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Severe hypertriglyceridemia in pregnancy and plasmapheresis: A case report

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Abstract

Introduction: Pregnancy in women with severe hypertriglyceridemia increases the risk of pancreatitis with its associated maternal and fetal morbidity and mortality.[1,2] Achieving safe levels of triglyceride in this population can be challenging. In this case report, plasmapheresis was performed as the patient was refractory to other treatment modalities.

Case: A 19-year-old, body mass index 19, non-English speaking background woman from Lebanon presented to the birthing unit at 24 + 6 weeks with worsening generalised abdominal pain. Upon extensive history and investigations, the woman was diagnosed with severe pancreatitis secondary to familial hypertriglyceridemia. With the aid of her endocrinologist in Lebanon and multidisciplinary care with internal endocrinology, dietitian and maternal–fetal medicine team at the hospital, the woman was treated with dietary modification with low-fat diet, insulin-dextrose infusion, subcutaneous heparin, subcutaneous insulin, oral antilipid and fat-soluble supplementation in various stages of her inpatient stay. However, these methods failed in maintaining the triglyceride level within a safe level. Subsequently, a multidisciplinary decision was made to commence plasmapheresis with albumin as the replacement fluid. The plasmapheresis was initially conducted once a week due to the rapid rise in triglyceride in the third trimester. She remained well in the third trimester, with good fetal growth and wellbeing. Induction of labour was organised at 37+ weeks which resulted in an uncomplicated birth and postnatal course.

Discussion: Triglycerides concentration rises 2.5-fold over pre-pregnancy levels, reaching a peak during the third trimester.[3,4] These changes are related to an increasing hepatic synthesis of very low-density lipoproteins and a reduction in the activity of lipoprotein lipase in relation to the high levels of estrogen.[1] Familial hypertriglyceridemia with TG levels >10 mmol/L (severe levels) is exacerbated by the physiologic hypertriglyceridemia of pregnancy.[5] As proposed by Wong et al.,[4] a hierarchical management strategy for familial hypertriglyceridemia includes a low-fat and low-glycemic carbohydrate diet with nutritional support, consideration of hospitalization for parenteral nutrition or intravenous insulin therapy and fibrate use after the first trimester. Once other methods of treatment have been exhausted, plasmapheresis may be the final treatment modality.[6–8] Although it is effective, plasmapheresis is invasive and short-lasting. Hence, may require multiple sessions to reduce the triglyceride levels as demonstrated in this case.[9,10]

Conclusion: Plasmapheresis was an effective and safe therapeutic modality in managing severe hyperlipidaemia in pregnancy, leading to a good outcome in this case. There is still scope for research for determining the optimal time to begin plasmapheresis, frequency, duration and the long-term effects on the mother and the baby.

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Protein chaperones and sFlt-1:PlGF ratio in preeclampsia: A case–control study

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Factor V deficiency in pregnancy

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Abstract

Aim: Early diagnosis of Factor V deficiency (FVD) and management with haematology expertise is crucial for a successful outcome in obstetric patients.

Introduction: Congenital Factor V deficiency (aka parahaemophilia; and Owren's disease) is a rare autosomal recessive disorder associated with abnormal Factor V plasma levels and activity. It is more common in those with consanguineous history. It affects one in one million persons, with the decreased Factor V levels interfering with fibrin formation. It may be associated with increased rates of recurrent miscarriage and fetal demise.

Clinical description: A 36-year-old G3P0 female, of Middle Eastern background, with consanguineous partner, was diagnosed with Factor V deficiency following recurrent second trimester spontaneous miscarriage. Examination of the placenta revealed a haematoma 40 mm × 20 mm with maternal bloods depicting Factor V levels of 3%. Fresh frozen plasma (FFP) infusions showed platelet increment from 3 to 33%. During her third pregnancy, she was managed with FFP infusions with haematology involvement. Cervical shortening and preeclampsia further complicated her pregnancy. Her cervical length remained stable with progesterone pessary. Cervical cerclage was avoided due to increased bleeding risk. She was induced at 38 + 5/40, delivering a live male with aid of forceps and episiotomy. Four units of FFP administered once labour established. In postpartum period, she was administered prophylactic FFP and tranexamic acid. She was also monitored closely with daily bloods and management of anaemia.

Discussion: Congenital Factor V deficiency is rare. Defined as those with increased prothrombin time, increased aPTT, but with decreased factor activity levels than 5%. Common symptoms include epistaxis, menorrhagia, postmenopausal bleeding, post-surgical bleeding. Increased bleeding poses an obstetric issue due to increased risk of recurrent miscarriages and fetal demise, especially in those with homozygous FVD. There are few case reports of successful pregnancies. Of most importance is early diagnosis and management, to minimize bleeding risk. Prophylactic FFP is used to correct abnormal activity levels intrapartum. Factor V levels 20–30% normal is considered safe. Mode of delivery is debatable and should be made on an individual basis. Once labour established, or <2 h prior to a planned caesarean section, 20 mL/kg FFP is administered. Postpartum 10 mL/kg BD is given targeting >20% Factor V activity levels for a minimum of three days before ceasing FFP infusions. Tranexamic acid 1 g TDS is used for minimum three days postpartum to decrease postpartum haemorrhage risk. Correction of anaemia, iron deficiency and mechanical prophylaxis is also ensured.

Conclusion: FVD is a rare hemophiliac disorder. It must be correctly identified and distinguished from FV Leiden mutations in that it causes increased bleeding risk, rather than increased clotting. Therefore, in homozygous women with <1% activity levels, early management with FFP is necessary to decrease risk of miscarriage and fetal demise.

Management of low-molecular weight heparin allergy in pregnancy

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Abstract

Background: One of the most frequent adverse effects of low-molecular weight heparin (LMWH) treatment is delayed-type reactions presenting as a pruritic and erythematous rash at the injection site.[1] In pregnancy, the rate of delayed skin reaction is significantly higher at 19.8% compared to the non-pregnant population.[2,3] Finding alternative treatment is challenging.

Aim: To describe two cases of LMWH allergy in pregnancy and discuss current literature available describing alternative antenatal and postnatal management.

Methods: Management of pregnancy and, maternal and neonatal outcomes of two cases of pregnant women that reacted to: (1) LMWH thromboprophylaxis (Woman 1) and (2) LMWH treatment for pulmonary embolism (Woman 2) are presented. Current literature for management of LMWH allergy in pregnancy was reviewed.

Results: Woman 1 is a 35-year-old female G3P2 with a history of preeclampsia and post-partum pulmonary embolism (PE) diagnosed following her second pregnancy. In this pregnancy, the woman was started on prophylactic LMWH. After reacting to two different LMWH brands, she was approved for a compassionate supply of danaparoid. The woman cross-reacted to danaparoid developing an erythematous rash at the injection site. Danaparoid was ceased and she was continued on aspirin mono therapy. Post-partum, compassionate supply of fondaparinux was given as an inpatient, and apixaban was started upon discharge as she did not breastfeed. She delivered a healthy baby via normal vaginal delivery at 38 weeks of gestation. Baby weighed 2.9 kg with an APGAR score of 9[1]. Woman 2 is a 39-year-old female, with pulmonary embolism detected at 32-week gestational age. She developed severe erythematous, painful rash on her abdomen and lower limb. Given the difficulty of obtaining compassionate supply of therapeutic danaparoid or fondaparinux and close proximity to delivery, she was admitted for heparin infusion with no adverse reaction and was discharged on warfarin postpartum. Vaginal delivery was induced at 37 weeks of gestation. Baby weighed 2.7 kg with an APGAR score of 9[5]. Neither woman suffered from post-partum haemorrhage.

Discussion: Heparins are bovine or porcine derived mucopolysaccharides. Alternatives to heparin include heparinoids, hirudin and fondaparinux. Danaparoid is a semi-synthetic mixtures glysoaminoglycans. Danaparoid has been previously reported to be safe in pregnancy with relatively high cross-reactivity in non-pregnant women.[3] Danaparoid is not available on Pharmaceutical Benefits Scheme (PBS). Fondaparinux is a fully synthetic pentasaccharide sequence binding to anti-thrombin to

enhance its ability to inactivate Factor Xa. Fondaparinux has been used as an alternative in women with non-immediate cutaneous reactions from heparin and heparinoids; however, it has been documented to cross the placenta and increase rates of post-partum haemorrhage.
Conclusion: Managing LMWH allergy in pregnancy can be challenging due to limitations of safe PBS available alternatives. Heparinoids and fondaparinux are reasonable alternatives in this setting.

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Body composition measurement in pregnancy using bioelectrical impedance analysis: An Microbiome Understanding in Maternity Study (MUMS) sub-study

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Abstract
Background: Bioelectrical impedance analysis (BIA) is a popular method of body composition analysis in pregnancy as it is safe, inexpensive and non-invasive. Reliable techniques to measure body composition are required for clinical and research purposes. However, reproducibility between BIA instruments when used in pregnancy is uncertain. Abnormal changes in maternal body composition have been linked to adverse pregnancy outcomes including gestational diabetes mellitus (GDM). This study aimed to (1) determine the reproducibility of BIA between three instruments and (2) investigate the association of body composition with GDM risk.
Methods: Prospective cohort study ($n = 117$) of women with singleton pregnancies participating in the Microbiome Understanding in Maternity Study (MUMS) at St George Hospital. Anthropometric measurements and body composition were measured at three time-points: $\leq$13 weeks of gestation (Trimester 1), 20–24 weeks of gestation (Trimester 2), 32–36 weeks of gestation (Trimester 3). Body fat percentage (BFP) and total body water (TBW) were measured by three BIA instruments: tetrapolar Bodystat 1500, tetrapolar RJL Quantum III and bipolar Tanita BC587. Bodystat was the reference method due to previous validation. GDM status was recorded after a 75 g oral glucose tolerance test performed at 28 weeks or earlier. Bland–Altman analysis was performed to determine agreement between BIA instruments. Logistic regression analysis was performed to determine any association of BFP with GDM risk.
Results: Method comparison reproducibility between Bodystat and RJL was higher than between Bodystat and Tanita for both BFP and TBW across all three trimesters of pregnancy. RJL significantly overestimated BFP by 3.3% ($p < 0.001$), with limits of agreement within $\pm$5% for all trimesters. Average BFP was not significantly different between Tanita and Bodystat, although limits of agreement were greater than $\pm$5%. Test-retest repeatability for all three instruments was excellent (ICC range 0.984–1.000) when tested on a subset of 49 women. The risk of GDM was independently associated with increased BFP in Trimester 1 (adjusted OR 1.12 per 1% increase, 95% CI 1.02–1.22, $p = 0.017$) and Asian ethnicity (7.45, 2.08–26.64, $p = 0.002$).
Conclusion: Test-retest repeatability of all instruments was excellent, while reproducibility amongst instruments was moderate. Therefore, a single BIA measure at each time-point is appropriate for assessing body composition in pregnancy; however, interchangeability between instruments cannot be assumed. In this cohort, GDM risk was modestly associated with increasing BFP. The importance of BFP to GDM pathophysiology, including relationship to microbial dysbiosis, is to be further studied in the MUMS cohort.

Bariatric surgery – Pregnancy outcomes

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Abstract
Maternal overweight, an obesity, is attended by particular risks to mother and infant. One method of treating weight – bariatric surgery – is increasingly available and being used by women of childbearing years. This presentation will discuss the benefits, risks and challenges for women undertaking bariatric surgery prior to pregnancy, in relation to their pregnancy outcomes.

Inflammatory bowel disease in pregnancy

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Abstract
Inflammatory bowel disease (IBD) affects patients in their peak reproductive years. Active IBD increases the risk of adverse pregnancy outcomes, including miscarriage, intrauterine growth restriction and preterm birth. Most women with IBD will require medication to control their disease, both before conception and during pregnancy and breastfeeding. Preconception counselling has been shown to improve pregnancy outcomes. Most IBD medications are considered safe during pregnancy and breastfeeding. A multidisciplinary approach, with the involvement of general practitioners, midwives, obstetric physicians, and obstetricians and gastroenterologists, is recommended. Three to six months before conception, women should be reviewed by their gastroenterologist for preconception counselling to confirm disease remission, receive education about pregnancy and IBD and have a pregnancy treatment plan established. Medical treatment should be optimised, with the aim of achieving sustained remission for at least three to six months before conception. Cessation or modification of IBD treatment is usually not necessary, with the exception of methotrexate, thalidomide and allopurinol, and any changes to medical therapy should be made in consultation with the treating gastroenterologist. Data on biologic use in pregnancy (TNFi, vedolizumab, ustekinumab) and Tofacitinib will be discussed. Fear of infertility is common among patients with IBD, but women with

quiescent IBD generally have normal fertility. Women with Crohn's disease may have reduced fertility if they have active disease or have had an ileo-anal pouch. There is no evidence that ulcerative colitis affects fertility. IBD does not affect fertility in men, but some medications, including sulfasalazine and methotrexate, may cause reduced sperm count and may need to be replaced with alternatives pre-pregnancy. Women should be reviewed once per trimester and more regularly if they have active disease. Inadequate gestational weight gain is a marker for intrauterine growth restriction and prematurity and should prompt extra growth scanning during pregnancy. Monitoring of faecal calprotectin level is helpful to detect relapse but is not yet reimbursed. Intestinal ultrasound is useful to assess activity up to gestational week 24 but is available in selected centres only. Flexible sigmoidoscopy is safe in all trimesters with careful positioning and anaesthetic support. Referral to a high-risk obstetric clinic should be considered for women with active IBD, complex abdominal surgery, ileostomy or an IBD-related indication for caesarean section, such as ileo-anal pouch or perianal fistula. The mode of delivery is primarily guided by obstetric indications. Disease flares during pregnancy can be managed as for non-pregnant women. Steroids including IV hydrocortisone can be used when necessary to treat active disease but should not be given in prolonged courses. Antitumour necrosis factor (TNFi) therapy can be initiated during pregnancy and response is usually rapid. Babies exposed to TNFi in utero should not receive live vaccines before one year. Breastfeeding is encouraged.

Literature review: Guidelines and evidence for post-natal follow-up in women diagnosed with intrahepatic cholestasis in pregnancy (ICP)

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Abstract

Introduction: Intrahepatic cholestasis in pregnancy (ICP, also known as obstetric cholestasis) affects between 0.1 and 2% of women during their pregnancy.[1] Although significant evidence exists for close review and medical intervention *during* pregnancy, the role of post-natal follow-up remains less clear. Repeat liver function tests at least two weeks after delivery are often suggested, with the view to further investigations (including those for genetic mutations) if abnormalities persist.[2–4] The aim of this literature review was to assess the evidence for follow-up based on recent literature, including clinical trials, reviews and local guidelines.

Methods and analysis: Medline (Ovid) and Pubmed databases were searched for articles published from 1989 to 2019 (current). Relevant key words such as "intrahepatic cholestasis in pregnancy", "obstetric cholestasis" were combined with Boolean operators targeted at follow-up studies and clinical trials. Current guidelines from institutions in Australia and United Kingdom were also reviewed. Case reports, opinion pieces and letters to the editor were not included. Papers obtained in addition to the database search were identified within relevant publications. The study aimed to follow PRISMA guidelines.

Results: Database search identified 502 potential articles. Following removal of duplicates and screening by title, abstract and full text, 26 studies were included. A further five records were retrieved through other sources, for a total of 31 articles. Four of these papers centred on post-partum outcomes and risk stratification for women who had been diagnosed with ICP. Conclusions from these works unfortunately conflicted with one another.[2,5] The majority of publications focused on antenatal care and fetal outcomes, with limited amounts of post-natal data. Women with significantly elevated bile salts or early onset of the disease were more likely to test positive for a genetic cause.[2] Guidelines from several institutions in Australia suggest GP follow-up ranging between 2 and 6 weeks post-partum.[4] RCOG guidelines provide a more comprehensive counselling guide, including contraceptive advice and risk of recurrence as well as liver disease in later life.[3]

Discussion: Whilst active management during pregnancy is crucial for maternal and fetal wellbeing, there remains significant potential for increased long-term morbidity in women diagnosed with ICP. This review explores the notion that health institutions have a responsibility to arrange adequate follow-up and counselling for women prior to discharge. In particular, women with early onset of the disease or severely deranged bile acids should be considered for additional testing including those for genetic mutations. General Practitioners also need to be alerted to the significance of persistently abnormal laboratory results in the post-partum period.

Conclusion: To date, there is not an adequate level of data available on long-term complications and follow-up for women diagnosed with ICP. However, current literature suggests the importance of close monitoring and counselling regarding risk factors.

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Disrespect and abuse during childbirth in Western Ethiopia: Should women continue to tolerate?

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Abstract

Background: Healthcare coverage in Ethiopia has improved dramatically in recent decades. However, facility-based delivery remains persistently low, while maternal mortality remains high. This paper presents the prevalence and associated factors of disrespect and abuse (D&A) during childbirth in public health facilities of western Oromia, Ethiopia.

Methods: A facility-based cross-sectional study was conducted among 612 women from February 2017 to May 2017. Exit interview with the mothers were conducted upon discharge from the maternity ward. We measured D&A during childbirth using seven dimensions. Multivariable logistic regression model was used to assess the association between experience of D&A and client characteristics and institutional factors.

Results: Three-quarters (74.8%) of women reported experiencing at least one form of D&A during their facility childbirth. The types of D&A experienced by the women were: physical abuse (37.1%), non-dignified care (34.6%), non-consented care (54.1%), non-confidential

care (40.4%), neglect (25.2%), detention (2.9%), and discrimination (13.2%). Experiences of D&A were 1.6 times more likely to be reported by women delivering at hospitals than health centers (OR: 1.64, 95% CI: 1.01, 2.66). Women without a companion throughout their delivery were almost 10 times more likely than women who had a companion to encounter D&A (OR: 9.94, 95% CI: 5.72, 17.28).

Conclusion: Three in four women reported experiencing at least one form of D&A during labor and delivery. This demonstrates a real disconnect between what the health system intends to achieve and what is practiced and calls for fundamental solutions in terms of both improving quality of facility-based delivery and ensuring women's right to receive health care with dignity.

Consistency with international guidelines regarding mothers with rheumatologic diseases exposed to tumour necrosis factor inhibitors (TNFi) during the ante- and postnatal periods and change over time

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Abstract

Background: Many women with rheumatologic diseases require ongoing treatment with tumour necrosis factor inhibitors (TNFi) during pregnancy to maintain remission or low disease activity. Until recently, there has been a paucity of published evidence regarding the safety of these medications during the ante- and postnatal periods to guide clinical practice.

Objectives: To observe compliance with current guidelines for TNFi therapy in Australian women with rheumatologic diseases during the ante- and postnatal periods and change over time.

Methods: Australian women with rheumatologic diseases, exposed to biologics (bDMARDs) and targeted synthetic disease modifying antirheumatic drugs (tsDMARDs) during the preconception, antenatal and/or postpartum periods were eligible to participate in the Pregnancy Exposed to Biological (PEB) study. Commencing in 2015, recruitment was via invitation from patient's treating rheumatologists, community groups, and social media. Following self-referral to the study, retrospective data were collected, including rheumatologic condition and recommendations provided to women by health professionals.

Results: Preliminary data are available regarding 37 infants born to 29 mothers from February 2009 to December 2018. Women exposed to non-TNFi bDMARDs and tsDMARDs were excluded, as these medications are not currently recommended for use in the perinatal period. In total, 32 women received TNFi. We assessed the outcomes of three domains: TNFi continuation during pregnancy, TNFi continuation during lactation and vaccination practice in exposed infants. Specialist society guidelines were published in January 2016 regarding the safety of TNFi during pregnancy.[1] Of the PEB participants who were pregnant prior to guideline publication, 67% (n = 16/24) ceased TNFi preconception. Of the PEB participants who became pregnant subsequent to guideline publication, only 25% (n = 2/8) ceased TNFi pre-conception. Overall, 40.6% (n = 13/32) women received a TNFi during the antenatal period consistent with guidelines, which improved from 33.3% (n = 8/24) pre-publication to 62.5% (n = 5/8) post-publication, and 84.4% (n = 27/32) women in PEB breastfed their infants. Prior to availability of evidence regarding the safety of TNFi during lactation, 79.2% (n = 19/24) of infants were breastfed. After publication, 100% (n = 32/32) infants exposed to TNFi were breastfed. In total, 96.9% (n = 31/32) infants exposed to TNFi in PEB were vaccinated. Rotavirus vaccine should have been delayed in 43.8% (n = 14/32) infants, but was not; 9.4% (n = 3/32) infants had live vaccines delayed until only three months; 3.1% (n = 1/32) infants had live vaccines unnecessarily delayed. Only 3.1% (n = 1/32) infants had live vaccines appropriately delayed until seven months. Compliance with vaccination recommendations increased from 43.5% (n = 10/24) pre-publication to 62.5% (n = 5/8) post-publication of guidelines.

Conclusion: Preliminary data from PEB suggest that there has been a shift in practice following the publication of specialist society guidelines and that increasing numbers of women are continuing their TNFi therapy during pregnancy and the postpartum period in keeping with current evidence. Compliance with vaccination recommendations could be improved to be more consistent with published international guidelines.

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Management of diabetes in labour – A low intervention model

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Abstract

Background: Gestational diabetes mellitus (GDM) and pre-GDM are common complications of pregnancy with recent changes to diagnostic criteria and obesity rates contributing to an increase in these diagnoses. It has been accepted doctrine in obstetric settings that "tight" but not "very tight" control of blood glucose levels (BGL) in women with diabetes in pregnancy is associated with improved maternal and neonatal outcomes. A significant part of a woman's experience of pregnancy is birth and delivery. Current guidelines on the management of labour for women with diabetes recommend a range of often intensive regimes aimed at maintaining maternal euglycemia to reduce the risk of neonatal hypoglycaemia. At our institution, we have been following a low intervention approach to management of maternal BGLs in labour for both GDM and pre-GDM women for more than 20 years. This includes issuing a personalised plan to each woman documenting the required frequency of capillary BGLs as well as a protocolised approach to the use of supplemental insulin and/or glucose. Insulin and dextrose infusions are rarely used, even for women with pre-gestational diabetes. Insulin pump therapy is continued throughout labour unless contraindicated.

Hypothesis: That less intensive monitoring and intervention of maternal BGL during labour in women with both GDM and pre-GDM is safe and will not increase maternal or neonatal adverse outcomes.

Methods: A retrospective audit of labour management and neonatal outcome for women with GDM or pre-GDM was performed. A period of 18 months was chosen because the introduction of an electronic maternity register allowed consistent acquisition of data. Individual

woman files were reviewed to confirm labour management and the indications for intervention for mothers or babies admitted to the neonatal critical care unit (NCC) for >24 h.

Results:

	Total	NCC admission >24 h	Neonatal death
All vaginal births			
All women	4251 (67%)	276 (6.4%)	22 (0.5%)
Type 1 DM	6	2 (33%)	0
Type 2 DM	4	2 (50%)	1 (25%)
All GDM	417	29 (6.9%)	2 (0.5%)
GDM: diet and exercise	247	17 (6.8%)	2 (0.8%)
GDM: insulin ± metformin	170	12 (7%)	0
Vaginal term births			
All women	3905 (62%)	117 (3%)	0.08%
Type 1 DM	3	0	0
Type 2 DM	2	1	0
All GDM	382	13 (3.4%)	1 (0.3%)
GDM: diet and exercise	224	6 (2.7%)	1 (0.4%)
GDM: insulin ± metformin	158	8 (5%)	0

Conclusion: A low intervention model of care for women with GDM and pre-GDM undergoing vaginal birth is desirable and safe. This model more closely meets women's desire for "a physiological labour and birth" and "if intervention was needed or wanted, women wanted to retain a sense of personal achievement and control through active decision-making".[1]

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Azathioprine toxicity in pregnancy

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Abstract

Introduction: Azathioprine and mercaptopurine are commonly used immunosuppressants in pregnancy due to lack of teratogenicity.[1] We present two cases of purine antimetabolite hepatoxicity in pregnancy managed as cholestasis of pregnancy, with one case subsequently re-diagnosed as acute fatty liver of pregnancy. Both had 6-methyl mercaptopurine (6-MMP) concentrations above 12,000 pmol/8 × 10^{8RBC} with normal 6-thioguanine (6-TG) and thiopurine methyltransferase concentrations. Liver dysfunction and antimetabolite concentrations normalised in both following cessation of the antimetabolite.

Case 1: A G1P0 woman with ulcerative colitis on 75 mg 6-mercaptopurine and sulphasalazine presented with itch at 30 weeks of gestation. At 34 weeks, bloods showed elevated liver function with AST 71 U/L, ALT 155 U/L, bilirubin 46 and fasting bile acids (BA) of 33 μmol/L. She was commenced on ursodeoxycholic acid but developed worsening jaundice, coagulopathy and hypoglycaemia necessitating emergency caesarean section. Mercaptopurine metabolites two weeks postpartum revealed 6-MMP concentration of 12,955 pmol/8 × 10^{8RBC} 6-TG of 150 mmol/8 × 10^{8RBC} that normalised following 6-mercaptopurine cessation. The woman is currently in mid-second pregnancy and has already required dose reduction of mercaptopurine due to rising 6-MMP levels.

Case 2: A G2P1 woman with lupus on long-term azathioprine 50 mg presented with itch at 27 weeks of gestation. Bloods showed elevation in bile acids 63 umol/L, AST 65 U/L and ALT 104 U/L and conjugated bilirubin of 10 μmol/L. 6-MMP levels were elevated at 14,153 pmol/8 × 10^{8RBC} and 6-TG levels were normal at 99 pmol/8 × 10^{8RBC}. Ursodeoxycholic acid was commenced with concurrent azathioprine cessation. Metabolites, bile acids and liver function normalised. Ursodeoxycholic acid was ceased with no recurrent liver dysfunction or bile acid elevation. Caesarean section was six weeks later at K36 + 1. The woman's first pregnancy was complicated by cholestasis of pregnancy diagnosed at K35 with emergency delivery due to rapidly rising bile acids despite ursodeoxycholic acid. Mercaptopurine metabolites were not assessed.

Discussion: Azathioprine and its metabolite 6-mercaptopurine inhibit purine synthesis, suppressing leukocyte and lymphocyte function. Acute cholestatic hepatitis is reported as a reversible complication of azathioprine toxicity[2,3] with toxicity mediated via glutathione depletion and hepatic necrosis.[4] Hepatotoxcity has been associated with 6-MMP concentration above 5900 pmol/8 × 10^{8RBC}·5 and may mimick cholestasis and acute fatty liver of pregnancy. 6-MMP concentrations increase in pregnancy, while 6-TG levels decline, returning to baseline postpartum.[6] An increased incidence of acute fatty liver of pregnancy has been reported in women with inflammatory bowel disease with 40% of affected women managed on mercaptopurine.[7] In summary, mercaptopurine hepatotoxicity may occur in pregnancy. We report the first two confirmed cases. 6-MMP levels should be performed in pregnancy in treated women to exclude toxicity as a cause of elevated bile acids or liver function tests.

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Xanthogranulomatous oophoritis with cyst rupture in the third trimester: A rare case report

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Abstract
Xanthogranulomatous inflammation of the female genital tract is a rare, non-neoplastic condition of which the exact pathogenesis is unclear. It is most commonly confined to the endometrium with very few cases involving the ovary previously reported. Here, we describe a case of RP, a 36-year-old female, gravida 3 parity 2, presenting with acute onset left lower quadrant pain and a palpable mass in the pelvic cavity at $30 + 6$ weeks of gestation. This was an IVF pregnancy and otherwise, until this point, uncomplicated. Ultrasound demonstrated an 8.5×5.7 cm complex cystic lesion (volume 161 cc), with peripheral nodularity/papillary projections, peripheral vascularity and internal echoes noted. Given the acute clinical presentation, and the rapid evolvement radiologically (not demonstrated at morphology ultrasound or on MRI one year prior) malignancy could not excluded. RP represented four days later with worsening left lower quadrant pain. She was systemically well with unremarkable pathology; however, on examination there were features of peritonism. An emergency midline laparotomy was performed: exploration revealed a ruptured left ovarian cyst with mucinous content. A left salpingo-oophorectomy was performed with peritoneal washings and omental biopsy. Histopathology findings demonstrated xanthogranulomatous oophoritis with a chronic abscess and no evidence of neoplasia. RP was covered with triple antibiotics and treated for post-operative ileus. Her labour was induced postdates, and she delivered and healthy infant male by vaginal birth at $41 + 5$ weeks. The case described raises two points for discussion. Firstly, the aetiology of xanthogranulomatous oophoritis and whether ovum pickup in an IVF pregnancy may be a potential risk factor to those already proposed.[1] Secondly, that this chronic inflammation will often mimic a malignant process both clinically and radiologically, posing a diagnostic dilemma. It is an essential entity that must be considered as a differential in a woman presenting with a pelvic complex cystic mass; indeed, with a histopathological diagnosis, radical surgery with significant associated morbidity may be avoided.

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Nurse-initiated maternal health screening: A pragmatic approach to improving follow-up after hypertension and diabetes in pregnancy

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Abstract
Background: Postpartum follow-up of hypertensive disorders of pregnancy and gestational diabetes (GDM) is essential in screening for undiagnosed chronic disease and for optimising long-term maternal health, especially prior to future pregnancy. Timely follow-up within three months after birth is recommended by international and national guidelines; however, it does not always occur. Maternal and Child Health Services (MCHS) is an existing primary healthcare service well attended (85% participation) and accessible to the target population. We hypothesised the inclusion of a short maternal health screen to routine MCHS visits eight months after birth was feasible and would help identify women who may benefit from further follow-up.
Methods: A maternal health screen was integrated into routine eight-month child visits over six months (2018–2019), with 45 MCHS nurses participating at 13 sites within two eastern Melbourne municipalities. The health screen included demographic information, determining a history of hypertension and diabetes, and measurement of blood pressure and body mass index. Mothers with abnormal results (BP $>$ 140/90 mmHg or no GDM follow-up to date) received a letter advising attendance with their general practitioner (GP) and listing sources of online education. Feasibility and acceptability were evaluated using a mixed methods design. Participating MCHS nurses undertook a voluntary survey at the conclusion of the study evaluating their perceptions and experiences, and participated in an additional qualitative survey and group discussion.
Results: Health screens were completed in 508 out of 575 eligible eight-month attendances (88.3%), with the commonest reasons for non-participation being time constraints or the mother not being present at the child's visit. The mean time taken per assessment, including explanation, consent, and documentation was 5.0 ± 2.2 min; 10.4% (53 of 508) of assessments had abnormal results triggering a GP-referral and were carried out as per above protocol in 86.8% of cases. The remainder was referred after regular data safety review. Surveyed nurses reported that mothers were highly receptive to participating; nurses were comfortable performing the health check, and felt it did not deviate from the core goals of MCHS care or negatively impact workflow (all questions answered: strongly agree/agree). Qualitative feedback key themes included: 'simple and effective', 'time is the largest barrier', 'strong enthusiasm and appreciation from mothers'.
Conclusion: Targeted maternal health screening is feasible and acceptable in the MCHS setting and has capacity to reach a substantial proportion of the target population. One in 10 women screened were referred for further management of either hypertension or GDM, indicating suboptimal management at eight months postpartum. While this type of community-based health screen does not replace current best-practice recommended follow-up, it may be a pragmatic option to identify women who need ongoing care after high-risk pregnancies. It may also improve community awareness of these conditions in otherwise well postpartum women.

Utilisation of Maternal and Child Health Services for postpartum follow-up after hypertension and diabetes in pregnancy

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Abstract

Background: Over a quarter of all pregnancies in Australia are affected by hypertension and/or gestational diabetes (GDM). Timely follow-up of these conditions after birth is essential for optimising long-term maternal health; however it does not always occur despite recommendations by international and national guidelines. Maternal and Child Health Services (MCHS) are well attended and accessible to Australian families, with over 85% participation in Victoria. We hypothesised a short maternal health screen incorporated into routine eight-month MCHS child visits may identify women with certain health risks who may have missed timely follow-up, allowing opportunity for further follow-up prior to future pregnancies.

Methods: Over six months (2018–2019), a short maternal health screen was incorporated into routine eight-month child visits at 13 MCHS sites across two eastern Melbourne municipalities. The health screen was completed on all consenting attending mothers and included basic questions regarding age, pregnancy and breastfeeding status, history of smoking, hypertension and diabetes/GDM, and measurement of blood pressure and body mass index (BMI). Women with abnormal results (BP $>$ 140/90 mmHg or no GDM follow-up to date) received a letter advising attendance with their general practitioner and directing them to sources of online education. Descriptive statistics were used to evaluate results. Associations were evaluated further by regression analysis with significance defined as $p < 0.05$.

Results: Five hundred and eight health screens out of 575 eligible eight-month visits (88.3%) were completed. Mean maternal age was 33.2 years, and 2.1% of the cohort reported they were currently pregnant. Self-reported active smoking rates were low at 2.4%, and the mean BMI was 25.1 kg/m^2 with 15.0% of women being obese (BMI $>$ 30). Mean blood pressure was 114/72 mmHg. Hypertension (BP $>$140/90 mmHg) was detected in 6.9% of participants and was associated with obesity (OR 5.8, 95% CI 2.7–12.6), a history of diabetes/GDM (OR 2.7, 95% CI 1.3–5.5), and hypertension in their most recent pregnancy (OR 9.7, 95% CI 4.6–20.4). Of the entire cohort, 11.0% (56 of 508 women) reported a hypertensive disorder in their most recent pregnancy. Of these, 37.5% reported they had not yet received a follow-up blood pressure check after hospital discharge, and 18.7% of all women reported GDM, and one in five of these women reported they had not yet had a follow-up screen for diabetes after delivery. Women with pregnancies complicated by diabetes or hypertension had the lowest uptake of breastfeeding.

Conclusion: This study highlights the need for improved postpartum follow-up after complicated pregnancies, and despite some women having received follow-up after hypertension in pregnancy, persisting hypertension was not uncommon. Many mothers prioritise their children's health over their own, and incorporating maternal health promotional activities such as screening and education into the MCHS setting, may be both beneficial and an astute use of existing services.

Blood pressure phenotypes and markers of endothelial dysfunction after hypertensive pregnancy

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Abstract

Background: The observed association between hypertensive disorders of pregnancy and increased long-term maternal cardiovascular risk remains poorly understood. Antenatal changes to circadian blood pressure patterns have been observed in women with preeclampsia. We hypothesised that these changes may persist postpartum, and may be accompanied by other hypertensive abnormalities and/or evidence of subclinical endothelial dysfunction.

Methods: A cross-sectional study of 88 postpartum women who experienced either a normotensive pregnancy (NP), gestational hypertension (GH) or preeclampsia (PE) was performed from 2014 to 2018. Women with known chronic hypertension prior to pregnancy or renal disease were excluded. At a median of eight months postpartum (range 6–12 months), participants underwent 'office' BP and 24-h ambulatory BP measurement (ABPM), serum creatinine/eGFR, serum sVCAM-1, sEng, sFlt-1, MPO and urine protein estimation. Regular medications including antihypertensives were continued. ACC/AHA Hypertension Guideline 2017 and ISSHP definitions were used. Kruskal–Wallis analysis of variance was used for between-group differences, with significance $p < 0.05$.

Results: Of the 88 participants, 40 experienced PE, 16 had GH, and 32 had NP. Median maternal age and gestation at delivery were comparable between groups; however significant baseline differences included a higher proportion of nulliparous women with PE, and a higher median BMI in women with GH. Some participants were taking antihypertensives during the study: 35.3% of women in the GH group and 10.3% of women with PE. Median 'office' BP was highest in the GH group at 144/86 mmHg, followed by 131/78 mmHg in the PE group and 119/74 in the NP group. Hypertensive phenotypes on ABPM were more prevalent after a hypertensive pregnancy compared with NP. Masked HT was present in 28.6% of GH, 24.1% of PE, and 9.2% of NP ($p = 0.002$), all of whom also had an 'office' BP $>$130/80 mmHg. Sustained HT was present in 33.3% of GH, 18.1% of PE, and 9.2% of NP ($p = 0.002$). Women with PE had the highest rates of nocturnal non-dipping phenotype (43.6%). There was no significant difference between groups in renal function or markers of endothelial dysfunction. However, a trend towards reduced eGFR in the GH group was observed compared to other groups, as was a trend towards higher VCAM-1 in the PE group.

Conclusions: Sustained HT, masked HT, and nocturnal non-dipping were frequently observed in women after hypertensive pregnancy using ABPM testing. As ABPM is not currently standard of care, such phenotypes may remain undiagnosed in asymptomatic postpartum women, representing a missed opportunity for risk modification. An 'office' BP threshold of $>$130/80 mmHg may help determine who would benefit from ABPM testing. Given the associations between both masked HT and nocturnal non-dipping with cardiovascular risk in the general population, postpartum follow-up after PE or GH should consider the routine addition of ABPM. Endothelial dysfunction may require a greater number of participants to further characterise.

Psychosocial issues and obesity in pregnancy

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Abstract

Obesity in pregnant women has a strong socioeconomic gradient. This has been clearly documented in the 2016 report from the Australian Health and Welfare Report. The psychosocial and socioeconomic contributors to the obesity epidemic will be considered. Data regarding the relationship between adverse childhood experiences, obesity, gestational diabetes and depression in pregnancy will be examined. The relationship between adverse childhood experiences and socioeconomic status will be considered. The neurobiological and physiological consequences of

adverse childhood experiences will be examined. The implications of this for health promotion and clinical care will be considered. Compassionate, trauma informed care is critical for women who struggle with obesity.

Pituitary disorders in pregnancy

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Abstract
Clinically significant pituitary adenomas are no longer considered rare with approximately 1 in 800–1000 people having a clinically significant adenoma. However, complex pituitary diseases are not commonly encountered in pregnancy due to a high prevalence of gonadotropin deficiency associated with these complex adenomas. This talk will focus on the pituitary conditions that obstetricians may encounter in their practice. It will reinforce the need for multidisciplinary care with a particular focus on endocrinologist involvement in co-ordinating hormonal management and involving specialist pituitary neurosurgeons when required. Prolactinomas are the commonest pituitary adenoma encountered and up-to-date information regarding prolactinoma will be presented with a focus on the risk of cabergoline associated valvulopathy in prolactinoma patients; at this time, there have been three confirmed cases in approximately 2000 cases of prolactinoma described, so the risk is low but important to discuss when commencing cabergoline therapy. Non-functioning pituitary adenomas are the second commonest adenoma type but less frequency occurring in pregnancy as the median age of these adenomas occurs in the fifth decade. Based on my research from St Vincent's Hospital Melbourne, I discuss that premenopausal females have very good hormonal outcomes post-surgery for non-functioning macroadenomas with a propensity to restore gonadal function. Based on this, I recommend early surgery for non-functioning adenomas prior to conception. Lastly, using case examples, I will demonstrate the complexities of managing pituitary hormone replacement in pregnancy.

Perinatal opportunities for addressing complex intergenerational trauma in Aboriginal and Torres Strait Islander communities

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Abstract
Complex childhood trauma can have profound and ongoing impacts on development and physical, social and emotional wellbeing. Aboriginal people are particularly affected due to a legacy of violence and destructive policies associated with colonisation. The long-lasting relational effects may be triggered during the transition to parenthood, causing emotional distress and impede the capacity of parents to nurture their children. Conversely, the transition to parenthood offers a unique life-course opportunity for healing and preventing intergenerational transmission, even after severe trauma. Yet, despite these opportunities for healing, particularly during frequent scheduled contacts with health care providers; and the risk of triggering due to the intimate nature of perinatal care – there are currently no systematic perinatal strategies for identifying and supporting parents experiencing complex childhood trauma.

In this presentation, Associate Professor Chamberlain will:

- Outline the physiology and epidemiology of complex trauma, with a specific focus on the impacts on health and health equity in Aboriginal and Torres Strait Islander communities.
- Discuss the important opportunities during the perinatal period, including findings from a comprehensive systematic review of the views of parents who have experienced maltreatment in their own childhood.
- Briefly introduce an Aboriginal-led NHMRC and Lowitja Institute funded project – *Healing the past by nurturing the future* – which aims to co-design culturally acceptable and feasible perinatal awareness, recognition, assessment and support strategies for Aboriginal and Torres Strait Islander parents who have experienced complex childhood trauma.

Visual disturbance in pre-eclampsia – Not always as it appears

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Abstract
Introduction: Somatotroph producing pituitary adenomas are one of the most common causes of acromegaly, though rare overall with an estimated prevalence of 8.6 per 100,000. They are exceedingly rare amongst pregnant women due to the negative impact that pituitary adenomas have on fertility. Review of the limited current literature shows that the vast majority of women with a somatotroph adenoma have stable disease during pregnancy. However, there are a handful of reported cases of tumour enlargement or new diagnosis during pregnancy. We report a case of somatotroph adenoma with unusual presentation during pregnancy, presenting a diagnostic challenge.
Case presentation: A low-risk 29-year-old nulliparous woman was reviewed at $36+6$ weeks of gestation due to hypertension at a routine antenatal visit. She reported six weeks of blurred vision and worsening oedema for the past week. On examination, she was hypertensive (BP 150/90) with gross proteinuria (Urine PCR 2309; normal <30). She described diplopia and had inconsistent ophthalmologic findings on examination with impairments of extraocular movements and visual field deficits, none of which were consistent with a diagnosis. She was induced at 37 weeks for worsening pre-eclampsia and underwent an intrapartum caesarean delivery for failure to progress. The delivery was uncomplicated with the infant delivered in good condition. Post-partum, the woman reported worsening visual symptoms despite a stable blood pressure and biochemistry. MRI revealed a $28\times17\times25$mm mass in the sellar and suprasellar region with apoplexy, causing significant mass effect on the optic chiasm. She underwent emergency stereotactic transnasal transsphenoidal resection of the pituitary mass. Post-operatively a hormone profile showed an extremely elevated IGF-1, growth hormone and marginally elevated prolactin, consistent with uncontrolled acromegaly. Pituitary histopathology was consistent with a pituitary adenoma with acute haemorrhage. Immunohistochemical staining showed diffuse positive GH and sparse positive prolactin staining, consistent with a somatotroph adenoma.
Discussion: This case demonstrates the diagnostic difficulty posed by pituitary tumours during pregnancy given symptoms which may mimic pregnancy associated physical changes as well as common pregnancy-associated pathologies. Furthermore, pregnancy amongst women with pituitary tumours, more specifically in acromegaly, is extremely rare, thus limiting clinical experience with these women. Importantly, several

factors may impact upon pregnancy outcomes in acromegalic women. Uncontrolled GH and IGF-I has been associated with increased rates of hypertensive disorders and gestational diabetes which themselves have significant implications for maternal and fetal wellbeing. Physiological pregnancy-associated pituitary hypertrophy may worsen the mass effect of a pre-existing tumour or rarely, somatotroph adenomas enlarge spontaneously during pregnancy. Either may lead to severe neurological compromise requiring immediate surgical intervention. Given the potential for both maternal and fetal morbidity, obstetric physicians must be astute in recognising subtle neurological changes which may deviate from typical pregnancy pathologies, investigating and managing appropriately to optimise pregnancy outcomes.

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Case report: Delayed diagnosis of uterine incarceration in a multiparous woman with anuric end-stage renal disease

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Abstract

Introduction: Uterine incarceration is a rare obstetric complication scarcely reported in the literature. Likewise, end-stage renal disease (ESRD) in pregnancy has limited literature to date and remains a challenging event for women. Both are associated with significant maternal and fetal morbidity.

Case presentation: This interesting case presents a 34-year-old Australian Indigenous pregnant woman with uterine incarceration on a complex medical background of ESRD on daily haemodialysis, Type 1 Diabetes Mellitus, positive anti-Ro antibodies, syphilis, anaemia, thrombocytopaenia, and several cardiovascular risk factors. In addition, her obstetric history included pre-eclampsia, intra-uterine growth restriction and pre-term delivery in all four of her previous pregnancies. The diagnosis of incarcerated uterus was delayed in the setting of chronic anuria due to her ESKD. A successful restitution of the incarcerated uterus was performed at 18 weeks of gestation. She underwent an emergency classical caesarean section at 27 + 5 weeks of gestation in the setting of impaired placental blood flow and intrauterine growth restriction. A female baby weighing 701 g was delivered and is currently doing well in Intensive Care Nursery.

Conclusion: This case report discusses the diagnosis of uterine incarceration and further highlights the challenges faced in the management of ESRD, T1DM, and other medical comorbidities in pregnancy. A multidisciplinary approach is strongly encouraged in these high-risk obstetric cases.

Transdermal granisetron in the treatment of hyperemesis gravidarum

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Abstract

Objectives: Hyperemesis gravidarum (HG) is a severe form of nausea and vomiting affecting 0.3–1% of pregnancies.[1] HG is a common cause of hospitalisation during pregnancy.[1] Treatment involves multiple pharmaceutical agents, causing significant tablet burden. This report aims to share our experience of using oral and transdermal granisetron to improve HG.

Clinical features: A 28-year-old, with unremarkable medical history, presented to Obstetric Medicine outpatient clinic at 24 weeks of gestation for HG management on the background of multiple hospital admissions. Her symptoms included unrelenting nausea with associated vomiting. This occurred throughout the day, and of particular concern, for three hours each morning. She was unable to tolerate any medications on waking. Interestingly, her symptoms were unrelieved by oral ondansetron and prochlorperazine. The woman experienced reduced oral intake, weight loss, inability to work and reduced quality of life.

Literature review: Granisetron is a selective 5-hydroxytryptamine receptor antagonist, indicated for chemotherapy-induced or post-operative nausea/vomiting.[2] Currently, there is limited safety and efficacy data for granisetron use in pregnancy. Studies by Aleyasin of 32 women, and Caritis of 16 women, concluded that oral and transdermal granisetron decreased nausea/vomiting in pregnancy.[3,4] A further study by Shapira of 80 women found no association with adverse neonatal outcomes.[5]

Pharmacological interventions, progress and outcomes: Oral granisetron dosed at night was trialled to improve morning emesis. This partially controlled symptoms and a change to transdermal form was suggested by the pharmacist due to altering pharmacokinetics.[2] Pharmacist advised on switch from oral to transdermal forms, adjusting the frequency of application, counselling and sourcing stock.

Conclusions: Granisetron, particularly in transdermal form, drastically improved symptoms of HG, evident by a reduction of nausea, cessation of vomiting, and improved oral intake. Granisetron in the future may form part of the standard therapy for HG although requires further research. This case highlights that alternative routes may be necessary in the treatment of HG.

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Two unusual cases of post-partum vertebral artery dissection

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Abstract
Although stroke is a rare event in the child-bearing age group, stroke events are more common in pregnancy with an estimated risk of 0.03%. The highest risks are peri- and post-partum. A range of aetiologies are recognised including ischaemia, cerebral venous sinus thrombosis and haemorrhage.[1] We describe two cases of stroke in the peripartum period caused by cerebral artery dissection, an unusual cause of pregnancy related stroke. Both occurred in association with hypertensive disorders of pregnancy: one in the context of severe early onset pre-eclampsia at 24 weeks of gestation and the other in a woman with well-controlled essential hypertension delivered at term. In both cases, there was clinical and imaging evidence that the dissections occurred prior to the presentation with hypertension. Despite aiming for tight blood pressure control below 140/90 mm Hg and appropriate timing of delivery, both women experienced new onset of neurological deficit within 10–14 days post-partum on a background of ongoing neck pain and headache for days prior. There was no evidence of haemorrhagic stroke or eclampsia. Management considerations in these cases included investigation for an underlying cardiac right–left shunt, assessment for underlying connective tissue disorders, the importance of specialised stroke services to provide timely assessment and management, the role of dual antiplatelet therapy or anticoagulation for stroke in the post-partum period and discussions regarding the risks of further pregnancies. Spontaneous carotid and vertebral artery dissections are rare causes of stroke with poorly understood pathogenesis.[2] However the incidence is higher in younger patients[3] and they are a known rare complication associated with hypertensive disorders of pregnancy.[4] Two or more vessels are involved in <15% of cervical artery dissections.[5] Women with a history of ischaemic stroke have a low risk of recurrence during subsequent pregnancies, with similar outcomes to those expected in the general population.[6] There is very little data on recurrence rate of cervical artery dissections (CAD) in subsequent pregnancies; however, studies of CAD in the non-pregnant population show that the rate of recurrence is low and mostly occur within three months of the initial event.[2,7] The risk of recurrence is higher in women with younger age (relevant to most pregnant women), a family history of CAD, an underlying connective tissue disorder, vascular Ehlers-Danlos syndrome or fibromuscular dysplasia.[2] Our case series highlights the clinical significance of neck pain in association with hypertensive disorders of pregnancy.

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Are aggressive treatment thresholds warranted in GDM?

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Abstract
Introduction: A lower threshold for diagnosing gestational diabetes mellitus (GDM) and more aggressive thresholds for pharmacological therapy may result in more women receiving interventions without proven benefit. We have audited outcomes for women with GDM diagnosed on the International Association of Diabetes and Pregnancy Study Group criteria but managed according to the Australian Carbohydrate Intolerance Study (ACHOIS) thresholds for pharmacological therapy.
Methods: Universal screening at the Gold Coast University Hospital identified women with GDM. All received diet and exercise advice and commenced home monitoring of blood glucose. Those deemed inadequately controlled were further treated with combinations of insulin and/or metformin. Thresholds for pharmacological therapy were based on the ACHOIS thresholds (fasting glucose > 5.5 mmol/l, 2 h post-prandial > 7.0 mmol/l). Pregnancy outcomes for all singleton pregnancies >27 gestation were audited from 1 June 2015 to 31 December 2017. Maternal and neonatal outcomes data for all women with GDM were compared with women without GDM.
Results: A total of 782 women had GDM and were compared with 8460 normal women. GDM women were older (31.3 ± 5.4 vs. 29.4 ± 5.4 yrs, $p < 0.0001$) and reported greater pre-pregnancy weight (76.7 ± 22.0 vs. 66.0 ± 15.7 kg, $p = 0.0001$); 296/782 women received pharmacological therapy. Whilst there was a higher rate of large for gestational age babies in the GDM group (13.8% vs. 10.3%, $p = 0.002$), there were no differences for pre-term delivery, small for gestational age babies or APGAR score < 7 at 5 min. GDM was protective for having a baby- > 4000 g and was associated with lower birthweight (3365 ± 525 vs. 3429 ± 533 g, $p = 0.001$) probably explained by an earlier delivery time (38.5 ± 1.5 vs. 39.3 ± 1.7 weeks). Rates of caesarean section, induction, special care nursery admission and neonatal hypoglycaemia were higher in GDM. Women requiring pharmacological therapy and their babies were significantly different to those women with GDM not requiring pharmacological therapy.
Conclusions: A conservative approach to management of women with GDM does not result in substantially worse outcome in terms of neonatal size, nursery admission or APGAR score. Such women do have higher rates of obstetric intervention.

Gut wall barrier function is impaired in women who develop pregnancy complications and is no longer associated with dietary fibre intake

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Abstract

Background: The gut wall barrier plays an important role in preventing translocation of gut bacteria, bacterial compounds and metabolites to the host. Dietary fibre intake, BMI and the composition of the gut microbiota are determinants of gut wall barrier function. Pregnancy alters the composition of the gut microbiota and increases gut inflammation but it is unclear if gut barrier function is affected by pregnancy complications and dietary fibre intake. This study aims to assess gut barrier function, gut microbiota composition and dietary fibre intake in 203 overweight and obese women at 28 weeks of gestation.

Methods: Gut microbiota composition was determined by sequencing the V6–V8 region of the 16S rRNA gene. Gut barrier function was measured through circulating zonulin levels in a sub-group of 71 participants (35 without and 36 with gestational diabetes or preeclampsia). Higher zonulin levels indicate a less intact gut wall barrier.

Results: Healthy women in the highest quartile of dietary fibre intake (~32 g/day) had significantly higher abundance of *Faecalibacterium*and lower abundance of *Collinsella* when compared to women with the lowest dietary fibre intake (~11 g/day). Dietary fibre intake was negatively correlated with zonulin levels (rho = −0.34; P = 0.04), whereas BMI (rho = 0.35; P = 0.04) and *Collinsella* abundance (rho = 0.26, P = 0.03) were positively correlated in healthy pregnant women. In women with pregnancy complications, circulating zonulin levels were increased by 2-fold compared with healthy pregnancies (46.8 (24.3–76.9) vs. 22.3 (14.2–35.3) mg/ml; P = 0.001) and not correlated with dietary fibre intake, BMI or abundance of *Collinsella* or *Faecalibacterium*.

Conclusion: In pregnancy, high dietary fibre intake is associated with increased gut barrier function. In women who develop complications of pregnancy, gut wall barrier function is impaired and is no longer regulated by BMI or dietary fibre intake. Increasing dietary fibre intake before the development of complications may improve overall inflammation through maintaining gut wall barrier function in pregnancy.

Lower abundance of the butyrate-producer Coprococcus in the gut microbiota of women with future preeclampsia

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Abstract

Background: The gut microbiota plays a role in maintaining human health and in the development or prevention of illness partially through the release of metabolites. During gestation, large changes to the composition of the gut microbiota occur. In early pregnancy, the capacity of the gut microbiota to produce the short chain fatty acid butyrate is inversely correlated with systolic blood pressure. However, it is unclear if the gut microbiota composition is altered in women developing hypertension or preeclampsia later in pregnancy. In the present study, we compare the gut microbiota composition and butyrate-producing capacity between women with future preeclampsia and normotensive pregnant women at 28 weeks of gestation.

Methods: The composition of gut microbiota was investigated by 16S rRNA sequencing of faecal samples obtained from pregnant women in the SPRING cohort (Study of Probiotics IN gestational diabetes) at 28 weeks of gestation. Gut microbiota composition was compared between pregnant women who developed preeclampsia (n = 11) and controls (n = 200). Quantitative real-time PCR was used to assess the density of the butyrate-producing genes *But* and *Buk*.

Results: Women who develop preeclampsia have significantly decreased abundance of the genera *Coprococcus*, *Parabacteroides*, *Roseburia*, Unclassified *Christensenellaceae* and Unclassified *Clostridiales*. Abundance of *Coprococcus*, which is known to express butyrate-producing genes, is significantly positively correlated with the gene density of the butyrate genes *But* (rho = 0.29, P_{adj} = 0.002) and *Buk* (rho = 0.25, P_{adj} = 0.012) and total butyrate production (rho = 0.22, P_{adj} = 0.078). Women who develop preeclampsia have lower gene density of *But* (P = 0.010), *Buk* (P = 0.038) and total butyrate production (P = 0.004).

Discussion: The results suggest that reduced capacity to produce butyrate by the gut microbiota is associated with increased risk of developing preeclampsia in pregnant women.

High dietary fibre intake alters the composition of the gut microbiota in women who develop hypertensive disorders of pregnancy

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Abstract

Background: The composition of the gut microbiota and its interaction with the host can be influenced by diet. Fibre is a major fuel source for the gut microbiota, which can convert fibre into short chain fatty acids. Pregnancy changes the composition of the gut microbiota and can lead to increased gut permeability and inflammation. This state of the gut may be altered in women who develop hypertensive disorders of pregnancy. This study observed the gut microbiota profile in women who experienced hypertensive disorders during late pregnancy and if it was related to dietary fibre intake.

Methods: Women were enrolled in the Study of PRobiotics IN Gestational diabetes (SPRING) randomised controlled trial. Thirty-two women who developed a hypertensive disorder and dietary fibre intake was classified as high or low (above or below 18.2 g/day). The microbiota was examined using 16S rRNA gene amplicon sequencing followed by Quantitative Insights Into Microbial Ecology (QIIME2) and Calypso analysis. Predictive function analysis was performed using PiCRUsT.

Results: There was no significant difference, in women with future hypertensive disorders, in alpha diversity with high- and low-dietary fibre intake. Of those women, the individuals with low fibre intake had lower beta diversity. Dietary fibre intake altered the relative abundance of microbial genera. High fibre intake reduced the abundance of *Collinsella*, *Anaerotruncus*, *Streptococuccus* and *Oscillospira* but increased the abundance of *Faecalibacterium, Coprococcus, Sutterella* and *Paraprevotella* abundance. Of the women with future hypertensive disorders, those with low fibre intake had up-regulation of pathways involved in glycerate breakdown, nitric oxide production and cardiac disease.

Conclusion: Women with hypertensive disorders in late pregnancy who consumed a high-fibre diet showed a different composition of the gut microbiota that was predicted to promote increased production of fermentation end products and stimulation of pathways to relieve the severity of hypertension.

Management and outcomes of anti-M alloimmunisation during pregnancy

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Abstract

Background: The incidence of haemolytic disease of the fetus and newborn (HDFN) caused by maternal alloimunisation to red cell antigens has been greatly reduced through appropriate transfusion practice, maternal screening and the widespread adoption of Rh D immunoglobulin prophylaxis. More than 60 red cell antibodies have been associated with HDFN.[1] Of these, antibodies to the M antigen are among the most common non-Rh antibodies identified in alloimmunised pregnancies. Anti-M antibodies are an unusual cause of HDFN, with only a very small number of cases reported.[2] Guidelines for Transfusion and Immunohaematology Laboratory Practice group anti-M with other non-Rh antibodies suggest titration and monitoring during pregnancy.[3] We investigated practice at a single large tertiary centre and propose a management protocol for anti-M alloimmunisation in pregnancy.

Aim: To examine the surveillance and management practices for women with anti-M alloimmunisation in pregnancy.

Methods: We undertook a retrospective cohort analysis of women who were found to have anti-M antibodies in pregnancy at the Royal Women's Hospital (RWH), Melbourne, from 2009 to 2019. Outcomes of interest included anti-M titres, need for Neonatal Intensive and Special Care Unit (NISC) admission, neonatal jaundice, peak bilirubin, phototherapy, and blood transfusion.

Results: Anti-M antibodies were found in 97 pregnancies in 77 women during 2009–2019 at the RWH. Women had a median number of three titrations (range 2–4 titrations) performed through pregnancy. Seventy-eight pregnancies had a maximum titre at or below 1:4, and the highest titre of 1:64 was observed in only one pregnancy. Sixteen neonates were admitted to the NISC, for which monitoring for jaundice was the primary indication in 4. Ten infants required phototherapy for jaundice; however, none had a positive direct antiglobulin test (DAT). Three of the infants not admitted to NISC had a positive DAT; however, none developed bilirubin levels requiring treatment. There were no cases of HDFN attributable to anti-M alloimmunisation. One neonate required blood transfusion due to anaemia of prematurity.

Discussion: Over the study period, we observed heterogeneous practices in both antenatal and neonatal surveillance. We observed no cases of NISC admission, neonatal jaundice, or HDFN attributable to anti-M alloimmunisation, and no intrauterine transfusions were performed in this cohort. We propose a standardised surveillance protocol adapted from international recommendations based upon clinical risk, value and change of maternal titres and utilisation of ultrasound. This protocol aligns with current antenatal surveillance practice, and will reduce both unnecessary investigation and cost.

Conclusion: Anti-M alloimmunisation was not associated with any adverse outcomes during pregnancy at our institution, although it is acknowledged that no patients had a titre greater than 64. Our findings are consistent with international literature, and implementation of the proposed surveillance protocol will reduce unnecessary burdens on patients.

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Persistent post-partum haemorrhage despite fibrinogen substitution in a woman with dysfibrinogenemia

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Abstract

Background: Hypofibrinogenemia and dysfibrinogenemia are congenital quantitative and qualitative disorders of circulating fibrinogen with heterogeneity in genotype and phenotype. Guidelines on optimal dosing of fibrinogen replacement therapy (FRT) to treat abnormal bleeding without causing thrombotic complications are not well defined. Fibrinogen dosing guidelines for pregnancy in a brief literature review include broad formulaic calculations including: Dose (g) = desired increment (g/L) × plasma volume, where plasma volume is 0.07 × (1-haemocrit) × weight (kg), or dosing of 20–100 mg/kg fibrinogen concentrate[1] with the aim of fibrinogen levels higher then 1.5 g/L during the peri-partum period.[2]

Aim: We describe two pregnancy and neonatal outcomes of a 30-year-old female with class 3 obesity, a history of back surgery and superficial thrombosis with known dysfibrinogenemia.

Methods: We reviewed fibrinogen levels, Hb and other clotting levels through pregnancy, peri- and post-partum. We documented use of blood product support, post-partum bleeding and neonatal outcomes.

Results: The woman had undetectable fibrinogen throughout pregnancy. She delivered two healthy babies but had significant post-partum haemorrhages with both deliveries despite receiving fibrinogen concentrate. She did not have any post-partum venous thromboembolic events.

Discussion: Dysfibrinogenemia in pregnancy can be associated with bleeding, thrombosis or pregnancy loss. Fibrinogen levels physiologically increase through pregnancy; however, this change is not necessarily protective against complications related to dysfibrinogenemia. The management decisions of dysfibrinogenemia during pregnancy are guided but a personal or family history of bleeding and thrombosis complications, and in its absence, expectant management has been recommended for pregnant woman. This includes individualised fibrinogen replacement schedules to correct fibrinogen levels to recommended fibrinogen activity level targets associated with a reduced risk of bleeding and pregnancy loss. However, there can be significant variability in fibrinogen concentrate doses required to maintain a certain fibrinogen activity as a pregnancy progresses.[3] Difficulty predicting and maintaining fibrinogen trough levels can contribute to persisting pregnancy complications despite FRT. The inability to accurately predict factor concentrate correction has understandably given pause to the use of central neuraxial anaesthesia and other instrumentation during delivery in this group of women.

Conclusion: This case highlights a unique case of congenital dysfibrinogenemia with both a thrombotic and bleeding phenotype, highlighting the highly variable nature of fibrinogen pharmacokinetics and the complexity of dosing regimens that need to be considered during antenatal and post-natal care.

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Metastatic uterine leiomyosarcoma at 26 weeks of gestation

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Abstract

Uterine leiomyosacoma is a highly malignant neoplasm which has been rarely described in pregnancy. A case of advanced metastatic uterine leiomyosarcoma presenting at 26 weeks of gestation is reported. The principles in investigating and managing invasive cancer in pregnancy are discussed, in addition to a specific discussion about uterine leiomyosarcoma. The incidence of cancer in pregnancy is increasing with advancing maternal age and higher rates of obesity. Cancer is now the second most common cause of death of women during reproductive years with an incidence of approximately 1/1000 pregnancies. Diagnosis may be delayed due to the symptoms and signs of malignancy being masked by or attributed to changes in pregnancy. The diagnosis of cancer in pregnancy provokes complex management issues balancing both short and long-term risks for both mother and baby. Every case needs to be individualised, with a multidisciplinary team of midwives, obstetricians, oncologists, surgeons, radiation oncologists, neonatologists and psychologists assisting the family to make informed decisions regarding the best treatment course for the mother and her baby.

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Malignancy in pregnancy – A review of diagnosis and management

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Abstract
This review of malignancy in pregnancy summarises the evidence regarding the safety of diagnostic imaging, procedures and treatment modalities for cancer for the pregnant woman and fetus. A general discussion about incidence, symptoms, investigation, diagnosis and treatment of malignancy in pregnancy is followed by a more detailed individual discussion of the more common malignancies that present in pregnancy, speicifically melanoma, breast cancer, cervical cancer, Hodgkin's disease, Non-Hodgkin's lymphoma, differentiated thyroid cancer, colorectal cancer and lung cancer. Malignancy in pregnancy is increasing in incidence with advancing maternal age and higher rates of obesity. Malignancy contributes significantly to indirect mortality in pregnancy and the 12-month postpartum. The symptoms can often be masked by, or attributed to pregnancy leading to a delay in diagnosis. This highlights the need to investigate concerning symptoms in a timely manner, and most imaging and diagnostic modalities can be safely used in pregnancy with minimal risk to the mother and fetus, when balanced against the possible risk of undiagnosed malignancy (cf. table 1). The diagnosis of cancer in pregnancy provokes complex management issues balancing both short- and long-term risks for both mother and baby. Every case needs to be individualised, with a multidisciplinary team of midwifes, obstetricians, oncologists, surgeons, radiation oncologists and neonatologists assisting the family to make informed decisions regarding the best treatment course for the mother and her baby. Management depends on the diagnosis and gestation. Surgery, chemotherapy and radiotherapy can be used in pregnancy in most cases. Mode and timing of delivery must be individualised to the woman, type of malignancy and fetal condition. Newer treatments including targeted therapies, monoclonal antibodies and immunotherapies are becoming available with limited data of their use in pregnancy. The efficacy of novel anticancer therapies highlights the need for international registries to accumulate safety data for these agents in pregnancy as expeditiously as possible given the proliferation of anti-cancer therapies, advancing maternal age and increasing incidence of malignancy in pregnancy.

Table 1. Fetal radiation dose with radiological examinations.

Imaging modality	Fetal dose (mGy)
Chest X-ray	0.0005–0.1
CT head	<0.5
CT chest	0.2
CT abdomen	4
CT abdomen/pelvis	13–25
18F-FDG-PET-CT	1–22
18F-FDG-PET-MRI	<5
^{99M}Technetium lymphoscintigraphy	0.5

18F-FDG: 8 F-2-fluoro-2-deoxy-glucose; CT: computed tomography; MRI: magnetic resonance imaging; PET: positron emission tomography.[1] Table reproduced with permission: Morton and Morton.[1]

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Management of peripartum therapeutic anticoagulation: A review of current practice and assessment of bleeding and thrombotic complications

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Abstract
There are no clear evidence-based consensus guidelines around peripartum cessation and re-initiation of therapeutic anticoagulation, and management differs between institutions. No large trials have reviewed timing of re-initiation of anticoagulation postpartum. This retrospective analysis reviews the peripartum management of 36 consecutive therapeutically anticoagulated women over 36 months at a quaternary obstetric referral hospital in Brisbane, with a focus on time to re-initiation. Complications of bleeding and thrombosis were audited out to 42 days postpartum. Our hospital uses a conservative protocol with cessation of enoxaparin 24 h ahead of planned induction of labour or operative delivery and re-initiation at 6 h postpartum – regardless of mode of birth. Seventy-eight percent of births were planned and vaginal delivery achieved in 61%; 7/36 (19%) had a bleeding event postpartum but none of the women required blood products, return to theatre or intensive care admission. There were no thrombotic complications. Our data suggest therapeutic enoxaparin can be safely re-initiated as per our protocol, without the need for complex intravenous unfractionated heparin regimens in the majority of women.

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Gestational weight loss in obese pregnant women

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Abstract

Background: Maternal obesity is associated with pregnancy complications such as gestational diabetes, pre-eclampsia and large-for-gestational age (LGA) infants. There is also increasing evidence of longer term effects in the offspring including premature cardiovascular disease and type 2 diabetes.[1] IOM guidelines recommend a total gestational weight gain of 5–9 kg for obese women.[2] However, while studies assessing maternal and neonatal outcomes in obese pregnant women with weight loss are limited, there is suggestion that lower weight gain or even weight loss can reduce a number of obesity-related complications. Studies supporting this have found a reduced risk of gestational hypertension and macrosomia.[3,4] Whilst some of these studies have found an increased risk of small-for-gestational age (SGA) infants, others have not found this association.[5–7] These studies contain small numbers of women with weight loss and several did not stratify women according to class of obesity. They also lack information regarding the circumstances of the weight loss. We present a case series of obese women who have lost weight during pregnancy with good pregnancy outcomes.

Methods: We report 18 obese women with pregnancies over the past two years with weight loss via improved diet and exercise during pregnancy. All women were managed by a private obstetrician and gynaecologist and private endocrinologist during their pregnancy. Women were given advice regarding minimising weight gain and were provided with a one-page handout with dietary advice. No woman in this group had prior bariatric surgery or hyperemesis gravidarum.

Results: Eighteen obese women were included. Eight women had Class I obesity (BMI 30–34.9), six women had Class II obesity (BMI 35–39.9) and four women had Class III Obesity (BMI $>$ 40). Weight loss ranged between 1 kg and 22 kg and was higher in women with Class II or III obesity. The average gestation at birth was 38.75 weeks (range 38 + 2 to 39 + 3). The average birth weight was 3341 g (range 2700–3984 g). There were no SGA or LGA infants in this cohort. Seventeen of 18 women had diabetes diagnosed during pregnancy, treated with a combination of Metformin and basal insulin. Three women also required rapid acting insulin. Eight women either had pre-existing hypertension or were hypertensive in the first trimester. Hypertension improved with weight loss with only one woman requiring antihypertensive treatment in the last two weeks of pregnancy.

Discussion: Controlling gestational weight gain can reduce the effect of obesity on adverse pregnancy outcomes. Long-term effects of gestational weight loss on the fetus are unknown and larger studies with long-term follow-up of offspring are required. However, the benefits of healthy weight loss in obese pregnant women to reduce complications, such as hypertension, diabetes and macrosomia, challenge IOM guidelines that weight loss in pregnancy is not recommended.

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Non-invasive cardiac and haemodynamic monitoring for prediction of severe pre-eclampsia at diagnosis

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Reducing anaemia during pregnancy through clinical practice improvement

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Abstract

Aim: Iron deficiency (ID) with or without anaemia continues to be a neglected issue in Australian women's health. Anaemia at delivery is a strong modifiable risk factor for transfusion in women with a postpartum haemorrhage (PPH).[1] A maternity blood management clinical practice improvement (CPI) was conducted to optimise antenatal haemoglobin and iron stores prior to delivery.[2] This is the second Australian health service implementing maternity CPI tools which included introduction of routine first trimester ferritin screening.

Methods: CPI tools (haemoglobin optimisation flowcharts and maternity oral iron patient handouts) were introduced at a tertiary hospital from November 2016 to March 2017. To assess if CPI effectiveness improves haemoglobin and iron stores, an Interrupted Time Series (ITS) analysis was performed using data collected for all deliveries from January 2016 to June 2018.

Results: There were 11,269 deliveries that had at least one Hb measured during pregnancy for the ITS analysis, which included a total of 31,055 haemoglobin and 4895 ferritin results. In 1550 women with haemoglobin and ferritin in the first trimester, non-anaemic ID was detected in 416 women (26.8%) following routine first trimester ferritin screening. These women would have missed treatment with oral iron if practice was reliant on testing haemoglobin alone. In comparison to the first trimester, the greatest numbers of anaemic episodes were observed in the postpartum period, with a probability difference of 49.7% (95% CI 47.8 to 51.6%). There is a clinically significant increase in the monthly average predelivery haemoglobin of 0.9 g/L (95% CI –0.4 to 2.2 g/L; $p = 0.16$), see Figure 1. This corresponded with a reduction in the monthly rate of anaemic women by 18% (RR 0.82, 95% CI 0.6 to 1.1; $p = 0.12$).

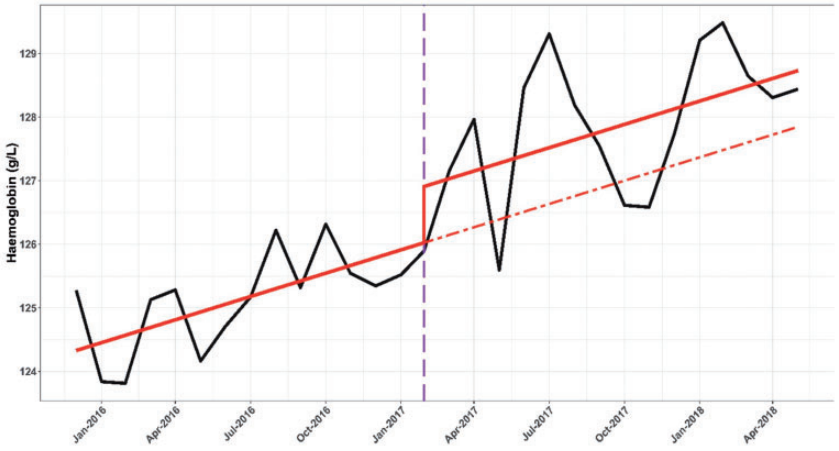

Figure 1. Monthly predelivery haemoglobin average.

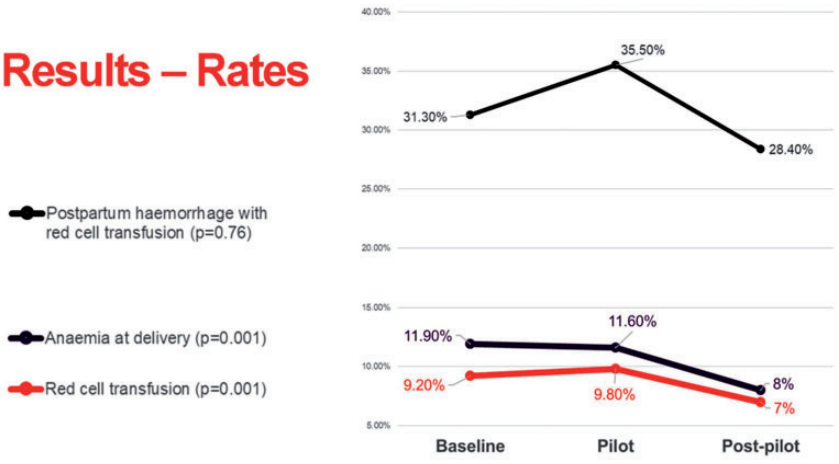

Figure 2. Anaemia at delivery, PPH and red cell transfusion rates.

There was a significant decrease in the rates of anaemia at delivery and decrease in red cell transfusion in anaemic women ($p = 0.001$), see Figure 2. While there was a change in anaemia rates, there was no change in rates of non-anaemic ID.

Discussion: South Australian iron deficient pregnant women were not captured through routine antenatal care with haemoglobin only screening based on most current antenatal guidelines. With an increase of predelivery haemoglobin by 0.9 g/L post-PBE CPI, the maternity PBM CPI tools facilitated the optimisation of haemoglobin at delivery, thereby delivering a change impact to a strong modifiable risk factor for transfusion in women with PPH. The maternity PBM CPI tools standardised practice with early identification of women who were iron deficient, which allowed adequate time to initiate appropriate oral iron therapy, reserving IV iron in circumstances where oral iron therapy fails or a very rapid restoration of iron stores is required.

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Severe gestational hypertriglyceridaemia complicated by acute pancreatitis

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Abstract

Context: Severe gestational hypertrigliceridaemia is rare but potentially life threatening. Triglycerides and total cholesterol increase in the third trimester of normal pregnancy in response to changes in levels of oestrogen, progesterone and human placental lactogen. These changes are exacerbated by pre-existing abnormalities of lipid metabolism. Maternal and fetal complications can be catastrophic.

Case: A 36-year-old woman (gravida 2, para 1) with unremarkable family history presented severe pancreatitis in the third trimester prompting emergency caesarean section when blood was noted to be lipaemic. She was diagnosed with severe gestational hypertriglyceridaemia (total cholesterol 40.8 mmol/L, triglycerides 118.1 mmol/L). Management with a seven-day insulin–dextrose infusion and dietary restriction, omega 3 fatty acid and niacin supplementation resulted in normalisation of the lipid abnormality by week six postpartum in the low-oestrogen lactating state. Genetic testing showed only heterozygosity of c.-644T>C, a variant of APOA5.

Evidence acquisition: We searched Ovid Medline for English language publications published since the last comprehensive literature review, 2011 (search terms pregnancy, hypertrigliceridaemia, pregnan*, gestation, hyperlipidaemia, hypertriglyceridaemia, chylomicronaemia). We identified 47 case reports.

Evidence synthesis: Severe gestational hypertriglyceridaemia with normal pre-pregnancy lipid profile is invariably due to polygenic mutations in lipid metabolism. Effective interventions in the reviewed cases include dietary restriction, omega 3 fatty acid supplementation, niacin supplementation, fibrate therapy, insulin infusion and plasmapheresis.

Conclusions: Severe gestational hypertriglyceridaemia is associated with significant risk of maternal and fetal morbidity and mortality. In our case of hypertriglyceridaemic pancreatitis with normoglycaemia, a tailored insulin–dextrose infusion provided an effective mainstay of acute therapy. We recommend that women with known lipid profile abnormalities or strong family history of hypertriglyceridaemia be screened in early pregnancy and have their lipid profile once in the first and second trimesters, and four to six weekly in the third trimester. Due to the significant risk of adverse outcome, these women should be managed in a multidisciplinary setting if possible. Further research is required to determine optimal evidence-based treatment and prevention. Our review of cases to date suggests that this condition can be managed effectively without the need for apheresis in the majority of cases.

Refractory hyperemesis gravidarum: Should empiric treatment for *Helicobacter pylori* infection be offered?

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Abstract

Introduction: Hyperemesis gravidarum (HG) affects 0.3–3% of all pregnancies. Severity of symptoms can cause complications, negatively impact function, cause anxiety leading to termination of pregnancy or even lead to avoiding future pregnancies. *Helicobacter(H) pylori* infection is considered as one of the multiple predictive factors for HG.

Case description: A 20-year-old female in her first singleton pregnancy presented at nine weeks of gestation with severe vomiting associated with electrolyte imbalances. She was treated symptomatically and discharged with anti-emetics and ranitidine. Subsequently, she had four more admissions for hyperemesis till 19 weeks of gestation with weight loss, ketosis and electrolyte disturbances leading her to request for termination of pregnancy. Her thyroid function showed gestational hyperthyroidism and liver function tests were normal. She was given intravenous steroids followed by oral steroids which did not help. Her urea breath test for *H. pylori* infection was requested during the last episode which was positive. Treatment with triple therapy led to complete resolution of vomiting and she successfully continued her pregnancy to term. Another 28-year-old lady with history of hypertension presented similarly in her first trimester of her first pregnancy for recurrent refractory hyperemesis with inability to take her anti-hypertensive medications resulting in multiple admissions for HG with hypertensive urgency. She was treated symptomatically with antiemetics, thiamine, intravenous labetalol, and steroids with Proton pump inhibitors. Her urea breath test was negative; however, empiric treatment for *H. pylori* resulted in resolution of symptoms at 20 weeks of gestation.

Summary: The most recent systematic review showed that in four studies, there was no association between *H. pylori* infection and HG, in contrast to two studies which demonstrated such an association. However, most international guidelines suggest consideration of testing for *H. pylori* infection in refractory cases of HG. Regular use of proton pump inhibitors leads to false negative results for both Urea breath tests and stool antigen test, and serology is not routinely done as it could be inaccurate in low prevalence areas. This leads to lack of timely treatment. Besides, use of steroids for HG may enhance symptoms and be ineffective in such cases. Hence, empiric therapy for *H. pylori* infection should be considered in the guidelines for refractory cases of HG.

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Agenesis of inferior vena cava with deep vein thrombosis and recurrent antepartum haemorrhage

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Abstract

Introduction: Absence or agenesis of the inferior vena cava (IVC) is an extremely rare entity. Its incidence varies from 0.00005% to 1% in the general population. There are few reports of this entity in a pregnant woman and this is the first published case in a woman with a history of deep vein thrombosis (DVT).

Clinical case: A 30-year-old nulligravid woman first presented to our institution for pre-conception counselling due to previous venous thromboembolism, absent infra-hepatic IVC and lifelong therapeutic anticoagulation with rivaroxaban. She was diagnosed in utero as having bilateral renal vein thrombosis, leading to a right-sided renal dysgenesis and a single functioning left kidney at birth. This was confirmed in adulthood via nuclear medical renal scan. The infra-hepatic IVC was absent; however, she had extensive collateralisation to allow venous drainage from the pelvic vessels to the supra-hepatic IVC. At age 21, while on the oral contraceptive pill, she developed a left ilio-femoral DVT. Thrombophilia screening was negative. On the advice of her haematologist, she commenced lifelong anticoagulation. Prior to conception, rivaroxaban was changed to therapeutic enoxaparin, 80 mg twice daily, given the permanent anatomic abnormality and previous DVT at a young age. She then developed recurrent antenatal bleeding with a known sub-chorionic haematoma identified from eight weeks of gestation. Furthermore, there was evidence of intrauterine growth restriction (IUGR). Our patient ultimately presented with preterm prelabour rupture of membranes (PPROM) at 27 weeks + 3 days of gestation and was delivered via lower segment caesarean section after intravenous heparin bridging. A midline skin incision was chosen due to the extensive collateralisation of pelvic vessels. After delivery, she was recommenced on enoxaparin 40 mg twice daily which was eventually restored to 80 mg twice daily. Birthweight of the male infant was 910 g (<10th centile) with APGAR scores of 1 at 1 min and 5 at 5 min.

Discussion: Absent IVC can be due to intrauterine or perinatal thrombosis; however, embryological dysgenesis seems to be the most commonly proposed origin. The cause for IUGR in this case may be related to the altered vascular anatomy. Appropriate management of antepartum haemorrhage in a pregnant woman requiring therapeutic anticoagulation is not well supported by current literature. The evidence to balance between bleeding and clotting is anecdotal at best.

Conclusion: We describe the first case of IVC agenesis in pregnancy complicated by IUGR, recurrent antepartum bleeding, PPROM and multiple adjustments of anticoagulation.

Balancing fetal goitrogens – Immunity vs. iatrogenic

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Abstract

Introduction: Managing Graves' disease during pregnancy requires balancing the goitrogenic effects of antithyroid drugs (ATDs) and TSH-receptor antibodies. Fetal thyroid dysfunction can be detected on ultrasound scanning based on the presence of a fetal goitre and markers of bone growth and fetal heart rate.

Case details: A 36-year-old primiparous woman with a long history of Graves' disease was managed with propylthiouracil (PTU) during pregnancy. Her TSH-receptor Ab was elevated at 8.4 mU/L and she was treated with PTU 25 mg three times a day. Between 18 and 30 weeks, fT4 remained between 11 and 12 mU/L (7–17 mU/L) and T3 was 4 and 4.5 mU/L (3.5–6) despite reduction in PTU dose. Her TSH-receptor Ab titre reduced during pregnancy but remained significantly elevated. At 34 weeks, a fetal goitre was detected with sonographic features consistent with fetal hypothyroidism that was confirmed on cordocentesis with an elevated fetal blood TSH. Thyroxine 400 mcg was infused into the amniotic fluid at 34 and 36 weeks with resolution of the fetal goitre and the baby was delivered with normal thyroid function at 40 + 2 weeks.

Conclusion: This case demonstrates the challenges faced by clinicians managing Graves' disease in pregnancy when TSH-receptor Abs remain elevated as well as the diagnosis and management of fetal thyroid dysfunction. Continuation of PTU despite a low-normal fT4 led to fetal hypothyroidism and goitre formation. Guideline recommendations for surveillance of fetal thyroid dysfunction are inconsistent. Moderate quality evidence supports routine use of fetal surveillance in women treated with ATDs in later pregnancy as well as the importance of achieving maternal T4 targets.

New generation antiplatelet agents reduce pathophysiological aspects of preeclampsia in human and mouse models of disease, representing exciting novel candidate therapeutics

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Abstract

Aim: Preeclampsia (PE) is a serious complication of pregnancy. Two of the major pathophysiological aspects are (1) the release of sFlt1 and pro-inflammatory mediators and (2) systemic maternal endothelial dysfunction, leading to hypertension and major end organ damage. New generation antiplatelet drugs (clopidogrel, prasugrel and ticagrelor) used in clinical cardiovascular disease have key properties to prevent and treat various pathogenic aspects of disease. Thus, they may be effective in preventing the development of preeclampsia.

Objective: To examine whether new generation antiplatelets can counter the pathophysiology in human and mouse models. Importantly,

comparing these new generation agents against aspirin (older generation antiplatelet), the current most widely prescribed drug to prevent preeclampsia.

Methods: Functional studies were performed on human primary: (1) cytotrophoblast, (2) endothelial cells and (3) PE placental explants. We tested the effects of new generation antiplatelets (clopidogrel, prasugrel, ticagrelor and aspirin) on human tissues at increasing doses (0–100 μM) to determine effects on oxidative stress, sFlt1 production, endothelial dysfunction (in a variety of in vitro models/assays). Importantly, we tested the new generation antiplatelets, in two mouse model of preeclampsia (placental sFlt-1 overexpression and systemic N-Nitroarginine methyl ester (L-NAME) infusion) and further functional vascular reactivity studies (using wire myography) on arteries from pregnant women and mice.

Results: New generation antiplatelet agents induced antioxidant cytoprotective gene expression, reduced reactive oxygen species (ROS) production. New generation antiplatelet agents potently reduced sFlt-1 secretion and pro-inflammatory cytokine production from preeclamptic placental explants. Additionally, these drugs mitigated endothelial dysfunction in human models of preeclampsia. Furthermore, they enhanced activity of endothelial nitric oxide synthase, the enzyme responsible for producing nitric oxide. New generation antiplatelets reduce vasoconstriction in human and mouse models of preeclampsia (ex vivo). Importantly, administration of prasugrel decreased the elevated blood pressure (BP) phenotype in two mouse models of preeclampsia. Of note, aspirin had modest to no effect in the majority of these models.

Conclusions: New generation antiplatelets demonstrate clear capability of curtailing various pathological stages of preeclampsia and thus represent exciting novel therapies to both prevent and treat preeclampsia. They outperformed aspirin in all assays examined, suggesting their effects may not be limited to early pregnancy mediation. Importantly, they are classified as category B/C drugs and warrant further investigation in human clinical trials.

Retrospective 10-year audit of pregnancies in solid organ transplant recipients at the Royal Brisbane and Women's Hospital

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Good at heart: Developing a tertiary perinatal cardiac service; the first eight years of experience

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Abstract

Background: Maternal cardiac disease is the most common cause of indirect maternal death, and women with pre-existing cardiac disease have complex medical, obstetric and anaesthetic requirements. A multidisciplinary perinatal cardiac service was commenced at our hospital in 2009 to optimise outcomes in women with cardiac disease.

Aim: To assess the maternal and perinatal outcomes of women referred to the perinatal cardiac clinic in the first eight years of service to evaluate clinical practice and inform future service provision.

Materials and methods: A single centre retrospective study of women referred to the Perinatal Cardiac Service between 2009 and 2016. Data collected included: demographic details; cardiac diagnosis; pregnancy and birth outcomes, including anaesthetic and delivery complications, and requirement for Intensive Care Unit (ICU)/High Dependency Unit (HDU) admission.

Results: A total of 170 women were referred for pre-pregnancy, pregnancy or postpartum care. Corrected congenital heart disease was the most common indication for referral (34%), followed by maternal cardiac arrhythmia (24%) and valvular disease (19%). The perinatal mortality rate was 2%, mean gestational age at delivery was 38w2d, fetal growth restriction (customized birthweight $<$10th centile) was 9%, although 23 (16%) pregnancies resulted in preterm birth. Maternal outcomes were favourable, although 51% of women required a caesarean section, and 23% who achieved a live birth required ICU/HDU admission, most commonly in those with cardiomyopathy.

Conclusion: This study confirmed that women with pre-existing cardiac disease are at increased risk of preterm birth and high acuity in the peripartum period but otherwise good maternal and perinatal outcomes. An integrated multidisciplinary perinatal cardiac service can optimise perinatal outcomes in women with cardiac disease.

Perinatal outcomes following intravenous compared with oral iron for the treatment of antenatal iron-deficiency anaemia

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Abstract

Background: While intravenous (IV) iron appears superior to oral iron for managing antenatal iron deficiency anaemia (IDA) with respect to maternal haematological improvements, impacts on maternal or neonatal clinical outcomes remain unclear.

Aim: To undertake a systematic review and meta-analysis to evaluate the effects of IV iron compared with oral iron for first-line treatment of antenatal IDA on perinatal outcomes.

Methods: Medline, Embase, Web of Science, Scopus, Cochrane Register of Controlled Trials were searched from first publication until January 2019. Bibliographies of articles were hand searched for additional studies. Two review authors independently assessed studies for inclusion, extracted data, and evaluated study quality. Quality of evidence was evaluated using the GRADE criteria. Meta-analysis was undertaken using fixed or random effects models where appropriate.

Results: Fifteen studies involving 1938 participants were identified. All were at high risk of bias in at least one domain, with the majority (10/15) undertaken in low- and middle-income countries. We identified low-quality evidence suggesting that administration of intravenous iron may reduce the requirement for blood transfusion at delivery (Peto Odds Ratio 0.19; 95% CI 0.05 to 0.78, 9 RCTs; Number Needed to Treat: 95; 95% CI 81 to 348). There was low to very low quality evidence that intravenous iron may lead to slight improvements in neonatal birth weight (mean difference 58 g; 95% CI 4–112, 8 RCTs) or lower the rate of breastfeeding cessation (Hazard Ratio 0.70; 95% CI 0.50–0.99, 1 RCT). While intravenous iron led to a greater improvement in maternal haematological indices at the time of delivery, no differences were evidence with respect to neonatal parameters.

Conclusions: We identified low-quality evidence suggesting that use of IV iron compared with oral iron may lead to a reduction in the risk of blood transfusion at delivery and improve neonatal birth weight, but the absolute treatment effects are small and were subject to high risk of bias. The current lack of high-quality evidence supporting improvements in maternal or neonatal clinical outcomes following intravenous iron use in pregnancy limits justification for routine first-line utilization over oral iron in clinical practice.

The BP2 (blood pressure postpartum) study: Protocol for a randomised trial of follow-up and lifestyle behaviour change strategies after hypertensive pregnancy

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Abstract

Introduction: Epidemiological studies have established at least a doubling of cardiovascular disease risk after hypertensive disorders of pregnancy (HDP), not explained by other cardiovascular risk factors in these women. A number of national and international societies, including Society of Obstetric Medicine of Australia and New Zealand and ISSHP, now recommend all women after HDP be advised of their increased cardiometabolic risks, see their general practitioner (GP) regularly, and adopt a healthy lifestyle. However, appropriately powered randomised trial evidence of whether early intervention after HDP improves cardiometabolic parameters (therefore potentially improving long-term health) is lacking.

Aims: Primary aim: in women with HDP, to compare the effect of three different management strategies in the first 12 months postpartum on maternal blood pressure (BP) and positive lifestyle behaviour change (LBC) as measured by maternal weight and waist circumference change. Secondary aims include assessing: effect on other maternal cardiometabolic parameters including vascular function, maternal serological and urine measures of cardiovascular risk, infant growth trajectory, maternal health-related-quality-of-life, and economic analysis. We hypothesise that the intervention arms will result in greater positive LBC and BP change than the usual care arm.

Methods: Three-arm multicentre randomised trial (sample size 500 from fvie socioeconomically diverse Sydney hospitals). Consenting women who complete baseline questionnaires randomised 1:1:1 at six months postpartum to either (1) Optimised usual care: Information package to woman and her GP, see GP for six months postpartum visit and health after HDP discussion, (2) Brief education intervention: Information package, attend postpartum clinic with obstetric physician and dietician six months postpartum for risk assessment and brief LBC counselling, (3) Extended lifestyle intervention: as per (2), additionally woman enrolled into six-month telephone-based LBC program (NSW Health Get Healthy Service) from 6–12 months postpartum. All women were seen 12 months postpartum for co-primary (BP change, weight change, waist

circumference change) and secondary outcome assessment. Data also collected from LBC program regarding engagement and retention of women in the program. The study is powered to detect a 4 mmHg difference in systolic BP between groups, or a 4 kg weight loss difference/2 cm waist circumference change.
Results: The recruitment commenced in January 2019, ACTRN12618002004246, and is aimed to conclude by the end of 2020.
Discussion: Current guidelines on managing long-term health after HDP are largely based on assumptions/extrapolation from other populations, which may not be applicable to postpartum women. BP2 will provide evidence regarding feasibility and effectiveness of early (6–12 months postpartum) LBC intervention and structured follow-up clinics in improving cardiovascular health markers after HDP.

Maternal multiple endocrine neoplasia type 1 is associated with an increased risk of gestational diabetes mellitus, hypertensive disorders and low birth weight

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Abstract
Introduction: Multiple endocrine neoplasia type 1 (MEN 1) is a highly penetrant autosomal dominant disease characterised by multi-system neoplasia including adolescent onset primary hyperparathyroidism and pituitary adenomas, particularly prolactinomas. Despite the early onset of endocrinopathies that may adversely impact reproductive health, information regarding the impact of maternal MEN 1 on pregnancy and neonatal outcomes is limited to case reports.
Methods: This study is a retrospective case series of pregnancy and fetal outcomes for mothers with MEN 1 who were cared for at the Royal Hobart Hospital between 1980 and 2018. Data were retrieved from medical records and Australian averages from the Australian Institute of Health and Welfare.
Results: Between 1980 and 2018, 27 women with MEN 1 had 93 pregnancies resulted in 75 live born infants. Miscarriage rate was not increased (18.8% vs. 20%, $p = 1.00$). There was no fetal death in utero. Women with MEN 1 were more likely to have gestational diabetes (56% vs. 8.9%, $p = 0.0006$), hypertensive disorders of pregnancy (25% vs. 7.6%, $p = 0.0187$) and their neonates were more likely to have a low birthweight ($p = 0.001$) compared to the Australian average. Caesarean deliveries (30.1% vs. 34%, $p = 0.7234$) and gestational length (39 vs. 38.6) were similar. Adverse events were not more frequently observed in women with antenatal hypercalcaemia when compared those with normocalcaemia.
Conclusion: Maternal MEN 1 is associated with an increased risk of gestational diabetes mellitus, hypertensive disorders of pregnancy and low neonatal birthweight. These risks were not attributable to isolated antenatal hypercalcemia.

The Cardiac-Obstetric Registry of South Australia (COROSA): Improving outcomes of pregnancy for women with heart disease. Analysis of retrospective cohort: 2013–2017

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Abstract
Women with pre-existing heart disease have a higher risk of developing complications and suffering poor outcomes, both during and after pregnancy. Optimal management for heart disease during pregnancy is poorly defined, with treatment varying significantly across sites. Our five-year retrospective approach studying this population aims to inform the ideal process for management and treatment of pregnant women with heart disease. Participants were retrospectively identified through ICD coding for inclusion into the study. All women with a diagnosis of pre-existing heart disease who received antenatal care at our tertiary centre between 2013 and 2017 were included in the retrospective cohort. We identified 677 women with ICD codes indicating a diagnosis of heart disease. A preliminary clinician review was required to screen for eligibility, with 69 women meeting the inclusion criteria. Analysis of the results showed that 33 women (48%) had a known arrhythmia, 19 (28%) had congenital heart disease, 15 (22%) had valvular heart disease, 5 (7%) had cardiomyopathy and 2 (3%) had ischaemic heart disease. Around half (48.5%) of participants developed an obstetric antenatal complication and one-quarter (26%) developed peri-delivery complications. The majority (53%) of these births were not normal vaginal deliveries. The Cardiac-Obstetric Registry of South Australia will continue to monitor outcomes of pregnant women with heart disease in our prospective cohort. Project outcomes will inform our clinical management of these women at our site and, in the future, within our state. Long-term follow-up will also improve access to care for these high-risk women and their children.

Saving mothers' lives in Australia

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Abstract
Maternal mortality rates in Australia have halved in the last 40 years, but have not changed significantly in the last decade. In the last decade, thromboembolism, amniotic fluid embolism, obstetric haemorrhage, hypertensive disorders and sepsis were the main causes of direct maternal deaths. Non-obstetric haemorrhage (CVA, ruptured splenic artery), cardiovascular disease, suicide and complications of substance abuse were the main causes of indirect maternal deaths. Aboriginal and Torres Strait Islander women continue to have a maternal mortality ratio almost four times than other Australian residents. Key to preventing maternal deaths and severe morbidity is the continuing review of confounding factors in relation to causation and the careful review of all cases to determine whether there were potentially preventable contributing factors. Increased attention needs to be placed on review of severe maternal morbidity and the contribution of contributing factors to these events.

Hyperemesis gravidarum and hCG-induced maternal thyrotoxicosis

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Abstract

Introduction: Human chorionic gonadotrophin (hCG) is produced in the placenta and is structurally homologous to thyroid stimulating hormone (TSH). When hCG is produced in excess, it can bind to maternal thyroid TSH receptors, resulting in an increase in maternal free T3 and free T4. Transient gestational thyrotoxicosis peaks in the later stages of the first trimester and usually self-resolves without significant complications. However, an excess of hCG production often manifested through severe hyperemesis gravidarum can induce maternal thyrotoxicosis. Differentiation between hCG-induced gestational thyrotoxicosis, Graves' disease and autoimmune thyroiditis is important given the differences in management. Here, we describe the presentation and management of two cases of hCG-induced gestational thyrotoxicosis, discuss its pathophysiology, clinical diagnosis and management.

Case one: A 25-year-old primip with a singleton pregnancy was admitted with significant dehydration, weight loss and end-organ impairment, with acute kidney and liver injury as a result of severe hyperemesis gravidarum at 10 weeks of gestation. Her TSH level was <0.02 mIU/L (0.27–4.2 mIU/L) with a free T4 level of >100 pmol/L (12–22 pmol/L) corresponding with a significantly elevated hCG level of 558,960 IU/L. TSH receptor antibodies were negative at <1.0 U/L. She was hypertensive with a blood pressure (BP) of 141/93 mmHg in the absence of a known hypertensive disorder; she was tachycardic despite intravenous fluids and her Sflt1/Plgf ratio was 167. She was treated with labetolol 50 mg TDS and propylthiouracil (PTU) 100 mg TDS. Her biochemical and clinical parameters improved along with notable improvement in her free T4 level to 41.7 pmol/L within three days. PTU was ceased 10 days after initiation. She remained biochemically euthyroid and normotensive thereafter without regular antihypertensives or PTU.

Case two: An 18-year-old G2P1 woman was admitted for syncopal episodes and hypokalaemia at 13 weeks of gestation. She had severe symptomatic intravascular volume depletion from severe hyperemesis gravidarum with a serum potassium and bicarbonate level of 2.3 mmol/L and 32 mmol/L, respectively. Further biochemistry assessment demonstrated maternal thyrotoxicosis with a TSH of <0.02 mIU/L and free T4 of 85.3 pmol/L. TSH receptor antibodies were negative at <1.0 U/L and her corresponding bHCG was 270,639 IU/L. She was commenced on PTU 100 mg QID and propranolol 40 mg QID with good effect.

Conclusions: In conclusion, these two cases illustrate the need to consider hCG-induced maternal thyrotoxicosis in women with severe hyperemesis gravidarum. In the acute setting, it may be difficult to distinguish this condition from hyperthyroidism (e.g. due to Graves' disease). While hCG-induced maternal thyrotoxicosis often self-resolves in the absence of significant clinical manifestation in the first trimester, women with a substantial overproduction of hCG may require PTU to manage the thyrotoxic effect in the short term.

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The P4 Study: Subsequent pregnancy maternal physiology after hypertensive and normotensive pregnancies

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Abstract

Background: Hypertensive disorders of pregnancy (HDP) are amongst the most common serious medical complications of pregnancy and are associated with increased risk of cardiovascular and metabolic disease later in life.

Methods: Prospective sub-study of the P4 (postpartum, physiology, psychology and paediatric) Study. Women were studied six months after normotensive (NP) versus hypertensive (HP) pregnancy and in the subsequent pregnancy (SP) (11–13 weeks of gestation). Measurements included blood pressure (BP), blood and urine tests (Urine ACR, HOMA-IR Score, LDL-Cholesterol), body composition (Fat %) and Postnatal Edinburgh Depression Scale (EDS). Following descriptive analysis, paired sample t-tests compared postpartum and SP measurements. Regression analysis examined whether maternal characteristics (age, ethnicity, education) and inter-pregnancy factors (interpregnancy interval, body mass index (BMI) change, breast feeding duration) explained cardiovascular/metabolic measurement (SP systolic and diastolic BP and body fat%) variability in the SP.

Results: This study included 31 women (21 NP, 10 HP). Women after HP had higher systolic BP six months postpartum (NP: 105 ± 11; HP: 113 ± 10; $p = 0.05$) and in the SP (NP: 102 ± 10; HP: 110 ± 8; $p = 0.04$) as well as diastolic BP six months postpartum (NP: 66 ± 8; HP: 72 ± 6; $p = 0.03$) and in the SP (NP: 63 ± 6; HP: 68 ± 5; $p = 0.04$). There was no significant difference in EDS between the NP and HP groups at either pregnancy. Physiological measures and risk markers six months postpartum remained similar in the SP irrespective of index pregnancy hypertensive status. Caucasian ethnicity was associated with higher SP systolic ($p = 0.002$) and diastolic ($p = 0.009$) BP, and a longer inter-pregnancy interval (IPI) was associated with higher fat% in the SP ($p = 0.03$).

Discussion: In this cohort, women after HP had higher BP than NP six months postpartum and early SP, demonstrating that women with a history of HDP maintain higher BP than those without. Additionally, within

groups (HP postpartum to SP, and NP postpartum to SP) physiological measurements remained similar over time indicating that these measurements in an index pregnancy are likely to be similar in the SP irrespective of hypertensive status. Caucasian ethnicity was associated with higher SP BP, and longer IPIs with higher fat%. All these factors may reflect a higher long-term cardiovascular risk for women with a history of HDP. The similar findings postpartum versus early SP also suggest that without postpartum intervention, women after HDP will continue to have more adverse cardio-metabolic profiles in subsequent pregnancies than their NP counterparts.

A rare cause of severe urgent hypertension in pregnancy: Mid-aortic syndrome

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Abstract
Mid-aortic syndrome (MAS) is defined as an obstructive lesion of the mid aorta, regardless of aetiology[1]. It is a variation of aortic coarctation commonly affecting the renal (>80%) and splanchnic (50–70%) branches of the aorta[2]. MAS is the most common clinical syndrome associated with stenotic aorto-arteriopathy in children, but remains a relatively rare complication of pregnancy. Severe cases of MAS are associated with significant morbidity and mortality, with hypertensive encephalopathy, congestive heart failure, and stroke all reported to develop in close to 50% of cases by the third or fourth decade, and a 20% survival rate after age 40 years[3]. We present the case of a 33-year-old female in her first ongoing pregnancy, who presented with an elevated booking blood pressure of 140/80 and commenced on labetalol. Her blood pressure escalated at 18 weeks of gestation and she was admitted with severe urgent hypertension with a blood pressure of 180/90. She underwent thorough investigation of secondary causes of hypertension. Her renal artery dopplers showed a >75% stenosis of the juxta-renal aorta and further imaging was recommended. An MRI confirmed abrupt narrowing of the abdominal aorta most pronounced at the coeliac trunk extending to the iliac bifurcation. In conjunction with the vascular surgery and renal teams a diagnosis of mid-aortic syndrome was reached and further investigation delayed to the post-partum period due to radiation exposure. She underwent weekly blood pressure review in the pregnancy unit, home blood pressure monitoring and second weekly growth and wellbeing ultrasounds, which remained normal with an estimated fetal weight on the 70th centile. Her blood pressure continued to require titration of medication, managed on three agents and commencement of aspirin; however, she never developed pre-eclampsia. She underwent an unsuccessful induction of labour at 37 weeks of gestation and on advice of the vascular surgeons delivered a healthy female infant via a classical caesarean section. This case provides important insight and experience into the complex multidisciplinary management of a rare cause of secondary hypertension in pregnancy.

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Two cases of postpartum atypical haemolytic uraemic syndrome in the pre- and post-eculizumab era

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Abstract
Introduction: There is diagnostic uncertainty in differentiating pregnancy-associated Atypical Haemolytic Uraemic Syndrome (aHUS) and conditions including Thrombocytopaenic Purpura (TTP), and pre-eclampsia/HELLP variant. aHUS can be associated with post-partum haemorrhage (PPH)[1]. We describe two cases managed as postpartum aHUS in the pre- and post-eculizumab era.
Case one (2008): A 31yo nulliparous female was induced at 41 weeks, vaginal delivery complicated by stillbirth. Over the next two days she developed thrombocytopaenia, mildly deranged liver function, dialysis dependent anuric renal failure and transfusion dependent microangiopathic haemolytic anaemia (MAHA), with normal complements. She commenced plasmapheresis for five days. On day 9, she became hypertensive, with massive PPH. Exploratory laparotomy revealed no bleeding source, however required uterine and ovarian artery ligation. Bleeding subsided by day 10. Subsequently, plasmapheresis and dialysis were ceased, biochemical parameters normalised, and blood pressure improved. She was discharged on day 15. On follow-up, she had normal blood tests, mild hypertension, a negative autoimmune screen, normal complements and mild reduction of ADAMTS13 (67%) inconsistent with TTP. She subsequently had two uncomplicated normotensive pregnancies, delivered healthy term babies, on aspirin prophylaxis. A decade post presentation, there has been no evidence for recurrent haemolysis, nor renal dysfunction.
Case two (2018): A 29yo nulliparous female was induced at 39 weeks of gestation, with vaginal delivery of a healthy baby, and intact placenta. She developed massive PPH on day 0 with 2.5 L blood loss, requiring five units of packed red cells and underwent examination under anaesthesia, which identified no bleeding source. She became thrombocytopaenic with oliguric acute kidney injury, low C3 0.82 g/L and C4 0.11 g/L, deranged coagulation profile, elevated lactate dehydrogenase, but normal liver function tests. On day 4, she developed MAHA and commenced plasmapheresis, followed by eculizumab. She remained normotensive with no neurological symptoms. ADAMTS13 returned normal excluding TTP, thus plasmapheresis discontinued. On day 6, she became fluid overloaded with marked renal dysfunction, requiring 24 h of dialysis. Following this, she recovered rapidly with resolution in biochemical abnormalities and discharged by day 11. Her autoimmune screen, shiga toxin, and aHUS screen (CFI, CFH, CFH Ab) and genotyping (CFH, CFI, MCP) were negative. She completed three months of eculizumab. One year after drug cessation, she remains well with normal renal function, complements and no haemolysis. She is planning her next pregnancy, with a multidisciplinary team to aid preconception counselling.
Discussion: These cases highlight the complexity of diagnosing pregnancy-associated aHUS, a potentially fatal condition in the absence of timely treatment. They have features suggestive of alternate conditions, including but not limited to HELLP/pre-eclampsia. With the

availability of eculizumab, diagnosis of this rare condition may become more common. It important to ascertain the correct diagnosis to optimise treatment, assist pre-conception counselling and advice on ongoing risk for chronic disease.

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Maternal and neonatal outcomes of over 100 very high-risk maternities managed in a multidisciplinary team model of care and what we learned!

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Abstract
Multidisciplinary care for very high-risk maternity patients is essential for the safety and wellbeing of the woman, but also the wellbeing of the staff entrusted with her care. Each month, our quaternary maternity facility conducts collaborative meetings to discuss 5–8 women (with the highest medical needs), with an emphasis on peri partum management. Obstetrics, anaesthetics, critical care (medical and nursing), obstetric medicine, midwifery and birth suite, and subspecialty physicians including nephrology, cardiology, haematology represent the quorum with representation from MFM, surgical specialties and oncology as required. Clinicians involved recognise the value of input from all parties and often unexpected group learning occurs. In the two years since inception, more than 100 maternities have been planned and documented via an electronic maternity care plan. Morbidities include adult congenital heart disease, aortopathy, prosthetic heart valves, solid organ transplants, VTE and malignancy. Obstetric and neonatal outcomes to date are remarkably positive, with a median gestational age at delivery of 38 weeks and median birth weight of 3048 g. There have been no maternal deaths and one neonatal death due to extreme prematurity. Operative delivery rates are high at 68% and approximately half nulliparous. As a result of the increased collaborative exposure to very high risk maternities, novel care pathways have been developed. An example of this is the ECMO protocol developed for maternity patients with acute, severe cardiovascular compromise. This pathway required multiple stakeholders and repeated simulation to ensure feasibility. In summary, prospectively gathered maternal and neonatal outcomes support the clinician consensus that well-planned MDT care is essential for the safety and wellbeing of these very high-risk women. The clinicians themselves draw reassurance and learning from the group process. An additional benefit is the development of pathways for infrequent but catastrophic events.

A retrospective case-based study on the detection and management of thrombotic thrombocytopaenic purpura in pregnant women presenting to a large obstetric centre in Australia

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Abstract
Severe thrombotic microangiopathy (TMA) can be an inherited or acquired disorder; however, there is an increase among women presenting during pregnancy. TMA in pregnancy is associated with a high mortality and morbidity to mother and infant; therefore, early detection and initiation of appropriate management is paramount. There is often clinical, and laboratory overlap in features between different types of TMA, and this can lead to diagnostic delay. Thrombotic thrombocytopaenic purpura (TTP) is a type of TMA that is related to severe ADAMTS13 enzyme deficiency. The consequence of this deficiency leads to microthrombi in small vessels, microangiopathic haemolytic anaemia and thrombocytopaenia overall leading to multi organ ischaemia. Current international evidence shows that there is an increased frequency of TTP presentations during pregnancy, current estimates sit around one case per 100,000 pregnancies. At present, there is negligible Australian literature with regard to TTP in pregnancy and whether there is any related neonatal outcomes. The primary objective of this monocentric retrospective study is to analyse the pregnant and puerperal population (and their infants) who have presented to the Mater Hospital (a large quaternary obstetric centre) over a 10-year period (from 1 March 2008 to 1 March 2018). The secondary objective is to infer the short-term maternal outcomes such as treatment duration, outcomes and relapse rates of TTP, and gain a basic insight into neonatal health by analysing data such as birth weight, APGAR scores and birth gestation. We identified our study population via electronic medical records and laboratory records analysing all consecutive patients who had an ADAMTS13 assay performed during the study period. For our study, we defined TTP as an ADAMTS13 activity level of $\leq$10%. One of the main difficulties with regard to the diagnosis of TTP is the prolonged turnaround time for the ADAMTS13 activity testing, this often means the clinician must make a rapid diagnosis and initiate treatment prior to the test result being available. A recent update to improve the pre-test probability of an accurate diagnosis of TTP was the development of the PLASMIC score. In addition to the analysis of epidemiological and clinical data, we aim to retrospectively apply the PLASMIC score to our data population and assess the external validity of this tool in a pregnant population. Interim analysis has identified 32 cases of TMA over the 10-year period, of these three patients had confirmed TTP; in total, there were five episodes of TTP between these patients and there was one case of intra uterine death. Ongoing data analysis continues. The overarching aim of this study to get a broad descriptive Australian perspective of disorder with high mortality and morbidity if undiagnosed and inadequately treated, and contribute to the international literature on a very rare disorder.

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Postpartum interventions to reduce long-term cardiovascular disease risk in women after hypertensive disorders of pregnancy: A systematic review

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Abstract

Introduction: Hypertensive disorders affect approximately 7% of pregnancies. Evidence now suggests diagnosis of a hypertensive disorder of pregnancy (HDP) independently increases that individual's risk of later cardiovascular disease (CVD) later in life. Focus on reduction or mitigation of this risk has been limited. This meta-analysis seeks to identify trialled interventions to reduce cardiovascular risk after HDP.

Methods: Online medical databases were searched to identify full-text published results of randomised controlled trials (RCTs) in women <10 years postpartum after HDP that trialled interventions to reduce cardiovascular risk. Outcomes sought included cardiovascular disease events, chronic hypertension, and other measures of cardiovascular risk such as obesity, smoking status, diet, and physical activity. There were no language restrictions. Publications from January 2008 to July 2019 were included.

Results: Two RCTs were identified. One, a trial of calcium versus placebo in 201 women with calcium commenced from the first follow-up visit outside of pregnancy and continued until 20 weeks of gestation if another pregnancy occurred. A non-significant trend towards decreased blood pressure was noted. The second RCT of 151 women tested an online education programme (versus general information to control group) to increase awareness of risk factors and personalised phone-based lifestyle coaching in women who had a preeclampsia affected pregnancy in the five years preceding enrolment. Significant findings included increase in knowledge of CVD risk factors, reported healthy eating and decreased physical inactivity; however, adoption of a promoted heart healthy diet and physical activity levels did not differ significantly between groups. Several observational studies after HDP, and one meta-analysis of studies of lifestyle interventions used to extrapolate likely benefits of lifestyle interventions, were identified which supported the use of lifestyle interventions. Several ongoing RCTs were also noted.

Discussion: There is a paucity of intervention trials in the early years after HDP to guide evidence-based cardiovascular risk reduction in affected women. Limited evidence suggests lifestyle intervention may be effective; however, degree of any risk reduction remains uncertain.

Conclusion: Sufficiently powered randomised controlled trials of appropriate interventions (e.g. lifestyle behaviour change, pharmacological) are required to assess the best method of reducing the risk of cardiovascular disease in this at-risk population of women.

The 'Links2HealthierBubs' cohort study: Protocol for a record linkage study on the safety, uptake, and effectiveness of influenza and pertussis vaccines among pregnant Australian women

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Abstract

Introduction/background and aims: Pregnant women and infants are at risk of severe influenza and pertussis infection. Inactivated influenza vaccine (IIV) and diphtheria-tetanus-acellular pertussis vaccine (dTpa) are recommended during pregnancy to protect both mothers and infants. In Australia, uptake is not routinely monitored but coverage appears sub-optimal. Evidence on the safety of combined antenatal IIV and dTpa is fragmented or deficient, and there remain knowledge gaps of population-level vaccine effectiveness. We aim to establish a population-based cohort of mother–infant pairs to measure the uptake, safety, and effectiveness of antenatal IIV and dTpa vaccines in three Australian jurisdictions.

Methods: 'Links2HealthierBubs' is an observational, population-based, retrospective cohort study established through probabilistic linkage of maternal, infant and child administrative health data in three Australian jurisdictions. The population-based cohort includes registered births between 2012 and 2017 in Northern Territory, Queensland, and Western Australia. Linkage to jurisdictional vaccination registers will be used to identify antenatal vaccination status and the gestational timing of vaccination. Information on maternal, fetal, and child health outcomes will be obtained through linkage to hospitalisation and emergency department records, notifiable diseases databases, developmental anomaly registers, birth and mortality registers.

Results: The Links2HealthierBubs cohort will include ~607,605 mother–infant pairs from Queensland, Northern Territory, and Western Australia. Cohort data will be used to evaluate the effectiveness and the risk of adverse events associated with IIV and dTpa during pregnancy and at birth in Australian mothers and infants. Initial analysis of 134,698 West Australian mothers who gave birth between 2012 and 2016 showed 9.0% were vaccinated for influenza alone, 9.3% for pertussis alone, and 7.0% for both vaccines. Data collection in Northern Territory and Queensland is ongoing.

Conclusions: Links2HealthierBubs is the first national population-based study to evaluate the impact of antenatal vaccination programmes in Australia. Results will be used to guide national maternal immunisation policy.

Recurrent pregnancy-related spontaneous pneumomediastinum

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Abstract

Spontaneous pneumomediastinum (SPM) with subcutaneous emphysema was first described by Laennac in 1819.[1] Pregnancy-related SPM is an uncommon disorder with an incidence of approximately 1 in 100,000 births and occurs almost exclusively with vaginal delivery. Ninety-one percent of cases occur in primiparas, typically of younger age with term pregnancy, and a history of difficult labour with prolonged second stage of delivery and excessive Valsalva manoeuvre. SPM may be accompanied by subcutaneous emphysema, pneumothorax and pneumopericardium. The proposed pathophysiology is rupture of pulmonary alveoli as a result of sudden increase in intrathoracic pressure, leading to dissection of air down bronchovascular sheaths into the mediastinum and subsequently along fascial planes into subcutaneous tissues.[2] SPM typically manifests in the second stage of labour with acute chest pain, dyspnoea, and subcutaneous swelling with palpable crepitus. Diagnosis is made on chest radiograph, although computed tomography of the chest is frequently performed to further define the pathology and exclude other sinister pathology such as oesophageal rupture.[2] The natural history from reported cases appears to be of a benign clinical course and conservative management with close observation is usually employed. Recurrent episodes of SPM are extremely rare with only 21 cases described thus far in literature, and to our knowledge no recurrent episodes related to pregnancy have been reported. We present the case of a 27-year-old female with a history of SPM with associated subcutaneous emphysema, pneumomediastinum and pneumopericardium in her first pregnancy in 2016, who suffered a recurrence of the condition in her following pregnancy in 2019. She had a vaginal birth after 62 min of second stage and then developed chest pain and facial swelling 5 min after birth. On examination, there was palpable crepitus over the left side of the face and neck. Chest X-ray demonstrated pneumomediastinum. She was managed conservatively, and her condition remained stable. She was discharged home on the fourth day after delivery following resolution of her symptoms. Health professionals should be aware of the risk of recurrent SPM in subsequent pregnancies in the absence of underlying pathology.

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Application of the sFlt-1:PlGF ratio to exclude pre-eclampsIa study: The ALEXIS Study

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Abstract

Background: Preeclampsia is a placental disorder defined by de novo hypertension in pregnancy with maternal organ dysfunction (i.e. renal, hepatic or central nervous system involvement) or fetal intrauterine growth restriction. Elevated levels of maternal anti-VEGF factor Soluble Fms-like Tyrosine Kinase-1 (sFlt-1) and reduced levels of pro-angiogenic Placental Growth Factor (PlGF) have been observed in women destined to develop preeclampsia. PROGNOSIS, published in NEJM 2016 evaluated the sFlt-1:PlGF ratio in predicting the development of preeclampsia. The prevalence of preeclampsia was 17.8% at four weeks. A ratio ≤ 38 was considered low risk for preeclampsia development at one week with a negative predictive value (NPV) of 99.3%. The positive predictive value (PPV) of a ratio >38 for preeclampsia prediction at four weeks was poor at 36.7%. This assay has gained popularity both as a test to exclude preeclampsia and for diagnosis of preeclampsia despite limited evidence for the latter. If validated in high prevalence cohort such a test may be useful in the management of high-risk women.

Aims: To compare the sFlt-1:PlGF ratio to a clinical prediction in order to predict the likelihood of development of preeclampsia in the following seven days in high-risk women and to determine whether the sFlt-1:PlGF ratio can be used in a high-risk clinic to guide frequency of clinical reviews.

Methods: Women at risk for pre-eclampsia were recruited from the Day Assessment Unit where comprehensive maternal and fetal clinical assessments were undertaken over a 4-h period. Four serial blood pressure readings were measured additional to blood tests, urinalysis and fetal cardiotocography (CTG) enabling the medical teams to formulate a clinical prediction as to whether preeclampsia was likely to develop within seven days. This was compared to the sFlt-1:PlGF ratio.

Results: One hundred and twenty-one women were recruited, 14 were excluded, eight diagnosed with preeclampsia on the day of recruitment. Fourteen women developed preeclampsia within one week and 32 developed preeclampsia by delivery or discharge. The sFlt-1:PlGF ratio < 38 ruled out the development of preeclampsia within one week with an NPV of 96% vs. 92% with the clinical prediction ($p =$ n.s.). The PPV of the sFlt-1:PlGF ratio (>38) was 33% vs. 30% for clinical prediction ($p =$ n.s.). The sFlt-1:PlGF ratio correlated with preeclampsia (Pearson correlation 0.518, $p < 0.01$) and was therefore specific for preeclampsia.

Conclusions: The sFlt-1:PlGF ratio was as effective as the clinical prediction in ruling out the development of preeclampsia in high-risk women at seven days. The ability of both the s-Flt-1:PlGF ratio and the clinical assessment in predicting preeclampsia were poor. This study does not support the routine clinical use of the s-Flt-1:PlGF assay.

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Impaired cardiovascular adaptation to pregnancy in women who deliver a small-for-gestational-age baby

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Abstract

Objectives: To evaluate and compare maternal haemodynamic changes across gestation in women who delivered a small-for-gestational-age (SGA) infant with those with uncomplicated pregnancies.

Design: Prospective observational cohort study from 2015 to 2018.

Setting: Lyell McEwin Hospital, Elizabeth Vale, South Australia.

Methods: Healthy, nulliparous women carrying a singleton pregnancy between 9 and 16 weeks' gestation were eligible for inclusion in the STOP Study. Haemodynamic profiles were obtained between 9–16 weeks' gestation and again at 32–36 weeks' gestation using the USCOMâ system to measure both peripheral and central blood pressures, Augmentation index (AIx, as a marker of vascular stiffness), cardiac output (CO) and systemic vascular resistance (SVR). After delivery, women were classified into uncomplicated ($n = 286$) or SGA pregnancies based on customized centiles ($n = 48$). Analysis was performed using one-way ANOVA and linear regression modelling after adjusting for age, BMI and smoking status. Women were excluded from analysis if they developed another complication of pregnancy (for example pre-eclampsia) in addition to carrying an SGA infant.

Main outcome measures: Maternal haemodynamic adaptation in uncomplicated pregnancies and those resulting in delivery of an SGA infant.

Results: Maternal haemodynamic adaptations across gestation were significantly different in women who delivered an SGA infant compared to those with uncomplicated pregnancies. At 9–16 weeks' gestation, women who later delivered an SGA baby had lower CO (median (IQR) 6.00 (5.43–6.83) vs. 6.25 (5.58–7.12) L/min, $p = 0.001$) and higher SVR (median (IQR) 1171 (989–1290) vs. 1092 (949–1219) dynes-s-cm^5, $p = 0.004$) than women with uncomplicated pregnancies. At 32–36 weeks' gestation, women with SGA pregnancies had lower CO (median (IQR) 6.26 (5.34–7.51) vs. 6.59 (5.73–7.54) L/min, $p = 0.002$), and higher SVR (medial (IQR) 1124 (956–1314) vs. 1021 (898–1203) dynes-s-cm^5, $p \leq 0.001$) than those with uncomplicated pregnancies. Women who delivered an SGA infant had a higher, but not quite statistically significant, AIx at 9–16 weeks' gestation ($p = 0.052$) which was significantly higher at 32–36 weeks' gestation ($p \leq 0.001$). Furthermore, they did not demonstrate the same physiological reduction in AIx across gestation observed in women with uncomplicated pregnancies ($p = 0.027$).

Conclusion: Women who delivered an SGA infant had lower CO, higher SVR and higher AIx than those with uncomplicated pregnancies across gestation. Women who deliver an SGA infant exhibit a maladaptive cardiovascular response to pregnancy. Early pregnancy haemodynamic parameters may suggest cardiovascular predisposition to deliver a small baby.

Intractable pruritus in early onset severe intrahepatic cholestasis of pregnancy (ICP) relieved by naltrexone

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Abstract

Case: A 35-year-old Kurdish woman G2P1 presented with pruritus at 16 weeks of gestation (16/40). History: severe ICP (maximum total bile acids (TBA) 251 μmol/L), gestational diabetes (GDM), and cholecystectomy (cholelithiasis) between pregnancies. Pruritus predominantly was nocturnal, affecting palms and soles. Ursodeoxycholic acid (UDCA), commenced at 20/40 (TBA 11 μmol/L, ALT 21 U/L, GGT 94 U/L), was up-titrated to 750 mg TDS by 28^6/40. Screening for underlying hepatic disease was negative. Recurrent GDM was diet-controlled. Mild hypothyroidism (TSH 5.0 mU/L) was treated with thyroxine. Rifampicin, commenced at 29^6/40, withdrawn (31^1/40) due to worsening transaminases: peak ALT 953 U/L (31^3/40), peak TBA 130 μmol/L. Cholestyramine, added at 31^1/40, up-titrated to 8 g BD. Hepatic MRI and liver histology: widespread perisinusoidal fibrosis, without evidence of steatosis or drug-induced liver injury. Severe pruritus persisted despite reasonable biochemical control of cholestasis (TBA 15–43 μmol/L). Pruritus worsening after liver biopsy was postulated secondary to oxycodone. IV naloxone provided relief of itch. Oral naltrexone 50 mg mane was therefore prescribed at 33/40. TBA 90 μmol/L (36^{+4}/40) prompted semi-urgent LSCS (36^{+5}/40). Naltrexone was withheld for 24 h. A healthy male infant was born (3700 g), APGAR score 9/9, clear liquor. Pruritus persisted for five days postpartum, while pain was mostly controlled with non-opioid analgesia. Biopsy review with immunostaining: poor expression of GGT at biliary canalicular margins, suggesting *ATP8B1* deficiency. Extensive genomic analysis demonstrated a heterozygous variant of unknown clinical significance in the epoxyhydrolase-1 (*EPHX1*) gene, previously associated rarely with autosomal recessive familial hypercholanaemia.[1]

Discussion: UDCA is currently first-line treatment for ICP, improving hepatobiliary secretion of bile salts and BA clearance across the placenta from fetus back to maternal circulation.[2,3] Data regarding effectiveness are conflicting.[4] Other agents include rifampicin[5] (pregnane-X receptor agonist) and cholestyramine[6] (anion exchange resin). Despite these therapies, our patient remained highly symptomatic. Pruritus can be severely debilitating. Many pruritogens (progesterone metabolites, histamines and autotaxin) have been postulated.[7] Underlying mechanisms of pruritus are complex and poorly understood. Opioid-induced itch is mediated centrally and via the opioid-receptors in the skin.[8] Endogenous opioids, including the μ-opioid-receptor (MOR1D), can influence modulation of itch but endogenous opioids are unlikely causative.[9,10] μ-Opioid antagonists exert anti-pruritic effects in some cholestatic patients.[11–15] Naltrexone is recommended as third-line therapy (after cholestyramine and rifampicin) for cholestatic liver diseases (not including ICP) for refractory pruritus.[16,17] Naltrexone use in pregnancy has been described in opioid-use disorder.[18] Available human data are reassuring. Animal studies using higher doses show some developmental changes[19] of uncertain relevance. Severe maternal symptoms in this case necessitated balancing risks of therapy against deteriorating maternal mental health and fetal prematurity. Liver immunohistochemistry points to a potential molecular

genetic aetiology.[20,21] The change in hormonal milieu of pregnancy might potentially mediate the change in phenotype.
Conclusions: Naltrexone can provide relief of symptoms in severe ICP. Liver immunohistochemistry can suggest molecular mechanisms in severe ICP.

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The acceptability and feasibility of implementing a fractional exhaled nitric oxide (FeNO)-based asthma management strategy into antenatal care: The perspective of pregnant women with asthma

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Abstract

Objective: This study aimed to explore the acceptability and feasibility of using Fractional exhaled Nitric Oxide (FeNO)-based asthma management in antenatal care in Australia from the perspective of pregnant women with asthma.
Design: A qualitative descriptive study involving semi-structured interviews with video elicitation.
Setting: Participants were recruited from the antenatal clinics of two tertiary referral hospitals in metropolitan NSW, Australia.
Participants: Eighteen pregnant women, in late gestation, enrolled in the breathing for life trial, a randomized controlled trial of FeNO-based asthma management (n = 11 received FeNO-based management, n = 7 usual care controls).
Measurements: A video demonstrating the use of FeNO in antenatal care was shown to the participants, they were then questioned regarding the acceptability and feasibility of this process. These interviews were digitally recorded, transcribed and analysed using qualitative content analysis.
Findings: Two main themes and eight sub-themes emerged from the data. Theme one was 'Feeling safe' with sub-themes: *Well monitored and managed; Accurately medicated; Increased understanding; Beneficial for me and my baby.* Theme two was 'Should be part of antenatal care' with sub-themes: *Quick and easy; Convenient; Don't mind who does it* and *Better asthma management.* Participants regarded FeNO-based management as quick and easy to do. Those who received the intervention were happy that their asthma was being well managed and expressed confidence in taking their prescribed medications due to being able to see tangible changes in their asthma symptoms and FeNO measurement. Those in the control group also stated they wanted to have their asthma managed in this way. Both groups expressed that they would

not mind which health professional provided the FeNO-based management as long as the staff were trained in the process.

Key conclusions and implications for practice: Pregnant women with asthma regard the FeNO-based asthma management strategy as acceptable as it would help them to 'feel safe'. From the women's perspective it appeared feasible to implement and therefore an implementation strategy should be developed to introduce FeNO-based asthma management into antenatal care.

The P4 Study: Maternal body composition and energy balance following normotensive vs. hypertensive pregnancies

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Abstract

Objectives: The postpartum period is characterised by metabolic demands which alter traditional physiological paradigms. Further complicating this period is a history of hypertensive disorders of pregnancy, particularly preeclampsia and gestational hypertension, which affect 6–8% of pregnancies. Recent studies indicate that the postpartum period is associated with changes in maternal body composition and energy balance; however, it remains unknown as to whether hypertensive disorders of pregnancy influence these associations. The aim of this study was to characterise body composition, energy expenditure, and energy intake within a postpartum population following normotensive and hypertensive pregnancies.

Methods: A cross-sectional study six-months following normotensive ($n = 248$), preeclamptic ($n = 80$), and gestational hypertensive ($n = 18$) pregnancies was conducted as part of the Postpartum Physiology, Psychology and Paediatric follow-up study (P4 Study). Metabolic measurements included: body composition via bioelectrical impedance analysis, 24-h energy expenditure via SenseWear Armbands, and energy intake via a three-day food diary. A reference range for percentage fat mass was constructed and the groups were compared. Hierarchical multiple regression analysis was conducted to examine the association between demographic (e.g. age, ethnicity, pre-pregnancy BMI) and obstetric factors (e.g. parity, breastfeeding status, pregnancy complications), and percentage fat mass at six months postpartum.

Results: The 90% reference range for percentage fat mass six months following a normotensive pregnancy was from 20.9% to 50.5%. Regression analysis revealed high pre-pregnancy BMI to be independently associated with an increased postpartum percentage fat mass ($p < 0.001$). At six months postpartum, women with previous gestational hypertension had a greater percentage fat mass and absolute fat-free mass when compared to normotensive women ($p < 0.001$); however, there was no significant difference in these parameters following preeclampsia. For the 91 women with complete energy balance data (normotensive: $n = 71$, preeclamptic: $n = 20$), daily total energy expenditure was not significantly different. Following preeclampsia, however, women had a lower activity-related energy expenditure ($p = 0.03$) and total energy intake ($p = 0.01$), leading to a more negative energy balance compared to their normotensive counterparts (-2007 kJ/24-h versus -571 kJ/24-h; $p = 0.03$). Both postpartum cohorts recorded a lower carbohydrate and a higher fat intake compared to the recommended dietary guidelines.

Conclusion: The mean percentage fat mass six months following a normotensive pregnancy was at the upper limit of the non-postpartum healthy range. Women with previous gestational hypertension demonstrated a significantly different body composition to normotensive women, characterised by a higher percentage fat mass six months postpartum. There was no significant difference in percentage fat mass following preeclampsia despite a lower activity-related energy expenditure. Furthermore, women with previous preeclampsia were identified as a group at higher risk of insufficient nutrient intake. Additional exploration of the lifestyle factors following hypertensive disorders of pregnancy is essential for the development of protocols aimed at reducing these women's cardiovascular disease risk.

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A new development for Maternal and Fetal Medicine Midwifery care provision in New Zealand

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Abstract

Counties Manukau is one of the New Zealand's fastest growing DHB populations with approximately 120,000 women of child-bearing age living in the area in 2018. It is home to New Zealand's second largest Maaori population and largest population of Pacific people, as well as a fast-growing Asian community. Our population is diverse and vibrant with strong cultural values. This newly developed Maternal and Fetal Medicine (MFM) Midwifery team has changed the way support is provided to women who require specialist care for either themselves or their babies in utero. Midwives within this team have a wealth of primary, secondary and tertiary care experience as well as skills and knowledge gained from both working within this specialist area and from the completion of the role specific orientation and education opportunities. We provide both clinic-based and case loading midwifery care to women and families who require specialist care. Our midwives provide both continuity of care and stream lined care pathways for women accessing either specialist maternal medicine services, fetal medicine services or often both. Midwives work within Specialist clinics offering midwifery support and in the community providing full ante and post natal care for a small caseload of women with complex care needs. We also provide support for community midwifery colleagues in a shared care capacity. This enables them to feel more confident with continuing full care for the women with high risk pregnancies in their caseload. The MFM team consists of four senior midwives, two specialist and two specialty midwives. They are part of a larger specialist team which includes our dedicated diabetes in Pregnancy Midwifery Team, plus a midwife dedicated to the care of women based at Auckland Regional Women's Correctional Facility.

The orientation programme required to be completed by each team member is rigorous and role specific. It focuses on both the roles and requirements of their position as well as in gaining knowledge of the external agencies and professionals that may be part of each woman's care package. Alongside, this is the expectation that each team member with complete the MFM Specific Complex Care Course through Auckland University of Technology, within the first year of employment. This course not only provides a comprehensive research and education background to the role but also allows for participants to gain experiential knowledge of the services that wrap around the women in their care through the 100 h of compulsory practicum placements. There is also an on-going Education Credentialing pathway ensuring that both practical skills and knowledge are researched based and up to date. This also provides a clear and formal career progression pathway is in place for midwives within the team.

Picking preeclampsia with pre-pregnancy proteinuria

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Abstract
Background: The diagnosis of preeclampsia in women with underlying kidney disease is complicated by physiological changes in proteinuria, renal function and blood pressure during healthy pregnancy. While it is known that diabetic nephropathy may be associated with a significant increase in proteinuria during pregnancy in the absence of preeclampsia, little is known regarding the progression of proteinuria in chronic kidney disease of other aetiologies.
Aim: To assess changes in urine protein:creatinine ratio (uPCR) in a variety of causes of chronic kidney disease, particularly as to whether the degree of change may be useful in the diagnosis of preeclampsia.
Methods: A retrospective audit of changes in uPCR in 68 pregnancies to women with preconception proteinuria. Greater than doubling of proteinuria was arbitrarily chosen as being significant based on physiological changes in healthy pregnancy.
Results: In 51 pregnancies (75%), the peak uPCR in the second half of pregnancy was less than double the value at the start of pregnancy. Where a greater than doubling of uPCR was seen, 12 of 17 women (70%) were judged clinically to have superimposed preeclampsia, three women had a flare in lupus nephritis, and two had diabetic nephropathy.
Conclusion: Larger studies of women with pregnancies complicated by chronic kidney disease would be valuable to determine whether changes in uPCR may be of value in the diagnosis of superimposed preeclampsia in women with chronic kidney disease with proteinuria.

Anaemia in CKD pregnancy

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Abstract
Aim: To determine the incidence, assessment and treatment of anaemia in pregnancy in women with chronic kidney disease (CKD).
Methods: A retrospective audit of the incidence, management and outcomes of anaemia in 63 pregnancies in 52 women with CKD at a tertiary referral obstetric hospital between January 2003 and December 2017 was performed.
Results: First trimester se creatinine was 90–129 mmol/L in 36 pregnancies (57%), 130–179 mmol/L in 13 pregnancies (21%), greater than 180 mmol/L but not yet receiving dialysis in nine pregnancies (14%), and five women (8%) were receiving dialysis prior to conception. Seventy-six per cent of these pregnancies were complicated by anaemia, which was severe in 14% of pregnancies. Results for serum ferritin were available for only 39 pregnancies (62%). In 37 of these 39 measures (95%), the serum ferritin was less than 100 ng/mL. Erythropoiesis stimulating agents (ESA) were used in 28% of mild, 38% of moderate, and 44% of severe (non-dialysis) CKD pregnancies without complication. FeI was administered in only nine non-dialysis pregnancies, all in third trimester, at a mean gestation of 28 weeks of gestation. Six of these were after 2014 when iron carboxymaltose became available. Mean increment in Hb with simultaneous ESA and FeI was from 84 to 109 g/L, from 81 to 105 g/L with ESA alone, and from 100 to 118 g/L with FeI alone. Severe anaemia was associated with earlier gestation and lower birthweight.
Conclusions: The cohort was remarkable for a low rate of testing for iron deficiency and low rates of FeI. Possible explanations include the primary medical care of women being by obstetric staff and not renal physicians, and concerns regarding the risk of anaphylaxis with older FeI preparations prior to 2014. Regular surveillance for iron deficiency and anaemia is indicated throughout pregnancy. FeI with low doses may be reasonable in first trimester given the absence of teratogenic effect in dialysis patients. Trials of lactoferrin in CKD pregnancy with iron deficiency may also be useful given high rates of non-adherence with oral iron.

Should POCUS be part of the bedside assessment in women with severe preeclampsia?

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Abstract
Pleural effusions and ascites are signs of severe preeclampsia and regarded as an indication for delivery given the potential for rapid progression and maternal respiratory compromise. Pleural effusions have been reported in 26% of women with severe preeclampsia and ascites in 21–30% of women with severe preeclampsia.[1] Ascites was observed in 76% of women with HELLP syndrome or acute fatty liver of pregnancy.[2] In a matched cohort study, maternal ascites in severe preeclampsia was an independent risk factor for maternal adverse outcome (RR 4.6) and perinatal adverse outcome (RR 2.1) compared with women with severe PET without ascites.[3] Point-of-care ultrasound (POCUS) is a rapid, effective, repeatable and safe diagnostic tool which may be performed at the bedside without exposure to ionizing radiation. An observational pilot study of 150 healthy parturients between 36 and 38 weeks of gestation found the lung ultrasound pattern matched the physiological pattern in non-pregnant women, suggesting lung US is a feasible and helpful diagnostic tool in pregnancy.[4] Cardiogenic pulmonary oedema may be differentiated from non-cardiogenic causes of dyspnoea on POCUS with a sensitivity of 94% and specificity of 92%.[5] Studies evaluating the potential role of POCUS in assessing severity of preeclampsia may be useful.

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An initiating mentorship program for pregnant women using a buddy system in Probolinggo, Indonesia: A pilot study

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Abstract
Introduction: The high maternal and infant mortality rate is a continuing problem in Indonesia. Many programs have been conducted by the government, such as the distribution of guideline books (KIA books) and performing pregnancy classes. However, the level of knowledge and awareness of pregnant women is still lacking especially in rural area. Besides, the small number of health providers and facilities available in the rural area also complicate the situation.
Purpose: (1) To increase the knowledge of pregnant women. (2) To provide an optimal support system for pregnant women.
Methods: The mentorship program was started with a pretest to assess the basic knowledge of pregnant women in Condong area, Probolinggo. The participants were paired based on their residence, education level, and risk level based on the *Poedji Rochjati* score. Each participant was arranged to perform a discussion with their partner using the KIA books. After that, a post-test was performed. Each pair was then tasked to do an independent discussion session at home within one week. A discussion material was provided. This activity aimed to assess the compliance of the participants and whether there is any direct positive impact. The participants were given a reference card, named 'Buddy card', as a guideline for the activity. The Buddy card contains important information for their pregnancy and also helps them to establish bonding with their partners. A questionnaire was given to assess their acceptance and attitude towards the buddy system.
Result: Of all participants (n = 8) following the complete procedure, it was known that the education levels varied, with majority of the participant are junior high school graduate. One person is paired with a cadre. Based on the post-test results, it was known that there was a pattern of increased knowledge with an average of 21.25% after the discussion (mean post-test: 93.75/100). Eleven people conducted an independent study session at home and showed improvement in their daily nutritional intake. Three women were recruited by cadre during home visit. Based on the Buddy card, it was discovered that the majority of participants were not aware of their emergency and personal telephone numbers, estimated dates and plans of deliveries. The majority of participants admitted that they never read the KIA books. The results of the questionnaire showed that the majority of participants had positive responses to the mentorship program.
Conclusion: This program showed benefit in increasing knowledge and providing a good support system for pregnant women. This activity received positive responses and therefore has a potential to be developed with a greater number of participants.

Scurvy in pregnancy as a result of bariatric surgery, disordered eating pattern and poor antenatal attendance

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Abstract
Background: Scurvy, the clinical syndrome of Vitamin C deficiency, is uncommon. It is associated with malabsorption syndromes, malnutrition, alcoholism, drug abuse, pregnancy/breast feeding and elderly patients. Vitamin C is an antioxidant and an important enzyme for collagen synthesis and prevention of tissue breakdown. Intake is generally met but content can be destroyed with cooking. It is also reported in post-bariatric surgery when altered eating patterns result in low supplement. Clinical presentation includes asthenia, mood disturbances, arthralgia, myalgia, gingival hypertrophy, spontaneous bleeding with subsequent anemia and in severe cases jaundice, fever and visceral bleeding. As clinical improvement can take four weeks, prompt diagnosis with timely replacement of Vitamin C in deficient patients is important.
Case presentation: A G2P0, 24-year-old 37/40 female with poor antenatal care was referred to obstetric medicine clinic for investigation of easy bruising for weeks. Medical history revealed gastric banding for morbid obesity, childhood trauma, domestic violence and previous THC use. She had a fetal death in utero at 20/40, two years ago. Her diet was poor; mainly fast food, minimal vegetable and fruit intake. Pertinent examination findings were BMI 35, pale skin and multiple ecchymosis over her upper and lower limbs. Severe nutritional deficiency was suspected. Multivitamins and Vitamin C were commenced immediately.
Investigations: Investigations revealed microcytic anemia, Vitamin B12, C, and D deficiency. Hb 105 g/L, MCV 78, Ferritin 5ug/L, Transferrin saturation 5%, Vitamin B12 Holo Asssay 33 pmol/L (>36), Vitamin C < 5 μmol/L (10–115), Vitamin D 49 nmol/L (>50). Folate, coagulation profile, liver and renal function tests were normal.
Treatment, outcome and follow-up: The woman was given an iron infusion, dietary advice and Vitamin D. She had an uncomplicated delivery at 39 weeks via C/section to a healthy 3.2 kg infant. She did not attend postnatal appointments. Her General Practitioner was informed with recommendations for follow-up.
Discussion: Adequate intake of macronutrients and micronutrients are essential during pregnancy to support maternal health and fetal growth and development. Following bariatric surgery, pregnant women are at greater risk of micronutrient (iron, folate, fat soluble vitamins) deficiencies. A joint 2013 clinical guideline recommended that women avoid conception 12 to 18 months after bariatric surgery to minimize potential adverse effect of post bariatric surgical nutritional deficiencies. Screening, dietetic input and close monitoring of pregnant women for nutritional deficiencies with timely and adequate supplementation is important throughout pregnancy and the postpartum period. Our case highlights a unique presentation of significant nutritional deficiencies in late pregnancy post gastric banding and poor antenatal attendance. Scurvy should be strongly considered in patients with spontaneous ecchymosis, especially in context of bariatric surgery. Untreated scurvy can increase morbidity and mortality during delivery. Prompt diagnosis and initiation of vitamin C is needed for rapid symptom resolution.

Anti-thrombotic and anti-platelet therapy and their influence on placental cell-free DNA release

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Abstract
Introduction: Anti-thrombotic and anti-platelet therapy have been implicated to improve pregnancy outcomes by promoting cell survival in placenta and restoring normal placental function. This has been suggested to be a possible cause for the increased rates of failed non-invasive prenatal testing results due to a low fetal fraction. This study aimed to measure cell-free DNA (cfDNA) release from placental tissue in vitro when treated with anti-thrombotic and anti-platelets drugs with the hypothesis that there will be a decrease in cfDNA release when treated with these drugs.
Methods: Healthy pregnant women presenting for term caesarean delivery at The Mercy Hospital for Women and Northern Health were recruited for this study. Human placental explants were cultured and treated in media containing various concentrations of enoxaparin (Clexane), aspirin, clopidogrel, prasugrel and ticagrelor. After 24 h of incubation, cfDNA was extracted from the media using the QIAGAN™ Qiaamp Circulating Nucleic Acid Kit, quantified using NanoDrop Microvolume Spectrophotometer and normalized to explant weight. Results were analysed on GraphPad Prism 7.0 software, using ANOVA (non-parametric), $p < 0.05$ was statistically significant.
Results: Five participants were included in this study for five samples of placental explants. Treatment of placental explants with 4.0 IU/ml Clexane caused a significant increase in the relative amount of cfDNA released compared to untreated control and other Clexane doses ($p = 0.009$). There were no statistically significant differences in amount of cfDNA release in other drug treatments.
Discussion: Clexane caused a significant increase in the amount of cfDNA released from placental explants contrary to our initial hypothesis, indicating a more complicated relationship between anti-thrombotic therapy and cfDNA release other than influencing cell survival. Further investigations are required to determine the underlying mechanisms in which anti-thrombotic therapy is involved in.

Management of hepatitis C infection in pregnancy

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Abstract
Hepatitis C is a chronic viral infection that causes liver fibrosis and steatosis, with cirrhosis occurring in 20% of untreated cases. It is most commonly spread by intravenous drug use, but is also seen in people from endemic areas. Until recently, hepatitis C affected approximately 1% of the Australian population, but this has reduced significantly with the funding and widespread prescribing of direct acting antiviral agents. Many people are unaware that they have hepatitis C, and pregnancy may be an opportunity to engage them in their own healthcare. At this stage, antiviral therapy for hepatitis C is not recommended during pregnancy (category B), although trials are occurring in the third trimester. The perinatal transmission rate is approximately 5%. There is an increased rate of preterm delivery, intrauterine fetal death, and low birth weight; however, this may be due to common associations with poor perinatal care, and drug and alcohol use. There is an association of chronic hepatitis C infection with intrahepatic cholestasis of pregnancy, and an association with poorer neonatal outcomes.

Cerebral venous thrombosis, a misdiagnosis with MR-venography

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Abstract
We present the case of a 28-year-old G3P2, referred with acute on chronic headache with associated visual disturbance at 30 weeks of gestation. The pregnancy was complicated by caesarean section scar implantation with thin anterior segment necessitating prolonged inpatient admission and gestational hypertension from k28. Medical history was significant for chronic headache with normal MRI brain three years prior, obesity (BMI 49), non-alcoholic fatty liver disease and depression. Medications included labetalol, folic acid, aspirin, moclobemide and prophylactic sodium heparin, 7500 IU twice daily. Physical examination revealed no neurological deficit, normal fundoscopy and no features of pre-eclampsia. The headache worsened and was investigated with time-of-flight MR-venography (MRV) which was reported to show a nonocclusive thrombus within the distal right transverse sinus, sigmoid sinus and right jugular vein. IV heparin was commenced for treatment of acute cerebral venous thrombosis. Ultrasound of her right internal jugular vein revealed a patent vein. Given the discrepancy, a CT head and venogram was performed, which showed no dural venous thrombus, indicating a false positive MR-venogram. The incidence of cerebral venous thrombosis (CVT) in pregnancy ranges from 1 in 2500 to 1 in 10,000 deliveries in Western countries[1–3] and 2% of pregnancy-associated strokes are attributable to CVT.[4] The majority occur in the puerperium.[3] Clinical features are highly variable and non-specific, with headache being the most frequent presenting symptom.[5] CT-venography (CT-V) or non-contrast time-of-flight MR-venography (TOF-MRV) are used for diagnosis in the pregnant woman. Studies have indicated sensitivity and specificity of 95% and 91%, respectively, for CT-venogram compared to digital subtraction angiography. CT-V is not prone to flow-related artefacts unlike TOF-MRV. Various image artefacts have been described for TOF-MRV, mimicking cerebral venous sinus thrombosis. These include in-plane saturation of spins and physiologic variants. A comparative evaluation of two-dimensional (2D) time-of-flight and three-dimensional (3D) contrast enhanced MRV revealed a sensitivity/specificity of 71.4%/55.6% for 2D TOF-MRV compared to 85.7%/97.2% with 3D MRV,[6] the latter of which is contraindicated in pregnancy. If TOF-MRV is utilised for diagnosis, multiple planes need to be acquired to adequately assess the abnormal flow in different sequences to confirm the presence of CVT. Radiation risk is a possible reason why MR-V may appear more appealing in the pregnant woman; however, the estimated fetal dose from a CT head according to Australian Guidelines is less than 0.005 mSv.[7] This case highlights the limitations and potential for false positive results if using TOF-MRV to diagnose cerebral venous thrombosis in pregnancy. Given potential risks of treatment dose anticoagulation, it is imperative to have a correct diagnosis. We suggest that CT-venogram should be used in the first instance for investigation of CVT, particularly when there is no focal neurological deficit.

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A mediastinal mass with severe superior vena cava compression

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Abstract

A 33-year-old G3P1 at 33 weeks of gestation presented with a two-week history of dry cough, orthopnea and upper limb swelling. The pregnancy was uncomplicated to date. She had no medical history or regular medications. On examination, facial and upper limb swelling, chest wall venous distention and a positive Pemberton's sign was noted. CT chest with contrast revealed a large soft tissue anterior mediastinal mass measuring $92 \times 50 \times 64$ mm, encasing the great vessels in the superior mediastinum, with superior vena cava compressed to a maximum diameter of 1 mm. Intravenous dexamethasone was commenced. A multidisciplinary team approach was undertaken with input from obstetrics, obstetric medicine, haematology, anaesthetics, cardiothoracic surgery and neonatology. Decision was made to postpone delivery and await urgent tissue diagnosis. A CT guided biopsy of the mediastinal mass was performed; histopathology revealed primary mediastinal large B-cell lymphoma (PMBCL). Steroids were continued in attempt to decrease the size of the mass. It was unchanged in size on imaging five days later. Management options included delivery vs. commencement of chemotherapy. Gestation and concern for fluid load required for chemotherapy in the setting of a 1 mm SVC were key factors in guiding management. The woman delivered a healthy baby via caesarean section with regional anaesthesia eight days post initial presentation. CHOEP-chemotherapy was commenced one-week post-partum. Maternal malignancy in pregnancy is rare, affecting 0.1% of pregnancies. Lymphoma is the fourth most common cancer in pregnancy, but the most frequent haematological malignancy.[1] Mediastinal tumours can initially cause symptoms and signs that can mimic normal pregnancy. PMBCL is a subtype of diffuse large B-cell lymphoma mainly affecting young females often presenting as bulky mediastinal tumour with compressive symptoms.[2,3] Fifty per cent present with superior vena cava syndrome.[2,4] PMBCL in pregnancy is rare, consequently there is little evidence surrounding the optimal management. Cytotoxic agents cross the placenta and decision to administer chemotherapy in pregnancy is complex and is based on tumour grade and gestation. Patients presenting in the first trimester requiring chemotherapy will often undergo termination due to teratogenesis but case reports of chemotherapy regimens including cyclophosphamide, doxorubicin, vincristine, prednisolone in the second and third trimesters appear to have acceptable maternal and fetal outcomes.[5,6] This case presents unique anaesthetic considerations, further highlighting the importance of MDT approach. General anaesthesia is widely accepted not to be an option due to concern for circulatory collapse and airway obstruction.[7,8] The diagnosis of lymphoma during pregnancy poses significant management challenges necessitating consideration of the fetus without compromising potential curative therapy for the mother. This case highlights the challenges of mediastinal masses in pregnancy and the importance of a multidisciplinary approach to malignancy in pregnancy.

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Evaluation of global coagulation assays for assessment of clotting function and risk of venous thromboembolism in pregnancy

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Abstract

Introduction: Women are at higher risk of venous thromboembolism (VTE) in pregnancy and postpartum. Current routine coagulation tests cannot discern the physiological hypercoagulability of pregnancy. Global coagulation assays (GCA) including thromboelastography (TEG), thrombin generation assay using calibrated automated thrombography (CAT) and fibrin generation assay using the overall haemostatic potential assay

(OHP) may be more representative of the coagulation process. We aim to evaluate the ability of GCA to detect the hypercoagulability of pregnancy and differentiate coagulability amongst pregnant women of varying VTE risk profile, with particular respect to BMI.

Methods: Women undergoing term elective caesarean section at a level 5 maternity hospital provided a single pre-operative blood sample for routine baseline blood tests and experimental testing with TEG, CAT and OHP. Data from 47 healthy non-pregnant women aged 18–45 years were used as controls. GCA results were compared between the pregnant and non-pregnant cohorts, and within the pregnant cohort by BMI category and antenatal VTE risk category, calculated using the Royal College of Obstetricians & Gynaecologists (RCOG) thromboprophylaxis risk assessment and management guidelines.[1] Data were analysed with SPSS using the Shapiro–Wilk, independent t-test, Mann–Whitney U test and a generalised linear regression model.

Results: Sixty women with term singleton pregnancies were included; 41.7% (n = 25) were obese (≥30 kg/m^2) at booking and 88.3% (n = 53) were multiparous. APTT and INR remained within normal range in pregnancy, while 98.3% (n = 59) had D-dimer level above the critical level of 500 mg/L as expected. Most GCA parameters were significantly more hypercoagulable in pregnant women compared to non-pregnant controls, particularly with increased maximum amplitude (clot strength) ($p < 0.001$), endogenous thrombin potential ($p < 0.001$) and fibrin generation ($p < 0.001$). Pregnant women with booking BMI ≥30 kg/m^2 had significantly higher maximum amplitude on TEG compared to pregnant women of normal BMI (18.5–25 kg/m^2) ($p < 0.001$). Statistical significance was maintained after controlling for age, parity, smoking status and diabetes. GCA parameters did not differ when comparing women of high and intermediate VTE risk with women of low risk, as determined by the RCOG clinical VTE risk assessment.

Discussion: GCA are able to detect the hypercoagulability of pregnancy and may potentially correlate with obesity in the pregnant population. GCA hold promise for understanding the mechanisms underlying the relationship between BMI and VTE risk during pregnancy. In the future, they may be used as adjuncts to risk factor-based criteria for VTE thromboprophylaxis during pregnancy and the puerperium.

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Dietary trends in Australian pregnant women: A MUMS sub-study

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Abstract

Introduction: Maternal dietary habits can directly affect the growing fetus. As dietary patterns are influenced by food availability and sociocultural factors, it is important to assess nutrient intake in an Australian population. The Australian Eating Survey (AES) is a food frequency questionnaire developed to assess dietary intake in Australian adults, providing a panel of macro- and micro-nutrients.

Table 1. Nutrient profiles in MUMS cohort, Trimester 1 and Trimester 3.

	Pregnancy trimesters			
	n	T1	n	T3
Energy (kJ)	86	7875.1 ± 2595.6	76	8485.2 ± 2489.8
Protein (g)		87.8 ± 36.7		94.3 ± 32.7
Fat (g)		71.5 ± 26.9		79.5 ± 26.2
Carbohydrate (g)		209.7 ± 70.0		223.9 ± 74.1
Sugar (g)		98.7 ± 46.1		114.6 ± 46.7
Fibre (g)		25.1 ± 9.6		24.8 ± 8.2
Vitamin C (mg)		152.4 ± 76.2		143.1 ± 60.2
Folate (Ng)		284.6 ± 107.4		285.8 ± 92.1
Magnesium (mg)		363.5 ± 107.2		387.3 ± 95.6
Calcium (mg)		995.7 ± 338.6		1176.8 ± 358.5
Iron (mg)		11.8 ± 4.4		12.2 ± 3.8
Zinc (mg)		11.6 ± 4.8		12.4 ± 4.3

Aims:

(1) To examine macro-nutrient and micro-nutrient intake in a longitudinal cohort of Australian pregnant women.
(2) To explore relationships between nutrient intake, body mass index (BMI), ethnicity and parity.
(3) Assess associations of average nutrient intake with the development of pregnancy complications: gestational diabetes mellitus (GDM), preeclampsia and gestational hypertension (GH).

Methods: A total of 117 women were recruited into the MUMS prospective longitudinal cohort at <13 weeks of gestation. Demographic data, including ethnicity, parity and BMI, was collected. The AES was emailed to participants at T1 and T3. Energy, protein, fat, carbohydrate, sugar, fibre, vitamin C, folate, magnesium, calcium, iron and zinc were examined. After descriptive analysis, linear mixed models were used to assess changes in nutrient profile from early to late pregnancy and correlations between demographic variables and individual nutrients. Generalised linear mixed model logistic regression was used to assess correlations of average nutrient intake with pregnancy complication development, presented as odds ratio (OR) with confidence interval (CI).

Results: Eighty-six of one hundred and seventeen surveys were completed following T1 visits (74%), 76/98 following T3 (78%). Forty-five women (38%) were high-risk due to pre-existing diabetes or hypertension, BMI ≥ 30, or past GDM or hypertension; 24 women had BMI ≥ 30 in T1 (21%), 39% were nulliparous, 57% were of Caucasian ethnicity and 24% Asian. Seventeen (15%) developed GDM, six (5%) developed preeclampsia and six (5%) developed GH. Descriptive nutrient statistics are shown in Table 1. Calcium intake increased most significantly, by approximately 20% ($p < 0.001$), fat intake increased by approximately 10% ($p = 0.018$), and sugar intake increased by approximately 15% ($p = 0.024$) between T1 and T3. In comparison to Caucasian subjects (reference group), Asian subjects consumed significantly more protein throughout pregnancy, estimated marginal mean 88.8 g vs. 106.3 g ($p = 0.031$). Increased GDM risk was associated with increased protein intake during pregnancy ($p = 0.037$, OR = 1.013, CI = 1.011–1.025) and increased zinc intake during pregnancy ($p = 0.036$, OR = 1.102, CI 1.006–1.207). Decreased preeclampsia risk was associated with increased calcium intake during pregnancy ($p = 0.046$, OR = 0.997, CI = 0.944–1.000).

Conclusion: In the MUMS cohort, some components of dietary intake changed modestly but statistically significantly from T1 to T3, with little relationship to BMI, ethnicity, or parity. Higher protein and zinc intake were associated with high GDM risk and higher calcium intake was moderately associated with lower preeclampsia risk. Relationship of nutrient intake patterns to microbial dysbiosis and pathological pregnancy outcomes is to be further studied in this cohort.

Cirrhosis/liver failure/liver transplants in pregnancy

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Abstract
Pregnancies in women with portal hypertension with and without cirrhosis have become more frequent. Treatment and management options for cirrhosis and portal hypertension have improved significantly as has management of infertility. Nevertheless, pregnancies in these women are associated with increase maternal and fetal risks. There is an increased risk of life-threatening hepatic decompensation and variceal bleeding due to physiological changes that occur in pregnancy. Pre-pregnancy planning is important for identification of women at high risk of adverse events. Pre-pregnancy planning also offers the opportunity for diagnosis and management of oesophageal varices and splenic artery aneurysms; with the aim of decreasing antepartum complications. These women should be managed at a tertiary referral centre with access to a multidisciplinary team. In women at high risk of varices endoscopy should be performed in the second trimester. Peri-partum planning and decisions involving mode of delivery need to be individualised to the clinical situation. Rates of peripartum haemorrhage are increased due to clotting abnormalities, thrombocytopenia and pelvic varices: active management of the third stage and close monitoring post-partum are recommended.

Thrombolysis in pregnancy: A case report and a literature review

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Abstract
Background: Physiological hypercoagulable state during pregnancy is thought to be the cause of the higher rates of thrombotic complications such as deep vein thrombosis and pulmonary embolism (PE) during pregnancy, some of which may be life-threatening. In the non-pregnant woman, the current guidelines suggest thrombolysis as the primary treatment in PE with haemodynamic compromise or shock. There is no available data from randomised controlled trials in pregnancy and information about safety of thrombolytics in pregnancy is sparse.
Case: A 35-year-old woman was brought in by ambulance with collapse and haemodynamic instability. She was 13 weeks pregnant with no complications up to that point. A bedside ultrasound in Emergency Department showed features of PE, and computed tomography pulmonary angiography (CTPA) confirmed large volume, acute bilateral pulmonary emboli involving both main pulmonary arteries extending into all lung lobes with features of right heart strain. The initial plan was to perform an embolectomy for assumed fear of thrombolysis resulting in pregnancy loss, so the woman was transferred to a tertiary centre where interventional radiology was available. Upon arrival to the tertiary centre, a decision was made for thrombolisation instead due to the woman being haemodynamically unstable. A 10 mg bolus of Alteplase was given intravenously followed by a 90 mg infusion over 2 h. Heparin infusion was commenced targeting activated partial thromboplastin time as per PE protocol. Patient made good progress following thrombolysis with signs of resolution on the follow-up echocardiogram. At 36 weeks five days of gestation, a healthy child was delivered with NVD.
Discussion: A review of the literature revealed 158 previously reported cases of pregnant women with serious thrombotic events, all of whom received some form of thrombotic treatment. Including our case, four maternal deaths (2.5%), 13 major bleeding episodes (8.1%), 14 mild/moderate bleeding episodes (8.8%), three fetal death (1.9%), one neonatal death (0.6%) and 11 miscarriages (6.9%) were described. This shows that the use of thrombolytic agents in pregnancy is associated with a relatively low reported complication rate, especially given the severe medical conditions for which they are indicated. Most importantly, the complication rate of thrombolytic treatment does not seem higher in pregnant women in comparison to the general population. Poor fetal outcome was associated with mothers with poor prognosis. These findings underscore the safety and efficacy of thrombolysis, which remains the only life-saving therapeutic method immediately available in severe forms of thrombotic events during pregnancy. However, caution should be exercised when drawing conclusions regarding maternal and fetal safety, given the lack of controlled clinical trials including pregnant women and the nature of the weak evidence level of the cumulative data presented in this review. Specific consensus recommendations are needed in the use of thrombolytics in pregnancy.

Risk stratification of pregnancy in women with heart disease

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Abstract
Pregnancy and childbirth are as safe in Australia and New Zealand as anywhere in the world. However, cardiovascular disease during pregnancy and peripartum remains a leading cause of maternal mortality and is associated with substantial morbidity. Cardiovascular disease affecting pregnancy is a diverse problem that includes a wide range of congenital and acquired diagnoses with differing prognostic implications. This talk will focus on models of risk stratification as a basis for multidisciplinary care to achieve best practice and outcomes. Disease-based and physiology-based models of risk stratification will be discussed with illustrative cases.

Iron deficiency and anaemia in pregnancy: Diagnosis and solutions

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Abstract
Iron deficiency and anaemia are highly prevalent conditions in pregnancy, especially in women in low-income countries. This presentation will explore the clinical implications of these conditions in pregnancy. The biology of iron homeostasis in pregnancy will be described. Approaches to testing for iron deficiency in pregnancy will be discussed. Prevention and treatment using iron interventions will be described. Finally, emerging studies providing evidence for iron interventions in pregnancy will be presented.

New-onset lupus nephritis in pregnancy

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Abstract

New diagnosis of systemic lupus erythematosus in pregnancy is uncommon with only a few published case series.[1–5] Compared with non-pregnant cohorts, atypical presentations are common, with lupus nephritis (LN) as the presenting diagnosis up to 66% of cases.[3,5] Differential diagnoses for new onset renal disease in pregnancy are wide-ranging and include more common forms of primary glomerular disease in reproductive age women including IgA nephropathy, focal segmental glomerulosclerosis, minimal change disease and membranous nephropathy.[7] In addition, early onset pre-eclampsia is an important differential diagnoses. Active lupus nephritis in pregnancy is associated with significantly increased risks of adverse obstetric outcomes[6] and it is therefore critically important to ascertain cause of nephropathy in antenatal women to allow institution of optimal management. The American College of Rheumatologists recommends that patients with clinical evidence of active LN undergo a renal biopsy so as to classify glomerular disease[8]; however, the procedure is noted to be associated with a significant increase in risk profile when performed during pregnancy. A 2013 systematic review of renal biopsies performed in pregnancy reported a 2% risk of major complications, including major bleeding and large peri-renal haematoma requiring transfusion. On the other hand, the study also identified therapeutic changes based on renal biopsy results in 66.1% of patients.[9] We present a case of a 27-year-old G3P0 who presented at 15 weeks of gestation with borderline hypertension (140/90) and severe proteinuria with a protein creatinine ratio of >600. She was asymptomatic of her blood pressure and her examination was unremarkable. Her medical history included Hashimoto's thyroid disease treated with thyroxine. Her creatinine levels pre-pregnancy and at presentation were normal; albumin was borderline low and a 24 h urinary protein was 2.86 g. The woman was subsequently referred to our tertiary centre and assessed in the combined renal-obstetric clinic. She underwent a renal ultrasound, which excluded renal artery stenosis, and autoimmune workup which revealed a positive ANA titre and lupus anticoagulant. Methyldopa was commenced for hypertension management and the woman was counselled regarding the benefits and risks of a renal biopsy in pregnancy which was undertaken without complication at 18 weeks of gestation. The biopsy result showed LN and the woman was commenced on prednisone, azathioprine and hydroxychloroquine with good control of disease and kidney function. The pregnancy was further complicated by gestational diabetes requiring insulin. Labour was induced at 36 weeks of gestation due to worsening blood pressure and superimposed preeclampsia. The woman proceeded to a caesarean section due to labour dystocia with delivery of a well-grown infant. Renal function and blood pressure improved with treatment postpartum and both mother and baby are doing well.

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Non-invasive cardiac and haemodynamic measurement for prediction of pre-eclampsia in high-risk women

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Abstract

Background: Preeclampsia is a disease of pregnancy, with the potential to cause significant maternal and fetal morbidity and mortality. Pregnant women with essential hypertension or gestational hypertension have a 20–25% risk of developing superimposed preeclampsia, well above the baseline 4% risk. Currently, there is no reliable method of predicting which of these women will develop preeclampsia. Cardiac output and peripheral vascular resistance may be useful parameters to predict preeclampsia. A non-invasive continuous-wave 2D Doppler (USCOM1) is available to measure cardiac parameters conveniently at the bedside. This is performed via a probe placed at the suprasternal notch measuring velocity time integrals of transaortic blood flood at the left ventricular outflow tract. Utilising an anthropometric algorithm incorporating the patient's height and the LVOT readings, stroke volume and cardiac output can be calculated. The USCOM machine has been validated for use in this population. Preliminary studies have shown changes in haemodynamic parameters in women who develop preeclampsia including increased systemic vascular resistance, lower cardiac output, increased systemic vascular resistance index and reduced cardiac index. A prospective observational study performed at a single-centre St George Hospital in Kogarah assessed women recruited from high-risk obstetric clinics, those attending day assessment unit and inpatients. The women undertook written informed consent prior to testing and completed a comprehensive health questionnaire inclusive of all past obstetric and medical history, medications, smoking history, booking blood pressure readings and ethnicity. Only women above 18 years of age were included and were excluded if they had underlying comorbid cardiac or renal disease. Control groups of normal pregnant women were recruited from antenatal clinic, and non-pregnant women of child-bearing age were recruited from amongst hospital staff. A period of 5 min of physical inactivity was required prior to the testing and pregnant women were positioned at 15° to avoid compression

of the SVC. All pregnancy outcome data were collected on women and their babies including birth weight, mode of delivery, gestation at delivery and need for antihypertensive medications. Records were made of women who demonstrated more severe features of pre-eclampsia.
Results: A total of 109 women with either EH or GH were recruited in the study, of which 32 developed PE. The women were similar at baseline with similar demographics. Our data failed to demonstrate a difference in any of the measured haemodynamic parameters between the women who did and did not go on to develop pre-eclampsia. The high rates of women medicated in this study may have influenced these results.

Case report: Operative management of hysterectomy in placenta increta

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Abstract
Placenta increta is an abnormal attachment of placenta in the myometrium. The incidence of placenta increta increases along with the increase rate of caesarean section. This condition can increase maternal morbidity and mortality due to postpartum hemorrhage. A 37-year-old postpartum female via vaginal delivery underwent an abdominal hysterectomy due to postpartum hemorrhage as a result of an abnormal attachment of the placenta. Ultrasonography showed that the placenta was implanted in the myometrium. Post-operative condition of the woman was good and showed no signs of abnormality.

There's a tweet for that – A hitchhiker's guide to Social Media in Obstetric Medicine

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Abstract
Social Media (SoMe) is an exciting innovation in clinical medicine presenting an unprecedented opportunity to share healthcare-related knowledge. Convectional research dissemination platforms like scientific journals are increasingly relying on innovative approaches to interact with their target audience, like the popularity of Visual Abstracts. SoMe has influenced how medical content is accessed by physicians, and patients, ultimately breaking down barriers across the world. In a time of easy-access information, making sense of the landscape and be challenging. The concepts of SoMe existed long before the acronym, yet, names are important to making ideas stick. Physicians' knowledge and use of SoMe platforms like Twitter has been steadily increasing across all specialities. The use of SoMe platforms like Twitter during conferences has gained increasing popularity in the medical community. There are many benefits including immediate and widespread dissemination of information, collaboration and engagement, spur discussions leading to new research questions and sharing data. Despite the increasing use of SoMe and the general integration in the routine clinical space, there remains some hesitancy at an individual level. Healthcare professionals have concerns about the use of SoMe pertaining to professionalism and privacy which are just. There has been an increasing number of articles about the strategies and professional standards of using platforms like Twitter. Obstetric Medicine strengthens and brings together the expertise of general and specialist physicians with that of obstetricians and midwives. The commendable feature of this discipline is that innately instils collaboration, something that will lend itself well to SoMe. We have come a long way from September 2008, when the first ever journal to focus on Medicine in Pregnancy – Obstetric Medicine Journal – was published. It has served as a source of information, exchange of ideas and stimulus to further conversations over the years. Medicine is now digital – it no longer is 'if' we should embrace SoMe but 'how' we do it. They are adjuncts, not replacements for current medical education approaches, and have an exciting future. Just as health coalitions work to disseminate key messages through traditional media, the use of SoMe could extend this beyond into the greater medical community and public alike, becoming an important public health tool.

Obesity in pregnancy

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Abstract
Obesity has a significant impact on fertility, perinatal outcomes, and the subsequent health of both mother and child. The rising prevalence of obesity presents the health service with many challenges, and our current care of the obese and morbidly obese patient is arguably 'wanting'. We remain somewhat haphazard and 'blunt' in many aspects of our care, and we can do better. Optimising care of the overweight woman in pregnancy is much more than simply determining if a BMI does or does not exceed your bariatric capability, and many strategies that we know can improve outcomes are being under-utilised. Pregnancy presents a 'window in care' that can impact on the future health of mother and child, and we are not yet making the most of the opportunity. The presentation will summarise what we know of the obstetric and health associations with increasing levels of obesity in pregnancy, review what managements have been shown to improve perinatal and health outcomes, and examine what needs to change. The specific care needs of the pregnant woman with extreme morbid obesity in pregnancy will also be discussed.

Maternal ketones in gestational diabetes mellitus: A clinical practice survey

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Abstract
Background: Elevated maternal ketones in women with GDM have been associated with low IQ in the offspring. There is currently a lack of guidance on how to manage elevated ketones in pregnancy. This study assessed whether clinicians review maternal ketones and change management accordingly.
Methods: Clinicians caring for women with GDM were surveyed about their clinical practice regarding maternal ketones. Data were collected on the measurement of ketones during pregnancy and whether levels alter patient management.

Results: One hundred and nine clinicians were included in the study. Seventy-two percent of clinicians never review maternal ketones. Of those that do, 77% change patient management based on the level, although the cut-off for changing management varied widely.
Conclusion: The majority of clinicians never review ketones in patients with GDM. This likely reflects the inconsistent evidence of the detrimental effects of maternal ketones on offspring and the lack of guidance regarding management of elevated ketones in pregnancy.

Ketonuria is associated with changes to the abundance of *Roseburia* in the gut microbiota of overweight and obese women at 16 weeks of gestation: A cross-sectional observational study

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Abstract
Objective: To assess for differences in the composition of the gut microbiota in pregnant women with and without ketonuria at 16 weeks of gestation.
Design: Cross-sectional observational study of 11 overweight or obese women with ketonuria at 16 weeks of gestation and 11 matched controls.
Methods: Faecal samples from 11 women with fasting ketonuria at 16 weeks of gestation were analysed and compared with samples from 11 matched controls. Gut microbiota composition was analysed by 16S rRNA sequencing to assess for differences between cases and controls.
Results: There was no difference in alpha-diversity between the two groups. However, significantly different beta-diversity was seen with supervised hierarchical clustering analysis. Both group comparisons and network analysis showed that women with ketonuria had an increased abundance of *Roseburia* in their microbiome.
Conclusion/discussion: The genus *Roseburia* is more abundant in the gut microbiota of pregnant women with ketonuria. *Roseburia* is a butyrate producing bacterium and may increase serum ketone levels.

A case of atypical PRES requiring decompression craniotomy following early onset preeclampsia

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Abstract
Posterior reversible encephalopathy syndrome (PRES) is a clinical–radiological entity that can present with a heterogenous spectrum of clinical and radiological findings. We present a case of an unusual presentation of PRES in a postpartum woman with haemolysis, elevated liver function tests and low platelet count (HELLP) syndrome. A 23-year-old G3P2 developed early onset preeclampsia (PET) at 30 weeks pregnant. She had PET in her first pregnancy but not in her second. She subsequently developed HELLP syndrome 10 days after initial diagnosis and was delivered by emergency caesarean section. At 36 h post-partum, she developed new onset neurological symptoms including nystagmus, unilateral facial weakness, facial paraesthesia and slurred speech. This occured following a period of persistent hypertension with a maximum systolic blood pressure of 170 mmHg during initial ICU admission at her regional hospital. A CT head and venogram were normal, but subsequent MRI performed the same day at the tertiary hospital was suspicious for a cerebellar and pontine infarct. She was initially suspected and treated as having a posterior circulation stroke, due to atypical early stage unilateral asymmetrical oedema in the pons and cerebellum. She rapidly deteriorated with significant cerebral oedema and a GCS of three requiring a decompression craniotomy. There were initial concerns for a poor outcome with major permanent disability. However, she underwent extensive rehabilitation with a stroke unit and has made a near complete recovery. Here we present this unusual case report as well as a review of the literature on atypical PRES in the context of preeclampsia. As with our case, individuals with atypical neuroimaging findings may initially be misdiagnosed; hence, clinicians require a low index of suspicion for PRES in such patents to ensure necessary serial neuroimaging occurs, and the diagnosis of PRES is accurately established.

Maternal and fetal implications of red cell alloimmunisation

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Abstract
Red cell alloimmunisation has the potential to impact both the mother and fetus during pregnancy. All women have blood group testing during the antenatal period as well as testing for the presence of red cell alloantibodies. The presence of antibodies may cause delay in accessing compatible blood for transfusion, and in rare cases blood may be unavailable. While blood transfusion is not commonly required in pregnancy, obstetric haemorrhage may occur requiring urgent and life-saving transfusion, and this is not always predictable. The principles of patient blood management can be used to guide prevention and management: optimisation of red cell mass during the antenatal period, transfusion strategies to prevent alloimmunisation in girls and women, and appropriate planning for blood support when alloantibodies exist. Red cell antibodies of the IgG class cross the placenta during pregnancy, with some antibodies known to cause haemolytic disease of the fetus and newborn (HDFN). The Rh system antibodies, particularly Anti D, as well as anti-K cause the most severe HDFN. The prevention of alloimmunisation to the D antigen through the use of Rh D Immunoglobulin during the late 20th century was a remarkable success, causing rates of disease and morbidity and mortality to drop. We will soon have the ability to target the antenatal use of Rh D immunoglobulin to those women carrying an Rh D positive fetus through the use of non-invasive prenatal testing. For women with clinically significant alloantibodies, antibody quantitation and titration is used to guide the commencement of fetal surveillance, with fetal anaemia detected by measured through velocity of blood flow in the middle cerebral artery. Blood selected for fetal transfusion must take into account both maternal and fetal compatibility requirements, as well as not causing the development of additional alloantibodies. In the most severe cases of disease where there is a risk of severe anaemia before transfusion is technically feasible, maternal plasma exchange and IVIG therapy have

been used. Novel drugs targeting IgG recycling or placental transport are about to enter into clinical trials for this disease.

Who should receive Ferinject and how quickly does it work? A retrospective analysis of 575 infusions at a quaternary maternity facility

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Abstract
The addition of Iron Carboxymaltose (Ferinject) to the Australian PBS in 2014 initiated a change in prescribing patterns for iron deficiency anaemia (IDA) in pregnancy,[1,2] IV iron is now easier to prescribe, stocked in most hospitals; and the new formulations, such as Ferinject, are considered safer and faster to infuse.[3] However, there are risks associated with use of IV iron.[4] There has been limited ongoing assessment of efficacy and safety of Ferinject use in pregnant women. This study aims to define the prescribing patterns, demographic correlations and outcomes in women prescribed Iron Carboxymaltose in pregnancy. We present a retrospective audit of 575 antenatal Iron Carboxymaltose infusions administered at a quaternary maternity facility between July 2017 and June 2018. This represents approximately 5% of total confinements for that period. The cohort includes both public and private maternity patients and examines the relationship between haemoglobin (Hb) and ferritin response over time (days). Multivariate modelling revealed maternal age and adherence to hospital protocol (defined as IV iron infusion when Hb <90 g/L) were associated with the Hb trajectory.[5] Of the total cohort, private maternities accounted for 68%, and prescription of IV iron that adhered to protocol (Hb < 90 g/L) accounted for 8.6% of infusions. Ferritin levels were available for 522 of 575 patients, with a mean of 9.5 μg/L (Hb <90 g/L) and 12.5 μg (Hb >90 g/L). Other indicators such as oral iron intolerance could not be assessed retrospectively from patient notes. The cohort was divided into infusions administered with Hb < 90 g/L and those >90 g/L. Ethnicity varied substantially between cohorts, with Caucasians representing 44% of Hb <90 g/L and 75% of Hb >90 g/L. The greatest response to treatment occurred in women under the age of 30, with an Hb <90 g/L pre-infusion, at a rate of 0.56 g/L/day of Hb. In summary, Iron Carboxymaltose administration in our facility is predominantly in privately insured, Caucasian women over the age of 30 with an Hb > 90g/L pre-infusion. However, the greatest response rate is seen in women of non-Caucasian origin, less than 30 years of age and with an Hb < 90g/L pre-infusion. These data should aid in targeted prescribing for safe and cost-effective administration.

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A case of severe hyperemesis resulting in subcutaneous emphysema

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Abstract
Background: Hyperemesis gravidarum (HG) is defined as significant vomiting resulting in weight loss greater than 5% of pre-pregnancy weight and ketonuria.[1] This can be associated with electrolyte, thyroid and liver function abnormalities. Case reports have shown HG leading to oesophageal rupture and pneumothorax, pneumomediastinum or pneumopericardium.[2]
Case presentation: A 35-year-old multiparous woman with severe HG was transferred from a regional hospital to Royal Brisbane & Women's Hospital (RBWH) with chest pain. She was 15 weeks pregnant. On examination, she was mildly dehydrated with a heart rate of 110 bpm. She had subcutaneous emphysema around her neck and no features of thyrotoxicosis or thyroid eye disease. There was normal fetal heart rate of 155 bpm was noted. Biochemical investigations showed elevated Troponin I without features of ischaemia on ECG. Thyroid function tests showed supressed TSH of <0.05 mU/L, T4 of 80 pmol/L and negative thyroid autoantibodies. Chest imaging revealed pneumopericardium and pneumomediastinum causing external compression of air on both the heart and thyroid gland. There was no indication of oesophageal rupture as she remained afebrile without features of sepsis. A barium swallow was not undertaken given the significant radiation risk to the fetus. She was treated for suspected alveolar barotrauma from her profuse vomiting and dry retching. She continued conservative management of her HG with anti-emetics and intravenous (IV) fluids, transitioning to oral diet as tolerated. This resulted in resolution of her HG, subcutaneous emphysema and improvement of her Troponin I and thyroid function tests.
Conclusion: This case highlights the importance of recognising the significant complications from severe HG. Most case reports showed oesophageal rupture as a cause of subcutaneous emphysema in women with HG, which is usually managed by keeping patients nil by mouth and on antibiotics.[3] Our case highlights tracheobronchial damage as one of the causes of subcutaneous emphysema without signs of sepsis, favouring conservative management with anti-emetics and IV fluids.

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Hidden trigger for serious medical complications in pregnancy. The Meth amphetamine crisis

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Abstract
We would like to describe two women recently delivered at King Edward Memorial Hospital in Perth with serious complications of methamphetamine use. The first patient was a 36-year-old indigenous woman in her first pregnancy who presented with severe headache at 30 weeks of gestation. Her only relevant medical history was that of type 2 diabetes for which she was prescribed insulin therapy. There was concern for regular compliance. She claimed her headache occurred after an assault by a relative. It was generalised and there was some bruising on her forehead. At a glance, she sat on the bed holding her head in her hands with severe discomfort. She had some associated nausea and no visual disturbance. Her blood pressure was normal and all of the investigations done for the possibility of PET were negative. An urgent MRI was organised to rule out intra-cerebral haemorrhage. The result revealed a significant ischaemic stroke of the cerebellum with some concern for obstructing hydrocephalus. She was transferred to the neurology ward at the local tertiary hospital where she was managed conservatively. Her symptoms improved and she was discharged after two weeks with no residual neurological signs. The underlying pathology was deemed to be cerebral vasoconstriction secondary to methamphetamine use prior to her symptoms. The MRA revealed normal cerebral vasculature. She was supported by the drug and alcohol service and delivered a healthy baby at 38 weeks of gestation. The second patient was a 25-year-old woman in her second pregnancy at 225 weeks of gestation presenting with palpitations and exertional dyspnoea. She had delivered her first child in 2017 and had similar symptoms through her pregnancy then. She had mild Fe deficiency which was treated with no change to her symptoms. She admitted to smoking methamphetamine and sought help to curb her use as she felt it was escalating in the current pregnancy. Clinical examination revealed sinus tachycardia of 110 beats per minute with no other features of cardiac failure. Echocardiography did not reveal LV dysfunction. She is currently being observed for concern of methamphetamine-related cardiomyopathy in pregnancy (MACE). We hope to describe the complications of stroke and cardiomyopathy in relation to methamphetamine use to highlight the need to consider this as a likely risk factor in women presenting with similar issues in a pregnancy. The current background to methamphetamine use in Australia and WA will also be presented. We feel that this is an important and escalating problem that will complicate pregnancies in the current landscape of escalating use and its very addictive nature.

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An unusual case of Graves' disease in pregnancy. A legacy effect of altezumab therapy

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Abstract
The woman has a medical history of relapsing, remitting multiple sclerosis. She first had clinical signs suggestive of this in 2003 and had multiple therapies including steroids, beta-interferon, and natalizumab. She had one planned uneventful pregnancy in 2015. Subsequently, she was thought to have had a relapse and was treated with alemtuzumab two doses a year apart after she embarked on a second pregnancy. All of her thyroid function tests were negative prior to and in the first trimester. In early second trimester, she had clinical features of a goitre and a resting tremor and her tests were consistent with thyrotoxicosis. She was commenced on carbimazole 5 mg BD. She required escalating doses throughout the second trimester, up to 10 mg TDS by 24 weeks. Her TRAb level was first noted to be raised at 24 weeks (18 U/L) and despite the increased carbimazole dose her thyroid function remained deranged. At 32 weeks of gestation, the woman continued to be clinically thyrotoxic. She was commenced on prednisolone therapy to counteract the profound immune response. Fetal ultrasound revealed evidence of fetal thyrotoxicosis. She improved on steroid therapy both clinically and biochemically. She was delivered for fetal concerns.
Discussion: This is an interesting case of hyperthyroidism in pregnancy, as unlike standard Grave's disease, autoimmune thyroid disease secondary to alemtuzumab therapy does not see an improvement with the immune suppression of pregnancy. It is the first documented case that we are aware of. Like cases of alemtuzumab-induced autoimmune thyroid disease reported outside of pregnancy, carbimazole treatment was not successful at improving thyroid function, and prednisolone therapy was required to reduce levels and the effect on the fetus. Alemtuzumab is a monoclonal antibody directed against CD52 lymphocyte receptors. It has been used successfully in relapsing multiple sclerosis. It has an association with the development of particularly autoimmune thyroid disease. This occurs late after treatment. As alemtuzumub-induced lymphopenia resolves slowly, immune reconstitution occurs with T cells having a stronger avidity for native tissue. It is during this time that the risk of autoimmune disease is greatest and Graves' disease can be relentless. Our case demonstrated that only until the addition of prednisolone that an effect on reducing TRab levels was seen with improvement in the fetal condition. This case highlights the importance of understanding the pathogenesis of thyroid disease post alemtuzumab therapy, particularly in pregnancy, where Graves' disease needs an immune suppressive approach to improve both maternal and fetal disease.

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Cytomegalovirus (CMV) and pregnancy: What do women and maternity health care providers need to know?

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Abstract
Congenital CMV is the most common congenital infection in the developed world. CMV is a highly prevalent infectious agent, with seroprevalence among women of reproductive age in Australia about 50%. Congenital CMV can range from asymptomatic infection to severe neurodevelopment impairment, as well as be a cause of fetal and neonatal death. Screening in pregnancy for CMV infection is not recommended in Australia and New Zealand, although pre-pregnancy or early pregnancy screening with CMV IgG for women at high risk of infection may be considered. Infection in children in day care is common, and excretion of virus occurs more frequently in children 1–2 years of age; hence,

parents with a child in day care are at particularly high risk of encountering CMV infection. Over half (59%) of women who develop CMV infection in pregnancy are symptomatic or have abnormal laboratory findings or both. Women with suspected CMV infection in pregnancy should have CMV serology testing for IgG and IgM, and IgG avidity if CMV IgG and IgM are positive. Diagnosis of primary CMV is based upon the new appearance of CMV-specific IgG in a woman who was previously seronegative, or the detection of CMV IgM antibody with low IgG avidity. Despite the high prevalence of congenital CMV infection and subsequent sequelae, awareness amongst maternal health care providers and the community is low. Recently released Royal Australian and New Zealand College of Obstetricians (RANZCOG) guidelines and NHMRC maternity care guidelines have recommended that women are given information about CMV prevention, as the prevention of maternal CMV infection currently relies on hygiene measures, with no effective CMV vaccine or prophylaxis therapies available. Fetal infection can occur through primary maternal CMV infection or maternal CMV reactivation or re-infection. If CMV infection occurs in pregnancy, outcomes depend on gestation and whether it is primary infection or not. Primary infection in the first trimester with a 30–40% risk of fetal transmission and a 30% risk of sequelae if there is fetal infection of around 20–45%% (i.e. overall 10% risk of sequelae). There are no currently licensed treatment options available to prevent fetal CMV infection or treat known or suspected fetal infection. However, both antivirals and hyperimmune globulin have been utilised in a range of different doses, gestations and clinical scenarios. This talk will discuss preventative behavioural measures, diagnosis and management of maternal and fetal CMV in pregnancy and the current role of therapy.

Rapid increase in intravenous iron use among women of reproductive age in Australia: A population-based study

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Abstract

Background: Iron deficiency anaemia (IDA) is a common problem in women of reproductive age, treated with oral or intravenous (IV) iron. There are three preparations of IV iron listed on the Australian Pharmaceutical Benefits Scheme (PBS). We aimed to determine the demographic characteristics and trends in use of IV iron among reproductive-aged women.

Methods: We used PBS dispensing claims from 2013 to 2017 of a 10% random sample of Australians. Rates and annual trends in dispensing of IV iron among reproductive-aged women (18–44 years) were assessed and extrapolated for the Australian reproductive-aged female population (N = 4,627,016).

Results: Between 2013 and 2017, PBS claims for IV iron increased over five-fold from 17,920 to 97,040 in reproductive-aged women. One in 50 women (2%) were dispensed at least one IV iron prescription in 2017. The most commonly dispensed iron preparation was ferric carboxymaltose (FCM) (72.3%), with use increasing rapidly since its 2014 PBS listing. IV iron was most commonly prescribed by general practitioners (43%), followed by other medical practitioners (36%) and specialists (21%). Over five years, the overall estimated PBS cost of IV iron was AUS$60 million with 97% attributable to FCM.

Conclusions: Intravenous iron usage in Australian women of reproductive age has increased significantly over a short time period, largely attributable to increased use of FCM. These data likely underestimate the total use of IV iron, as dispensings to public hospital inpatients may not be included. Further research to evaluate IDA treatment including clinical outcomes and cost effectiveness is required.

Effect of aspirin on placental growth factor (PlGF) in pregnancy and the development of preeclampsia

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Abstract

Introduction: Placental growth factor (PlGF) is a proangiogenic protein that plays an important role in placental angiogenesis. Low first-trimester circulating PlGF in maternal plasma has been shown to be associated with an increased risk of preeclampsia. Prophylactic aspirin is given to women who are at risk of developing preeclampsia and has been shown to have a risk reduction of up to 60%. However, the effect of aspirin on maternal circulating PlGF in high-risk pregnant has not been adequately explored.

Objective/hypothesis: To examine the relationship between aspirin ingestion and plasma PlGF level in high-risk pregnant women and its effects on obstetric outcomes.

Methods: In a longitudinal multicentre cohort study of 220 high-risk women, plasma was collected at a four-weekly interval between 12 and 36 weeks of gestation. Aspirin adherence was verified by platelet function analyzer (PFA100) and plasma salicylate acid detection (liquid chromatography, mass-spectrometry (LCSM)) at each time point and plasma PlGF was measured through human PlGF Quantikine® ELISA Kit. Statistical analysis was done with the use of t-test and repeated measure ANOVA with SPSS.

Results: Only high-risk women who were biochemically ≥90% adherent to aspirin were analysed (n = 82) and compared against high-risk women who were not on aspirin (n = 42). A statistically significant increase in PlGF by 31% at 12 weeks, 71% at 16 weeks, 107% at 20 weeks, 169% at 24 weeks, 315% at 28 weeks, 268% at 32 weeks and 330% at 36 weeks of gestation in high-risk pregnant women on aspirin was observed compared to the non-aspirin high-risk group ($p < 0.001$). Clinically, women in the aspirin group had a lower incidence of preeclampsia (14% vs. 40%, $p < 0.001$), intrauterine growth restriction (IUGR) (4% vs. 11%, $p = 0.003$), delivery before 37 weeks (0.6% vs. 19%, $p = 0.05$), with a higher rate of reduction in antihypertensive agents antenatally (30% vs. 1%, $p < 0.001$). A further subanalysis did not demonstrate a difference in the percentage of PlGF raise between 100 mg and 150 mg of aspirin (p = NS).

Discussion: Aspirin upregulates maternal circulating PlGF from 16 to 36 weeks of gestation. This corresponded with an observed improvement in

obstetric outcomes in the group of high-risk pregnant women on aspirin, with a lower rate of preeclampsia, IUGR, delivery before 37 weeks of gestation and with a higher rate of reduction in antihypertensive agents antenatally.

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A mixed method analysis on factors that influences adherence to aspirin therapy in the prevention of preeclampsia amongst high-risk pregnant women

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Abstract

Background: Non-adherence with medications in pregnancy is increasingly recognized and often results in a higher rate of preventable maternal and fetal morbidity and mortality. In keeping with this, non-adherence with prophylactic aspirin amongst high-risk pregnant women has been shown to be associated with a higher incidence of preeclampsia, preterm delivery, and intrauterine growth restriction. Yet, the factors that influence adherence with aspirin in pregnancy, from a patient's perspective, remains poorly understood and warrants further investigation to help clinicians and patients achieve the desired clinical outcome.

Aim: Our study is aimed at understanding the factors, from a patient's perspective, that influences adherence with prophylactic aspirin amongst high-risk pregnant women.

Methodology: We utilized an exploratory sequential mixed methods approach in conducting a multi-centre quantitative ($n = 122$) and qualitative ($n = 6$) survey of high-risk pregnancy women recruited from three high-risk pregnancy clinics within the South Western Sydney Local Health District, Australia. Data obtained were analyzed against women's adherence with aspirin utilizing phi correlation (φ) with significance set at <0.05.

Results: Two key themes, from a patient's perspective, that influenced adherence with aspirin in pregnancy were identified: (1) pill burden and non-intention omission and (2) communication and relationship with health care provider (HCP). Pill burden and its associated non-intentional omission were both strongly correlated with reduced adherence ($\Phi = 0.8$, $p = 0.02$; $\Phi = 0.8$, $p < 0.01$), whilst the use of reminder strategies was found to strongly minimize accidental omission and improve adherence ($\Phi = 0.9$, $p < 0.01$). Consistent communication between HCP and a good patient–HCP relationship was found to be strongly associated with improved adherence ($\Phi = 0.7$, $p = 0.04$; $\Phi = 0.9$, $p \leq 0.01$) and more importantly was found to play an important role in alleviating factors that had potentials to negatively influence adherence with aspirin in pregnancy.

Conclusion: Our study identified factors that both positively and negatively influenced adherence with aspirin amongst high-risk pregnant women. The findings of this study highlight the importance of recognizing the impact of pill burden in pregnancy and the need to counsel women on the utility of reminder strategies to minimize non-intentional omission. More importantly, this study emphasizes the importance of a positive patient–HCP relationship through effective and consistent communication to achieve the desired maternal and fetal outcomes in high-risk pregnancies

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An update on the clinical impact of aspirin non-adherence and resistance amongst high-risk pregnant women: A multicentre, longitudinal cohort study

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Abstract

Introduction: Aspirin is known to be beneficial in preventing preeclampsia; however, current studies suggest that 30–40% of high-risk pregnant women develop preeclampsia despite the use of aspirin. The influence of aspirin resistance or non-adherence has been described in non-obstetric studies but has not been adequately examined in the high-risk pregnant population and could potentially contribute towards this observation. Our recent pilot study demonstrated that non-adherence

with aspirin amongst high-risk pregnant women is underrecognized and was associated with an increased rate of preeclampsia, premature delivery and intrauterine growth restriction (IUGR). We now present an update of our completed multicentre, longitudinal cohort study.

Objective/hypothesis:

- To examine the prevalence of aspirin non-adherence and resistance amongst high-risk pregnant women through biochemical assessment of adherence with the use of platelet function analyzer (PFA100) and plasma salicylate acid (SA).
- To compare the reliability of self-reported adherence (SRA) to biochemical analysis of adherence.
- To examine the obstetric outcomes based on the maternal biochemical adherence with aspirin.

Methods: We recruited 154 high-risk pregnant women across three high-risk pregnancy clinics within the South Western Sydney Local Health District. Simultaneous blood collection and SRA was conducted at a four-weekly between 12 and 36 weeks of gestation. Blood samples were assessed for PFA-100 and SA through liquid-chromatography, mass-spectrometry. Non-adherence was defined as a normal PFA-100 and non-detectable plasma SA in <90% of time points. Value of 90% is based on current evidence. Aspirin resistance was defined as a normal PFA-100 despite detectable plasma SA. Chi-square analysis, four-way ANOVA and multi-variant analysis were done utilizing SPSS.

Results: Women who were commenced on aspirin after 16 weeks of gestation (n = 9) were excluded for this analysis. No women were found to be aspirin resistant and 64(44%) women were non-adherent. Non-adherence was associated with a higher rate of preeclampsia (7% vs. 38%, $p = 0.03$), anti-hypertensive requirement (10% vs. 46%, $p < 0.001$), delivery prior to 37 weeks (6% vs. 25%, $p = 0.02$) and IUGR (4% vs. 20%, $p = 0.03$). Further sub-analysis of the non-adherent group (<90% adherence) did not demonstrate a difference in the obstetric outcome between groups of varying degree of adherence (<30% vs. 30–60% vs. 61–89% of adherence, p = NS). Agreement between verified biochemical adherence and SRA was poor with a kappa coefficient of 0.4.

Discussion: Non-adherence with aspirin amongst high-risk women is high and is associated with a significantly higher rate of preeclampsia, IUGR and delivery <37 weeks of gestation. Self-reported adherence is not representative of biochemically assessed adherence. This study also supports the finding in a recent study that demonstrated the need for high-risk women to be ≥90% adherent with aspirin to effectiveness minimize their risk of preeclampsia.

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Assessment of the aspirin-triggered lipoxin pathway (ATL) and its influence on the pro-inflammatory cytokine profile of high-risk pregnant women

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Abstract

Introduction: The prophylactic benefit of aspirin in the prevention of preeclampsia is widely recognized. However, the mechanism by which aspirin prevents preeclampsia remains unclear. Recent non-obstetric studies have described an anti-inflammatory effect of aspirin through the aspirin-triggered lipoxin (ATL) pathway. ATLs are the epimeric form of endogenous lipoxin A4, which is a potent immunomodulator and antioxidant. The anti-inflammatory role of aspirin on the pro-inflammatory pathophysiology of preeclampsia, however, has not been examined and remains unknown.

Objective/hypothesis: To examine

- For a difference in endogenous lipoxin A4 production between normal and high-risk pregnancy
- For the extent of ATL production with the use of aspirin in high-risk pregnant women
- For the effect of aspirin on the pro-inflammatory TH1/TH2 cytokine profile which has been identified in high-risk pregnant women.

Methods: In a longitudinal multicentre cohort study of 220 high-risk women, plasma was collected at a four-weekly between 12 and 36 weeks of gestation. Samples were analyzed for plasma lipoxin and ATL through liquid chromatography, mass-spectrometry (LCMS). Selected Th1/Th2 cytokines, IL10, TNFα, IFNγ, IL8 and IL1β in maternal plasma was assessed using high-sensitivity multi-bead Luminex® assay. Repeated measure ANOVA and t-test with SPSS was utilized for analysis. Samples of women with normal pregnancy (n = 20) were obtained from a historical cohort.

Results: Only high-risk pregnant women who were biochemically ≥90% adherent to aspirin were analyzed (n = 82) in comparison to high-risk pregnant women who were not prescribed aspirin (n = 42). Women with normal pregnancy were found to have a higher plasma level of endogenous lipoxin A4 by 180–195% ($p < 0.001$) at all time points compared to high-risk pregnant women. The use of aspirin in high-risk pregnant women demonstrated a significant reduction of IL-8 from 12 to 36 weeks of gestation ($p < 0.001$), TNFα from 24 to 36 weeks of gestation ($p = 0.02$) and increase in IL-10 from 16 to 36 weeks of gestation ($p = 0.03$). Differing doses of aspirin (100 mg vs. 150 mg) resulted in a difference in degree of ATL production (an increase by 35% with 150 mg aspirin ($p = 0.02$)), IL-10 upregulation (an increase by 18% at 16 and 20 weeks of gestation with 150 mg of aspirin ($p = 0.01$)), IL-8 downregulation (a decrease by 20% at 20 and 24 weeks of gestation with 150 mg of aspirin ($p < 0.001$)) and TNFα downregulation (a decrease by 18% at 28–34 weeks of gestation with 150 mg of aspirin ($p = 0.02$)).

Discussion: Endogenous lipoxin A4 production is lower in high-risk pregnant women compared to normal pregnant controls. Aspirin results in ATL production and reduction of pro-inflammatory cytokines (IL-8, TNFα) with an increase in anti-inflammatory cytokine (IL-10). This, therefore, highlights the potential anti-inflammatory role of aspirin through the ATL pathway in the prevention of preeclampsia.

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An unexpected find at caesarean section

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Abstract

Introduction: An 18-year-old primigravida was referred from a Hinterland regional hospital to the Obstetrics and Gynecology department of the Georgetown Public Hospital Corporation for the management of breech presentation @ 36 weeks and four days gestational age. The woman's history was unremarkable for any pathology. Her height of fundus was noted to be small for her gestational age and when calculated, her estimated fetal weight was noted to be less than the first percentile for her gestational age (WHO estimated Fetal weight chart). That ultrasound was also remarkable for Oligohydramnios. A repeated ultrasound at the Georgetown Public Hospital revealed the same findings as to the prior one. After reviewing the case with the consultants of the department, a collective decision was made to deliver this woman via an elective caesarean section. The next day, a primary low transverse caesarean section was performed. After the neonate was delivered by breech extraction, the caesarean team was surprised by the deformities presented to the lower extremities of the neonate. The Pediatrics team was promptly contacted, and they diagnosed with neonate with sirenomelia or mermaid syndrome.

Discussion: Sirenomelia is an extremely rare congenital, multi-organ malformation that is incompatible with life.[1,4] The incident in human is estimated to be around one per 100,000 births and seems to be more prevalent in the male fetus with a ratio of 2.7–1.[1,5] These neonates are born with numerous malformation that affects the renal, urogenital, skeletal, gastrointestinal, nervous and vascular system making this syndrome incompatible with life.[2,4,5] Although the etiology of this multisystemic condition is unknown, investigators believe that genetical and environmental factors play a role.[1,3,4] Some risk factors include maternal diabetes, teratogens and maternal age younger than 20 years old.[2] These neonates have one umbilical artery that has an abnormal origin high on the abdominal aorta that gives rise to one single artery instead of the normal two that branches off into the caudal region of the fetus.[1,4] This causes agenesis of the midline structures and deficient blood flow to the lower extremities resulting in their abnormal development.[4]

Conclusion: Second-trimester ultrasounds are sensitive for detecting features consistent with this malformation.[1] Unfortunately, the woman had two ultrasounds done by distinct radiologists at different institutions and neither was capable of recognizing these malformations. More than half of the neonates who are born with this pathology would demise in utero and those who survive, only live for a few minutes to a maximum of two days.[3] Sadly, this neonate demised after 20 min of life.

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The use of intravenous iron in pregnancy: For who and when? A survey of RANZCOG fellows

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Abstract

Background: Iron deficiency anaemia (IDA) affects 11–18% of Australian pregnant women.[1] IDA is associated with adverse maternal and neonatal outcomes including blood transfusion, postpartum depression, preterm birth and small for gestational age.[2–4] Newer preparations of intravenous iron and increased screening for iron deficiency in pregnancy have resulted in increased use in pregnancy.[5]

Aims: (1) To establish the current patterns of intravenous iron use by Fellows of the Royal Australian and New Zealand College of Obstetricians (FRANZCOG) when treating iron deficiency and IDA in pregnancy and immediately postpartum. (2) Assess FRANZCOG opinions regarding potential trial of intravenous iron for first-line treatment of IDA in pregnancy.

Materials and methods: Online survey of RANZCOG Fellows, distributed by the RANZCOG. Survey included clinician demographics, current intravenous iron prescribing practices in pregnancy and immediately postpartum, perceived advantages and disadvantages of intravenous iron

in pregnancy, and attitudes towards a potential trial of first-line intravenous iron use in IDA in pregnancy. Results were analysed descriptively, and responses were compared by clinician demographics using Chi-squared or Fisher's exact testing.

Results: Of 484 respondents (21% of FRANZCOG), 457 were currently practicing obstetrics and were included in the analysis. Most respondents prescribed intravenous iron in pregnancy (96%) and/or postpartum (85%). Most (98%) of those who prescribed intravenous iron prescribed it for IDA rather than for iron deficiency without anaemia (53%). Intravenous iron was most commonly prescribed for IDA second-line to failed oral iron supplementation and first-line in special circumstances (59%). Ferric carboxymaltose was the preparation most frequently prescribed (90%). IV iron was most frequently used in the third trimester (97% for IDA, 53% for ID without anaemia). Perceived advantages of IV iron included improving iron status in those with poor oral iron tolerance (92%) or adherence (76%), or for those in late pregnancy/special circumstances (76%). Major perceived disadvantages of IV iron included adverse maternal outcomes (58%), need for venepuncture (57%) and practicalities of administration (44%). Intravenous iron prescribing in pregnancy was associated with shorter time since FRANZCOG completion ($P = 0.014$), practice in public hospital ($P = 0.008$) and higher hospital birth numbers ($P = 0.011$). Half of respondents (54%) stated they would consider a randomised controlled trial of first-line intravenous iron for IDA in pregnancy, with the haemoglobin threshold of <100 g/L considered acceptable.

Conclusions: Almost all FRANZCOG prescribed intravenous iron for IDA, while half prescribed it for ID without anaemia. Mostly IV iron was used for second-line treatment; however, over half of FRANZCOG used it as first-line treatment. Further research is required into the optimal treatment of IDA and iron deficiency without anaemia with both oral and intravenous iron, taking into account important clinical outcomes and cost effectiveness.

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Familial hypocalciuric hypercalcemia: Amniocentesis to guide management

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Abstract

Introduction: Hypercalcaemia poses a unique challenge in pregnancy as first-line therapy is intravenous fluids (IVF). Consequently, many antenates are at risk of potential fluid overload from excessive hydration. Here a case of familial hypocalciuric hypercalcemia (FHH) is described where amniocentesis aided in minimising need for aggressive use of IVF.

Case: A 28 yo G3P1 was referred at $19 + 5$ with a history of FHH for management. She was found to be heterozygous for calcium sensing receptor mutation (CaSRm) following the delivery of her first child in 2018. Her child was subsequently diagnosed with the same mutation. She denied symptoms nor a history of nephrolithiasis, osteoporosis, fractures, hypertension, or pancreatitis. She had a miscarriage at first pregnancy at 13 weeks. A strong familial history of CaSRm was described with possible paternal death secondary to FHH. Her corrected Ca was 3.16 mmol/L and was commenced on twice a week IVF and polythiouracil. At $24 + 5$, she developed dyspnoea, and central chest pressure following IVF. She was not clinically overloaded. ECG demonstrated sinus rhythm, CXR found marked pulmonary congestion and cardiomegaly, lower limb dopplers were negative, and echo revealed normal LV size and function. IVF was ceased and a short course of frusemide was prescribed. Given ongoing hypercalcaemia and need for IVF, amniocentesis was offered to identify CaSRm in current pregnancy to avoid ongoing IVF. She was agreeable, with results revealing fetal CaSRm. Regular IVF was ceased.

Discussion: FHH is a rare, benign, autosomal dominant condition with a prevalence of 1:70,000.[1] It results from a CaSRm where the parathyroid, kidneys, and bones are unable to ascertain calcium levels in the blood.[2] Thus, bone leaching and hypocalcuria are prominent features of FHH with a normal or slightly elevated parathyroid hormone.[2] It rarely requires parathyroidectomy unless there is recurrent pancreatitis.[1,2] Mainstay of therapy is to exclude compounding vitamin D deficiency and IVF.[2] Direct maternal risks from FHH are limited. However, many fetal complications have been described.[3] Risks include seizures, tetany, IUGR, fetal death in utero, and neonatal death secondary to fetal hypoparathyroidism.[3] To prevent these, IVF is commenced early. However, physiological changes in pregnancy including decreased vascular resistance, and increased activity of renin-angiotensin-aldosterone system, puts antepartum women at a risk of fluid overload.[4] Given advances in gene testing and ability for quick results, early amniocentesis should be suggested to women to avoid fluid overload.

Conclusion: FHH is a rare form of hypercalcaemia. Treatment in pregnancy is designed to avoid fetal hypoparathyroidism. Unfortunately, given antenates propensity to become fluid overloaded, IVF hydration is difficult. In this case, amniocentesis was utilised to avoid further fluid overload in a woman with symptomatic pulmonary oedema.

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Maternal mortality and morbidity – Australasian maternity outcomes surveillance system (AMOSS)

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Abstract

Background: Maternal mortality remains rare in Australia with the most recent maternal deaths in Australia 2006–2016 reporting 226 maternal deaths in Australia or a maternal mortality ratio of 7.0 deaths per 100,000 women who gave birth in Australia. The Australasian Maternity Outcomes Surveillance System (AMOSS) was established in 2009 as a national surveillance and research system of severe and rare conditions in pregnancy, many of which remain the leading causes of maternal mortality in Australia. The aim of this presentation is to describe the maternal morbidity and mortality associated with these severe maternal morbidity conditions in the context of maternal health surveillance in Australia.

Method: Population-based surveillance of women giving birth with AMOSS conditions between 2009 and 2019 in Australia and New Zealand. Conditions studied were categorised using the CDC severe maternal morbidity framework and included six indicators: five severe maternal morbidity conditions amniotic fluid embolism, eclampsia, antenatal pulmonary embolism, massive obstetric haemorrhage requiring rapid blood transfusion and renal disease in pregnancy; and one intervention peripartum hysterectomy.

Results: Of the 702 women with severe maternal morbidity who gave birth in Australia and were included in the study, there were seven maternal deaths. The overall case fatality rate for the five severe maternal morbidity indicators was 1.3%, ranging from no deaths in eclampsia, massive obstetric haemorrhage, and renal disease in pregnancy to 15.4% in women with an AFE. The case fatality for women having a peripartum hysterectomy was 0.6% with the underlying conditions being placenta accrete. The overall admission to ICU/HDU rate was 69.1%, with 48.7% admitted to ICU and 20.4% admitted to HDU.

Conclusions: National surveillance and research of severe maternal morbidity and mortality should be an essential component of maternal health policy. Rare and serious conditions in pregnancy are underresearched with limited information on the incidence, management and maternal outcomes, and patient experience. This information is critical to developing an evidence base to inform women centred care and for use in counselling, education and training of the maternity workforce. Maternal mortality is an essential outcome of maternity care but a wider set of clinical and patient measures are indicated to better inform maternity policy and practice.

Microbiome Understanding in Maternity Study (MUMS): Study protocol and recruitment data

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Abstract

Introduction: Alterations in the maternal microbiome may facilitate the normal adaptive changes throughout pregnancy for biological advantage. However, increasing rates of pre-pregnancy obesity, metabolic abnormalities, reduced physical activity and the proinflammatory environment related to the modern-day lifestyles may be leading to preconception dysbiosis and maladaptation.

Objective/hypothesis: This mother–infant cohort aims to characterise maternal microbial signatures and their associations with pathological pregnancy phenotypes, particularly Gestational Diabetes Mellitus (GDM), hypertensive disorders of pregnancy (HDP) including gestational hypertension (GH) and preeclampsia (PE), and excessive gestational weight gain (GWG). The MUMS aim is to explore longitudinal differences in the faecal, oral and vaginal microbiome over the course of a pregnancy and the first year post-partum in women who have complicated and uncomplicated pregnancies.

Methods: MUMS is an Australian prospective longitudinal cohort of 100 mother–infant pairs. Recruitment occurs in the first trimester ≤ 13 weeks of gestation. Visits will occur in trimester one ($\leq$13 weeks of gestation), trimester two (20 to 24 weeks of gestation) and trimester three (32 to 36 weeks of gestation), time of birth, then six weeks, six months and 12 months post-partum. Maternal and infant biological samples will be collected at seven time points. Simultaneous clinical, medication, anthropometric, body impedance analysis, dietary, physical activity and psychological data will also be collected. Faecal shotgun metagenomic analysis will be conducted and 16S rRNA gene sequencing will be conducted on the oral and vaginal specimens.

Results: One hundred and seventeen pregnant women were recruited to MUMS in 2018, with 100 completing all three pregnancy visits and due to give birth by mid-July 2019. Within the cohort, 46 women were classified as high risk: 8 had previous GDM, 7 previous GH or PE, 29 a booking body mass index (BMI) ≥ 30, and 3 women has pre-gestational diabetes. Consistent with the hospital's demographics, average maternal age in the cohort is 32.5 ± 4.9 years, booking BMI 25.7 ± 5.3 kg/m^2, 45 (45%) women are nulliparous. The cohort is ethnically diverse: 52% identify as Caucasian, 34% Asian, 6% Middle-Eastern, 5% Latino/Hispanic and 4% other ethnic backgrounds. Complication rates during the current pregnancy for the MUMS cohort includes 13 women with a hypertensive disorder of pregnancy (5 PE, 8 GH) and 18 women with GDM including five diet controlled and 13 requiring a hypoglycaemic agent; three oral and 10 insulin. The in-depth microbiome analysis is currently pending and will occur for all the longitudinally collected pregnancy samples with clinical correlation.

Discussion: Pregnancy and post-partum microbiome analysis may provide additional insight into the role of the microbiome during pregnancy and the implications of pathological pregnancy phenotypes on women and their offspring.

Paroxysmal nocturnal haemoglobinuria and aplastic anaemia: A rare condition in pregnancy demonstrating benefit of a multidisciplinary approach

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Abstract
Background: Paroxysmal nocturnal haemoglobinuria (PNH) is a disease characterized by intravascular haemolytic attacks, haemoglobinuria, anaemia, thrombocytopenia, a thrombotic tendency and increased susceptibility to infection. Related mortality is mostly due to either thrombosis or thrombocytopenia associated with haemorrhage. It is also associated with aplastic anaemia (AA) and pancytopenia arising from unexplained bone marrow hypocellularity. Pregnant women with both PNH and AA are at risk of thromboembolic events resulting in serious maternofetal consequences. Management of these patients includes avoidance of infection and anaemia, countering the risks of thrombosis with bleeding, managing the risks of treatment while reducing the risk of fetal death and prematurity, ideally by a multi-disciplinary team.
Case report: A 31-year-old Malaysian with a history of a termination of pregnancy for anaemia was referred to the high-risk Antenatal Clinic in KKH early in her second pregnancy. She had a medical history of auto-antibody-negative hyperthyroidism, cervical dysplasia for which she had had a loop excision, aplastic anaemia complicated by PNH, for which she had received a bone marrow transplant and multiple blood transfusions with haematology follow-up. She was already on tinzaparin 0.5 mL daily, folic acid, prednisolone 7.5 mg daily, pyridoxine 50 mg daily and iron supplementation. She was subsequently referred and followed up by an obstetric medicine physician in addition to her regular obstetrician. Thyroid function tests at 20 weeks showed a TSH <0.01 mIU/L and FT4 27.8 pmol/L. She commenced Carbimazole 15 mg daily which was then increased to 30 mg by 30 weeks. For the AA, she had three blood transfusions through pregnancy which kept her haemoglobin above 8 g/L. The prednisolone for her thrombocytopenia was tapered down and stopped once the platelet count had stabilised at $70–80 \times 10^9$/L. Tinzaparin was switched to clexane 60 mg BD at 16 weeks because of transaminitis. During the third trimester, she was advised early induction of labour in view of her history. Peri-partum management was coordinated by a multidisciplinary team to ensure optimal outcome. She subsequently had an uneventful normal vaginal delivery; delivering a female weighing 2.38 kg with APGAR scores of 9/9.
Conclusion: Patients with PNH and AA must be closely monitored throughout pregnancy and postpartum because of the increased risk of both maternal (11.6%) and fetal mortality (7.2%). There is little published data supporting specific treatment recommendations, which tends to be individualised and based on the physician's experience. This case demonstrates the importance of a multidisciplinary team approach in the care of rare but high-risk conditions complicating pregnancy to achieve the best maternofetal outcomes.

Anaemia in pregnancy with an unexpected aetiology

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Abstract
Haematinic deficiency is commonly encountered in pregnancy. The causes of anaemia are diverse, with some potentially life-threatening. This case highlights the importance of investigating anaemia when haematinics are normal prior to considering pregnancy. A 31-year-old pregnant woman presented at 21 weeks of gestation with progressive fall in her haemoglobin. She had chronic mild normocytic anaemia prior to pregnancy (90–100 g/L) with normal haematinics. She was known to cardiology with anomalous pulmonary venous drainage, PDA (repaired at nine months of age), SVT (ablated), pacemaker for second-degree heart block and an occluded SVC (surgically corrected). She also had a hypoplastic left thumb, repaired cleft lip/palate and seasonal asthma. She had two previous first trimester miscarriages without any known fetal anomalies. Medications were aspirin 100 mg daily and a pregnancy multivitamin. Clinically she was of normal stature, was euvolaemic and had normal respiratory/gastrointestinal examinations. Haemoglobin immediately prior to pregnancy was 96 g/L, normocytic. This dropped progressively throughout pregnancy to a nadir of 68 g/L at 21 weeks and she developed macrocytosis. She had moderate ovalocytes with occasional tear drop cells, normal platelet/white cell counts, normal haematinics and inappropriately low-normal reticulocytes of 42×10^9/L. Initial haematological investigations were negative (haemolysis, PNH, parvovirus, haemoglobin electrophoresis, paraproteins, Fanconi's anaemia). Bone marrow aspirate was declined. She underwent whole genome sequencing which showed RSP 19 mutation consistent with Diamond-Blackfan anaemia. She required only one unit of packed red blood cells throughout the pregnancy at 21 weeks to maintain haemoglobin above 70 g/L. Antenatal scanning showed short femur lengths and slowing growth. Caesarian section was performed at $33 + 4$ weeks due to concern regarding fetal anaemia (female baby, 1814 g with APGAR score $7 + 8$). The baby had mild transient haemolytic anaemia managed conservatively and genetic screening is pending. Maternal haemoglobin at delivery was 104 g/l and has remained above 90 g/l since delivery. Diamond-Blackfan anaemia is an autosomal dominant condition characterised by macrocytic anaemia, red-cell aplasia, congenital malformations in up to 50% and growth retardation in 30%.[1] Haematologic complications manifest in 90% by the first year of life. It has a variable phenotype and is treated with steroids if significant anaemia (improves blood count in 80%). Blood transfusion may be required, with stem cell transplant reserved for severe cases. There is an increased long-term risk of solid organ tumours, AML and MDS; therefore, long-term haematology follow-up is essential. Reduced fertility, miscarriage, placental abruption, stillbirth and pre-eclampsia are more common in this population.[2,3] This diagnosis was unexpected given it is usually diagnosed at a young age; however, she is likely of mild phenotype, hence the diagnosis later in life. Pre-conception investigation of abnormal results is essential and management of Diamond-Blackfan anaemia in pregnancy should be in a multidisciplinary high-risk clinic.

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Management of heparin allergy in pregnancy

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Abstract

Venous thromboembolism (VTE) prophylaxis in pregnancy is managed with low-molecular weight heparin, which is safe and effective. However, this can become complicated in a woman with heparin allergy when approaching delivery. This review discusses the management of Enoxaparin allergy in pregnancy and the balance of risks and benefits with alternate anticoagulants in terms of immunogenicity and mode of delivery. Fondaparinux is an established alternate anticoagulation option in Enoxaparin allergy. It is safe and effective in pregnancy with reduced immunogenicity compared with Enoxaparin.[1] However, due to its long half-life, delivery options are restricted. In the event of emergency caesarean section with Fondaparinux on board, delivery is under general anaesthetic.[2] Guidelines suggest withholding fondaparinux 3–4 days prior to considering regional anaesthesia.[3] This is in stark contrast to Enoxaparin, which is withheld for only 12 h prior to surgical procedure/regional anaesthesia at prophylactic dose and 24 h at treatment dose.[3] Nadroparin has a similar half-life to Enoxaparin and is a potential alternative to Fondaparinux, allowing greater options for delivery.[1,4,5] It is cheap, effective and safe in pregnancy. It does, however, have a risk of cross-reactivity in Enoxaparin allergy.[1,4,5] Three women with established Enoxaparin allergy and managed on Fondaparinux were reviewed in late third trimester of pregnancy. All wanted to avoid the risk of delivery by general anaesthetic and were trialled on Nadroparin. Two of the three women (both on prophylactic Nadroparin) developed localised skin reaction within 2–4 h of taking the first dose. One continued on Nadroparin despite her reaction and delivered at term by induction of labour with epidural and vaginal delivery without complications. The second returned to Fondaparinux and delivered at term by caesarean section under general anaesthetic without complications. The third tolerated Nadroparin (treatment dose) without any reaction and delivered via emergency caesarean with regional anaesthesia at term for pre-eclampsia (no complications). Some studies have suggested that heparin allergy has a higher incidence in pregnancy with an estimated risk of 19.8% compared with 10.3% in non-pregnant women[2] with others refuting this.[5] Risk further increases with older age, obesity and longer exposure to heparin.[4] The result of this case series is in line with previous studies highlighting the immunogenic effect of nadroparin (estimated reaction rate of approximately 60% in treatment naive pregnant women, and cross-reactivity of 33% in those with Enoxaparin allergy trialled on alternate heparins).[2,4,5] At present, recommendation remains with Fondaparinux. Further options for anticoagulation in pregnancy are required to allow greater delivery options for women with heparin allergy.

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Diagnostic imaging for suspected pulmonary embolism during pregnancy and postpartum: A retrospective radiation dose study

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Abstract

Background: Pulmonary embolism remains a leading cause of maternal mortality. Computed tomography pulmonary angiography (CTPA) and ventilation/perfusion (V/Q) lung scintigraphy are commonly used for investigation of pulmonary embolism; however, both are associated with small levels of radiation exposure. Our study aimed to review diagnostic imaging within our institution for clinically suspected pulmonary embolism during pregnancy and the puerperium and to calculate the associated radiation exposure to patient, breast and fetus in these populations. We also evaluated the diagnostic efficiency of CTPA and V/Q imaging in this population.

Methods: We performed a retrospective analysis on pregnant and postpartum women referred for CTPA or lung scintigraphy for suspected pulmonary embolism at our institution between 2013 and 2018. Patients were stratified by pregnant/postpartum status, and imaging protocol. Radiation dose estimates for maternal effective dose, breast-absorbed dose and uterus/fetal-absorbed dose estimates were calculated for CTPA and lung scintigraphy. Images were categorised for diagnosis as negative/very low probability, non-diagnostic/indeterminate, or high probability/positive for pulmonary embolism based on radiological report findings. Suboptimal CTPAs were reviewed by an experienced, independent consultant radiologist for diagnosis categorisation.

Results: In total, 471 women underwent diagnostic imaging for suspected pulmonary embolism between 2013 and 2018, including 284 pregnant women and 187 postpartum women. The overall incidence of positive pulmonary embolism was 5.4%. CTPA was more commonly used for initial imaging than V/Q-SPECT protocols (overall 61.8% vs. 38.2%, respectively; pregnant 51.8% vs. 48.2%, postpartum 77% vs. 23%, respectively). CTPA was associated with higher maternal effective dose (mean difference 2.93 mSv, $p < 0.001$) and breast absorbed dose (mean difference 7.67 mGy, $p < 0.001$) than VQ-SPECT. Fetal radiation dose exposure was comparatively low between groups. CTPA and V/Q-SPECT were associated with indeterminate rates of 3.0% and 5.5% ($p = 0.176$), respectively.

Discussion/conclusion: Our study demonstrated differences in radiation dose exposure between CTPA and V/Q-SPECT imaging. The results are concordant with recent findings with CTPA being associated with higher maternal effective and breast absorbed dose, while fetal radiation dose was comparably low in both groups. The diagnostic yield of CTPA and V/Q-SPECT are similar. The findings of this large retrospective audit of pregnant and postpartum women investigated for suspected pulmonary embolism provide institution specific information that will allow clinicians to appropriately weigh risks and benefits of the modalities. As one of the largest studies of pregnant women undergoing CTPA for suspected pulmonary embolism, our research provides a significant contribution to the evidence base of CT scanners and associated radiation dose exposure during the investigation of PE during pregnancy and the postpartum.

Thromboprophylaxis dosing for venous thromboembolism prevention in pregnancy

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Abstract
Background: Venous thromboembolism (VTE) is among the three major causes of death in pregnancy however can be challenging to diagnose. Prevention with appropriate thromboprophylaxis is therefore essential. Low-molecular weight heparins (LMWH) are the mainstay of prophylaxis with established safety in pregnancy. In an era of diverse body shapes and increasing prevalence of obesity, the concept of fixed dose, one-size fits all thromboprophylaxis is unrealistic. Current international guidelines suggest weight-based dosing especially in obesity; however, this is based on retrospective studies and extrapolations from non-obstetric literature.
Objective: To summarise the existing prospective clinical data on weight-based dosing of LMWH in pregnancy to determine whether a weight-based dosing regimen is necessary for prevention of VTE in pregnancy and post-partum.
Methods: A systematic search of Pubmed and Embase databases from inception till February 2019 using the terms "pregnancy", "thromboembolism "and "low-molecular weight heparin" was performed, resulting in 417 studies. Studies that were not in English, were retrospective or were not clinical trials were excluded. Full-text review of the remaining 43 studies and references was performed by a single reviewer. Studies that titrated dosing according to Anti-Xa levels or had primary outcomes reported as measures of thrombin generation were further excluded.
Results: On review of 417 articles, only four studies with a total of 1059 patients were prospective clinical trials appropriately addressing weight-based dosing of LMWH in pregnancy. Studies were diverse with regard to study design, dosing, risk profiles and outcome measures. One study was a randomised controlled trial and others were observational and cohort studies. Three studies focused on women post-caesarean section, specifically with elevated BMI in two studies. One observational study found five incidences of VTE all in high and very high-risk groups. Three other studies relied on maintenance of Anti-Xa levels within prophylactic range as their main outcome measure, a surrogate for reduced VTE incidence. In all three studies, weight-based dosing resulted in most women (70–88%) with Anti-Xa levels in the appropriate prophylactic range. This was higher than alternative regimens of BMI-stratified or fixed-dosing with only 26% and 14% of women in the prophylactic range, respectively. No study demonstrated significant adverse events with weight-based dosing of LMWH.
Conclusions: Despite being a major preventable cause of morbidity and mortality, high-level evidence is lacking for thromboprophylaxis in pregnancy. Existing prospective data focuses on post-caesarean section prophylaxis in women with increased BMI. Current studies however are inadequately powered to determine if weight-based thromboprophylaxis vs. standard dosing regimens result in reduced rates of VTE.

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Preeclampsia: Still a disease of theories?

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Abstract
Defective placentation is associated with persistence of a high-resistance uterine circulation, impaired placental perfusion and a placental 'stress' response leading to the development of preeclampsia. It has been proposed that early-onset preeclampsia comprises a disease entity which is distinct from late-onset preeclampsia. The latter has been attributed to as yet undefined "maternal" factors, while the former has been dubbed as "placental" preeclampsia – a rather simplistic dichotomy. There are inconsistencies with the placental origins hypothesis, especially when considering the lack of a causative association with abnormal placental histology or lack of impaired fetal growth in the majority of cases (a TED Talk on this topic can be accessed here: http://bit.ly/2i1SqDk). An alternative explanation is that preeclampsia is secondary to maternal cardiovascular maladaptation in pregnancy. After all, the primary derangement in preeclampsia involves widespread and profound effects on the heart and endothelial system. The concept that placental dysfunction is secondary to a maternal disorder is not new when one considers the clinical similarities between preeclampsia and gestational diabetes – both pregnancy-specific conditions that are cured by birth. It is accepted that gestational diabetes develops when the maternal pancreas is unable to manage the glucose load of pregnancy. Emerging evidence demonstrates that pregnancy presents a substantial cardiovascular load on the maternal heart, and that cardiovascular dysfunction precedes the disorder, predominates in the clinical syndrome and – most significantly – persists postpartum. To date, the placenta has been considered in isolation without regarding the fact that its functioning is dependent on adequate perfusion by the maternal circulation. The involvement of the cardiovascular system in the pathogenesis of preeclampsia and placental dysfunction has significant implications for screening, triage, diagnosis, peripartum care and postnatal management of women at risk of preeclampsia.

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Influenza in pregnancy

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Abstract
Influenza infection places a significant burden on the community each year. Due to changes in the respiratory and immune systems, pregnant women are susceptible to severe infection with increased hospitalisations and complications compared to the non-pregnant population. Diagnosis is via nasopharyngeal swab but treatment with anti-viral medication (oseltamivir) should be commenced empirically if there is a high clinical suspicion. The influenza vaccine in pregnancy is the best defense against infection and is recommended by all relevant bodies. The safety of the influenza vaccine has been proven with multiple studies and a systematic review showing no increase in congenital abnormalities, fetal death, preterm birth, low birth weight and small for gestational age. Maternal influenza immunisation in pregnancy not only protects the mother but also protects the fetus and the infant by passage of antibodies across the placenta. Infants born to mothers who have been immunised are less likely to have laboratory-confirmed influenza infection and are also less likely to have acute respiratory tract and febrile illnesses in the first months of life. Despite this evidence, immunisation rates in Victoria generally range from 30 to 60%. Improving access and education for health care providers and pregnant women is important to increase immunisation rates and decrease influenza infections in pregnancy.

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Therapeutics in preeclampsia

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Abstract
Preeclampsia is a major pregnancy complication that threatens the lives of both mothers and babies. Once diagnosed, there is no treatment that can slow or ameliorate the disease besides delivering the baby and placenta. Over the last two decades, there have been accelerating efforts to discover effective treatments for preeclampsia that could be used to quench the disease, which could allow pregnancies that are preterm to safely continue to advance in gestation. Many of the candidate treatments have arisen in light of our better understanding of the pathophysiology inciting the organ injury that occurs with preeclampsia. Most of the treatments proposed or are being tested in clinical trials target two aspects of the disease: either the placental disease, the maternal blood vessels, or both. This lecture will update delegates on global efforts to find a new treatment for preeclampsia. I will discuss lead preclinical concepts as well as trials that have been done, or are now underway.

Project FIXIOL: Fixing the induction of labour process at a Tertiary Metropolitan Hospital of Western Australia (WA)

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Abstract
Introduction: We undertook a medical service improvement project aimed to improve the experience of women undergoing induction of labour (IOL) at a Tertiary Metropolitan Hospital in Western Australia (WA). The study was driven by patient and staff dissatisfaction with the current process and growing concerns as our IOL rate soars to over 30%. These high-risk women contribute a large burden of workload within the Maternity department and a streamlined process is essential.
Methods: We utilised the DMAIC model of service improvement with focus on cross-sectional stakeholder input throughout the root cause and improvement phase.
Results: A robust stakeholder solutions generation session led to seven improvement goals. This first of which was the implementation of a new IOL Policy for the hospital via collaborative policy-making. This will be released in line with the opening of a dedicated 'IOL Suite' where women are co-located during admission with a dedicated Midwife on 12 h shifts. In addition to this, we formulated a novel admission form that will document the continuum of examinations and management which was previously duplicated between many sources. We will audit qualitative and quantitative results throughout the implementation but current staff feedback is exceedingly positive.
Discussion: With growing capacity and access concerns, the pressures of a rising IOL rate have resulted in a disjointed process that does not provide continuity of care. We hope that our service improvement project can provide insight into a stakeholder driven vision to provide access to individualised care appropriate for the level of antenatal risk that exists for women undergoing IOL. This project motivated all members of the Maternity Department to allocate resources effectively with the hope to improve IOL outcomes, as well as patient and staff satisfaction.

Sleep-disordered breathing in gestational hypertension and preeclampsia: Impact on maternal and fetal outcomes

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Abstract
Introduction: Hypertensive Disorders of Pregnancy (HDP) include Gestational Hypertension (GH) and Preeclampsia (PE), both associated with worse maternal and perinatal outcomes. Sleep-disordered breathing (SDB) is reported to occur more commonly in HDP, although the confounding effect of obesity has been variably accounted for. SDB could amplify the adverse consequences of HDP given similar pathological pathways. We aimed to (i) confirm if the link between SDB and HDP persists

after controlling for obesity and (ii) determine if SDB increases the risk of adverse outcome among women with HDP.
Methods: Women diagnosed with HDP and normotensive BMI- and gestation-matched controls underwent PSG with time-synchronised fetal heart rate monitoring in the third trimester. Fetal growth was assessed by ultrasound and maternal venous and fetal cord blood were sampled at delivery for markers of HDP severity and fetal growth.
Results: Forty women with HDP and 40 matched controls were recruited. The frequency of SDB (RDI $\geq$ 5) in the cases was 52.5% compared to 37.5% in the controls ($p = .18$), but more severe SDB (RDI $\geq$ 10) was twice as common in women with HDP (35% vs. 15%, $p = .04$). SDB had no impact on outcomes for GH and PE women, including gestation at diagnosis, severity of hypertension or biomarkers of disease severity. There was no temporal relationship between maternal apnoea and fetal distress on CTG, but severity of SDB was weakly related to overall fetal heart rate decelerations in controls with well-grown fetuses ($r = .44$, $p = .02$). The presence of SDB had no effect on birthweight centile, third trimester fetal growth trajectory or regulators of fetal growth in cord blood. Among the HDP women, infants of those with SDB were larger at birth ($p = .02$).
Discussion: Mild SDB occurs in half of women with HDP, but also in over a third of BMI-matched normotensive women, suggesting the link between SDB and HDP is in part due to the confounding effect of obesity. SDB did not affect the course of GH or PE nor adversely affect fetal health. Given the high prevalence of mild SDB and that only more severe SDB was related to HDP, a threshold for clinical significance likely exists. Future research needs to identify the relevant threshold for SDB in pregnancy, and proposed causative pathways to inform clinical trials investigating the role of CPAP to improve pregnancy outcomes.

Pregnancy after bariatric surgery: A literature review

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Abstract
Introduction: In Australia, maternal obesity has become a common obstetric problem due to its contribution to adverse pregnancy outcomes such as gestational diabetes, large-for-gestational-age infants, preterm birth and stillbirth. Bariatric surgery has become an increasingly popular and successful intervention for individuals with obesity and therefore obstetric units are caring for more women who have had such procedures.
Objective: The aim was to review the published literature on pregnancy-related risks and benefits associated with bariatric surgery.
Discussion: Patients who underwent bariatric surgery prior to pregnancy had lower rates of gestational diabetes mellitus and large-for-gestational-age infants compared to women without a bariatric surgery history but similar characteristics. However, important studies have shown that there was a higher risk of small-for-gestational-age and intrauterine growth restriction. Micronutrients essential for growth and development especially in the pregnant population were seen to be depleted. However, the degree of micronutrient deficiencies in pregnant women after bariatric surgery is not well established.
Conclusion: Although bariatric surgery is associated with a reduction in the risk of several adverse obstetric outcomes, this subpopulation of pregnant women should be assessed early and monitored closely so as to identify poor outcomes such as SGA and micronutrient deficiencies. Pregnancy care should involve a multidisciplinary approach which includes the obstetrician, physician, bariatric surgeon and dietician.

Cardiovascular outcome in pregnancy in Far North Queensland

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Abstract
Background: In Far North Queensland, cardiovascular disease, namely rheumatic heart disease (RHD), remains an important health issue.[1] In pregnancy, pre-existing and antenatal cardiac disease are both associated with adverse maternal and neonatal outcomes.[2] There is limited literature on cardiovascular disease in pregnancy, which this study seeks to expand.
Methods: A retrospective study was conducted between June 2010 and June 2017 at Cairns Hospital. Patients with cardiovascular disease in pregnancy, which included pre-existing and antenatal conditions, were identified via the clinical coding database. Patient demographics, details on cardiovascular disease, echocardiogram results, delivery and maternal and neonatal outcomes were recorded. Cardiac risk score was also calculated and included some of the risk factors (Table 1).[1]
Results: A total of 63 women were included in this study. *Demographics*: Median age was 28 (range 16 to 45), and the majority of women were of Indigenous background (74.6%, n = 47). *Cardiovascular disease*: The predominant cardiovascular condition was RHD (58.7%, n = 37), with other conditions less common which included non-RHD valvular heart disease (7.9%, n = 5), coronary artery disease (4.8%, n = 3) and non-valvular arrhythmia (17.5%, n = 11). Echocardiogram revealed 25.4% had no valvular heart pathology, whilst 38.1% and 36.5% had one and more than one valvular pathology, respectively; 14.3% of women had mixed mitral valve disease (n = 9) and 19% had mitral and aortic valve disease (n = 12). Mean cardiac risk score[1] was 0.64 ± 0.817. *Outcome:* Median gestational age at delivery was 38 weeks, with 42.9% delivered via spontaneous vaginal delivery (n = 27), 15.9% with assisted vaginal delivery (n = 10) and 34.9% required caesarean section (n = 22). There were eight maternal cardiac complications which included acute pulmonary oedema (n = 1), new arrhythmia (n = 3) and need of a cardiac procedure (n = 4). Although cardiac risk score was not statistically associated with maternal complication, score of >1 had higher complication rates. Neonatal outcome included one case of stillbirth. Median APGAR was 9 ± 1.34 and 9 ± 0.87 at 1 and 5 min, respectively. Median birth weight was 3100 ± 631.87 g.
Conclusion: Despite the burden of cardiovascular disease, there was a low risk of maternal and neonatal adverse outcome found in this study. Cardiac risk score >1 was associated with a higher maternal cardiac complication rate.

Table 1 Cardiac risk score – some of the risk factors.[1]

History of acute pulmonary oedema or significant arrhythmias
Dyspnoea with slight exertion on presentation – New York Heart Association score III
Mitral or aortic valvular stenosis with area $<1.5\ cm^2$
Pulmonary hypertension with systolic pulmonary artery pressure >50 mmHg
Left ventricular dysfunction with ejection fracture < 60%

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Acute fatty liver of pregnancy from 18 weeks of gestation

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Abstract

Background: Acute fatty liver of pregnancy (AFLP) is rare and can be potentially fatal. In most cases it presents with non-specific symptoms, which can progress quickly to fulminant liver failure. Classically, it occurs after 30 weeks of gestation, and here we report the earliest case.

Case presentation: A 28-year-old nulliparous woman who had conceived via in vitro fertilization (IVF) pregnancy reported constant epigastric pain and nausea from 18 weeks. Background medical history included an early pregnancy loss at eight weeks of gestation in 2018, also conceived via IVF, and thyroid peroxidase antibody positivity. At 19 weeks and six days of gestation, she was transferred to our institution for ongoing management. Liver function tests (LFTs) were markedly deranged, with a predominant transaminitis (Table 1). At 19 weeks and six days, total Swansea score was 5. Fetal ultrasound at 19 weeks and four days of gestation showed severe symmetrical intrauterine growth restriction (IUGR) with all fetal biometric parameters less than the first centile. Placental and fetal Doppler studies were abnormal: umbilical artery pulsatility index (PI) 5.11 and resistance index (RI) 1.00 with absent end diastolic flow; middle cerebral artery PI 1.56, RI 0.77 and cerebroplacental ratio PI 0.31.

Management: Given the potentially poor maternal prognosis with continuation of the pregnancy and the terminal prognosis of a pre-viable fetus, the decision was made to terminate the pregnancy at 19 weeks and six days of gestation. Medical termination was commenced with misoprostol; however, despite five doses there was no significant cervical change. At 20 weeks of gestation, Swansea score reached 6 with the addition of elevated bilirubin (Table 1). An emergency surgical hysterotomy was performed and a stillborn male infant was delivered. From day 1 post-delivery, LFTs showed improvement. Liver biopsy one week following delivery showed mild to moderate diffuse microvesicular steatosis, widespread ballooning and apoptotic hepatocytes.

Conclusion: We present a case of AFLP from 18 weeks of gestation, which is the earliest report in the current literature. Our case defies the typical presentation of AFLP in the third trimester and highlights the need to consider AFLP in the differential diagnosis for patients presenting with non-specific symptoms and liver dysfunction.

Use of intravenous fluids in labour – A single centre retrospective study

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Abstract

Introduction: Intrapartum intravenous fluid therapy (IVT) is postulated to reduce labour duration and caesarean section rates. However, evidence is scarce and the World Health Organization does not recommend IVT to shorten labour duration.[1] The optimal IVT regimen and risks and benefits of IVT remain unknown. Our study explored the local practice of intrapartum IVT prescriptions and associated maternal and neonatal risks and benefits.

Methods: Women who underwent labour with a gestational age of $\geq$20/40 from 1 January 2019 to 28 February 2019 at the Mercy Hospital, Heidelberg, were identified through the hospital database of all births. Women with known in utero fetal deaths during labour and elective caesareans were excluded. Patient demographics, co-morbidities, and outcomes of interest including IVT prescriptions; labour duration; mode of delivery; usage of epidural anaesthesia, oxytocin and intravenous antibiotics; maternal fluid overload (hypoxia, peripheral oedema, chest X-ray showing pulmonary oedema, diuretic use); maternal and neonatal serum biochemistry; APGAR scores, neonatal weight loss within 72 h of delivery; and neonatal intensive care (NICU) admission rates were collected and compared.

Results: Two hundred and seventeen women (aged 32 $\pm$ 4.7 years; gestational age 39/40 $\pm$ 2.1) were assessed, with 131 receiving IVT. A median of 2 $\pm$ 1.3 L of IVT was administered and the median infusion rate was

Table 1. Trajectory of pathology.

	Laboratory specific reference range	19 wks + 6 days	20 wks	Day 1 post-op	Day 20 post-op
ALT	<34 U/L	**675**	**3600**	**2690**	29
AST	<31 U/L	**556**	**4580**	**2790**	25
Total bilirubin	<20 μmol/L	11	**30**	**23**	8
APTT	24–39 s	**60**	**68**	**44**	
INR	0.9–1.2	1.1	**1.3**	**1.5**	
White cell count	5.7–16.9 × 10^9/L	**14.1**	**16.3**	**22.2**	6.6
Swansea score		**5**[a]	**6**[b]	**6**[b]	**7**[c]

wks: weeks; post-op: post-operative. Values presented in bold are greater than the laboratory specific reference range.
[a]Abdominal pain, leucocytosis, elevated transaminases, coagulopathy and bright liver on ultrasound.
[b]Addition of elevated bilirubin.
[c]Addition of liver biopsy findings of microvesicular steatosis.

209 ± 250 ml/h. Only compound sodium lactate solution was prescribed. There were more primigravids in the IVT cohort (mean parity 1 ± 0.8 vs. 2 ± 1.2, $p < 0.01$) compared to the no IVT cohort. Both cohorts had no renal or cardiac disease and there was no significant difference in rates of gestational diabetes (17% vs. 7%, $p = 0.06$) and pre-eclampsia (3% vs. 1%, $p = 0.41$). The IVT cohort had significantly higher rates of instrumental deliveries (26% vs. 9%, $p < 0.01$), emergency caesareans (16% vs. 3%, $p < 0.01$) and NICU admissions (14% vs. 3%, $p < 0.01$); longer mean labour duration (346 vs. 268 min, $p < 0.01$); and larger mean postpartum blood losses (511 vs. 317 ml, $p < 0.01$). Women receiving IVT had significantly higher rates of labour induction (64% vs. 3%, $p < 0.01$); usage of epidural anaesthesia (56% vs. 3%, $p < 0.01$), oxytocin (97% vs. 77%, $p < 0.01$) and intravenous antibiotics (30% vs. 13%, $p < 0.01$). There was no difference in maternal and neonatal serum biochemistry, neonatal weight loss within 72 h of birth, and APGAR scores between women who received IVT and those who did not. There were no cases of maternal fluid overload.

Conclusion: Intrapartum IVT is associated with longer labour and higher rates of instrumental deliveries and emergency caesareans. However, IVT also correlated with higher postpartum blood loss; usage of epidural anaesthesia, oxytocin, and intravenous antibiotics; and higher rates of labour induction and NICU admissions. IVT may therefore reflect a more complicated intrapartum course. Intrapartum IVT was not associated with maternal or neonatal harm. Further studies are required to evaluate the effectiveness and safety profile of IVT in labour.

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Target organ changes at six months and two years following pre-eclampsia – The P4 study

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Abstract

Background: Pre-eclampsia (PE) commonly involves the kidneys and liver, and increases the risk of future cardiac and renal disease. The impact of PE on future liver function is unknown. In this study, we report cardiac, renal and hepatic function at six months and two years postpartum in women with prior normotensive pregnancy (NP) or pre-eclampsia (PE).

Methods: In the ongoing, prospective P4 study, 302 NP women and 90 PE women have been assessed at six months, and 94 NP women and 39 PE women at two years postpartum. Demographic data and medical history are recorded. At each assessment, biometric measures, blood and urine samples are collected, and 24-h blood pressure monitoring is performed. Transthoracic echocardiogram is performed in a sub-group (six months, n = 54NP, 43PE). Results are expressed as mean ± SD. The full methodology is available at Davis et al.[1]

Results: Compared with NP, PE had higher BMI at six months (25.0 ± 5.1 vs. 27.8 ± 5.9 mmHg, NP vs. PE, $p < 0.00001$) but the difference was not significant at two years (25.7 ± 6.7 vs. 27.1 ± 7.2 mmHg, NP vs. PE, p = N.S.). Twenty-four hour BP was higher in the PE group at six months (107/67 ± 7/5 vs. 115/72 ± 8/7 mmHg, NP vs. PE, SBP $p < 0.001$, DBP $p < 0.001$), not significant at two years (109/68 ± 9/8 vs. 112/72 ± 12/8 mmHg, NP vs. PE, SBP p = N.S, DBP p = N.S.). PE had greater left ventricular mass index (51.6 ± 12.1 vs. 53.8 ± 13.2, NP vs. PE, $p < 0.01$), interventricular septal thickness (45.6 ± 3.1 vs. 46.4 ± 4.1 mm, NP vs. PE, $p < 0.01$) and posterior wall thickness (7.8 ± 1.1 vs. 8.4 ± 1.1 mm, NP vs. PE, $p < 0.01$) at six months. E/A ratio was lower (1.6 ± 0.4 vs. 1.4 ± 0.3, NP vs. PE, $p < 0.05$) and E/E′ ratio was higher (7.4 ± 1.5 vs. 8.8 ± 2.2, NP vs. PE, $p < 0.005$) in PE compared to NP at six months. Peripheral pulse pressure was higher in PE at six months (39.7 ± 5.0 vs. 42.7 ± 4.9 mmHg, NP vs. PE, $p < 0.001$) but not two years (40.4 ± 4.2 vs. 40.5 ± 7.2 mmHg, p = N.S.). Urinary albumin:creatinine ratio (ACR) was higher in PE at six months (1.2 ± 3.6 vs. 2.2 ± 3.2, NP vs. PE, $p < 0.01$) but not at two years (1.0 ± 2.0 vs. 0.8 ± 1.2, NP vs. PE, p = N.S.). ALP (78 ± 21 vs. 83 ± 21 IU/L, NP vs. PE, $p < 0.05$) and GGT (14 ± 14 vs. 20 ± 24 U/L, NP vs. PE, $p < 0.005$) were higher in PE at six months but there were no differences at two years. AST and ALT were similar between groups.

Conclusion: Pre-eclampsia was associated with differences in BMI, BP, cardiac structure and diastolic function, ACR and liver function tests at six months, but not at two years postpartum (although with smaller and incomplete sample size). The six-month differences may be relevant to future risk of cardiovascular, renal and hepatic disease in these women.

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The diagnosis and management of patients with adrenal disorders during pregnancy

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Abstract

This presentation will summarize current knowledge regarding the diagnosis and management of patients with adrenal disorders during pregnancy. This will include adrenal insufficiency, Cushing's syndrome, primary aldosteronism, pheochromocytoma and adrenocortical carcinoma.

Acute hepatitis C infection in pregnancy, a case report of second trimester diagnosis and term delivery

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Abstract

This is a case report describing a conservative approach to the management of acute Hepatitis C virus (HCV) infection in pregnancy. A 27-year-old gravida 3 para 2 woman presented with jaundice and systemic illness in her 27th week of gestation. Investigations demonstrated elevated bilirubin, ALT and AST, with a fasting bile acid level of 50. Hepatitis serology and quantitative HCV-RNA demonstrated an acute HCV infection, and first trimester antenatal screen had been negative. The woman was commenced on Ursodeoxycholic acid and observed closely during her pregnancy. Her biomarkers peaked four weeks after her initial diagnosis to levels exceeding that usually seen in acute HCV infection.[1,2] She symptomatically and biochemically improved but developed itch in her 36th week of gestation and a presumptive diagnosis of intrahepatic cholestasis of pregnancy (ICP) was made. Induction proceeded at 37 weeks of gestation and a well neonate was delivered. The immediate neonatal period was complicated by newborn jaundice but responded quickly to usual therapies. Serological testing of the newborn was deferred to six months post-partum and for community follow-up. In the literature, acute HCV in pregnancy is limited to case reports only.[3–7] The incidence of this infection is likely to be under-represented by the literature and this paucity leads to difficulty in management decisions and counselling for women as to potential outcomes. This poster gives a brief summary of reported cases, including others with concurrent intrahepatic cholestasis. With greater reporting of this infection in pregnancy, a correlation between ICP and acute HCV may be identified, as well as confirming if, in the immune-compromised pregnancy state, and ALT levels exceed that expected in the non-pregnant woman.

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Pregnancy in women with a Fontan circulation

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Abstract

Background: The Fontan circulation results from the Fontan operation, performed for a number of severe congenital heart defects where there is insufficient ventricular muscle to achieve a biventricular repair. This results in the ventricular chamber (regardless of whether it is a right or a left ventricle, morphologically) being utilised as the systemic chamber. The venous return to the lungs is achieved by passive flow, with no intervening ventricular pump. Physiologically, these individuals are usually mildly cyanosed and have reduced exercise capacity on formal testing. The single ventricle is thought to display abnormal mechanics that affect both systolic and diastolic function. A whole of life experience does not yet exist, as this operation was first described in 1971.

Pregnancy and the Fontan circulation – the experience: Worldwide, the experience in the care of these women during pregnancy is small. A recent systematic review has described the main maternal complications as being supraventricular arrhythmias, heart failure and embolic events. The rate of livebirths is low (45%) due to a high miscarriage rate, and the babies are often delivered early and small. Bleeding, both ante- and post-partum is a common obstetric complication. The Australia and New Zealand Fontan Registry is the largest registry of individuals with a Fontan circulation in the world. Insights from this Registry will be presented.

Pregnancy and the Fontan circulation – management: These women should all be managed through pregnancy in a multidisciplinary and tertiary referral setting. Pregnancy management starts with contraceptive advice and pregnancy education. This should commence around puberty, be repeated frequently, and be re-discussed at transition to an adult congenital cardiology service. The importance of a planned conception that follows medical assessment (cardiac and high-risk obstetric, at a minimum, and additionally a haematologist if the woman is anticoagulated) cannot be over emphasised. In some cases, individualised risk assessment may result in advice that conception is contraindicated. It is important to support these women and their families through exploration of alternate parenthood opportunities if desired. As pregnancy progresses, the members of the multidisciplinary care team need to expand to include midwives, neonatologists, obstetric, and often also cardiac, anaesthetists and nurses. Women should be monitored in a high acuity setting (e.g. a coronary care unit) for a minimum of 48 h to ensure diuresis with the post-partum fluid shifts and ideally tolerance of the letdown reflex associated with breastfeeding initiation.

Concluding remarks: Although no cases of maternal death in pregnancy were identified in the literature, data on the outcomes of complex congenital heart disease as a whole do show an increase. Whether pregnancy for these women modulates their longer term outcomes remains unknown. An international registry is currently being created with the hope of answering the post-partum outcome questions.