

## PREGNANCY AND HYPERCALCEMIA: A CASE REPORT AND MANAGEMENT PROPOSAL.

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**Case Report.** We present a case of severe hypercalcemia in a woman at 14 weeks' gestation. She had an undetectable PTH level and elevated PTHrP. A pelvic ultrasound and abdominal MRI showed a 9-cm fibroma and bilateral nephromegaly, with a hyperechoic cortex and diminished corticomedullary differentiation. Otherwise an extensive evaluation including a bone marrow aspirate and thoracic MRI was normal. After aggressive hydration and administration of furosemide, calcitonin, and cinacalcet, severe symptomatic hypercalcemia persisted. After termination of pregnancy at 16 week' gestation, she received pamidronate and calcium level normalised. The PTHrP became undetectable. The bone pain resolved completely only after removal of the fibroma 6 weeks later. Histopathological studies of both the placenta and fibroma showed immunohistochemical reactivity for PTHrP.

**Discussion.** Hypercalcemia is a rare pathology in pregnancy, with significant maternal morbidity as well as neonatal morbidity and mortality. It is probably underdiagnosed because of the nonspecific symptoms mimicking those of pregnancy and modification of the calcium levels by decreased albumin values. Pregnancy presents a challenge as regards to the radiologic investigations and especially the therapeutic options. We present a unique situation where the origins of the PTHrP secretion was uncertain and where the severity of the hypercalcemia in spite of treatment led to an interruption of pregnancy. We discuss the association of hypercalcemia and fibroid tumors and the use of Cinacalcet rarely reported in pregnancy and of bisphosphonates considered teratogenic. We also propose an algorithm for the investigation of hypercalcemia in pregnancy.

## KINGELLA KINGAE ARTHRITIS IN PREGNANCY: A CASE REPORT AND REVIEW OF THE LITERATURE.

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**Case Report.** We report a case of *Kingella kingae* septic arthritis in a pregnant woman. During the first trimester of pregnancy she complained of the right knee. The analysis of the joint effusion in another center yielded negative results. In our center, the Gram staining performed on a sample of the joint exudate revealed the presence of some Gram negative bacilli. While the culture of the liquid remained negative, a multiplex PCR-based assay revealed the presence of the bacteria. Blood cultures remained sterile. The woman was treated with intravenous ceftriaxone with complete resolution of the arthritis.

**Discussion.** To our knowledge, this is the first report of a *Kingella kingae* arthritis acquired during pregnancy. *Kingella kingae* is a Gram-negative beta-hemolytic coccobacillus usually carried in the oropharynx. It has been described as a common cause of osteo-articular infections in children and less frequently of invasive infection in immunocompromised adults. Due to specific isolation techniques required, delay in diagnosis can compromise patient outcome and the use of molecular detection assays is more efficient. We discuss the facts that 1) the use of a multiplex PCR-based assay adapted to children pathogens provided the diagnosis and could be used in adults; 2) the modification of the immune system during pregnancy may have promoted the infection.

Case Report: An unusual cause of recurrent second trimester death of male fetuses over four generations.

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The proband was the first pregnancy for a woman in the fourth generation of a family with a history of second trimester fetal deaths of males. There were 11 cases of intrauterine fetal death of males in the preceding three generations. Most deaths occurred on or before 20 weeks gestation. Hydrops fetalis was diagnosed at death in this most recent case. A fetal whole genome chromosome microarray was normal.

Whole genome sequencing was performed on samples from 5 obligatory carrier females, the normal male offspring of a carrier, and a tissue sample from the affected fetus.. (See pedigree.) Analysis of the data showed a mutation in the FOXP3 gene – D303fs. This unique mutation caused a frame shift resulting in premature termination.

Mutations in this gene are associated with the IPEX syndrome. (Immune dysregulation, Polyendocrinopathy, Enteropathy, X linked syndrome.) There are a total of about 70 mutations reported, in this gene which codes for a transcriptional regulator critical to the function of Tregulator cells, and thus the ability to suppress immune responses to self. Most cases present with complex autoimmune disorders in early childhood. Recently two, more severe, mutations have been reported in two families with male fetal deaths. Hydrops fetalis has been diagnosed in affected fetuses due to severe autoimmune hemolytic anemias.

This case demonstrates that genetic evaluation in cases of recurrent unexplained fetal death and stillbirth should not stop with chromosome studies, including microarray analyses. Whole genome sequencing is now available, and will likely lead to more diagnoses, and possibilities for management than ever before.

**Title:** Reduction in Narcotic Analgesic Use on Labor and Delivery Unit: Examining the effects of institutional policy

**Principal Investigators:**

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-Diana Kolettis, M.D., PGY3, Obstetrics and Gynecology

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**Background:** Post operative pain control is an issue not only of patient satisfaction, but also patient safety. Compared to other surgical subspecialties, there is a paucity of literature on effective methods to decrease post operative narcotic use in obstetric units, especially in the postpartum period. Our study evaluates how a protocol of non-narcotic anesthetics used in the immediate post operative period effects the oral narcotic requirements of our post-cesarean patients.

**Methods:** This is a retrospective cohort study at a tertiary care academic center where a new post operative pain management protocol was implemented. Cesarean sections performed prior to and after implementation of this protocol were dichotomized into “standard protocol” and “Ketorolac protocol” groups. Medical records were reviewed for perioperative characteristics, pain scores, narcotic use post operatively and length of hospital stays.

**Results:** Two hundred and eight cesarean sections were identified during the study period. One hundred and ten women were in the standard group and 95 were in the Ketorolac group. On average, the standard group received 5.39 doses (STD 4.682) of Hydrocodone10Acetaminophen (H10A) and the Ketorolac group received 3.44 doses (STD 4.544) of H10A. After secondary analysis, a significant difference between the amount of Hydrocodone5Acetaminophen required by the standard and Ketorolac groups was identified in those undergoing primary cesarean section (3.84 vs 2.39, respectively.  $p= 0.031$ ). Those who underwent repeat cesarean section had similar outcomes as the total sample, in that the Ketorolac group required less doses of H10A. (5.49 Standard, 3.13 Ketorolac,  $p = 0.026$ )

**Conclusion:** The administration of scheduled intravenous Ketorolac for analgesia after both primary and repeat cesarean sections can reduce the amount of oral narcotic medications used by patients in the post operative period.

## **Obstetric medicine participation in MoreOB activities**

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**Background:** MoreOB (Managing Obstetrical Risk Efficiently) is a multidisciplinary on-site program aimed at creating a culture of patient safety in obstetrical units. Based on High Reliability Organization (HRO) principles, it promotes a common knowledge base, communication strategies and practice evaluation. The Quebec government supports the implantation of MoreOB in all maternity services. The tertiary care teaching hospital in Sherbrooke, Québec has integrated this program for obstetrical personnel since 2008.

### **Workshop development**

The obstetric medicine service collaborated with the MoreOB team to develop two workshops on issues identified as priorities by obstetrical personnel: severe hypertension and respiratory distress. A multidisciplinary team (obstetrician, general practitioner, obstetrical resident, obstetrical nurse and obstetric medicine physician) developed the interactive case scenario workshops, emphasizing content of existing protocols (severe hypertension) and integrating elements of teamwork and cooperation.

### **Workshop participation and impact**

Multidisciplinary groups of 10-12 participants attended a one hour workshop. Each session had 2-3 instructors from the multidisciplinary developing team. Participation was as follows: Workshop #1 (severe hypertension): 65 nurses, 9 midwives, 16 GP's, 17 OBGYN residents and 9 OBGYN staff and #2 (respiratory distress): 65 nurses, 8 midwives, 19 GP's, 14 OBGYN residents and 10 OBGYN staff.

Knowledge improvement on multiple choice questions on severe hypertension was remarkable: 78% on pretest; 93.8% on post-test and 87.4% after one year. Evaluation of workshops was extremely positive; all professional groups felt the experience was pertinent to practice and appreciated the multidisciplinary learning setting.

### **Conclusion**

Obstetric medicine involvement in MoreOB activities promotes knowledge acquisition and a team approach to care. Whether this translates into practice improvement has not yet been formally evaluated.

# **Grapefruit juice as a treatment for intractable pruritis in severe intrahepatic cholestasis of pregnancy**

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## **Abstract**

### **Background**

Intrahepatic cholestasis of pregnancy (ICP) is a medical condition specific to pregnant women, usually appearing later in the pregnancy. It is a typically benign, yet somewhat incapacitating condition which usually resolves after delivery. Delivery remains the mainstay therapy for severe ICP. A few treatments exist, notably ursodeoxycholic acid, used mainly for symptomatic relief of ICP. Combination therapy for severe pruritis is less well tolerated. Alternate avenues for severe symptomatic treatment are needed. We report here the unusual treatment of grapefruit juice for severe cholestasis in pregnancy.

### **Method and results**

We present the cases of 3 patients with severe symptomatic cholestasis in pregnancy. Two patients had an ABCB4 mutation (revealed retrospectively) and the third patient had primary biliary cirrhosis with a probable autoimmune hepatitis overlap syndrome. A partial response was seen with ursodeoxycholic acid treatment in combination with rifampin and cholestyramine. They were successfully managed with 1000 cc daily intake of grapefruit juice. Symptoms resolved and a net decrease of bile salts and hepatic enzymes occurred. No cases of gestational diabetes were seen in these patients.

### **Discussion and conclusion**

Grapefruit juice contains flavonoids which have been shown to inhibit cytochrome P450 enzymes 1A, 2A et 3A. By a mechanism yet to be clearly determined, grapefruit juice ingestion decreased pruritis, bile salts level and liver enzymes in all 3 cases of severe ICP presenting to our center.

## VALIDATION OF THE PHILIPS INTELLIVUE MP50 IN PREGNANCY

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**Objective:** To study the accuracy of the Philips IntelliVue MP50 monitor in normotensive and hypertensive pregnancy.

**Methods:** The European Society of Hypertension International Protocol (ESHIP) for the validation of blood pressure (BP) measuring devices is used to validate this upper arm automatic oscillometric monitor: sequential BP values are obtained alternating between Philips IntelliVue MP50 device and the E-Sphyg2 monitor on auscultatory mode (American Diagnostic Corporation) used as a substitute of the mercury sphygmomanometer.

**Results:** Thirty nine women are included at a mean gestational age of  $32.8 \pm 6.1$  weeks. 61% are Caucasians, 31% are obese, 18% are normotensive women, 23% have chronic hypertension, 59% have preeclampsia and 44% receive antihypertensive medications. For systolic BP (SBP), the differences between the 2 devices are:  $\leq 5$  mmHg 80.3%,  $\leq 10$  mmHg 95.7% and  $\leq 15$  mmHg 99.1%. For diastolic BP (DBP), the differences are:  $\leq 5$  mmHg 75.2%,  $\leq 10$  mmHg 97.4 and  $\leq 15$  mmHg 100%. The means of the differences between the 2 devices are  $0.05 \pm 4.04$  mmHg for SBP and  $-1.9 \pm 2.95$  mmHg for DBP. Two differences among 3 measurements are within 5 mmHg in 34 women for SBP and in 32 women for DBP. No differences among 3 assessments are within 5 mmHg in 3 women for SBP and in 2 women for DBP. Thus, the device passes the ESHIP requirements.

**Conclusions:** The Philips IntelliVue MP50 is suitable for blood pressure monitoring in normotensive and hypertensive pregnant women.

# **Use of Extracorporeal Membranous Oxygenation in the Peripartum Period**

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## **Background:**

In cases of hypoxic and/or hypercarbic respiratory failure during pregnancy, the use of extracorporeal membranous oxygenation (ECMO) has been reported to have an overall maternal survival rate of 77% and fetal survival rate of 65%, with the majority of the reported cases from the H1N1 epidemic<sup>1</sup>.

## **Case Review:**

We present our institutional experience of four peripartum patients requiring ECMO support from March 2014 - December 2015.

A 23 year old, with heritable pulmonary arterial hypertension on intravenous prostacyclin analogue therapy, presented three weeks postpartum with human metapneumovirus infection and required 10 days of awake veno-arterial (VA) ECMO for worsening hypoxic respiratory failure with subsequent right ventricular failure for 10 days.

A 22 year old patient (G4 P1) with severe asthma presented at 17 weeks gestational age (GA) presented with status asthmaticus and received veno-venous dual lumen (VVDL) ECMO for 7 days for worsening hypoxic and hypercarbic respiratory failure. Patient delivered at term.

A 32 year old woman (G5P1) presented at 29 week GA with hypoxic and hypercarbic respiratory failure in the setting of rhinovirus/enterovirus infection and asthma. Worsening hypercarbia and intermittent fetal heart decelerations prompted VVDL ECMO for 6 days. Patient delivered at term.

A 36 year old woman (G7P4) presented after premature rupture of membranes at 21 weeks GA complicated by septic shock and ARDS. Persistent hypoxemia despite maximal ventilatory support led to initiation of VV ECMO for 6 days.

All patients were successfully discharged from the hospital.

## **Conclusion:**

In well selected peripartum patients, ECMO may be a safe rescue modality.

## **Works cited:**

1. Moore SA, Dietl CA, Coleman DM. Extracorporeal life support during pregnancy. *J Thorac Cardiovasc Surg* 2016; 151: 1154-60



## **A Fortuity of Rarities: A Complicated Case of Acute Fatty Liver of Pregnancy**

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### **Background:**

Acute fatty liver of pregnancy (AFLP) is a rare complication typically affecting pregnant women in the third trimester and is associated with severe maternal morbidity and mortality.

We describe a case of AFLP in a patient with Osteogenesis imperfecta, complicated by acute pancreatitis, encephalopathy and prolonged diabetes insipidus resulting from a pituitary hemorrhage.

### **Case:**

A 32 year-old, Gravida 1, with a past history significant for osteogenesis imperfecta, presented at 37 weeks gestation with a 4 week history of nausea and vomiting. Lab studies were consistent with severe preeclampsia/HELLP syndrome. Within hours of an emergent cesarean section she was noted to be hypoglycemic and lethargic. Repeat lab studies showed worsening transaminases, hypernatremia, coagulopathy and a significant elevation of lipase. Large volume urine output was noted, suggesting diabetes insipidus (DI). We began to favor AFLP as the diagnosis at this point due to this presence of hypoglycemia, DI resulting from decreased clearance of vasopressinase and encephalopathy. Supportive care was continued and clinical picture improved over the next four days. However, despite improvement in liver function, DI persisted. On postpartum day #10, an MRI was performed which revealed posterior pituitary hemorrhage. Treatment with desmopressin was initiated with dramatic improvement in serum sodium and urine output. Notably, there was no evidence of hypotension or postpartum hemorrhage in this patient.

### **Discussion:**

This case illustrates how the unexpected course of DI, an expected complication of AFLP, led to a diagnosis of posterior pituitary hemorrhage. Our case was also complicated by pancreatitis, a potentially lethal complication of AFLP.

## Postpartum Transient Pulmonary Hypertension: Fact or Fiction?

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**Background:** "Pulmonary hypertension is a feared complication during pregnancy. Limited information is available on pulmonary hypertension diagnosed postpartum for the first time. We describe three cases of pulmonary hypertension, first noted in the postpartum period, with varied presentation and management.

Case 1: A healthy 34 year old, presented 7 days postpartum, with dyspnea and, bilateral lower leg edema. Clinical presentation was consistent with pre-eclampsia and pulmonary edema pre-eclampsia. An echocardiogram showed right ventricular systolic pressure (RVSP) of 70 mmHg. CT angiogram did not show pulmonary embolism. Following diuresis, pulmonary pressures normalized within a week. A right heart catheterization revealed normal pulmonary artery pressures.

Case 2: An obese 40 year old, presented with severe dyspnea and orthopnea on postpartum day 19. Work-up was consistent with pulmonary edema secondary to severe pre-eclampsia. An echocardiogram revealed normal biventricular function and RVSP of 59 mmHg., She was managed with diuretics and antihypertensives agents. An echocardiogram preformed a month later was normal.

Case 3: A healthy 32 year old presented 5 days postpartum with fever, flank pain and dysuria and was treated for suspected pyelonephritis. Two days after admission she developed dyspnea. A CT angiogram showed prominent pulmonary arteries but no pulmonary embolism. An echocardiogram showed RVSP of 60 mmHg and no cardiomyopathy. A VQ scan was indeterminate. Therapeutic anticoagulation was initiated. RVSP measured one month later was normal.

**Conclusion:** Peripartum pulmonary hemodynamics, particularly in pre-eclamptic women, are not well described, leading to widely differing management strategies. Further research in this area is warranted for appropriate risk stratification and development of management protocols.

Title: Preconception Counselling: Characterizing the role of obstetric medicine in preconception counselling.

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Background: Preconception counselling is recommended by provincial, national and international organizations as a strategy to improve maternal and neonatal outcomes during pregnancy. Maternal morbidity and mortality is strongly associated with co-existing medical disorders, many of which can be optimized prior to pregnancy. Thus, obstetrical internists play important roles in the prevention of serious maternal morbidity and mortality.

Purpose: Calgary has a dedicated preconception clinic that involves a collaboration between specialists in obstetric medicine and maternal fetal medicine with a goal of improving maternal and fetal outcomes. The actual roles that the clinic plays in the care of women planning pregnancy is unknown. The objectives of this study are: (1) to review the patient population seen in clinic (i.e., the reasons for referral and medical comorbidities) and (2) to describe the types of recommendations made during the consultation process.

Methods: This retrospective chart review includes all women seen in the Calgary Preconception Clinic from September 2014-August 2015 (N=113). Using standardized data collection forms the following data is being gathered: reason for referral, demographics, medical comorbidities, medications, physical exam findings, investigations and recommendations. The types of recommendations will be categorized as: advice/education; clinical/laboratory follow-up; medical interventions (e.g., medication adjustment or health promotion); or optimization of medical comorbidities.

Results: Data has been collected from all charts and analyses are in progress. Results will be presented at the NASOM meeting.

Conclusion: The results will serve as the first of three steps in the evaluation of the utilization and impacts of Calgary's preconception clinic.

**Oxidative and Carbonyl Stress in Pregnant Women with Obstructive Sleep Apnea**  
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**Introduction:**

Obstructive sleep apnea (OSA) in pregnancy is associated with poor pregnancy and fetal outcomes. Oxidative stress in the setting of intermittent hypoxemia and sympathetic activation may play a role in the association of OSA and pregnancy outcomes. We hypothesize that pregnant women with OSA have a pronounced oxidative stress profile.

**Methods:**

A case-control study of oxidative markers was performed using serum of pregnant women with or without OSA. Second trimester serum was tested for oxidative and carbonyl stress serum markers by established spectrophotometric/fluorometric methods. Multiple linear regression analysis was used with a model including age, body mass index at delivery, and history of diabetes.

**Results:**

Twenty three OSA cases and 41 controls were identified. Levels of advanced oxidation protein products (AOPP) a marker for oxidative stress, and advanced glycation end products (AGEs), a marker for carbonyl stress, were lower in women with OSA than in controls (AOPP 5.4 vs. 6.4  $\mu\text{mol/g}$ ,  $p\text{-value} = 0.0427$ ; AGEs 19432.0 vs 27344.4,  $p\text{-value} < 0.0001$ ). There was also a statistically significant increase in antioxidant power, measured by total antioxidant capacity (TAC) (618.2 vs 586.4  $\mu\text{mol/L}$ ,  $p\text{-value} < 0.0001$ ) in women with OSA versus controls. AGEs remained significant even after adjusting for confounders. The use of CPAP in 4 patients did not impact the findings.

**Conclusion:**

The results of the present study suggest that pregnant women with OSA have higher circulating antioxidative and lower carbonyl stress markers compared to controls. It is possible that OSA may have a protective effect on the oxidative stress profile in pregnant women.

## **Obstructive Sleep Apnea, Insulin Resistance and Cortisol Levels in Pregnant Women with Gestational Diabetes Mellitus**

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### **Background:**

Obstructive sleep apnea (OSA) is associated with gestational diabetes mellitus (GDM). This propensity towards heightened insulin resistance may be related to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. We hypothesized that OSA is prevalent among pregnant women with GDM and that women with OSA will have higher levels of insulin resistance and a dysregulated hypothalamic pituitary adrenal (HPA) axis.

### **Methods:**

A cohort of 25 pregnant women diagnosed with GDM answered sleep questionnaires and underwent in-home sleep studies. The presence of OSA was defined by apnea hypopnea index (AHI)  $\geq 5$  events per hour. Insulin resistance was derived from measurements of fasting glucose and C peptide levels with a calculation of the Homeostasis Model of Assessment of insulin resistance (HOMA-IR). Salivary cortisol levels were obtained at bedtime, at wake and 45 minutes after waking.

### **Results:**

Mean age was  $30.6 \pm 4.4$  with pre-pregnancy BMI  $33.1 \pm 7.1$ , majority Caucasian. 8.7% of all participants had chronic hypertension. OSA was diagnosed in 4 (16%) of all patients, three with mild OSA and one with moderate OSA. There were no significant correlations between AHI and HOMA-IR. There was a significant correlation between HOMA-IR and bedtime cortisol levels. Morning cortisol levels were lower in women with OSA and had a weak negative correlation with AHI, but did not reach statistical significance.

**Conclusions:** OSA is prevalent in women with gestational diabetes despite the use of in-home sleep studies and conservative hypopnea criteria. OSA may be associated with a blunted cortisol response in pregnant women with GDM.

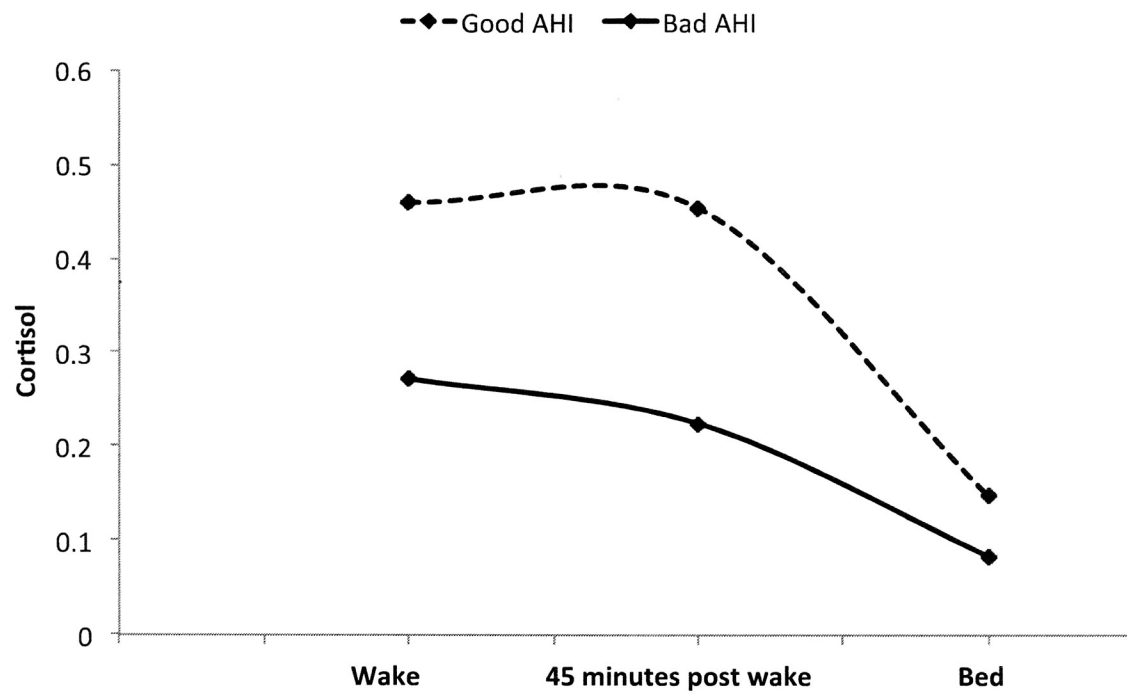


Figure 1: AHI and cortisol levels. Good AHI <5; Bad AHI  $\geq$  5

## Sleep characteristics, Insulin resistance and Cortisol Levels in Pregnant Women with Gestational Diabetes Mellitus

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### Rationale:

Short sleep duration has been associated with abnormal glucose metabolism in pregnancy. We hypothesized that sleep disturbances are prevalent among pregnant women with GDM and are associated with worse insulin resistance and disruptions in cortisol levels, reflective of HPA axis function.

### Methods:

Data was collected from a cohort of 25 pregnant women with GDM. Epworth Sleepiness Scale (ESS) to assess daytime somnolence (normal  $\leq 10$ ), Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality (normal  $\leq 5$ ) were obtained. Insulin resistance was derived from measurements of fasting glucose and C peptide levels and calculated by the Homeostasis Model of Assessment-Insulin Resistance (HOMA-IR). Salivary cortisol levels were obtained at bedtime, at wake and 45 minutes after wake.

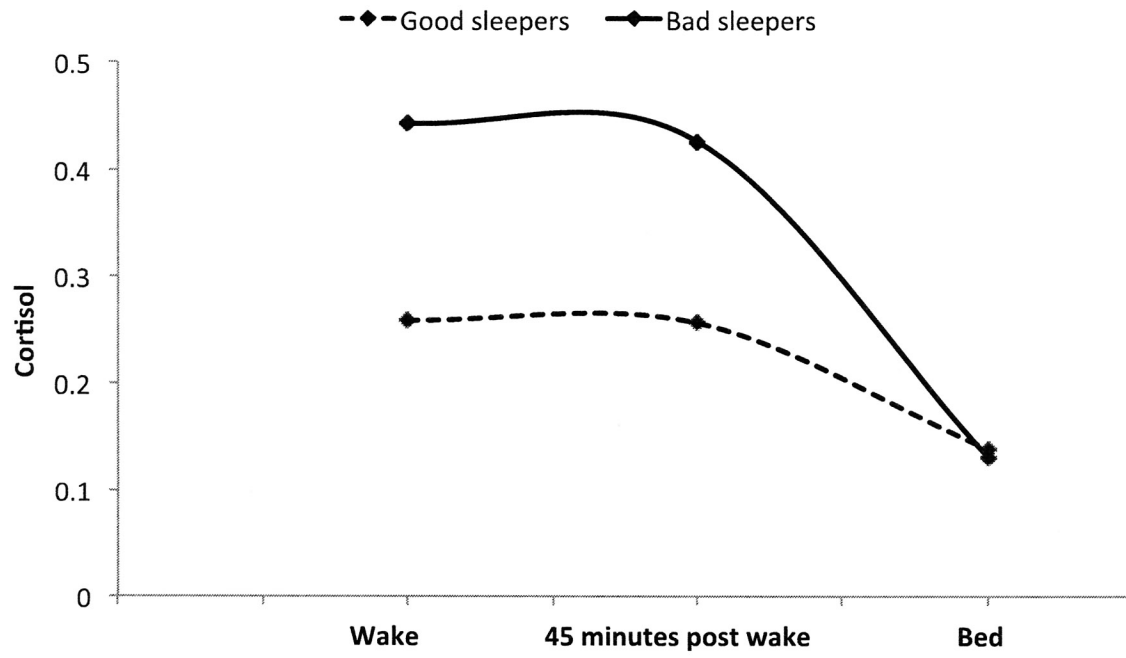
### Results:

Mean age was  $30.6 \pm 4.4$  with pre-pregnancy BMI  $33.1 \pm 7.1$ , majority Caucasian. There were statistically significant differences from normal values in PSQI ( $p < 0.001$ ) and ESS ( $p < 0.01$ ) scores. PSQI score suggesting poor sleep was reported in 92% of subjects; excessive daytime sleepiness was reported in 29% of all subjects. There were no significant correlations between PSQI score or ESS score and insulin resistance measured by HOMA-IR. Cortisol levels were higher in women with poor sleep quality. There was a weak to moderate positive correlation between ESS scores and cortisol awakening response ( $r=0.29$ ) and bedtime cortisol ( $r=0.48$ ).

### Conclusions:

Sleep disturbances are very common in women with GDM and may impact HPA axis function. There are no significant correlations between poor sleep and the degree of insulin resistance.

Figure 1: Cortisol levels and sleep quality. Good and bad sleepers were categorized based on PSQI  $\leq 5$  or  $>5$ .





## Abstract for North American Society of Obstetric Medicine (NASOM)

**Title:** Severe maternal morbidity during delivery hospitalizations in women with hypertensive disorders of pregnancy

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**Background and Purpose:** Hypertensive disorders of pregnancy (HDP) are: common complications of pregnancy; associated with increased maternal morbidity; and require increased antenatal and postpartum care. This study aimed to determine the association between HDP and (1) severe maternal morbidity and (2) prolonged hospital length of stay (LOS) >7days during the delivery hospitalization.

**Methods:** This population-based retrospective cohort study used the Discharge Abstract Database to examine all delivery hospitalizations between 2010-2012 in Alberta. The primary outcomes included severe maternal morbidities and LOS. Descriptive statistics and logistic regression were used in data analysis.

**Results:** In this cohort (n=130,420), HDP cases comprised four groups: preeclampsia (PE, n=1,853), gestational hypertension (GHTN, n=6,127), chronic hypertension (CHTN, n=563), and preeclampsia superimposed on CHTN (PE-CHTN, n=183). Compared with normotensive women (n=121,695), women with PE and GHTN had a higher likelihood of experiencing severe morbidity (defined as: post-partum hemorrhage, embolism, shock, sepsis, uterine rupture, venous thrombosis and tear) with adjusted OR=1.32, 95%CI 1.17-1.49, adjusted OR=1.23, 95% CI 1.14-1.32, respectively. Women with PE-CHTN and PE had significantly prolonged LOS (adjusted OR=37.24, 95% CI 26.07-53.21, adjusted OR=19.6, 95%CI 16.3-22.53 respectively). LOS was independently associated with the four types of HDP, early preterm delivery, cesarean section, maternal morbidities and the Bateman obstetric comorbidity score.

**Conclusion:** Women with HDP had significantly higher risks of severe maternal morbidity and prolonged LOS. Early prediction of HDP and preventative interventions during pregnancy may be important in reducing both the burden of adverse maternal outcomes and the rates of health service utilization.

# Markers of Vascular Dysfunction After Hypertensive Disorders of Pregnancy: A Systematic Review and Meta-Analysis

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**Background and Purpose:** Women with prior hypertensive disorders of pregnancy (HDP) are at twice the risk of cardiovascular disease (CVD) compared to women with prior normotensive pregnancy, possibly due to vascular dysfunction after the pregnancy. The aim of this systematic review and meta-analysis is to summarize evidence of vascular dysfunction at least three months following HDP, as measured by several different modalities.

**Methods:** Articles in all languages were retrieved from MEDLINE, Embase, BIOSIS Previews, CINAHLPlus, and Cochrane. Studies included were observational with HDP as the main exposure and measurements of vascular dysfunction via imaging modalities or serum biomarkers as the main outcome, assessed at least 3 months postpartum. We pooled results of modalities reported in more than three studies using a random effects model and report weighted mean difference with 95% confidence interval between measures of vascular dysfunction in women with and without prior HDP.

**Results:** Of 6109 potentially relevant studies, 72 were included that evaluated 10 imaging modalities and 11 serum biomarkers. There was significant vascular dysfunction in women post-HDP when measured by carotid-femoral pulse-wave velocity (0.64m/s [0.17 to 1.11]), carotid intima-media thickness (0.025mm [0.004 to 0.045]) and augmentation index (5.48% [1.58 to 9.37]), while no difference was observed in pooled biomarker values, except for soluble fms-like tyrosine kinase (6.12pg/ml [1.91 to 10.33]). Vascular dysfunction in women with prior HDP compared to controls was greater when assessments were done in younger women (<40 years).

**Conclusion:** Pooled data from studies evaluating vascular imaging suggest that some vascular dysfunction persists following HDP. The serum biomarkers measured following HDP in these studies may not accurately reflect underlying dynamic endothelial damage.

**The cost-effectiveness of first trimester screening and early preventative use of aspirin in women at high risk of early pre-eclampsia**

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**Background:** Pre-eclampsia (PE) remains a leading cause of maternofetal morbidity and mortality. A first-trimester screening algorithm predicting risk of early pre-eclampsia was developed and validated. Early prediction coupled with initiation of aspirin at 11-13 weeks to high risk women effectively reduces prevalence of early-onset PE.

**Objective:** This study aimed to evaluate cost-effectiveness of a first-trimester screening program coupled with early use of aspirin in women at high risk of developing early PE versus current practice.

**Methods:** A decision analysis was performed based on a theoretical population of live births in Canada/year (n=386,400). The clinical and financial impact of screening using the Fetal Medicine Foundation (FMF) algorithm for prediction of early PE coupled with use of low dose aspirin in high risk pregnancies was simulated and compared with current practice. The probabilities at each decision point and associated costs of resources were calculated based on published literature and databases.

**Results:** Of 386,400 births per year, estimated prevalence of early PE in the screening group was 716 (0.2%) versus 2068 (0.5%) in the current practice group. This corresponds to an estimated cost of \$8,580,403.75 compared to \$24,465,320.70 with current practice for diagnosis and management of women with early PE, a cost-savings to the Canadian health care system of approximately \$15,884,917/year.

**Conclusion:** Implementation of a first-trimester screening program for PE and intervention with aspirin in those deemed high risk for early PE has potential to prevent a significant number of early PE cases with a substantial associated cost-savings to the health care system.

# EARLY DETECTION OF GLOMERULAR INSULT DURING PREGNANCY IN WOMEN WITH DIABETES: PRELIMINARY DATA.

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## Introduction

Diabetes increases the risks of preeclampsia (proteinuria/hypertension) and diabetic nephropathy (albuminuria), and both conditions can be revealed during pregnancy. Proteinuria is a hallmark of glomerular diseases but recent studies suggest that the presence of podocytes in urine (podocyturia) could be an earlier marker. The aim of this study is to measure the occurrence of different glomerular markers in pregnant women with diabetes.

## Method

50 women with either diabetes diagnosed prior to pregnancy or insulin-treated gestational diabetes ( $\geq 12$  weeks of gestation) are recruited. Urine samples are collected every 4 weeks until delivery. Protein/creatinine ratio (PCR) and albumin/creatinine ratio (ACR) are measured at the CHUS biochemistry laboratory and podocytes are quantified using the qPCR method, using podocin as a specific marker and GAPDH as internal control. Descriptive data are presented as median [IQR]. Variations of glomerular marker at each trimester are assessed with the Kruskal-Wallis test.

## Results

Preliminary analysis includes 28 participants (aged 34 [31;39], body mass index  $32\text{kg}/\text{m}^2$  [24;42]) and a total of 88 samples collected at 11[10;14] weeks of pregnancy (n=5), 23[20;27] weeks (n=40) and 34[31;37] weeks (n=43). The comparison of the PCR and ACR for the 3 trimesters does not show significant variations (PCR: 0,05[0,05;0,09] vs 0,05[0,05;0,12], ACR: 0,25[0,25;0,70] vs 0,25[0,25;1,20], p=0,2 and 0,5 respectively).

## CONCLUSION

Our preliminary analysis shows that proteinuria and albuminuria do not differ between each trimester. Podocyturia's analysis is in progress and we anticipate that this marker will contribute in detecting participants who will progress towards overt glomerular insult.

## Newly Diagnosed Heart Block in Pregnancy

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Cardiac conduction disorders are rarely first diagnosed in pregnancy. A small number of published case reports suggest the conduction delay will progress with advanced pregnancy and potentially resolve in the post-partum (1, 2).

We present two cases of new heart block in pregnancy.

Patient One (G2P0) is without personal or family history of cardiac disease. She is in the Navy and prior to pregnancy exercised at a high level without difficulty. At 15 weeks gestation, she presented to the emergency room complaining of 1 week of intermittent palpitations that worsened acutely with dyspnea and chest tightness. ECG revealed sinus rhythm with severe first degree AV block (PR > 400 ms) and intermittent second degree Mobitz Type 1. Lyme serology was negative. On echocardiogram her EF is 50% with mildly reduced right ventricular systolic function. Subsequent cardiac monitoring showed intermittent episodes of complete heart block and first and second degree AV block. The patient is being closely monitored without a pacemaker due to absence of significant symptoms and having an adequate junctional escape rhythm. Her EDD is 7/18/16 and we will be able to report on the outcome of this pregnancy.

Patient Two (G2P0) is also without personal or family history of cardiac disease. At 11 weeks, she complained of palpitations. 48-h Holter revealed a sinus rhythm with intermittent episodes of second degree Mobitz Type II AV block. Her EDD is 10/31/16, we will be able to report on the workup results and progress through pregnancy.

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## Refractory Immune Thrombocytopenia in Pregnancy

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Immune Thrombocytopenia (ITP) occurs in < 1% of pregnancies (1). More than 20% of adults with ITP also have elevated Antinuclear Antibodies (ANA) yet do not fulfil diagnostic criteria for Systemic Lupus Erythematosus (SLE). Elevated ANA in primary ITP is a known risk factor for resistance to classical treatments. Hydroxychloroquine (HCQ) is a suggested treatment for ITP patients with elevated ANA with and without SLE (2).

We present a case of a 19 year old nulliparous pregnant patient with refractory ITP and elevated ANA (titer 1: 10,240) treated with HCQ. She was diagnosed at age 16 years. Her platelets ranged from 4,000- 27,000 and she had little or no sustained response with IVIG, prednisone, and Rituximab. For the two years prior to pregnancy she remained on active monitoring alone without treatment. At 12 weeks gestation, platelet count was 19,000 and HCQ was started. Two weeks later, with a platelet count of 14,000, prednisone was added. As the pregnancy progressed, her platelet count slowly improved and the dose of prednisone was tapered down. At 36 weeks, 4 days gestation, she presented with ruptured membranes and breech fetal presentation, platelets were 53,000. She underwent a Cesarean section under general anesthesia without complications, prior to the procedure she was transfused platelets and received stress dose steroids. At four months post-partum, the patient remains on HCQ and prednisone, platelets are 48,000.

There are no current reports in the literature on the use of HCQ for refractory ITP and elevated ANA in pregnancy.

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NASOM Abstract Mahajan A, MD CCFP1; Kemp A, BSc2; Hawkins TL, MD MSc3; Nerenberg K, MD MSc3; Metcalfe A, PhD4

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Background and Purpose Hypertensive disorders of pregnancy (HDP) are a leading cause of preventable maternal morbidity and mortality in Canada, particularly amongst women with postpartum presentation of HDP. Women with postpartum HDP often present to the Emergency Department (ED), where they may experience delayed recognition and treatment of hypertension leading to serious adverse clinical outcomes. To address this care gap, our interdisciplinary team developed an ED-specific management protocol for postpartum HDP.

The objective of this study is to describe the current management and clinical outcomes of women with postpartum HDP presenting to Calgary EDs, prior to implementation of the novel protocol.

Methods A retrospective study of postpartum women attending Calgary EDs is currently being performed. The Discharge Admission Database was used to randomly select 50 cases (ICD-10 codes for HDP related, diagnoses, e.g., abdominal pain, headache). The hospital charts will be reviewed for: maternal demographics; obstetrical history; and ED clinical findings, investigations and management. Results will be summarized with descriptive statistics. Predictors of clinical outcomes and management will be assessed through logistic regression.

Anticipated Results We anticipate identifying important gaps in the clinical management of women with postpartum HDP that are associated with adverse clinical outcomes. We will then to repeat this study six months after implementation of the ED protocol to evaluate the use of the protocol, and changes in ED management and clinical outcomes (through a pre-post intervention comparison).

Conclusions This three-step study will inform the development of provincial strategies for postpartum HDP management.

## **Obstructive uropathy and acute kidney injury in pregnancy**

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### **Background**

Functional hydronephrosis is a common change in the urinary tract during pregnancy. However, complete ureteral obstruction by the gravid uterus is a rare cause of AKI in pregnancy. Treatments include amniocentesis, bilateral ureteral stenting, percutaneous nephrostomy tubes, hemodialysis, and when feasible, delivery or cesarean section.

### **Case**

A 33-year-old G1P0 woman presented at 27 weeks gestation with a twin pregnancy complaining of left-sided flank pain. Blood and urine tests revealed hematuria and no proteinuria, and creatinine continued to rise and pain worsened following admission. Renal ultrasound revealed left hydronephrosis and a small perinephric fluid collection at the left lower renal pole. On hospital day four, the patient noticed a "blood clot" in the toilet after voiding, which was sent to the lab. Due to worsening renal function, the patient underwent cystoscopy and ureteroscopy. No stone was identified, but a stent was placed into the left ureter, improving pain but not reducing creatinine levels. Spontaneous delivery of the first baby boy occurred 36 hours after stent placement, followed by delivery of the second baby boy 10 hours later. Brisk diuresis ensued and creatinine improved. Lab testing later reported the "blood clot" to be a calcium phosphate stone.

### **Discussion**

The timing of the events and imaging suggest that flank pain was caused by ureterolithiasis and forniceal rupture, while AKI was due to obstructive uropathy from the gravid uterus. Passage of the stone and stent placement alleviated the patient's flank pain, while spontaneous delivery resulted in rapid resolution of AKI.



## **Obstetric Medicine Health Services Utilization in a Canadian Urban Centre**

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Background and Purpose: Obstetric medicine (ObMed) is an emerging clinical area that provides medical care for women with medical co-morbidities before, during and after pregnancy. Data on ObMed service utilization in North America is scarce. This information is important for program planners in creating sustainable ObMed services that meet their patients' needs. One model of an ObMed clinical service was established in 2001 at a tertiary care centre in Calgary, Alberta; by 2010, out-patient services were expanded to include a total a 5 sites. The objective of this study was to describe the ObMed clinical service utilization in Calgary over a one-year period.

Methods: Prospective evaluation of all out-patient ObMed services from January 1 to December 31, 2015, using an administrative information system (Clinibase). Visits were categorized as either consultation or follow-up, as well as by timing (preconception, antepartum or postpartum). Time from referral to consultation was also recorded. Results were summarized using descriptive statistics.

Results: Overall, 1,752 outpatient ObMed in-person visits for 954 patients were recorded; 85% of visits occurred antepartum, 9% preconception and 6% postpartum. About half of the women (44%) had  $\geq 1$  follow-up visit and  $>50\%$  were seen for  $>1$  medical diagnosis. Mean time from referral to consultation was 23 days.

Conclusions: This ObMed service utilization study from a Canadian tertiary care centre identified that a large proportion women were seen for multiple medical co-morbidities on  $>1$

occasion mostly during pregnancy. This information may guide ObMed clinical service planning locally and at other centres.

# **Pulmonary Hemorrhage in Pregnancy: A Case Report and Review with Diagnostic Considerations**

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**Background:** Hemoptysis and massive pulmonary hemorrhage in pregnancy occur very infrequently, but carry potentially deadly consequences. Early intervention and diagnosis are important for good outcomes.

**What the case adds to the existing literature:** The management and workup of a patient with massive pulmonary hemorrhage arising from a synovial sarcoma

## **Case Description:**

29 y.o. multiparous, otherwise healthy African American woman, required induction of labor at 31 weeks' gestation for severe preeclampsia. During labor (at 8cm cervical dilation), she had hemoptysis with desaturation which resolved after administration of supplemental oxygen. Soon after vaginal delivery, she had recurrent hemoptysis and respiratory failure requiring endotracheal intubation and ICU transfer. Massive pulmonary hemorrhage involving the entire left lung was confirmed on imaging and bronchoscopy. She had a prolonged hospital course requiring blood transfusion, chest tube, tracheostomy due to prolonged intubation, and dialysis for acute kidney injury. No immediate etiology was determined with negative tests for angiography, rheumatologic and infectious causes, negative anti-glomerular basement membrane antibody and no significant past medical or family history. She eventually recovered kidney function but continued to have pulmonary issues necessitating transfer to pulmonary rehabilitation center. Three months later, she was extubated and tracheostomy closed. Subsequent imaging revealed persistent opacification of lower half of left lung. Recurrence of hemoptysis few months later, prompted evaluation revealing metastases in liver and contralateral lung. Liver biopsy confirmed diagnosis of monophasic synovial sarcoma originating in the left lung/pleura. She is currently undergoing chemotherapy.

**Discussion:** Massive pulmonary hemorrhage in pregnancy is a very rare, potentially life-threatening condition. Reported causes in a young patient include pulmonary arteriovenous malformations including hereditary hemorrhagic telangiectasia, hemosiderosis, celiac disease, infections, Goodpasture syndrome, and systemic lupus erythematosus. However, malignancy is another important cause and should be looked for if other tests are non-diagnostic, even in a young woman.

## **Attitudes of Obstetrical Medicine Specialists about out-of-office blood pressure measurement in Canada for the diagnosis of white coat hypertension**

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Accurate blood pressure (BP) measurement is of critical importance and should be performed both in-office and out-of-office, as recommended by Canadian Hypertension Education Program (CHEP) guidelines. Out-of-office measurements include home BP measurements or 24h ambulatory blood pressure measurement (ABPM), with the 24h ABPM being preferred. In pregnancy, the gold standard to assess for hypertensive disorders of pregnancy is in-office BP. White coat hypertension (normal out-of-office BP readings and elevated in-office readings) is common during pregnancy, with a prevalence of 30% and is associated with 40% progression to gestational hypertension and 8% to preeclampsia. Furthermore, women with white coat hypertension have a trend towards increased frequency of c-section delivery compared with normotensives women. Therefore, it is important to accurately differentiate women with true gestational hypertension from white coat hypertension, as we do not want to subject women to unnecessary medications or surgeries. To diagnosis white coat hypertension, out-of office BP measurements are essential, either through home BP measurement or 24h ABPM. It is unclear how Obstetrical Medicine specialists in Canada assess for white coat hypertension in pregnancy. Therefore, we will conduct a survey of Obstetrical Medicine specialists to better understand their preference and practice of out-of office BP measurements. The objective of this questionnaire will be to better understand how 24h ABPM and home BP measurements are used in decision-making regarding therapies amongst Obstetrical Medicine specialists in Canada.

## Chronic Thrombotic Thrombocytopenic Purpura In Pregnancy: Cases & Literature Review

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**Background:** Thrombotic thrombocytopenic purpura (TTP) in pregnancy is fatal if appropriate treatment is not promptly initiated. Chronic forms of hereditary or acquired TTP can have a more subtle presentation. No consensus on most appropriate intervention exists to ensure successful pregnancy outcomes in these women.

**What the cases add to existing literature:** Management of women with prior episodes of TTP in pregnancy, compilation of cases, and review of literature.

**Case Description:** 34 y.o. G1P0 Caucasian female had history of acquired TTP diagnosed 8 years prior, treated with corticosteroids and plasmapheresis. After 4-year remission, an infected pilonidal cyst provoked recurrence. In current pregnancy, she presented in first trimester with petechiae, numbness, and 9,000 platelets. Despite treatment with plasmapheresis and corticosteroids, she had three relapses, requiring admission at 25 weeks gestation for severe fetal growth restriction and mild pre-eclampsia. Plasmapheresis was continued 2x/week, while corticosteroids were tapered four weeks after attaining normal platelet count. She required Cesarean delivery at 30 weeks gestation for severe pre-eclampsia. After two plasmaphereses in the postpartum period, she has since been in remission.

26 y.o. G5P2121 African-American obese female was diagnosed with TTP in her second pregnancy when presented with fetal demise at 24 weeks, abdominal pain, and 14,000 platelets. She was treated with plasmapheresis, corticosteroids, and Rituximab. Relapse two years later led to hypertension, headaches, and numbness. After aggressive treatment, work-up revealed positive anticardiolipin antibodies. She had a miscarriage two years after this episode. In the next pregnancy, she was treated for TTP and antiphospholipid syndrome with aspirin and low molecular weight heparin, delivering at 37 weeks for superimposed pre-eclampsia. Lost to follow-up, she presented one year later with left middle cerebral artery stroke, treated with anticoagulation. Pregnancy at six weeks was diagnosed and patient chose medical termination of pregnancy.

**Discussion:** In patients with a chronic recurrent form of hereditary or acquired TTP, appropriate clinical management during pregnancy can result in successful outcomes for patient and child, though incidence of pregnancy complications remain high.

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## Abstract for NASOM 2016 Annual Meeting

### Adolescent Pregnancy Clinic: Issues and Trends in Caring for this Vulnerable Population

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Adolescent pregnancy is the leading cause of mortality in girls aged 15-19 worldwide <sup>1</sup>. Approximately 16 million girls aged 15-19 and approximately 1 million girls under 15 give birth every year<sup>2</sup>.

Adolescents have many issues that are unique to their age group including higher rates of STIs, drug and alcohol abuse, nutritional deficiencies such as anemia and intimate partner violence (1).

The Adolescent Pregnancy Clinic in Edmonton is unique in that all patients are seen by a Nurse Practitioner, registered dietitian and registered social worker.

#### Methods

We conducted a 1 year retrospective chart review of pregnant adolescents seen in the Adolescent Pregnancy Clinic at the Royal Alexandra Hospital in Edmonton, Alberta. We looked at characteristics including age, ethnicity, history of drug and alcohol use, history of sexually transmitted infections, educational level achieved, intimate partner violence and prior involvement with child and family services.

#### Purpose

Having a clinic that provides multidisciplinary comprehensive care focusing on improving outcomes for mothers and their infants is the purpose of our clinic.

#### References

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**Oxidative and Carbonyl Stress in Pregnant Women with Obstructive Sleep Apnea**  
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**Introduction:**

Obstructive sleep apnea (OSA) in pregnancy is associated with poor pregnancy and fetal outcomes. Oxidative stress in the setting of intermittent hypoxemia and sympathetic activation may play a role in the association of OSA and pregnancy outcomes. We hypothesize that pregnant women with OSA have a pronounced oxidative stress profile.

**Methods:**

A case-control study of oxidative markers was performed using serum of pregnant women with or without OSA. Second trimester serum was tested for oxidative and carbonyl stress serum markers by established spectrophotometric/fluorometric methods. Multiple linear regression analysis was used with a model including age, body mass index at delivery, and history of diabetes.

**Results:**

Twenty three OSA cases and 41 controls were identified. Levels of advanced oxidation protein products (AOPP) a marker for oxidative stress, and advanced glycation end products (AGEs), a marker for carbonyl stress, were lower in women with OSA than in controls (AOPP 5.4 vs. 6.4  $\mu\text{mol/g}$ , p-value = 0.0427; AGEs 19432.0 vs 27344.4, p-value < 0.0001). There was also a statistically significant increase in antioxidant power, measured by total antioxidant capacity (TAC) (618.2 vs 586.4  $\mu\text{mol/L}$ , p-value < 0.0001) in women with OSA versus controls. AGEs remained significant even after adjusting for confounders. The use of CPAP in 4 patients did not impact the findings.

**Conclusion:**

The results of the present study suggest that pregnant women with OSA have higher circulating antioxidative and lower carbonyl stress markers compared to controls. It is possible that OSA may have a protective effect on the oxidative stress profile in pregnant women.