Compliant women had a lower incidence of late-onset preeclampsia (4.1% vs 59% %, p<0.001), lower blood pressure (p=0.01) and were more than 34 weeks of gestation at delivery (96% vs 81%, p=0.02). Furthermore, the incidence of early-onset preeclampsia (2% vs 18%, p=0.001) and IUGR was lower (4.1% vs 23% p=0.003), favouring > 90% compliance.

Discussion
Aspirin non-compliance is more likely than aspirin resistance and self-reporting is not a reliable measure. Women who are non-compliant have worse clinical outcomes.

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The efficacy of Recombinant human soluble thrombomodulin in preeclampsia
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Introduction
Recombinant human soluble thrombomodulin (rhTM) is a novel anti-coagulant agent that regulates the imbalanced coagulation system by reducing the excessive activation of thrombin. rhTM potentially reduces the morbidity and mortality in patients with sepsis-induced disseminated intravascular coagulation (DIC). However, the efficacy of rhTM in obstetric DIC, especially in patients with preeclampsia, has not yet been established.

Objectives
We performed this study to examine whether the administration of rhTM was a potentially effective treatment for DIC and organ damage in preeclamptic patients.

Methods
This is a single-center, retrospective cohort study conducted between January 2007 and December 2017 using the records of our hospital. The eligibility criteria were known or suspected obstetric DIC documented on the basis of clinical and laboratory data. Baseline imbalance between patients with and without treatment of rhTM was adjusted using an inverse probability of treatment weighting using propensity scores composed of the following independent variables: initial platelet counts, D-dimer levels, fibrinogen levels, and prothrombin time–international normalized ratio. We evaluated laboratory changes and clinical outcomes in the early phase of obstetric DIC in preeclampsia patients.

Results
In total, 21 patients admitted to our department during the study period fulfilled the required criteria; of these, 10 and 11 patients were included in the rhTM and control group, respectively. After adjustment, treatment with rhTM was associated with significant improvements in platelet counts (p=0.036), D-dimer levels (p=0.009), compared with the control group. Serum creatinine level was significantly improved in rhTM group (p=0.036), but other laboratory data of organ damage and failure showed no significant difference between the two groups.

Discussion
rhTM administration was associated with clinical and laboratory improvement in patients with DIC caused by underlying obstetric conditions in patient with preeclampsia. Further clinical research is needed to clarify the optimal application of rhTM in patients with preeclampsia.
Comparison between frequency of thrombophilia in patients with and without severe preeclampsia in a Brazilian Tertiary Center.
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INTRODUCTION: In the last two decades studies have associated thrombophilia with the risk of developing severe preeclampsia (PE). Few of them, however, have been conducted in Latin America to assess the importance of thrombophilia in these patients. OBJECTIVE: Evaluate thrombophilia frequency among patients with and without severe preeclampsia in a Brazilian Tertiary Center. METHODS: From October 2009 to October 2015, a retrospective case-control study was conducted in pregnant women with severe PE and compared to normal pregnant women at Hospital das Clínicas, FMUSP. The patients with PE who had no gestational trophoblastic disease, foetal malformation or chromosomal abnormalities and who underwent thrombophilia screening during the postnatal period were included. Pregnant women without comorbidities and normal obstetric outcome were included to make up the normal group, and were screened for thrombophilia during prenatal care (when functional dosages were abnormal, they were repeated in the postnatal period). Factor V Leiden (FVL), G20210A prothrombin mutation (PM), antithrombin, protein C, protein S, homocysteine, lupus anticoagulant, and anticardiolipin IgG and IgM antibodies were analysed. The frequency of thrombophilia in the two groups was compared. RESULTS: We included 199 patients with severe pre-eclampsia and 50 normal pregnant women. In patients with severe PE we found 55 (27.6%) women that had at least one thrombophilia (14 Antiphospholipid Syndrome,10 heterozygous PM, 10 protein S deficiency, 9 hyperhomocysteinemia, 9 heterozygous FVL, 2 antithrombin deficiency, 4 association of thrombophilia). In the control group 2 (4%) women had positive thrombophilia research (1 heterozygous PM and 1 heterozygous FVL), p<.001. DISCUSSION: Our results show a higher rate of thrombophilia among the patients with severe PE (p<.001), but the frequency of thrombophilia in our population seems lower than European and American studies. Different ethnicities found in our population are probably the reason for that.

An Interdisciplinary Collaboration to Enhance Consent for Imaging for VTE in Pregnancy: a Quality Improvement Project
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Introduction
Imaging for VTE in pregnancy is common, but the decision between VQ scan and CTPA often causes anxiety amongst women and health care professionals. Ensuring the patient is aware of the rationale, risks, and benefits requires a good understanding of the technicalities of each scan, as well as the ability to express relative risks in terms the patient can understand. We identified a need for an accurate patient information leaflet (PIL), as well as the need to improve staff education and confidence. We used an interdisciplinary approach, incorporating the recent updates to Ionising Radiation (Medical Exposure) Regulations and latest ARSAC research into our educational material and guidelines.

Methods
Multi-specialty survey
We designed and disseminated a short survey amongst health care professionals to assess their confidence about counselling women. 124 people completed this survey (obstetricians, physicians, midwives, and radiographers) and it was clear that staff were particularly underconfident about VQ scans. Over 99% of survey participants indicated they would find an education session useful in addition to a new PIL, with several expressing they were shocked how little they knew. Areas that revealed particular uncertainty included advice for pregnant staff caring for women having VQ scans, and the risks associated with both VQ and CTPA.

Patient information leaflet
We designed a PIL to cover all the essential areas about the use of chest radiography, ultrasonography, VQ and CTPA in pregnancy and commonly asked questions associated with these investigations.

Education session
These were introduced at both hospitals in our Trust.

Conclusions
The survey results, patient information leaflet and results of a post-implementation survey will be presented. As a result of this project, we hope to demonstrate that women are more informed when these tests are being performed, and that staff feel more confident.
A pharmacokinetic assessment of aspirin through timed analysis of plasma salicylate acid level: an analysis of difference in gender, dose and preparation of aspirin.

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Introduction
The benefit of aspirin in preventing preeclampsia is well established. Recent data, however, suggest variability in outcomes with its use. Two potential contributing factors are the dose and preparation of aspirin.

Objective/Hypothesis:
To determine the:
- Pharmacokinetics of 100mg coated (Coated100) vs 100mg non-coated (NonCoated100) vs 150mg non-coated (NonCoated150) aspirin
- Pharmacokinetics of the above in male vs non-pregnant vs gestation-matched pregnant female subjects

Methods
Three subjects from each group were given Coated100, NonCoated100 or NonCoated150 aspirin at different times. Blood samples were collected pre-ingestion, 1-hour post, 2-hours post, 4-hours post, 6-hours post, 12-hours post and 24-hours post-ingestion of aspirin. Samples were analysed for plasma salicylate acid (SA) utilising a validated liquid chromatography mass-spectrometry (LCMS) methodology. The differences in the area under the curves (AUC) were analysed using Kruskal-Wallis and Mann-Whitney-U (SPSS).

Results
The AUCs of Coated100, NonCoated100 and NonCoated150 were different across all three groups of subjects (p<0.001). When compared between dose-matched differing preparations, there was no significant difference in AUCs between Coated100 and NonCoated100 in all groups (p=0.2). When compared for preparation-matched differing doses, AUCs for NonCoated150 and NonCoated100 was significantly different (p=0.001). The was a statistically significant difference in AUCs between the sexes (p = 0.04) and a difference in AUCs between pregnant and non-pregnant females with lower AUCs in pregnant females (p = 0.03). The difference in AUCs between pregnant and non-pregnant females, however, was lost when corrected for 150mg of aspirin(p=0.98).

Discussion
The pharmacokinetics of aspirin between male, non-pregnant and pregnant female differs, with lower AUCs in pregnant females. There is no difference in the dose-matched AUCs between coated and non-coated aspirin but a difference was noted in AUCs between preparation-matched 100mg and 150mg of Aspirin. The clinical significance of this in the high-risk pregnant women is yet to be examined, however, potentially supports the need for a higher dose of aspirin in pregnant women.

The Characteristic of PE (Preeclampsia) Complication at Lupus on Pregnancy


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BACKGROUND
Indonesia had the serious challenge of highly maternal mortality over last ten years reflecting the real national health problem. There was 305 maternal death /100.000 deliveries, where 3 major possible cause of PE, PPH and infection persisted. Recently the new comer of diseases was standing tightly behind them: lupus on pregnancy

MATERIAL & METHOD
This was a retrospective study from medical records. Fifty two cases of Lupus from 4592 pregnancy during 4 years (1.13%) have been observed in DR. Soetomo Teaching Hospital (tertiary hospital) Surabaya, Indonesia from January 2013 through December 2016.

RESULTS
Sixteen cases of lupus were complicated by PE (30.7%), and 37.5% cases with Lupus Nephritis (that mostly
showing increased serum creatinin level > 1.4 mg%). The maternal age were 25-34 years old (62.5%) and 62.5% were multigravida. Almost half cases (43.75%) got flare, leading to 25% early termination, while the remaining casesed (75%) were conservatively managed until 34 weeks gestation. Fetal outcome reported as 11 cases (68.75%) having birthweight > 2 kg, with 37.5% asphyxia (low apgar score).

**DISCUSSION**

Pregnancy was discouraged in women affected by SLE, due to the disease becoming more aggresive during pregnancy and a poor pregnancy outcome was frequently reported. During pregnancy, the maternal immune system adapts to allow the growth of a semi-allogenic fetus. Significant immunological changes occur including suppression of type-2 helper cells (Th2), but the upregulation of Th1 cytokines in pregnancy may increase the risk for Th1-mediated diseases.

The aboved concept was reflected at our study where most cases were sucessfully managed conservative until 34 weeks gestation and majority baby born with birthweight > 2 kg.

**CONCLUSIONS**

Our results suggest that lupus women are much more likely to develop worsening maternal spesifically preeclampsia and fetal outcomes when they become pregnant.

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Obstetric Hemolytic Uremic syndrome (P-AHUS): prognostic markers

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Pregnancy carries a high risk for various forms of thrombotic microangiopathy(TMA), including thrombotic thrombocytopenic purpura and P-AHUS. Preeclampsia (PE) and HELLP might be a trigger of P-aHUS.

**OBJECTIVES:** to describe the subpopulation of P-aHUS patients, to search clinical and anamnestic prognostic markers of the course of the disease.

**METHODS:**

The throughout analysis of 36 cases of p-aHUS. The median age of patients was 30 years (25-33). All patients received plasma therapy (30-40ml/kg), in 13 cases Eculizumab was administered. The patients were divided into two groups: Gr.1 have consisted of patients surviving the episode of TMA (n=25, Md 30 years (25-34)), gr.2- those who did not (n=11, Md 35 years (32-44)). Groups were compared using following criteria: age, amount of pregnancies and deliveries in anamnesis, gestational complications in previous pregnancies, volume of surgical treatment, treatment with antibiotics, antithrombotic therapy, organ lesions, laboratory markers.

**RESULTS:**

Gr.2 had a greater number of previous pregnancies and births (3 pregnancies (2.25, 4), P = 0.03, 2 (2, 3) births, P = 0.03), a greater frequency of surgical interventions (including caesarian section) in a larger volume than the cesarean section (30.6% gr1, 63.6% gr2, P = 0.01) and greater frequency of previous PE/HELLP. Gr2 had a higher rate of developing acute heart failure (27.3% vs 4%, p=0.1), respiratory distress syndrome (90.9% vs 60.0%, p=0.01), acute cerebrovascular events ( in total and ischemic stroke, 27.3% vs 0%, p=0.01). The superimposed sepsis was more frequently observed in the gr.2 (45.5% vs 0%, P=0.01).

**CONCLUSIONS:**

The revealed regularities allow us to assume the presence of the following triggers for the development of p-aHUS: surgical interventions and gestational complications in previous pregnancies, volume of surgical treatment, treatment with antibiotics, antithrombotic therapy, organ lesions, laboratory markers.

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The causal pathway from pre-eclampsia to postpartum hemorrhage: a hypothesis

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**Introduction:** Pre-eclampsia is a risk factor for postpartum hemorrhage (PPH). However, the mediator responsible for the progression of this relationship is unknown.

**Objective:** To evaluate the proposed mediating effects of placental abruption and thrombocytopenia on the pre-
Methods: Data were derived from the miniPIERS (Pre-eclampsia Integrated Estimate of Risk) multi-country prospective cohort of 2081 women admitted with any hypertensive disorder of pregnancy in a less-resourced setting. Pre-eclampsia was defined broadly as hypertension with proteinuria or maternal end-organ involvement; PPH as postpartum bleeding requiring blood transfusion or hysterectomy; thrombocytopenia as <50x10^9/L platelets without blood transfusion; and placental abruption as clinically diagnosed. In a mediation analysis, the association between PPH and pre-eclampsia (compared with a group of women with chronic or gestational hypertension) was estimated using logistic regression, then adjusted for concurrent diagnoses of thrombocytopenia, placental abruption, or both.

Results: Pre-eclampsia was confirmed in 1238 women (59.5%), of whom 19 (1.5%) had thrombocytopenia (OR 3.00, 95% CI [0.87–10.32]; p=0.08) and 57 (4.6%) had placental abruption (OR 2.51 [1.36–4.61]; p=0.003). PPH occurred in 39 women (3.2%) with pre-eclampsia (ORadj 2.01 [1.02–3.94]; p=0.04); PPH risk was attenuated by adjustment for thrombocytopenia (OR 1.87 [0.95, 3.70]; p=0.07), placental abruption (OR 1.86 [0.94, 3.68]; p=0.07), or both (OR 1.74 [0.88, 3.45]; p=0.11).

Discussion: In the miniPIERS cohort, a diagnosis of pre-eclampsia (compared to chronic or gestational hypertension) was associated with PPH. This association was attenuated by adjustment for thrombocytopenia, placental abruption, or both, suggesting that these factors could mediate the relationship between pre-eclampsia and PPH. These findings should be replicated in larger data sets.

Cardiovascular risk after hypertensive disorders of pregnancy in women with and without inheritable thrombophilia, preliminary results

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Introduction: Women who develop hypertensive disorders of pregnancy (HD) are at increased risk for cardiovascular disease later in life. Presence of inheritable thrombophilia is associated with poor placentation in HD. It is unknown whether the combination of inheritable thrombophilia and early-onset HD (HD <34 weeks) influences the risk for cardiovascular disease later in life.

Objective: To compare cardiovascular risk factors 12.5 years in women after early-onset HD with and without inheritable thrombophilia.

Methods: We compared two prospective cohorts of women with a history of early-onset of HD. Women with inheritable thrombophilia (protein C deficiency, protein S deficiency, heterozygous factor V Leiden mutation and heterozygous prothrombin gene G20210A mutation) were compared to women without thrombophilia. Women with pre-existing hypertension were excluded. Physical examination was performed and cardiovascular parameters in serum were measured.

Results: Sixteen women with inheritable thrombophilia and 98 without thrombophilia were included. Seventy-five percent of all women developed one or more cardiovascular risk factor(s). Hypertension was present in 31.3% of women with thrombophilia and 33.7% without (p=1.000), increased body mass index >25kg/m^2 in 43.8% with thrombophilia and 53.1% without (p=0.593) and hypercholesterolemia in 31.3% with thrombophilia and 43.9% without (p=0.420). Differences were not significant.

Discussion: Our preliminary findings demonstrated similar cardiovascular risk factors in women after early-onset HD with and without inheritable thrombophilia. It raises the question whether there is a difference between the pathophysiological origin of HD between women with and without thrombophilia. In general, the role of thrombophilia in the development of cardiovascular risk factors is unclear. However, in this subgroup of women with a history of early-onset HD, thrombophilia does not modify the development of cardiovascular risk factors.
Monday October 8, 2018

Biomarkers and risk factors

Posters

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Risk factors for labor onset hypertension: a novel category among hypertensive disorders of pregnancy
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Introduction: Eclampsia and stroke during pregnancy are major causes of maternal death in the world. We have experienced cases in which pregnant women developed hypertension firstly after the onset of labor (labor onset hypertension; LOH). While they might be the risk for eclampsia and stroke during labor, their detail pathophysiology has not been well examined.

Objective: Our aim is to clarify the perinatal outcomes of and risk factors for LOH.

Methods: A total of 1349 parturient women that did not exhibit preeclampsia or gestational hypertension prior to labor were examined. The patients were classified into 4 groups, the normotensive (n=1023) (whose systolic blood pressure (SBP) remained below 140 mmHg throughout labor), mild LOH (n=241) (whose maximum SBP during labor ranged from 140-159 mmHg), severe LOH (n=66) (whose maximum SBP during labor ranged from 160-179 mmHg), and emergent LOH groups (n=19) (whose maximum SBP during labor was greater than 180 mmHg). The perinatal outcomes and patient characteristics of the 4 groups were compared.

Results: Twenty-four percent of the pregnant women who remained normotensive throughout pregnancy developed hypertension during labor. One of the patients in the emergent LOH group developed eclampsia. Blood pressure at delivery and the frequencies of hypotensor use, interventional delivery, and low Apgar scores differed significantly among the 4 groups. The following risk factors for severe/emergent LOH were extracted: being aged more than 35 years, a body mass index at delivery of >30, an SBP at 36 weeks’ gestation of 130-134 mmHg, an SBP at admission of 130-139 mmHg, proteinuria, and severe edema.

Discussion: The risk factors for severe/emergent LOH were identified in this study. In high risk cases, repeatedly measuring maternal blood pressure during delivery might help to detect critical hypertension early. LOH might be a novel category among hypertensive disorders of pregnancy.

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Maternal recall of a history of early-onset preeclampsia, late-onset preeclampsia or gestational hypertension: a questionnaire study
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Objective
To study women’s ability to recall hypertensive disorders in pregnancy in their fifth decade of life and to differentiate between those with early-onset, late-onset preeclampsia and gestational hypertension.

Design
Questionnaire study.

Setting
Tertiary hospital in the capital of the Netherlands.

Population
Women who delivered between 2006 and 2011, 5-10 years post index pregnancy, with either a history of early-onset preeclampsia, late-onset preeclampsia, gestational hypertension, uncomplicated pregnancy or preterm birth.

Methods
Recall was assessed using a questionnaire and compared to medical records.

Main Outcome Measures
Accuracy of the questionnaire to detect early-onset-, late-onset preeclampsia and gestational hypertension. Sensitivity and specificity with 95% confidence intervals were calculated. Besides, the influence of facilitating factors on correct recall were assessed by logistic regression analysis.
Results
Questionnaire based recall had a sensitivity of 98.1% (95% CI: 93.4–99.8) and specificity of 94.2% (91.3–96.3), recall of late-onset preeclampsia a sensitivity of 68.2% (55.6–79.1) and specificity of 91.1% (88.0–93.7) and recall of gestational hypertension had a sensitivity of 29.0% (20.6–38.5) and specificity of 97.9% (95.9–99.1). Lower gestational age at delivery was associated with higher rates of correct maternal recall (OR 0.734, 95% CI: 0.658–0.819).

Conclusions
Early-onset preeclampsia can accurately be assessed using a simple questionnaire. Recall of late-onset preeclampsia and gestational hypertension was not accurate. These last mentioned women often overstated their risk by recalling a more severe hypertensive disorder. In clinical practice this would be suitable to detect most women at risk.

Absence of the corpus luteum in early pregnancy increases the risk of preeclampsia
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Introduction: Assisted reproductive technology is associated with an increased risk of preeclampsia, but the reasons are poorly understood. The corpus luteum (CL) produces multiple vasoactive hormones in the first trimester of pregnancy which could affect initial placentation and later development of preeclampsia.

Hypothesis: We hypothesized that non-physiologic states present in in-vitro fertilization (IVF) such as absence of the CL could increase the risk of preeclampsia.

Methods: 892 infertile women were enrolled in this prospective cohort study. Four categories based on CL status were defined: (1) absence of the CL; (2) single CL; (3) multiple CL associated with ovulation induction; (4) multiple CL associated with controlled ovarian stimulation for IVF and fresh embryo transfer. Analysis focused on singleton pregnancies conceived with autologous oocytes resulting in live birth (n=683). Multivariable logistic regression was used to control for covariates.

Results: Compared with conceptions occurring in the presence of one CL, conceptions occurring in the absence of a CL were associated with a higher incidence of preeclampsia (12.8% vs 4.8%, P=0.02) and preeclampsia with severe features (9.6% vs 1.4%, P<0.001). Compared with FET occurring in the absence of one CL (modified natural cycles), FET occurring in the absence of a CL (programmed cycles) were associated with a higher incidence of preeclampsia (12.8% vs 3.9%, P=0.02) and preeclampsia with severe features (9.6% vs 0.8%, P=0.002).

Absence of CL and programmed FET were predictive in multivariable regression models for preeclampsia (OR 2.73; 1.14–6.49 and 3.55; 1.20–11.94) and preeclampsia with severe features (6.45; 1.94–25.09 and 15.05; 2.59–286.27) compared to presence of one CL or FET in a natural cycle.

Discussion: Among singleton pregnancies after infertility resulting in live birth, those conceived in the absence of a CL were at increased risk for development of preeclampsia and preeclampsia with severe features.

Signal analytes in hiv-associated pre-eclampsia
Sayuri Padayachee
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Background: Sub-Saharan Africa remains the epicentre of the HIV pandemic. In South Africa, 35.8% of maternal deaths are ascribed to non-pregnancy related infections, namely HIV infection. The prevalence rate of HIV in pregnancy in KwaZulu-Natal is an estimated 37.7%. Furthermore, in women of reproductive age, the incidence of HIV infection is high (18.8%). The shallow trophoblast invasion and the lack of physiological conversion of the maternal spiral arteries into small bore low resistance conduits is the primary cause behind the pathogenesis of pre-eclampsia. HIV-positive patients on highly active antiretroviral therapy (HAART) are pre-disposed to pre-eclampsia development. Trophoblast cells are stimulated to invade the maternal decidua by interacting cytokines and growth factors in the local environment through signal transduction pathways. Aberrant cell signaling and signaling molecule function impedes trophoblast invasion necessary for a healthy pregnancy, leading to endothelial dysfunction. As a
result, the expression of cell signaling analytes may potentially be a predictive marker for patients at risk to pre-eclampsia development. This study investigated the expression of STAT-3 and MEK-1 in HIV-associated pre-eclampsia, as a diagnostic tool of abnormal placentation in pre-eclampsia.

Method: STAT-3 and MEK-1 expression were analysed by the Bio-Plex Multiplex immunoassay in 80 normotensive and pre-eclamptic women further stratified by HIV status.

Results: STAT-3 expression differed by pregnancy type (p=0.001) and not HIV status (p=0.0859), while MEK-1 differed by HIV status (p=0.0102) and not pregnancy type (p=0.1526).

Conclusion: This study demonstrated a downregulation of STAT-3 and MEK-1 in pre-eclampsia, corroborating limited trophoblast invasion. HAART and non-phosphorylation of HIV regulatory proteins may account for the downregulation of STAT-3 and MEK-1, respectively. Additional studies are required to further investigate the role of signal transduction pathways and its effect on HAART in pre-eclampsia development.

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Correlation between mcp-1 and tnfα in maternal plasma, fetal plasma and placenta in patients with pre-eclampsia.
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INTRODUCTION: Monocyte chemotactic protein-1 (MCP1) main function is to recruit monocytes and other leukocytes into sites of inflammation. Inflammatory mediators, such as TNFα, regulate its expression.

OBJECTIVES/HYPOTHESIS: To analyze MCP1 levels in maternal, fetal plasma and placental in women with pre-eclampsia (PE) and correlate with TNFα. We hypothesized a positive correlation between both molecules.

METHODS: Case-control study, 117 pregnant women consented to participate, PE (50)/controls (67). MCP1 and TNFα were quantified using MagPlexTH-C microsphere system and were analyzed using ANCOVA method, adjusted by BMI, gestational age at delivery (GA) and maternal age. To estimate the difference between groups, the mean ratio (MR) and the 95% confidence interval (CI) were calculated. The analysis between MCP1 and TNFα was made by Pearson’s correlation.

RESULTS: Increased MCP1 were observed in fetal plasma of preterm (GA<37 wks) PE pregnancy (p=0.029). In placenta a correlation between MCP1 vs. placenta weight (PW) (r=0.313, p=0.020), and MCP1 vs. BMI (r=0.366, p=0.004) was seen. Also, in fetal plasma, in PE group, MCP1 vs. GA (r=-0.645, p<0.001), birth weight (BW) (r=-0.603, p=0.001) and PW (r=-0.512, p=0.001) was seen. High levels of TNFα were found in the maternal plasma in PE group (MR=1.29, 95% CI: 1.04 - 1.61, p=0.021). Increased levels of TNFα in fetal plasma from preterm PE (GA<37 wks) and in placenta from early preterm PE (GA<34 wks) (p<0.05), was seen. In placental tissue, a correlation between MCP1 vs. TNFα, entire group (r=0.568, p=0.001) and in PE group (r=0.694, p<0.001) was found.

DISCUSSION: We observed a strong direct correlation between MCP-1 vs. TNFα in placenta PE groups, which suggests a possible regulation of TNFα molecule by MCP-1. Also, we observed that higher the levels of MCP-1 in fetal plasma, the lower the GA, FW and PW, which might indicate the involvement of MCP-1 in preterm delivery.

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Specifics of laboratory data changes in pregnant women with pre-eclampsia
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From a modern scientific point of view, metabolism is one of the main processes of vital activity, this is due to the universal role of lipids in homostatic functions, the mobile ability of their metabolism to adapt to various states of the organism.

Purpose of the research. To study some parameters of the lipid and protein blood spectrum in pregnant women with pre-eclampsia.

Material and methods of investigation. In order to determine the characteristics of the lipid spectrum of the blood, 70 women were examined in the II-III trimester of pregnancy, of which the main group consisted of 50 pregnant women with mild and severe degree of PE by 30 and 20 women in each subgroup respectively and after delivery.
Results of the study and their discussion. During the study of the parameters of lipograms of blood serum in mothers with pre-eclampsia. The level of total lipids reached up to 6.9±0.3 g/L and 8.9±0.4 g/L (p<0.05), that is 1.4 and 1.8 times the control figures, the content β-lipo-proteids - 4.130±1g/l and 4.83±0.4 g/l(p<0.05), which is 1.5 and 1.7 times higher than the similar parameter of the control group, the concentration of cholesterol was 6.62±0.2 g/L and 8.13±0.3 mMol/L (p<0.05) or 1.2 times and 1.5 times higher than the control indicator, the content of triglycerides 2.6±0.27 and 3.81±0.3 mmol/l (p<0.05), that is, 2.4 times and 3.5 times higher than the same indicators for a physiologically occurring pregnancy. The level of phospholipids in our patients was 1.81±0.1g/l and 1.41±0.2 g/l(p<0.05), that is, 1.5 times and 1.9 times lower level of control indicators.

Conclusions. Therefore, with the progression of PE, a significant increase in the basic indices of lipograms and a decrease in the level of phospholipids and albumin occurs.

An interesting case of relation between placenta volume, uterine artery PI in early pregnancy and the prognosis of pregnancy
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Objective
We reported an association between placenta volume in early pregnancy and birth weight. We report our experience with an interesting case to support it.

Methods
During pregnancy 11-14 weeks, the placenta volume was measured using Vocal mode manual trace of Voluson730/E8. The index of the placenta volume is PQ (placental quotient: placental volume/crown-rump length, normal 0.997) The normal of the PQ was measured from 270 cases that we experienced in our department.

Results
Case is in 34 years old, first pregnancy was established by timing. She was admitted because of hypertensive disorder of pregnancy from pregnancy 24 weeks, in 26-3 weeks her fetus was death intra-uterine, and it was delivered in 564 g (-2.6SD) girl. PQ was 0.632 at 11-2 weeks, UA-PI was 1.21 in pregnancy 20 weeks. Second pregnancy, 37 years old, pregnancy was established in IVF-ET, and she was delivery by a cesarean section because of breech presentation 2,498 g (-0.7SD) boy in 37-0 weeks. PQ was 1.076 at 11-5weeks, PQ was 0.851 at 13-5weeks, UA-PI in pregnancy 20 weeks was 0.41. Third pregnancy was established spontaneously, 38 years old. She was admitted because of FGR from pregnancy 30 weeks. An emergency cesarean section was performed due to delivery progressed in 32-2 weeks 1,038 g (-3.1SD) girl. PQ was 0.547 in 12-4weeks, PQ was 0.412 in 14-4weeks, UA-PI was 0.39 in pregnancy 20 weeks.

Discussion
We experienced 1 case 3 delivery to suggest to relation between an early placenta volume, UA-PI and the birth weight. The case that a placenta volume in early pregnancy was small and UA-PI was high needed management as a high risk of FGR and hypertensive disorder in pregnancy.

A study to investigate Calcium mechanisms in women at high risk of pre-eclampsia through analysis of putative protein markers. A sub-study of The Calcium and Pre-eclampsia (CAP) study (a WHO collaboration)
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Introduction
The mechanisms by which calcium reduces the severity of preecclampsia are currently not established.

Objective/Hypothesis
Blood samples were studied from participants in CAP, a recent study of the efficacy of giving calcium prior to
pregnancy to reduce preeclampsia. The aim was to characterize blood biomarkers in order to identify potential mechanisms by which calcium might exert an effect on preventing preeclampsia. Identifying these mechanisms could guide additional interventions.

Methods
Women with previous preeclampsia were randomised to calcium 500mg/day or placebo prior to pregnancy. From 20 weeks' gestation both groups received 1500 mg/day Ca as recommended by WHO. Blood samples were obtained pre-pregnancy and at 8, 20 and 32 weeks' gestation with biomarkers chosen to assess placental, angiogenic, vasoconstrictor/dilator, endothelial and immune function.

Results
Altogether 111 women were included in this sub-study. Eleven women (20%) in the placebo group and nine (16%) in the calcium group developed preeclampsia.

Biomarker comparisons (calcium vs placebo)
Most biomarkers increased over time with similar increases observed across calcium and placebo groups. AT1-AA and Endothelin were relatively constant over time, Copeptin values were higher in the calcium group (pre-pregnancy through to week 8).

Biomarker comparisons (preeclamptic vs non-preeclamptic women)
Biomarkers levels were similar, on average, between women who went on to develop preeclampsia and those who did not. Slight differences were observed for some biomarkers with directionality of results similar to reported values (e.g. PI GF lower and Activin-A, s-ENG and PI GF higher in women who developed pre-eclampsia). Copeptin values were higher in the preeclamptic women prior to pregnancy and at weeks 8 and 20.

Discussion/Conclusion
This small study did not demonstrate any obvious difference in analytes assessing relevant pathophysiological pathways for preeclampsia with calcium treatment. This exploratory study was not powered to detect or exclude relevant effects with certainty.

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Maternal hypertensive disorders in pregnancy and the association with embryonic growth trajectories.
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Introduction
Embryonic development is under the constant influence of the intrauterine environment. This environment is determined not only by genetic factors, but also by maternal health conditions. A strong association between hypertensive disorders (pre-eclampsia and pregnancy induced hypertension) and both intrauterine growth restriction and low birth weight have been described. However, these associations are mainly limited to second and third trimester foetal growth parameters and birth weight. The association between these hypertensive disorders of pregnancy and first trimester growth parameters have not been investigated yet.

Objective/hypothesis
In line with the findings on second and third trimester foetal growth, we hypothesize that embryonic (first trimester) growth is reduced in women with pregnancies complicated by hypertensive disorders.

Methods
Within a large population-based cohort in Rotterdam, The Netherlands, we assessed whether there is an association between maternal hypertensive disorders in pregnancy (both pregnancy induced hypertension and preeclampsia) and embryonic growth, defined as crown-rump-length (CRL) and embryonic volume (EV) using logistic regression analysis. Embryonic volume was measured using 3D ultrasound and virtual reality techniques, which enabled us to take this accurate parameter for embryonic growth into account.

Results
We included 1631 pregnancies in the analysis. In our first crude model, CRL has a statistically significant association with hypertensive disorders in pregnancy (p = 0.042). This accounts for a decrease of -0.22 SD CRL in women with a pregnancy complicated by a hypertensive disorder, compared to women without a hypertensive disorder.

Discussion
Our preliminary results suggest that embryonic (first trimester) growth is associated with hypertensive disorders in pregnancy. Additional analysis in which we adjust for confounding factors are currently being conducted. These will clarify the pathway through which embryonic growth is impaired. Moreover, the association with embryonic volume is being analysed, since this is a more accurate parameter for embryonic growth compared to the crown-rump-length.
Is serum 25-hydroxyvitamin D associated to blood pressure in pregnancy and preeclampsia development?
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Background: Preeclampsia (PE) involves hypertension, proteinuria and circulatory impairment in late pregnancy. We aimed to elucidate associations between serum 25-hydroxyvitamin D (25(OH)D) in early and late pregnancy, blood pressure (BP) measured throughout pregnancy, and development of preeclampsia.

Methods: We included 2,111 singleton pregnant women from the Odense Child Cohort, an unselected, prospective study in Denmark. Associations between 25(OH)D and PE were assessed by adjusted multivariate regression analysis, adjusted for first trimester BP. The inter-association between BP, 25(OH)D and PE was further investigated using PATH analysis.

Results: Blood pressure was higher at all time in women who developed PE. Serum 25(OH)D in early and late pregnancy was inversely correlated to BP in second and third trimester. Concentrations of 25(OH)D at gestation 12 weeks were inversely associated with PE, aOR 0.99 p=0.046, while continuous 25(OH)D at gestation 29 weeks was not significantly associated to PE. S-25(OH)D below the median at 12 weeks (<66nmol/L) and 29 weeks (<79nmol/L) were associated with increased odds of preeclampsia; aOR = 0.54, p=0.009 in late pregnancy. PATH analysis of the interrelation between early pregnancy 25(OH)D, blood pressure and PE demonstrated that early pregnancy 25(OH)D was inversely associated to later BP, but not directly associated with PE.

Conclusion: Decreased 25(OH)D in both early and late pregnancy increased the odds of PE, and 25(OH)D was inversely associated with BP later in pregnancy. Our findings support a role for vitamin D in the pathogenesis of PE. Further data analysis will elucidate the correlations between maternal blood pressure and 25(OH)D concentrations to angiogenetic factors sFlt-1 and PlGF, measured in the same cohort.

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Development of a phenotyping algorithm for Hypertensive Disorders of Pregnancy (HDP) in large-scale prospective genome cohort study
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Background
To elucidate genetic and environmental factors causing hypertensive disorders of pregnancy (HDP) in large-scale cohort study, we need to conduct precise phenotyping on subjects in cohort study. However, large-scale phenotyping by medical doctors' diagnoses is impracticable with regard to cost-effectiveness. Here, we developed a rule-based HDP phenotyping algorithm. Our algorithm enables us to identify HDP patients and classify them into subtypes using large-scale cohort dataset.

Methods
We developed a phenotyping algorithm according to the HDP diagnosis criteria of Japan Society of the Study of Hypertension in Pregnancy (JSSHP). Our phenotyping algorithm was applied to 22,257 mothers with pregnancy recruited by the BirThree Cohort Study of Tohoku Medical Megabank. To validate consistency between our algorithm-based phenotype and medical doctor's diagnoses, an independent medical doctor examined medical records and made clinical diagnoses on 50 subjects.

Results
By conducting our phenotyping algorithm, 1,939 (8.71%) subjects were phenotyped with HDP patients. Among them, HDP patients were phenotyped with subtypes as follows; 995 (4.47%) patients with gestational hypertension (GH), 318 (1.43%) patients with super-imposed pre-eclampsia (SuPE), and 626 (2.81%) patients with pre-eclampsia (PE). As for consistency between our algorithm-based phenotype and diagnose, 36 cases shows consistency for subtypes and timing of onset, whereas 14 cases shows no consistency; 10 cases were inconsistent in onset of HDP, 2 cases were in subtypes and the remaining 2 cases were in timing of onset.

Discussion
In this study, we developed high-performance HDP phenotyping algorithm. The major part of the reasons of inconsistency was that postpartum hypertension was phenotyped in non-HDP group by our algorithm. This misphenotyping was caused by that postpartum blood pressure was not included in cohort data but included in
medical records. In future, we will develop not only rule-based but also machine-learning based phenotyping algorithm to perform more precise phenotyping in large scale clinical information.

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Multiplex analysis of maternal circulating cardiovascular risk biomarkers in preeclampsia
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Introduction
Preeclampsia is a hypertensive pregnancy disorder that occurs after week 20 of pregnancy, associated with an increased risk for maternal cardiovascular disease (CVD) later in life. The risk is increased with early onset of the disease and delivery of a growth restricted child. The mechanisms underlying these associations are not well established.

Objective/hypothesis
We aimed to measure the level of circulating biomarkers associated with cardiovascular risk, and hypothesized that the level of these markers at the time of delivery differed between early-onset preeclampsia (EPE), late-onset preeclampsia (LPE) and normotensive controls (NC), as these groups differ in future risk for CVD.

Methods
The level of 92 biomarkers associated with CVD risk, including markers of inflammation, endothelial function and cardiac stress, were measured in maternal plasma collected at the time of delivery using the Olink Proseek multiplex CVD I assay. The patient group consisted of EPE (n=37, delivery < week 34), LPE (n=29, delivery ≥week 34), and normotensive controls delivered at term (n=49).

Results
The levels of 82 biomarkers were detectable and included in the data analysis. Using the Kruskal Wallis test, 47 of the biomarkers were found to be significantly different between groups after correction for multiple testing (p<0.05). Applying the Dunn’s post hoc test to the significant markers, we found that the MMP-3, and ST2 markers were significantly elevated, and MMP-1 significantly reduced, in the EPE group only.

Discussion
ST2 is an established marker of endothelial inflammation and cardiac stress, while MMPs have a major function in vascular remodeling and angiogenesis. Altered levels of these markers could indicate specific CVD-related biological processes active mainly in the EPE subtype, potentially linked to the elevated risk of future CVD seen in this group. Future work should assess postpartum levels of the same markers.

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Association between adverse maternal clinical outcomes and imbalance of cytokines and angiogenic factors in preterm preeclampsia
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Introduction: Preeclampsia (PE) is a pregnancy specific syndrome, characterized by abnormal levels of cytokines and angiogenic factors, suggesting that immunological factors play a role in the disease development.

Objective: The objective of this study was to determine whether immunological markers are associated with the gestational age and with the disease severity at the time of the disease diagnosis.

Methods: Ninety-five women who developed PE were stratified for gestational age as preterm PE (<37 weeks) and term PE (≥37 weeks of gestation) and compared for disease severity (blood pressure ≥ 160x110mmHg, proteinuria ≥2g/24h, imminent eclampsia, eclampsia and HELLP syndrome) as well as plasma concentration of immunological markers. The concentrations of angiogenic factors: placental growth factor (PIGF) and vascular endothelial growth factor (VEGF), anti-angiogenic factors: Fms-like soluble tyrosine kinase (sFlt-1) and soluble endoglin (Eng), as well as the cytokines: tumor necrosis factor alpha (TNF-α) and Interleukin 10 (IL-10) were determined by immunoenzymatic assay (ELISA). Results were analyzed by non-parametric test with significance set at p < 0.05.

Results: The comparison between preterm and term PE showed higher percentage of severe cases in the preterm PE (76.7%) than in the term PE (23.3%) group. Similarly the concentrations of TNF-α, TNF-α/IL-10 ratio, sFlt-1, sEng and sFlt-1/PIGF ratio were significantly higher in the preterm PE group. On the other hand, concentrations of PIGF,
VEGF and IL-10 were significantly lower in the preterm PE group. Negative correlations between TNF-α and IL-10 (\( r = -0.5232; \ p < 0.05 \)) and between PI GF and sFlt1 (\( r = -0.4156; \ p < 0.05 \)) were detected only in the preterm PE group. **Discussion:** Pregnant women with preterm PE showed an imbalance between immunological markers, with predominance of anti-angiogenic factors and TNF-α, associated with adverse maternal clinical outcomes.

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Evaluation of sFlt-1/PIGF Ratio for Improving Clinical Management of Pre-eclampsia: Experience in a tertiary hospital
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**INTRODUCTION:**
Management of pregnant women with gestational hypertension (GH) varies according to the severity of the disease. An imbalance of soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PIGF), is involved in pre-eclampsia (PE) pathogenesis. An elevated ratio (>110) is highly predictive of PE, whereas the diagnosis of PE can be ruled out within one week for low ratio (<38).

**OBJECTIVE:**
The main objective of this study was to assess whether the cutoff value in late pregnancy (>34 weeks) help to management the preeclampsia.

**METHODS:**
We performed an observational study to evaluate serum sFlt-1/PIGF ratio (Roche Diagnostics Cobas e411 system) for differential diagnosis and the severity of disease from 2018 February to April (three months). Thirty-seven women with singleton pregnancies diagnosis with suspected preeclampsia were enrolled. Serum sFlt-1 and PIGF were measured when they admitted (>34 weeks). The sFlt-1, PIGF, and the maternal clinical data were obtained.

**RESULTS:**
Among the 37 patients included, 25 had a sFlt-1/PIGF ratio lower than 38; only one diagnosis with PE leading to a negative predictive value of 96%. Two patients diagnosed with clinical PE as the ratio higher than 110. For the rest 10 patients had a sFlt-1/PIGF ratio between 38 to 110, four of them diagnosis with clinical PE. There were five patients with thrombocytopenia, the sFlt-1/PIGF ratio were all lower than 38 and rule out for HELLP. All patients were delivered without adverse maternal and neonatal outcomes.

**DISCUSSION:**
The serum sFlt-1/PIGF ratio showed high value of differential diagnosis for ruling out PE. In our data, four of ten patients had a sFlt-1/PIGF ratio between 38 to 110 diagnosed with clinical PE, the cutoff value may be considering more clinical experience. Using these biomarkers in routine management of PE may improve clinical management of suspect patients. It need more clinical experience in future.

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Predictive Value of the sFlt-1/PIGF Ratio in Pre-eclampsia with or without Fetal Growth Restriction
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**Introduction:** Preeclampsia is a pregnancy-specific multisystemic disorders with an incidence of 2.5% worldwide. Placental deficient was thought to be the main reason for preeclampsia. Reduced uteroplacental blood flow can also cause fetoplacental restriction (FGR).

**hypothesis:** Evaluating serum soluble fms-like tyrosine kinase-1 (sFlt-1), serum placental growth factor (PIGF) and the sFlt-1/PIGF ratio in preeclampsia with or without FGR can help clinicians to make decision.

**METHODS:** 17 singleton pregnancies women was diagnosed as preeclampsia with (n=5) or without FGR (n=12) in third trimester (>28 weeks) from March to April 2018. Serum sFlt-1 and PIGF were estimated when they admitted. The sFlt-1, PIGF, and the maternal basic data were obtained. This study was approved by the Ethics Committee for Guangzhou Women and Children’s Medical Center.

**RESULTS:** The sFlt-1/PIGF ratio in preeclampsia with FGR group was significantly increased compared with another group (227.3±80.51 vs. 121.15±55.80, P=0.007). The mean systolic pressure (157±9 vs. 142±11 mmHg) and diastolic pressure (100±6 vs. 92±7 mmHg) were higher in FGR group (P<0.05). Comparison based on gestational week, the fetal birth weight still lower in FGR group (1814±708 vs. 2648±646g, P=0.03).

**CONCLUSION:** High serum levels of sFlt-1 and low serum levels of PIGF have been proposed as useful predictors for the subsequent development of preeclampsia. Abnormal placental implantation with endothelial dysfunction may
also result in FGR. The sFlt-1 and PlGF are the inflammatory factors from placenta which may indicate the inflammation of maternal-fetal interface. Coincidence of the high ratio in these two obstetrical complications may suggesting that an inflammatory mechanism may have an important role in preeclampsia with FGR. The higher ratio might predict preeclampsia with FGR, which can influence clinical intervention.

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Non-invasive study of haemodynamic parameters in normotensive versus hypertensive pregnancies
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Background/Objectives: Major physiological cardiovascular system adaptations during pregnancy include decreased systemic vascular resistance (SVR) and increased cardiac output (CO). In hypertensive disorders of pregnancy, especially preeclampsia, these usual cardiovascular adaptations may be deficient. This study aims to evaluate differences in cardiac function and haemodynamic parameters using point-of-care, non-invasive testing, in women with normotensive and hypertensive (chronic hypertension, CH, gestational hypertension, GH, preeclampsia, PE) pregnancies.

Methods: Normotensive (NT, n=70) and hypertensive (HT, n=65; 23 CH, 22 GH, 20 PE) pregnant women aged 18-45 with a singleton pregnancy studied cross-sectionally from 20 weeks’ gestation in this ongoing prospective study. Haemodynamic parameters were obtained non-invasively via the Ultrasound Cardiac Output Monitor (USCOM) and liquid crystal sphygmonanometer. Women are followed prospectively and pregnancy outcomes, including preeclampsia development, ascertained.

Results: There was no statistically significant difference in average stroke volume (73mL/NT, 69mL/CH, 70mL/GH, 73mL/PE; p=0.838), cardiac output (5.9/5.7/5.5 and 5.7L respectively; p=0.802) and cardiac output index between groups (3.2/2.8/2.7/2.9L/min/m²; p=0.16) between groups. Pre-eclamptic pregnancies had significantly higher SVR (1851±1111 versus 1215±396 dyne/sec/cm⁵; p≤0.001) and systematic vascular resistance index (3653±2189 versus 2274±912dyne/sec/cm⁵/m²; p=0.001) than NT pregnancies. As expected, HT participants had significantly higher mean arterial pressure, systolic (110±12, 129±11, 129±10, 138±12; p=0.001) and diastolic blood pressure (70±9, 79±8, 87±12mmHg respectively; p=0.001) than NT.

Conclusions: In this pilot study of non-invasive (USCOM) haemodynamic measurements, significant differences in systemic vascular resistance, but not overall cardiac output, were seen between normotensive and hypertensive pregnancies. A larger sample size is needed for further investigation, including determining whether USCOM may be useful in predicting which pregnancies will progress from gestational hypertension and/or chronic hypertension, to preeclampsia.

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Elecsys® and Kryptor immunoassays for the measurement of sFlt-1 and PlGF to aid preeclampsia diagnosis: are they comparable?
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Introduction
In pregnant women with suspected preeclampsia, the soluble Fms-like tyrosine-kinase 1 (sFlt-1)/placental growth factor (PIGF) ratio is used as a biomarker to aid diagnosis. sFlt-1 and PIGF levels are measured using Elecsys® (Roche) or Kryptor (BRAHMS) immunoassays; Elecsys® sFlt-1/PIGF ratio cut-offs 85 and 110 may indicate preeclampsia.

Objectives
To perform method comparisons between the Elecsys® versus Kryptor immunoassays for sFlt-1 and PIGF measurement, and assess diagnostic performance for preeclampsia/HELLP syndrome in a large cohort.

Methods
Analyses included 396 serum samples from a case-control study in 113 pregnant women with preeclampsia or HELLP syndrome and 270 controls. sFlt-1 and PIGF were determined using Elecsys® and Kryptor sFlt-1 and PIGF immunoassays, and gestation-specific cut-offs <33 and >85 for early-onset preeclampsia (ePE; 20-0+33+6 weeks) and <33 and >110 for late-onset preeclampsia (loPE; ≥34+0 weeks) were assessed. Method comparisons were
based on Passing-Bablok regression, and Bland-Altman plots (CLSI EP09-A3). ROC analysis was performed for all sFlt-1/PIGF cut-offs.

**Results**

Mean (±2 SD) differences between Elecsys® and Kryptor values were: sFlt-1, 173.13pg/mL (6237.66, -5891.40); PIGF, 102.71pg/mL (186.06, -391.48); and sFlt-1/PIGF ratio, 151.74 (1085.11, -781.63). Elecsys® and Kryptor immunoassays showed high correlation: Pearson’s correlation coefficient (r), 0.913; slope, 1.06; intercept, -358.19pg/mL (sFlt-1), and Pearson’s r, 0.945; slope, 0.79; intercept, -17.89pg/mL (PIGF), resulting in ~20% lower values for PIGF. Sensitivities and specificities using the sFlt-1/PIGF 85 cut-off (eoPE) were 88.0%/100.0% (Elecsys®) and 90.4%/96.2% (Kryptor), and using a sFlt-1/PIGF 110 cut-off (loPE) were 51.3%/96.5% (Elecsys®) and 78.9%/90.1% (Kryptor). Using Elecsys® and Kryptor sFlt-1/PIGF ratios, 0% and 3.8% of women were falsely ruled-in for eoPE, and 3.5% and 9.9% for loPE.

**Discussion**

Despite high correlation between Elecsys® and Kryptor immunoassays, substantial differences were observed between Elecsys® and Kryptor sFlt-1/PIGF and PIGF. sFlt-1/PIGF cut-offs 85 and 110 showed lower specificity on Kryptor versus Elecsys®, resulting in more false-positive preeclampsia diagnoses.

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**Identification of new candidate proteins involved in preeclampsia**

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**INTRODUCTION:** Preeclampsia is a major disease of pregnancy, affecting 2% to 8% of pregnant women. It is characterized by arterial hypertension and proteinuria occurring from the 20th week of amenorrhea. The STOX1 overexpressing mice develop a preeclamptic syndrome. This model is very relevant to identify potential new actors in preeclampsia because the phenotype is both precocious and severe.

**OBJECTIVES:** Using this mouse model of severe PE, we aim to identify plasma proteins quantitatively modified during pregnancy with a global proteomics approach in the blood and to validate these proteins on human placental cell models.

**METHODS:** We provoked preeclamptic gestations in mice by crossing WT females with transgenic STOX1 males. Blood was taken at E6.5 of gestation and plasma was analyzed using ITRAQ mass spectrometry to identify proteins of differential abundance. In parallel, we developed BeWo cells stably overexpressing STOX1. BeWo is a choriocarcinoma cell line in which fusion is induced by forskolin treatment and reproduces therefore the physiology of villous trophoblast that syncytialize into syncytiotrophoblast. We are validating the link between STOX1 overexpression and sLIFR production by qRT-PCR and ELISA in this cell model.

**RESULTS:** We identified 15 proteins differentially present, two of which have human homologs: sLIFR (soluble Leukemia Inhibitory Factor Receptor) and TTR (transthyretin) respectively increased and decreased in the preeclamptic mice. In the BeWo cells, after fusion or in the presence of STOX1, alternative splicing of LIFR mRNA increases, leading to more secretion of sLIFR in the supernatant.

**DISCUSSION:** An early excess of sLIFR could trap Leukemia Inhibitory Factor (LIF) at early stages of embryo implantation and development. Given the primordial role of LIF in implantation in mice and humans, this could lead to a defective implantation and/or placentation possibly causing embryo resorptions or a preeclamptic phenotype.

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**Association between laboratory abnormalities and obesity with time of birth and perinatal outcome in preeclampsia.**

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**Introduction:** Laboratory abnormalities and obesity may be associated with perinatal outcomes in patients with preeclampsia. Analysis of these factors may guide damage prevention strategies.

**Objective:** To associate laboratory variables and maternal body mass index (BMI) with childbirth outcome before 34 and 37 weeks and perinatal outcomes in cases of pre-eclampsia.

**Methods:** Cohort study. Location: Guilherme Álvaro Hospital, Santos / Brazil; (May/ 2017 - April/ 2018). Inclusion:
women with pre-eclampsia (NHBPEP; 2000) and preterm delivery. Group 1: delivery <34 weeks. Group 2: childbirth <37 weeks. Measured at admission: uric acid (> 6 mg/dl), liver enzymes (AST > 34 U/I and ALT > 35 U/I), obesity (BMI > 30), neonatal ICU admission. Statistical analysis: Fisher’s exact test (significance p <0.05). The work has ethical approval.

Results: Sample size: 90 patients. Group 1: AST elevation in 53.3% of the patients (p = 0.001); ALT elevation in 46.7% (p = 0.001), uric acid elevation in 28.6% (p = 0.068) and 12.5% were obese (p = 0.044). Group 2: AST elevation in 30.2% of the patients (p = 0.001); ALT elevation in 23.3% (p = 0.004); uric acid elevation in 20% (p = 0.085) and 24.4% were obese (p = 0.047). Of the total sample, 45.6% of newborns were admitted to the neonatal ICU.

Discussion: In Group 1, with more severe prematurity, hepatic damage and elevated uricemia were more frequent. In Group 2, obesity was more prevalent, corroborating with the literature (Chaemsaihtong P, 2018). The neonatal ICU admission of the total sample was significantly elevated. This behavior of the indirectly recognized target organ damage and lipotoxicity, associated with the severity of prematurity, may represent indicators regarding the higher expression of preeclampsia causing preterm delivery, the need to guide prophylaxis strategies and eventually prognostic counseling. Enlarging the sample may add information.

Keywords: laboratory, obesity, premature, birth.

CD163-mediated hemoglobin-scavenging system, haptoglobin phenotype and preeclampsia risk
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Introduction: Preeclampsia (PE) is a multisystemic disorder which complex pathophysiology involves both oxidative stress and endothelial dysfunction as key factors. The CD163-mediated haptoglobin (HP) hemoglobin-scavenging system has been proposed as an important pathway for diverse disease states due to its anti-inflammatory and pro-angiogenic effects. The human HP locus is polymorphic, yielding three distinct phenotypes characterized by different antioxidant and pro-angiogenic properties.

Objective: We aimed to determine whether HP phenotype was associated with PE risk and to assess the relationship between HP phenotype and first-trimester concentrations of HP, soluble form of the hemoglobin-scavenger receptor CD163 (sCD163), placental growth-factor (PIGF) and soluble fms-like tyrosine kinase-1 (sFlt-1).

Methods: Case-control study of 452 pregnant women selected from a prospective cohort of singleton pregnancies that underwent first-trimester aneuploidy screening in a routine care low-risk setting. The study sample included 204 women who subsequently developed PE and 248 women with normal pregnancies who were matched for gestational age. HP phenotypes were determined by polyacrylamide gel electrophoresis (PAGE). First-trimester serum PIGF, sFlt-1 and HP concentrations were determined by automated electrochemiluminescence/immunoturbidimetric methods (Roche Diagnostics), while sCD163 levels were determined by enzyme-linked immunosorbent assay (R&D Systems).

Results: Although HP phenotype alone did not affect overall PE risk, we found significantly higher HP concentrations between preeclamptic and normal women with HP2-1 (122.0/107.1 mg/dL, P=0.01) and HP2-2 (101.0/82.0 mg/dL, P=0.001) phenotypes. HP2-2 phenotype was also associated with high levels of sCD163 (472.6/418.6 ng/mL, P=0.02) that were significantly higher among women who subsequently developed PE (511.5/430.8 ng/mL, P=0.04). Finally, PIGF and sFlt-1 levels presented significantly different patterns between preeclamptic and normal pregnancies, being the strongest association in women with HP2-1 and HP2-2 phenotypes.

Conclusion: These findings suggest that HP phenotype could be useful in combination with first-trimester inflammatory and angiogenic markers to identify subsets of women with increased risk of PE development since early pregnancy.
Measurement of serum angiogenic markers at the 2nd trimester can predict fetal growth restriction (FGR)
mothers who will subsequently develop preeclampsia (PE).
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Objectives:
It is reported that FGR and PE are associated with abnormal profiles of angiogenic markers in maternal circulation. Mothers with FGR fetuses are at increased risks for developing PE. The aim of our study is to determine the cut-off levels of maternal serum angiogenic markers to develop PE subsequently among FGR mothers.

Methods:
This study included women with singleton pregnancies diagnosed with FGR before 24 weeks of gestation (n=50). The protocol was approved by ethics committees and participants provided written informed consents. The serum levels of PIGF, sFlt-1, sEndoglin and sFlt-1/PIGF ratio were measured at 20-24 weeks of gestation. The cut-off value of each angiogenic factor was determined by ROC curve analysis for identifying mothers with FGR at risk of developing PE.

Results:
The prevalence of patients with FGR preceding PE was 40% (n=20/50). The mean of onset period of subsequent PE was 30.1±4.8 weeks of gestation. The mean gestational age at delivery of PE+FGR group and FGR only group was 32.4±5.4 vs 37.2±4.9 weeks respectively. We compared serum levels of angiogenic factors among PE+FGR and FGR only groups. In the PE+FGR group, the level of PIGF was significantly decreased, and the levels of sFlt-1, sEndoglin, and sFlt-1/PIGF were significantly increased as compared with FGR only group. The optimal cut-off levels were PIGF level<27.4 pg/mL (AUC=0.93), sFlt-1 level >1823.3 pg/mL (AUC=0.884), sEndoglin level >7.41 ng/mL (AUC=0.967), and sFlt-1/PIGF ratio >7.42 (AUC=0.941). sEndoglin and sFlt-1/PIGF ratio were the most powerful predictors for developing PE with sensitivity of 88.9% and 86.7%, and specificity of 92.6 and 92.0% respectively.

Conclusions:
Angiogenic factors measured in maternal sera between 20 and 24 weeks of gestation can identify mothers diagnosed with FGR who subsequently develop PE. Measurement of these markers may contribute to the risk assessment of mothers with FGR, and their clinical outcomes.

Hair cortisol concentration and reported anxiety are elevated in preeclampsia
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Introduction: While some studies argue that maternal stress during pregnancy is a risk-factor for preeclampsia (PE), other studies do not support this hypothesis. These studies did not incorporate physiological stress measures and recall bias may explain their results.

Objective: To investigate whether maternal stress during pregnancy, as measured by questionnaires and cortisol concentrations in hair, differ between a group of women with early onset PE, late onset PE and uncomplicated pregnancies.

Methods: This multicentre case-controlled study included women with early-onset PE (<34wks gestation; n=15), late-onset PE (>34wks gestation; n=18), and uncomplicated pregnancies (n=26). At admission to the hospital (early-onset PE and late-onset PE), or at term pregnancy (controls), mothers filled out stress and anxiety questionnaires. Participants also donated a strand of hair at admission, not influenced by corticosteroid administration. The average hair growth rate is 1cm a month, with the hair closest to the scalp representing the most recent part of pregnancy. Cortisol concentration in hair were analyzed in three periods: 3 months before conception (preconception), 0-3 months of pregnancy (1st trimester) and 3-6 months pregnancy (2nd trimester).

Results: ANOVA’s showed that reported anxiety levels were higher in women with preeclampsia compared to the controls (p<0.01). Furthermore, a repeated measurements ANOVA showed that cortisol trajectories from preconception to the 2nd trimester differed between early onset preeclampsia, late onset preeclampsia and uncomplicated pregnancies (p=0.04). Post-hoc analyses indicated that mothers with early-onset PE showed steeper increases in cortisol, with significantly higher cortisol concentrations during the second trimester.

Discussion: These results indicate that measures of psychosocial anxiety and physiological stress differ between early-onset PE, comparing to late-onset PE and uncomplicated pregnancies. Late-onset PE might be associated
with a higher level of preconceptional cortisol concentration, although these results were underpowered, cortisol concentrations may be utilized to assess the differentiation between early-onset and late-onset PE.

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Anthropometric aspects and hematimetric parameters in gestations complicated by hypertensive syndromes

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Introduction: Possible markers of severity in hypertensive syndromes of the pregnancy-puerperal cycle could be identify and guide conduct timely in order to reduce maternal and perinatal risks.

Objectives: To analyze the relationship between the anthropometric aspects and the hematimetric parameters comparing in pregnant women with preeclampsia(PE), hypertension chronic(HC) and without comorbidities.

Methods: Cross-sectional study developed at Hospital Guilherme Alvaro, Santos/Brazil and at Municipal Maternity of São Vicente/Brazil (May-September 2017). Group PE: pregnant women with PE and HC Group: pregnant women with HC (NHBPEP, 2000). Control group(C): healthy pregnant women. Variables analyzed: body mass index(BMI), abdominal circumferences(CA), complete blood count. Exclusion criteria: diabetes, collagenosis, smoking, twin pregnancy and fetal abnormalities. Fisher’s exact test was used and was considered as the significance p<0.05.

Results: 68 pregnant women were selected. The mean BMI found in group C was 29.45, in the HC group of 35.5 and in the PE group 38.8. We also observed that pregnant women in the PE group had an average CA19.21 cm higher than pregnant women in group C. It was identified that CHCM is superior in the PE group. There was statistical significance in the levels of neutrophils and lymphocytes in the groups with hypertensive syndromes.

Discussion: Elevation of BMI/CA in PE patients are risk factors for cardiovascular diseases according to the literature (Rezende, 2006). There was an increase in CHCM in cases of endolymphatic injury related hemolysis (HC and PE). Considering the exclusion of patients with other comorbidities, capable of influencing CHCM, this one presented as a potential marker of abnormalities. The increase in the level of lymphocytes in the PE group found in the study, with statistical significance, opposes the literature reporting otherwise (Vázquez, 2004). The increase in neutrophils found in group C (p= 0.007), especially at the end, is consistent with the literature (Souza, 2002).

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Clinical utility of sFlt1/PlGF in the management of hypertensive pregnancies in India

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Angiogenic biomarkers have been shown to predict adverse maternal/perinatal outcomes. This study explored the outcomes of hypertensive pregnancies using sFlt1/PlGF ratio in the third trimester. A single site prospective cohort study was done at a tertiary center in India. Singleton pregnancies with chronic/gestational HTN between 28 to 37 weeks were enrolled. sFlt1/PlGF was measured in serum samples on Roche platform. The results were stratified as Screen negative, Borderline positive or Screen positive (Table 1). All patients were delivered based on clinical parameters.

Data on 31 pregnancies (resulting in 85 samples) was analyzed using sFlt1/PlGF ratio (cases) and compared with 93 contemporaneous pregnancies who were monitored without the biomarkers (controls). With the biomarkers, there was an increase in diagnosis of preeclampsia and IUGR along with higher rates of preterm delivery less than 30 weeks with an increase in the NICU stay. However, there was a significant reduction in rates of adverse maternal outcomes. 9 cases with maternal (peripartum) complications in controls included 2 cases of abruption, 6 cases of HELLP/partial HELLP and 1 case of pulmonary edema as compared to only 1 case of pulmonary edema among cases. No cases of IUFD was reported with biomarkers (Table 2).

Serial testing with sFlt1/PlGF in the third trimester could help avert serious adverse maternal and perinatal outcomes in hypertensive pregnancies. Larger prospective studies are needed.
Demographic characteristics and angiogenic profile in relation to fetal sex
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Fetal sex has been shown to alter maternal milieu, with patients carrying a male fetus having an altered inflammatory response in pregnancy. Angiogenic biomarkers sFlt1 and PlGF are associated with preeclampsia, however the difference in angiogenic profile with respect to the fetal sex is not previously analyzed.

In this retrospective cohort analysis, women with preeclampsia and normal pregnancy were enrolled upon admission to labor and delivery. Blood samples were collected and were assessed for angiogenic factors using an automated platform. Clinical and demographic information was abstracted from medical records and presented as median (interquartile range) or n (%).

A total of 299 normotensive and 130 women with preeclampsia were enrolled. Equal number of patients had male fetuses among preeclampsia and normotensive parturients (55.9% and 50.2% respectively). Among both normotensive and women with preeclampsia, no difference was observed in demographic characteristics between male and female fetuses, including age (normotensive), body mass index, smoking or racial status, blood pressure, gestation age at delivery or birthweight (all p > 0.10). Normotensive mothers carrying a male fetus had significantly high sFlt1 (3168 [IQR: 2160-4945] vs 2678 [IQR: 1752-4271]; p = 0.01), lower PlGF (175 [IQR: 97-367] vs 215 [IQR: 124-426]; p = 0.05), and higher sFlt/PlGF ratios (18 [IQR: 7-44] vs 12 [IQR: 5-30]; p = 0.01). This difference between fetal sexes was not observed in the angiogenic profile of patients with preeclampsia; however, we did observe a higher maternal age (27 vs 24 years, p=0.03) and rates of cesarean section, among patients with male fetuses in this cohort (54.7%vs 37.3%; p = 0.04).

Our study demonstrates that normotensive women carrying a male fetus have significantly worse angiogenic profile as compared to those carrying a female fetus. No such relationship exists for preeclamptic pregnancies. Further studies are needed to elucidate this mechanism.

Endothelin-1 is elevated prior to the development of term preeclampsia and is exacerbated in established severe early onset preeclampsia.
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INTRODUCTION: Preeclampsia (PE) is a serious complication of pregnancy, the pathophysiology remains unclear and diagnosis and treatment strategies are limited. The potent vasoconstrictor endothelin-1 (ET-1) has been implicated in the pathogenesis of PE. Previously we observed ET-1 levels were significantly higher in a cohort of women at high risk of developing PE as early as the first trimester. We set out to measure ET-1 in the circulation in women destined to develop PE, and in women with established severe PE.

METHODS: Plasma samples were collected as part of two separate studies and used to assess ET-1 levels by ELISA. Plasma was collected from women 1) from a case control prospective cohort study (Fetal Longitudinal Assessment of Growth; FLAG) at both 28 (n=106 Controls and n=38 PE) and 36 weeks (n=99 Controls and n=39 PE) gestation, prior to diagnosis of term PE; and 2) with established severe early onset PE (< 34 weeks; n=25 Controls vs. n=33 PE).

RESULTS: Plasma ET-1 levels were significantly higher in women destined to develop term PE (FLAG cohort) at 28 (p<0.001: Area under the ROC curve 0.68) and 36 weeks gestation (p<0.05: Area under the ROC curve 0.61) prior to disease onset. ET-1 was significantly increased in women with severe early onset PE (p<0.0001) compared to gestation matched controls. There was almost perfect discrimination between cases and controls (Area under the ROC curve 0.99).

CONCLUSIONS: We identified increased ET-1 levels in women destined to develop term PE and massively elevated levels in women with severe early onset PE. ET-1 may provide a useful biomarker alone or in combination with other markers to predict PE. ET-1 has potent vasoconstrictory activities, and likely plays considerable roles in the pathogenesis of PE; neutralising ET-1 action may offer therapeutic strategies to treat PE.
sFlt-1 and PlGF as predictors of fetal and neonatal outcomes in a high-risk cohort
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Introduction: Studies have reported an association between umbilical cord blood levels of PlGF (placental growth factor) and soluble fms-tyrosine kinase-1 (sFlt-1) and neonatal complications, including bronchopulmonary dysplasia (BPD).

Objective: To determine whether maternal serum levels of sFlt-1, PlGF and their ratio in women with suspected or with confirmed preeclampsia are associated with the development of BPD and other neonatal complications, independent of gestational age in preterm neonates.

Methods: In patients submitted with suspected or clinically confirmed preeclampsia maternal blood was sampled for determination of serum levels of sFlt-1, PlGF and their ratio. Women with singleton pregnancies, delivering before 34 weeks of gestation were included. Fetal/neonatal outcomes were death, SGA (birthweight <10th percentile), Apgar score below 7 (after 5 minutes), length of stay at the neonatal intensive care unit (NICU), respiratory distress syndrome (RDS), BPD, and sepsis. Odds Ratios between values of sFlt-1, PlGF and sFlt-1/PlGF ratio and outcomes were evaluated using logistic regression analysis without and with adjustment of gestational age.

Results: A total of 143 singleton deliveries were analyzed. The median GA was 28.2 weeks (range 20.0–33.6) at study entry and 29.2 weeks (20.6–34.0) at delivery. Fetal/neonatal death occurred in 17, birthweight <10% in 18, Apgar score < 7 in 12, RDS in 80 BPD in 19 and sepsis 36 pregnancies. ORs were present for the association between the PlGF and BPD, fetal death, RDS and SGA, and were respectively 16.3 (3.0–89.1), 4.8 (1.2–19.1), 2.2 (0.8–5.8) and 3.0 (0.7–12.9). However, significant association were no longer found after correcting for gestational age at delivery.

Conclusions: There is no direct connection between the biomarkers and adverse neonatal outcomes. Maternal PlGF and sFlt-1/PlGF-ratio are predictors of prematurity, and therefore indirectly related to complications such as BPD, RDS and SGA.

Risk Factors associated with Hypertensive Disorders of Pregnancy within an Urban Indigenous Population in South Western Sydney
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Australia

Background: The prevalence of hypertensive disorders of pregnancy (HDP) in Australia’s urban Indigenous women is unknown.

Aim: To explore the risk factors associated with HDP for a cohort of urban Indigenous women in South-Western Sydney, Australia

Methods and Materials: This study was conducted in partnership with the Tharawal Aboriginal Medical Service (TAMS). Women (18-45 years) were recruited at the clinic and community events. The quantitative questionnaire included obstetric history, personal and family history of hypertension. Anthropometric measurements and blood pressure were conducted. Rates were compared with Australian Bureau of Statistics (ABS) national rates.

Results: Eighty three participants completed the questionnaire. The rate of ever having HDP in a pregnancy was 36.1%. The overall ABS rate was 9.8% and for Indigenous women, 14%. The mean maternal age at first pregnancy was 20.8 years (S.D. 3.7 years). The mean body mass index (BMI) of the sample population (n=81) was 32.2kg/m² (S.D. 9.5kg/m²) and BMI was not related to HDP (p = 0.197). Of those questioned, 25.3% had an individual history and 63.9% had a family history of hypertension. The effect of family history of hypertension (p = 0.020) (OR 4.29; 95%CI; 1.42-12.93) and individual history of hypertension (p<0.001) (OR 15.69; 95%CI; 4.50-54.76) were associated with HDP.

Conclusion: There was a higher rate of HDP in urban indigenous women compared to the national Indigenous prevalence. The family history, or individual history of hypertension were the most significant risk factors and BMI was not identified as a risk factor for HDP in this population.
Fetal programming

Posters

Maternal blood pressure and hypertensive disorders during pregnancy and childhood respiratory morbidity. the generation r study.
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Introduction Preeclampsia is associated with an increased risk of bronchopulmonary dysplasia, wheezing and asthma in later childhood.

Objective To examine the associations of maternal blood pressure and hypertensive disorders in pregnancy with the risk of lower lung function, wheezing and asthma in childhood.

Methods In a population-based prospective cohort study (n=4,894 mother-child pairs) we measured maternal blood pressure in early, mid and late pregnancy. Information about gestational hypertension and preeclampsia was obtained from medical records. At age 10 years, spirometry was done in the children. Current wheezing and asthma in children aged 10 years were assessed by parental questionnaires. We used multivariate linear and binary logistic regression models to examine the associations of maternal blood pressure and hypertensive disorders during pregnancy with lung function, wheezing or asthma.

Results We observed consistent associations of higher maternal blood pressure in early pregnancy and lower child FEV₁/FVC (Z-score (95% CI) -0.03 (-0.05, -0.01)), and a higher risk for current wheezing and current asthma in the child in late pregnancy (odds ratios (95% CI): 1.07 (1.02, 1.12), 1.06 (1.00, 1.11), respectively). Maternal hypertensive complications during pregnancy were not related to child lung function, current wheezing or asthma.

Conclusion Higher blood pressure in pregnant women was associated with lower lung function and increased risks of current wheezing and current asthma in their offspring. The associations may be trimester specific.

The 3d-pd features of fetal middle cerebral with severe preeclampsia
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Background The prevalence of preeclampsia was approximately 4.0% and 2.88% of all pregnancies worldwide and in mainland China. It is mainly characterized by the poor remodeling of the uterine spiral artery and the superficial implantation of placenta, which will contribute to maternal and neonatal complications.

Objective The aim was to explore the changes of fetal middle cerebral artery flow indices and its relationship with severe preeclampsia.

Methods From August 2016 to February 2017, 56 women with severe preeclampsia who hospitalized in the obstetric ward of the first affiliated hospital, Xi’an Jiaotong University were included as research group. 64 normal pregnant women without any complications during the same period were randomly selected as the control group. The matching principles are ± 3 years age of maternal age and ± 3 of gestational weeks. Color Doppler ultrasound were performed by GE Voluson E8. PI and RI of fetal middle cerebral artery and of umbilical artery were tested. VI, FI and VFI was calculated by VOCAL.

Results The UA-PI was 0.94 (0.57-1.55) and UA-RI was 0.61(0.44-0.83) in research group . CPR(PIMCA/PIUA)was significantly lower in research group[ 1.63 ( 0.73-3.02%) vs. 1.85 ( 0.67-3.02% ,p= 0.019]. There were no significant differences in MCA-PI . MCA-RI and VI, FI and VFI of MCA between the two groups. There was a negative correlation between CPR and stillbirth or neonatal death in the research group (r was -0.294 and -0.306,p was 0.047 and 0.039 respectively). In the adverse perinatal outcome of research group , CPR was 1.66 ( 0.73-3.02% It was significantly higher compared with that of good perinatal outcome. When the cut-off values of CPR was taken as 1.05, 1.10, 1.15, respectively , the sensitivity was 7.7%,12.8%, 17.9% and specificity was 100%, 100%, 87.5%,
respectively, for predicting adverse perinatal outcome.

Conclusion CPR could be used as predictive index for adverse outcome with severe preeclampsia.

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Neonatal outcome after natural course of preterm IUGR fetuses with abnormal umbilical Doppler flow in combination with preeclampsia

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Introduction: The natural course of preterm IUGR pregnancies with absent or reversed end diastolic flow (AREDF) in the umbilical artery and preeclampsia has not been investigated so far.

Objectives: Determine neonatal outcome of preterm IUGR pregnancies with AREDF and preeclampsia after expectant obstetric management.

Methods: Patients were admitted between 2004 and 2014 in the Erasmus Medical Centre with preterm IUGR. Inclusion criteria: singletons, IUGR, 24-32 weeks, birth weight 500-1250 grams. Admission was on clinical grounds and/or because of AREDF. Patients were allocated to the AREDF group or the normal end-diastolic flow (NEDF) group. After expectant management, pregnancies were terminated because of fetal distress or for maternal reasons.

Short-term primary outcomes: idiopathic respiratory distress syndrome (IRDS), sepsis, bronchopulmonary dysplasia, necrotizing enterocolitis, intraventricular hemorrhage, composite neonatal outcome and perinatal mortality. Long-term primary outcome: cognitive and motor neurodevelopment at two years of age with Bayley III (BSID III).

Results: 433 women with preterm IUGR were admitted, 184 met the inclusion criteria, 33 were also diagnosed with preeclampsia. AREDF had no adverse effects on perinatal morbidity and mortality. NEDF seemed to increase the risk for IRDS (P=0.021). Between the two groups, no differences were found on cognitive (P=0.078) and motor development (P=0.568). There were no differences in gestational age at delivery. Expectant management had positive effects on sepsis and perinatal mortality. Delivery was postponed between 1 day and 10 weeks. Preeclampsia had no additional adverse effects on the prevalence of perinatal morbidity and mortality (P=0.402) and cognitive and motor neurodevelopment (P=0.611 and P=0.640).

Discussion: No significant differences in neonatal outcome were found between the AREDF and NEDF group irrespective of co-existing preeclampsia after expectant management. It seems that postponing the delivery reduces perinatal morbidity and mortality. NEDF seemed to increase the risk of IRDS.

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Neighbourhood deprivation and foetal growth: the Generation R study.

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Introduction: Embryonic development is affected by multiple parental lifestyle factors and environmental exposures. Neighbourhood deprivation is associated with lower birth weight and higher preterm birth rates. However, the effects of living in a deprived neighbourhood on embryonic and foetal growth have not been explored yet.

Hypothesis

We hypothesized that living in a deprived neighbourhood is negatively associated with embryonic and foetal growth. Therefore, our objective was to assess the association between neighbourhood deprivation and embryonic and foetal growth parameters.

Methods

We evaluated the association between living in a deprived neighbourhood and embryonic and foetal growth parameters in 1614 mothers with a reliable first day of last menstrual period and a regular menstrual cycle. Foetal measurements included crown rump length (CRL), head circumference (HC), femur length (FL), biparietal diameter (BPD), abdominal circumference (AC) and estimated foetal weight (EFW).

Results

A total of 1614 pregnant women were included. Most were of Western ethnicity (70.7%) and nulliparous (59.0%).
Almost every pregnancy was spontaneously conceived (95.7%). The score for neighbourhood deprivation is determined for all 4-digit zip codes and takes income, education and employment into account. A low score represents a deprived neighbourhood.

Using linear mixed models, we found a statistically significant association between the neighbourhood deprivation score and FL (adjusted $\beta -1.06$ [95% CI: -1.98, -0.15]) and EFW (adjusted $\beta -0.96$ [95% CI: -1.89, -0.04]), but not with CRL, HC, AC and BPD.

**Discussion**

This population-based study shows that residing in a deprived neighbourhood is statistically associated with some, but not all, foetal growth parameters. Possibly, foetal growth parameters have different degrees of receptivity to external factors such as neighbourhood deprivation.

The effects we found remained above and beyond individual SES, for which we adjusted. This suggests a separate neighbourhood level effect on embryonic and foetal growth.

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**Neurodevelopmental outcomes at five years after early-onset fetal growth restriction, analyses in a Dutch subgroup participating in a European management trial**


**The Netherlands**

**Introduction:** Extreme early-onset fetal growth restriction (FGR) is associated with severe neonatal morbidity and long-term sequelae at age two and above. In a European trial on timing of delivery in early-onset FGR, developmental outcome was assessed at age two. No further follow up was scheduled. The Dutch follow-up program gave the opportunity to study developmental outcome at corrected age five years in a (Dutch) subset of the participating FGR children.

**Objective/ hypothesis:** To explore developmental outcomes at five years after extreme FGR and their perinatal risk factors.

**Methods:** Retrospective data analysis of prospective follow-up of infants born very preterm after FGR. At five years of age IQ, movement ABC-II (M-ABC-II-NL) and neurosensory outcomes were assessed.

**Results:** Seventy-four very preterm FGR children underwent follow-up at five years. They had a mean gestational age at birth of 30 weeks and birth weight of 910 grams. 7% of the children had a Bayley score <85 at two years. Mean five years' full scale IQ (FSIQ) was 98, 16% had a FSIQ <85, and 35% had one or more IQ scores <85. Motor score $\leq 7$ was seen in 39%. Neurodevelopmental impairment increased from 6.8% at age two to 15% at age five. An abnormal IQ scale score was related to birthweight and severity of FGR, and abnormal motor score to male sex and bronchopulmonary dysplasia (BPD).

**Discussion:** Overall, mean cognitive outcome at five years was within normal range, but 35% of the children had any abnormal IQ score, depending on the IQ measure, and motor impairment was seen in 39% of the children. Severity of FGR was the most important risk factor for cognitive outcome.

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**Immunology**

**Posters**

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**Decidual killer immunoglobulin-like receptor (kIr)2d1 expression and the onset of preeclampsia, birth weight and placental weight in early and late onset preeclampsia**

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Successful remodelling of spiral artery ensures adequate uteroplacental perfusion and sufficient nutrient supply to the fetus. HLA-C interaction with maternal KIR determines the outcome of spiral artery remodelling. Strong inhibitory KIR2DL1 lower the expression of cytokines and angiogenic factors affecting uteroplacental perfusion and nutrient
supply.

Material and methods: We analysed the decidual expression of KIR2DL1 in early and late preeclampsia groups by quantitative immunohistochemistry using anti human-KIR2DL1/CD158a antibody and its correlation with preeclampsia onset, birth weight and placental weight. 35 patients, 14 patients with early onset preeclampsia (EO-PE) and 21 with late preeclampsia (LO-PE) were analysed.

Results: There was a significant difference between the expression of KIR2DL1 between the EO-PE and LO-PE group (p<0.001) with a strong negative correlation between decidual expression of KIR2DL1 and preeclampsia onset (p<0.001, r=−0.723), birth weight (p<0.001, r=−0.770) and placental weight (p<0.001, r=−0.770).

Conclusion: In patients with EO-PE, the higher placentals of KIR2DL1 and inhibitory KIR2DL1 contributes to earlier onset of preeclampsia, lower birth weight of the baby and low placental weight. The strong negative correlation might be due to much lower expression of cytokines and angiogenic factors in higher KIR2DL1 expression samples. The different expression of KIR2DL1 between EO-PE and LO-PE is in line with current concepts on different pathophysiologic pathway leading to these different PE phenotypes.

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Significant increase of soluble B7-H4 in women at high-risk for preeclampsia in the first trimester: a potential immunobiological biomarker for immunologically-mediated pregnancy complications?

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Introduction: The successful outcome of pregnancy requires adequate immune tolerance. A lack of appropriate tolerance might cause placental dysfunction and pregnancy complications such as preeclampsia (PE). Members of the B7 family play an essential role in maintaining immune tolerance in pregnancy by effecting T cells. B7-H4 is responsible for the negative regulation of T-cell-mediated immune response and might play an important role in PE. We currently revealed that sB7-H4 is involved in the spontaneous onset of labor and is elevated in early pregnancy in women with a preterm premature rupture of the amniotic membranes (pPROM). Thus, here we investigated the association between PE and sB7-H4 levels.

Material and Methods: Maternal serum levels of sB7-H4 were determined by enzyme-linked immunosorbent assay in first trimester with elevated risk for PE < 1 in 100 (n=48) compared to controls (n=47). In third trimester serum levels (n=166) as well as placental mRNA expression were determined in early- and late-onset PE, intrauterine growth restriction (IUGR), and in healthy controls.

Results: In women at elevated risk for PE in first trimester significantly higher levels of sB7-H4 were detected compared to controls (p<0.0001). sB7-H4 has some predictive ability to identify cases with an elevated risk for PE with area under the curve (AUC) value of 0.88 (95% CI 0.8−0.94), sensitivity of 89.6% and specificity of 80.0%. In third trimester, the highest serum levels of sB7-H4 and placental B7-H4 mRNA were observed in women with early-onset PE (p=0.01 and p=0.006, respectively) and late-onset PE (p=0.03 and p=0.004, respectively) compared to healthy controls, but not in IUGR.

Conclusion: sB7-H4 is involved in the regulation of immune tolerance in women with PE in the third trimester. In the first trimester, sB7-H4 might serve as a predictive immunobiological biomarker for women who are at elevated risk of developing PE.

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Silibinin regulates the NF-κB pathway and NLRP1/NLRP3 inflammasomes induced by monosodium urate in monocytes from preeclamptic women and THP-1 cells

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Introduction: Preeclampsia (PE) is characterized by a state of abnormal activation of the innate immune system. It’s associated with hyperuricemia and elevated serum levels of inflammatory cytokines. Uric acid crystals can activate
inflammasome, a multiprotein structure important for processing and release of inflammatory cytokines. The imbalance between pro- and anti-inflammatory cytokines in PE seems to be dependent on the deficiency of regulatory factors capable of modulating inflammatory response, which could be alleviated by administration of substances with anti-inflammatory and modulatory properties such as silibinin (SB).

**Objective:** The study aimed to evaluate the modulatory effect of silibinin on NLRP1 and NLRP3 inflammasomes and on NF-κB pathway activation in monocytes from preeclamptic women stimulated with monosodium urate (MSU).

**Methods:** Twenty preeclamptic women, 20 normotensive pregnant women (NT) and THP-1 cells were cultured with or without SB and MSU. Gene expression of NLRP1, NLRP3, Caspase-1, TLR4, MyD88, NF-κB, IL-1β, IL-18, TNF-α and IL-10 was performed by qPCR. Inflammatory cytokines and p65NF-κB activity were evaluated by ELISA.

**Results:** Monocytes of preeclamptic women presented higher endogenous activation of the inflammatory genes, as well as p65NF-κB basal activity and the inflammatory cytokines production than NT group. MSU stimulation increased the expression of these parameters, whereas SB treatment reduced them. Additionally, THP-1 cells had a similar immunological response profile of monocytes from preeclamptic women when cultured with or without MSU and SB.

**Conclusion:** These results suggest the MSU participation in the systemic inflammatory response, characteristic of preeclampsia, and that silibinin treatment is capable of modulating the sterile inflammation established in monocytes of preeclamptic women, demonstrating that this flavonoid plays a relevant role in the regulation of the inflammatory response in preeclampsia.

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**Haptoglobin deficiency in the inflammatory process of preeclampsia**

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**Introduction:** Preeclampsia is a specific pregnancy syndrome characterized by a systemic inflammatory response associated with the production of proinflammatory cytokines and with the presence of molecular structures associated with stress and cell death and called “danger signals” or damage associated molecular patterns (DAMPs). HMGB1 is a proinflammatory cytokine and considered as DAMP, can interact with the acute phase protein haptoglobin, an endogenous HMGB1 inhibitor, forming complexes that can be removed from the circulation by interaction with CD163 receptor, present on the surface of monocytes/macrophages.

**Objective:** This study aimed to analyze the levels of haptoglobin, HMGB1 and inflammatory cytokines in the plasma of pregnant women with PE.

**Methods:** The plasma was obtained from 90 pregnant women, 30 pregnant women with severe preeclampsia (severe PE), 30 pregnant women with mild preeclampsia (mild PE) and 30 normotensive pregnant women (NT). The concentrations of haptoglobin, HMGB1 and IL-1β, IL-6, IL-10, TGF-β and TNF-α cytokines were determined by ELISA. The results were analyzed using parametric tests at 5% significance level.

**Results:** Plasma levels of haptoglobin and IL-10 were significantly lower in the severe PE group whereas the concentrations of TNF-α, IL-1β and TGF-β were higher in the severe PE group in comparison to the mild PE and NT. On the other hand, the results of HMGB1 and IL-6 only showed difference between pregnant women with PE and NT. **Discussion:** The high endogenous concentration of HMGB1, IL-1β, IL-6, TGF-β and TNF-α in the plasma of pregnant women with PE confirms the inflammatory activation profile of this pathology, while the lower concentrations of haptoglobin and IL-10 suggest a deficiency in a mechanism capable of correcting this inflammatory process in PE.

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**Regulatory (auto-) antibodies against G-coupled receptors in women ten years after early-onset preeclampsia: Results from the PREVFEM study**

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Introduction:
Preeclampsia (PE) is associated with an increased cardiovascular risk in later life, especially in women after early-onset PE. We and others have shown that activating antibodies against angiotensin II receptor type 1 (AT1-) are present in women with PE, even after pregnancy. Further, regulatory (auto-)antibodies against G-coupled receptors (GPCR) have been shown to contribute to cardiovascular disease.

Hypothesis:
We tested the hypothesis that regulatory autoantibodies’ titers are elevated in women with a history of early-onset PE and correlate to physiological parameters and clinical outcomes.

Methods:
We investigated data from PREVFEM (Preeclampsia Risk EValuation in FEMales) retrospective matched case-control study, which was performed in Zwolle, The Netherlands, from 2008 until 2010. All women registered in the early PE database as well as an equal number of age-matched females without PE from the regular obstetric database in the same time period (1991-2007) were invited to participate in the PREVFEM study. Autoantibodies against AT1-, β1- adrenergic receptors, endothelin I receptor A (ETAR), protease-activated receptor 1 (PAR1) and C-X-C3 chemokine binding receptors (CX3R) were determined in 609 samples (306 cases and 303 controls) by using commercially available ELISA (Celltrend, Luckenwalde, Germany).

Results:
The titer levels of AT1-, β1-, ETAR-, PAR1- and CX3R- autoantibodies were not significantly different between control and former PE groups 10 years after index pregnancy. Former PE women showed a significantly higher prevalence of hypertension (43% vs. 17%, p < 0.0001). Furthermore, we found a significant association of AT1- and ETAR- autoantibodies levels with the heart rate, but no relationship between blood pressure and autoantibodies’ titers.

Discussion:
Regulatory autoantibodies against GPCR do not identify women at higher risk for cardiovascular disease 10 years after early-onset PE. The need to search for biomarkers identifying women at risk before cardiovascular symptoms is continuing.

Vitamin D decreases gene and protein expression of NLRP3 inflammasome in placental explants cultured with hydrogen peroxide from women with preeclampsia
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Introduction: Pregnancies complicated by preeclampsia (PE) are associated with placental oxidative stress and related to the activation of NLRP3 inflammasome, an important complex for activation of caspase-1, interleukin-1 beta (IL-1β) and high-mobility group box-1 (HMGB1). The hyperactivation of NLRP3 inflammasome in placental tissues may be involved in the huge systemic inflammatory state in PE, which could be modulated by administration of substances with anti-inflammatory properties such as vitamin D (VD).

Objectives: This study aimed to evaluate vitamin D immunomodulatory effect on the NLRP3 inflammasome in placental explants from normotensive (NT) and preeclamptic women cultured with hydrogen peroxide.

Methods: Placental explants from 7 PE and 7 NT women in the third trimester of pregnancy were obtained from women undergoing elective cesarean section. Explants were cultured with or without H2O2 and H2O2 plus VD. NLRP3, HMGB1, caspase-1 and IL-1β gene expression were analysed by qPCR. Protein expression were determined by western blotting or ELISA.

Results: Endogenous gene expression of NLRP3 and HMGB1 were significantly higher in PE than in NT explants. NLRP3, caspase-1, IL-1β and HMGB1 gene expression were higher in cultures treated with H2O2 compared to control cultures, while explants treated with H2O2 plus VD led to lower gene expression in NT and PE groups. High protein expression of NLRP3, caspase-1, IL-1β and HMGB1 was detected in explants cultured with H2O2 compared to controls whereas cultures treated with H2O2 plus VD decreased this protein expression compared to H2O2 stimuli.

Conclusion: Vitamin D was able to decrease the gene and protein expression of NLRP3 inflammasome and HMGB1 production in placental explants cultured with H2O2 in PE and NT groups. These results suggest that vitamin D may play an immunomodulatory role in the systemic inflammatory response present in preeclampsia.

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Higher levels of memory T-cell subsets in decidua parietalis compared to basalis tissue of uncomplicated term pregnancies
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Introduction: During pregnancy, tolerance towards the fetus is induced by adaptations in the maternal immune system. Maladaptation of the maternal immune system is associated with pregnancy complications like preeclampsia and fetal growth restriction. Memory T-cells might play an important role in fetal-maternal tolerance. It is at the fetal-maternal interface where the maternal immune system especially needs to create tolerance towards the fetus. Decidua basalis is the maternal part of the basal plate whereas decidua parietalis is the maternal part of the fetal membranes. Decidual distribution pattern of memory T-cells during pregnancy is not known.

Objective: Since it is unknown how memory T-cells are distributed in decidual tissue, memory T-cells in decidua basalis and decidua parietalis were evaluated.

Methods: Lymphocytes were isolated from decidua basalis and decidua parietalis from uncomplicated term pregnancies. Using flowcytometry, subsets of memory T-cells (central, effector, regulatory, and tissue resident) of uncomplicated term pregnancies were analysed (n=27). To compare different subsets of memory T-cells between decidual tissues, a student’s t-test (p<0.05) was used.

Results: Levels of memory T-cells (CD45RO+) were higher in decidua parietalis compared to decidua basalis in both CD4+ and CD8+ cells. Moreover, CD8+ central memory cells (CD45RO+CCR7+) and CD8+ tissue resident cells (CD45RO+CD103+) were higher in decidua parietalis compared to decidua basalis. Lastly, activation status (CD69+) was higher for all memory subsets (except for CD4+ effector memory T-cells) in decidua parietalis compared to decidua basalis.

Discussion: This study shows that memory T-cell subsets are differently distributed in decidua parietalis and basalis, with higher percentages of memory T-cell subsets as well as more activated memory T-cell subsets found in decidua parietalis compared to decidua basalis. Since memory T-cells are found to be present at higher percentages in decidua parietalis, this could suggest that these cells are especially important for creating tolerance to the fetal membranes.

TNFα impairs cerebral blood flow autoregulation during pregnancy
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Background: Cerebral complications are a leading cause of morbidity and mortality in preeclamptic pregnancies, accounting for approximately 40% of all preeclampsia/eclampsia related deaths. However, the underlying pathophysiological mechanisms remain unclear. Given the central role of the ischemic placenta in driving preeclampsia, we hypothesized that circulating factors released from the ischemic placenta directly impair cerebral vascular function and blood brain barrier permeability. Specifically, the role of TNFα, an inflammatory cytokine increased in the placenta and circulation of preeclamptic pregnancies, was examined.

Methods: Pregnant Sprague Dawley Rats were infused with vehicle or TNFα (200 ng/day i.p, from gestational day 14 to 19). Evan’s blue extravasation was measured in the cerebral cortex as an indicator of blood brain barrier (BBB) permeability, and brain water content was assessed as an indicator of cerebral edema at the time of euthanasia. In a separate experimental group, rats were infused with vehicle or TNFα in order to examine the impact on cerebral blood flow (CBF) autoregulation during pregnancy. CBF was measured by laser Doppler flowmetry under anesthesia. Rats were intubated and ventilated in order to maintain constant blood gases, and mean arterial pressure was elevated step-wise from 100-190 mmHg by infusion of phenylephrine to determine changes in CBF.

Results: Infusion of TNFα in pregnant rats caused a significant 10 mmHg increase in arterial pressure (n=12, p<0.05). Brain water content was increased in TNFα infused rats (p<0.05), mainly in the anterior cerebrum, and significantly increased BBB permeability in the hippocampus (p<0.05). TNFα infusion impaired CBF autoregulation in pregnant rats with increased CBF flow at 180 mmHg (253±16 vs 188±9, n=6, p<0.05). Peak carbon dioxide was not different between groups.

Conclusions: These data suggest that increasing TNFα to levels observed during preeclampsia results in cerebral vascular changes that may mechanistically underlie the increased risk for encephalopathy.
INTRODUCTION - The etiology of pre-eclampsia (PE) is not yet fully understood, though current literature indicates an upregulation of inflammatory mediators produced by the placenta as a potential causal mechanism. Vitamin D is known to have anti-inflammatory properties and there is evidence of an inverse relationship between dietary calcium intake and the incidence of PE.

METHODS: We studied 150 patients attended by the Obstetrics Department of the Barbacena Medical School and the Federal University of Juiz de Fora. All patients underwent vitamin D dosing in the first, second and third trimesters of pregnancy. The cutoff point was 30 mcg / dl and out of pregnancy 20 ng / ml.

RESULTS: The median vitamin D level in pregnant women was considered low (<30 ng /ml), with an average of 22 ng/ml, requiring replacement. There was no association between vitamin D dosage and preeclampsia (p> 0.05).

CONCLUSIONS: The authors report the importance of maintaining normal levels of vitamin D in pregnant women, considering the formation of the fetus, but there was no association between vitamin D and preeclampsia in this study.

Peripheral maternal haemodynamic gestation across pregnancy in gestational diabetes mellitus
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Introduction: Haemodynamic maladaptation has been associated with gestational diabetes mellitus (GDM), a risk factor for hypertensive disorders of pregnancy. Recent RCT’s suggested that metformin treatment may reduce the risk for preeclampsia in very obese women.

Objectives: To evaluate maternal haemodynamics across gestation in uncomplicated pregnancies and those complicated by GDM.

Study design: Prospective cohort study from 2015-2018 of healthy, nulliparous, singleton-bearing women. Maternal haemodynamics assessed at 11 and 32 weeks’ gestation in pregnancies complicated by GDM, grouped by treatment: diet, metformin or insulin, compared to uncomplicated pregnancies using mixed-effects linear modelling.

Main outcome measures: Maternal haemodynamics assessed by Uscom BP+ [peripheral and central blood pressure (BP), and augmentation index (Aix)] in uncomplicated pregnancies and those complicated by GDM.

Results: Eighty-five women developed GDM (insulin: 19, metformin: 12, diet: 53) and 294 women had uncomplicated pregnancies. All 379 women showed a mean increase in peripheral systolic BP (SBP; 2.89mmHg, 1.75-4.02), peripheral diastolic BP (DBP; 2.06mmHg, 1.20-2.92), peripheral mean arterial pressure (MAP; 1.85, 0.90-2.80), central DBP (2.36mmHg, 1.49-3.22), central MAP (1.39mmHg, 0.55-2.24) but not peripheral pulse pressure (PP) nor central SBP across gestation. Central PP decreased across gestation (2.88mmHg, 2.14-3.63), as did Aix (18.22%, 16.57-19.96).

Aix decreased less in women with diet-controlled GDM (9.27%, 4.78-13.77) and metformin-controlled GDM (8.76%, 0.33-17.18), but not in those with insulin-controlled GDM, compared to uncomplicated pregnancies. Changes across gestation for peripheral SBP, DBP, MAP, PP and central SBP, DBP, MAP and PP were not different in women with GDM compared to those with uncomplicated pregnancies.

Conclusion: Across gestation, Aix decreased less in women with diet-controlled and metformin-controlled GDM, compared to those with uncomplicated pregnancies. Those with insulin-controlled GDM showed comparable haemodynamic adaptation to those with uncomplicated pregnancies. This suggests that women with diet-controlled or metformin-controlled GDM have cardiovascular maladaptation to pregnancy which disappears with insulin treatment.
The P4 study: postpartum maternal and infant faecal microbiome 6 months after hypertensive versus normotensive pregnancy
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TITLE: The P4 study: postpartum maternal and infant faecal microbiome 6 months after hypertensive versus normotensive pregnancy

Introduction: There is increasing evidence inside and outside pregnancy of the importance of the microbiome to human health, including hypertension and cardiovascular health. How the microbiome changes and affects pregnancy outcomes including hypertensive disorders (HDP) is still unclear, and postpartum data is lacking.

Objective/hypothesis: To explore differences in faecal microbiome six months post-partum between women and their infants who had normotensive pregnancies (NP) versus those who had gestational hypertension or preeclampsia (HP).

Methods: Subgroup pilot study within the P4 study (Postpartum Physiology, Psychology, and Paediatrics Study) of 18 mother-infant pairs 6 months postpartum after NP or HP. Mothers collected a stool sample from themselves and their infants, with samples aliquoted and stored at -80°C. DNA was extracted from samples at the same time point using the PSP Spin Stool DNA Plus Kit, and 16S sequencing analysis performed.

Results: Ten NP and 8 HP (6 preeclampsia, 2 gestational hypertension) mother-infant pairs participated. They were predominantly primiparous (n=16) with vaginal birth (n=14). Apart from one HP woman with cholestasis, no other pregnancy complications, or medical history was present in the remaining cohort. At the time of faecal microbiome analysis 8 women were using a form of hormonal contraception (oral or implantable), and one HP woman remained on an antihypertensive. All women had blood pressures in the normal range, systolic 90-124, diastolic 60-76. Ten women had high BMI (eight 25-29.9, two 30+), and their gestational weight gain had ranged from 1 to 23 kg (average 11.1kg). At the time of assessment all infants had started solids. Eight were exclusively breastfed, one bottle fed and nine mixed. Three infants had been exposed to a course of antibiotics and one had a multivitamin. Sequencing results in process and to be presented.

Discussion: Postpartum microbiome analysis may provide additional insight into HDP, particularly relationship to long-term cardiovascular disease.

Key words: hypertension, microbiome, preeclampsia, postpartum

The gut microbiome in pregnant mice: relation to maternal immune responses?
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Introduction: Pregnancy is associated with maternal immunological adaptations in order to tolerate and support the development of the semi-allogeneic fetus.

Hypothesis: Since intestinal microbiota are linked to immune modulations, we hypothesized that intestinal microbiota are altered during pregnancy to support maternal immune adaptations.

Methods: Pregnant (day 18) and non-pregnant C57BL/6 and BALB/c mice were sacrificed and feces and colonic tissue were harvested. Fecal microbiota composition (MITchip) and intestinal gene expression (microarray (Affymetrix)) were evaluated.

Results: Pregnancy influenced intestinal microbiota diversity and composition in a mouse strain dependent way. Pregnant BALB/c mice had, among others, a higher abundance of various Lactobacillus species (e.g. L. paracasei et rel. and L. plantarum), Allobaculum et rel., Roseburia intestinalis et rel. and Eubacterium hallii et rel., as compared to non-pregnant BALB/c mice. The microbiota composition in C57BL/6 mice hardly changed during pregnancy. Additionally, intestinal immunological pathways were changed during pregnancy, again in a mouse strain dependent way. For example, pathways related to B cell development and CD28 signaling in T helper cells were only affected in C57BL/6 mice, while IL-10 signaling was only affected in BALB/c mice. Using advanced statistics, we combined microarray data with microbiota composition data from BALB/c mice and found many correlations between the presence of various pregnancy affected intestinal bacteria and immunological genes. Various bacteria with a higher abundance in pregnant mice (such as Allobaculum et rel.) correlated with clusters of genes, with many genes involved in immune responses (for instance T cell development).

Conclusion: Our data support a role for the microbiome in adapting immune responses in pregnancy. However,
also other factors are involved, since in C57BL/6 mice many immunological changes take place in the absence of microbiome changes. Follow up studies are needed to study the exact relationship between intestinal bacteria and maternal immune responses in pregnancy.

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**Association Between Body Mass Index and Preeclampsia**

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**Introduction:** Lipotoxicity is a consequence from low grade inflammation caused by obesity. Women presenting body mass index (BMI) above 35kg/m² have four times higher risk of preeclampsia development (Bianco, 1998).

**Objective:** To characterize the association of BMI and maternal and perinatal variables between puerperas with and without preeclampsia.

**Method:** Transversal study, Hospital Guilherme Álvaro-Santos/Brazil, (January/2015-March/2016). Anthropometric data was collected from 160 women (immediate postpartum), 75 patients without preeclampsia (control group) and 85 with preeclampsia (case group). Variables: blood pressure (hospital admission), gestational age at childbirth and immediate perinatal outcome.

**Results:** Average mother age and BMI were 25 years and 26kg/m² for the control group, in the group case: 29 years and 35kg/m². Patients with preeclampsia showed higher blood pressure: medium level of 136mmHg (sistolyc) and 85mmHg (diastolic). 84% of the deliveries in the case group were cesarean sections and the majority of these women had gestation resolution above 37 weeks. Newborns out of pre-eclampsia mothers weighed among 2685g and five-minute Apgar score was 8,7. Those neonates presented higher admission rates in a ICU (36.5%) and 12% were small for gestational age. Cesarean in 84% of births in the case group and 40% case of births occurred in prematurity. Newborns of mothers with preeclampsia weighed on average 2685g, average 5' Apgar score of 8,7, higher rates of admission to ICU (36.5%) and 12% were small for gestational age.

**Discussion:** Was observed in women with preeclampsia higher average BMI and blood pressure values and their newborns showed smaller weight and 5' Apgar score, need frequent admission to ICU and prematurity. Reproductive counseling appears to be relevant to the obese women to warn about potential complications, it’s important to adopt strategies for assistance to this population to qualify the attendance, particularly in actions preventive and possible reduction in the rate of cesarean section that could magnify risks.

**Maternal Mortality**

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**Examination of the eclamptic attack 5 case that we experienced recently**

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Introduction: The management comes to be carried out, and the eclamptic attack that often occurs cause of hypertensive disorders of pregnancy is a tendency to decrease. In our hospital, there were five (0.296%) cases of eclamptic attack by 1685 delivery during 17 months from February, 2016 to June, 2017.

Result: Five cases were primipara, and the age was 28-40 years old. Two patients were cared for by obstetric opening type practice, two cases were cared by in-hospital midwifery of our hospital, and there were not high-risk pregnancy. One patient performed a medical examination in our hospital obstetrics for 40-year-old advanced age first childbirth. All patients did not detect hypertension, proteinuria during a pregnancy period together. Two cases were intrapartum eclampsia, and three cases were puerperal eclampsia. Blood pressure was increased all cases during a birth process temporarily, but the blood pressure just before eclamptic attack all five cases were normal. One puerperal eclampsia case of the blood pressure was high after eclamptic attack, and it was given an antihypertensive agent, but recovered immediately, and the antihypertensive medications became needless four hours later. One patient of the puerperal eclampsia had history of hypoglycemia, but there was not hypoglycemia at attack. Because it was all a convulsive seizure from normal blood pressure, we performed head CT of all cases, three patients performed the MRI, the organic disease was not found of all cases.
Discussion: By the simulation education and the team approach in medical care to cope with a maternal sudden change, we came to rarely experience eclamptic attack from hypertensive disorders of pregnancy. However, the eclamptic attack occurs from a case of the normal blood pressure like our case. Therefore it is important that we learn the skill that can urgently always support for sudden abnormality from normal.

Quality of Care for Hypertensive Disorders in Pregnancy in Primary Health Care settings in Southern Nigeria: Women’s Perspectives from Capacity Enhancement Interventions
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Introduction: Quality of care, defined by WHO as effective, efficient, accessible, patient-centered, equitable and safe care, may have a multiplier effect on positive maternal and neonatal outcomes. No study in Nigeria has explored post-intervention experiences of women with hypertensive disorders in pregnancy (HDPs) on care quality at primary and referral levels.

Objectives: To understand the quality of care received by women with HDP during antenatal care (ANC).

Methods: Case studies were conducted with thirty-four women whose pregnancies were complicated by hypertension and managed by community health extension workers (CHEWs) until delivery, as part of implementation research on task-shifting. Results were analyzed with Nvivo 11.

Results: Diagnosis and treatment of HDP were based on WHO recommendation—blood pressure (BP) and urine protein measurements. Women identified and managed for HDP consistently reported receiving feedback and counselling on their BP measurements, and less frequently on urine protein tests. Although CHEWs prescribed antihypertensives, women could not recall the specific medications given. Often referred to higher-level hospitals within reasonable distance given antihypertensives unavailability, women lament about the long distance to referral facilities which leads to delays in accessing treatment. While some women recounted satisfactory provider-client interactions, others expressed negative experiences, including disrespect and abuse, which led to the refusal of treatment. The absence of a perceived particular caring provider often leads to women declining care. Some women reported that providers prescribed antihypertensives that were difficult to purchase locally. Gaps in communicating diagnosis to patients resulted in women being aware of their HDP status, but unaware of the seriousness of the conditions.

Conclusions: Despite positive experience with of evidence-based quality care, drug availability and supply, referral mechanisms, communication on the types of HDPs and names of prescribed drugs were generally insufficient. CHEWs should be mentored and supported to provide patient-centered care with respect for human dignity.

Risk of maternal near miss with elective caesarean delivery in women with hypertension in pregnancy in Brazil.
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Introduction: Hypertensive disorders of pregnancy (HDP) contribute significantly to maternal near miss (MNM), most of them are preventable and associated with some delay in obstetric care little use of evidence-based guidelines.

Objective: The aim of this study is to analyse the association between elective caesarean section (CS) and MNM in women with HDP.

Methodology: This study is based on data from Birth in Brazil Survey, a nationwide hospital-based study conducted between 2011 - 2012, including 23,894 women. The women selected had 34 - 42 weeks, and were attended in public hospitals. Cases of placenta previa, HIV, multiple pregnancy, foetal distress before labour and non-cephalic presentation were excluded. A directed acyclic graph was constructed to select the variables for minimum adjustment. Multiple logistic regression analysis was performed to evaluate the association between MNM and elective CS.

Results: The prevalence of HDP was 12.6% (2,999). After exclusions, 1,950 women were analyzed, 54% had an elective CS and 10.5% induction of labour. MNM was associated with elective CS (OR 2.2, 95% CI 1.1 - 4.5), age ≥ 35 years (OR 2.0, CI 95% 1.0 - 4.1), and nullipara (OR 2.0, 95% CI, 1.1 - 3.9). In the multiple logistic regression woman undergoing elective CS had as odds ratio of 2.13 (95% CI 1.02 - 4.43) for MNM, even controlled by maternal age,
Confidential review of maternal deaths in the Community Level Interventions for Pre-Eclampsia (CLIP) Mozambique Trial
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Introduction: Computer based algorithms, such as the WHO’s verbal autopsy tool (InterVA), are often used to attribute cause of death (COD) in low-resource settings despite their variable agreement with physician review. After a large scale community-level intervention trial for pre-eclampsia in Mozambique, maternal deaths were assessed in order to identify COD and barriers to care.

Objective: To compare COD for women who died in the Community Level Interventions in Pre-eclampsia (CLIP) Mozambique Trial (NCT01911494), 2015-2017, by physician review vs. the InterVA output.

Methods: Two physicians independently reviewed maternal mortality data from the trial (i.e., verbal autopsy [2012 WHO Instrument], baseline data and outcomes, and in the intervention arm, data from a mobile health application that included blood pressure readings), and assigned COD (by International Classification of Disease-Maternal Mortality). Disagreement was resolved by a third reviewer. Assigned COD was compared between physician review and InterVA output (set for high prevalence of malaria and HIV) using Cohen’s Kappa.

Results: Of the twenty-one (0.14%) maternal deaths reported, most were postpartum (14/21, 66.7%), and due to indirect causes (12, 57.1%). Malaria during or prior to pregnancy (14/21, 66.7%) and HIV/AIDS (11/21 reported, 52.3%) were found to significantly affect pregnancy. The three most common causes of death were 1) non-obstetric complications, 2) obstetric hemorrhage and 3) pregnancy-induced hypertension. Agreement between physicians and InterVA was fair, $\kappa=0.40$ [0.10 - 0.69]). Compared with InterVA, physicians were more likely to assign COD due to non-obstetric complications, specifically infectious diseases (9/21, 42.9%), including malaria and HIV/AIDS.

Discussion: Addressing infectious diseases, such as malaria and HIV/AIDS, obstetric hemorrhage and pregnancy-induced hypertension as most important causes of death is important to reduce maternal mortality in Mozambique. We found a fair level of agreement between COD assigned by InterVA and physician review at an individual case level, particularly for indirect causes of death.

Severe Maternal Morbidity and Pathological Puerperium: the Impact of Hypertensive Syndromes
Brazil

Introduction: Recognizing severe maternal morbidity (MMG) allows the adoption of effective measures, with emphasis on the contribution of hypertensive syndromes (HS).

Objective: To analyze the characteristics and maternal-neonatal outcomes of the hypertensive syndrome selected as severe maternal morbidity and/or pathological puerperium.

Method: Cross-sectional study (November/2017-March/2018), location: Complexo Hospitalar dos Estivadores/Instituto Social Hospital Alemão Oswaldo Cruz-Santos/Brazil. 70 women with at least one of Santos criteria derived from the definition of MMG of the World Health Organization (2009), Waterstone et al. (2001), Mantel et al. (1998), seeking to homogenize/facilitate this definition according to clinical/laboratory/management and/or recognized as pathological puerperium: ≥ three days of hospitalization. Variables analyzed: diagnosis of hypertension (NHBPEP/2000), age, parity, blood pressure, gestational age and way of delivery, adequate prenatal care (≥06 appointments), maternal complications and immediate perinatal outcomes.
**Results:** We identified that 53 (75.7%) patients had HS. Average age: 28 years. Previous pregnancies: 35 (66%). Adequate prenatal care: 49 (92.4%). Cesarean section in 73.6%. Signs of severity in 62.3%, HELLP syndrome (28.3%) and eclampsia (3.8%), used magnesium sulfate (69.8%) and admission to an adult ICU (7.5%). Neonatal: 5’ Apgar score of 8-10 (96.2%), prematurity (20.8%) and neonatal ICU admission (24.5%).

**Discussion:** A high HS rate was observed among women with MMG and with prolonged hospitalization with their risks/costs. The numerically adequate number of prenatal consultations questions the quality of the care (not evaluated). There is a need to reflect on strategies that enhance vaginal delivery and reproductive planning. The frequency of complications demonstrated the severity of the clinical expression and the expressive neonatal impact: prematurity and need for ICU neonatal admission, although the Apgar score frequently above 07, reinforces the need for recognition of SH regarding its frequency and extension of postpartum complication.

**Mental Health**

**Posters**

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**Associations between postpartum depression and hypertensive disorders of pregnancy**

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**OBJECTIVES:** to identify the possible relationships between PPD and HDP in women in a public maternity, and the associated factors. **STUDY DESIGN:** Prospective cross-sectional study with 168 puerperal women diagnosed with HDP (hypertensive women) and their controls (normotensive women) and their newborns. Diagnosis of SAH was indicated when systolic pressure was 140 mmHg or higher or diastolic pressure was 90 mmHg or higher; the diagnosis and severity of the disease were based on blood pressure, proteinuria, and clinical and laboratory findings. The Edinburgh Postnatal Depression Scale (EPDS) was used to assess the risk of postpartum depression. Scores ≥ 12 were considered to indicate the presence of depressive symptomatology. **MAIN OUTCOME MEASURES:** probability of depressive symptoms according to the EPDS. **RESULTS:** The probability of postpartum depressive symptoms was positively related with the diagnosis of hypertensive disorders of pregnancy (rS = 0.219, p ≤ 0.004), premonitory signs (rS = 0.171, p = 0.027), use of magnesium sulfate (rS = 0.199, p = 0.010), and DBP (rS = 0.165, p = 0.033), and use of milk formula during hospitalization (rS = 0.152, p = 0.048). **CONCLUSIONS:** puerperal women diagnosed with HDP are more likely to have depressive symptoms.

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**Impact of preeclampsia/HELLP on occupational activity afterwards: a pilot study.**

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**Introduction:** Women with a history of preeclampsia (PE)/HELLP syndrome have a twofold increased risk for cardiovascular disease (CVD). The psychosocial impact of such a high risk pregnancy is huge, especially in the first year postpartum. Women after PE/HELLP more often report anxiety, depressive symptoms, and display impaired memory and cognitive function that could affect their occupational activities. Follow-up of women with a history of PE/HELLP to assess occupational activity has not been done before.

**Objective/hypothesis:** The aim for this pilot study was to assess whether occupational activity is altered in women with a history of PE/HELLP.

**Methods:** An online survey was done among members (n = 211) of the Dutch HELLP Foundation (‘HELLP stichting’). Data were collected on medical and obstetric parameters. Work-related characteristics (work exposure, job control and job demands) and work related fatigue were measured using the short Copenhagen Psychosocial Questionnaire (COPSOQ-II), the “need for recovery scale” (NFR) and “recovery opportunities scale”.

**Results:** A total of 138 women (mean age 35.6 ± 5.7 years) completed all questionnaires. Participants were almost 5 years postpartum (mean 5 ± 4.9) and most were diagnosed PE/HELLP (80.4%). Only 11 participants (8%) reported to have fully recovered after pregnancy. Of the women who reduced working hours after index pregnancy (n = 127, mean reduction 9.3 hours; p < 0.01), this was not intended in 32.3%. The main reason for reducing the number of working hours was persisting mental and physical symptoms after PE/HELLP. Respondents scored high on chronic
stress indices, both for COPSOQ-II and NFR scale, respectively mean 63.4± 17.9 and 69.9 ± 26.9 (mean NFR in general population 27.3 ± 29.6).

Conclusion: Occupational activity is affected by PE/HELLP, with an increased risk for less recovery and stress related problems.

The P4 study: Gaining insight into women’s mental health and birth experience 6 months after a normotensive or hypertensive pregnancy
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Introduction: Pregnancy and childbirth are usually positive experiences. However, when complications occur, it may be emotionally traumatic. There is limited research reporting women’s mental health after hypertensive pregnancy and their perspective on the experience.

Objectives: To compare depression, anxiety and PTSD symptoms between women who were normotensive (NT) and hypertensive (HT) in pregnancy and to compare their birth experience.

Methods: Prospective sub-study of the P4 (Postpartum, Physiology, Psychology and Paediatric) study. Women were studied 6 months after NT or HT pregnancy. Each woman completed questionnaires comprising the Edinburgh Postnatal Depression, General Anxiety Disorder, Posttraumatic Stress Diagnostic and Maternal Infant Bonding Scales and questions, rated on a Likert Scale, regarding birth experience.

Results: 321 women (237 NT, 84 HT) completed the questionnaires. Both groups were similar in demographics. The HT group experienced more intervention during labour and birth; more had their labour induced (29% NT, 70% HT, p<0.001), a caesarean section (18% NT, 33% HT, p<0.001), or required admission to ICU (2% NT, 18% HT p<0.001). More women in the HT group met the threshold for possible depression (2% NT, 7% HT p=0.03) and reported their birth as a traumatic event (1% NT, 7% HT, p=0.006). None reported PTSD symptoms that met the diagnostic criteria. There were no statistical differences in anxiety or mother-infant bonding scores. Women in the NT group were 3-5 times more likely to respond positively regarding labour and birth.

Discussion: Six months postpartum, women with a previous HT pregnancy report significantly worse psychological health and birth experiences. Care providers need to include mental health support as part of routine care for women with a HT pregnancy.

'It was my body. It was happening to me. I should have known.' Women's knowledge and information needs in pregnancies complicated by pre-eclampsia.
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Introduction
Raised blood pressure (BP) is a common problem in pregnancy which can lead to significant morbidity and mortality for mother and child, particularly when accompanied by proteinuria or other metabolic changes (pre-eclampsia). Consequently, blood pressure and urinary protein are monitored by health professionals throughout pregnancy. There is little research on the psychological consequences of experiencing pre-eclampsia, although women’s perceptions and experiences suggest they are physically and emotionally distressed (Furuta 2014). Women’s knowledge about hypertension in pregnancy and pre-eclampsia, and their information needs during and after pregnancy, are largely unknown.

Methods
In depth semi-structured interviews were carried out with women in the UK who had experienced pre-eclampsia or HELLP syndrome about their experiences of pregnancy and its complications. Interviews were audio recorded and transcribed for analysis. Thematic analysis was undertaken based using constant comparison.

Results 17 women were interviewed. Women often didn’t know how serious blood pressure problems in pregnancy could be, and described knowledge journeys from largely ignorance to becoming experts. Women often struggled to understand and make sense of information they were given, especially while they were ill. They described pinch points when information was particularly important: on receiving diagnosis, admission to hospital, during labour and at discharge. Although women and their relatives could go online, information and communication from health
professionals was key. In the absence of verbal explanations, sometimes women interpreted body language and glanced looks.

**Discussion**

Our analysis highlights the lack of knowledge that women have about hypertension in pregnancy and its risks. If they develop complications their learning curve is steep and often frightening. The need for clear communication from health professionals and more reliable information about the risks and reality of pre-eclampsia are needed.

**Outcome/Treatment/Management**

**Posters**

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**Perinatal care for zambian pregnant women complicated with preeclampsia: the medication rooted in the region to stabilize its local management in zimba.**

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**BACKGROUND:** Preeclampsia (PE) is a hypertensive disorders of pregnancy (HDP) that is associated with proteinuria or some organ failure and it is still a major cause of perinatal death worldwide. Maternal mortality in developing countries is high due to PE. To reduce the maternal mortality in Zambia, it is important to survey the status of PE and prevent eclampsia. At first, we aimed at surveillance of obstetric status in Zambia.

**OBJECTIVES:** In this study, we surveyed detailed obstetric profile including PE morbidity in local area of Zambia and aimed at raising awareness of PE statistics at a low-income local area in Zambia.

**METHODS:** All deliveries from January through December in 2017 at Zimba Mission Hospital, Zambia were enrolled in this study. The number of patients complicated with preeclampsia and eclampsia were analyzed, and the clinical condition, the treatment, and the outcome were also analyzed.

**RESULTS:** Among the 1,712 deliveries in Zimba, 42 women (2.6%) were complicated with HDP (gestational hypertension (GH): 17, PE: 25). There was two still births in PE. All eclampsia (n = 8; 19.0%) happened out of hospital and the patients were taken to our hospital. Magnesium sulfate was administered to PE patients by intramuscular injection to prevent the occurrence of eclampsia along the suitable protocol for low-income pregnant women proposed by University Teaching Hospital (UTH) in Zambia and no eclampsia happened later.

**CONCLUSIONS:** We surveyed and evaluated the obstetric profile and morbidity of PE. The protocol for preventing eclampsia by UTH was suitable for a local clinic and hospital for low-income pregnant women in Zambia. However, the morbidity of eclampsia is still high out of hospital. We have to educate pregnant women about the seriousness of PE and encourage to measure BP of pregnant women in local clinic and hospital in Zambia.

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**Breastfeeding practices in the first 6 months after delivery: effects of arterial hypertension**

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**Objective:** To identify the effects of systemic arterial hypertension (SAH) on breastfeeding practices in the first 6 months after delivery. 

**Study Design:** It is a prospective cohort study enrolling 168 mother-newborn pairs (SAH group n=42, Normotensive group n=124). SAH diagnosis criteria was established as systolic pressure ≥140mmHg or diastolic pressure ≥90mmHg, while its severity was categorized according blood pressure, proteinuria, clinical and laboratory analysis. Demographic, clinical and social information were collected from the patient’s medical records. Mothers were phone interviewed 30, 60, 120 and 180 days after delivery, in order to collect information about the newborn’s feeding practices and possible difficulties in breastfeeding. 

**Main Outcome Measures:** Lactation practices (eg. exclusive breastfeeding, breastmilk and other liquids/solids, or not breastfeeding) within the first 6 months after delivery. 

**Results:** SAH during gestation displayed greater difficulties in maintaining exclusive breastfeeding over time, when compared to normotensive mothers. There was a greater introduction of milk formulas in the SAH group at hospital admission (p<0.0001). Additionally, SAH group precociously reported higher frequencies of predominant
breastfeeding practices and presented shorter duration of breastfeeding after 6 months after delivery. **Conclusions:** Women with SAH are at risk of using complementary breastfeeding and having a shorter duration of breastfeeding.

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**Evaluation of the clinical impact of the revised ISSHP and ACOG definitions on preeclampsia and on severe preeclampsia**

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**Background:** In 2013/2014 both ISSHP and ACOG revised their original statement and postulated new criteria for (severe) preeclampsia, by which the diagnosis preeclampsia can also be established in the absence of proteinuria when other specific symptoms are present.

**Objective:** What is the clinical impact of the use of three different new criteria for the diagnosis of preeclampsia and severe preeclampsia?

**Methods:** Retrospective cohort study of all pregnant women who gave birth in the Erasmus MC between 01-01-2014 and 01-01-2016. Hypertensive disorders of pregnancy (HDP) were defined when ≥2 times during pregnancy high blood pressure (≥140mmHg systolic and/or ≥90mmHg diastolic) was measured. All HDP cases were then classified according to the ISSHP 2001, ISSHP 2013/2014 and ACOG 2013 criteria.

**Results:** In our cohort (N=4395) 878 patients had HDP (20.0%). The ISSHP 2014/ACOG 2013 criteria cause a significant increase in patients with (superimposed) preeclampsia versus the ISSHP 2001 criteria, from 272 patients (6.2%) to respectively 360 (8.2%)/290 (6.6%) (p<0.001/p=0.001). This increase is due to non-proteinuric preeclampsia cases. Use of the ACOG 2013 criteria increases severe preeclampsia cases from 113 (2.3%) using ISSHP 2013 to 154 (3.5%) (p<0.001). Severe hypertension occurred less in pregnancies complicated by non-proteinuric preeclampsia (p<0.001/p=0.019). Prematurity, perinatal death and maternal complications were not different in pregnancies complicated by non-proteinuric or proteinuric preeclampsia.

**Discussion:** Implementation of the ISSHP 2014/ACOG 2013 criteria causes a shift from gestational hypertension and chronic hypertension towards (superimposed) preeclampsia (relative increase 10%/2%) and severe preeclampsia (4.6%). Since women with preeclampsia have an increased risk of developing cardiovascular disease later in life, we recommend further research into the course and prognosis of especially non-proteinuric preeclampsia.

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**Very preterm preeclampsia and treatment by heparin-mediated extracorporeal LDL-precipitation (H.E.L.P.) apheresis: The Freiburg Preeclampsia H.E.L.P.-Apheresis Study**

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**Objective:** Soluble Fms-like tyrosine kinase-1 (sFlt-1) is thought to be causative in the pathogenesis of preeclampsia (PE) and specific removal of sFlt-1 via dextran sulfate cellulose (DSC)-apheresis was suggested as a cure to allow for prolongation of pregnancy in preterm PE. However, in addition a deranged lipoprotein metabolism may impact endothelial and placental function in PE. Lipoprotein-apheresis by heparin-mediated extracorporeal LDL-precipitation (H.E.L.P.) was previously applied and has been shown to alleviate symptoms in PE. This clinical trial reevaluates the clinical efficacy of H.E.L.P.-apheresis in PE considering sFlt-1.

**Methods:** Open pilot study assessing the prolongation by H.E.L.P.-apheresis in 6 women (30-41 years) with very preterm PE (24+4 to 27+0 gestational weeks (GW)) (NCT01967355) compared to a historic control-group matched for GW at admission. Clinical outcome of mothers and babies, and pre- and post H.E.L.P.-apheresis levels of sFlt-1 and PI GF were monitored.

**Results:** In apheresis patients (2-6 treatments), average time from admission to birth was 15.0 days (6.3 days in controls; p=0.027). Lung maturation was induced in all treated cases, and all children were released in healthy condition. Apheresis reduced triglycerides and LDL-cholesterol by more than 40%. Although H.E.L.P.-apheresis
induced a transient peak, baseline levels did not change and rather stabilized sFlt-1 levels at pre-apheresis levels.

**Discussion:** Lipoprotein-apheresis proved again to be safe and prolongs pregnancies in PE. However, without changing sFlt-1 levels below baseline lowering lipids or other yet undefined factors appear to be of more relevance than reducing sFlt-1.

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**Is Home Blood Pressure Monitoring In Hypertensive Disorders Of Pregnancy Consistent With Clinic Recordings?**

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**OBJECTIVES**

To assess the agreement of home blood-pressure monitoring (HBPM) and office blood pressure measurements in a cohort of pregnant women with Hypertensive Disorders of Pregnancy (HDP).

**METHODS**

This was a cohort study at St George's Hospital. The inclusion criteria were chronic hypertension, gestational hypertension or high risk of developing preeclampsia, no significant proteinuria and no hematological or biochemical abnormalities. The blood pressure measurements at home and the corresponding hospital visit for that gestational age were coupled for analysis. Differences between home and office blood pressure measurements were tested using Wilcoxon signed rank test or paired t-test and they were also visually assessed with Bland-Altman plots. Subgroup analyses were performed in the following gestational age windows: <14 weeks, 15 to 22 weeks, 23-32 weeks and 33-42 weeks' gestation.

**RESULTS**

A total of 294 blood pressure measurements from 147 women were included in the analysis. The systolic HBPM measurements were significantly lower than office measurements [median (IQR): 132.0mmHg (123.0-140.0mmHg) vs 138.0mmHg (132.0-146.5mmHg), p<0.001]. When stratified according to gestational age, systolic measurements were significantly lower for all periods except at 23-32 weeks' gestation (p=0.057). The HBPM diastolic measurements were also significantly lower than office measurements [median (IQR): 85.0mmHg (77.0-90.0mmHg) vs 89.0mmHg (82.0-94.0mmHg), p<0.001]. When stratified according to gestational age, diastolic HBPM measurements were significantly lower for the periods 5-14 weeks (p<0.001), 15-22 weeks (p=0.008) and 33-42 weeks (p<0.001). The incidence of clinically significant systolic and diastolic hypertension using office blood pressure measurements were 4 times higher compared to HBPM measurements (p<0.001 and p=0.005, respectively).

**CONCLUSIONS**

HBPM has the potential to reduce unnecessary medical interventions in women with HDP, but this must be carefully weighed against the risk of increasing adverse outcomes. Prospective studies investigating the use of HBPM in pregnant women are urgently needed to determine the relevant thresholds and monitoring frequency.

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**Metformin for the prevention of hypertensive disorders of pregnancy in women with gestational diabetes and obesity: a systematic review and meta-analysis**

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**Objectives:** Metformin has been reported to reduce the risk of preeclampsia. It is also known to influence soluble fms-like tyrosine kinase-1 (sFlt-1) levels, which correlate significantly with the gestation of onset and severity of preeclampsia. The main aim of this meta-analysis was to determine whether metformin use is associated with the risk of hypertensive disorders of pregnancy (HDP).

**Methods:** MEDLINE, Scopus and the Cochrane Library were searched for relevant citations. Randomized controlled trials on metformin use, reporting the incidence of HDP were included. Studies on populations with a high probability of metformin use prior to randomization were excluded. Random-effects models with Mantel-Haenszel were used for subgroup analyses. Moreover, a Bayesian random-effects meta-regression was used to synthesize the evidence.
Results: In total, 3337 citations matched the search criteria. After evaluating the abstracts and full text review, 15 studies were included in the review. Metformin use was associated with a reduced risk of PIH when compared to insulin (RR: 0.56, 95% CI: 0.37-0.85, I² = 0, 1260 women) and a non-significantly reduced risk of preeclampsia (RR: 0.83, 95% CI: 0.60-1.14, 1724 women). When compared to placebo, metformin use was associated with a non-significant reduction of preeclampsia (RR: 0.74, 95% CI: 0.09-6.28). Metformin use was also associated with a non-significant reduction of any HDP (RR: 0.71, 95% CI: 0.41-1.25, I² = 0, 556 women) when compared to glyburide. When studies were combined with Bayesian random-effects meta-regression, the posterior probabilities of metformin having a beneficial effect for the prevention of preeclampsia, PIH and any HDP were 92.7%, 92.8% and 99.2%, respectively when compared to any other treatment or placebo.

Conclusions: There is a high probability that metformin use is associated with a reduced HDP incidence when compared to other treatments and placebo.

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Introduction: Preeclampsia contributes significantly to maternal and neonatal morbidity and mortality worldwide. Maternal folic acid supplementation is recommended peri-conceptionally for the prevention of neural tube defects. Research suggests an association between folic acid supplementation during pregnancy and a reduced risk of preeclampsia.

Objective: A systematic review and meta-analysis was conducted to review the evidence of an association between maternal folic acid supplementation during pregnancy and preeclampsia risk.

Methods: The protocol for this review was prospectively registered with PROSPERO (CRD42015029310). Multiple scientific databases and unpublished literature were searched for relevant studies. Two reviewers independently reviewed studies against a priori inclusion and exclusion criteria. Study data was extracted and quality of each included study assessed. Meta-analysis was conducted to examine the effect of maternal folic acid supplementation on preeclampsia risk. Sub-group analysis was used to explore any sub-group differences between folic acid taken alone or in/alongside a multivitamin, on preeclampsia risk.

Results: Meta-analysis of eight cohort studies showed a significantly lower risk of preeclampsia with folic acid supplementation in comparison to no folic acid (Odds Ratio = 0.78 [95% CI = 0.63 – 0.98]). Heterogeneity between studies was moderately high (I-squared = 67%). No significant subgroup difference was found between folic acid taken alone vs folic acid taken in or with a multivitamin on the risk of preeclampsia (Chi-squared = 0.34 (p = 0.56); I-squared = 0%).

Discussion: This systematic review and meta-analysis found a modest association between maternal folic acid supplementation and reduction in preeclampsia risk, however the overall level of available evidence for the association is low. Further, well-designed prospective studies investigating this relationship are required. These should clearly define the duration and regularity of supplementation, control for the presence of multivitamins, measure folate biomarkers to validate maternal self-report of supplementation, and differentiate between preeclampsia sub-types in their outcomes.

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Hypertensive Disorders of Pregnancy: Australian Population Data 2004-2013
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Introduction: Australia is a high-immigration country, with over a quarter of annual births to overseas-born mothers. How Australian hypertensive disorders of pregnancy (HDP) rates vary by country of birth (COB) is unclear.

Objective/hypothesis: 1) Examine Australian incidence of HDP by mother’s COB 2) Compare small-for-gestational-age (SGA) rates by HDP category using Australian birthweight charts and INTERGROWTH-21st fetal growth charts.

Methods: Population-based cohort study using all singleton birth records (Australian Perinatal Data Collection) 1 January 2004-31 December 2013. Hypertensive disorder status was categorized as no hypertension, pre-existing hypertension-only (EH), pregnancy hypertension-only (gestational hypertension and preeclampsia: GHIPE), and both pre-existing and pregnancy hypertension.

Results: Of 2.78 million singleton births, 72.8% had Australian-born mothers, 8.8% European, 2.9% Middle
Eastern/North African, 1.9% Chinese, 2.0% Indian, 1.2% Vietnamese, 1% Filipino, 4.7% other Asian, 4.6% other. For the 2.36 million (85%) where HDP status available, 5.9% had an HDP recorded: 4.9% GH/PE, 0.8% EH, 0.1% both. HDP varied substantially by maternal COB, from 2.1% in Vietnamese-born to 6.5% in Australian-born mothers. Chinese (2.3%), Middle-Eastern/North African (3.2%) and Indian-born (4.3%) mothers also had substantively lower HDP rates than Australian-born. Filipino-born (6.4%) did not. SGA rates were higher in women with HDP than without (p<0.001). These rates also varied substantially by which growth chart was used: Australian birthweight centiles 9.2% SGA if no HDP, 10.8% EH, 12.7% GH/PE, 13.7% both, INTERGROWTH-21st 3.5% SGA if no HDP, 5.6% EH, 7.4% GH/PE, 9.8% both. 

Discussion: HDP rates varied substantially by COB, and were more than double in Australian-born mothers than some immigrant groups. Reasons for this could include differing HDP risk-factor profile among immigrant populations. Rates of SGA at birth were higher in women with HDP than without, but varied substantially depending on whether birthweight or prescriptive fetal growth (INTERGROWTH-21st) charts were used, which has implications for clinical practice.

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The profile of early versus late onset preeclampsia-eclampsia at Kenyatta National Hospital: a retrospective cohort study
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Introduction
Pre-eclampsia, a major cause of maternal and neonatal morbidity and mortality can be classified as early (before or at 34 weeks) or late (after 34 weeks) onset. The clinical characteristics and outcomes of early onset preeclampsia-eclampsia (EO-PE) versus late onset pre-eclampsia-eclampsia (LO-PE) in low resource settings have not been previously described.

Objective
To compare the clinical characteristics and outcomes of early versus late onset pre-eclampsia-eclampsia.

Methods
Retrospective hospital records were examined for 620 women who received care for preeclampsia-eclampsia during pregnancy, labor and delivery or postpartum (≤12 weeks) at Kenyatta National Hospital between September 2015 and October 2017. Descriptive statistics and bivariate analysis were conducted using Stata® 13.

Results
Out of 620 records reviewed, 44% (n=273) exhibited EO-PE while 56% had LO-PE, 126(23%) were referred from other facilities. Women with EO-PE were likely to be younger (mean 29.2, Standard deviation (SD) 6.11 years) compared to those with LO-PE (mean 27.8 years, SD 6.34 years; p < 0.008). Compared with LO-PE, EO-PE was associated with greater odds of severe preeclampsia (OR2.63; 1.73-3.71; p<0.001), including HEEELLP syndrome (OR: 2.63; 11.99-10.19; p<0.001), renal dysfunction (OR: 3.46; 2.16-5.62 p<0.001), still births (OR=4.96; 3.10-8.05; p<0.001) and neonatal death (OR: 8.51; 3.82-21.37; p<0.001). Neonates born after EO-PE had increased odds of respiratory distress (OR=16.99; 9.02-32.28; p<0.001) and birth asphyxia (OR: 1.89; 0.70 - 4.79; p<0.142). The result further shows that EO-PE was associated with higher odds of prolonged maternal hospitalization beyond 7 days (OR=5.76; 3.94-8.42; p<0.001) and antepartum hemorrhage (OR=5.80; 1.14 -56.40; p<0.001).

Discussion
Early compared to late onset pre-eclampsia is more severe and is associated with greater odds of adverse maternal and perinatal outcomes compared in low resource settings. There is need to improve awareness to improve early detection among pregnant women.

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Using blood pressure Self-monitoring in pregnancy: A systematic review and individual patient data meta-analysis
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Introduction: Hypertensive disorders during pregnancy result in substantial maternal morbidity and are a leading cause of maternal deaths worldwide. Self-monitoring of blood pressure might improve the detection and management of hypertensive disorders of pregnancy but few data are available, including regarding appropriate thresholds.

Objective: This systematic review and individual patient data analysis aimed to assess the current evidence regarding differences between clinic and self-monitored blood pressure through pregnancy.

Methods: MEDLINE and ten other electronic databases were searched for articles published up to and including July 2016 using a strategy designed to capture all the literature concerning self-monitoring of blood pressure during pregnancy. Investigators of included studies were contacted requesting individual patient data: self-monitored and clinic blood pressure and demographic data.

Results: Twenty one studies that utilised self-monitoring of blood pressure during pregnancy were identified. Individual patient data from self-monitored and clinic readings were available from seven plus one unpublished paper (eight studies, n=758) and two further studies published summary data. Analysis revealed a mean self-monitoring - clinic difference of ≤1.2mmHg systolic BP throughout pregnancy, though there was significant heterogeneity (difference in means I²>80% throughout pregnancy). Although the overall population difference was small, though levels of ‘white coat hypertension’ were high, particularly towards the end of pregnancy.

Discussion: The available literature includes no evidence of a systematic difference between self and clinic readings, suggesting that appropriate treatment and diagnostic thresholds for self-monitoring during pregnancy would be equivalent to standard clinic thresholds.

Reversible cerebral vasoconstriction syndrome associated with pregnancy in peripartum period
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Introduction
Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by reversible multifocal narrowing of the cerebral arteries, generally preceded by thunderclap headaches with or without associated neurological deficits. RCVS develops a unique set of clinical imaging. Though RCVS is typically considered benign and self-limited disease, some reports showed that the patients with RCVS had a higher proportion of non-benign outcomes. Here, we present 6 cases of RCVS associated with pregnancy.

Methods
Patients were retrospectively identified at TOYOTA Memorial Hospital, from 2010-2017. We diagnosed RCVS based on the presence of reversible vasoconstrictions of cerebral arteries in magnetic resonance angiography (MRA) and neurological symptoms in peripartum period. These vasoconstrictions disappeared in the follow-up MRA within 3 months. Clinical course of these patients were collected.

Results
The average age was 36.8 years old and 4 patients were primipara. Four patients were complicated with preeclampsia or eclampsia. Headache was the initial symptom in 3 patients and only 1 patient developed typical thunderclap headache. Four patients developed RCVS in peripartum period, and 2 patients in postpartum period. Intracranial hemorrhage and non-aneurysmal subarachnoid hemorrhage were detected in 1 patient respectively and PRES was detected in 3 patients. Magnesium sulfate was administered in 2 patients who presented with convulsion related to intracranial hemorrhage or eclampsia. No patient developed neurological sequela after the resolution of vasoconstrictions.

Discussion
Frequency of a typical thunderclap headache is relatively low in RCVS associated with pregnancy. RCVS can be associated with PRES and eclampsia closely. Prompt recognition and early imaging studies are essential for the diagnosis of RCVS associated with pregnancy.
Introduction
Hypertensive disorders of pregnancy (HDP) complicate approximately 10% of pregnancies worldwide. Limited data exists about the information needs of women with HDP.

Objective/Hypothesis
To identify the information needs of women with HDP.

Methods
We analyzed retrospective data, covering July 2013 to March 2017, from The Preeclampsia Registry (TPR), an online survey hosted by the US-based Preeclampsia Foundation. Participants access and enroll in TPR via social media and web searches. We restricted our analysis to women who self-reported a history of HDP and responded to the open-ended question, “Is there any information that you could have had at the time of this pregnancy that would have been helpful?” Narrative responses were coded, reconciled, and thematically analysed by multiple coders using an inductive approach.

Results
Of 3,285 participants enrolled during the study period, 898 (27%) completed the survey, self-reported a history of HDP, and responded to the open-ended question. Participants were from the United States (86%) and from 27 other countries. Most participants (85%) were not satisfied with the information they received. About 23% were completely unaware of HDP. Participants specified they needed information about symptoms (25%), causes (9%), and long-term complications (3%) of HDP. They also felt ill-informed about postpartum HDP (4%) including its prevalence, symptoms, and treatment. Among these participants, 60% indicated they were unaware HDP could occur postpartum. Finally, 17% indicated disappointment in the quality of their provider or care received, mostly due to inadequate communication about their symptom experiences and feeling that their illness concerns were dismissed.

Discussion
Most women with a history of HDP in our analysis were not satisfied with the information they received. Unfamiliarity with HDPs, desire for greater knowledge, and poor provider-patient communication and relationship, present opportunities for patient and provider education.

Severe hypertension and maternal organ involvements were closely related in the disease of hypertensive disorders of pregnancy.
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Purpose: Severe hypertension (sevHT, over 160/110mmHg) is supposed to be pathogenesis of maternal organ involvements in the disease of hypertensive disorders of pregnancy. It remains that to what extent each target organ is to be damaged in sevHT.

Methods: 2746 pregnant women managed in our tertiary perinatal center from 2013 to 2016 were entered in this study retrospectively. All cases with sevHT were managed expectantly in the same antihypertensive protocol. Disease type was defined by restrictive criteria in irrespective of organ involvements.

Result: 192 cases of 2746 found sevHT and 91 cases was in antepartum (AP), 90 in intrapartum (IP) and 21 in postpartum (PP). 9 cases (11%) of 91 cases in AP showed gestational hypertension (GH), 47 (58%) preeclampsia and 22 (27%) preeclampsia superimposed on chronic hypertension (PES). 11% of GH in AP, 58% of PE in AP, 41% of PES in AP, 11% in IP and 29% in PP complicated with organ involvements. HELLP related involvements such as elevated liver enzymes, low platelets count or renal impairment were observed in 34% of PE in AP, 27% of PES in AP and 14% in PP. Hyperpermeability involvements such as pleural edema or massive ascites were diagnosed in 9% of PE or PES in AP. About CNS involvements, eclampsia were observed in 4% of PE in AP, cerebral vascular
spasms 6% of PE in AP, 5% of PES in AP, 1% in IP and 14% in PP.
Conclusions: SevHT found in 7% (192 of 2746). CNS involvements found 9% of preeclamptic disease. HELLP related involvements related to the preeclamptic disease. Hyperpermeability involvements had even 11% in GH in preeclamptic disease. We showed maternal organ involvements were closely related with preeclamptic disease with sevHT. Also hyperpermeability involvements related with GH with sevHT. In discussing non-proteinuric preeclampsia, hyperpermeability disorders play important role.

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Circadian rhythm does not influence the secretion of melatonin in pregnant women
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Introduction: Melatonin is vital for pregnancy success. Reduced levels of melatonin are seen in the pregnancy disorder preeclampsia. In non-pregnant individuals melatonin is mainly produced in a circadian regulated fashion by the pineal gland, during pregnancy the human placenta also produces melatonin which reaches a peak at term. The melatonin levels in pregnant women are twice that of non-pregnant women. Interestingly it has been reported that there were no difference in melatonin levels in pregnant women between daytime and night time at delivery. Whether the increased maternal melatonin is produced by placenta or pineal gland has not been investigated.

Objectives: In this study we investigated melatonin levels in healthy pregnant women during the day.

Methods: Blood samples from 22 healthy pregnant women were collected at 6:00am, 12:00am, 6:00pm and 12:00pm at term (>37 weeks) before delivery and within 48 hours after delivery. Additional blood samples from 26 healthy pregnant women were also collected at the time of delivery. Serum melatonin levels were measured using ELISA (LifeSpan BioSciences, USA).

Results: The maternal melatonin levels at 6:00am or 12:00am or 6:00pm or 12:00pm before delivery ranged from 446pg/mL to 496pg/mL. There was no difference in melatonin levels among the four different time points before delivery (p>0.05, ANOVA). However, the averaged maternal melatonin levels after delivery was 522pg/mL at 12:00pm, which was significantly higher than that at 6:00am (448pg/mL), 12:00am (422pg/mL), or 6:00pm (418pg/mL) (p<0.001). There was no difference in the maternal levels of melatonin among other three time points after delivery (p>0.05, ANOVA). Furthermore, there was no difference in melatonin levels at delivery between daytime (6:00am to 10:00pm) and night-time (10:00pm to 6:00am).

Conclusions: Our study demonstrates that the maternal melatonin levels remain constant throughout the day rather and are not regulated by circadian rhythms during pregnancy.

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Evaluation of the PIERS on the MOVE mobile health tool for pre-eclampsia triage: the users' perspective
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Background
The PIERS on the Move (POM) mobile health (mHealth) application was implemented as part of a complex community health system intervention in the CLIP (Community Level Interventions for Pre-eclampsia; NCT01911494) Trials. In this context, community health workers (CHWs) were trained to use the app and to take on new clinical skills, such as measuring blood pressure and assessing symptoms.

Objective
To evaluate the perceived impact on pre-eclampsia knowledge, self-efficacy and CHW role from use of the POM app.

Method
This study used mixed methods including closed and open-ended survey questions and focus group discussions (FGDs) based on the SALT (Stimulate, Appreciate, Learn, Transfer) approach. All health care workers who participated in the CLIP Trials in Pakistan and India were eligible to participate. A random sample, stratified by age and years of experience, was drawn to target participants for qualitative evaluation after completion of recruitment for the Trials. Survey results were summarized and qualitative data analyzed using grounded theory.

Results
In India, 24 CHWs completed the survey and were interviewed. In Pakistan, 219 CHWs completed the survey and
18 participated in 3 follow-up FGDs. CHWs in both countries reported a high level of pre-eclampsia knowledge and self-efficacy. Qualitative data analyzed from the interviews in India and FGDs in Pakistan indicate a high level of job satisfaction with themes emerging related to positive ability to manage pregnancy complications; happiness with supporting healthy pregnancy and birth and satisfaction with new knowledge and responsibilities. Challenges reported included initial difficulties learning to use a smart phone and technical issues with the device itself (battery life and screen size).

Conclusions
This study supports the ability and desire of community health workers to use mobile health tools such as the PIERS on the Move app to support their performance of clinical tasks related to pre-eclampsia care.

Implementation of the PIERS on the Move mobile health app in the Community Level Interventions for Pre-eclampsia Trials
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Background
The PIERS on the Move (POM) app was implemented as part of a complex health system intervention in the CLIP (Community Level Interventions for Pre-eclampsia; NCT01911494) Trials in India, Pakistan and Mozambique. POM guides community health workers through an antenatal/postnatal assessment and provides recommendations for referral to a nearby facility with immediate treatment with MgSO₄ and methyldopa when hypertension is detected, based on disease severity.

Objective
To evaluate the implementation of the POM app based on population coverage, compliance and recommendation acceptance.

Methods
As per the protocol, coverage was measured as the proportion of women receiving one or more POM home visit out of all pregnancies registered in the intervention area and compliance was measured as the proportion of women receiving the minimum standard of monthly POM home visits. Acceptance of recommendation and was summarized and rates of outcome for women in intervention areas with and without a recommendation presented.

Results
In total 21,416/36,077 eligible women received 151,893 POM visits (76.2% antepartum, 23.8% postpartum) during the CLIP Trials. Coverage was 90.0% in India, 56.6% in Pakistan and 61.2% in Mozambique. Compliance rates were 55.4% in India; 63.4% in Pakistan; and 77.0% in Mozambique. Rate of triage recommendation was 5.6% (1,194/21,416) of the covered population in total. The primary reason for referral was non-severe hypertension. Women's acceptance of recommendations was 77.0% overall. In intervention clusters, the rate of adverse maternal outcomes in women who received recommendations compared to those who did not was higher in India (11.7% vs 4.3%) and Mozambique (11.3% vs. 7.7%) but similar in Pakistan (5.0% vs. 5.0%).

Conclusion
During the CLIP Trials there was good coverage and compliance and a high rate of community acceptance of triage recommendations after implementation of the POM app but limited apparent impact on maternal health outcomes.

A qualitative inquiry into women's preferences for treatment of hypertension in pregnancy.
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Background
National and international clinical practice guidelines recommend two treatment approaches for management of pregnancy hypertension: ‘less tight’ control aiming to minimise antihypertensive therapy, and ‘tight’ control aiming to normalise blood pressure (BP). Consistent with prior small trials, the CHIPS trial (Control of Hypertension In Pregnancy Study) found that ‘tight’ (vs. ‘less tight’) control was associated with lower maternal risk without an
increase in perinatal risk. However, treatment choice should reflect both evidence and women’s values, yet, information on the latter is lacking.

**Objective**
The study aimed to develop an understanding of what women value when choosing a treatment approach for hypertension in pregnancy.

**Methods**
A qualitative approach was used. Semi-structured focus groups and individual interviews were conducted in an iterative fashion, with memoing and debriefing after each group or interview. All interactions were transcribed for thematic analysis grounded in a critical realist perspective. Codes were developed inductively and collected into themes that were reviewed with the research team for face validity.

**Results**
Thirteen women participated in two focus groups and five individual interviews. Thematic analysis yielded four themes:

- Individualized information. Participants emphasized individualized information and doubted “average” information.
- Understanding of pregnancy. Many participants understood pregnancy as a time-limited situation emphasizing infant health during pregnancy and delaying maternal health concerns.
- Medication drives preference. Participants varied significantly in willingness to take medication, and desire to avoid medication often drove treatment preference.
- Short- vs. long-term risks. Most participants prioritized long-term risks over short-term risks.

Additionally, seven attributes were identified as important to consider: likelihood of medication, and caesarean delivery; and risk of severe hypertension throughout pregnancy, preeclampsia, infant being born small for gestational age, and delivery before 34 weeks.

**Discussion**
Next steps will be applying these preferences to: (1) determine how patients make trade-offs between attributes; and (2) develop patient-oriented clinical endpoints.

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**PREDICTING MATERNAL MORBIDITY IN HYPERTENSİON IN PREGNANCY WITH THE 'SHRUNKEN PORE SYNDROME' RATIO FOR OPTIMAL TIMING OF DELIVERY**

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**Introduction:** Hypertension in pregnancy is still associated with a considerable risk of severe maternal morbidity due to difficulties in appropriately timing delivery. Timing based on gestational age alone or already manifest progression of maternal disease has proven to be too blunt an instrument to prevent maternal morbidity.

**Objectives:** Our aim was to evaluate a previously described marker of glomerular endothelial damage, the “shrunken pore syndrome ratio”, to determine whether women with hypertensive disorders of pregnancy should be considered low-risk or high-risk for developing maternal complications if delivery is delayed.

**Methods:** Women admitted to the perinatal ward at the Skane University Hospital in Lund during the year of 2016-09-01 to 2017-08-31 under the diagnosis of hypertension in pregnancy were invited to join the study. After delivery and discharge from the hospital all registered measures of renal function were analysed.

A cut-off of 0.60 was used to distinguish high-risk women from low-risk women. A “shrunken pore syndrome ratio”, SPS-ratio, of 0.60 or less was considered to define high risk for maternal complications, since this ratio reflects a reduction in the glomerular pore size, previously associated with endothelial damage.

**Results:** We included 61 patients in the study, of which two were excluded due to chronic hypertension, and one due to delivery before samples were taken. Of the remaining 58 patients 13 were defined as low-risk women according to the SPS-ratio of which only one (7.7%) developed severe maternal disease. Among the 45 high-risk women 18 women (40%) developed serious disease whereas 27 (60%) could avoid complications.

**Discussion:** The SPS-ratio seems promising as a predictive marker for maternal morbidity and its performance as a tool in the monitoring of progressing disease should be evaluated further for an improved management. With delivery before the SPS-ratio decreases to or below 0.60 maternal complications might be avoided.
Optimising the monitoring and management of raised blood pressure during and after pregnancy - developing an self-monitoring intervention in the English NHS
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Introduction
Raised blood pressure (BP) is a common problem in pregnancy and may develop into pre-eclampsia in the presence of proteinuria or other metabolic changes. Raised BP and pre-eclampsia affect about one in ten women and are a major cause of death and prematurity birth worldwide. While maternal deaths from pre-eclampsia in the UK are lower than ever, there is still room for improvement in detecting and managing hypertensive women in pregnancy. Asking women to self-monitor their own blood pressure might improve outcomes. Pilot work has suggested that, with support from midwives and doctors, it is possible for women to monitor BP and urine safely, potentially identifying problems earlier and controlling BP better. We aimed to develop a comprehensive self-monitoring interventions for a full trial.

Methods
Focus groups and interviews were undertaken with NHS staff (obstetricians, community and hospital midwives). We conducted ‘think alouds’ with women talking through their experiences of using a self-monitoring app and the trial materials.

Results
Focus groups and interviews were conducted with 144 NHS staff (obstetricians, community and hospital midwives, GPs, trainees, pharmacists and healthcare assistants) at seven different hospital sites. Areas important to staff included: providing clear patient information as BP in pregnancy is a complex phenomenon and not the only indicator of pre-eclampsia; concerns about the use of validated monitors and reliability of readings; supporting staff in decision-making in the context of discrepant readings.

Discussion
Our analysis suggests SMBP will be welcomed by staff, while highlighting potential barriers. This has helped develop user-friendly, accessible patient-facing materials. A large multi-centre, randomized-controlled trial, underpinned by theories of behaviour change, is now underway in the UK to determine the usefulness of SMBP in the detection and management of raised BP during pregnancy.

Why do we have too many caesarean sections in Brazil, even in patients with pre-eclampsia?
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Introduction: Hypertension in pregnancy, especially pre-eclampsia (PE), may result in maternal and perinatal complications and the best form of treatment is the interruption of gestation through the safest method for the mother and baby. In Brazil, there are high rates of Cesarean (CS) among patients with PE. Would it be possible to change these routines to reduce risks and costs associated with the actual patterns of care?

Objective: To assess the type of delivery in patients with PE in a public maternity in Sao Paulo (Brazil) and propose changes in this pattern.

Methodology: Retrospective Cohort of 117 patients with PE treated in a reference center (MEVNC) in 2016 and 2017. Maternal variables were assessed and related to childbirth and perinatal period. Baseline characteristics and labor and delivery characteristics according to PE early and late were analyzed.

Results: The average maternal age was 29.0 years, 51.3 being nulliparous and the BMI average was 29.1. Mild PE was present in 85.0%. The overall cesarean rate was 32.0%. Among patients with early PE the rate was 72.0% while in patients with late PE the rate was 77.0%. The reasons for CS were maternal risk in 30.7% and fetal risk in 22.7%.

Discussion: The overall rate of CS of the institution being on average, 34%. However in patients with PE CS rates
are very high. Our results contrast with the literature, when compared with different places. Two aspects could be considered: insecurity related to maternal prognosis and the difficulties of assessing fetal well-being. Two interventions could be tested to modify this pattern: the adoption of the model PIERS for maternal care and fetal monitoring for fetal scalp samples for pH and lactate evaluation. In this way, the introduction of these alternatives could innovate the current standard of clinical practice.

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Casual and home blood pressures measuring for epidemiological study among pregnant women: The TMM BirThree Cohort Study
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Introduction: We previously reported that blood pressure measured at clinic during antenatal care is higher than that measured at home. However, it is still unknown if blood pressure measured not under medical environment but under research environment is different from that measured at home.

Hypothesis: We hypothesised that blood pressure measured at epidemiological research centres is not much higher than that measured at home.

Methods: We used the data of 1,940 pregnant women who participated in the Tohoku Medical Megabank Birth and Three-Generation Cohort Study (the BirThree Cohort Study), which is conducted in Japan. The BirThree Cohort Study invited pregnant women to our research centres for measuring casual blood pressure twice at each visit. Participants visited the centre once or twice in total during pregnancy. The BirThree Cohort Study also asked pregnant women to measure blood pressure at home in the morning for a week if the participants agreed to measure that. The difference between casual blood pressure and home blood pressure was calculated individually first, and then the mean of the difference among all participants was calculated on each of the first, second and third trimesters.

Results: The mean systolic/diastolic casual blood pressures were 100.1±13.1/63.1±9.3mmHg at the first trimester, 103.6±9.0/61.4±7.6mmHg at the second trimester, and 105.3±8.9/63.1±7.8mmHg at the third trimester. As for home blood pressure being available on 895 pregnant women, 108.6±8.9/66.4±8.5mmHg at the first trimester, 104.0±9.7/61.0±6.9mmHg at the second trimester, and 106.9±9.8/63.2±7.5mmHg at the third trimester were observed. The difference between mean casual and home blood pressures at each trimester were: 1.7±11.9 mmHg, -0.3±7.6 mmHg, and -1.7±8.2 mmHg.

Discussion: Although the number of pregnant women among each trimester was disproportionate, the difference between casual and home blood pressures was small. Even casual blood pressure was tended to be smaller than home blood pressure after the second trimester.

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The Great East Japan Earthquake and hypertensive disorders of pregnancy: The TMM BirThree Cohort Study
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Introduction: We experienced a devastating disaster, the Great East Japan Earthquake, in 2011. Some previous studies showed that disasters affected maternal blood pressure and their health. Its longer effect on pregnant women is necessary to investigate.

Objective: The purpose of this present study was to investigate if maternal disaster exposure affected their blood pressure.

Methods: The relationship between disaster exposure and maternal outcomes was retrospectively analyzed using the data of 4,426 women who were recruited to the Tohoku Medical Megabank Birth and Three-generation Cohort Study, which was conducted in the years 2013 to 2017. Women were classified into three groups by the severity of the destruction of their house: group A, no destruction/did not live in the disaster-hit area; group B, half/a part of the house was destroyed; and group C, house totally/mostly destroyed. Multiple logistic regression analysis was
performed to investigate the relationship between disaster exposure and hypertensive disorders of pregnancy, adjusting for body mass index, age, smoking, drinking, income, parity, and multiple pregnancy.

**Results:** Of 4,426 women eligible for the analyses, the houses of 489 women (11.0%) were totally or mostly destroyed, and the houses of 1,706 women (38.5%) were half or partly destroyed. Those whose houses were not destroyed or did not live in the area affected by the disaster included 2,231 women (50.4%). The prevalence of hypertensive disorders of pregnancy in groups B and C were 0.82 and 1.47 times higher than in group A, but there was no statistical significance.

**Discussion:** Involvement in a disaster event about three to six years before pregnancy was not related to a higher prevalence of hypertensive disorders of pregnancy.

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**Prescription of Antihypertensive Drugs in Pregnancy: a study based on health insurance claims data**

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**Introduction:** Hypertensive disorders of pregnancy occurs in 5-10% of pregnant women, but information about antihypertensive drugs prescribed to patients with hypertensive disorders of pregnancy is limited.

**Objective:** To clarify the prescription of antihypertensive drugs to pregnant women based on claims data.

**Methods:** Based on health insurance claim (claims) data at the Japan Medical Data Center, data were extracted about pregnant women with a hypertension-related diagnosis (ICD-10 classification: O10-O16) during pregnancy between January 1, 2008 and May 31, 2010. Information about gestational age and start date of medical care in claims for the mothers was extracted, and based on diagnostic information related to labor and delivery/miscarriage and records of treatment, pregnancy duration for each woman was estimated. Information on drug prescriptions during pregnancy was extracted from medical records or records of dispensed prescriptions.

**Results:** From among 2173 pregnant women, information about prescription status during the entire pregnancy could be obtained for 567 women, and of these, 160 women (28%) had been prescribed an antihypertensive drug during pregnancy. The most frequently prescribed antihypertensive drug was nifedipine tablets/capsules (41%), followed by methyldopa tablets (27%) and hydralazine HCl powder/tablets (22%). In addition, diuretics were used in 33%, and renin-angiotensin system drugs were used in 3% of cases.

**Discussion:** Safety has not been established for many of the antihypertensive drugs prescribed to women with hypertensive disorders of pregnancy based on our study results. This suggests an urgent need to establish a safety evaluation system for these drugs in Japan.

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**Sociodemographic profile of pregnant women affected by preeclampsia**

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**Introduction:** Preeclampsia (PE) causes morbidity and mortality in several women in the productive phase, including definitive sequels. Recognizing the socio-demographic profile of pregnant women may justify the allocation of resources to promote an effective care for this population.

**Objective:** To describe the socio-demographic profile of pregnant women diagnosed with preeclampsia.

**Method:** Retrospective study of medical records of 98 patients. Place: Hospital Guilherme Álvaro Santos / Brazil, (from May 2017 to April 2018). Variables analyzed: Previous history of systemic arterial hypertension (SAH) and preeclampsia, first-degree relative with SAH, recreational drug use, cohabitation with the partner, preeclampsia, employment status, years of schooling, average number of pregnancies and body mass index (BMI). For all the information in the sample, a description of the data was made through numerical means and descriptive measures of variables with the intention of searching for clues about the behavior of the phenomena studied. The study has ethical approval.

**Result:** We identified that 53.1% had previous SAH; 29% reported a history of preeclampsia; 83% had first-degree relative with SAH; 19% used recreational drugs; 32% lived with partner; 38% were unemployed. How many means: the time of schooling was of 10.23 years; that of pregnancies of 2.27 previous; and the BMI of 31.93 (obesity).
Discussion: These data suggest that it is necessary to create strategies for reproductive planning access for this population because several women were in the third gestation and advised of the risks identified in their own history as relatives with SAH. Avoiding additional complications due to drug use, especially among obese women, hypertensive and with a history of pre-eclampsia and that these guidelines need to be reinforced also by low education. These aspects can be recognized by the anamnesis itself, which can optimize resources and optimize financial resources.

ASPECTS OF INITIAL CLINICAL EVALUATION OF THE PREGNANT WOMAN WITH PRE-ECLAMPSIA

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Introduction: Current diagnostic criteria for pre-eclampsia include organic dysfunctions. Recognizing predictive signs of complications in the initial clinical evaluation could optimize resources guiding care strategies. Objective: To describe the status of pre-eclampsia patients in the initial evaluation by clinical and laboratorial parameters. Methods: Retrospective study approved by Ethics Committee. Location: Guilherme Álvaro Hospital, Santos, São Paulo/Brazil; (May 2017 - April 2018). Inclusion: 85 patients with pre-eclampsia, according to NHBPEP (2000) criteria. Analyzed Variables: Gestational age and severe admission complications, pressure values, symptomatology (visual, headache, epigastralgia) and medication use. For the sample's information, numerical means and descriptive measures were used. Results: The means of gestational age was 31.7 weeks, systolic and diastolic blood pressures 137.51 and 83.34 mmHg respectively and weight 91.67 kg. 18.8% of urine dipsticks tests were negative or trace. The symptomatic evaluation, 11.8% was visual (scotoma), 21.2% headache and 12.9% epigastric pain. For medication, 23.5% used Acetylsalicylic acid (ASA), 89.4% methylidopa and 28.2% corticosteroid. About 1.2% of the patients presented placental abruption, 1.2% eclampsia and 5.9% thrombocytopenia as severe complications at admission. No fetal or maternal death occurred in the current analyzed population. Discussion: Early clinical evaluation may demonstrate the potential risk of prematurity associated with pre-eclampsia, once the mean of gestacional week was 31 weeks. A considerable fraction of the analyzed women presented obesity and serious clinical expressions of pre-eclampsia, although approximately 20% was not recognized by the initial proteinuria test screening. An expressive amount of the patients used ASA, without a characterization about the use. Most patients used at least one hypotensive agent, which could be an exaggerated expectation for these drugs. Although just a few patients presented serious complications these risks should not be neglected, mainly the thrombocytopenia. We also observed that some clinical-laboratory data can guide actions since the admission of the pregnant woman.

Contextualizing care for women with pre-eclampsia and eclampsia in Ethiopia: exploring policy and implementation environments

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Background: Effective management of pre-eclampsia and eclampsia (PE/E) depends how policy environments relate to health service delivery interfaces. Less known is how these contextual factors intersect with the lived experience of care provision and use.

Objective: To explore the policy and health systems environment around PE/E to improve care provision and use in Ethiopia.

Methods: Institutional ethnography was used to assess viewpoints across multiple primary data sources (n=95) and a desk review of peer-reviewed publications and maternal health-related textual guidelines and policies (n=43). In-depth interviews were conducted with women who experienced pre-eclampsia (n=17), health extension workers (n=17), health workers (nurses/midwives/doctors) (n=22), and policymakers and stakeholders at kebele, woreda, zonal, regional and national levels (n=21). Sixteen focus group discussions engaged men and women of reproductive age in select areas.

Results: Despite a progressive maternal health policy environment around task shifting and expanding service access, including to PE/E care, there remains ambiguity of provider roles in PE/E diagnosis and management. No document delineates cadres to administer the loading dose of magnesium sulphate (MgSO4) or antihypertensive
Drugs nor details pre-referral care and referral processes sufficiently. All respondents describe the visibility of guidelines and protocols in facilities influence care provision. Downstream effects of professional practice norms, supervisory structures, and provider abilities manifest in the lack of confidence among providers at all levels of the health system to administer MgSO$_4$. Supply chain bottlenecks limit the use of essential PE/E drugs and commodities at health centers and health posts, curtailing providers’ ability to manage and refer women in a timely way.

**Conclusions**: A health system’s ability to effectively manage pre-eclampsia and eclampsia depends on various contextual factors, including an amenable policy environment, supportive health worker practice norms, and supply chain functioning. Factor confluence has implications for quality of care and outcomes experienced by women with PE/E.

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**Chronic hypertension and pregnancy: what is the quality of francophone websites?**

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**Objective**: To evaluate the quality of francophone-oriented-patients websites about chronic hypertension and pregnancy.

**Methodology**: Three instruments were used by 4 assessors to evaluate 12 most browsed websites. The first instrument evaluates the readability for a patient, the pictorial outlook and gives a general evaluation (3 questions, total score range 0-9). The second instrument judges the quality and quantity of information provided by each website, according to a pre-established list of items concerning health habits, medications, maternal and neonatal complications, postpartum evolution and breastfeeding (35 items, total score range 0-105). The third instrument, the Discern instrument, assesses the reliability and the quality of information about pharmacologic treatments (16 questions, total score range 16-80). Agreement between the observers was analysed with the Kendall coefficient of concordance (p<0.05).

**Results**: Six websites were affiliated with medical journals or associations, 2 with media providers, 2 with web providers, 1 with a health care provider and 1 was commercial. Five websites were considered suitable for non-medical readers and only 3 had a favorable general evaluation. None of the websites obtained a score of at least of 50 (for a maximum score of 105) for their content with the second instrument. The Discern instrument, assessed the reliability and the quality of information about pharmacologic treatments (16 questions, total score range 16-80). Agreement between the observers was analysed with the Kendall coefficient of concordance (p<0.05).

**Conclusion**: French-speaking people have access to very poor quality websites to gather information about chronic hypertension and pregnancy.

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**Challenges to using antihypertensive drug during pregnancy by primary health care provider in primary and secondary level facility in Bangladesh**

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Background: One of the most life threatening condition for pregnant women is hypertensive disorder in pregnancy. In Bangladesh, pre-eclampsia and eclampsia causes 20% of death, the second largest cause of maternal mortality. The correct knowledge of primary health care providers (PHCs), who are the first contact point for antenatal care (ANC) clients, are important to detect and manage hypertension in pregnancy.

**Objectives**: We examined primary health care provider’s knowledge and current management practices to identify and treatment of hypertensive disorders in pregnancy.

**Methods**: This is a cross sectional study. A semi-structured questionnaire survey was conducted among primary health care providers those are provided services at primary level from May to June 2017 in 4 upazilla of Comilla and Tangail District. Total 101 primary health care providers including Family Welfare Visitor (FWV), Sub Assistant Community Medical Officer (SACMO) and Nurses were interviewed. Data entry was conducted using CSPro and analysis was conducted using stata software version 12.0.

**Results**: More than 90% primary health care providers clearly define the sign/symptoms and consequences of pre-eclampsia/eclampsia. Only 30% primary health care providers clearly classify the hypertensive disorders in
pregnancy. 54% PHC provider said, it is difficult to identify hypertension in the facility due to 37% service provider did not measure blood pressure. 80% FWV/Nurses and 90% SACMO heard about alpha-methylidopa as an anti-hypertensive drug during pregnancy. FWV/Nurse and SACMO have idea about Labetelol (18% vs. 8%) and Nifedipine (6% vs. 11%) and almost all of the service provider did not know about the proper dose and time schedule of use.

Discussion: This study found gaps in knowledge regarding classification of hypertensive disorders in pregnancy, anti-hypertensive drugs, dose and schedule. PHC providers should equipped with the appropriate knowledge, skills and training for the management of hypertension in pregnancy.

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Is longer admission to delivery for expectant management in Pre-eclampsia associated with increased risk of maternal outcomes?
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Introduction: Gestational age (GA) of pre-eclampsia onset is of clinical importance and affects management. Expectant management has been recommended for preterm pre-eclampsia to improve perinatal outcomes. However, prolonged pregnancy could expose the mother to higher risk of adverse outcomes.

Objective/hypothesis: We sought to compare characteristics of women admitted with pre-eclampsia at different GAs and examine whether longer admission to delivery is associated with higher rates of adverse maternal outcomes.

Methods: Data used for this study were derived from the fullPIERS prediction model external validation cohort, which included 2427 women admitted with pre-eclampsia, diagnosed according to the SOGC. The data were collected from 2003 to 2016 from tertiary hospitals in Canada, United Kingdom, Finland and USA. Demographic characteristics, clinical management practices and rates of adverse outcomes for women admitted with preterm pre-eclampsia (i) before 32 weeks, (ii) between 32 and 33+6 weeks and (iii) between 34 and 36+6 weeks) and were compared with (iv) term pre-eclampsia (> 37 weeks’ gestation). The odds of experiencing adverse maternal outcomes with increasing admission to delivery interval was calculated.

Results: Majority of the women (46.4%) had term pre-eclampsia (Table 1). In general, women with preterm pre-eclampsia appeared to be younger, have multiple pregnancies and more likely to smoke compared with term pre-eclampsia. Women with preterm pre-eclampsia were also more likely to be administered treatment (corticosteroids, Magnesium sulphate and antihypertensive therapy). Longer admission to delivery was associated with a higher rate of adverse outcomes (OR 1.02 (95%CI: 1.00-1.03) although this association was non-significant after adjusting for GA at admission (ORadj: 1.0 (95%CI: 0.98-1.01) as well other demographic factors.

Discussion: Our findings supports reports that women with early-onset pre-eclampsia have significantly worse maternal and perinatal outcomes despite receiving more interventions. However, the higher rates of maternal outcomes were not associated with longer admission to delivery interval.

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Comparison of management of women admitted with preterm pre-eclampsia between AlerePETRA and Non-AlerePETRA groups in the fullPIERS external validation data
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Introduction: There is uncertainty regarding expectant management of pre-eclampsia especially on administration of antenatal corticosteroids and prolongation of pregnancy. Management often varies depending on location and associated guidelines, even among high-income countries.

Objective/hypothesis: To compare management of women admitted with pre-eclampsia in the PETRA site (USA) versus non-PETRA sites (Canada, UK and Finland) according to a risk prediction probability (fullPIERS) for women admitted with pre-eclampsia.

Methods: We used data derived from the external validation dataset of the fullPIERS risk prediction model for pre-eclampsia. The fullPIERS probability of experiencing an adverse maternal outcome for each woman was calculated and women were grouped into <10%, 10-29% and 30% probabilities. Women admitted with pre-term pre-eclampsia
were then grouped according to data collection sites (PETRA vs Non PETRA) and their management and outcomes were compared.

**Results:** Majority of the women (82%) were classified into the low risk group had term pre-eclampsia and 5.5% into the high risk group. Women in NonPETRA data appeared to be older, smoke more and admitted at a later gestational age than PETRA data across all PIERS probability ranges. There was lower administration of corticosteroid and antihypertensive for women but higher administration of MgSO₄ for women in PETRA data compared to NonPETRA sites. The women in the PETRA data were also more likely to have a shorter admission to delivery for women except in the highest PIERS risk range. There was no clear pattern in difference between the two groups for the occurrence of adverse maternal and perinatal outcomes except for smaller babies in the PETRA group.

**Discussion:** These findings show variation in pre-eclampsia management between the USA and other high income countries (Canada, UK and Finland). However, it is unclear if and how these managements affect pregnancy outcomes for women admitted with pre-eclampsia suggesting the need for further studies.

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Pregnancy characteristics, management and outcomes according to different definitions of pre-eclampsia and other hypertensive disorders of pregnancy

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**Introduction:** The classification of hypertensive disorders of pregnancies (HDPs) especially pre-eclampsia (PET) vary according to different guidelines. Pregnancy characteristics, management and outcomes of women admitted with HDPs may differ by these definitions.

**Objective:** To compare characteristics, management and outcomes associated with different definitions of PET and other HDPs.

**Methods:** Dataset of 1972 women admitted with pre-eclampsia in a tertiary hospital in Canada from 2011 to 2016 was used for this study. Women were grouped into 8 groups: (1) chronic hypertension (CH), (2) gestational hypertension only; PET defined by (3) Hypertension and Hyperuricaemia only (4) Hypertension and accelerated hypertension only (5) Hypertension and proteinuria only (6) Hypertension and proteinuria only (7) PET defined by hypertension, proteinuria, and HELLP syndrome and (8) PET defined by hypertension, proteinuria, and either hyperuricaemia or accelerated hypertension. The demographic characteristics, management and adverse outcomes rates for the different groups of HDPs were compared.

**Results:** Majority of the women (32.3%) fell under group 8. Women in Group 1 were more likely to be older and multiparous but with the lowest rate of multiple pregnancy. Women in Group 2 were admitted at a later gestational age (GA) with the highest rate of smoking and had the least interventions (administration of antihypertensive, MgSO₄ and antenatal corticosteroids, and caesarian delivery); consecutively group 7 had the earliest GA at admission, lowest smoking rate and most administrations with the highest rates of multiple pregnancy and adverse maternal and perinatal outcomes.

**Conclusion:** The different definitions of HDPs were associated with differences with demographics, management and outcomes. Women in group 2 appeared to have the least adverse maternal and perinatal outcomes while women in group 7 (PET with both proteinuria and HELLP syndrome) had worse outcomes. These differences in outcomes by definitions may aid in directing the management of HDPs.

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Why are pregnant women not screened for Hypertensive disorders of pregnancy (HDP) in Kinshasa, Democratic Republic of the Congo?

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**Introduction**

Screening for HDP during antenatal visit allows identification of high-risk women, and initiation of early preventive interventions to improve pregnancy outcomes. In Kinshasa however, the majority of pregnant women attending antenatal clinics are not screened for HDP.
Objective
To identify factors associated with the lack of screening for HDP within antenatal clinics in Kinshasa.

Methods
We conducted a facility-based cross-sectional study in 58 clinics (30 primary, 26 secondary and 2 tertiary), and selected 580 pregnant women by systematic sampling. Data were collected by observation during antenatal consultation, interview and review of antenatal records. A pregnant woman was considered as not screened for HDP if she did not receive blood pressure measurement, proteinuria testing and assessment for at least one of clinical risk factors from the American College of Obstetricians and Gynecologists. To identify factors associated with the lack of screening for HDP, we applied a weighted multivariate logistic regression model using generalized estimating equations.

Results
Of 580 pregnant women included, 73% were not tested for proteinuria, 40% were not assessed for risk factors, 4% did not have their blood pressure checked, and 74% were not screened for HDP. In the multivariate analysis, gestational age less than 20 weeks (AOR = 4.38; 95% CI, 1.68-11.41; p=0.003), primary level of education (AOR = 1.94; 95% CI, 1.02-3.68; p=0.043), attending in a public (AOR = 5.80; 95% CI, 1.82-18.47; p=0.003), or in a primary clinic (AOR = 3.52; 95% CI, 1.35-9.17; p=0.01), or in a clinic were additional payment is required for proteinuria testing (AOR = 3.43; 95% CI, 1.31-9.00; p=0.012), were associated with the lack of screening for HDP.

Discussion
The majority of pregnant women attending antenatal care in Kinshasa are not screened for HDP. There is a need of increasing awareness of health providers in the screening for HDP to improve pregnancy outcomes in Kinshasa.

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Study of Maternal and Perinatal Variables in Preeclampsia According to its Clinical Expression
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Introduction: The severity of the clinical expression of preeclampsia determines maternal-fetal repercussions. Recognize indicators of severity may guide the adoption of behaviors in a timely manner.

Objective: To relate maternal characteristics and perinatal outcomes in patients with severe preeclampsia and without signs of severity.

Method: Cross-sectional study. Location: Hospital Guilherme Álvaro-Santos/Brazil, January/2015-May/2016. Patients with preeclampsia (NHBPEP/2000) were divided into two groups: no signs of severity (control) and severe (study). Maternal variables: age, body mass index (BMI), parity, prenatal care, gestational age at birth, serum creatinine, aspartate aminotransferase (AST) and alanine (ALT); and neonatal: weight and admission to the Intensive Care Unit (ICU). Statistical analysis: Fisher's exact test (p significant<0.05).

Results: The preeclampsia group presented more commonly than women without signs of severity: age ≥40 years (6%), obesity (56.5%) and nulliparity (38%) against 0%, 61.5%, 6.7%, respectively. Absence of prenatal care 24% against 6.7%. The childbirth occurred between 29-346/7 weeks in 36% in the group with severe preeclampsia, whereas in the preeclampsia without signs of severity: 6.7%. Average weight of newborns of 3205g and 02 (13.3%) ICU admissions, against 2528g and 21 (42.9%). The average creatinine level was similar; AST and ALT was 18.67 and 12.53 in the control group compared to 22.63 and 15.65.

Discussion: Similar rates of severe preeclampsia were found in the literature. (Batista, 2009). The severe expression of preeclampsia was associated with women in the extremes of age, with previous gestation, obesity and with worse perinatal performance. Noting that these women lack counseling and qualified care. Inadequate follow-up of prenatal care may be explained by the greater number of hospital admissions in severity. It is proposed a reflection on strategies to increase vaginal parturition in this group. The variations of AST-ALT indicate hepatic involvement anterior to the renal, which will be clearer with the continuation of the study.
Profile of Pregnant Women Affected by Severe Preeclampsia

Introduction: The clinical expression of severe preeclampsia is associated to the worst maternal and neonatal outcomes. Identify the profile of women with this condition may target the adoption of care effectively.

Objective: Analyze the profile and major complications of pregnant women affected by severe preeclampsia.

Method: transversal study. Location: Complexo Hospitalar dos Estivadores/Instituto Social Hospital Alemão Oswaldo Cruz–Santos/Brazil (november/2017–march/2018). The study include 43 pregnant women admitted with the diagnosis of severe PE according to the criteria of NHBPEP (2000), as: blood pressure ≥160/110mmHg, proteinuria 2.0g/24h or +2 dipstick, serum creatinine >1.2mg/dl (new onset), platelets <100,000/mm(3), microangiopathic hemolysis (increased lactate dehydrogenase), elevated alanine aminotransferase or aspartate aminotransferase, persistent headaches or other cerebral or visual disturbance, persistent epigastric pain or eclampsia. Analyzed variables: age, parity, adequate prenatal care (≥ 06 appointments), blood pressure on admission, childbirth, evolution to HELLP syndrome/eclampsia, use of magnesium sulfate (MgSO4) and admission in Intensive Care Unit (ICU).

Results: They were identified 43 women with serious preeclampsia. Average maternal age: 29.49 years, history of previous gestations (55.81%). The prenatal had more than six appointments for 30 women (69.8%). Cessarian labor: 65.1%. Evolution to complications: HELLP syndrome (16.3%), Eclampsia (4.6%), used magnesium sulfate (93%) and admission in Intensive Care Unit (37.2%).

Discussion: A gravity recognized condition reaches in this priority area women in productive phase with potential socioeconomic impact, often multiparous and at least 30% not prenatal care with lots of appropriate appointments probably for early admission. The frequency of complications and caesarean sections also leads to the need for recognition of the problem of public life, as the need for appropriate guidance and access to qualified services for it attendance.

Creating biobanks in low and middle-income countries to improve knowledge - The PREPARE initiative
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The Millennium Development Goal 5, a project signed in 2000, intended to improve maternal health and reduce maternal mortality by 75% by 2015. Despite all efforts, little progress has been achieved in low and middle-income countries (LMIC) and 99% of all maternal deaths related to preeclampsia (PE) still occur in these settings. It is important to determine whether women in LMIC, where pre-eclampsia carries a greater risk than in high-income countries (HIC), have unique risk factors. Some variances may alter the risk, severity and pertinent pathophysiology of PE. We posit based upon this, that women from LMIC may have biomarkers specific to this population. Discovering such specific biomarkers and testing the relevance of biomarkers developed in HIC populations could increase the clinical usefulness of these analyses increasing cost effective approaches for prediction of PE. Here we briefly describe our platform to develop the PREPARE – biobank in tertiary hospitals or basic units for antenatal care from 6 different cities in Brazil. The PREPARE – Biobank has been developed with two arms. The first arm is a cross-sectional study that will collect clinical information and biosamples from more than 1000 women who develop preterm PE. The second arm is a
cohort study of 7000 women. It will collect clinical information and longitudinal biosamples from women at three times during pregnancy, <16 weeks, between 28 and 32 weeks and at delivery or diagnosis of adverse outcomes.

The biobank will be supported and complemented by a Brazilian database using the CoLab COLLECT Database. All data has been recorded and stored in a secure on-line system provided by MedSciNet group. We believe the combined approach of testing the value of established approaches and searching for unique biomarkers and pathophysiological features in LMIC settings using biobanks and databanks will help to achieve the MDG 5.

Characteristics of women with preterm pre-eclampsia enrolled to the PREPARE Trial - preliminary data
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Introduction: Pre-eclampsia is a major cause of short and long-term morbidity for affected offspring, including injuries from birth asphyxia and iatrogenic prematurity. This is a special problem in Brazil since pre-eclampsia accounts for higher prevalence of preterm births comparing with high-income countries. Objective: To reduce preterm births related to pre-eclampsia. Methodology: This is a multicentre study with a stepped wedge design involving seven tertiary centres in Brazil that will receive an intervention based on risk stratification. All data have been recorded in the CoLab COLLECT Database. Results: Table 1 presents the characteristics of 634 women with preterm pre-eclampsia enrolled to the study between January 2017 and March 2018. Conclusion: The PREPARE study will allow to establish reliable characteristics of women with preterm pre-eclampsia in Brazil.

Data expressed in numbers and percentage unless stated otherwise; BP= Blood Pressure; BMI= Body Mass Index
Tuesday October 9, 2018

Endothelium/Lipids/Oxidative stress

Poster pitches

Effects of syncytiotrophoblast extracellular vesicles (STBEVs) on endothelium-dependent vasodilation in uterine arteries from lectin-like oxidized LDL receptor-1 (LOX-1) overexpressing mice during pregnancy
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Introduction: Placental factors, such as syncytiotrophoblast extracellular vesicles (STBEVs), have been suggested to contribute to maternal endothelial vascular dysfunction in women with preeclampsia (PE). The lectin-like oxidized LDL receptor-1 (LOX-1) is a multi-ligand scavenger receptor; and in women with PE both STBEV levels and LOX-1 expression are elevated. We used heterozygous LOX-1 overexpressing (LOX-1OE) mice to further investigate the role of LOX-1 and STBEVs in vascular dysfunction during pregnancy.

Hypothesis: We hypothesized that STBEVs activate LOX-1 and contribute to vascular dysfunction in mouse uterine arteries of LOX-1OE mice, but not in WT controls.

Methods: Uterine arteries were obtained from late pregnant (gestational day 18; term = day 19) LOX-1OE mice (carrying a bovine LOX-1 transgene) and WT controls (+/−). Isolated vessels were incubated overnight in the absence (n=8) or presence of STBEVs (200 μg/ml, n=5-7) from control pregnant women. Using wire myography, endothelium-dependent vasodilation responses to methacholine (MCh) were assessed with or without L-NAME (pan nitric oxide synthase inhibitor), superoxide dismutase (SOD) or oxidized LDL (oxLDL).

Results: Endothelium-dependent vasodilation to MCh was unchanged following STBEV-incubation in both mouse strains. In WT mice, nitric oxide did not contribute to vasodilation, while there was a nitric oxide contribution to vasodilation in STBEV-incubated arteries (p<0.01), and in control and STBEV-incubated arteries from LOX-1OE mice (p<0.01). Reduction of oxidative stress via SOD-incubation did not affect MCh-responsiveness. LOX-1 activation with oxLDL reduced vascular responses to MCh in LOX-1OE, but not WT mice (p<0.05), independent of STBEV-exposure.

Discussion: Interestingly, both LOX-1OE and STBEV-exposure increased nitric oxide contribution to relaxation; perhaps as a compensatory mechanism. OxLDL (a potential contributing factor in women with PE and dyslipidemia) impaired endothelial-dependent relaxation in the presence of increased LOX-1 expression during pregnancy. These data suggest that increased LOX-1 expression in women with PE could contribute to impaired vascular function.

Maternal lipid profile in early pregnancy as marker for adverse perinatal outcomes
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Introduction: Metabolic syndrome, characterized by abdominal obesity, insulin resistance, hypertension and hyperlipidemia has become a major health problem of the modern world. Metabolic syndrome is associated with adverse perinatal outcomes, such as a neonate born large for gestational age (LGA). Little is known about the role of maternal lipid concentrations in this association. Possibly, an atherogenic lipid profile in early pregnancy is a risk factor for adverse perinatal outcomes.

Objective: To determine the association of maternal glucose and lipid concentrations in early pregnancy with perinatal outcomes: LGA, small for gestational age (SGA), and spontaneous preterm birth (sPTB).

Methods: We included 5692 women from The Generation R Study; a prospective population-based birth cohort. Maternal glucose and lipid concentrations including triglycerides, total-cholesterol, high-density lipoprotein-cholesterol (HDL-c) were measured in early pregnancy (median 13.4 weeks). Low-density lipoprotein-cholesterol (LDL-c), remnant-cholesterol and non-HDL-c were calculated. A birth weight above the 90th percentile was defined
as LGA and below the 10th percentile as SGA. Spontaneous birth before 37 weeks of gestation was defined as sPTB.

**Results:** Triglycerides and remnant-cholesterol were positively associated with the risk for LGA. These associations were partly mediated by maternal glucose concentrations in early pregnancy (10.9% and 9.0% respectively). HDL-c was negatively associated with the risk for LGA. Women with an atherogenic lipid profile (high triglycerides with either high total-cholesterol, high remnant-cholesterol or low HDL-c) were most at risk for a LGA child. We observed no associations between lipid concentrations in early pregnancy and the risk for SGA or sPTB.

**Discussion:** An atherogenic lipid profile in early pregnancy is associated with a higher risk for a LGA child. This association is partly mediated by maternal glucose concentration in early pregnancy. Assessing maternal lipid profile in early pregnancy might help to identify high-risk pregnancies in an early stage.

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**Placental oxidative stress, angiogenic factor and maternal endothelial function in pregnant women with normotensive fetal growth restriction**

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**Introduction:** Placental oxidative damage may increase the production of anti-angiogenic factors, resulting in maternal endothelial dysfunction in pregnant women with preeclampsia (PE). Endothelial dysfunction is observed in women with a history of normotensive fetal growth restriction (FGR). However, placental oxidative stress, angiogenic factors and maternal endothelial function in those women remain unclear.

**Objectives:** This study aimed to assess the relationship between placental oxidative stress, angiogenic factors and maternal endothelial function in pregnant women with normotensive FGR.

**Methods:** A total of 21 women with uncomplicated pregnancies, 17 women with early-onset preeclampsia (PE), 18 with late-onset PE, and 14 with normotensive FGR were evaluated. We measured to determine serum parameters of oxygen free radicals (d-ROMs), PIGF and sFlt-1 as maternal anti-angiogenic factor, placental oxidative DNA damage, and flow-mediated vasodilation (FMD) as a marker of maternal endothelial function. Immunohistochemical analysis was performed to measure the proportion of placental trophoblast cell nuclei staining positive for 8-hydroxy-2’-deoxyguanosine (8-OHdG) and redox factor-1 (ref-1), which are markers of oxidative DNA damage.

**Results:** Maternal serum d-ROMs, sFlt-1 concentrations, and FMD did not significantly differ between control and normotensive FGR groups. The proportion of nuclei staining positive for 8-OHdG was significantly higher in the normotensive FGR group relative to the control group, but ref-1 were not significantly differences among all groups.

**Conclusion:** Our findings demonstrate that although placental oxidative DNA damage was observed in both women with PE and those with normotensive FGR, pregnant women with normotensive FGR show no increase in the concentrations of sFlt-1 and d-ROMs, or a decrease in FMD.

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**The effect of pitavastatin and pravastatin on omental and chorionic plate artery function in normal pregnancy and pre-eclampsia**

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**Introduction:** There are no effective therapies for pre-eclampsia (PE), which remains a leading cause of considerable maternal-fetal morbidity and mortality. Statins, widely utilized in cardiovascular disease, represent a candidate therapy for PE. Determination of statins’ ability to ameliorate the observed endothelial dysfunction in PE is lacking.

**Objective:** To determine the effect of short-term pitavastatin and pravastatin exposure on endothelial function in NP CPAs and omental arteries (OAs) from normal and PE pregnancies.

**Methods:** CPAs and OAs from normal pregnancy (NP; N=43 placentas, N=20 biopsies) and PE (N=18 placentas, N=5 biopsies) pregnancies were mounted on a wire myograph. Contraction was assessed with KPSS (120mM) and thromboxane-mimetic U46619 (0.1nM–2μM). Arteries were incubated for 2h with 1μM pitavastatin or pravastatin; time-controls in parallel. U46619 dose–response curves were repeated or NO-donor SNP (1nM–100μM) or endothelium-dependent bradykinin (0.1–1000nM/L) following U46619 pre-constriction. All data are mean±SEM.

**Results:** Neither statin significantly altered vascular reactivity in NP CPAs. CPAs show blunted SNP-induced...
relaxation in PE vs. NP (38±10% vs. 28±12% respectively; p=0.038; Two-way ANOVA). Additionally, 1µM pitavastatin attenuated PE CPAs vasoconstriction compared to control (Emax, 152±30% and 165±33% respectively; p=0.013; Two-way ANOVA) but vasodilation was unaffected. In NP OAs, 1µM pravastatin reduced vasoconstriction compared to time-control (111±20% and 123±23% respectively; p=0.044; Two-way ANOVA) but did not affect vasodilation. Preliminary PE OA data suggests neither statin had a significant effect on vasoconstriction or vasodilatation (P>0.05; Two-way ANOVA; N=5).

**Discussion:** Data suggests statins are unlikely to be deleterious to placental vascular function in NP. Pitavastatin (PE CPAs) and pravastatin (NP OAs) have the ability to blunt agonist-induced vasoconstriction. Future work will focus on whether pitavastatin and pravastatin improve endothelial function in OAs from women with PE.

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**The role of vitamin D in cell-cell interaction of endothelial cells and trophoblasts in a preeclampsia-like model**

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**Objective:** The obstetric history of women is an important part of their cardiovascular risk profile, but also of their offspring. Preeclampsia is a separate, independent risk factor. We hypothesize that fetal endothelial cell functional limitations can already be demonstrated in pregnancies complicated by preeclampsia and that therapeutic use, e.g. with 1.25 (OH)2 Vitamin D3 can balance the negative effects of preeclampsia on cell function.

**Methods:** Human umbilical venous endothelial cells (HUVEC) and endothelial colony-forming cells (ECFC) were obtained from umbilical veins and cord blood. Furthermore, a trophoblast cell line (HTR8-SVneo) as well as human uterine venous endothelial cells (HUUtMVEC) were available. Serum from uncomplicated and preeclamptic pregnancies was collected. Functional properties such invasion and migration as well as cell interaction of endothelial cells and trophoblasts were investigated with or without 1.25 (OH)2 Vitamin D3 treatment.

**Results:** In a co-culture and invasion model of HUVEC and ECFC as well as of HUtMVEC and HTR8, the simulation of preeclampsia-like conditions led to a reduced invasion of ECFC or trophoblasts into an endothelial cell monolayer consisting of mature endothelial cells. Vitamin D neutralized the evoked negative effects on functional properties. Furthermore, immunocytochemical studies revealed a cell-cell interaction between immature and mature endothelial cells as well as mature endothelial cells and trophoblasts.

**Discussion:** Limited functional capacity of fetal endothelial cells under preeclamptic conditions suggests that pathogenic factors of the dysfunctional placenta adversely affect fetal endothelial cells and thus contribute intracellularly to cellular changes. Physiological concentrations of vitamin D promote important cell functions of endothelial cells. Whether the observed cellular changes persist in the neonatal period and childhood and are a possible early marker of an increased cardiovascular risk of the progeny of preeclamptic pregnancies has to be investigated by further studies.

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**Reduced barrier function of the microvascular endothelial glycocalyx in women with a history of preeclampsia, one year after delivery**

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**Introduction** The endothelial glycocalyx is a proteoglycan- and glycoprotein-rich layer at the interface of the flowing blood and the cell membrane. It regulates key endothelial functions and is critical for vascular health. The effects of glycocalyx damage (e.g., proteinuria, pro-coagulation, inflammation, vasospasm) suggest that the glycocalyx might have an important role in the pathophysiology of preeclampsia and increased risk of later life cardiovascular disease in these women.

**Hypothesis** We hypothesized that, 1 year after delivery, non-pregnant women with a history of preeclampsia evidence microvascular endothelial glycocalyx damage compared to non-pregnant controls who had a normotensive, uncomplicated pregnancy.

**Methods** Glyocalyx damage was assessed using sidestream dark field imaging and was defined as deeper penetration of RBCs into the glycocalyx of the sublingual microcirculation (5-25µm diameter). Twenty-one women with a history of normotensive pregnancy (NP) and 10 women with prior preeclampsia (PE) were examined at one
year after delivery. We compared movement of RBCs into the glycocalyx (perfused boundary region, PBR), microvascular density (total length of perfused microvessels/mm²), and RBC filling percentage (percentage of time in which vascular segments are perfused).

**Results** Glycocalyx PBR was significantly increased in women with prior PE compared to NP (2.32±0.22µm PE vs. 2.1±0.22µm NP, P<0.05). Microvascular density was marginally reduced in prior PE (372±157 mm/mm² PE vs. 493±218 mm/mm² NP) (P<0.13). RBC filling percentage was significantly reduced in women with prior PE (68±1.6% PE vs. 73±1.1% NP, P<0.05).

**Discussion** One year after delivery, the sublingual microvascular glycocalyx is functionally damaged in women with prior preeclampsia as indicated by an increase in PBR (magnitude similar to end-stage renal disease). There is also evidence of impaired microvascular perfusion. Glycocalyx degradation may contribute to increased risk of later life cardiovascular disease in women with a history of preeclampsia. Funded by NIH-NICHD (P01 HD030367, R21 HD083659), and AHA 16SFRN27870000

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**Sublingual Microvascular Density and Glycocalyx Barrier Dynamics, During and After Normal and Preeclamptic Pregnancy**

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**Introduction**: The apical surface of the vascular endothelium comprises a complex meshwork of membrane-bound proteoglycans and glycoproteins, the glycocalyx. The glycocalyx has important vasoregulatory roles; e.g., growth factor binding, signal transduction, coagulation and permeability. Glycocalyx damage has been implicated in several vascular diseases.

**Hypothesis**: Glycocalyx structural barrier integrity and microvascular perfusion are reduced in women with preeclampsia (PE).

**Methods**: We evaluated 17 women with PE and 27 with uncomplicated pregnancy (NL), just prior to delivery (LD) and at 24-48 hours postpartum (PP). The sublingual microvasculature was interrogated using sidestream-darkfield imaging to compare glycocalyx integrity, microvascular density and percentage of perfused vascular segments. Glycocalyx integrity (for vessels 5-25 µm) was measured as depth of the RBC accessible region (AR), in which greater AR signifies diminished ability of glycocalyx to exclude RBCs. Plasma soluble syndecan-1, a shed glycocalyx component, was measured by ELISA.

**Results**: Microvascular density (segments/mm²) was greater in NL-LD (478±28) compared to PE-LD (378±35 p=0.002), decreasing in both NL-PP (355±28) and PE-PP (306±35). Perfusion was not different between groups. AR in NL-LD (2.33±0.05 microns) was surprisingly greater than PE-LD (2.17±0.06 p=0.03), or NL-PP (2.19±0.05 p=0.05) but not different from PE-PP (2.26±0.06). The change in AR between timepoints (LD-PP) indicates postpartum improvement in barrier function in NL (but not PE) group (-0.09±0.4 vs 0.08±0.3 p=0.05).

Maternal plasma syndecan-1 was higher in NL-LD (1126±110.3ng/mL) compared to PE-LD (715.5±112.1 ng/mL; p=0.008), and declined in both groups PP (NL-PP 210±98, PE-PP 173±120; NS).

**Conclusion**: Women with PE exhibited a reduction in functional microvascular density compared to NL. The increase in RBC accessibility (AR) in NL compared to PE was opposite to our hypothesis. This reduction in endothelial glycocalyx barrier function was accompanied by a higher level of circulating syndecan-1 prior to delivery in NL. The physiologic significance of these glycocalyx changes remain to be determined. **Funding** PO1-HD-30367,R21-HD-83659,AHA16SFRN27810001

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**Quercetin protects against the vascular contractile effect of placental secreted messengers released under placental hypoxia: an in-vitro model of preeclampsia**

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**Introduction**: Placental hypoxia is a crucial factor in the pathogenesis of preeclampsia resulting in hypoxic stress. Upon this stress the placenta will release placenta secreted messengers (PSMs) which will cause maternal
endothelial dysfunction. Previous research suggests that the antioxidant quercetin exerts anti-hypertensive effects and endothelial relaxation via NO release.

**Objective:** To determine the vascular effect of PSMs released under hypoxia and to study the protective effect of quercetin on this process.

**Methods:** In this study 44 non-complicated placentas (GA > 37 weeks) were used. PSMs were generated by exposing healthy term placentas to hypoxia. Chorionic arteries were incubated with these PSMs +/- quercetin 3 and 20 µM and contractile responses were recorded over a two-hour period. PSMs generated under normoxic conditions were used as control. Endothelial dysfunction induced by PSMs was assessed by analyzing changes in contractile responses to KCl (62.5 mM) before and after exposure to the PSMs.

**Results:** PSMs released under hypoxia induced an increased contraction in chorionic arteries compared to PSMs released in the presence of quercetin and normoxic conditions (39.1 µm ± 5.9 vs. quercetin 3 µM: 17.5 µm ± 1.6 vs. quercetin 20 µM: -8.5 µm ± 2.2 vs. normoxic: 0.5 µm ± 0.8, p < 0.001). A decreased change in contractile response to KCl (62.5 mM) was observed for PSMs released in the presence of quercetin (20 µM) (72.5 µm ± 6.0 vs. quercetin 3 µM: 40.1 µm ± 3.3, p < 0.05 and quercetin 20 µM: 3.5 µm ± 0.6, p < 0.001). No changes in contractile response to KCl was observed for the control condition (0.0 ± 0.2, p < 0.001).

**Discussion:** Quercetin shows promising results for the protection against the PSMs released under preeclampsia-like stress conditions like placental hypoxia, which could eventually be used for prevention and/or treatment of preeclampsia.

**Late breaking abstracts**

**Effect of high dose folic acid supplementation throughout pregnancy on preeclampsia (FACT): a double-blind, randomized controlled, international multi-centre trial**

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**Introduction**

Previous studies on the association between folic acid supplementation and preeclampsia have shown promising findings on the potential protective effect of folic acid. Given the potential benefits of folic acid on preeclampsia, supplementation of folic acid in pregnant women with 4.0-5.0 mg/day beyond the first trimester has become widespread.

**Objective**

To determine the efficacy of high dose folic acid supplementation for prevention of preeclampsia in women with at least one of these risk factors: pre-existing hypertension, pre-pregnancy diabetes (type I or II), twin pregnancy, preeclampsia in a previous pregnancy, or body mass index (BMI) ≥ 35 (kg/m²).

**Materials & Methods**

This was a randomized, phase III, double-blinded, placebo-controlled, international multi-center trial at 70 obstetrical centres in five countries (Argentina, Australia, Canada, Jamaica, UK). Eligible women were randomized to receive either daily high dose folic acid (four 1.0 mg oral tablets) or placebo from 267 - 1637 weeks’ gestation until delivery. Clinicians, participants, adjudicators, and all study staff were masked to study treatment allocation. The primary outcome was preeclampsia defined as diastolic blood pressure ≥ 90 mmHg on two occasions ≥ four hours apart and proteinuria which developed in women greater than 20 weeks gestation.

**Results**

A total of 2464 pregnant women with at least one high risk factor for preeclampsia were randomized between 2011 and 2015; 2301 were included in the intention to treat analyses, with 1144 assigned to the folic acid group. Preeclampsia occurred in 169 (14.8%) women in the folic acid group and 156 (13.5%) in the placebo group (relative
risk 1.10, 95% confidence interval 0.90 to 1.34; P=0.37). No evidence of differences was found between the groups for any other adverse maternal or neonatal outcomes.

**Conclusion**
Folic acid supplementation with 4.0 mg/day beyond the first trimester does not prevent preeclampsia in women at high risk for preeclampsia.

**Posters**

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**Vitamin D enhances endothelial integrity and antagonizes inflammatory effects**
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Introduction: Preeclampsia, is associated with chronic inflammation, endothelial dysfunction and higher cardiovascular morbidity in later life. During the past two decades endothelial progenitor cells (EPCs) have come into research focus as a potential biomarker for cardiovascular risk. Endothelial colony-forming cells (ECFC), a subgroup of EPCs, display high regeneration ability, play a role in vasculogenesis and have the capacity of de novo vessel formation. ECFC number and function is impaired in preeclampsia and we recently demonstrated that vitamin D antagonizes the negative functional impact of preeclampsia on ECFC.

Objective/Hypothesis: In this study, we addressed the question whether vitamin D has vasoprotective effects by improving ECFC barrier function and adhesion molecule expression.

Methods: Using electrical impedance monitoring to test endothelial integrity, immunocytochemistry for characterization of protein localization and flow cytometry to determine protein expression as well as an in-vitro chemotaxis assay, we investigated the effect of vitamin D on ECFC endothelial barrier and integrity under healthy and inflammatory conditions.

Results: Inflammation, simulated using TNF-alpha, enhanced the permeability of an ECFC monolayer (p<0.005). This was accompanied by an increased formation of intercellular gaps, stress fibers and delocalization of VE-Cadherin, an adhesion protein important for monolayer integrity. Vitamin D alone stabilized the ECFC monolayer (p<0.002). Further, it rescued the TNF-alpha effect by an increased formation of adhesion junctions via VE-Cadherin. Vitamin D also enhanced adhesion protein surface expression and lead to an increase of chemotactic migration alone (p=0.03) and in combination with TNF-alpha (p=0.03).

Discussion: Vitamin D is important for endothelial barrier integrity and antagonizes inflammatory effects, as observed in preeclampsia, by improving endothelial interconnection through adhesion proteins.

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**Concomitant intrauterine growth restriction alters the lipoprotein profile in preeclampsia**
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Introduction: Preeclampsia (PE) is a heterogeneous disorder that can be subgrouped according to clinical and pathophysiological features. PE can be accompanied by intrauterine growth restriction (IUGR) and both diseases share common features. Alterations in lipid metabolism have consistently been reported for both diseases.

Objective/Hypothesis: We investigated whether characteristic lipid changes can be related to either of both diseases. We hypothesized that in general IUGR displays a low cholesterol phenotype while pure PE is rather associated with high triglyceride concentrations.

Methods: Serum lipid profile of patients with IUGR (n=52), hypertensive IUGR (HIUGR, n=28), and PE without IUGR (n=56) were compared to a control group (CTRL, n=167). Additionally, lipid components in serum of severe early-onset cases (<34th weeks of gestation) of normotensive IUGR, hypertensive IUGR (HIUGR), and PE without IUGR (each n=10) were analyzed by extensive lipid subfractionation and compared to 30 control patients.

Results: Triglycerides are elevated in PE. However in IUGR LDL-cholesterol is reduced, irrespective of additional PE (IUGR 79 mg/dL; HIUGR 74 mg/dL vs. CTRL 133 mg/dL). The ApoB-profile shows a higher level of VLDL-ApoB in PE and a lower level of LDL-ApoB in IUGR, as expected. Interestingly, the HIUGR group shows features of both
groups, high VLDL-ApoB level and a low ApoB level in the LDL-subfractions. **Discussion:** The presence of IUGR in PE alters lipid profiles. Study groups have to be selected carefully to avoid misinterpretation.

**Significance of systemic vascular disorders in gestational complications in pregnancy**
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Many pathogenetic similar disorders of pregnancy, including preeclampsia, placenta abruption, pregnancy losses, have been attributed, at least in part, to defects in the tightly regulated systemic vascular changes necessary to support a healthy pregnancy. Evaluation of the levels of endogenous regulators makes it possible to determine the risk of the realization of these pathological conditions from the early stages of pregnancy.

**Study objective:** To evaluate the role of endogenous regulators of angiogenesis in the development of recurrent miscarriage and preeclampsia.

**Methods:** Immunological and biochemical study of peripheral blood of pregnant women divided into three groups: 43 patients with recurrent pregnancy losses, 46 with preeclampsia and 34 women of the control group. To explore the plasma levels of endothelin-1, VEGF and PI GF and activity of NO system we studied the angiogenesis process.

**Results:** The level of endothelin-1, in women with recurrent miscarriage and with preeclampsia, were significantly higher in both groups by 2.2 and 1.8 times (p < 0.05), than in control group. The level of total nitrite (NO2⁻ total) in the first and second main groups was 1.6 and 1.8 times lower than in the control group (p = 0.024 and p = 0.014). Reduction in the level of vasodilators, established in the first and second groups, suggesting as an endothelial dysfunction. The PI GF and sVEGF-R1 levels decreased on the background of an increasing in the VEGF in the first and second groups compared to controls (p <0.001). The changes in the concentration of VEGF, PI GF and sVEGF-R1 occur from early gestation before the onset of miscarriage symptoms and manifestations of preeclampsia.

**Conclusions:** The pathogenetic mechanisms of development of preeclampsia and reproductive losses are associated with a violation of the functional state of the endothelium and the inferiority of the processes of angiogenesis.

**High density lipoproteins lose their antioxidant protective effect during pre-eclampsia.**
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**Introduction:** Pre-eclampsia (PE) is a hypertensive disorder of pregnancy associated with abnormal placentation leading to poor placental perfusion, oxidative stress, and inflammation, which then leads to the dysfunction of the maternal endothelium. High density lipoproteins (HDL) exert protective effects on the vascular endothelium especially an antioxidant effect. However, HDL can become dysfunctional and lose these protective properties. A dyslipidemia characterized by low plasma levels of HDL, elevated triglycerides, and high levels of low density lipoprotein (LDL)-cholesterol associated with an increased LDL oxidation has been described in PE.

**Objective/hypothesis:** We hypothesized that HDL become dysfunctional in PE especially with regard to their antioxidant properties and fail to protect the maternal endothelium. Our study is therefore investigating these antioxidant properties.

**Methods:** We conducted a case-control study in 10 pregnant women with early severe PE paired for age and gestational age to 10 control healthy pregnant women. We isolated HDL from patients and control women by ultracentrifugation, and then incubated cultured human endothelial cells with the purified HDL, LDL and CuSO4 for 6 hours. Then, we measured TBARs (ThioBarbituric Acid Reactive Substances) produced in culture supernatants to evaluate the HDL antioxidant protective effect.

**Results:** The TBARs levels in culture supernatants were significantly raised when the endothelial cells were incubated with
HDL purified from PE women rather than with HDL purified from control women (respectively 3.24±1.25 µM versus 2.50±0.95 µM, mean ± SD, p=0.02). These data show that HDL from PE patients have less antioxidant effect than HDL from pregnant controls.

**Discussion:**
In our study, we found that HDL isolated from PE patients lose their antioxidant properties, which could explain the increase of oxidized LDL previously described in the PE. These dysfunctional HDL could fail to protect the vascular endothelium; such mechanism could be involved in the physiopathology of the PE endothelium dysfunction.

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**The microvascular endothelial glycocalyx: impaired barrier function in preeclampsia with small gestational age neonates**

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**Introduction**
The glycocalyx, the endothelial lining of membrane-bound proteoglycans and glycoproteins, serves as a functional barrier between flowing red blood cells (RBC) and the endothelial cell membrane. Recent studies suggest that damage to the glycocalyx, which can be reflected by deeper radial penetration of RBC into the glycocalyx, contributes to microvascular dysfunction.

**Hypothesis**
We hypothesized that women with preeclampsia, especially those who deliver a small-for-gestational age neonate (PE+SGA, birthweight<10th percentile), evidence an increase in RBC penetration into the sublingual microvascular glycocalyx compared to normotensive controls (NP).

**Methods**
We compared 30 women with a normotensive pregnancy (NP) to 30 women with preeclampsia (PE), matched for gestational age at time of analysis and presence/absence of labor. Using sidestream dark field imaging of the sublingual microcirculation, we measured 1) the accessibility of the RBC into the glycocalyx layer (perfused boundary region, PBR), defined as the difference between median and maximal RBC column widths, and 2) the microvascular density (total length of perfused microvessels/mm² area). In healthy vessels, PBR is relatively small due to limited penetration of RBC into the glycocalyx.

**Results**
We observed no significant group differences in microvascular density (229±75 mm/mm² PE, 247±88 mm/mm² NP, P=0.48) or PBR (2.20±0.22 µm PE, 2.14±0.30 µm NP, P=0.14). However, the subset of women with PE+SGA (n=12) evidenced a significant reduction in vascular density (205±67 vs 306±71 mm/mm², P<0.01) and an increase in PBR (2.27±0.17 vs 2.15±0.29 µm, P=0.05) compared with their matched NP (n=12).

**Discussion**
The increase in RBC encroachment (PBR) into the microvascular glycocalyx in PE+SGA compared to NP indicates a change in glycocalyx structure which may be associated with a reduced vascular protective function of the glycocalyx, possibly contributing to endothelial and microvascular dysfunction. Funded by NIH-NICHD (P01 HD0030367, R21 HD083659), and AHA 16SFRN27870000

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**Changes in endothelial glycocalyx between the first and third trimester in high-risk and low-risk pregnancies**

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**Introduction**
Pregnancy is associated with several physiological cardiovascular adaptations that begin during early pregnancy and reach a maximum around 30 weeks of gestation. However, little is known about microvascular pregnancy adaptations. The endothelial glycocalyx can be noninvasively visualized using Sidestream Dark Field (SDF) imaging and the Perfused Boundary Region (PBR) reflects its health status, with a high PBR indicating damage. It is possible that the glycocalyx adapts during pregnancy, even in women with known microvascular dysfunction.

**Objective**
This study aims to assess changes in endothelial glycocalyx between the first and third trimester of gestation and the differences between high-risk and low-risk pregnancies.

**Methods**
A single center prospective cohort study was performed. High-risk pregnancies consisted of pregnant women with suspected microcirculatory endothelial dysfunction, based on pre-specified vascular health complications. Low-risk
pregnancies did not show any signs of vascular impairment at the time of measurement. PBR was measured sublingually using the Glycocheck™ at around 12 and 30 weeks of gestation.

**Results**
In total, 19 patients were included of which 13 were low-risk and 6 were high-risk. Mean PBR at 12 weeks was 1.83 (±0.25) and 2.05 (±0.27) at 30 weeks (p=0.041). In low-risk pregnancies PBRs of 1.86 (±0.24) and 2.02 (±0.30) were seen at 12 and 30 weeks, respectively (p=0.036). For high-risk pregnancies PBR values were 1.79 (±0.27) and 2.12 (±0.19) (p=0.029). No significance was detected between high-risk and low-risk pregnancies at 30 weeks of gestation.

**Discussion**
This research detected a significant change of PBR between the first and third trimesters of pregnancy, indicating microvascular adaptation to pregnancy. This change was visible in both high-risk and low-risk pregnancies, but no substantial difference was observed between both groups at 30 weeks. Further research is needed to determine whether these adaptations are a cause or consequence of cardiovascular adaptations during pregnancy.

### Pravastatin to treat early fetal growth restriction
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**Introduction:** Despite a progress in prophylaxis, placental disfunction-related diseases such Preeclampsia (PE) and Fetal Growth Restriction (FGR) are still lack in useful treatments beyond delivery. Pravastatin has been proposed as a safe drug able to restore the balance of antiangiogenic factors and reduce oxidative stress, which are known pathogenic mechanisms in placental disfunction.

**Objective:** To analyse the sFlt-1/PlGF ratio values in patients suffering early FGR before and after being treated with Pravastatin compared with non-treated FGR controls.

**Methods:** Women affected by early onset FGR defined as EFW ≤3rd centile, before 28+0 gestational weeks, with or without Doppler impairment, were offered to participate in the study. After signing the informed consent, 26 patients received 40 mg of Pravastatin daily since inclusion until delivery. The sFlt-1 to PlGF ratio was measured in maternal serum using the fully automated Elecsys sFlt-1 and PlGF assays on an electrochemiluminescence immunoassay platform cobas e analyzers. One measurement was obtained before introducing Pravastatin (M0) and one or more determinations were performed later on during the treatment (M1) and/or at delivery (Mf).

Data from other 16 pregnancies affected by early onset FGR, whom two or more sFlt1 to PlGF ratio values were available, were used as control group.

**Results:** Gestational age at delivery was inversely correlated with ratio values at the moment of inclusion (M0) in both groups. Ratio values tended to decrease after introducing Pravastatin (mean M1-M0=-32.38) while increased in controls (mean M1-M0=66.54). However these differences were not statistically significant (p=0.143)

**Conclusion:** The effectiveness of Pravastatin on improving the antiangiogenic profile by reducing sLFT1/PLGF leads researchers to consider it as a promising option to treat placental disfunction. Higher ratio levels early in pregnancy correlate with earlier gestational age at delivery. Thus, further studies should focus on introducing Pravastatin as soon as possible.

### Placenta

**Poster pitches**

### Possible roles of (pro)renin receptor induced by hypoxia in trophoblasts
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**Objectives:** Elevated soluble (pro)renin receptor [s(P)RR] concentration in maternal blood is associated with gestational hypertension and preeclampsia. Placental ischemia is a presumed trigger of gestational hypertension, and because placenta has abundant expression of (P)RR, the binding of which with pyruvate dehydrogenase E1
beta subunit (PDHB) is recently reported to maintain oxidative metabolism, we hypothesized that placental (P)RR may be induced by hypoxia and have a role in the pathogenesis or maintenance of hypertensive disorders of pregnancy.

**Methods:** Expression and functional analyses were performed using human trophoblast cells, JAR and JEG3. Endogenous expression of (P)RR and PDHB were confirmed in two trophoblast cell lines, and (P)RR showed co-immunoprecipitation and co-immunofluorescence with PDHB mainly in mitochondria. Subjecting the cells to hypoxia in a chamber system increased s(P)RR protein expression by $4.3 \pm 0.4$ fold ($1\%$ O$_2$ for 8 hours, N=6, $P<0.05$). While hypoxia reduces PDH activity in several non-trophoblast cell lines, hypoxia treatment did not alter PDHB expression or PDHB activity in trophoblasts; however, knockdown of (P)RR by siRNA in trophoblasts significantly reduced PDHB protein expression and PDH activity under hypoxia. Acetyl-CoA, the product of PDH activity, was also significantly reduced by (P)RR siRNA under hypoxia.

**Conclusion:** Induction of s(P)RR in trophoblasts may serve to maintain oxidative metabolism and efficient energy production during hypoxia. While increased serum s(P)RR concentration in maternal blood may reflect placental ischemia, whether elevated s(P)RR leads to deleterious effects on the mother such as by activating systemic renin angiotensin system remains to be determined.

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**LXR and ABC-Transporter-Expression Patterns in the Placenta in IUGR**

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**Introduction:**
Atherogenic lipid oxidation and cholesterol accumulation is increased in the placenta in IUGR. Both, hypoxic conditions and the formation of small molecules like oxysterols however are involved in cellular cholesterol homeostasis by regulating the cholesterol efflux ABC-transporter expression ABCA1 and ABCG1 via activating liver-X-receptors (LXR).

**Objectives/Hypothesis:** Since it is assumed that hypoxia and oxysterol production or accumulation is increased in the IUGR placenta we questioned whether the LXR-ABCA1 pathway is activated to counteract cholesterol excess.

**Methods:** Placentas of 40 IUGR and 40 controls (CTRL) arranged in tissue micro arrays (TMA) were analyzed immunohistochemically for LXRα, LXRβ, ABCA1, and ABCG1. The expression was assessed in trophoblasts and endothelium cells semi-quantitatively using Immunoreactivity-Score (IRS). Expression values were related to maternal and fetal lipid profiles. Expression patterns were statistically accomplished via the Mann-Whitney test.

**Results:** The LXRα und ABCA1-expression was increased in trophoblasts as compared to controls (LXRα Median IRS (95%CI) IUGR= 6.3 (5.59-7.06), CTRL= 4.8 (4.51-5.85), p=0.0207; ABCA1 Median IRS (95%CI) IUGR= 7.0 (6.33-7.87), CTRL= 3.9 (3.87-5.67), p=0.0001). No differences were found in LXRβ and ABCG1 expression patterns.

**Discussion:** An increased expression of cholesterol transport molecules in trophoblasts may be a compensatory mechanism against toxic effects of cholesterol excess and oxidation within the placenta.

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**Disulfiram inhibits placental sFLT-1 secretion**

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**INTRODUCTION**
Preeclampsia is associated with elevated placental secretion of the anti-angiogenic factor sFLT-1. Surprisingly, little is understood about its regulation, identifying such mechanisms may uncover therapeutic leads.

**OBJECTIVES**
Our objective was to determine the effects of disulfiram, a 20S subunit proteasome inhibitor, on placental secretion of sFLT-1 and endothelial dysfunction.

**METHODS**
Primary trophoblast were isolated from normotensive term placenta, treated with disulfiram and mRNA expression of sFLT-1 variants and protein secretion assessed. To assess the effects of disulfiram on the 20S subunit of the proteasome, primary trophoblast were treated with disulfiram in the presence of Suc-LLVY-AMC fluorogenic
substance. Next, we investigated the effect of disulfiram on endothelial dysfunction using isolated primary human umbilical vein endothelial cells (HUVECs) treated with 5% preeclamptic serum +/- disulfiram. The effect of disulfiram on markers of endothelial dysfunction were measured via qRT-PCR for vascular cell adhesion molecule-1 (VCAM-1) and adhesion of fluorescently labelled peripheral blood mononuclear cells (PBMCs) to HUVECs.

RESULTS
Disulfiram significantly reduced mRNA expression of the sFLT-1 variants, sFLT-1-i13 and sFLT-e15a. This translated into a significant and dose dependent reduction in the protein secretion of sFLT-1. In primary trophoblast disulfiram did not inhibit the 20S subunit of the proteasome, evidenced by no change in cellular fluorescence following addition of Suc-LVY-AMC. Treating primary HUVECs with serum from preeclamptic women induced endothelial dysfunction with significantly increased mRNA expression of VCAM-1 as well as the adhesion of PBMCs to HUVECs. Disulfiram reduced VCAM-1, with expression reduced below control levels, however, did not alter the adhesion of PBMCs to primary HUVECs.

Conclusions
We have identified disulfiram to quench placental sFLT-1 secretion via a mechanism independent of inhibiting the 20S subunit of the proteasome. Understanding of the mechanisms by which disulfiram inhibits sFLT-1 secretion may assist in identifying therapeutic targets. Interestingly, disulfiram also reduced markers of endothelial dysfunction.

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Lipoprotein turnover and possible remnant accumulation in preeclampsia: Insights from the Freiburg Preeclampsia H.E.L.P.-Apheresis Study
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Introduction: Preeclampsia is a potentially life threatening disease occurring in pregnancy. The only causative cure consists in delivery with all the risks for a premature fetus. In preeclampsia, the lipid metabolism is substantially altered and lipid apheresis is being explored as a possible therapeutic approach to prolong preeclamptic pregnancies and allow further maturation of the fetus. In the Freiburg H.E.L.P.-Apheresis Study, 6 early onset preeclamptic patients were treated with H.E.L.P. apheresis.

Objective/Hypothesis: Detailed analysis of apheresis-induced dynamics in serum lipid parameters.
Methods: 6 early onset preeclamptic patients underwent repeated apheresis treatments (n=23). We evaluated parameters of the lipoprotein metabolism in 6 preeclamptic patients in detail.
Results: Reduction of lipoproteins by apheresis was lower than theoretically expected. Lipids reached previous pre-apheresis levels before the next apheresis even though apheresis was repeated within 2.9 ± 1.2 days. Fractional catabolic rates and synthetic rates were found to be substantially elevated, with fractional catabolic rates for ApoB / LDL-cholesterol being 0.7 ± 0.3 / 0.4 ± 0.2 [day⁻¹] and synthetic rates being 26 ± 8 / 17 ± 8 [mg·kg⁻¹·day⁻¹]. The distribution of LDL subclasses after apheresis shifted to larger buoyant LDL, while IDL levels remained unaffected.
Discussion: Apheresis induced changes in lipoprotein profiles point to an underlying remnant removal disease like imbalance in plasma lipid conversion during preeclamptic conditions.

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Placental structure and vascularization in IVF/ICSI-pregnancies compared to naturally conceived pregnancies
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Objectives: Although pregnancy rates of artificial reproductive techniques (ART) pregnancies have been optimized, these pregnancies have a higher risk of pregnancy complications due to impaired placenta function during early pregnancy and thereby affecting placental vascularization, structure and later on fetal growth. The aim of this study is to investigate if there are placental ultrasonographic differences between ART- and naturally conceived pregnancies.
Methods: A cross-sectional pilot study included 35 ART- and 30 naturally conceived (NC) pregnancies at the Maastricht University Medical Centre, between October 2017 and March 2018. Inclusion criteria were singleton pregnancies (NC, IVF/ICSI), maternal age ≥ 18 years and body-mass-index (BMI) < 35kg/m². Characteristics were collected via electronic health records. Ultrasounds were performed by two trained ultrasonographers at 12 and 16 weeks of gestation, using an abdominal transducer and predefined settings. Vascularization index (VI) was calculated offline, using 4D-View (VOCAL).

Results: Placental calcifications at 12 and 16 weeks of gestation showed no significant difference between the ARTand NC-group. However, placental lakes at 16 weeks were more prominent in the ART-group (59.5%) compared to the NC-group (26.1% (p=0.017). Vascularization index at the umbilical cord insertion (UCI) and in the peripheral parts of the placenta was measured. At 12 weeks, the ART-group compared to the NC-group, showed a lower VI at the UCI (0.73±0.81% vs. 2.00±2.46%, p=0.156) and in the peripheral parts of the placenta (1.73±3.43% vs. 4.14±4.92%, p=0.023). At 16 weeks, no significant differences were found.

Conclusions: Reduced early placental vascularisation in ART compared to NC-pregnancies may reflect the underlying aetiology of impaired placentation. These results provide promising possibilities for a more extended prospective trial and using placental ultrasonography as a predictor in the future.

Fetal microchimerism in pregnancy and placental dysfunction
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Introduction:
During pregnancy, bidirectional cell trafficking occurs, generating cellular fetal microchimerism (cFMC). cFMC describes fetal cells that enter maternal tissues and blood, potentially persisting for decades. In the long-term, cFMC may be associated with maternal disease risk (e.g. autoimmunity) and protection (e.g. cancer). In pregnancy, circulating cFMC is augmented in preeclampsia. Preeclampsia is characterized by placental dysfunction, but the underlying mechanisms remain elusive. Other disorders associated with placental dysfunction include HELLP, pregnancy induced hypertension, fetal growth restriction, and pregestational or gestational diabetes mellitus (DM).

Objective/hypothesis:
We hypothesize that placental dysfunction in general, not limited to preeclampsia, correlates with augmented cFMC in maternal circulation

Methods:
Pregnant women were recruited to the Oslo Pregnancy Biobank (2001-2017) at the time of delivery, prior to active labor. We analyzed 28 pregnancy samples (preeclampsia, n=9, pregestational or gestational DM, n=7, uncomplicated pregnancies, n=6). Buffy coat was isolated from maternal peripheral blood and fetal cord blood. To identify fetus-specific polymorphisms, the samples were genotyped by high resolution sequencing of the human leukocyte antigen (HLA) loci DRB1, DQA1, and DQB1. We identified cFMC using validated HLA polymorphism-specific quantitative polymerase chain reaction assays.

Results:
Our preliminary results showed that of 9 preeclampsia samples, 5 (55.6%) were positive for cFMC; of 7 diabetes samples, 4 (57.1%) were positive. In the control group, only 1 of 6 (16.7%) had cFMC.

Discussion:
We conclude that at the time of delivery, women with preeclampsia or DM (pregestational or gestational) may harbor circulating cFMC more frequently than women with uncomplicated pregnancies. One possible explanation is that dysfunctional placentas could be prone to fetal cell “leakage”. We speculate that circulating cFMC may promote generalized maternal endothelial inflammation contributing to hypertension and proteinuria, immediately and long-term. A larger cohort is required to investigate cFMC in a wider range of pregnancy complications associated with placental dysfunction.
Do Calcium Channel Blockers Modulate Fetoplacental Blood Flow? A Study Using Parallel Wire Myography
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Introduction: Calcium channel blockers treat maternal hypertension in pregnancy. The effect of newer calcium channel blockers on placental vascular function remains unknown. This study aimed to determine the effect of calcium channel blockers on placental chorionic plate proximal resistance arteries in comparison to maternal omental arteries.

Methods: Chorionic plate and omental arteries from healthy term pregnancies delivered by caesarean section were studied using parallel wire myography (n=80; N=10). Arteries were normalised at 0.9 of L5.1 kPa in 5% O2 and L13.3 kPa in 20% O2 respectively, approximating physiologic vascular pressure and oxygen tension. Arteries were contracted with thromboxane-mimetic U46619 to determine and maintain optimal physiologic vascular tone (EC80). Nifedipine, Nicardipine and Clevidipine were added in incremental doses from 10⁻¹⁰M to 10⁻⁵M to create dose-dependent relaxation curves. Omental arteries were incubated for 30 minutes at the highest dose (10⁻⁵M) to further evaluate full effect (n=16; N=4).

Results: Omental arteries demonstrated similar contractility to chorionic plate arteries (8.90kPa±0.681 vs 8.85kPa±0.603). Chorionic plate arteries did not relax with Nifedipine, Nicardipine or Clevidipine (110.73%±7.518 vs 118.88%±9.379 vs 113.16%±5.163). Omental arteries demonstrated a trend towards larger relaxation with all calcium channel blockers at the highest dose of drug concentration. This was confirmed with highest dose incubation of omental arteries, that showed Nifedipine, Nicardipine and Clevidipine relaxed omental arteries (52.31%±16.294 vs 57.12%±8.621 vs 79.95%±14.862; One-way ANOVA, p<0.05).

Conclusion: Chorionic plate arteries demonstrated reduced vasodilatory responses to calcium channel blockers compared to omental arteries. This suggests calcium channel blockers show limited effect on placental blood flow through proximal resistance arteries.

Late breaking abstracts

Does pre-eclampsia predicts attention-deficit/hyperactivity disorder in offspring? Findings from ALSPAC Birth Cohort Study
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Background: Attention-deficit/hyperactivity disorder (ADHD) is a prevalent heterogeneous neurodevelopmental syndrome associated with various environmental factors. This study examined the association between maternal pre-eclampsia and offspring ADHD at 7- and 10-years.

Methods: We used data from the Avon Longitudinal Study of Parents and Children (n=7200+). ADHD was diagnosed using parent reported Development and Wellbeing Assessment (DAWBA). Logistic regression and Generalized Estimating Equation (GEE) models were used to examine the association between maternal preeclampsia and ADHD in offspring.

Results: The overall prevalence of ADHD was 2.04% and 1.62% at ages of 7 and 10 years, respectively. GEE analysis showed that pre-eclampsia was associated with increased risk of ADHD in offspring (adjusted odds ratio [OR] = 2.94, 95% confidence interval [CI]: 1.40-6.15). The results of multivariable logistic regression analysis, at each time point, also showed that preeclampsia increased risk of ADHD by more than 2.75-fold.

Conclusion: This study suggests that offspring of mothers with pre-eclampsia are at increased risk of ADHD adding to the growing evidence that uterine environment is a critical determinant of neurodevelopmental outcome. If our findings are replicated by others, early screening for ADHD and other developmental delays may be recommended in offspring of women with pre-eclampsia.
Hypertensive disorders of pregnancy and childhood depression: evidence from the ALSPAC birth cohort study
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2The University of Queensland, Australia

Background: Around 10-15% of global pregnancies are complicated by hypertensive disorders of pregnancy (HDP) which in turn accounts for up to 16% of maternal deaths worldwide. HDP are also responsible for various adverse perinatal outcomes and are associated with an increased risk of offspring cardiovascular, immune, and metabolic disorders later in life. However, little is known about the impact of HDP on offspring mental health outcomes.

Objective: This study aimed to investigate the association between HDP and the risk of depression in childhood.

Methods: We used data from the Avon Longitudinal Study of Parents and Children (ALSPAC), a prospective longitudinal birth cohort study in Avon, United Kingdom. Childhood depression at the age of 7 years was diagnosed using parent reported Development and Wellbeing Assessment (DAWBA).

Results: Among those children who had data on childhood depression at age 7 (n=7847), 15.9% were exposed to HDP. Children of women with HDP had an increased risk of depression at 7 years (OR= 2.4, 95%CI: 1.23-4.71). Results were adjusted for a wide range of confounding variables including maternal depression and anxiety during pregnancy.

Conclusion: To our knowledge, this is the first study to investigate associations between maternal HDP and childhood depression. Our study suggests that fetal exposure to maternal hypertensive disorders of pregnancy increased the risk of childhood depression and adds to the body evidence indicating that the uterine environment is a critical determinant of neurodevelopmental and psychiatric outcomes. Early screening for childhood emotional problems in offspring of women with HDP may be warranted.

Posters

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Angiotensin ii modulates the pathogenesis of preeclampsia through sflt-1 production from extravillous cytotrophoblast.
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INTRODUCTION: Preeclampsia (PE) is characterized by disturbed extravillous trophoblast migration toward uterine spiral arteries leading to increased uteroplacental vascular resistance and by vascular dysfunction resulting in reduced systemic vasodilatory property. It is known that such pathogenesis is mediated by soluble fms related tyrosine kinase 1 (sFlt-1) and Endoglin (sEng). Our objective was to evaluate the effect of angiotensin II (AngII) on the production of sFlt-1 and sEng from cytotrophoblast.

METHODS: Plasma concentration of sFlt-1 and sEng in our PE model mouse was calculated with AngII receptor subtype 2 (AT2) stimulator (C21). Jar cell and HTR-8 cell was cultured and stimulated by AngII with or without AngII receptor subtype 1 (AT1) inhibitor and AT2 inhibitor. The concentration of sFlt-1 and sEng was calculated in culture medium of the cells using ELISA.

RESULTS: C21 reduced plasma concentration of sFlt-1 resulted in improved hypertension and proteinuria but did not affect that of sEng. sFlt-1 concentration in the medium of HTR-8 was reduced by AT1 inhibitor and stimulated by AT2 inhibitor. sFlt-1 production of Jar cell could not be responded by AngII.

CONCLUSIONS: This study demonstrated that extravillous trophoblast (HTR-8) could produce sFlt-1 in response to AT1 and AT2; however, cytotrophoblast (Jar) could not be responded by AngII. It is suggested that extravillous trophoblast could be involved in the pathogenesis of PE through the effect of AngII and C21 could be a candidate of new therapy of PE.
**Tonicity responses by TonEBP and SMIT in human primary term cytotrophoblasts**

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**Introduction:** Previously, we and others have demonstrated that in pregnancy enhanced intake of salt (NaCl) lowers maternal blood pressure and improves pregnancy outcome; the reasons why are unknown. It has been shown in non-renal tissues such as the skin interstitium, that in response to high salt, macrophages upregulate tonicity-responsive enhancer binding protein (TonEBP), which regulates transcription of sodium-myo-inositol cotransporter (SMIT). We hypothesised that placental trophoblasts are able to respond to salt in a similar manner.

**Objectives:** To use human primary term cytotrophoblasts (CTBs) to evaluate how the placenta responds to hypertonicity.

**Methods:** CTBs were incubated with 3 different salt concentrations (110, 140 and 170mM NaCl) for 6 or 24 hours. mRNA expression of TonEBP and SMIT were measured by RT-PCR and normalised to the geometric mean of the reference genes Cyclophilin A, HPRT1 and YWHAZ.

**Results:** After 6h incubation with high salt (170mM NaCl), TonEBP and SMIT mRNA levels were upregulated (p<0.01) compared to 110mM NaCl. After 24h incubation with high salt, TonEBP mRNA was no longer upregulated in CTBs. However, SMIT mRNA levels stayed upregulated also after 24h incubation with high salt (p<0.05).

**Conclusion:** The results of this study indicate that TonEBP regulates transcription of SMIT in human primary term cytotrophoblasts and that this regulation can be enhanced following treatment with NaCl. The TonEBP response enables cells to survive hypertonic conditions via the accumulation of organic osmolytes. The results of the CTBs confirm our results in three human trophoblast cell lines (HTR8/SVneo, JEG3, BeWo).

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**Placental pathology and neonatal outcome in relation to uterine artery Doppler velocimetry in pregnancies complicated by placenta syndrome**

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**Objectives:** High resistance utero-placental circulation leads to placenta insufficiency related complications for both mother and fetus. The objective of this study was to evaluate the relationship between abnormal uterine artery pulsatility index (UtAPI) Doppler measurements, neonatal outcome and placental histological findings in placenta syndrome (PS) pregnancies.

**Methods:** A retrospective pilot study was performed on singleton pregnancies complicated by PS (pre-eclampsia and/or foetal growth restriction). UtA, umbilical (UmbA) and middle cerebral artery (MCA) Doppler measurements were collected within the last two weeks prior to delivery. Patients were divided into two groups according to UtAPI values, in which UtAPI>p95 was considered abnormal. Histological lesions were classified according to the criteria of the Society for Pediatric Pathology. Statistical analysis was performed using independent T-, Mann-Whitney U- and Fisher’s exact test. Multivariate analysis was used to correct UtAPI for gestational age (GA) at delivery and parity.

**Results:** The UtA-PI>p95 group (n=25) showed a higher rate of premature delivery (p=0.025), caesarean section (p=0.007) and NICU-admission (p=0.001) compared to the UtA-PIp95 group showed a significantly higher UmbA-PI (p=0.004) with absent or reversed flow (p=0.002), a lower MCA-PI (p=0.010) and cerebro-placental ratio (p<0.001). The predictive ability of the corrected UtA-PI was significant for macroscopic infarction (OR= 1.033 (95% CI 1.007-1.059) p=0.011), intervillous fibrin (OR=1.033 (95% CI 1.005-1.061) p=0.022) and decidual atheropathy (OR=1.059 (95% CI 1.002-1.119) p=0.043). Overall, UtA-PI was able to predict maternal vascular malperfusion lesions (OR=1.048 (95% CI 1.011-1.087) (p=0.011)).

**Conclusions:** In pregnancies complicated by PS, UtA-PI>p95 showed a moderate predictive ability for placental underperfusion independently of GA at delivery and parity. Furthermore, neonatal outcome and Doppler measurements were poorer.
Spiral arterial blood flow during pregnancy: a systematic review and meta-analysis
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Objectives: To evaluate the physiological adaptation of blood flow in human uterine spiral arteries throughout the course of normotensive and hypertensive pregnancies based on existing literature.

Methods: A systematic literature review and meta-analysis on the change of arterial uterine spiral arteries, measured by Doppler ultrasonography, was conducted. Literature search was performed in Pubmed, EMBASE and Cochrane Library. The search was limited to papers published in English. Both first and second selection were performed by two independent researchers. Weighted means of the Doppler indices were calculated for the three pregnancy trimesters.

Results: Seven longitudinal prospective and four cross-sectional studies were included with publication dates ranging from 1995 to 2015. Ultrasound measurements were performed at certain gestational ages using transvaginal or transabdominal transducers. In normotensive pregnancies, pulsatility index (PI) decreased from 0.76 (95% CI: 0.65-0.86) in the first trimester to 0.51 (95% CI: 0.45-0.57) (p<0.001) in the second trimester and to 0.51 in the third trimester (95% CI: 0.47-0.54) (p=0.960). Resistance index (RI) decreased from 0.49 (95% CI: 0.45-0.53) in the first trimester to 0.40 (95% CI: 0.36-0.43) (p<0.001) in the second trimester and to 0.37 in the third trimester (95% CI:0.35-0.38) (p=0.960). Although PI and RI tend to be higher in the hypertensive pregnancies, no significant difference with normotensive pregnancies during gestation was observed.

Conclusions: PI and RI in uterine spiral arteries both decreased with advancing gestational age with the largest decrease between the first and second trimester. This is in concordance with previous histological hypertrophic decidual vasculopathy- and Doppler uterine artery findings. Longitudinal studies examining comprehensively the predictive value of spiral artery Doppler for hypertensive pregnancies are yet to be determined.

Evidence of senescence in post-mature and pathological human placentas; a possible contributing factor in pre-eclampsia?
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Introduction: Cell senescence, which can be activated by oxidative stress and DNA damage, has also been implicated in cell fusion. Placental oxidative stress is a key intermediary event in the pathophysiology of pre-eclampsia.

Objectives/hypothesis: The aim was to examine senescence markers in normal placentas across gestation, and in pathological and post-mature pregnancies. Inducers of oxidative stress were used to mimic senescence changes in term explants.

Methods: Placental samples were collected with ethical approval. First and second trimester samples were from surgical terminations; term and pre-term controls, and early-onset pre-eclampsia (PE+IUGR) placentas were from caesarean deliveries. Paraffin and EM blocks of post-mature placentas (7-21 d post-term) were from an archival collection. Oxidative stress was induced by subjecting term explants to cyclical hypoxia-reoxygenation (HR) or H2O2 (0-1 M) for 24-48 h.

Results: p21 was increased significantly in term homogenates compared to first and second trimester samples, and was significantly higher in both preterm controls and PE+IUGR compared to term controls. Immunostaining revealed nuclear localisation of p21 and phosphorylated histone, γH2AX, in the syncytiotrophoblast, with abundant foci in pathological and post-mature placentas. Abnormal nuclear appearances were observed in post-mature placentas. Sudan-Black-B staining demonstrated abundant expression of lipofuscin, an aggregate of oxidised proteins, lipids and metals, in post-mature and pathological placentas. In addition, an increased percentage of nuclei were positive for 8-hydroxy-2’-deoxyguanosine, a marker of oxidised DNA, in pathological placentas compared to age-matched controls. These changes could be mimicked in vitro by challenge with HR or H2O2.

Conclusions: Evidence of senescence markers increases with gestational age in normal placentas, and is exaggerated in post-mature and pathological placentas. Oxidative stress triggers these changes in placental
explants, and may be the precipitating insult in vivo. The consequent pro-inflammatory senescence-associated secretory phenotype may contribute to the pathophysiology of early-onset pre-eclampsia.

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**Preeclamptic decidual stromal cells fail to decidualize during co-culture with placental villous explants**

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**Introduction:** Sustained stromal cell decidualization at the maternal fetal interface is vital to the development of placenta and fetus. Recent reports suggest that defective decidualization of endometrial stromal cells (ESCs) may contribute to the development of preeclampsia (PE). We hypothesize that there may be defective communication between the placenta and stromal cells in PE that contribute to suboptimal decidualization. Our aim is to study the interaction between placenta and decidual cells in an ex vivo co-culture model with respect to decidualization and sFlt1 production.

**Methods:** Primary decidual stromal cells (DSCs) were isolated from term placentas of normotensive (n=4; NT-DSCs) and preeclamptic (n=3; PE-DSCs) pregnant women. Villous explants (VE) were prepared from NT placenta (n=3) and stored in liquid nitrogen by the process of vitrification. DSCs were subjected to co-culture with VE for 72 h. Prolactin (PRL) and sFLT1 mRNA expression in VE and DSCs were determined by qRT-PCR. Group means were analyzed by one-way ANOVA. p≤0.05 is considered significant.

**Results:** Co-culturing VE with NT-DSC induced a significant increase in the DSC PRL expression (4.78±1.64 fold against control 1.0, p=0.005) compared to 1.93±0.40 in PE-DSCs. VE co-cultured with NT-DSCs showed a significant downregulation of DSC sFlt1 expression (0.34 ± 0.10; p=0.02) but not when co-cultured with PE-DSCs (0.37 ± 0.17, p = 0.07). PRL mRNA levels did not significantly change in VE. However, VE co-cultured with NT-DSCs showed a significant downregulation of sFlt1 mRNA expression.

**Conclusion:** VE interaction with NT-DSC induced decidualization and downregulation of sFlt1 in the DSCs as well as sFlt1 expression in the VE. This effect was not observed in co-cultures of VE with PE-DSCs. These findings suggest that in addition to being defective to hormone-induced decidualization, PE-DSCs are defective in their interaction with placenta that is necessary for optimal post-implantation decidualization and downregulation of sFlt1.

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**Phenotype restoration of trophoblasts in preeclampsia by Low Level Light Therapy (LLLT)**

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**Introduction:** In our previous work we demonstrated the importance of altered extracellular matrix (ECM) in disease processes and how treatment with 670nm LLLT can restore cell behavior.

**Objective:** To study the signaling properties of altered ECM in preeclampsia, its contribution to preeclampsia, and the possibility of a novel therapeutic modality restoring the trophoblast phenotype with LLLT.

**Methods:** To study signaling pathways we decellularized placentas from healthy and preeclamptic subjects with 1%SDS followed by triton X and thorough wash steps. First trimester human trophoblasts (HTG8) were cultured on these two different matrices. This allows us to study trophoblast behavior in their proper microenvironment and follow the trophoblast phenotype changes. Immunohistochemistry and western blot analysis were performed with a focus on PLGF, ERRg, FoxP3, and HLA-G expression comparing the different matrices. Readouts are fluorescence intensity and western blot density in arbitrary units (AU). Furthermore, 670nm light treatment was applied to HTG8s at an energy level of 4J/cm² once and cellular changes were studied 24hours later.

**Results:** Our results show that the expression of PLGF in HTG8s was decreased from 102AU to 68 AU comparing control with preeclamptic matrix. ERRg expression was significantly reduced in HTG8s from 80.33AU to 18.6AU. FoxP3 expression was decreased from 109.38AU to 82.1AU. HLA-G expression was significantly decreased from 105.94 to 49.48AU. LLLT restored the phenotype of HTG8s cultured on preeclamptic matrix to the phenotype of HTG8s cultured on control placenta. Statistics were performed using the Student’s t-test.

**Discussion:** Our data demonstrate for the first time that the ECM of the placenta and therefore the microenvironment has great impact on trophoblast signaling. Preeclamptic ECM alters the trophoblast phenotype and LLLT restored the phenotype to the phenotype found in trophoblasts cultured on control ECM.
Imaging the Placental Glycocalyx
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Introduction: Glycocalyx is a gel-like mesh which lines the luminal surface of vascular endothelium and has an important role in vessel function and permeability. Disruption of glycocalyx has been implicated in the endothelial dysfunction in pre-eclampsia. There is increasing evidence for a significant glycocalyx present at the maternal-fetal interface of the human placenta. Due to the unstable nature of glycocalyx in-vivo it has previously been difficult to demonstrate and study.

Objectives: To confirm the presence of the placental glycocalyx of the fetal capillary endothelium and syncytiotrophoblast and to develop a reliable imaging protocol to observe this ex-vivo.

Methods: Term placentae were collected from uncomplicated pregnancies at caesarean section and processed in one of two ways. 1) Electron Microscopy: placental glycocalyx was labelled using perfusion or immersion with Alcian Blue in glutaraldehyde. Samples were post fixed, embedded and sectioned for imaging with transmission electron microscopy (TEM). Glycocalyx depth was measured perpendicular to the phospholipid bilayer. 2) Lectin Staining. Biopsies were fixed in 4% paraformaldehyde, paraffin embedded and sectioned. Glycocalyx was labelled with FITC-conjugated wheat germ agglutinin (WGA) and membrane labelled with octadecyl rhodamine B chloride (R18) and imaged using confocal microscopy. The distance between the peak signals of FITC-WGA and R18 was used to measure glycocalyx depth. Results presented as mean glycocalyx thickness ± SEM.

Results: TEM demonstrated glycocalyx depth of 57.1 ± 5.8 nm at the fetal capillary and 62.2 ± 3.7 nm at the syncytiotrophoblast. Glycocalyx depth using lectin staining was significantly greater 279.3 ± 42.6 nm and 893.7 ± 150.1 nm at the capillary and syncytiotrophoblast respectively.

Conclusion: The placenta maintains a significant glycocalyx at the syncytiotrophoblast and fetal capillary endothelium in term uncomplicated pregnancy. The absolute depth of glycocalyx varied depending on the imaging modality used. Correlative fluorescence and electron microscopy techniques would help further define this.

Investigation of placental proteome of pregnant stroke-prone spontaneously hypertensive rats
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Investigation of placental proteome of pregnant stroke-prone spontaneously hypertensive rats
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Introduction: The stroke-prone spontaneously hypertensive rat (SHRSP) obtained by selective inbreeding of the Wistar-Kyoto (WKY) strain is a well-characterized model of cardiovascular disease. The phenotype of the pregnant SHRSP is reflective of the clinical condition of maternal chronic hypertension during pregnancy.

Objective: We investigated whether placental proteomics can identify candidate molecules involved in placental dysfunction in pregnant SHRSP.

Method: Placental proteome of pregnant WKY and SHRSP (n=5) at gestational day 18 were analyzed using label-free proteomics. Identification and quantitation of protein was performed using LC-MS/MS connected to an LTQ Orbitrap hybrid mass spectroscopy. Functional annotation and gene ontology of proteome was carried out using bioinformatics tools such as DAVID, STRING and Cytoscape.

Result: Comparison of SHRSP and WKY identified total of 1318 proteins, amongst these 686 were extracellular exosomes proteins, followed by 663 cytoplasm, 486 nucleus and 383 membrane proteins. There were 363 differentially expressed proteins (p value <0.05), of which 115 and 227 protein were found to down-regulated and up-regulated in SHRSP respectively, with a fold change cut-off >1.3. Protein interaction networks and gene ontology analysis of these proteins identified major biological process such apoptosis, inflammation, oxidative stress, cell adhesion and migration. We also found 7 and 14 proteins to be uniquely identified only in WKY and SHRSP respectively (p value < 0.05).

Discussion: The study shows characteristic proteomic pattern in placenta of SHRSP. Further studies into the differentially expressed candidate proteins will give insight into the placental dysfunction in hypertensive pregnancy.

Keyword: Placenta, Proteomics, Hypertension, SHRSP
Peculiarities of placental expression of erythropoietin in preeclampsia

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Introduction: The role of erythropoietin (EPO) in the pathogenesis of preeclampsia (PE) is important and associated with the anti-apoptotic and angiogenic effects of the hormone.

Objectives: The aim was to study the peculiarities of placental expression of erythropoietin in preeclampsia.

Methods: In the cross-sectional cohort study we included 55 pregnant women: group 1 (control) – 11 women without PE; group 2 - 14 women with mild PE; group 3 - 30 women with severe PE. Immunohistochemical studies of the placenta (syncytium, capillary endothelium, macrophages of villi stroma) were performed to evaluate the expression of EPO (primary specific anti-Epo (N-19): sc-1310-R (Santa Cruz Biotechnology, Inc., California, USA) in 10 randomly selected areas using an objective micrometer under light microscope at a magnification of 400 high-power field. The mean for 10 fields was used as the cell count for that section.

Results: In group 1 EPO expression was more often detected in the villous syncytiotrophoblast (19.73 ± 0.54, \( p_{s-e} = .005 \)) compared with the capillaries endothelium (9.46 ± 0.60, \( p_{s-e} = .003 \) and stromal macrophages (12.27 ± 0.51, \( p_{s-m} = .003, p_{s-m} = .005 \)). In mild PE expression of EPO in the syncytium (26.20 ± 0.46, \( p_{1-2} < .001 \)), in capillaries endothelium (18.87 ± 0.50, \( p_{1-2} < .001 \)) and macrophages of the villi stroma (19.87 ± 0.48, \( p_{1-2} < .001 \)) was significantly higher comparing with group 1. The highest levels of EPO expression were in severe PE - in syncytium (33.06 ± 0.76, \( p_{1-3} < .001; p_{2-3} < .001 \)), vascular endothelium (26.00 ± 0.40, \( p_{1-3} < .001; p_{2-3} < .001 \)) and macrophages of the stroma (27.29 ± 0.52, \( p_{1-3} < .001; p_{2-3} < .001 \)).

Discussion: It has been suggested that in severe PE, placental hypoxia could induced EPO expression in placenta (syncytium, capillary endothelium, macrophages of villi stroma).
Quercetin protects against the vascular contractile effect of placental secreted messengers released under placental hypoxia
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Introduction: Hypoxia is a crucial factor in the pathogenesis of preeclampsia resulting in hypoxic stress in the placenta. Upon this stress the placenta will release placenta secreted messengers (PSMs) which will cause maternal endothelial dysfunction. Previous research suggests that the antioxidant quercetin exerts anti-hypertensive effects and endothelial relaxation via NO release.

Objective: To determine the vascular effect of PSMs released under hypoxia and to study the protective effect of quercetin on this process.

Methods: In this study 44 non-complicated placentas (GA > 37 weeks) were used. PSMs were generated by exposing healthy term placentas to hypoxia. Chorionic arteries were incubated with these PSMs +/- quercetin 3 and 20 µM and contractile responses were recorded over a two-hour period. PSMs generated under normoxic conditions were used as control. Endothelial dysfunction induced by PSMs was assessed by analyzing changes in contractile responses to KCl (62.5 mM) before and after exposure to the PSMs.

Results: PSMs released under hypoxia induced an increased contraction in chorionic arteries compared to PSMs released in the presence of quercetin and normoxic conditions (39.1 µm ± 5.9 vs. quercetin 3 µM: 17.5 µm ± 1.6 vs. quercetin 20 µM: -8.5 µm ± 2.2 vs. normoxic: 0.5 µm ± 0.8, p < 0.001). A decreased change in contractile response to KCl (62.5 mM) was observed for PSMs released in the presence of quercetin (20 µM) (72.5 µm± 6.0 vs. quercetin 3 µM:40.1 µm± 3.3, p < 0.05 and quercetin 20 µM:3.5 µm± 0.6, p < 0.001). No changes in contractile response to KCl was observed for the control condition (0.0 ± 0.2, p < 0.001).

Discussion: Quercetin shows promising results for the protection against the PSMs released under preeclampsia-like stress conditions like placental hypoxia, which could eventually be used for prevention and/or treatment of preeclampsia.

Translational research
Poster pitches
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Investigational RNAi therapeutic targeting angiotensinogen (AGT) ameliorates the preeclamptic phenotype in rodent models of preeclampsia
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Introduction: Preeclampsia is a common and devastating pregnancy disorder, featuring hypertension and proteinuria. Studies have demonstrated that dysregulation of Renin-Angiotensin-System (RAS) is involved in the pathogenesis of the disease; however, treatment with a RAS-blocker is contraindicated due to fetal toxicity.

Objective: RNA interference (RNAi) is a potent means of gene-specific silencing. We sought to demonstrate maternal-specific RAS blockade by targeting maternal hepatic angiotensinogen (AGT) using small interfering RNA (siRNA). In this study we tested the ability of AGT-targeting siRNA to ameliorate symptoms of preeclampsia in two rat models, without inducing a placental pathology or affecting fetal health.

Methods: Two animal models of preeclampsia were used. The first model (transgenic) acts by upregulation of the circulating and uteroplacental Renin-Angiotensin-System (RAS). The second model is a surgical model that induces ischemia/reperfusion injury and subsequent local and systemic inflammation restriction (RUPP). Beginning on day 3 of gestation, transgenic rats were dosed subcutaneously with 10 mg/kg siRNA every third day through gestation day 15. In RUPP rats, siRNA was subcutaneously injected once (10mg/kg) on day 12 of gestation.

Results: The major finding is that RNAi therapeutics targeting maternal hepatic AGT ameliorated the preeclamptic phenotype in both models. We were able to selectively reduce maternal RAS signaling while preserving the fetal RAS. In the transgenic model, silencing of hAGT leads to a reduction of blood pressure and urinary albumin
Magnesium deficiency induces hypertension associated with suppression of catechol-O-methyltransferase

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Introduction: Eclampsia is a severe complication of hypertensive disorders of pregnancy (HDP). Magnesium (Mg) sulfate is conventionally used as an initial treatment or as a prophylaxis of eclampsia without established mechanism. Serum Mg concentration ([Mg]) is known to be suppressed in preeclamptic women. Catechol-O-methyltransferase (COMT), the Mg dependent enzyme, deficiency leads to hypersensitivity of pressure response against angiotensin II (AgII). Here, we hypothesize that Mg deficiency suppresses COMT levels and leads to hypertensive disorders.

Methods: 7 weeks male/female DBA/2J mice were fed either Mg deficient food (30mg Mg/kg) or control food (800mg Mg/kg). For male mice, low-dose AgII (AgII: 70ng/kg/min) or PBS was infused on 17th day after Mg deficient/control food was administered. Mice were sacrificed on 27th day.

Results: Serum Mg level of the Mg deficient group (Mg-) had decreased to 1/4 of the control group (Cont) on 10th day. In Cont, body weight (BW) had increased to 30% in male mice and 20% in female mice on 27th day; in Mg-, BW was unchanged and lighter compared to Cont. In male mice, the average systolic BP (sBP) was higher in Mg- compared to Cont regardless of AgII infusion. The difference in sBP between Mg- and Cont was 7~10mmHg during 14th to 25th day. In female mice, sBP was not altered in Mg-. The COMT levels in heart, liver, kidney were significantly low in Mg- compared to Cont.

Discussion: The sBP difference between two groups was significant, which implied that the Mg deficiency induced hypertension. COMT expression was lower in Mg deficient group, suggesting that the Mg deficiency might induce hypertension by suppressing COMT expression.

Integrins (a1, b1 and a6, b4) differentially modulate trophoblast-endothelial interaction in vitro

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Introduction: During normal trophoblast invasion, integrin a6b4 are downregulated and a1b1 are upregulated in invasive cytotrophoblast cells. In preeclampsia, both interstitial and endovascular invasion are shallow and cytotrophoblast fail to upregulate a1b1 and downregulate a6b4. Objective: This study aims to investigate role of integrin a1b1 and integrin a6b4 during trophoblast integration into endothelial cellular networks in vitro. Methods: Red fluorescent-labeled human uterine myometrial microvascular endothelial cells (UmMVECs) were seeded on Matrigel to form endothelial networks. Green fluorescent-labeled trophoblast HTR-8/SVneo cells pre-incubated with 20 μg/ml of neutralizing antibodies (anti-a1, b1, b6, b4, a1b1 or a6b4) for 1 hour were then co-cultured with the endothelial networks with the neutralizing antibody for 24 hours. Fluorescent images were captured and quantified by image J. Free soluble fms-like tyrosine kinase-1 (sFlt-1), placenta growth factor (PIGF), matrix metalloproteinases 2 and 9 (MMP-2 and MMP-9) from conditioned media were measured by ELISA. Cells were retrieved to examine mRNA expression of invasion markers of tissue inhibitor of metalloproteinase-1 (TIMP-1) and plasminogen activator inhibitor type 1 (PAI-1) by quantitative PCR. Results: The integration of trophoblast cells into endothelial cellular networks was significantly inhibited by anti-b1 (72±3%, p<0.0001), and increased by anti-a6 (119±5%, p<0.01). In the conditioned medium, MMP-2 was significantly inhibited by both anti-a1 (72±1%, p<0.001) and anti-b1 (85±2%, p<0.05), however, MMP-9 production was inhibited by anti-a1 only (73±5%, p<0.001). The sFlt-1 production was also inhibited by anti-a1 (73±5%, p<0.001). There were no changes in PIGF production. The mRNA of TIMP-1 expression was significantly inhibited by anti-a1 (41±5%, p<0.01) and anti-b1 (37±7%, p<0.001). The PAI-1 mRNA expression (385±70%, p<0.0001) was increased by anti-a1b1. Discussion: We have shown that anti-integrin b1, not
anti-integrin α1 inhibited and anti-integrin α6, not anti-integrin B4 increased endothelial-trophoblast cellular integration in vitro. The matrix degradation enzymes (MMP-2 and MMP-9) and their associated inhibitors (TIMP-1 and PAI-1) may involve in this process.

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Nicotinamide alleviates preeclampsia-like features and lupus nephritis in pregnant MRL/lpr mice treated with LPS
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【Introduction】Systemic Lupus Erythematosus (SLE) increases the risk of unfavorable pregnancy outcomes including preterm birth and preeclampsia (PE). Flare-up of SLE during pregnancy or after birth is also problematic. TLR4 signaling is known to exacerbate both SLE and pregnancy. We have shown that nicotinamide (NAM), a non-teratogenic amide of vitamin B3, reduces inflammation and oxidative stress, and improves PE-like phenotype in mouse models of PE (Takahashi N, et al. PNAS 2016). 【Objective】The aim of the present study is to establish a mouse model to study pathogenesis and treatment of SLE patients suffering from PE, and to test whether nicotinamide (NAM) is beneficial to preeclamptic SLE mice. 【Methods and Results】We administered low dose LPS, a TLR4 ligand, to pregnant lupus-prone MRL/lpr mice, and analyzed maternal and fetal outcomes. LPS increased blood pressure, caused fetal growth restriction (FGR), and exacerbated glomerulonephritis in MRL/lpr-LPS mouse. We conclude that this is a suitable model to study pathogenesis of pregnancy in SLE. We next examined a therapeutic effect of NAM on the pregnancy outcome and lupus nephritis in pregnant MRL/lpr mice given LPS. NAM (500 mg/kg) was administered on 13.5-17.5 dpc, and data and samples were collected on 18.5 dpc. NAM decreased maternal blood pressure, prolonged pregnancy period, and corrected FGR. NAM significantly improved glomerular injury and inflammatory cell infiltration, which was accompanied by reduced expression of inflammatory cytokines in their kidneys. NAM also decreased the level of plasma anti-dsDNA antibody and lymphadenopathy. 【Discussion】NAM alleviates PE-like features, FGR, and lupus activity in MRL/lpr-LPS model. NAM may be a novel therapeutic option to benefit pregnant SLE patients.

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A novel pre-eclampsia model induced by renal artery clipping
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Background: Pre-eclampsia affects approximately 2 to 8% of pregnant women, causing proteinuria and blood pressure above 140 x 90 mmHg after the 20th week of gestation. If left untreated, PE can lead to the occurrence of self-sustained seizures (Eclampsia) that could eventually evolve to coma, and death of the mother and fetus. In the present study, an experimental model of hypertension was induced in pregnant rats that, later, received a seizure-trigger injection of pentylenetetrazol (PTZ) aiming to mimic the eclampsia clinical picture. Methods: Wistar rats were divided into four groups: non-pregnant (NP), pregnant (P), hypertensive (H) and pregnant hypertensive (HP). Hypertension (H and HP) was induced via clipping of the left renal artery. Subsequently, all animals were injected with PTZ and behavioral and electroencephalographic (EEG) changes were recorded. Results: In opposition to control animals (NP and P), those from the H and HP groups presented a steady increase in BP that was first noticed two weeks after the renal artery clipping. PTZ injection at pregnancy days 18, 19 and 20 was able to induce behavioral and electrographic seizures in all groups although the number and the duration of each fit were higher in HP animals when compared to other groups. Besides, EEG analysis revealed that signal power and amplitude during the seizure events were significantly higher in the HP group. Conclusion: Renal artery clipping in pregnant female rats was able to induce signs similar to those observed in preeclampsia. Besides, PTZ administration was able to induce behavioral and electrographic seizures significantly more intense in the HP group than those observed in the control groups (NP, P, H).
Joint exposure to antiangiogenesis and inflammation in pregnant mice results in sex specific growth restriction patterns

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Introduction: Preeclampsia is a multifactorial pregnancy disorder presented with angiogenic imbalance and low-grade systemic inflammation. However, animal models which represent these variety of pathophysiological conditions are missing.

Objective/hypothesis: We aimed to establish a novel double hit preeclampsia animal model in order to mimic the complex multifactorial conditions that are present during preeclampsia and to investigate the early consequences to the fetus.

Methods: C57Bl/6 mice on gestational day GD 8.5 were injected with adenovirus overexpressing sFlt-1 (1x10⁹ PFU in 100 ml) or empty adenovirus. On GD 10, a second hit was introduced with a low dose of lipopolysaccharide (LPS, 25 µg/kg, i.p.) or PBS. Between GD 16.5 and 17.5, 24-hour urine was collected. Blood pressure and blood analysis were performed on GD 18.5. Fetuses and placentas were collected at GD 18.5.

Results: Animals exposed to sFlt-1 and LPS showed increased blood pressure and albumins in 24-hour urine. sFlt-1 concentrations were 2x higher in the double hit preeclampsia group. Blood pressure values were positively correlated with the sFlt-1 concentrations. Fetuses were growth restricted and subclassification based on sex showed that females have symmetrical growth restriction accompanied with smaller placentas in comparison to male fetuses. In continuation male fetuses showed asymmetrical growth restriction, accompanied by brain sparing.

Discussion: Our results show that combined exposure to sFlt-1 and LPS mimics the symptoms of preeclampsia in a mouse model and affects fetal growth in a sex-specific manner.

Metabolomic analysis of preeclampsia in mouse overproducing sFlt-1

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Preeclampsia (PE) constitutes a leading cause of maternal morbidity and mortality. Although alterations in circulating angiogenic factors are pathogenic, the detailed pathological mechanisms of PE remain unclear. In this study, we performed mass spectrometry (MS)-metabolomics of the plasma and placenta of mice overproducing sFlt-1 to elucidate the pathological conditions of PE. In addition, we evaluated the effect of nicotinamide on metabolic changes in PE. To generate the PE model, recombinant adenovirus to overproduce sFlt-1 was administered to mice (C57BL/6) at 8.5 dpc. Plasma and placenta samples were harvested at 12.5 dpc for metabolomics and gene expression analysis. Blood pressure of PE mice was significantly increased, and fetal weight was significantly decreased. Metabolomics revealed that levels of acylcarnitines in the plasma and placenta were significantly higher in PE mice than controls. In addition, placental acetylcarnitine were increased in the labyrinth as assessed by MS imaging. In the labyrinth, although the levels of metabolites involved in the TCA cycle did not change, those involved in glycolysis and ATP production were decreased in PE mice. Nicotinamide treatment normalized acylcarnitine levels and ATP content in the placenta. Furthermore, nicotinamide increased the levels of NAD⁺ and the amount of metabolites in glycolysis and TCA cycle that are produced in the enzymatic reactions requiring NAD⁺. These results indicate that in the PE placenta ATP production is diminished, and fatty acid oxidation is accelerated, and consequently, blood carnitine and acylcarnitines were increased. Targeting this metabolic alteration in the placenta using nicotinamide may be useful to treat PE.
A Novel Peptide-Based Antagonist of sFlt-1
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Introduction: Preeclampsia (PE) is a multifactorial disease in which little progress has been made to develop adequate therapy. One of the etiologies of this maternal syndrome includes a rise in maternal anti-angiogenic factors, such as sFlt-1. Here we describe a novel therapeutic antagonist of sFlt-1 based on placental growth factor (PIGF).

Hypothesis: We hypothesize that our novel therapeutic, ELP-PIGF, will attenuate the hypertension and endothelial dysfunction in the preclinical RUPP model of placental insufficiency.

Methods: Animals were received on GD11 and received the sham or RUPP surgery on GD14 along with drug or vehicle administration. On GD18, carotid catheters were placed for blood pressure measurement on GD19. Western blots used serum samples with an antibody specific for PIGF (Abcam) and were normalized to the amount of serum loaded per well.

Results: Untreated HUVEC cells had significantly greater tube formation compared to cells treated with sFlt-1 (44.6 ± 7.4 tubes/field vs 29.3 ± 6.4 tubes/field, p<0.5). Treatment of HUVECs with both sFlt-1 and ELP-PIGF completely normalized the tube formation, such that there was no difference between this group and untreated cells (41.9 ± 4.3 tubes/field vs 44.6 ± 7.4 tubes/field, p=0.998). RUPP animals had significantly increased blood pressure compared to normal pregnant counterparts (116.7±19.6 mmHg vs 92.4±3.32 mmHg, p<0.01). Administration of ELP-PIGF attenuated RUPP hypertension (116.7±1.96 mmHg vs 105.6±4.70 mmHg, p=0.051). Western blots showed a trend for decreased circulating PIGF (1.0±0.18 vs 0.73±0.11 fold change, p=0.26, n=4) in RUPP animals, with a near-significant trend towards increased endogenous free PlGF with ELP-PIGF administration (0.73±0.11 vs 1.79±0.35, p=0.051, n=4).

Discussion: Angiogenic imbalance is one of the best characterized contributors to the development of preeclampsia, largely lead by elevated sFlt-1. Our promising data suggest that our novel drug, ELP-PIGF, may work to correct this imbalance and potentially serve as a therapeutic for preeclampsia.

Late breaking abstracts

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The impact of the HYPITAT I trial on obstetric management and maternal and neonatal outcome in women with gestational hypertension or preeclampsia in the Netherlands
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Objective: The HYPITAT-I trial, conducted between 2005-2008, showed that in women with hypertensive disorders at term, induction of labor reduces maternal high-risk situations compared with expectant management. We evaluated the impact of the HYPITAT-I trial on obstetric outcome in the Netherlands.

Methods: We studied 143,749 women with gestational hypertension or preeclampsia and a singleton fetus in cephalic position delivering between 36.0 to 40.6 weeks’ gestation (the hypertensive disorders group), using data from the Dutch National Perinatal Registry between 2000 and 2014. For comparison we used the period before (2000-2005) and after the HYPITAT-I trial (2008-2014). We compared induction of labor rates, mode of delivery, maternal-, and perinatal complications. We differentiated between hospitals that had recruited for HYPITAT-I and hospitals that had not. Women without hypertensive disorders in pregnancy were used as reference group (n=1,649,510).

Results: In the hypertensive disorders group, the induction of labor rate increased from 51.1% to 64.2% (RR 1.26; 95% CI 1.24-1.27). Maternal mortality decreased from 0.022% to 0.004% (RR 0.20; 95% CI 0.06-0.70). Perinatal death reduced from 0.49% to 0.27% (RR 0.54; 95% CI 0.45-0.65). Both the increase in induction rates and the reduction in hypertensive complications were more pronounced in hospitals that recruited for HYPITAT.

Induction of labor increased in the reference group; the increase in the hypertensive disorders group was significantly higher (4.6% vs. 13.1% (OR 1.10 (95% CI 1.07-1.12); p<0.001). The increase in emergency cesarean sections and the decrease in placental abruptions was significantly higher in the reference group compared to the
hypertensive disorders group. The reduction in maternal and perinatal death did not differ significantly between the hypertensive disorders group and the reference group.

Conclusion: The HYPITAT-I trial resulted in an increased induction rate in term pregnancies complicated by hypertensive disorders in the Netherlands, which improved maternal and perinatal outcome.

Posters

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Potential therapeutic in preeclampsia: effect of resveratrol on endothelial cells incubated with plasma from pregnant before clinical onset of disease
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Introduction: Resveratrol is a compound presented in high quantity in red grapes that contribute to healthy endothelial function. We are exploring an in vitro model of preeclampsia incubating plasma with endothelial cell cultures. In this study we collected samples before clinical onset of preeclampsia that is relevant because a dietary intervention may reduce risk to develop preeclampsia.

Objective: to verify if resveratrol induces production of NO, improve cell viability and modulate expression of heme oxygenase-1 (HO-1, enzyme inducible by oxidative stress) in endothelial cells incubated with plasma from case and control pregnant.

Methods: We collected blood at 20-25 weeks of gestation from matched healthy pregnant during all gestation (control, n=5) and pregnant who subsequently develop preeclampsia (case, n=5). Plasma was incubated (10% v/v) for 24 hours in HUVECs with or not 30 µM trans-resveratrol. Cellular viability was measured using MTT assay, HO-1 by ELISA and nitrite (NO metabolite) by Griess. P value < 0.05 was considered statistically different.

Results: We found similar levels of cell viability and nitrite levels between case and control, supplemented or not with resveratrol (all P>0.05). Concerning HO-1 levels, we found that cultures incubated with plasma from case presented higher levels of HO-1 compared to control. When resveratrol was added, this difference diminished, although plasma from case induce higher HO-1 expression compared to control.

Discussion: Our study demonstrates that plasma from case induce expression of HO-1 suggesting presence of inducers such as oxidative stress even before clinical onset; and when resveratrol is added reducing of HO-1 expression in case cultures demonstrated lower cell-stress. Our results suggest that a diet rich in resveratrol may help to prevent endothelial injury decrease risk to develop preeclampsia, as supported by literature in cardiovascular diseases.

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A peptide antagonist in a genetic rat angiotensinogen x renin model of preeclampsia
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Introduction: Preeclampsia is a pregnancy-related disorder characterized by hypertension and excess protein excretion in the urine. It is the most common hypertensive disease of pregnancy and affects about 5-8% of pregnancies. The Renin-Angiotensin-System (RAS) is involved in the pathogenesis of the disease; however, treatment with a RAS-blocker is contraindicated due to fetal toxicity.

Objective: The rat angiotensinogen renin cross model has been described as a rodent model that recapitulates many of the changes observed in human preeclampsia. This experimental rat model of preeclampsia will be used to test the hypothesis that peptide antagonists targeting the RAS system impact both maternal and fetal outcomes.

Methods: Sprague-Dawley (SD) rats harboring the human angiotensinogen (hAGT) gene [SD-Tg(hAGT)L1623] were mated with male SD rats bearing the human renin (hREN) gene [SD-Tg(hRen)L10J] to produce a model of preeclampsia (PE) in the dams. These pregnant dams developed hypertension on day 13 of pregnancy (plug-
recognition was assigned as day 1) and albuminuria. At day 15 of gestation when the animals were already hypertensive, a RAS peptide antagonist was administered via mini-osmotic pumps sc.

Results: The major finding of the study was that a peptide antagonist targeting RAS ameliorated the preeclamptic phenotype. In the transgenic model, treatment led to a reduction of blood pressure and urinary albumin excretion. The improvement of intrauterine growth retardation (IUGR) indicates an improved fetal development.

Discussion: RAS peptide antagonist ameliorates the preeclamptic phenotype of the rat model due to the reduction of blood pressure and albuminuria. Furthermore an improvement of the fetal outcome was observed by an amelioration of the IUGR.

Trans-resveratrol Increases Nitric Oxide and Heme-oxigenase-1 Production and Decreases ROS Levels In Endothelial Cells Incubated With Plasma From Preeclamptic Patients
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Introduction: Preeclampsia is characterized by hypertension and proteinuria at ≥ 20 weeks of gestation and it is the leading cause of fetal-maternal morbidity and mortality worldwide. The pathophysiology of this syndrome is complex and involves several processes. One of these, widely validated in the literature is oxidative stress, which is the prevalence of free radical production and/or reduction of antioxidant activity. Trans-resveratrol is an antioxidant that acts by several mechanisms, including eNOS and heme-oxigenase-1 (HO-1) stimulation and reactive oxygen species (ROS) scavenging, and it has been studied in the management of preeclampsia.

Objective: To evaluate the effect of trans-resveratrol incubated with plasma from healthy pregnant (HP) and preeclamptic patients (PE) on nitrite (nitric oxide metabolite), HO-1 and ROS levels in human umbilical vein endothelial cells (HUVECs).

Methods: HUVECs were co-incubated with trans-resveratrol (1 uM) and 10% (v/v) plasma from HP and PE (n=4 and 8, respectively) for 24h. Nitrite, HO-1 and ROS levels were measured by Griess assay, ELISA and DCFH fluorescent dye, respectively.

Results: Nitrite and HO-1 concentrations were reduced in PE compared to HP (Nitrite: 1.5±0.5 vs. 4.9±0.8 uM, p=0.004; HO-1: 297±42 vs. 590±147 pg/mL, p=0.038, respectively). Trans-resveratrol significantly increased nitrite and HO-1 concentrations only in PE (Nitrite: 3.0±0.6 vs. 1.5±0.5 uM, p=0.002; HO-1: 336±46 vs. 297±42 pg/mL, p=0.038, respectively). ROS levels was not significantly different between PE and HP (14.6x10⁻³±1.9x10⁻³ vs. 11.1x10⁻³±3.0x10⁻³ fluorescence intensity, p=0.316, respectively), however trans-resveratrol significantly decreased ROS only in PE (9.9x10⁻³±1.5x10⁻³ vs. 14.6x10⁻³±1.9x10⁻³ fluorescence intensity, p=0.005, respectively).

Discussion: Trans-resveratrol was able to increase nitrite and HO-1 concentrations and to decrease ROS levels in HUVECs incubated with plasma from preeclamptic patients. Our results showed that trans-resveratrol is acting through different mechanisms contributing to reduce oxidative stress, which suggests that it could be beneficial in the management of preeclampsia.

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Catechol-O-methyltransferase deficiency leads to hypersensitivity on the pressor response against angiotensin II
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Catechol-O-methyltransferase (COMT) metabolizes 2-hydroxyestradiol into 2-methoxyestradiol (2-ME); COMT deficiency has shown to be associated with hypertension in men and preeclampsia, the disease associated with hypersensitivity of pressor response against angiotensin II (Ang II). Here, we found that COMT deficiency could explain the hypersensitivity of pressor response against Ang II in mice because of the lack of 2-ME–dependent suppression of angiotensin II receptor type 1 (AT1R). Male C57BL/6 mice were subjected to COMT inhibitor (COMTi: 25 mg/kg per
day) or oil (control) for 4 weeks, with or without low-dose Ang II infusion (ANGII: 70 ng/kg per minute) for the last 3 weeks. The Ang II-infused mice were treated with 2-ME (10 ng/d) or vehicle for the last 1 week. We obtained the following experimental groups: control, ANGII, COMTi, COMTi+ANGII, and COMTi+ANGII+2-ME. We performed similar experiments using the in vivo administration of small interfering RNA of COMT instead of COMTi. Neither ANGII nor COMTi exhibited significant alterations in systolic blood pressure. Compared with ANGII or COMTi, COMTi+ANGII displayed significantly higher systolic blood pressure, albuminuria, and glomerular endotheliosis; 2-ME normalized such alterations. Similar phenotypes were observed in COMT small interfering RNA–treated mice. In the aorta of COMT-deficient mice, AT1R expression was increased; 2-ME suppressed AT1R expression. The 2-ME exhibited peroxisome proliferator–activated receptor γ agonistic activity in vitro and ex vivo plasma from pregnant female mice as well. In vitro, 2-ME suppressed both basal and Ang II–induced AT1R levels in a peroxisome proliferator–activated receptor γ–dependent manner. The 2-ME is relevant to combat COMT deficiency–associated hypertensive disorders via suppression of AT1R by its peroxisome proliferator–activated receptor γ activity.

Preeclamptic plasma affects gene expression in human endothelial cells and vascular smooth muscle cells
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Introduction: One of the main preeclampsia features is maternal vascular dysfunction. In rat experimental preeclampsia we have previously shown that this includes changes in vascular gene expression (Lip et al. Sci. Rep. 7, 14807(2017)).

Objective: We tested whether vascular gene expression in experimental preeclampsia can be induced by incubation of human endothelial and vascular smooth muscle cells with preeclamptic plasma in vitro.

Methods: Human umbilical vein endothelial cells (HUVEC) and human aortic vascular smooth muscle cells (VSMC) were incubated with 15% plasma from early-onset preeclamptic (n=5), healthy pregnant (n=5) or non-pregnant women (n=5) for 24 h. RNA was isolated from the cells and RT-PCR was performed to determine gene expression. We measured top dysregulated vascular genes in experimental preeclampsia (KCNA6, ESM1 for HUVEC and TTN, ACTC1, CHRNA3 for VSMC). Additionally, we measured expression of genes which might be altered in the vasculature during preeclampsia (NOS3, EDN1, PTGIS, CXCL8 for HUVEC and MYL6, MYL9, ACTG2 and ACTA2 for VSMC).

Results: Stimulation of HUVEC with preeclamptic plasma induced upregulation of KCNA6, ESM1 and CXCL8 compared to healthy pregnant plasma, while expression of NOS3, EDN1 and PTGIS was not affected. Stimulation of VSMC with preeclamptic plasma induced upregulation of ACTC1 compared to healthy pregnant plasma and upregulation of CHRNA3, MYL6, ACTG2 and ACTA2 compared to plasma from non-pregnant women, while expression of TTN and MYL9 was not affected.

Discussion: Using gene expression array data from the vasculature of a preeclamptic rat model, we selected potential targets to be upregulated in endothelial cells and vascular smooth muscle cells by preeclamptic plasma. The upregulation of genes by preeclamptic plasma may suggest that these gene are upregulated in vivo in preeclamptic women inducing vascular dysfunction in this condition. We next aim to determine which factors in the circulation of preeclamptic women induce these effects.

Combination sulfasalazine and metformin are additive in reducing placental secretion of antiangiogenic factor sFlt
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Introduction
Preeclampsia is associated with increased placental secretion of antiangiogenic factors sFlt-1 and sENG and a reduction in angiogenic proteins placental growth factor secretion (PIGF) and vascular endothelial growth factor (VEGF). We have identified two medications, safe in pregnancy, that mitigate key aspects of preeclampsia in vitro. We have demonstrated metformin and sulfasalazine independently reduce placental sFlt-1 secretion and vessel
dysfunction.
In this study we investigate the possibility of combining these medications to reduce the dose required to mitigate key aspects of preeclampsia; sFlt-1 and sENG secretion and PI GF and VEGF expression, using primary human tissues.

Methods
Metformin and sulfasalazine, at low doses individually and in combination, were administered to primary trophoblasts and placental explants and sFlt-1 secretion assessed. At the mRNA level there are two sFlt-1 splice variants; the primate and placental specific isoform sFlt-1 e15a and the predominately vascular isoform sFlt-1 i13. Both were measured following combination treatment. In addition the expression of angiogenic factors PI GF and VEGFa were assessed.

Results
Combining low-dose metformin and sulfasalazine additively decreased sFlt-1 secretion from primary trophoblast compared to either drug alone. Similarly, an additive decrease in sFlt-1 e15a and i13 was identified following combination treatment. In placental explants, combination treatment also additively decreased sFlt-1 secretion.
Low dose sulfasalazine potently upregulated PlGF expression in primary trophoblasts and this was maintained with the addition of metformin. Metformin and sulfasalazine individually increased VEGFa, and this effect was additive when the two drugs were combined.

Conclusion
Combination metformin and sulfasalazine additively reduced sFlt-1 secretion and the expression of its splice variants, sFlt-1 e15a and i13. Furthermore, in combination metformin and sulfasalazine upregulate angiogenic factor VEGFa. Therefore we conclude that they might be promising combination therapeutics that could reduce the burden of this devastating disease.

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BKCa channels; a new target to treat maternal hypertension?
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Introduction: Severe hypertension is a common indication for delivery amongst women with pre-eclampsia (PE), contributing to iatrogenic prematurity and its associated complications. Large-conductance calcium-activated potassium channels (BKCa), which promote vasorelaxation, are downstream targets of many vasoactive agents, including nitric oxide and angiotensin II. Estrogen-mediated increases in uterine artery BKCa activity are an important physiological adaptation to normal pregnancy. However, the role of BKCa has not been assessed in the wider systemic vasculature in either normal pregnancy or pregnancy pathologies. Outwith pregnancy, BKCa activity is reduced in association with PE risk factors, including age, hypoxia and diabetes. Furthermore, 5,6-EET, a BKCa inhibitor, is reported to be increased in the serum of women with PE.

Objectives: To determine the effect of BKCa activation on systemic resistance arteries of pregnant women and whether this is different in PE.

Methods: Resistance arteries (<400µM) dissected from omental biopsies of women with uncomplicated, term pregnancy (NP) or PE were assessed by wire myography. Arteries submaximally constricted (EC80) with the thromboxane-mimetic U46619 were treated with a specific BKCa channel activator NS11021 (10^-9^-10^-5 M) or appropriate vehicle (Control). Relaxation was compared by 2-way ANOVA with Sidak’s post-tests (p<0.05).

Results: NS11021 induced a substantial relaxation of omental resistance arteries obtained from women with either NP (N=10; final relaxation Control 23±8% Vs. NS11021 76±4%; p<0.001) or PE (N=9; final relaxation Control 38±8% Vs. NS11021 81±4%; p=0.006). There was no significant difference in the relaxation observed between women with NP and PE.

Discussion: Systemic arteries from women with both NP and PE relax in response to activation of BKCa channels. Direct BKCa activation provides an opportunity to bypass the inherent vascular dysfunction of PE to achieve comparable vasorelaxation in women with PE. On-going work will determine whether BKCa-activating compounds can offer a new treatment for maternal hypertension in PE.
Maternally Sequestered Biologics for Treatment of Preeclampsia

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Introduction. Preeclampsia is a hypertensive syndrome of pregnancy with few pharmacological treatment options. The risk of for adverse fetal effects is a major limitation for drug development. Our lab has developed a protein-based drug carrier called elastin-like polypeptide (ELP) that is capable of stabilizing therapeutic proteins or peptides in the maternal circulation while preventing their placental transfer.

Objective/Hypothesis. We hypothesize that ELP can be optimized for maternally sequestered drug delivery by altering the polymer length. We further hypothesize that ELP can be fused to vascular endothelial growth factor (VEGF) to restore angiogenic balance while preventing fetal exposure to the therapeutic.

Methods. A library of ELP carriers ranging in size from 25 to 110 kDa was created. The pharmacokinetics, biodistribution, and placental transfer of each agent were determined in a rat pregnancy model. A 60 kDa ELP domain was fused to human VEGF-A121, and the pharmacokinetics were determined following repeat dosing intravenous or subcutaneous administration.

Results. The plasma half-life of ELP was inversely related to its molecular weight. As the size of the molecule increased, the renal ELP deposition decreased and the placenta and other maternal organ levels increased. Within the placenta, ELP was localized broadly in the labyrinth and along the chorionic plate. No ELP crossed the placental barrier at any size tested. When fused to VEGF, daily IV dosing lead to a 2.1 +/- 1.1 hour half-life after each injection. SC administration lead to an increase in plasma ELP-VEGF levels over the first three hours, followed by a slow clearance phase over 24 hours that was accompanied by dispersal of the protein from the SC injection site.

Discussion. This work demonstrates the utility of ELP as a tunable, long-circulating, non-toxic, maternally sequestered drug carrier. The ELP-VEGF fusion protein has potential as a novel biologic for treatment of preeclampsia.

Pharmacokinetics of Placental Protein 13 (PP13) after intravenous and subcutaneous administration in rabbits
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Human placental protein 13 (PP13) is a galectin predominantly expressed by the placenta. Low serum concentrations of PP13 in early pregnancy indicate a higher risk to develop preeclampsia. The pharmacokinetic disposition and bioavailability of PP13 were determined by single intra-venous and subcutaneous (S.C.) administration to twelve healthy New Zealand white rabbits. The serum pharmacokinetic values were determined by ELISA assay, and are best described by a two-compartment model. Both volume of distribution (Vd) and the area under the curve (AUC) were dose dependent for the IV group (p<0.01). PP13 elimination half-life was also found to be different between the groups (p<0.01). The bioavailability of PP13 following S.C. administration was found to be 57%. This study shows that the concentration of total PP13 released into the maternal circulation during pregnancy might be much higher than previously estimated.
Introduction: It is unknown if and how right ventricle changes during gestational hypertension.

Purpose: The purpose of this study was to determine right ventricle dimensions, systolic and diastolic function changes in gestational hypertension (GH).

Methods: Study included 60 pregnant women. 35 with GH and 25 normotensives as control. Echocardiography was performed to evaluate right ventricle and atrial size (RV diastolic diameter at the base and mid level, proximal and distal dimension of outlet tract, RA volume), systolic function (TAPSE, FAC, S’, IVCT, ET, GLS), RV index of myocardial performance (RIMP), and diastolic function ( E/A, EDT, E/e’, RAVsI, IVRT) of the right ventricle. Echocardiography was performed in the third trimester and 6 weeks after delivery.

Results:
1. Participants with GH during pregnancy had normal values of right ventricle and atrial size, systolic function, and diastolic function except E/e’, whose mean value was 6.354±2.100.
2. Women with GH had larger RA volume (33.66±11.8 vs 24.75±9.1, p<0.016) than controls. GH women had lower s’ (0.113±0.023 vs 0.146±0.026 p<0.0005), higher RIMP (0.570±0.151 vs 0.435±0.122 p<0.047), while other parameters of systolic function remained without significant difference.
3. Some parameters of diastolic function did differ: E/a was significantly lower in group with hypertension(1,1±0,26 vs 1,4±0,21 p<0.0005), EDT was longer (182,72±24 vs 160,1±18,6 p<0.0005) and prolonged IVRT in hypertensive patients(73,38±12,12 vs 59.73±12.402, p<0.029) was found.
4. All changed echocardiographic parameters became improved six weeks after delivery, the difference persisted only in s’ (0.119±0.014 vs 1.45±0.021 p=0.003) which remained significantly lower.

Conclusion: Right ventricle dimensions are not significantly affected by gestational hypertension. Both systolic and diastolic function of right ventricle changed in gestational hypertension during pregnancy. After delivery, changes were reversible, but only s’ remained lower, as a suggestion of not fully recovered systolic function.

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3d versus 2d echocardiography assessment of maternal cardiac remodeling in gestational hypertension

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Introduction: Considering that the left ventricle (LV) is losing its standard elliptical shape during pregnancy and that these changes are more pronounced if pregnancy is complicated by hypertension, we assumed that there was a difference in geometric remodeling of the LV evaluated by 2D compared to 3D echocardiography in gestational hypertension (GH).

Objective: To establish the difference between 2D and 3D evaluation of maternal cardiac remodeling in GH and reversibility of these changes after delivery.

Methods: 55 women with GH and 26 normotensive pregnant women as controls underwent a complete echocardiography in the third trimester and 6 weeks after delivery, to assess parameters of chamber quantification, wall thickness and LV myocardial mass index. The LV remodeling was determined as normal geometry (NG), concentric hypertrophy (CH), eccentric hypertrophy (EH) and concentric remodeling (CR) according to the reference values of Relative wall thickness and LVmass index due to recommendations of European Association of Cardiovascular Imaging and American Society of Echocardiography.

Results: Hypertensive women had statistically significant higher values of almost parameters of the LV geometry, that caused most abnormal geometry in women with GH (p<0.0005). Considering the difference between values of LVmassi evaluated by 3D and 2D, there was also the difference in geometric remodeling but only in GH group. Thus, evaluated by 3D, NG was presented in GH in 25% vs 26.8% measured by 2D (p<0.0005), CR in 38,3% vs 40,5% (p<0.0005), CH in 28,3% vs 26.3% (p<0.0005), and EH in 8,3% vs 6,4% (p<0.0005). Also all changed echocardiographic parameters became improved six weeks after delivery. Only 25.8% previously hypertensive women had CR, but without significance 3D versus 2D assessment.

Conclusion: There was
statistically significant difference between 3D and 2D estimation of the maternal cardiac remodeling in gestational hypertension.

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Blood Pressure after PREeclampsia/HELLP by SELF monitoring (BP-PRESELF): rationale and design of a multicenter randomized controlled trial
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Background: Hypertensive pregnancy disorders (HPD) such as preeclampsia (PE) or the hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome are associated with an elevated cardiovascular disease (CVD) risk. Standardized prevention guidelines after pregnancy in these high-risk women are lacking. Hypertension is the first emerging risk factor after PE/HELLP pregnancies and is acknowledged as a major risk factor for CVD. Premature hypertension leads to various manifestations of end-organ damage at young age. Timely treatment of elevated blood pressure is mandatory, despite many of these women have long-term undetected and untreated hypertension before adequate treatment is initiated.

Hypothesis: The aim of our study is to assess whether home blood pressure monitoring (HBPM) in women with a previous pregnancy with PE/HELLP is a valuable tool for early detection of hypertension.

Methods: Women with a history of PE/HELLP syndrome (both early and late) aged 40-60 years are invited to participate. They are randomized between HBPM or ‘usual care’. Patients with a history of CVD, known hypertension and/or use of antihypertensive medication are excluded. The primary outcome is to evaluate feasibility and usability of HBPM after 1 year of follow-up. Secondary outcomes will be to assess the effectiveness of blood pressure (BP) home monitoring to detect hypertension, the efficacy of BP treatment, quality of life (QoL), health-related symptoms, work ability and life-style behaviour.

Discussion: The results of this study will provide information for optimal preventive strategies to detect hypertension in women after PE/HELLP.

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Repeatability of USCOM®-measured cardiac output in normotensive non-pregnant and pregnant women
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Objectives: To investigate the repeatability of ultrasonic cardiac output monitor (USCOM) measurements of cardiac output in normotensive non-pregnant and pregnant women.

Study design: Using the USCOM, cardiac output was measured, five times successively within 5 minutes in normotensive non-pregnant (n = 30) and pregnant (n = 30) women of any gestation with uniform technique by a single operator. The data were analysed using multi-level modeling and intra-class correlation.

Results: There was no statistically significant variation in cardiac output with repeated measurement in normotensive non-pregnant or pregnant women. The intra-class correlation for cardiac output measurements was 0.921 (95% CI 0.887-0.947).

Conclusions: No extra information is added by making more than one USCOM measurement on the same woman under the same conditions in normotensive pregnant and non-pregnant women. The USCOM demonstrates excellent repeatability in this population. This finding should provide reassurance that single measurements using this system are of value in research and clinical practice.

Keywords: USCOM, cardiac output, pregnancy, pre-eclampsia
Cardiovascular risk factors in young women after hypertensive disorders during pregnancy
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Introduction: Hypertensive disorders during pregnancy (HDP) are associated with later maternal cardiovascular disease risk. It is important to understand the pathophysiological mechanisms before the development of the cardiovascular complications.

Objectives: The study aimed to scrutinize cardiovascular risk factors and biomarkers among young women with and without prior hypertensive disorders during pregnancy.

Methods: Retrospective cohort study. The study included 77 women: gr. 1 - with prior HDP (n=33) aged 41 (40-43) years, gr. 2 – without prior HDP (n=44) aged 39 (33-43) years. Inclusion criteria: age 18-44 years, prior delivery. Exclusion criteria: diabetes mellitus, secondary hypertension. We measured serum glucose, insulin, HOMA-IR, leptin, lipids, PAI-1 and blood pressure (BP). Left ventricular mass index (LVMI) was estimated by transthoracic echocardiography. Data are presented as M±SD and Me (Q25 –Q75).

Results: The average postpartum period was 15 (12-19) years in gr. 1 and 12 (5-19) years in gr. 2, NS. Women in gr. 1 more often had hypertension (n=27; 82% vs n=9; 20.5%; RR 4.0 95%CI [2.2-7.3], p<0.001), obesity (n=20; 39% vs n=6; 13.6%; RR 4.5 95%CI [2.1-10.1], p<0.001) and smoking (n=9; 27% vs n=6; 13.6%; RR 2.0 95%CI [0.8-5.1]) compared to gr. 2. Levels of glucose (5.5±0.7 vs 5.2±0.6) mmol/L, leptin (42 [30-50] vs 24 [13-32]) ng/ml, PAI-1 (460 [407–472] vs 382 [222-416] ng/ml) and LVMI (120±24 vs 86±15) g/m² were statistically higher in gr. 1 vs gr. 2, p<0.05.

Discussion: Taking into account the high frequency of cardiovascular risk factors and biomarkers in young women, we noticed that women who had prior HDP should be informed about the increased risk for hypertension later in life. The present study indicates that women with prior HDP should also receive lifestyle counseling aimed at optimizing body weight and to control lipid and glucose levels for long-term follow-up.

Central and uterine haemodynamics in hypertensive disorders of pregnancy
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Background: Placental disorders such as hypertensive disorders of pregnancy (HDP) and are associated with de-novo changes in uterine artery pulsatility index (PI) and cardiovascular indices. The aim of this study is to explore the relationship between central and uterine haemodynamics in pregnancies complicated by HDP compared to controls.

Methods: A prospective study involving ongoing third trimester pregnancies complicated by HDP, as well as healthy controls. Maternal central haemodynamics were measured using an USCOM-1A® device and uterine artery Doppler assessments were carried out by a standardised technique. Indices that varied physiologically with gestation or maternal characteristics were corrected for by calculating multiples of the median (MoM).

Results: The study included 211 HDP and 446 control pregnancies. Compared to controls, HDP pregnancies had significantly (all p<0.01) lower cardiac output (0.98 vs 0.94 MoMs), higher systemic vascular resistance (1.0 vs 1.3 MoMs) and higher uterine artery PI (0.96 vs 1.2 MoMs). Subgroup analysis demonstrated more severe alterations in cardiac output and systemic vascular resistance with preterm vs term HDP. In both HDP pregnancies, there was a significant positive correlation between systemic vascular resistance and uterine artery PI (r= 0.192, p<0.01 and r= 0.239, p< 0.01 respectively).

Conclusion: HDP pregnancies are associated with altered central maternal haemodynamics - namely reduced cardiac output and increased systemic vascular resistance. Maternal haemodynamics is further deranged with more severe phenotypes of HDP. Changes in third trimester uterine artery PI are likely to be a consequence rather than the cause of modified central haemodynamics in HDP.
The management of pregnant women with chronic kidney disease: An 8-year review in a tertiary care center
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Objective: The management and treatment of kidney disease has advanced, and women who are pregnant and give birth have also increased recently. On the other hand, pregnancy with kidney disease causes preeclampsia (19 to 30%), intrauterine fetal death (16 to 20%), postpartum renal failure (3 to 5%). The purpose of this study was to review the maternal and neonatal outcomes in pregnant women with chronic kidney disease (CKD), and to evaluate the appropriate management that may contribute to obstetric outcomes.

Methods: We conducted a retrospective review of 126 births and 129 neonates in 110 CKD patients who were seen at Osaka University Hospital between January, 2010, and December, 2017.

Results: The mean patient age was 33.5 (18 to 49) years, and the nulliparity rate was 61%. The most frequent disease was IgA nephropathy (43/126; 34%) and the second was lupus nephritis and renal transplantation (both were 15/126; 12%). Second trimester abortion and preterm delivery occurred in 5% and 20% of the patients, respectively. There was no maternal and neonatal death. Fetal growth restriction and preeclampsia occurred in 10% and 25% of the patients, respectively. Two patients with lupus nephritis and one with Henoch-Schönlein purpura nephritis had severe preeclampsia occurred before 20 weeks gestation. sFlt1/PIGF ratio were 427, 865 and 1183, respectively.

Conclusions: To predict and prevent the adverse events in the care of pregnant women with CKD is important for good maternal and neonatal outcomes. Furthermore, Henoch-Schönlein purpura nephritis that had been already ameliorated may be also a risk factor for severe preeclampsia.

Hypertensive disorders of pregnancy increase the risk for chronic kidney disease: A population-based retrospective study
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Introduction: Hypertensive disorders of pregnancy (HDP) and chronic kidney disease (CKD) are well-known risk factors for cardiovascular disease (CVD) in later life. However, few studies have investigated the association of HDP with CKD. Moreover, these studies utilized either registry- or clinical-based data and did not include subclinical CKD patients.

Objective: To address this gap in the literature, we investigated whether HDP is related to CKD, diagnosed based on the estimated glomerular filtration rate (eGFR), in later life.

Methods: We designed a population-based, retrospective study, and reviewed the results of blood and physiological examinations as well as the results of pregnancy data available in patients’ Maternity Health Record Books for 312 women.

Results: We identified 15 women with a diagnosis of CKD based on the eGFR, and 14 women with HDP. We found that women who experienced HDP had a high risk of CKD in later life compared with women without HDP (odds ratio (OR): 4.854; 95% confidence interval (CI): 1.042–22.621). Compared with normotensive women, those who were hypertensive at the time of the examination were significantly associated with CKD (OR: 3.109; 95% CI: 1.213–11.510).

Discussion: Awareness regarding the risk for CKD and CVD in a relatively young age can enable women to prevent diseases effectively.
Proteinuria concentration of pregnant women with preeclampsia: this value would be an indicator of pregnancy interruption?
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Introduction: Proteinuria (≥ 300mg/24hs) is one of the parameters that define preeclampsia. According to the literature, proteinuria concentration ≥ two or five grams defines severe preeclampsia, and massive proteinuria is defined by at least 10g. Objective: To identify and classify the severity of proteinuria in preeclamptic pregnant women. Methods: We studied 101 preeclamptic women, who received obstetric care during the year of 2015 at the Maternity of the Botucatu Medical School Hospital, Botucatu, SP, Brazil. Proteinuria was classified as mild (300-1999g), two severe grades (2000-4999g and ≥5000g) and massive (≥10,000). The following parameters were evaluated: demographic [age, race, marital status] and obstetric characteristics [parity, gestational age at pregnancy resolution, forms of preeclampsia (superimposed or not upon chronic hypertension, early or late onset, mild or severe, and type of delivery)]. Results: In the studied population predominated the age between 20 and 35 years old, white race and stable union. Parity was similar between primiparous and multiparous, with 41.6% of prematurity and 69.3% of caesarean section. In the characterization of pre-eclampsia predominated pure (80.2%), severe (73.3%) and late (81.2%) forms. Among the parameters of severity, predominated hypertensive crisis (49.5%), proteinuria (33.7%) and imminent eclampsia (22.8%). The median values and range of proteinuria were 900mg/24h (300mg - 36,014mg), and classified as mild (66.4%) or severe ≥2,000mg (33.6%). Considering severe ≥5,000mg) and massive proteinuria the values were 22.7% and 10.8%, respectively. Discussion: Proteinuria was a parameter of severity in one third of cases of preeclampsia, with 10.8% of massive grade. In our service, one year of follow-up of pregnant women, who developed severe preeclampsia showed persistence of proteinuria and/or albuminuria in 27% of patients. However, there is no literature indication of which proteinuria concentration should be an indicator for gestation interruption in order to avoid future impairment of renal function of these women.

Dye-densitometry analysis of maternal circulating blood volume and cardiac output in hypertensive disorder in pregnancy
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In hypertensive disorder in pregnancy (HDP), blood pressure increases due to vasospasm caused by vascular endothelial cells disorders. Simultaneously, vascular permeability increases, therefore result in decrease and concentration in circulating blood volume.

DDG analyzer is a method which enables us to calculate cardiac output, circulating blood volume (CBV), and other indicators simultaneously, non-invasively and continuously. Several serum biomarkers are reported as indicators of early detection of HDP. However, there is no report to show correlation with serum biomarkers and CBV of HDP. We identified serum biomarkers which correlate with CBV measured percutaneously.

We assigned 120 women with singleton pregnancies who underwent Caesarean section during March 2000 to April 2007 at Saitama Medical University. According to pregnancy induced pregnancy (PIH) criteria of Japanese Society of Obstetrics and Gynaecology 2005, patients are enrolled in three groups: normal(NP, n=60), gestational hypertension(GH, n=12), and preeclampsia(PE, n=48). CBV and cardiac output are measured just before the operation with DDG-2001(Nihon Koden, Japan). Tukey-Kramer method or Steel-Dwass method are used to calculate significant difference between three groups, and Spearman’s correlation coefficient is used to identify correlation.

CBV is significantly low in PE subjects compared to NP subjects, but there is no significant difference in cardiac output. Negative correlation between biomarkers and CBV are as follows: in NP subjects, BUN, AST, and ALT. In GH subjects, Hct. In PE subjects, UA , BUN, and ALT. In our study, DDG analyzer revealed CBV is significantly low in PE subjects compared to NP subjects. There is a possibility that CBV has correlation with severity of HDP.

We identified UA, BUN, and especially Hct reflect decrease of CBV. To evaluate severity of HDP and consider timing of termination, blood pressure and proteinuria are important indicators, but with these biomarkers safer labour management could be possible.
Maternal cardiovascular function at 35-37 weeks' gestation: Normal vs Hypertensive disorders of pregnancy

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OBJECTIVE

To examine the effects of maternal characteristics and obstetric and medical history on maternal cardiovascular parameters (MCPs) at 35-37 weeks' gestation using bioreactance (NICOM). To investigate the potential value of combining maternal factors with multiples of the normal median values of MCPs at 35-37 weeks' gestation in the prediction of pre-eclampsia (PE) and gestational hypertension (GH).

METHODS

In 3013 singleton pregnancies maternal characteristics and medical history were recorded; uterine artery pulsatility index (UtA*: PI), mean arterial pressure (MAP) and MCPs were measured. In those who remained normotensive, multivariable regression analysis was used to determine significant predictors of the MCPs among gestational age (GA), maternal characteristics and medical history. Multivariable logistic regression analysis was then used to determine if the maternal factors and MCPs made a significant contribution to predicting PE and GH. The performance of screening was determined by the area under ROC curves.

RESULTS

Multivariable regression analysis demonstrated that significant independent prediction of MCPs including cardiac output, cardiac index, total peripheral resistance, stroke volume, MAP and heart rate, significant prediction was provided by GA, maternal characteristics and medical history. In pregnancies that subsequently delivered with PE or GH, total peripheral resistance and MAP were higher and maternal cardiac output was lower. The increases in total peripheral resistance and MAP were inversely related to gestational age at delivery. The performance of screening for PE and GH achieved by maternal characteristics and medical history was improved by the inclusion of MAP, but not by UtA*: PI or MCPs.

CONCLUSION

MCPs are affected by maternal characteristics and medical and obstetric history, and they should therefore be converted into multiples of the normal median adjusted for significant independent predictors before their inclusion in combined screening for PE. In women developing term PE, total peripheral resistance and MAP are increased and maternal cardiac output is reduced. However, assessment of MCPs at 35-37 weeks' gestation is unlikely to improve the performance of screening for PE provided by maternal factors and MAP alone.

PREGNANCY IN RENAL TRANSPLANT PATIENTS: RENAL FUNCTION MARKERS AND MATERNAL-FETAL OUTCOMES

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Introduction: Progressive proteinuria and glomerulosclerosis characterize chronic allograft nephropathy. Podocytes are fundamental cells for maintaining the functionality of glomerular filtration barrier. Failure to achieve this task due to reduced podocyte number and results in progressive glomerular dysfunction, causing proteinuria and glomerulosclerosis and ultimately leading to end-stage kidney disease. Assessment of podocyturia and its correlation with other renal parameters could help with the diagnosis and definition of prognosis of the glomerulopathies, thus contributing to risk reduction.

Objective: To evaluate podocyturia and other renal parameters as functional markers in pregnant women with kidney grafts.

Methods: In this cross-sectional and prospective study, 43 pregnant women with kidney grafts had their Mid-stream urine samples collected to determine proteinuria, including retinol-binding protein (enzyme immunoassay using monoclonal antibodies), albumin/creatinine ratio (immunoturbidimetry), protein/creatinine ratio (the alkaline picrate colorimetric method), and podocyturia (indirect immunofluorescence).

Results: 43 women who got pregnant after renal transplantation were included. Podocyturia was not significantly correlated with other renal function markers. A gradual increase was observed in the following parameters during pregnancy and puerperium: serum creatinine levels (P < 0.001), proteinuria (P < 0.001), urinary protein/creatinine ratio (P < 0.001), and albumin/creatinine ratio (P < 0.001). Elevated serum creatinine levels, urinary
albumin/creatinine ratio, and retinol-binding protein levels in the third trimester were associated with prematurity (P < 0.001). Preeclampsia was the main cause of renal function decline at the end of pregnancy (65.0% of cases).

Conclusion: Proteinuria, urinary protein/creatinine ratio, and retinol-binding protein levels were elevated in patients with preeclampsia. Proteinuria (or more specifically, urinary protein/creatinine ratio) and albumin/creatinine ratio has also used as a marker of CKD progression. We observed that urinary podocyte excretion occurs in pregnant women with kidney transplant. Using these markers to assess renal function during pregnancy may be clinically useful for early diagnosis and follow-up of glomerular injury, eventually preeclampsia. It may be also associated to its severity or activity.

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A multimarker model for aberrant cardiac geometry after PE
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A multimarker model for aberrant cardiac geometry after PE
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Introduction: One out of four former preeclamptic women shows aberrant cardiac remodelling consistent with subclinical heart failure (HF). These women are prone for the development of remote symptomatic HF, stressing the need to develop a predictive multimarker model for persistent aberrant cardiac geometry postpartum.

Objective: To develop a potential predictive multimarker model for aberrant cardiac remodelling in former PE patients.

Methods: In this cross-sectional study, we included 752 women with a history of PE. These women underwent cardiovascular screening between 6 months and 5 years postpartum consisting of echocardiography, systolic and diastolic blood pressure (sys- and diasBP), plasma volume (PV) measurements and venapunction to assess uric acid, C-reactive protein (CRP) and fibrinogen. Determinants for cardiac geometry (left ventricular mass (LVM) and relative wall thickness (RWT)) where assessed with cardiac ultrasound. We used ANCOVA to perform univariate and multivariate analysis.

Results: Multivariable analysis showed that both SysBP and PV were independently correlated with RWT and LVMi ((b=0.06, 95% CI 0.03-0.08 and b=26.24, 95%CI18.07-34.41, P<0.01 respectively) (b=0.02 95%CI=0.04-0.00, P<0.05 and b=9.01, 95% CI=2.81-15.35, P<0.01 respectively). CRP ((b=0.00, 95% CI=0.00-0.01, P<0.01) and uric acid (b=0.02, 95% CI=0.00-0.03, P<0.05)) where only independently related to RWT. Fibrinogen did not relate to either LVM or RWT.

Discussion: This study shows a potential role for SysBP, PV, CRP, and uric acid as markers to predict persistent aberrant cardiac remodelling in former preeclamptic women. Future studies should evaluate the predictive value of this model prospectively.

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Echocardiographic Assessment of Left Ventricular Systolic Function in Preeclampsia complicated by Pulmonary Oedema
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Introduction: Acute pulmonary oedema remains a life threatening complication of pre-eclampsia. The systolic left ventricular function in patients with pre-eclampsia and pulmonary oedema is not clear.

Hypothesis: We hypothesise that pulmonary oedema complicating pre-eclampsia is associated with the presence of a higher incidence of LV systolic dysfunction compared to LV function in patients with pre-eclampsia without pulmonary oedema.

Methods: Obstetric patients admitted to the Obstetric Critical Care Unit at Tygerberg Academic Hospital with pre-eclampsia complicated by pulmonary oedema were prospectively studied. The study design was a prospective case control study. Patients admitted during February 2016 and February 2017 with pre-eclampsia and pulmonary oedema, pre-eclampsia without pulmonary oedema and a normal control group were prospectively enrolled. An echocardiogram was performed on all the groups. LV function was mainly assessed by the LV ejection fraction (LVEF) estimation by the Teicholz and Biplane method and the lateral S wave tissue. Mean differences in the pre-eclampsia groups were compared to the normal control group. The primary objective was to compare the left
ventricular systolic dysfunction function. Ethics permission was obtained and the statistical analysis was performed by the Biostatistics Unit of the University of Stellenbosch.

**Results:** Twenty-one patients with pre-eclampsia and pulmonary oedema, 21 pre-eclampsia patients without pulmonary oedema and 21 normal patients were included in the study. The mean percentage difference in terms of lateral tissue doppler S wave displacement was calculated as follows: 19% lower in the patients with pulmonary oedema and 5% lower in the pre-eclampsia patients compared to the normal control group (p=0.31) Diastolic dysfunction was present in 48% of patients with pulmonary oedema compared to 33% of the control group without pulmonary oedema (p=0.12)

**Conclusions:** Blood pressure control and afterload reduction remains one of the most important measures in the management of pre-eclamptic patients with or without pulmonary oedema.

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(ISSHP) Evaluation of urinary biomarkers to develop a new method for screening of preeclampsia - Systematic Review and Meta analysis
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**Introduction**
Taking advantage of the multiple mechanisms involved in preeclampsia, a wide variety of candidate biomarkers for prediction and screening of preeclampsia has been found. However, there is scant scientific evidence to validate its use in clinical practice.
The development of a urinary marker for the screening of preeclampsia is attractive given the simple collection and the feasible development of a point-of-care method.
Our objective is to determine which biomarkers have the greatest potential to develop a urinary clinical marker for the screening and diagnosis of preeclampsia.

**Methods**
Study designs
We will include accuracy diagnostic test studies, prospective and retrospective comparative cohort studies, case-control or nested case control studies and cross-sectional studies.
Participants
Only studies examining pregnant women with gestational age between 20 weeks to 12 weeks postpartum will be included.
Interventions and outcomes
Every urinary marker demonstrating clinical relevance for screening of preeclampsia in humans will be included. Each biomarker will be evaluated for its diagnostic performance of preeclampsia. Secondary endpoints will be (i) diagnostic performance for detection of maternal organ failure, (ii) fetal growth restriction and (iii) Interval of time between presence of the marker and development of the clinical disease.
Search strategy and data extraction
Search will be performed in MEDLINE, EMBASE, CINAHL, LILACS, Web of Science, Scopus, ProQuest, Opengrey, OTSeeker and Maternity and Infant Care Database with a predefined search strategy. Two independent reviewers will conduct the screening and eligibility process based on inclusion and exclusion criteria. We will evaluate risk of bias in diagnostic accuracy studies according to Quality Assessment of Diagnostic Accuracy Studies (QUADAS) II instrument. Observational studies will be evaluated with the Newcastle-Ottawa Scale (NOS).

**Conclusion**
We will determine which are the best candidates to focus clinical research and to design a new diagnostic urinary marker of preeclampsia.

**Late breaking abstracts**

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THE ECLAMPSIA MATERNAL MORTALITY IN DR SOETOMO GENERAL HOSPITAL JANUARY 2015 - DECEMBER 2017: EVIDENCE FROM DR SOETOMO GENERAL HOSPITAL
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Introduction
The incidence of Eclampsia in developed country is 1,5-10 cases per 10,000 delivery. The incidence of Eclampsia in developing country is 6-157 cases per 10,000 delivery. More than 50,000 women annually because of Eclampsia. Maternal Mortality Ratio more than 1-2% in developed country. Maternal Mortality Ratio more than 10 % in developing country.

Objective
To know the incidence of Eclampsia and Case Fatality Rate of Eclampsia in dr. Soetomo General Hospital from January 2015 – December 2017.

Methods
This research was Case Control Study.

Results
There was 134 Eclampsia cases with 35 maternal death cases. The highest percentage of Eclampsia was maternal age 20-35 year old (62,7%). Place of delivery at Soetomo Hospital 84,18%, hospitalized 1-5 days 49,3%, gestational age ≥ 36 weeks 81,7%; Multigravida 84,3%, performed Caesarean Section (74,6%). Case fatality rate from maternal age ≤ 20 year old 34,6%, the address out of Surabaya 66,46%, place of delivery out of Soetomo General Hospital has highest case fatality rate (31,8%), the highest case fatality rate from duration of hospitalization was 6-10 days (50%), the gestational age ≤ 34 weeks gestation (58,3%), the highest case fatality rate was primigravida 57,1 % and the case fatality rate of vaginal delivery 14,28%.

Conclusion
Eclampsia was highest in age 20-35 years old, the case fatality rate was highest in age ≤ 20 years old. The duration of hospitalization the highest was 1-6 days hospitalization, the highest case fatality rate was 6-10 days hospitalization. The highest eclampsia incidence was ≥ 36 weeks gestation, the highest case fatality rate was ≤ 34 weeks gestation. The incidence of Eclampsia was highest in Multigravida, the highest case fatality rate was primigravida. The highest mode of delivery was Caesarean Section, case fatality no different between caesarean and vaginaly.

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Uterine vessels vasodilation effect of Placental Protein 13 (PP13) after subcutaneous slow-release administration in rats
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Abstract
Introduction: Placental protein 13 (PP13) is a placental specific galectin that is present only in primates. Low maternal serum concentrations of PP13 in early pregnancy are associated with elevated risk for a subsequent development of preeclampsia, being the leading cause of maternal and perinatal mortality and morbidity. Our previous studies have shown that PP13 lowers blood pressure in pregnant rats affecting the size and weight of pups and placentas and induces vasodilation of resistance arteries through endothelial signaling involving both eNOS and prostaglandin-2 pathways. This study aims to investigate PP13 on the entire vascular system of the maternal uterus.

Methods: Sixteen non-pregnant female Sprague-Dawley rats received mini osmotic pumps in periscapular region by subcutaneous (S.C.) implantation. The administration of recombinant PP13 (rPP13), histidine-tagged PP13 (HisPP13), or saline, by slow-release osmotic pumps lasted over a seven-day period. The rats were sacrificed six days after pumps emptied and their uteri were harvested, fixed, processed for histology and samples sections were stained with Hematoxylin-Eosin for morphometric analysis.

Results: The uterine vasculature was visibly more dilated in the group exposed to the rPP13 compared to the control (saline) group and HisPP13 was less effective. Morphometric analysis confirmed that the entire vascular system (veins and arteries included) was significantly expanded by PP13 although uterine vein dilation was more pronounced compared to the corresponding arteries.

Conclusion: PP13 appears to be an effective molecule for preconditioning the uterine vascular system to accommodate the anticipated increase in blood flow during pregnancy. The effect is not only physiological but also structural and is maintained after the protein is washed out of the circulation. The larger vein expansion compared to the arteries implies that these vessels may be more dependent on PP13 than the arteries, where additional pathways may be involved.
VEGF FUNCTIONALIZED BEADS IN MICROFLUIDIC DEVICE TO RESTORE THE PHYSIOLOGICAL SFLT-1/PLGF BALANCE IN PREECLAMPSIA
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Background: Soluble Fms-like tyrosine kinase-1 (sFlt-1) is an antiangiogenic protein believed to mediate the maternal symptoms of preeclampsia. Removal of circulating sFlt-1 with therapeutic apheresis is growing in interest.

Objective: We propose a specific and competitive apheresis system to capture sFlt-1 with VEGF functionalized magnetic beads. This competitive biomimetic binding approach would capture the circulating sFlt-1 while releasing PlGF thereby increasing the bioavailability of PlGF and potentiating its proangiogenic effects on maternal endothelial function.

Methods: Biotinylated VEGF functionalized magnetic Streptavidin Dynabeads M-280® were used as supports for the capture of sFlt-1. Experiments were carried out in different media (PBS, conditioned media from human trophoblastic cell culture and human plasma) and then in a dynamic microfluidic device as an approach to a real apheresis system. The concentrations of sFlt-1 and free PlGF in solution were measured with ELISA kits (Quantikine® R&D).

Results: In static conditions (2h30, 37°C), with 50 µg of beads and 105 pmol/mg of beads (surface saturation rate of 35%), with human pregnant plasma, we obtained a decrease of 33±13% of sFlt-1 (5972 pg/mL to 3596 pg/mL) and an increase of 27±10% of PlGF (190 pg/mL to 245 pg/mL); n=4. In dynamic conditions (resident time of 8.6 s, total volume 150 µL, flow rate of 1 µL/min), using the same functionalized magnetic beads (mass and ligand), with human pregnant plasma from preeclampsia, we obtained a capture of 46±14% of sFlt-1 (17913 pg/mL to 10191 pg/mL) and an increase of 64±32% of PlGF (36.3 pg/mL to 60 pg/mL); deressing the sFlt-1/PlGF ratio between two or three times after treatment; n=3.

Conclusions: The proof of concept of the capture of sFlt-1, the dissociation of the complex sFlt-1-PlGF and the release of free PlGF with VEGF-coated beads has been established in human plasma.

IS AUTOMATED BLOOD PRESSURE MONITORING RELIABLE IN PREGNANCY?
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Introduction:
The use of automated home BP monitors or Ambulatory blood pressure monitoring may help in accurate assessment of blood pressure patterns throughout pregnancy and early detection of preeclampsia.

Objective: To determine whether out of office BP monitoring is comparable to conventional BP measurements in pregnancy.

Methods: A prospective study was conducted in Department of OBG at JSS Hospital from July 2016 - June 2017. 90 women, 18 – 35 years, with no risk factors like multiple pregnancy, molar pregnancy, chronic hypertension, renal, cardiac, connective tissue disorders, diabetes and thyroid disorders were divided into two groups.

Office BP and Self Home BP monitoring with OMRON HEM 7130 automated BP monitor (n=50).
Office BP and 24 hour Ambulatory BP measurement using Welch Allyn 6100P Ambulatory BP monitor (n=40).
Office BP was recorded at 8 -14 weeks, 16 – 20 weeks, 22 – 28 weeks and 32 -36 weeks.

Results: SPSS 21 was used for statistical analysis.

In women with self home monitoring, the systolic pressure at home was less than the office measurements, but the difference was not statistically significant. Diastolic and mean arterial pressures showed minimal variations between the mean of the office and home BP recordings.

In women with ambulatory BP monitoring, the mean ambulatory systolic and diastolic pressures did not show significant difference when compared to office BP. The night time ambulatory pressures when compared to office recordings also did not show significant changes. There was no night time dip in BP in majority of women.

Conclusion: Self monitoring of BP is an inexpensive and reliable tool to monitor blood pressure in pregnancy, and may be an effective screening method for early detection of hypertensive disorders in pregnancy. Ambulatory BP monitoring is also an effective method, which may be used in high risk women, for early detection of hypertension.
Trophoblasts-specific Atg7 knockout-mediated poor placentation resulting in gestational hypertension in dams.

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Introduction: Preeclampsia is a serious pregnancy complication that is mediated with fetal growth restriction, fetal or maternal death. During the process of developing preeclampsia, placental growth is impaired, poor placentation, followed with the elevated production of anti-angiogenic factors. Preeclampsia is not a single etiological disease, but the role of autophagy, a mechanism of maintaining cellular homeostasis, is still unknown for preeclampsia.

Objective/hypothesis: We aims to clarify the role of autophagy for placentation as well as preeclampsia.

Methods: We established a placenta-specific Atg7 knockout (cKO) placenta using Atg7flx/flx blastocysts transduced with Cre protein by a lentiviral vector, which infected with trophectoderm, but not inner cell mass. Placental structures were evaluated morphologically and histologically. Apoptosis was evaluated with TUNEL assay, and autophagy inhibition was confirmed with RT-PCR or western blotting.

Results: SQSTM1/p62, a marker of autophagy inhibition, was highly accumulated in the giant trophectoblast cells and the spongiotrophoblast layer, in cKO placentas. Placental size was significantly smaller in cKO, which was accompanied with smaller spongiotrophoblast layer, than controls, meanwhile fetal size in cKO did not change. In dams, blood pressure significantly elevated in cKO, but proteinuria was not observed. In addition, increase of apoptotic cells in the spongiotrophoblast layer, reduction of migrating trophoblasts into the maternal decidua, and impairment of vascular remodeling in the spiral arteries were seen in cKO placentas. As a cause of poor placentation, relative expression of PlGF mRNA was significantly decreased in cKO placentas than control. In addition, TFEB expression, a master regulator of autophagy, was decreased in cKO placentas, and the decreased TFEB was also seen in severe human preeclamptic placentas.

Discussions: Impaired autophagy in trophoblasts leads to poor placentation complicated with maternal hypertension in mice, but also could be a risk of human preeclampsia. Autophagy might be a new target of therapeutic intervention for preeclampsia.

Maternal hepatic perfusion in patients with hypertensive disorders of pregnancy and HELLP syndrome

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Objective
Our purpose was to assess maternal hepatic perfusion in women with hypertensive disorders of pregnancy and HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome by using doppler ultrasound.

Design
Prospective observational study

Methods
This study included 12 women with severe preeclampsia, 9 women with HELLP syndrome and 45 healthy pregnant controls at 25–36 weeks of gestation. Dual hepatic perfusion was assessed by evaluation of common hepatic artery blood flow and portal vein blood flow. Angle-corrected time-averaged flow velocity and the cross-sectional area of these two blood vessels were measured by using Doppler ultrasonography Total liver blood flow was taken as the sum of flow volumes in the common hepatic artery and portal vein.

Results
The total liver blood flow was 2.8 ± 0.7 L/min in control, 2.5 ± 0.6 L/min in severe preeclampsia. While on the other hand, the total liver blood flow decreased significantly to about 40% of control in women with HELLP syndrome( 1.1 ± 0.3 L/min)

Conclusion
The total liver blood flow decreased significantly in women with HELLP syndrome compared with normal pregnant women and severe preeclampsia.
Characterization of ELABELA in pregnancy during women with chronic hypertension
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Introduction: ELABELA (ELA) is a circulating peptide involved in the regulation of volume status, vasodilation, hypertension, and angiogenesis. Trophoblast invasion and placental angiogenesis are impaired in ELA knockout (KO) mice and endogenous ELA appears to prevent preeclampsia (PE) while exogenous administration of ELA reverses PE phenotype in the ELA KO mice (Ho et al. Science 2017). Women with chronic hypertension are at an increased risk for developing PE but little is known about ELA pathophysiology in human pregnancies including those complicated by chronic hypertension. We aimed to characterize circulating levels of ELA levels throughout pregnancy in women with chronic hypertension and investigate their association with blood pressure, proteinuria and development of PE.

Methods: We performed a prospective cohort study of 106 pregnant women with chronic hypertension (RO1 HL 48846. PI: P. August). Circulating levels of ELA were measured using ELISA at baseline (<20 weeks), 20 weeks, 28 weeks and 36 weeks of gestation, and postpartum.

Results: ELA levels increased early in pregnancy peaking at 20 weeks to a median of 59 pg/mL (Interquartile range 49.8; 59 pg/mL) and decreased to 43.5 (30.9; 87.1) pg/mL by 36 weeks. There was no difference in levels of ELA in women who developed PE compared to those who did not; 59 vs. 59; 80 vs.73; 58 vs. 45; 44 vs. 41; 61 vs 66 pg/ml at baseline, 20 weeks, 28 weeks, 36 weeks and post-partum, respectively. ELA was not associated with mean arterial pressure or proteinuria.

Conclusion: This first-time characterization of ELA profile in pregnancies complicated by chronic hypertension identified a rise in maternal plasma in mid-pregnancy but the ELA levels were not associated with PE unlike the ELA KO mouse model.

Impact of gestational weight gain on the incidence of preeclampsia in obese women
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Introduction: The increasing occurrence of obesity among pregnant women may increase the occurrence of preeclampsia. In addition to obesity, gestational weight gain (GWG) also has an impact on the course of pregnancy.

Objective: Our study aimed to analyze the effect of GWG on the incidence of preeclampsia in obese pregnant women in Slovenia.

Methods: We conducted a retrospective observational survey, which included 21,316 obese women (pre-pregnancy body mass index >30 m2/kg) with singleton pregnancies without any known previous diseases from 2002 to 2015. We obtained aggregated data from the National Perinatal Information System of Slovenia. The relationship between preeclampsia and the GWG (according to the Institute of Medicine) adjusted for maternal age, parity, gestational age at delivery, and year of childbirth, was determined with multivariable logistic regression. We calculated adjusted odds ratio (aOR) for the incidence of preeclampsia with a 95% confidence interval with a two-way test. A statistically significant p-value < 0.05 was taken into account.

Results: The average GWG in obese women decreased over the observed period from 11.0 kg to 9.9 kg. Despite the increase in the proportion of obese women, we observed a reduction in the incidence of preeclampsia in the hole population from 1.9% to 1.6% with the highest reduction in obese women (from 7.5% to 4.4%). In obese women, a less than adequate GWG reduced the risk of preeclampsia by 40% (aOR=0.61, 0.49–0.74), while excessive increase increased the risk of preeclampsia by 42% (aOR = 1.53; 1.34–1.75). For every kg of GWG less, the incidence of preeclampsia decreased by 1.68% (95% CI=0.75%–2.62%).

Discussion: A less than an adequate GWG independently reduces the incidence of preeclampsia among obese women. With adequate control of GWG in obese women, the incidence of preeclampsia could be further reduced. Additionally, the optimal GWG in obese women should be re-evaluated.
The Characteristic of PE (Preeclampsia) Complication at Lupus on Pregnancy
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BACKGROUND
Indonesia had the serious challenge of highly maternal mortality over last ten years reflecting the real national health problem. There was 305 maternal death/100.000 deliveries where 3 major possible cause of PE, HPP and infection persisted. But recently the new comer of diseases standing tightly behind them, that lupus on pregnancy beside pregnancy with cardiac disease.

MATERIAL & METHOD
It was retrospective study, which obtaining the relevant data on clinical records. Fiftytwo cases of Lupus from 4592 pregnancy during 4 years(1.13%)have been observed in DR. Soetomo Teaching Hospital Surabaya, Indonesia from January 2013 through December 2016 which serving as the highest level in National Referral.

RESULTS
Over period 16 cases of PE complication(30.7%)appeared and from tho these also found 37.5% were accompanied by Lupus Nephritis that mostly showing creatinin serum level > 1.4 mg%. These collected cases ranged 62.5% with of 25-34 years, 62.5% multigravida. Almost the half cases(43.75%)got flare leading 25% terminated earlier, but the remained mostly 12 cases(75%)with conservative management reaching 34 weeks gestation. Fetal outcome reported as 11 cases(68.75%)having above 2 kg body weight with 37.5% asphyxia.

DISCUSSION
Pregnancy was discouraged in women affected by SLE, due to the disease becoming more aggresive during pregnancy and a poor pregnancy outcome was frequently reported. During pregnancy, the maternal immune system adapts to allow the growth of a semi-allogenic fetus. Significant immunological changes occur including suppression of type-2 helper cells(Th2), but the upregulation of Th1 cytokines in pregnancy may increase the risk for Th1-mediated diseases.

The aboved concept was reflected at our study where mostly 12 cases(75%) with success conservative management reaching 34 weeks gestation and fetal outcome 11 cases(68.75%)having above 2 kg body weight as well.

CONCLUSIONS
Our results suggest that lupus women are much more likely to develop worsening maternal and fetal outcomes when they become pregnant.

Neonatal asphyxia diagnosis in newborns of pregnancies with hypertensive disorders attended at a School Hospital in Porto Alegre/RS, Brazil: a retrospective cross-sectional study.
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Objectives: To verify the relation between hypertensive disorders in pregnancy and arterial blood gas analyses collected at birth in newborns attended at a School Hospital.

Methods: A retrospective cross-sectional descriptive study including newborns born between 2011 and 2016, at the Obstetric Center of a School Hospital (Porto Alegre, RS, Brazil), with hypertensive disorders in pregnancy, compared to a births without hypertensive disorders, with gestational age above 35 weeks. The clinical diagnosis of asphyxia was performed through the collection of the umbilical cord blood gas analyses at birth. Bivariate comparisons were carried out using for independent samples (Chi-Square, t Student’s or Mann-Whitney test). The significance was set at 5%. The Ethical Institutional Review Board approved this project (CAAE: 57087916.3.0000.5327).

Results: It was included 9212 medical records of newborns, 376(4.1%) with hypertensive disorders in pregnancy and 8836(95.9%) controls. The majority of women was white (75.4%), nulliparous (41.9%), with median[95%CI] gestational age of 39.39[39.36-39.42] weeks. No differences were found in the incidence of asphyxia by pH between both groups (Chi-Square test, p=0.412) or by base excess (Chi-Square test, p=0.976). The rate of cesarean section was higher in hypertensive women (44.94%) than in a term pregnancies (30.36%) (Chi-Square test, p<0.0001).

Conclusions: Women with gestational hypertension have increased caesarean sections, but there is no increase in neonatal asphyxia in their newborns.
Comparison between newborn's arterial blood gas analyses of various hypertensive disorders in pregnancy: a retrospective cross-sectional study.
Marcelo Marsillac Matias, Charles Francisco Ferreira, Daniele Camila Maltauro, Handria Rodrigues Silva, José Geraldo Ramos, Sérgio Martins-Costa
Universidade Federal do Rio Grande do Sul, Porto alegre, Brazil

Objectives: To verify the relation between umbilical blood cords collected at birth in newborns attended at a School Hospital, considering the various types of hypertensive disorders in pregnancy.

Methods: A retrospective cross-sectional descriptive study of newborns, born between 2011 and 2016 at the Obstetric Center of a School Hospital (Porto Alegre, RS, Brazil), over 21 gestational weeks, in order to compare hypertensive disorders in pregnancy. The clinical neonatal diagnosis of asphyxia was performed through the collection of the umbilical cord blood gas analyses at birth. Bivariate comparisons were carried out using for independent samples (Chi-Square, t Student’s or Mann-Whitney test). The significance was set at 5%. The Ethical Institutional Review Board approved this project (CAAE: 57087916.3.0000.5327).

Results: A total of 376 newborns’ medical records were included, 197(52.39%) with chronic hypertension, 84(22.34%) with mild preeclampsia, 32(8.99%) with severe preeclampsia, 49(13.03%) with gestational hypertension and 14(3.72%) with other conditions. The majority of women was white (68.88%), nulliparous (54.79%), with median[95%CI] gestational age of 38.86[37.86-39.72] weeks. The presence of neonatal asphyxia diagnosis by pH or base excess were not different between groups ([https://br.search.yahoo.com/search;_ylt=AwrJ7KJibDlbz8sAaQXz6Qt.;_ylu=X3oDMTBzamNxcGJpBGNvbG8DYmYxBHcvMxBH2aWQDBHNIywNyZWw: ?p=kruskal+wallis+test&type=D211BR105G0&ei=UTF-8&fr2=rs-top&fr=mcacef, p=0.73 and p=0.116, respectively). The cesarean section rate was 44.95%.

Conclusions: The umbilical cord blood gas analyses revealed not being related to the type of hypertensive disorders in pregnancy.

Continuous versus discontinuous Magnesium Sulphate treatment during expectant management of severe preeclampsia
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Introduction: Expectant management with close monitoring in severe preeclampsia before 34 weeks, improves neonatal outcomes. Magnesium Sulphate (MS) is essential to avoid maternal complications.

Hypothesis: Continuous administration of MS prolongs pregnancy more days than discontinuous administration. Secondary objectives were to compare the prevalence of maternal and neonatal complications according to the treatment regime.

Methods: This is an open-label, randomized, parallel-group phase IV clinical trial. Women admitted with severe preeclampsia between 24-34 weeks of gestation and suitable for expectant management, were randomly allocated to one of two different groups of treatment with MS: continuous treatment (CT) from diagnosis until 24-48 hours after delivery or discontinuous treatment (DT), in which MS was stopped after de first 24 hours from diagnosis and restarted when there was any indication for delivery until 24-48 hours after delivery.

Results: Between April 2012 and May 2016, 92 women were enrolled and randomly allocated to CT (45) or DT (47). Median gestational age at enrollment was 30.0 weeks (interquartile range [IQR]: 28.0-31.0) in CT and 29.0 (IQR: 27.0-32.0) in DT group (p=0.550). Median days of pregnancy prolongation was 5.0 (IQR: 3.0-9.0) in the CT group and 4.0 (IQR: 2.0-7.0) in the DT (p=0.125). No significant differences were seen in maternal adverse composite outcomes in CT 9/45 (20%) vs. DT 12/47 (25.5%) (p=0.622). There were no cases of eclampsia nor maternal death. There were only 2 neonatal deaths, both in the CT group (p=0.238). No significant differences were seen in neonatal adverse composite outcomes in CT 17/52 (32.7%) vs. DT 19/54 (35.2%) (p=0.786). Severe side effects related to MS were not observed in neither group.

Discussion: Continuous administration of Magnesium Sulphate in severe preeclampsia before 34 weeks, does not prolong pregnancy more days than discontinuous treatment. Maternal and neonatal outcomes do not differ from one group to the other.
RISK OF PREECLAMPSIA IN WOMEN WITH PLACENTA PERCRETA
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Introduction
Placenta accreta has been described as a protective factor for developing preeclampsia and it has been proved that sFlt-1 is downregulated in trophoblastic villi of women with placenta increta and accreta. We hypothesize that the greater the trophoblast invasion power the lesser the risk of developing preeclampsia. Thus, placental percretism (PP) could be considered as a protective factor. Our objective is to determine the risk of preclampsia in women with PP, treated at the National Institute of Perinatology in Mexico.

Material and methods
We conducted a comparative cohort study among pregnant women with PP diagnosed by ultrasound or MRI and confirmed by histopathology. In all cases, patients were followed 12 weeks postresolution, to discard preeclampsia according to ACOG criteria. They were matched for gestational age, maternal age and body mass index (BMI) with two healthy women.

Results
Frequencies were determined in 184 women: 47 with PP (Group 1) and 137 healthy women as control group (Group 2). There was no difference in maternal age (28.8 Vs 30 p = 0.8), BMI (27.8 vs. 27.2 p = 0.41) or gestational age (36.4 vs. 37.1 p = 0.002).
Neither was there difference in the incidence of risk factors: chronic arterial hypertension (3/47 vs 6/137, p = 0.69), obesity (0/47 vs. 1/13, p = 0.76), history of preeclampsia (3/47 vs. 9/137, p = 0.9), systemic eritematosus lupus (0/47 vs. 2/137, p = 0.55), hypothyroidism (1/47 vs. 2/137, p: 0.17) or hyperthyroidism (0/47 vs. 2/137, p= 0.55).
The calculated risk for the preeclampsia in women with PP had an OR 0.12 (95% CI 0.016-0.91).

Discussion
According to our study, PP is a protective factor for preeclampsia development. Similar results have been reported previously in placenta previa and accretism, nonetheless few studies have focused on PP, and none has confirmed the diagnosis by histopathology.

Preeclampsia and Gestational Hypertension: Role of Anti-angiogenic factors, sFlt-1 and sEng
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The etiological basis of Preeclampsia, PE, a multi-systemic disorder of Pregnancy, is largely attributed to dysregulation of various placental factors. The major among them, the anti-angiogenic (sFlt-1 and sEng) and angiogenic factors (PIGF and VEGF), have been shown to be critically involved in the onset and progression of PE. In the present study, we have tried to explore the possible role of the circulating anti-angiogenic markers in the serum of the patients with hypertensive disorder of pregnancy (including Gestational Hypertension (GH) and PE) and Normotensive (NT) pregnancy. The anti-angiogenic protein, sFlt-1 was found to be significantly increased (p<0.05) in the PE samples compared to the NT during the 3rd trimester and at term, (8.71±1.9 ng/ml, n=6, vs. 3.95±0.38 ng/ml, n=111, 15.2±4.1 ng/ml, n=7, vs. 6.6±0.43 ng/ml, n=111), while in the GH samples, it was found to be significantly increased (p<0.05) only at the term, compared to the NT samples (12.3±3.4 ng/ml, n=7, vs. 6.6±0.43 ng/ml, n=111). The levels of sEng, were found to be significantly increased (p<0.05) in the PE samples compared to the NT samples at the 2nd trimester, 3rd trimester and at term, respectively (6.9±2.3 ng/ml, n=7, vs. 3.8±0.26 ng/ml, n=106, 13.1±2.1 ng/ml, n=7, vs. 7.9±0.38 ng/ml, n=106 and 14.9±2.2 ng/ml, n=7, vs. 10.0±0.42 ng/ml, n=106). None of the samples from GH patients, from any trimesters showed any difference in the levels of sEng compared to the NT samples. Interestingly though, the levels of both the anti-angiogenic proteins, sFlt-1 and sEng were found to be more than two folds increased in the 1st and 2nd trimester and 0.5 - 1.5 folds increased in the 3rd trimester and term, in PE samples compared to the GH samples, but were not significant. A more critical role of sEng in the progression of PE is hence determined in the present study.
SILIBININ DOWNREGULATES THE INFLAMMATORY RESPONSE IN MONOCYTES OF PREGNANT WOMEN WITH PREECLAMPSIA

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Introduction: Preeclampsia (PE) is a gestational specific syndrome characterized by a maladaptation state of the immunological tolerance, identified by oxidative stress and abnormal activation of the innate immune system. The imbalance between pro- and anti-inflammatory cytokines in PE could be dependent on the deficiency of regulatory factors capable of modulating inflammatory response. This imbalance could be improved by administration of flavonoids with anti-inflammatory properties such as silibinin (SB).

Objective: This study aimed to evaluate the immunomodulatory effect of silibinin on the cytokine production and the NF-κB pathway activation of monocytes from pregnant women with PE.

Methods: Monocytes from pregnant women with PE were cultured with or without silibinin for 18 h and supernatant of culture was employed for determination of IL-1β, IL-6, IL-8, IL-10 and TNF-α by Cytometric Bead Array (CBA), and IL-12p70 and IL-23 concentrations by ELISA. Nuclear extract from each culture condition was employed to determine the level of p65NF-κB by using a transcription factor ELISA kit. The results were analyzed using nonparametric tests with 95% of significance level.

Results: Endogenous levels of IL-1β, IL-6, IL-8, IL-12p70 and TNF-α produced by monocytes from preeclamptic women were significantly higher, whereas the IL-10 levels were lower when compared to the monocytes treated with SB. The IL-23 levels did not show significant difference between both treatments. NF-κB levels in monocytes of pregnant women with PE were decreased when treated with silibinin.

Discussion: Silibinin treatment decreased the production of pro-inflammatory cytokines, while the IL-10 levels were increased. SB was also able to decrease the NF-κB concentration in nuclear extract of monocytes, suggesting that this flavonoid may contribute to suppress the inflammatory effects observed in PE.

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Comparison of long-term neurological prognosis in the children born from mothers with hypertensive disorders of pregnancy and intracranial imaging by MRI

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Objective: We evaluated the correlation between intracranial imaging by MRI (Kidokoro score: KS) and development at age of 3 in the children born from mothers with hypertensive disorders of pregnancy (Child-HDP) or spontaneous preterm birth (Child-PTB).

Methods: Eighteen cases of Child-HDP and 41 cases of Child-PTB managed in our hospital from 2006 to 2015 were selected. They were all evaluated intracranial abnormality by MRI before discharge from NICU and development at age 3 by Bayley. Poor development was defined as cerebral palsy, mental retardation, and low score of Bayley. KS which can accurately evaluate intracranial lesions was used in this study. The gray matter score and the white matter score are included in KS.

Results: 1) The rate of KS was 12.2% (Normal), 41.5% (Mild), 31.7% (Moderate) and 14.6% (Severe) in Child-PTB, while that was 50.0%, 14.6%, 11.1% and 0% in Child-HDP. 2) In Child-PTB, delivery weeks of gestation tended to correlate according to severity of KS (28.9wks of Normal, 28.2wks of Mild, 27.3wks of Moderate and 25.9wks of Severe, p=0.082), and the frequency of poor development also tended to correlate (0% of Normal, 11.8% of Mild, 7.7% of Moderate and 50.0% of Severe, p=0.058), but not in Child-HDP. 3) There was a significant difference between development and KS in Child-PTB (7.0±9.8 of good development vs 13.7±1.8 of poor, p<0.01), but not in Child-HDP.

Conclusion: The positive relationship was observed between intracranial imaging by MRI and long-term prognosis at age of 3 in children born from PTB mothers, while there was no correlation in HDP cases. In HDP cases, neurodevelopment might be recognized as functional damage rather than organic damage.
Combining Metabolite Biomarkers and Placental Growth Factor Yields a Prognostic Test for Preterm Pre-eclampsia.

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Objective
We have previously reported candidate metabolomic biomarkers that predict pre-eclampsia (PE) in nulliparous women. Here we report the precise chemical identities and performance of a novel propriety biomarker-only test capable of the accurate prediction of PE in early pregnancy.

Methods
We developed a library of quantitative mass spectrometry assays for bloodborne metabolites implicated in PE, prioritising metabolites discovered in New Zealand/Australian subjects from the SCOPE cohort (http://www.scopestudy.net). Using this assay library, a nested case:control study of 97 PE cases (23 developed preterm PE), and 335 controls from European SCOPE subjects was analysed, using EDTA 15 +/-1 weeks plasma. 44 metabolites (%CV =<25%), proteins PlGF, sENG and s-Flt1, and simple clinical risk factors, were considered for biomarker analysis. The prognosis of all-, preterm- and term PE was investigated. The prognostic performance of single- and multivariable predictors was quantified using AUROC and detection at predefined Positive and Negative Predictive Values.

Results
We found that 13 metabolite biomarkers exhibited prognostic capabilities across multiple prognostic viewpoints (AUROC, rule-in, rule-out) and across different PE outcomes. Dilinoleoyl-glycerol (DLG) (AUC=0.70; 95%CI [0.59-0.82]) performed similar to PlGF (AUC=0.73; 95%CI [0.61-0.85]) for preterm PE. Combining PlGF, DLG, with ergothioneine and leucine/isoleucine resulted in a 90% detection for preterm PE at PPV=0.07.

Discussion
Here we present a biomarker panel of 3 metabolites + 1 protein capable of the accurate prediction of PE at 15 weeks’ gestation. Interestingly, the three metabolomic biomarkers map onto complementary pathways: DLG, a diacylglycerol, may mediate insulin resistance, ergothioneine associates with mitochondrial oxidative stress, and amino acids leucine/isoleucine inform about placental nutrient uptake. Taken together with PlGF, a marker for placental insufficiency, this 3+1 panel more comprehensively encapsulates the different aspects of the preterm pre-eclampsia syndrome, thus delivering accurate biomarker-only prognosis in nullparous, which was -until now- not achievable.

SAFETY OF AMLODIPINE IN EARLY PREGNANCY

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Amlodipine is used for the treatment of hypertension, but reports on its use in early pregnancy are limited. In the present study, we recruited 233 pregnant women with chronic hypertension and investigated the morphologic abnormalities in their offspring after treatment with amlodipine or other antihypertensives in early pregnancy. Specifically, we evaluated 50 women exposed to amlodipine in the first trimester (amlodipine group, Group A), 54 women exposed to antihypertensives other than amlodipine (other antihypertensive group, Group O), and 129 women not exposed to antihypertensives (no-antihypertensive group, Group N). Morphologic abnormalities occurred in 2 women in Group A (4.0%), 3 women in Group O (5.6 %), and 6 women in Group N (4.7 %). Teratogenic risk was
not clearly increased in Group A compared with the other 2 groups. Maternal hypertension may itself increase the risk of morphologic abnormalities, and further research is needed.

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Maternal and fetal complications in post kidney transplantation (KT) women
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BACKGROUND: An important benefit of kidney transplantation (KT) in child-bearing women is opportunity to become pregnant.

OBJECTIVE: To identify factors associated with maternal and fetal complications.

MATERIALS AND METHODS: The cohort consisted of 64 post KT women. 18 patients had CKD stages 1-2, 25 – 3rd, 3 – the 4th. The immunosuppression therapy during pregnancy had been fully known for 53 patients: 2- monocomponent therapy with tacrolimus(t), 16 - 3component (t or cyclosporine(c)+azathioprine+corticosteroids), 35 - 2component (t/c+corticosteroids).

RESULTS: Main maternal complications (31.25%) were preeclampsia (PE), progressive hypertension in 46.87% and anemia in 65.63%. 3 patients became pregnant less than 1 year after KT had PE. The main fetal complications were intrauterine growth restriction (IUGR) (20.31%), preterm deliveries (31.25%). Anemia in the 1st trimester (Hb1) significantly associated with lower GFR in the 1st trimester (cor=0.65, p=0.015), higher creatinine in the 3rd trimester (cor=0.687, p=0.036), longer interval between KT and pregnancy (IKTP) (cor=0.58, p=0.014). Longer IKTP was associated with lower risk of PE (t-test p=0.037) and lower Hb1 (cor=0.58, p=0.014). Higher proteinuria in the 1st trimester was significantly associated with higher risk of PE (cor=0.646, p=0.032). Lower Hb in the 2nd trimester was associated with higher risk of PE (t-test p=0.036). Lower GFR in the 1st trimester correlated with lower Hb in the 3rd trimester (cor=0.69, p=0.038). “T” was associated with lower risk of PE (t-test p=0.098).

CONCLUSION: KT pregnancies have a higher risk of PE, preterm delivery and IUGR. An anemia and the short IKTP associated with PE. The possible reason for better outcomes in women with longer IKTP is absence of KT related TMA. The major risks to the fetus are mainly related to prematurity. We suggest that “T” is preferable to avoid maternal complications.

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Confirmation that the placenta is a significant source of circulating PI GF in normal pregnancy
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Introduction: Previous studies have shown conflicting evidence regarding the role of the placenta in the production of PI GF in normal pregnancies. These studies have not used automated assays or analyzed postpartum levels. We set out to determine whether PI GF is placentally derived in normal pregnancy.

Methods: Blood samples were collected on the day of caesarean section from the maternal antecubital fossa (peripheral) and uterine vein (UV) both taken before delivery of the feto-placental unit. Post-natal blood samples were collected at day 1-2 from the antecubital vein. Serum samples were assayed on the Roche e411 analyzer.

Results: Seventeen (uterine and periphery) paired samples were collected. Median gestational age was 39.4 (IQR 39.1-40) weeks. Mean UV PI GF was 177.3 (SD +/- 83.9) and mean periphery PI GF was 130.5 (SD +/- 73.2); (n=17 paired samples, paired t test=0.0004). Postnatal samples showed a 79% drop of PI GF postpartum (mean PI GF: 23.2 (SD +/-7.4); n=10; paired t test: p=0.003).

Conclusion: There is a significantly higher level of PI GF closer to the UV than in the periphery. Additionally PI GF levels drop significantly when the placenta has been removed. i.e. postnatally. This is in keeping with the placenta being a significant source of PI GF production in normal pregnancies.
Disruption of the balance of oxidative stress-associated angiogenesis in preeclampsia may cause future cardiovascular complications: VEGFR/Flt1 point-of-view
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Introduction: During pregnancy, the oxidative stress-induced angiogenesis involves hypoxia-inducible factor/vascular endothelial growth factor (VEGF). In preeclampsia (PE) endothelial dysfunction of maternal vessels could be associated with plasma concentration of VEGFR/Flt1.

Objectives/Hypothesis: To study the possible role of VEGFR/Flt1 as a biomarker of oxidative stress status in women that had preeclampsia.

Methods: We studied a case-control study of 142 pregnant women with normal blood pressure (NBP) in pregnancy (NT) and 185 PE; a prospective sub-sample of 138 women of which 90 had PE during pregnancy, 2 to 16 years ago. This reclassification led to the identification of 4 groups: PE and NBP in pregnancy who developed and didn’t develop hypertension (HT) (PE>HT; PE>NT; NBPP>HT; NBPP>NT). The anthropometric, demographic, hemodynamic and biochemical parameters (hepatic function, lipid profile) were determined by conventional methods. The levels of VEGFR/Flt1 were determined by ELISA method (R&D Systems). Statistical analysis were binary logistic regression and comparison of means, considering significant results for P<0.05.

Results: There were no significant differences in the levels of VEGFR/Flt1 between PE and NBPP women, nevertheless, 2 to 16 years old after pregnancy, women that developed HT presented significantly higher levels of VEGFR/Flt1 in relation to NT ones (n=27 HT: 41.4±7.6 vs n=31 NT: 35.2±1.3 pg/mL, P=0.003). This increment was associated to the previously PE status, since, for women that had PE, we found significantly higher levels of VEGFR/Flt1 for women that developed HT comparing with women actually NT (n=21 PE>HT; 41.8±8.0 vs n=21 PE>NT: 34.2±7.3, P=0.003). An important note is that PE>HT women (mean: 37.1±1.05 years old) are significantly older than women PE>NBPP (mean: 32.3±0.9 years old) (P=0.001).

Discussion: Our results suggested that the hypoxia status during pregnancy associated with preeclampsia could interfere with aldosterone levels and the future angiogenic profile, throughout VEGFR/Flt1, possible inducing future cardiovascular risk.
consultations in 62.5%) with difficulties to get to the hospital (28.2%). Comorbidities: systemic arterial hypertension (58.5%), overweight/obesity (68.4%), at least one previous pregnancy (85.3%). Seventy-one percent (71%) had HPD: overexposed pre-eclampsia (41%), preeclampsia (37%), HELLP syndrome (13%), severe chronic hypertension (6%) and eclampsia (3%). The mean gestational age at delivery was 33 weeks and the prevalent type of delivery was cesarean section (86.1%).

Discussion: The antenatal comorbidities and the predominance of unplanned pregnancies may represent limitations in qualified preconceptions. There seems to be difficulty in providing prenatal care, since risk conditions were not timely intercepted. Further studies may increase the recognition of local conditions and the contribution of hypertensive states to SMM, eventually contributing to the adoption of strategies to minimize this problem.

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Relation between sFlt-1/PlGF ratio and clinical decision making in pregnancies with placental disease - a real world analysis
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Background: The sFlt-1/PlGF ratio has been established in clinical routine for prediction and aid in diagnosis for preeclamptic pregnancies. The value of that biomarker reflects severity and progression of the disease and correlates negatively with the time interval to delivery. Aim of this pilot study was to analyze the relation of the implemented angiogenic biomarker and different cluster of decision of iatrogenic delivery.

Patients and methods: This monocentric retrospective preliminary analysis includes 69 cases with preeclampsia, HELLP syndrome or IUGR. sFlt-1/PlGF ratio was measured at admission and prior to delivery. Indication and urgency of iatrogenic delivery was analyzed and related to angiogenic status.

Results: Decision for delivery was based on maternal condition in 25 cases (sFlt-1/PlGF ratio at admission median 95.5), fetal condition in 19 cases (sFlt-1/PlGF ratio median 165.9) and combined in 25 cases (sFlt-1/PlGF ratio median 189.5). Pregnancies delivered due to fetal indication showed the highest sFlt-1/PlGF ratio: median 317.1 fetal vs. 188.9 maternal and 231.3 combined, n.s. There was no significant difference of the sFlt-1/PlGF ratio between elective (n=13), urgent (n=55) and emergency (n=1) deliveries. Pregnancies with urgent/emergency delivery had a significantly lower gestational age at delivery (34 wks / 36 wks vs. 39 wks elective, p< 0.001).

Conclusion: An increased sFlt-1/PlGF ratio characterizes as expected pregnancies with anti-angiogenic placental disease. In clinical routine, this biomarker serves as a diagnostic tool for a potentially maternal and/or fetal adverse outcome. The lacking difference of the sFlt-1/PlGF ratio between different degrees of urgency of iatrogenic delivery indicates that the biomarker contributes to decision making but does not guide it exclusively.

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Mild preeclampsia delivery at 37 week: Epidemiological profile and perinatal outcomes
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INTRODUCTION
Systematic delivery approach in pregnant women with preeclampsia could avoid risks to both mother and newborn. A study about these outcomes could guide this practice.

OBJECTIVE
Identify epidemiological profile and maternal and neonatal outcomes in normal pregnancies at term with mild preeclampsia.

METHODS
Prospective study with 104 pregnant women was developed in Guilherme Álvaro Hospital/Santos/SP/Brazil (March/2016-June/2017). Study group: 52 with preeclampsia (NHBPEP 2000), >37 weeks. Control group: 52 with single and live fetus, >38 weeks, without comorbidities. Study group exclusion criteria: twin pregnancy, fetal anomalies, gestational age <37 weeks. Control group exclusion criteria: twin pregnancy, gestational age <38 weeks, cesarean/forceps/induced vaginal delivery, comorbidities. Maternal variables: age, gestational age at delivery, body mass index (BMI), previous preeclampsia, intensive care admission (ICU), delivery route. Neonatal variables: birth
weight, adequacy weight for gestational age, Apgar score, ICU admission, acute respiratory distress syndrome (ARDS), jaundice, intrahospital mortality. Statistical comparisons were made using Fisher’s exact test and Student t test. Data analysis was performed by calculating odds ratio adoption hypothesis and the rejection level of 0.05.

RESULTS

Comparison between preeclampsia and normal pregnancies in maternal and neonatal outcomes (p<0.05): study group: higher age (30), previous preeclampsia (19.2%), BMI (33.3%), admission SBP (132mmHg), and c-section (68.5%). Their newborns: lower gestational age at birth (37 weeks), Apgar Score (7/8), higher occurrence of small for gestational age (11.5%). There is a lack of significance in some variables, however, newborns of mothers with preeclampsia are more susceptible to ICU admission (25.5%), ARDS (19.6%), jaundice (7.8%).

DISCUSSION

The study group results are in accordance to literature. Results show a lack of statistical significance in neonatal outcomes. There was no maternal and neonatal death, and no maternal hospitalization in ICU, which makes us consider that providing delivery in a systematic way by reaching term, may constitute a possible method to anticipate problems.

Nicardipine as a new treatment option for severe hypertension in pregnancy: 9 years of clinical experience

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Objective

It is mandatory that women who develop severe hypertension during pregnancy have to be stabilized with a combination of magnesium sulphate and intravenously administered antihypertensives. It is still questionable which antihypertensive is best to be used in this situation. The primary goal of the present study is to confirm our hypothesis that nicardipine is an effective and safe option to treat severe hypertension during pregnancy.

Methods

Multicentre, retrospective cohort study in two tertiary care hospitals.

Primary outcomes: successful treatment (SBP <160 mmHg and DBP <100 mmHg), time period until successful treatment and maternal safety.

Categorical data are presented as n (%), and tested using Chi-square test. Non-parametric data were presented as median (min-max) and/or interquartile ranges, and tested using Mann-Whitney U test. Parametric data were presented as mean (SD), and tested using independent samples T-test. Statistical analyses were performed with SPSS (version 24; SPSS, Chicago, IL, USA).

Results

Nicardipine was successful in 100% of the 803 cases of severe hypertension during pregnancy; 77.4% of women were successfully treated within two hours, time period until success 77 minutes, 42.7% experienced maternal hypotension within the first two hours. One case (0.1%) of clinical relevant hypotension was described. In all other cases of hypotension this could be resolved after discontinuation or dosage reduction. There were no other serious maternal or neonatal complications due to the use of nicardipine.

Discussion

In this largest cohort study so far our hypothesis was confirmed that nicardipine is an effective, fast and safe treatment option to treat severe hypertension in pregnancy that.
INTRODUCTION
Gestational hypertensive syndrome is an expressive cause of maternal and neonatal morbidity and mortality, studying it contributes to guide approach strategies.

OBJECTIVE
Compare maternal and perinatal outcomes among pregnancies with hypertensive syndromes and gestations without comorbidities.

METHODS

RESULTS
Preeclampsia group presented higher: admission SBP (136mmHg), c-section (89.5%), small for gestational age (28.9%), need for neonatal ICU (44.7%), lower: gestational age at delivery (36 weeks), birth weight (2645g), Apgar Score (7/8). Chronic hypertension group presented higher: maternal age (32 years), previous c-section (0.80), BMI (34); lower: weight gain (7.9kg). Gestational hypertension group presented higher: previous preeclampsia (24%), birth weight (3281g). Control group presented lower maternal age (25 years), higher weight gain (12.7kg), gestational age at delivery (39 weeks). Despite the non-statistical significance, the preeclampsia group presented higher: maternal ICU, respiratory and non-respiratory neonatal complications. There were 4 neonatal deaths only in hypertensive group.

DISCUSSION
The results are in agreement with the literature about maternal epidemiological characteristics and need for neonatal ICU in preeclampsia group, and c-section in general hypertensive pregnant women. Although not significant in this study, the higher respiratory and non-respiratory neonatal outcomes are more related to preeclampsia, consistent with most studies.

Preventive subfascial application of absorbable hemostatic material in patients with HELLP syndrome may help to reduce the incidence of wound complications
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Objective: to evaluate the effect of preventive subfascial use of the absorbable hemostatic material on the incidence of wound complications in patients with confirmed HELLP syndrome.

Methods: Retrospective descriptive study evaluating the effect of adjunctive peroperative subfascial application of hemostatic material (oxidized regenerated cellulose) on the incidence of subfascial hematoma and the need for relaparotomy in pregnancies complicated by HELLP syndrome (class I and II). The patients were divided into 2 groups (before the use of hemostatic material (2005-2013) and after the use of hemostatic material was introduced into the clinical practice (8/2013-2017).

Results: 124 patients between 2005-2017 have been included (group 1; N=95, group 2; N=34). In group 1 the incidence of relaparotomy was 10.2% (10 cases) and subfascial hematoma 9.4% (9 cases), while in group 2 there were no patients with subfascial hematoma and 1 patient indicated for relaparotomy (2.9%).

Conclusion: We suggest that the routine and preventive subfascial application of absorbable hemostatic material in patients with HELLP syndrome might have an impact on reducing the incidence of subfascial hematoma and the need for relaparotomy. Due to the limited size of the sample no statistical methods were applied. Further research is needed to confirm the hypothesis.

Discussion: Wound hematoma and infection are frequent phenomena in women with HELLP syndrome undergoing Cesarean section (Curtin,Audibert, Haram). Very often the complication develops with the delay in spite of the meticulous hemostasis and/or drainage. In 2013 we started to apply an absorbable hemostatic material into the subfascial space, without the use of drains, in order to achieve a better local hemostasis. The results seem to be promising even though the relative small size of the sample does not allow a valid statistical analysis yet.

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The effect of changing food habits on the management of hypertension in pregnant women
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Introduction: Hypertension is defined as blood pressure higher than 140/90 mm Hg in the arteries. The condition is a serious concern for some pregnant women. It can sometimes cause severe health complications for both mother and fetus. According to (NHLBI), overweight or obesity is one of the predisposing factors for high blood pressure during pregnancy, which is due to nutritional or dietary regimen. Focus on gaining a healthy amount of rice as the most important food crop of developing countries was studied for weekly recipes.

Methods: During 18 months (2014 to 2016), a clinical trial was conducted to test the affect of a diet of rice on 200 pregnant women with BP systolic pressure ≥ 145 mm Hg and BP diastolic ≥ 85 mm Hg at the Gynecology Clinic, Arefian General Hospital, Urmia, Iran.

Results: For the control group including 100 pregnant women with hypertension the normal diet of 600 gr cooked rice weekly vs the study group which ordered by decreasing use up to 200 gr weekly, without the replacement of other grains. The blood pressure was measured for both groups at the end of 7 days. Our findings of systolic and diastolic BP showed at least 15 mm Hg and 10 mm Hg dropped BP in the study group comparing the control group.

Conclusion: The condition of changing food habits, caused decreasing risk of BP events in pregnant women.