James A. Low Research Day
Department of Obstetrics & Gynaecology

PROGRAMME
April 9, 2021

Queen's UNIVERSITY

Content

Queen's University is situated on the territory of the Haudenosaunee and Anishinaabek.

Ne Queen's University e'tho noṅwe nikanónhsote tsi noṅwe ne Haudenosaunee tánon Anishinaabek tehatihsnónhsahere ne óhontsa.

Gimaakwe Gchi-gkinoomaagegamig atemagad Naadowe miinwaa Anishinaabe aking.

To acknowledge this traditional territory is to recognize its longer history, one predating the establishment of the earliest European colonies. It is also to acknowledge this territory's significance for the Indigenous Peoples who lived, and continue to live, upon it and whose practices and spiritualities were tied to the land and continue to develop in relationship to the territory and its other inhabitants today.

Schedule

James A. Low Research Day

Friday, April 9, 2021

8:40	Land Acknowledgement (Dr. Jennifer McCall)
8:45	Opening Remarks (Dr. Graeme Smith)
8:50–10:00	**Oral Session |** *Moderator: Dr. Maria Velez*
8:50	**O1 Jessica Blom** Endometriosis is a Possible Risk Factor for Premature Cardiovascular Disease
9:00	**O2 Hossai Furmli** Comparing reproductive health outcomes among immigrant, refugee and Canadian born women: A population-based cohort study.
9:10	**O3 Anique Le Roux** Therapeutic Journey of Adolescents with Severe Dysmenorrhea and Endometriosis
9:20	**O4 Noor Shakfa** Improving genotype specific chemotherapy response in ovarian cancer via cGAS-STING pathway activation
9:30	**O5 Aline Atallah** Transgenerational Effects of Aberrant inflammation in Rat Pregnancy
9:40	**O6 Jean-François Paré** Classical monocytes from patients with pregnancy complications exhibit lower inflammatory response in the third trimester of pregnancy and after delivery

9:50–10:00	**HEALTH BREAK**

10:00–10:50	**Poster Session ROOM 1: Basic Science |** *Moderator: Dr. Samantha Benton*
	P1 Sydney Vanderkooi Exploration of the mechanism of human oviduct-specific glycoprotein (OVGP1) on enhancing sperm capacitation.
	P2 Alex Sadler Cigarette smoking in pregnancy increases mitochondrial fission in the human placenta.
	P3 Megan Cull Do Sca-1 positive trophoblasts cells contribute to an adaption or pathology in the placenta?
	P4 Yousra Tera Platelet Activation and Platelet Indices as Markers for Disease Progression in Women with Breast Cancer
	P5 Deyang Li Interferon associated adaptive immune resistance represented by immune checkpoint expression and immune cell localization in high-grade serous ovarian cancer
	P6 Matthew Gynn The effect of cigarette smoke extract and aspirin on mitochondrial dynamics in placental cells in-vitro
	P7 Ahmad J.H. Albaghdadi Tacrolimus Promotes First Trimester Extravillous Trophoblast Cells Migration and Modulates Their Nitric Oxide Synthase Activity In Vitro

10:00–10:50	**Poster Session ROOM 2: Clinical Science I |** *Moderator: Dr. Olga Bougie*
	P8 Sydney Flatt Evaluation of a Postpartum Cardiovascular Risk Screening Clinic: An Analysis of Interpregnancy and Subsequent Pregnancy Outcomes
	P9 Stefan Jevtic Physicians' Knowledge and Management Practices of COVID-19 Coagulopathies in Pregnancy
	P10 Skylar Tierney Hormonal contraception and thrombosis: identifying the gaps in knowledge among young women
	P11 Madeleine Powell Risk of Premature Ovarian Insufficiency following chemotherapy for AYA breast cancer: a population-based cohort study
	P12 Tiffany Chih Risk of preeclampsia in pregnancies conceived by assisted reproductive technology: a systematic review and meta-analysis of cohort studies
	P13 Eva Bruketa Maternal Obesity and Stillbirth-Related Placental Morphology: A Matched Case Control Study
	P14 Eva Bruketa Maternal Obesity and Stillbirth-Related Placental Morphology: A Matched Case Control Study

10:00–10:50	**Poster Session ROOM 3: Clinical Science II |** *Moderator: Dr. Maha Othman*
	P15 Sasha Letourneau Trends in urological injuries following gynecologic oncological surgeries in Kingston.
	P16 Grace S. Yin Investigating the uniformity of catheter-associated urinary tract infections (CAUTIs) related attitudes, beliefs, and practices amongst obstetrics and gynecology physicians at a Tertiary Care Hospital.
	P17 Michael Merrick Infertility treatment, multiple gestation, and multifetal reductions: a population-based cohort study.
	P18 Adelaide Burrows Preoperative factors of endometrial carcinoma in patients undergoing hysterectomy for atypical endometrial hyperplasia
	P19 Dia Kapoor An umbrella review of the risk of autism spectrum disorder in children conceived from assisted reproductive technology.
	P20 Flavia Elias Reproductive disorders and pregnancy outcomes in pregnancies conceived by Assisted Reproductive Technology: an overview and meta-analyses.
	P21 Emily Richmond Understanding caesarean delivery in women with subfertility and infertility treatment using the Robson Classification: A population-based cohort study

10:50–11:00	**HEALTH BREAK**

	Keynote Speaker | *Moderator: Dr. Maria Velez*
11:00–11:55	**Dr. Maria B. Ospina** Ehawawisit (With Child): A Mixed-Methods Evaluation of Maternal and Perinatal Health among the Métis in Alberta?

11:55	**Closing Remarks |** Dr. Maria Velez

Zoom Links

James A Low Research Day - Main Room
https://queensu.zoom.us/j/98994115414?pwd=bmRNRXBscENheXA1T3JGZ1BMb2pwdz09
Meeting ID: 989 9411 5414
Passcode: 736495
Find your local number: https://queensu.zoom.us/u/acTUCSxSlm

James A Low Research Day - Poster Session Room 1
https://queensu.zoom.us/j/96718460816?pwd=Z2RQcVhJTW1sSWVOTmtrbENGb0xrZz09
Meeting ID: 967 1846 0816
Passcode: 852413
Find your local number: https://queensu.zoom.us/u/addHsKkQcd

James A Low Research Day - Poster Session Room 2
https://queensu.zoom.us/j/97932813791?pwd=MitnZmFmYlB6bVlHbDFXdmJtdWVudz09
Meeting ID: 979 3281 3791
Passcode: 974083
Find your local number: https://queensu.zoom.us/u/aWA4ukBbE

James A Low Research Day - Poster Session Room 3
https://queensu.zoom.us/j/94640225844?pwd=K21qWEFXUzZNL0lHM1I5T2RLM21QUT09
Meeting ID: 946 4022 5844
Passcode: 661595
Find your local number: https://queensu.zoom.us/u/awjukPqBe

Keynote Speaker

Ehawawisit (With Child): A Mixed-Methods Evaluation of Maternal and Perinatal Health among the Métis in Alberta?

Dr. Maria B. Ospina, MSc, PhD
Assistant Professor
Departments of Obstetrics & Gynecology and Medicine
University of Alberta

Dr. Maria Ospina is an assistant professor with the Department of Obstetrics & Gynecology, a clinical epidemiologist, and population health researcher. She is a Canada Research Chair in Life Course, Social Environments and Health and member of the Women and Children's Health Research Institute. She has developed an innovative multidisciplinary translational research program to understand how the first 1,000 days of human life influence future health: DMETRE (Developmental Maternal and perinatal Epidemiology and Translational Research Evidence: Data, Birth, Babies + Beyond). DMETRE is based on a knowledge-to-action approach in which epidemiological methods are applied to produce maternal and perinatal epidemiological knowledge in relation to three main themes:

- Developmental Trajectories of Chronic Diseases
- Pathways of Inequalities in Maternal and Perinatal Health
- Synthesis of Maternal and Perinatal Research Evidence

Her work is supported by the Canadian Institutes of Health Research, PolicyWise for Children and Families, the Lung Association, the Alberta Health Services Strategic Clinical Network, and through the generosity of the Alberta Women's Health Foundation through the Women and Children's Health Research Institute.

Abstracts

Oral Presentations

Endometriosis is a Possible Risk Factor for Premature Cardiovascular Disease

Jessica N Blom (R2),[1] Maria P Velez,[1,2] Chad McClintock,[2] Jessica Pudwell,[1] Susan Brogly,[2,3] Olga Bougie.[1]

[1]Dept OBGYN, Queen's University, Kingston Health Sciences Centre, Kingston, ON, Canada; [2]ICES Queen's, Kingston, ON, Canada; [3]Dept Surgery, Queen's University, Kingston, ON, Canada

INTRODUCTION: Although cardiovascular disease (CVD) remains the leading cause of premature death in women worldwide, screening, diagnosis and treatment strategies were developed based on the male CVD experience. Female specific risk factors for CVD must be identified to improve patient outcomes. Endometriosis affects up to 10% of the female population, and may increase one's risk for CVD through chronic inflammation and early menopause. The OBJECTIVE of this study was to determine the association between a diagnosis of endometriosis and subsequent risk of CVD.

METHODS: We conducted a population-based cohort study using administrative health data from ICES in Ontario. The incidence of CVD and cardiovascular health outcomes was compared between women with endometriosis (exposed) and 2 age-matched women without endometriosis (unexposed) from 1993-2015 who were 18-50 years old upon enrollment. Women were considered to have endometriosis if they had a confirmed surgical diagnosis at any time (ICD9-617, ICD10-N80), or if they had 2 codes indicating a medical diagnosis (OHIP dx617). Exclusion criteria included CVD parameters at baseline. The primary outcome was composite hospitalizations due to CVD events. Secondary outcomes included composite CVD events of interest. Outcomes were based on previously validated composites. Cox-proportional hazards models were used to estimate hazard ratios (HR) by endometriosis status while adjusting for sociodemographic and prior health factors.

RESULTS: A total of 500,559 patients were enrolled in the study (166,853 exposed and 333,706 unexposed). Average age of enrollment was 36.4 years for both groups. Women with endometriosis had a higher incidence of hospitalization for CVD (197 cases / 100,000 person-years) as compared to unexposed (164 cases / 100,000 person-years) and a significantly reduced time to event (HR 1.16; 95% CI 1.11-1.20; $p<0.001$). Similarly, the incidence of secondary CVD events was higher in the exposed group (292 cases / 100,000 person-years) as compared to unexposed (224 cases / 100,000 person-years) and the time to event was reduced (HR 1.25; 95% CI 1.21-1.29; $p<0.001$).

CONCLUSION: This is the first population-based study to examine the association between endometriosis and CVD. Our results indicate that endometriosis may be a risk factor for the development of premature CVD. Further studies will need to be conducted to elucidate the potential mechanism, including the mediating role of surgical menopause.

FUNDING: CIHR

Comparing reproductive health outcomes among immigrant, refugee and Canadian born women: A population-based cohort study

Hossai Furmli (PGY2)[1], Jessica Pudwell[2], Rebecca Griffiths[3], Michael Green[1,3], Maria Velez[2,3].

[1]Queen's University Department of Family Medicine; [2] Queen's University Department of Obstetrics and Gynecology; [3] ICES Queen's

INTRODUCTION: Although cardiovascular disease (CVD) remains the leading cause of premature death in women worldwide, screening, diagnosis and treatment strategies were developed based on the male CVD experience. Female specific risk factors for CVD must be identified to improve patient outcomes. Endometriosis affects up to 10% of the female population, and may increase one's risk for CVD through chronic inflammation and early menopause. The OBJECTIVE of this study was to determine the association between a diagnosis of endometriosis and subsequent risk of CVD.

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FUNDING: CIHR

Therapeutic Journey of Adolescents with Severe Dysmenorrhea and Endometriosis

Anique Le Roux (Meds 2022)[1], Jennifer McCall (R3)[2], Jessica Pudwell[2], Jamie Pyper[3], Olga Bougie[2].

[1]Queen's University School of Medicine; [2] Queen's University Department of Obstetrics and Gynecology; [3] [1]Queen's University Faculty of Education

OBJECTIVE: Endometriosis in adolescents is underrecognized and understudied, leading to delayed diagnosis and reduced quality of life. We aimed to appreciate the diagnostic and therapeutic journey of adolescents with endometriosis, including disease presentation, obstacles to diagnosis and management, and the impact of endometriosis on their life.

STUDY METHODS: Women under twenty-eight years with severe dysmenorrhea were included. Participants were identified through a retrospective review of gynecology rosters at Kingston General hospital and invited to complete a questionnaire assembled from the World Endometriosis Research Foundation and the SF36 questionnaire. A mixed study design was utilized. Participants were further invited to complete a semi-structured phone interview. Questionnaire data was analyzed using descriptive statistics. Interviews were coded inductively using the constant comparative analysis method by two analyzers and inter-rater reliability was calculated. Thereafter, both sets of data were compared using a cross-sectional method. The study was approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (HSREB) (approval number #6029585).

RESULTS: We reviewed 23 charts. 23 participants were invited to participate in the study, 8 declined or never responded, 10 participants completed the survey and 5 participated in the interview. Onset of pelvic pain was reported at a mean age of 13.9 years (SD 1.9). Of surveyed participants, 50% identified that they have an endometriosis diagnosis, diagnosed at a mean age of 19.2 years (SD 2.6). Mean dysmenorrhea pain score was 8.3 (SD 1.8) on a 10-point severity scale. 90% reported severe pain requiring bed rest and medication. When experiencing pelvic pain, 90% of participants reported dyspareunia. Initial presentation to health care was through an emergency department visit for the majority (16/23) of patients. Mean age of interview participants was 23.6 (SD 2.61). Thematic analysis of patient interviews revealed three major themes: (1) endometriosis broadly impacts all aspects of an individual's life, (2) systemic unawareness and misunderstanding regarding endometriosis and women's health, especially in adolescents, by both health care providers and the public create delays for diagnosis and therapy, and (3) and the journey with disease begins long before diagnosis and creates a culture of self-directed care.

CONCLUSIONS: Adolescents with endometriosis encounter multiple obstacles. From our analysis, patients with endometriosis present with symptoms at a young age and often self-manage before receiving a formal diagnosis. Quality of life is reduced in all aspects of a person's life. There is a delay in diagnosis due to a knowledge translation gap with awareness and understanding regarding female reproductive health.

FUNDING: Queen's University Department of Obstetrics and Gynecology

Improving genotype specific chemotherapy response in ovarian cancer via cGAS-STING pathway activation

Noor Shakfa*, Elizabeth Lightbody, Deyang Li, Juliette Wilson-Sanchez, Gwenaelle Conseil, Afrakoma Afriyie-Asante, Stephen Chenard, Ali Hamade, Madhuri Koti
**PhD Candidate, Department of Biomedical and Molecular Science*

BACKGROUND & OBJECTIVE: Ovarian cancer is the most lethal gynaecologic malignancy, accounting for ~152,000 deaths globally each year. High-grade serous ovarian carcinoma (HGSC) is the most common subtype, with a 5-year survival rate of 45%. Although most patients show initial response to treatment, over 70% of cases will relapse due to developed chemotherapy resistance. Our work aims to counter the chemoresistance seen in HGSC patients via immune sensitization. Previous studies from our group have demonstrated the variable tumor immune microenvironment states that associate with platinum chemotherapy response. We further showed the significance of the interferon (IFN) induced chemokine CXCL10 as a key mediator of tumor infiltrating immune cell recruitment. Using the ID8-Trp53−/− murine model of HGSC, we demonstrated the potential of Stimulator of Interferon Genes (STING) pathway activation in enhancing response of HGSC tumors to carboplatin chemotherapy and sensitizing them to immune checkpoint blockade therapy through a heightened type 1 IFN response. CXCL10 production via IFN1 is also governed by genes that regulate cellular DNA damage repair pathways. Evolving evidence indicates a role of BRCA1 and PTEN genes in mediating cellular IFN1 responses. Losses in the function of these genes is widely prevalent in a large proportion of HGSC tumors, where tumors with BRCA1 mutations (~25% of HGSC cases) have higher CD8+ T cell infiltration in contrast to those with loss of PTEN (~10% of cases). We hypothesized that HGSC tumors with loss of PTEN expression can be rendered susceptible to immune mediated killing via activating the STING pathway.

STUDY METHODS: TIME of tumors generated from ID8 Trp53-/-; Brca1-/- cells and those from ID8 Trp53-/-; Pten-/- cells were characterized. The response of these distinct cells (in vitro), and tumors (in vivo) to combination carboplatin and STING agonist therapy was determined. Local and systemic immune responses post-treatment were measured using our immune profiling protocols.

RESULTS: Tumors generated from ID8-Trp53−/−; Brca1−/− cells and those from ID8-Trp53−/−; Pten−/− cells in C57BL6 mice showed significant immunologic differences through local and systemic immune profiling. The addition of STING agonist treatment significantly increased chemosensitivity and improved overall response in mice implanted with ID8-Trp53−/−; Pten−/− cells compared to those treated with carboplatin alone, altering immune responses.

CONCLUSION: This study is foundational to inform rational combinations of STING pathway activating therapies in HGSC, augmenting responses to existing chemotherapy regimens and prolonging survival rates in patients.

FUNDING SOURCES: Canadian Institutes of Cancer Research & Ontario Ministry of Research and Innovation Early Researcher Award.

Transgenerational Effects of Aberrant inflammation in Rat Pregnancy

Aline Atallah (MSc), Takafumi Ushida, Nicole Protopapas, Shannyn Macdonald-Goodfellow, Charles Graham and Tiziana Cotechini

OBJECTIVES: Children born to women who experience pre-eclampsia are at increased risk of developing cardiovascular (CV) and metabolic disease in adult life, while daughters experience an increased risk of developing pregnancy complications themselves. Though aberrant maternal inflammation contributes to the pathophysiology of pregnancy complications, its generational impact on the development and persistence of risk factors for CV and metabolic disease and pregnancy outcomes in offspring remains unclear. Using a rat model of inflammation-induced pregnancy complications, we examined whether aberrant inflammation in pregnancy leads to the development of known CV and metabolic disease risk factors in offspring, and whether female offspring develop pregnancy complications during their reproductive life.

METHODS: Pregnant Wistar rats (F0 generation) were administered low-dose lipopolysaccharide (LPS; 10-40ug/kg) or saline on gestational days 13.5-16.5 and allowed to deliver F1 offspring. Cardiovascular and metabolic parameters were evaluated in F1 offspring at 24-weeks of age using glucose tolerance test and cardiac growth-related gene expression. To evaluate the generational effect of pregnancy complications, F1 females were mated to non-experimental male rats. F1 dams were sacrificed on gestational day 17.5 and fetal weights of the F2 generation were assessed. Placentas from the F2 generation were processed for immunohistochemistry to assess the expression of the glucose transporter, GLUT1.

RESULTS: F1 offspring born to LPS-treated dams exhibited increased cardiac growth-related gene expression and abnormal glucose metabolism compared with F1 offspring born to saline-treated dams. Weights of F2 fetuses from LPS-treated grandmothers were significantly reduced compared with weights of F2 fetuses from saline-treated control grandmothers. Compared with controls, F2 fetuses from LPS-treated grandmothers displayed reduced GLUT1 immunoreactivity in the labyrinth zone of the placenta.

CONCLUSION: Abnormal maternal inflammation may contribute to increased risk of CV and metabolic disease in affected offspring. Moreover, our data provide evidence of a generation impact of pregnancy complications in subsequent generations, which may be mediated by impaired glucose transport to the neonate. Management of inflammation during pregnancy may be an important strategy to prevent pregnancy complications and their transgenerational effects.

FUNDING SOURCE: CIHR

Classical monocytes from patients with pregnancy complications exhibit lower inflammatory response in the third trimester of pregnancy and after delivery

Jean-François Paré (Research Associate), Kira King, Graeme N. Smith, and Charles H. Graham

Department of Biomedical and Molecular Sciences and Obstetrics and Gynaecology, Queen's University

Aberrant inflammation has an important role in the pathophysiology of pregnancy complications and could contribute to the subsequent increased risk of metabolic diseases in the mother. We are investigating the role of trained immunity, a.k.a. innate-immune memory, in the hyper-inflammatory status of patients with pregnancy complications, more specifically the contribution of monocytes. We purified classical monocytes from third-trimester maternal blood and at six months post-delivery from patients with normal pregnancy, preeclampsia (PE), or intra-uterine growth restriction (IUGR). To evaluate the acquisition of trained immunity in these cells, we quantified their release of pro-inflammatory cytokines following exposure to a heterologous stimulus, lipopolysaccharide (LPS). We also investigated the epigenetic changes associated with pregnancy complications by quantifying chromatin accessibility at promoter regions of pro-inflammatory genes. We found that, in patients with pregnancy complications, the release of pro-inflammatory cytokines from classical monocytes was dampened when compared with monocytes from patients with normal pregnancy. We also found that chromatin accessibility at pro-inflammatory genes was reduced in pregnancy complications cases, as demonstrated by lower tri-methylation at lysine 4 residue of histone 3 (H3K4me3) at these genomic sites. Moreover, classical monocytes from some mothers who had pregnancy complications remained hypo-responsive six months after delivery. These results indicate that classical monocytes from patients with pregnancy complications may have acquired a tolerance phenotype due to prior hyper-activation, and/or that other subsets of leukocytes (e.g. non-classical monocytes, natural killer (NK) cells) could mediate the inflammation associated with pregnancy complications. Further tests with various stimuli and other leukocytes subsets will help us elucidate the complexity aberrant inflammation associated with pregnancy complications.

FUNDING SOURCE: CIHR

Abstracts

Poster Presentations
Basic Science

Exploration of the mechanism of human oviduct-specific glycoprotein (OVGP1) on enhancing sperm capacitation

Sydney Vanderkooi (M.Sc. Candidate), Yuewen Zhao, Patricia Lima, and Frederick W. K. Kan.
Department of Biomedical and Molecular Science. Queen's University.

OBJECTIVE: Worldwide, 15% of couples suffer from infertility, where male infertility is the sole or contributing cause in about 50% of all infertile couples. Many infertile couples seek fertility treatment with in vitro fertilization (IVF). Since defective sperm-egg binding and penetration are the major causes for zero or low fertilization rates with standard IVF, there is a need to further improve the efficacy of this technique. The mammalian oviductal cells synthesize and secrete a major glycoprotein know as oviductin, or oviduct-specific glycoprotein (OVGP1). This protein has been implicated in enhancing mammalian sperm capacitation, sperm motility, sperm penetration and sperm-egg binding. Despite mimicking the physiological condition of the female oviductal fluid, the culture medium of IVF lacks OVGP1 which is normally present in the lumen of the oviduct in vivo. Our lab has successfully produced recombinant human OVGP1 (rHuOVGP1), which has been shown to enhance tyrosine phosphorylation of sperm proteins in the tail, a biochemical hallmark of capacitation, enhance the potential of sperm undergoing acrosome reaction, and increase sperm-egg binding. We set out to explore the mechanism of human OVGP1 in enhancing several key events of sperm capacitation. A major mechanism of inducing sperm capacitation is through the increase of intracellular calcium concentration ([Ca2+]i). The cation channels of sperm (CatSper) have been found to control the entry of Ca2+ ions into the sperm tail during capacitation and to be required for male fertility. Progesterone (P4) is known to bind to the plasma membrane P4 receptor of sperm and activate the CatSper channels, thus inducing the influx of Ca2+. Results in our lab have shown that P4 can also enhance tyrosine phosphorylation levels of sperm proteins alone and yield further increase when combined with rHuOVGP1. In the present study, we hypothesize that human OVGP1 enhances sperm capacitation through increasing [Ca2+]i possibly in a manner similar to P4 in increasing [Ca2+]i during sperm capacitation. There are two main objectives: first, to determine whether rHuOVGP1 increase [Ca2+]i levels alone and in combination with P4; second, to examine the localization of this [Ca2+]i increase.

STUDY METHODS: Experiments were carried out using fresh human sperm obtained from FlowLabs. The principal tests performed include fluorometric flow cytometry and confocal microscopy with live cell imaging. Statistical analysis was performed using student t-test and two-way ANOVA.

RESULTS: Results obtained to date indicate that rHuOVGP1 can increase [Ca2+]i levels in human sperm in a dose-dependent and time-dependent manner during capacitation. Our results demonstrate that both rHuOVGP1 and P4 can each increase [Ca2+]i levels alone and yield further increase when used in combination.

CONCLUSION: In the present study, we unravelled one mechanism of human OVGP1 in enhancing sperm capacitation, which is through the increase of [Ca2+]i in sperm. The present research is of significance to the field of infertility treatment as better understanding the mechanism that regulates the function of OVGP1 could lead to its supplementation to culture medium of IVF, potentially improving its success rates.

FUNDING: CIHR

Cigarette smoking in pregnancy increases mitochondrial fission in the human placenta

Alex Sadler, Nichole Peterson, Matt Glynn, Jonathan Ausman, Graeme Smith

Department of Obstetrics and Gynecology and Queen's University

OBJECTIVES: The aim of this study is to characterize mitochondrial dynamics (mitochondrial fission and fusion) in placentae of women who smoke in pregnancy relative to their non-smoking controls. Our secondary aims are to identify the components of cigarette smoke (Cigarette smoke extract (CSE) versus Carbon Monoxide (CO)) that are responsible for shifts in mitochondrial dynamics using an in vitro cell model of SV Neo cells.

STUDY METHODS: Nine pregnant cigarette smokers and BMI-matched controls were recruited from the antenatal clinic. Smoking status was confirmed by ELISA urine cotinine analysis. Placentae were collected within 10 minutes of delivery, according to protocol. Markers of mitochondrial fission were measured by protein expression of P-DRP1/DRP1 (dynamin-related protein 1) using western blot (WB). Mitochondrial fusion was measured by protein expression of OPA1 (optic atrophy 1) using WB. SV Neo cells were cultured and exposed to CSE at concentrations of 0.1%, 1% and 2%, at timepoints of 30 minutes, 1, 4, and 24 hours, and protein expression of P-DRP1/DRP1, and OPA1 measured by WB. SV Neo cells were exposed to media infused with 250 ppm CO at 30 minute, 1 hour and 4 hour timepoints; P-DRP1/DRP1 and OPA1 protein expression was measured by WB. Cigarette smoke extract (CSE) and Carbon Monoxide (CO) doses and time response curves were determined, and optimal conditions identified for future replication.

RESULTS: Urine cotinine analysis using ELISA confirmed smoking status ($p<0.001$). P- DRP1/DRP1 protein expression was increased three-fold in women who smoke in pregnancy ($p=0.0094$), and this associated with a decrease in OPA1 protein expression relative to controls ($p=0.0015$). Mitochondrial isolation confirmed decreased OPA1 in the mitochondrial compartment ($p=0.017$). Preliminary time-response experiments identified a one-hour timepoint as optimal, based on CO-dissipation in curve. OPA1 protein expression decreased relative to the mean of control at CSE concentrations of 0.1% (0.5:1) and 0.5%, (0.77:1), and increased at 1% CSE concentration (1.25:1).

CONCLUSIONS: Whole placentae protein expression of P-DRP1/DRP1 and OPA1 show increased mitochondrial fission in women who smoke in pregnancy, and this associated with decreased mitochondrial fusion, as confirmed by mitochondrial isolation. CSE is identified as having a dose-related effect on OPA1, where lower concentrations of 0.1% and 0.5% associated with decreased protein expression, but the 1% dose associated with increased protein expression. Replication of this experimental design, including those with CO infused media, is required.

FUNDING SOURCE: CIHR

Do Sca-1 positive trophoblasts cells contribute to an adaption or pathology in the placenta?

Megan Cull (1st year MSc), Dr. David Natale
Department of Obstetrics and Gynecology and Queen's University

OBJECTIVES: Stem Cell Antigen-1 (Sca-1) is a cell surface marker that allows for the isolation of proliferative, multipotent mouse trophoblast stem (mTS) cell-like cells from the mid-gestation placenta. In response to placental stress, Sca-1+ trophoblast (TB) increase in frequency, though whether these Sca-1+ TB cells contribute to placental pathology or confer an adaptive potential is unknown. I hypothesize that Sca-1+ TB cells maintain full differentiation potential and provide a placental adaptation in response to stress. My research project will define whether Sca-1 identifies a TS cell expansion in response to stress and will determine (1) if Sca-1+ TB contribute to placental development and (2) the role of Sca-1+ TB in the placenta and the TS cell niche.

STUDY METHODS: Tamoxifen-inducible Sca-1-CreERT2 mice and Rosa26-Brainbow reporter mice will be used together with a Reduced Utero-placental Perfusion Pressure (RUPP) model to identify and conduct lineage tracing of the Sca-1+ TB in response to stress. When activated, the Sca-1+ TB in the resulting placentae will express one of 4 colours (red, green, yellow, blue) from the Rosa26Brainbow transgene. The RUPP model involves surgical ligation of the maternal ovarian arteries to gradually restrict placenta blood flow and is a well-established placental stress model. At E14.5, mice will undergo RUPP or Sham surgeries, followed immediately by tamoxifen injection. Placentae will be collected at E16.5 and E18.5. Sca-1+ cells (and daughters) will be identified by expression of fluorescent reporter proteins. Contribution to the placenta will be assessed by a combination of fluorescent microscopy and dual Immunohistochemistry/In Situ Hybridization for differentiated TB genes to identify the timing of how Sca-1+ TB differentiate and contribute in response to placental stress. RNA-sequencing will be used to define the population, and in all assessments, embryo/placental sex will be considered as a biological variable. To complement the in vivo work and to assess whether Sca-1 is critical to the TB response to stress, I will use the mTS in vitro culture model. Hypoxic (1% O2) and normoxic (5% CO¬¬2 in air) culture conditions will be used together with a short hairpin (sh)RNA-mediated knockdown and over expression (OE) with Sca-1 constructs transfected into mTS cells. Cells will be collected and counted to assess proliferation, and RNA collected for analysis of TS and differentiated TB gene expression by qRTPCR.

RESULTS: I expect that Sca-1¬+ TB cells contribute to placental adaptation and have an enhanced proliferative status in response to stress, suggesting stemness. In collected placenta, expression of fluorescent reporter proteins will identify Sca-1+ cells (and daughters). I anticipate seeing clusters of the same colour, identify individual cells that proliferated and gave rise to daughter cells, rather than a single-coloured cell or a multicoloured cluster which would identify non-dividing Sca-1+ cells. From the mTS in vitro culture model, if functionally required, shRNA-mediated knockdown should reduce proliferation and stemness, while OE should do the reverse. If Sca-1 identifies a quiescent population that proliferates in response to stress, OE should increase proliferation and reduce differentiation, while knockdown in hypoxic conditions should compromise the cells.

SIGNIFICANCE: In other organs, Sca-1+ cells promote adaptive responses to stress. My project will, for the first time, using lineage tracing and ablation studies, determine whether Sca-1+ TB confer adaptive potential in the mouse placenta in response to stress. Understanding whether mid-late gestation TS cells confer adaptive potential is highly relevant as human TS cells, which have been recently characterized, may offer a potential target to treat placental pathologies in the future.

FUNDING SOURCE: NIH/NICHD

Platelet Activation and Platelet Indices as Markers for Disease Progression in Women with Breast Cancer

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OBJECTIVE(S): To systematically evaluate platelet activation and platelet volume indices in women with BC in chemo-naïve locally invasive and metastatic disease.

STUDY METHOD(S): Patients were recruited from oncology center at our local hospital between 2019 to 2020 following ethics approval. Patient groups included: 80 locally invasive BC patients (stages I,II,III), 20 metastatic (stage IV) and 100 age-matched controls. Platelet activation in response to ADP was assessed by light-transmission aggregometry. Platelet P-selectin (CD62P) expression with and without ADP stimulation was assessed by flowcytometry. Comprehensive analysis of platelet count and all platelet volume indices (PVIs) (MPV, PDW, MPV/P and PDW/P). Data were analyzed in relation to tumor pathology, hormone receptors (ER, PR, HER-2) and proliferation index Ki-67. Regression analyses were conducted for prediction of poor prognosis, tumor aggression and metastatic potential.

RESULTS: There was significant increase in platelet aggregation (MA), CD62P expression, CD62P+ADP, MPV, PDW, MPV/P and PDW/P in the metastatic group compared to the locally invasive group. Tumor size and grade were significantly correlated with ADP-MA, CD62P, CD62P+ADP, MPV, PDW, MPV/P and PDW/P. The area under curve showed (0.98, 0.9, 0.97, 0.93, 0.66, 0.7, 0.8, 0.73) for ADP MA, CD-62, CD-62P+ADP, CD-62P Diff., MPV, PDW, MPV/P, PDW/P) respectively. Univariate regression analysis showed significance for MA, CD62P, CD62P+ADP, CD-62P Diff., PLTs count, MPV, PDW, MPV/P, PDW/P.

CONCLUSION(S): PVIs (MPV/P and PDW/P) can be used as simple, easily available and low cost predictors for cancer progression and poor prognosis. Also, MA and CD62P+ADP can be regarded significant predictors for metastatic BC.

ABBREVIATION(S): MPV: mean platelet volume, PDW: platelet distribution width, MPV/P: MPV divided by platelet count. ADP-MA: maximum platelet aggregation with ADP, CD-62P and CD-62P+ADP: P-selectin expression at basal level and with ADP. CD-62P Diff: difference between basal and activated CD-62P.

FUNDING SOURCE: Egyptian ministry of higher education research fund.

Interferon associated adaptive immune resistance represented by immune checkpoint expression and immune cell localization in high-grade serous ovarian cancer

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OBJECTIVE(S): High-grade serous carcinoma (HGSC) is a deadly malignancy leading to ~70% of the 140,000 ovarian cancer deaths globally each year. Resistance to platinum chemotherapy followed by recurrence and an incurable disease occurs in most HGSC patients. Contemporary immune checkpoint blockade therapies have shown minimal efficacy in this cancer. Our previous investigations established that tumour interferon (IFN) activation status and CD8+ T cell density are predictors of chemotherapy response in HGSC. Furthermore, we also showed that IFN induced chemokine CXCL10 is a key determinant of increased survival via immune cell recruitment in the tumour immune microenvironment (TIME). Given that signal transducer and activator of transcription 1 (STAT1) is central to the feed forward loops of cellular IFN responses, we investigated STAT1 associated transcriptomic alterations and spatial profiles of immune cells in 204 pre-treatment HGSC tumours.

STUDY METHODS: A pre-selected subset of 43 sensitive (high STAT1 protein) and 17 resistant (low STAT1 protein) tumours previously characterized for STAT1 expression and CD8+ TIL density was subjected to RNA sequencing. Multiplex immunofluorescence based spatial profiling of CD8+ T cells, FoxP3+ T regulatory T cells, CD68+M1, and CD163+ M2 macrophages and expression of PD-L1, PD-1, IDO1 immune checkpoints was performed in all 204 pre-treatment tumors.

RESULTS: RNA-sequencing based whole transcriptomic profiling revealed that higher STAT1 expression significantly correlated with higher immunomodulatory gene expression, including immune checkpoints and activators, in both chemotherapy sensitive and resistant tumours. Findings were independently validated in a cohort of 379 HGSC tumour RNA-Seq profiles from The Cancer Genome Atlas Network ovarian cancer dataset.

CONCLUSION(S): Findings from our study provide evidence for IFN mediated adaptive immune resistance in the HGSC TIME and will potentially inform the design of rational chemo-immunotherapy approaches.

FUNDING SOURCE: CIHR

The effect of cigarette smoke extract and aspirin on mitochondrial dynamics in placental cells in-vitro

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BACKGROUND: Cigarette smoking has been shown to decrease the risk of preeclampsia and is attributed to carbon monoxide. The mitochondrial dynamics (a balance between fission and fusion of cell mitochondria) are shifted towards fission in preeclampsia. Our hypothesis is that the cigarette smoke pushes cells towards an increase in mitochondrial fusion, explaining the differences in preeclampsia in smokers vs. non-smokers. To address this hypothesis, we attempted to separate the components of cigarette smoke into carbon monoxide and the remaining cigarette smoke extract and subsequently test the effects on placental cell mitochondrial dynamics. We additionally tested a potential rescue agent aspirin that could potentially mimic the effects of cigarette smoke on placental cell mitochondrial dynamics to reduce the risk of preeclampsia.

METHODS: We cultured placental SV-NEO cells in RPMI media (5% FBS) for either 30 minutes, 1 hour or 4 hours in the presence of either carbon monoxide bubbled-media (CO-media), cigarette smoke extract-media (CSE-media), low dose aspirin media, and a combined ASA/CSE-media. Cells were harvested at the specified time points and cell lysates were prepared for Western Blot analysis. Cell lysates were blotted for OPA-1 (a protein marker for mitochondria fission) and DRP1P/DRP1 (a protein marker for mitochondrial fusion). Protein bands were normalized to GAPDH controls and analyzed using the ImageJ software.

RESULTS: Our results show no significant changes ($P > 0.05$) in mitochondrial fusion when SV-NEO cells are treated with either CSE, ASA or both. There are technical limitations in assessing CO-media treated cells at this current time.

CONCLUSIONS: Our results suggest that the changes in mitochondrial dynamics are not due to the non-CO components of cigarette smoke. We cannot conclude if carbon monoxide affects mitochondrial dynamics at the present time. Furthermore, ASA does not seem to show promise as a therapeutic to push mitochondrial dynamics towards fusion.

Tacrolimus Promotes First Trimester Extravillous Trophoblast Cells Migration and Modulates Their Nitric Oxide Synthase Activity In Vitro

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OBJECTIVES: To test the hypothesis that, independent of its immunosuppressive properties, low-dose tacrolimus can influence uterine spiral artery remodeling through, at least in part, the promotion of the migration of the first-trimester extravillous trophoblasts and the modulation of the activity of their Nitric Oxide Synthase (NOS) enzyme.

STUDY METHODS: The HTR8/SVneo cells (an immortalized human first-trimester extravillous trophoblast cell line) were cultured under normoxic conditions (5% O2), and were treated with low-dose tacrolimus (10ng/ml), the NOS inhibitor Nω- Nitro-L-Arginine methyl ester (L-NAME) (50 mMol) or a combination of the two treatments for specified time periods. Cells were collected at 12, 24 and 48 hours after treatment and were subjected to Western blot analysis for the detection of eNOS, p-eNOS-Ser 1197, p-eNOS-Tyr495, STAT3 and pSTAT3. The effect of the three treatment conditions on the HTR8/SVneo cells migration was assessed using a standard wound-scratch assay and was recorded in real time using IncuCyte zoom live-cell imager. Moreover, NO production in treated cells was analyzed by fluorescent microscopy and flow-cytometry using the NO sensitive fluorescent probe DAF-FM.

RESULTS: Our results showed the following: 1) a low-dose tacrolimus of 10ng/ml was sufficient to significantly ($p < 0.001$) stimulate the migration of the HTR8/SVneo cells and abrogate the suppressive effect of L-NAME on this process likely through the activation of STAT3 pathway, 2) low-dose tacrolimus prevented L-NAME-induced suppression of NO production in treated HTR8/SVneo cells and 3) low-dose tacrolimus stimulated the phosphorylation of the endothelial NOS (eNOS) activation domain p-eNOS-Ser1179 in treated HTR/SVneo cells.

CONCLUSIONS: Data obtained in this research suggest an immune-independent mode of action of low-dose tacrolimus in positively influencing uterine spiral artery remodeling through, at least in part, promoting the migration of the first-trimester extravillous trophoblasts and modulating the activity of their Nitric Oxide Synthase (NOS) enzyme.

FUNDING SOURCE: This work was supported in part by CIHR.

Abstracts

Poster Presentations
Clinical Science I

Evaluation of a Postpartum Cardiovascular Risk Screening Clinic: An Analysis of Interpregnancy and Subsequent Pregnancy Outcomes

Sydney Flatt (Meds 2023), Jessica Pudwell, Graeme N. Smith

OBJECTIVES: At the maternal health clinic (MHC), women with certain pregnancy complications are seen for appointments focusing on lifestyle modification and future pregnancy counselling. This study's objective is to determine whether women who attended the MHC following a pregnancy complicated by gestational diabetes mellitus (GDM) or a hypertensive disorder of pregnancy (HDP) have improved interpregnancy and subsequent pregnancy outcomes, compared to non-attendees.

STUDY METHODS: A retrospective cohort study was conducted on all pregnancies ≥20 weeks gestation at Kingston Health Sciences Centre from April 2010-Dec 2019. Women with ≥2 deliveries were eligible for inclusion, with 2 pregnancies per woman included. This identified 178 patients who attended the MHC, and 133 who did not. Continuous variables with normal distribution were assessed with independent sample t-tests. Continuous variables without normal distribution and ordinal variables were assessed with Mann–Whitney U tests. Categorical variables were assessed with Pearson's Chi-squared tests. Preterm delivery, HDP and GDM recurrence, HDP and GDM progression, change in first trimester blood pressure and pre-pregnancy weight were examined using multivariate regression modeling. Probability values <0.05 determined significance.

RESULTS: MHC attendance was associated with improvements in interpregnancy weight reduction (P=0.002), fewer interpregnancy type II diabetes diagnoses (P<0.001), and a later gestational age at delivery (P<0.001). There was no observed difference in subsequent pregnancy complication recurrence rate of GDM (P=0.731) or an HDP (P=0.139) between cohorts.

CONCLUSIONS: In our examination of MHC outcomes, we found improvements in certain interpregnancy and subsequent pregnancy outcomes. These results support the continued development and funding of these clinics.

Physicians' Knowledge and Management Practices of COVID-19 Coagulopathies in Pregnancy

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BACKGROUND: Coronavirus disease 2019 (COVID-19) occurs following infection with the highly transmissible, and potentially fatal, severe-acute-respiratory-syndrome-coronavirus-2 (SARS-CoV-2) virus. Infection can be complicated by coagulopathy featuring abnormal coagulation parameters, thrombo-inflammation, and thrombocytopenia, collectively termed COVID-19 associated coagulopathy (CAC). Data concerning CAC prevalence and management in pregnancy is limited. Evaluation of physician experiences in assessing and managing CAC is essential to identify current practice patterns and knowledge gaps.

AIMS: To determine physician experiences and practice patterns relevant to CAC prevention and management in pregnancy.

METHODS: A cross-sectional, international study with self-administered online questionnaire using the RedCap online platform; supported by the ISTH Subcommittee on Women's Health Issues in Thrombosis and Hemostasis.

RESULTS: Of 115 physicians who opened the survey, 74 (38% Maternal-Fetal Medicine, 31% Haematology/Thrombosis) provided responses conducive to analysis. There were 1503 reported cases of COVID-19, from which 1288 contained data regarding disease severity. Sixty-five percent of COVID-19 infections were mild while only 4% were severe. Of all reported cases, 1% developed CAC, of which 63% were in the severe spectrum of COVID-19 infection. The most frequently identified abnormalities included thrombocytopenia, elevated CRP, D-dimer, and lymphopenia. Low-molecular-weight heparin was the anticoagulant of choice, provided by 67% of respondents, with 56% using standard-prophylactic dosing for CAC. Thrombosis occurred in 6 patients on anticoagulation; 50% were receiving standard prophylactic dosing, while the remaining 50% were unspecified. Anticoagulation duration depended on disease severity and additional thrombosis risk factors.

CONCLUSION: CAC is uncommon in pregnancy with a predilection for higher disease severity. Anticoagulation practices vary and may not reflect current guideline recommendations. Development of thrombosis has been observed in CAC on standard prophylactic anticoagulation, thus emphasizing the need for re-evaluation of anticoagulant regime in severe cases. Urgent research is required to determine appropriate anticoagulant dosing and duration in these patients.

Hormonal contraception and thrombosis: identifying the gaps in knowledge among young women

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OBJECTIVES: To determine the current level of knowledge about hormonal contraception among young women so they may be better informed about the risks and various choices available to them regarding hormonal contraception.

METHODS: 681 female participants aged 18-30 years in various academic programs in two post-secondary instructions: Queen's University and St. Lawrence College. Participants completed anonymous online survey exploring three sections: demographics, use/type/duration of hormonal contraception, and knowledge of risks and benefits associated with hormonal contraception including thrombosis. Mann Whitney U test and Spearman Correlation were used to determine differences in knowledge level about contraceptives across age groups, education levels, as well as use/type/duration of hormonal contraception.

RESULTS: Of the 681 participants, 476 were users of hormonal contraception (264 >1 year) and 199 non-hormonal contraception users. 55% have a high school diploma, 21% have a college diploma, 20% have a bachelor's degree, and 4% have a post-graduate degree. The knowledge level of hormonal contraception risks was associated with duration of use and overall knowledge level of thrombosis and hormonal contraception. The knowledge level of thrombosis was positively correlated with duration of use, education level and age. Participants with higher level of education had an increased knowledge surrounding thrombosis. Those that have been using hormonal contraception for 5 years or longer had a significantly higher level of knowledge of thrombosis and risks of hormonal contraception than that of users with a shorter duration of use.

CONCLUSION: Misconceptions remain among young women concerning benefits and risks of hormonal contraception and formal educational intervention can address these misunderstandings to better inform young women.

FUNDING SOURCE: St. Lawrence College Ignite Fund

Risk of Premature Ovarian Insufficiency following chemotherapy for AYA breast cancer: a population-based cohort study

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OBJECTIVES: To determine the risk of Premature Ovarian Insufficiency (POI) following chemotherapy for breast cancer in female adolescent and young adult (AYA) with cancer in Ontario.

METHODS: Retrospective population-based cohort study of women aged 15-39 years with a diagnosis of breast cancer between January 1st, 1992 to December 31st, 2011 in Ontario, Canada. Participants were identified using the Ontario Cancer Registry and using health administrative data accessed through ICES datasets. Participants were categorized into women who had undergone chemotherapy treatment and those who had not. The use of chemotherapy treatments was determined using OHIP billing codes (G381 or G345). Incidence of POI was found using patient visits coded as OHIP billing diagnosis of menopause (ICD 9 code 627) before age 40. Modified Poisson Regression models were used to calculate the relative risk (RR) of POI in women exposed to chemotherapy and unexposed AYA breast cancer survivor, relative to an age-matched cancer-free population. Patient factors such as age, parity at time of cancer, socioeconomic estimates (e.g., income quintiles, deprivation index, and census subdivision, rurality) and immigration status were considered in adjusted models.

RESULTS: We identified 3903 women with breast cancer and 19,515 non-cancer patients. Among participants with breast cancers, 3053 (78.2%) underwent chemotherapy treatment and 850 (21.8%) were unexposed. The mean age of both the exposed group and unexposed group was 35 years old. The unexposed group had lower rates of parity (41.2%) compared to the exposed group (52.7%). There was no significant difference in socioeconomic estimates between exposed and unexposed groups. Relative to non-cancer patient, the risk of POI was higher in women who underwent chemotherapy treatment (RR= 6.25; 95% CI [5.15-7.58]), and in those who did not receive chemotherapy (RR=2.12; 95% CI [1.37-3.28]).

CONCLUSION: This population-based cohort study found a significant association between chemotherapy treatment for AYA breast cancer and increased risk of POI. It is also interesting that women with breast cancer who did not receive chemotherapy, were also at a higher risk of POI relative to women without cancer. Further investigation into the effect of specific chemotherapies and other factors that can contribute to POI in women with breast cancer is needed.

FUNDING SOURCE: The Canadian Institute of Health Research (CIHR).

Risk of preeclampsia in pregnancies conceived by assisted reproductive technology: a systematic review and meta-analysis of cohort studies

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OBJECTIVES: Aims of the meta-analysis are to assess whether in vitro fertilization and intra-cytoplasmic sperm injection (IVF/ICSI) increase the risk of preeclampsia and to identify potential risk factors.

METHODS: Relevant cohort studies published between 1990 and 2020 were identified from EMBASE, MEDLINE, and Cochrane Library or manually using a structured search strategy. Eligibility and quality of studies were evaluated by two reviewers independently (HC, FE). Exposures were IVF, ICSI, multiplicity, oocyte donation, and type of embryo transfer; the outcome of interest was preeclampsia. The pooled results were analyzed using RevMan and reported in odds ratios (OR) with 95% confidence intervals based on random effects models.

RESULTS: Seventy-eight studies were included after a screening of 2098 abstracts and 494 full text articles. Compared to spontaneous pregnancies, IVF/ICSI singleton pregnancies (OR = 1.59; 95% CI = 1.46 – 1.73; I2 = 72%) and multiple pregnancies (OR = 1.14; 95% CI = 1.06 – 1.23; I2 = 0%) were both associated with higher odds of preeclampsia. Pregnancies with oocyte donation had the highest odds of preeclampsia out of all groups analyzed (OR = 4.96; 3.52 – 7.00; I2 = 29%). Frozen embryo transfer resulted in higher odds of preeclampsia (OR = 1.82; 1.71 – 1.95; I2 = 0%) than fresh embryo transfer (OR = 1.48; 1.37 – 1.60; I2 = 39%).

CONCLUSION: Our findings support that IVF/ICSI pregnancies have a higher incidence of preeclampsia compared to spontaneous conceptions. Oocyte donation and frozen embryo transfer contribute particularly to a higher risk. Care plans for IVF/ICSI pregnancies need to be implemented to decrease the risk of preeclampsia and to allow for timely diagnosis.

FUNDING SOURCE: The Canadian Institute of Health Research (CIHR).

Maternal Obesity and Stillbirth-Related Placental Morphology: A Matched Case Control Study

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OBJECTIVES: One in three adults in Canada has obesity. The pregnancies of patients with obesity and placental complications are at an increased risk of stillbirth. The axes of the placenta (breadth and length) are modified independently and the thickness, surface, and shape (degree of ovality) are modified by both maternal and fetal factors. The objective of this study was to compare the placentas of pregnancies resulting in stillbirth to those of livebirths, born to females with obese and normal pre-pregnancy BMI (ppBMI).

METHODS: Information on all patients with a stillbirth at ≥20 weeks' gestation at Kingston Health Sciences Center (KHSC) from January 1st, 2010 to December 31st, 2020 was obtained from the BORN Database and KHSC delivery record. Case-control matching was performed in a 1:3 ratio; 3 obese ppBMI (≥30.0kg/m2) and 3 normal ppBMI (<25.0kg/m2) controls. Matches were based on maternal age (+/- 5 years), parity (parous/nulliparous), and gestational age (preterm/term). Patients with missing ppBMI, twin pregnancy, a known congenital anomaly, or with missing placental data were excluded. Patient characteristics and placental morphology were compared between the stillbirth and control groups. Placental morphology measurements were examined using linear regression, controlling for confounding factors. Data was analysed using SPSS v26.

RESULTS: Included in the analysis were 30 stillbirths, 90 normal ppBMI control and 90 obese ppBMI control patients. The stillbirth and livebirth controls did not differ significantly in the proportion of male fetus, nor in the proportion with pregnancy complications or pre-existing conditions. Despite matching for term/preterm, stillbirths compared to both sets of controls occurred at an earlier gestational, however only stillbirths compared to obese ppBMI livebirths had a significantly smaller birth weight (median 2401 vs 2912 g, p=0.014).

CONCLUSION: Placentas of stillbirths are smaller than those of livebirths across all dimensions measured except thickness. After adjustment, placental weight and placental length maintained significance. Placental Efficiency (inferred via placental weight : birth weight) did not significantly vary.

FUNDING SOURCE: This research was supported by the Thomas M. and Louise A. Brown Research Studentship.

Placental Morphology in Females with Obesity

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OBJECTIVES: One in three adults in Canada as obesity. The axes of the placenta (breadth and length) are modified independently and have been associated with disorders later in the fetus's life. Placental thickness, surface, and shape (degree of ovality) are also modified by both maternal and fetal factors. The objective of this study was to examine the relationship between placenta morphology and obesity.

METHODS: Information on all patients in 2019 who delivered at ≥20 weeks gestation at Kingston Health Sciences Center (KHSC) was obtained from the BORN Database and KHSC delivery record. Exposure was determined based on pre-pregnancy BMI (ppBMI); normal (<25.0kg/m2) or obese (≥30.0kg/m2). Patients with a ppBMI <18.5 or 25.0-29.9 kg/m2, missing ppBMI, twin pregnancy, a known congenital anomaly, or with missing placental data were excluded. Patient characteristics and placental morphology were compared between groups. The placental morphology measurements were examined using linear regression, controlling for confounding factors. Data was analysed using SPSS v26.

RESULTS: Included in the analysis were 521 normal and 407 obese ppBMI patients. The groups did not differ in age (30.2±4.9), in the proportion of male fetus (53.3%), nor in the proportion that delivered preterm (8.2%). A greater proportion of the obese patients were parous (62.7% vs 52.0%, p=0.001). The mean birth weight of infants born to obese patients was higher (3535±588 vs 3327±578, p<0.001).

CONCLUSION: Females with obesity are more likely to be parous and give birth to heavier babies than normal weight females, as expected based on the literature. Females with obesity have statistically significantly larger placentas across all dimensions measured (weight, length, width, thickness, surface area). When adjusted for controls, only placental weight and ratio of Placenta Weight: Birth Weight maintained statistical significance, averaging 27.5 grams heavier and a 0.52% larger ratio.

FUNDING SOURCE: This research was supported by the Thomas M. and Louise A. Brown Research Studentship.

Abstracts

Poster Presentations
Clinical Science II

Trends in urological injuries following gynecologic oncological surgeries in Kingston

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INTRODUCTION: Urologic injuries are common during abdominopelvic surgeries, occurring in 0.2-3% of all gynecological or pelvic procedures. Common urological injuries during obstetrical and gynecological surgeries include bladder (65-71%), ureters (62-71%) and vesico-vaginal fistulae (2%). To our knowledge, no studies have specifically explored the incidence of urologic injuries during gyncecologic oncological surgery.

OBJECTIVE: To characterize the incidence of and risk factors associated with urologic injury among patients undergoing gynecologic oncological surgery in Kingston, ON.

METHODS: All surgeries performed by fellowship trained gynceology-oncologists in Kingston, ON, between January 1, 2018 – December 31st, 2019 were included in a retrospective chart review. Surgeries with extremely low likelihood of involving urologic injury (e.g. inguinal/femoral lymph node dissection) were excluded. Collected data included patient demographic information, surgical data, histopathologic diagnosis, and urologic injury details. The primary study outcome is incidence of urologic injury. As a secondary outcome, this study also investigates potential risk factors associated with urologic injury. Descriptive analysis will be used to determine incidence while risk factors for urologic injury will be modeled using factor analysis, which is underway.

RESULTS: Of the 332 procedures were reviewed, 291 were included in the analysis. Fourteen (4.8%) patients suffered a urologic injury, including 12 bladder and 2 ureteric injuries. Three injuries were intentional. Table 1 summarizes the key differences among injury versus non-injury groups.

CONCLUSION: Identification of potential risk factors for urologic injuries in gynecologic oncological surgery may increase awareness and decrease injury incidence, improving patient outcomes.

Table 1: Comparison of characteristics among patients in the injury versus non-injury groups

	Urologic Injury N=14	**No urologic injury N=277**	**P-Value**
Age (yrs), Mean ± SD	**62.6** ± 12.2	**62.1** ± 62.7	**0.878**
BMI (kg/m^2), Mean ± SD	**31.9** ± 9.3	**31.9** ± 9.3	**0.518**
Prior Abdominal/Pelvic surgery, n (%)	**14** (100%)	**253** (91.3)	**0.615**
Metastasis, n (%)	**5** (35.7%)	**77** (27.8%)	**0.279**
Mass size (cm), Mean ± SD	**6.9** ± 4.4	**8.1** ± 7.1	**0.975**
Laparotomy, n (%)	**13** (92.9%)	**203** (73.3%)	**0.200**
Cystoscopy, n (%)	**5** (35.7%)	**43** (15.5%)	**0.062**

Investigating the uniformity of catheter-associated urinary tract infections (CAUTIs) related attitudes, beliefs, and practices amongst obstetrics and gynecology physicians at a Tertiary Care Hospital

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OBJECTIVE: Catheter-associated urinary tract infections (CAUTIs) are a leading contributor to urinary tract infections (UTIs) acquired in the hospital. This project aimed to assess percent agreement of physician practices, beliefs, and attitudes of catheterization practice, and its perceived necessity in 10 surgical procedures with the goal of reducing CAUTIs through future standardization in practice.

METHODS: All staff and resident physicians in the Department of Obstetrics and Gynecology at Queen's University were surveyed via an electronic questionnaire. The questionnaire distributed collected information on 4 broad categories: 1) demographics of position in the hospital and years of experience, 2) beliefs regarding CAUTIs - their prevalence, seriousness, and general use (agree/disagree statements), 3) beliefs regarding effective practices in preventing CAUTIs (effective/ineffective), and 4) agreement regarding whether catheterization should be routine practice for 10 listed procedures (always catheterize, sometimes catheterize, never catheterize options). Data was graphed in Microsoft Excel and used Cohen's Kappa to represent the inter-rater agreement with SPSS Statistics software.

RESULTS: Out of 40 faculty members and residents emailed, 12 responded (response rate of 30%). The hospital positions of the respondents were as follows: 58% Faculty (7/12), 25% Senior Resident (3/12), 18% Junior Resident (2/12). There were no significant differences in CAUTI beliefs found (p=0.64). Regarding agreement for 10 listed procedures, the highest level of agreement for catheterization of surgical procedures was 92% for Total Abdominal Hysterectomy (always), Hysteroscopy Dilatation and Curettage (never), and NOVOSURE (never). Laparoscopic Bilateral Salpingo-oophorectomy and Laparoscopic Salpingectomy had lowest levels of agreement. There were no statistically significant relationships between number of correct answers and participant's level of training with regards to CAUTI beliefs.

CONCLUSION: This study served its exploratory purposes well with regards to identifying baseline beliefs amongst residents and staff within the department as an appropriate first step towards formulating standardized recommendations for specified procedures. It is recommended that a departmental roundtable be organized to discuss whether consensus can be reached to determine standard catheterization practices, particularly for procedures with high levels of catheterization practice agreement. Future seminars regarding catheterization procedures aimed at standardizing practices can be carried out as a CME opportunity with the goal of reducing the incidence of CAUTI within the Department of Obstetrics and Gynecology.

Infertility treatment, multiple gestation, and multifetal reductions: a population-based cohort study

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OBJECTIVE: To evaluate the association between mode of conception, multiple pregnancies, and multifetal reductions in Ontario between 2006 and 2014 and comparing two periods (2005-2010 and 2011-2014).

METHODS: A population-based cohort study of births between April 1st, 2006 and March 31st, 2014 in Ontario was conducted through ICES (www.ices.on.ca). All births (live and stillbirth) during this period were identified using the Better Outcome Registry & Network (BORN) and Niday Perinatal Databases. These databases were used to classify each delivery according to the mode of conception: spontaneous, subfertility, non-invasive IT (ovulation induction or intrauterine insemination), or invasive IT (in vitro fertilization or intracytoplasmic sperm injection). The primary outcome, multiple gestation pregnancy, was determined using the BORN and Niday Perinatal databases and the secondary outcome, multifetal reductions, was determined using Ontario Health Insurance Plan (OHIP) billing codes and Mother-Baby (MOMBABY) codes. Rates of multiple gestation pregnancies and selective fetal reductions by mode of conception were calculated and a modified Poisson regression was used to calculate the relative risk (RR) of each outcome. The analysis was stratified by estimated conception date in order to compare the time periods of 2005-2010 and 2011-2014. Confounding factors including maternal age, income quintile, rurality, immigration status, obesity, parity, pre-existing diabetes, and chronic hypertension were controlled for.

RESULTS: Of the 921,624 eligible pregnancies, 807,705 (87.6%) were by spontaneous conception, 92,171 (10.0%) in women with subfertility, 10,535 (1.14%) by non-invasive IT, and 11,213 (1.22%) by invasive IT. Multiple pregnancies occurred in 1.23% of women who conceived spontaneously, 3.45% in those with subfertility, 12.01% in non-invasive IT, and 25.41% in invasive IT. Compared to spontaneous conception, the risk of multiple pregnancy increased by the degree of IT invasiveness: adjusted RR 9.24 (95% CI 8.73-9.78) for non-invasive IT and adjusted RR 19.15 (95% CI 18.34-19.99) for invasive IT. The risk of multifetal reduction was higher for both non-invasive IT (adjusted RR 8.60, 95% CI 6.04-12.24) and invasive IT (adjusted RR 6.66, 95% CI 4.76-9.31) compared to spontaneous conception. Additionally, pregnancies conceived between 2011-2014 had a lower risk (RR 0.89, 95% CI 0.87-0.92) of multiple pregnancy compared to 2005-2010 after adjustment for confounders.

CONCLUSION: This study provides evidence of the increased risk of multiple pregnancies and multifetal reductions from non-invasive and invasive IT compared to spontaneous conception. The lower risk of multiple pregnancies among births between 2011-2014 compared to 2005-2010 is an important finding that may be explained in part due to public funding of IVF in Quebec in 2010 and advocacy efforts for single-embryo transfer in IVF.

FUNDING SOURCE: The Canadian Institute of Health Research (CIHR).

Preoperative factors of endometrial carcinoma in patients undergoing hysterectomy for atypical endometrial hyperplasia

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OBJECTIVE: To identify clinicopathological preoperative factors associated with concurrent endometrial carcinoma in patients undergoing surgical management of atypical endometrial hyperplasia.

METHODS: The charts of all patients who underwent hysterectomy at a tertiary care hospital for preoperatively diagnosed atypical endometrial hyperplasia from April 2017 to April 2020 were retrospectively reviewed. Clinicopathological characteristics of patients were extracted. Patients who did not undergo hysterectomy or who had evidence of simple hyperplasia or carcinoma on initial biopsy were excluded. Univariate analysis was performed. A multivariate regression model for progression to endometrial carcinoma was developed.

RESULTS: A total of 126 patients were included. Of these patients, 19 (15.1%) had a final diagnosis of endometrial carcinoma, whereas 86 (68.2%) retained the diagnosis of atypical endometrial hyperplasia and 21 (16.7%) were found to have no residual atypical endometrial hyperplasia. The odds of a patient being diagnosed with endometrial carcinoma were 6.1 times higher (95% CI 1.32, 27.68) if they had an endometrial stripe thickness of >1.1cm and 13.5 times higher (95% CI 3.56, 51.1) if there was histological suspicion of carcinoma. The odds of a patient being diagnosed with endometrial carcinoma were significantly lower if a patient had an initial diagnosis of atypical endometrial hyperplasia in a polyp (OR, 0.07; 95% CI 0.02, 0.34).

CONCLUSION: Our results suggest that an endometrial stripe thickness of >1.1cm, a histological suspicion of carcinoma on preoperative pathology, and the absence of polyp involvement on initial diagnosis are the strongest predictors of endometrial carcinoma at the time of hysterectomy in patients with atypical endometrial hyperplasia.

An umbrella review of the risk of autism spectrum disorder in children conceived from assisted reproductive technology

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OBJECTIVE: The association between the use of assisted reproductive technology (ART) and autism spectrum disorder (ASD) in conceived children has been explored in several studies; however, the results remain inconclusive. A systematic review of reviews (umbrella review) and a meta-analysis was conducted to evaluate the association between ART and ASD in offspring.

METHODS: A literature search using the OVID platform (MEDLINE, Embase, APA PsycInfo, Joanna Briggs Institute, Cochrane, and CINAHL) was conducted to identify systematic reviews and new primary studies related to ART and ASD. The meta-analyses of existing and new primary studies were performed to estimate Risk Ratios (RR) and Odds Ratio (OR) using the random-effects model in RevMan 5.3.

RESULTS: In total, 20 studies (11 cohorts and 9 case-control) were included. In relation to the method of fertilization, five cohort studies did not differentiate between In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (IVF/ICSI). Six cohort studies analyzed IVF alone, and three studies reported on ICSI. The risk of ASD was not observed in the IVF/ICSI cohorts, which presented with a RR=1.40 (95% CI: 0.90-2.17, p=0.14, I2=95%). Similarly, in the case of IVF alone compared to SC, the risk of ASD was null (RR= 2.18, 95% CI: 0.73-6.52; p=0.16, I2=97%). Both had pooled analyses with high heterogeneity. The ICSI group compared to SC showed a null association as RR= 3.74 (95% CI: 0.43-32.56, p=0.23, I2=95%) with high heterogeneity. In case-control studies, patients with subfertility without infertility treatment had a higher risk of ASD (OR=1.51, 95% CI= 1.09-2.10, p=0.01, I2=0%). However, when considering different types of infertility treatment (i.e., Ovulation Induction, Intra Uterine Insemination, IVF, or ICSI), no association was found (OR=1.71, 95% CI= 0.93-3.11, p=0.08, I2=79%). The heterogeneity among the studies was high.

CONCLUSION: At present, there is no significant evidence that ART increases the risk of ASD in children. However, conflicting results in existing primary studies and systematic reviews, along with a lack of data on specific types of ART procedures, indicate that large-scale and high-quality studies focusing on specific forms of ART such as IVF, ICSI, and type of embryo transfer are still required. Any potential association between a history of infertility and ASD needs further investigation.

FUNDING SOURCE: The Canadian Institute of Health Research (CIHR).

Reproductive disorders and pregnancy outcomes in pregnancies conceived by Assisted Reproductive Technology: an overview and meta-analyses

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OBJECTIVE: This overview aims to compare rates of clinical pregnancy (CP), miscarriage, and live birth (LBR) in pregnancies conceived by Assisted Reproductive Technology (ART) in women with endometriosis, adenomyosis, and fibroids relative to women without these reproductive disorders.

METHODS: Systematic reviews/meta-analyses were identified from MEDLINE, Embase, and Cochrane Library (August 2020). The quality of the studies was evaluated using Amstar 2. Meta-analyses were carried out to estimate Odds Ratios (OR) using random effects models including primary studies included in the meta-analyses. Heterogeneity above 50% was considered high.

RESULTS: In total, 2021 studies were screened, and eight systematic reviews/meta-analyses met the inclusion criteria. Six were of moderate and two of low quality. All the studies considered IVF or combined IVF/ICSI pregnancies. Women with endometriosis presented lower CP (OR 0.88; 95% CI 0.79, 0.99, I2= 69% - 54 studies), but no association with miscarriage (OR 1.81; 95% CI 0.62, 5.26, I2=37%, 3 studies) or LBR (OR 0.87; 95% CI 0.70, 1.08, I2=0% - 14 studies). Women with adenomyosis had lower CP (OR 0.55; 95% CI 0.39, 0.78, I2= 49% – 10 studies), increased odds of miscarriages (OR 2.50; 95% CI 1.45, 4.33, I2= 51% – 9 studies), and decreased LBR (OR 0.45; 95% CI 0.24, 0.86, I2= 65% – 5 studies). Women with fibroids had lower CP (OR 0.69; 95% CI 0.59, 0.82, I2= 61% - 30 studies), increased odds of miscarriages (OR 1.35; 95% CI 1.10, 1.65, I2= 0– 24 studies), and decreased LBR (OR 0.67; 95% CI 0.55, 0.80, I2= 55% – 21 studies).

CONCLUSION: Endometriosis, adenomyosis, and fibroids are associated with decreased clinical pregnancy rates in ART. While adenomyosis and fibroids increase the rate of miscarriage and live birth, endometriosis is not associated with these outcomes. Future studies need to investigate the mechanism associated with these adverse outcomes and treatment options.

FUNDING SOURCE: The Canadian Institute of Health Research (CIHR) and the Department of Obstetrics and Gynecology, Queen's University.

Understanding caesarean delivery in women with subfertility and infertility treatment using the Robson Classification: A population-based cohort study

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OBJECTIVE: Caesarean section (CS) is more common in pregnancies conceived using infertility treatment (IT) compared to spontaneous conceptions, but the reasons remain unclear and confounded. We assess the association between mode of conception and CS in Ontario using the Robson Classification.

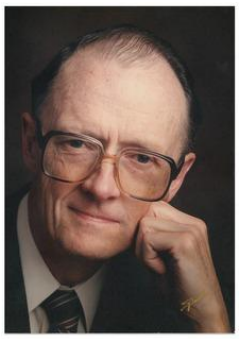
METHODS: We conducted a population-based cohort study of hospital births from April 2006 to March 2014 through ICES. Exposures were spontaneous conception (reference); subfertility without IT (history of an infertility consult without IT); non-invasive IT (OI, IUI); and invasive IT (IVF, ICSI). Births were classified into Robson groups based on parity, previous CS, gestational age, onset of labour, fetal presentation, and number of fetuses. CS rates were calculated overall and by each Robson group. Modified Poisson regression generated relative risks (RR) were reported for the association between exposure and CS rates, adjusting for demographics and pre-existing conditions.

RESULTS: In 921,023 births, CS rates were 26.9% with spontaneous conception, 36.3% with subfertility without IT, 38.8% with non-invasive IT, and 50.6% with invasive IT. Compared to spontaneous conception, the risk of CS rose by IT invasiveness: RR 1.17 (95% CI 1.16-1.18) with subfertility without IT; RR 1.21 (95% CI 1.18-1.24) in non-invasive IT; and RR 1.39 (95% CI 1.36-1.42) in invasive IT. Within each Robson group, similar patterns of RRs were seen, but with markedly differing rates. Group 5 (multiparous, singleton, cephalic, > 37 weeks, with at least one previous CS) contributed the most to the increased rate of CS in women with subfertility without IT (26.8%), and Group 8 (multiple pregnancy) contributed the most in women with IT, especially invasive IT (34.9%).

CONCLUSION: In Ontario, caesarean section is relatively more common in women with subfertility and those receiving IT. Multiple pregnancy contributes the most to the increased CS rates in women who use IT to conceive.

FUNDING SOURCE: The Canadian Institute of Health Research (CIHR) and the Queen's School of Medicine McLaughlin Summer Studentship.

Remembering Dr. Low



James A Low, MD
1925-2015
Professor and Head of the Department of Obstetrics & Gynaecology and Chief of Service at KGH from 1965 to 1985

Dr. Low came to Kingston in 1965 to assume the position of Professor and Head of Obstetrics & Gynaecology, Queen's University and the Chief of Service at the Kingston General Hospital. During the twenty years as Head, he was instrumental in shaping the Queen's Department of Obstetrics & Gynaecology into one of the most respected academic clinical departments and one of the most sought after postgraduate residency programs in the country. Furthermore, during his tenure as the Head, the department became recognized for academic excellence at the national and international levels in the areas of maternal-fetal medicine, urogynecology and gynecologic oncology. It was through the philosophy and ideals of Dr. Low that the department continues to flourish and remains to this day one of the country's more successful academic departments of obstetrics and gynaecology.

At various times during his career, Dr. Low served as Secretary/Treasurer, Vice President and President of the Association of Professors of Obstetrics and Gynaecology of Canada (APOG), Chair of the Specialty Committee for Obstetrics & Gynecology and Chair of the Manpower Committee for the Royal College of Physicians and Surgeons of Canada, Chair of the Postgraduate Manpower Committee of the Council of Ontario Faculties of Medicine, Chair of the Perinatal Medicine Committee for the Society of Obstetricians and Gynaecologists of Canada (SOGC) and member of the Editorial Board for the two most prestigious journals in our specialty; Obstetrics & Gynecology and the American Journal of Obstetrics & Gynecology.

From his first peer-reviewed publication in 1959 to finishing his last manuscript the week before he died, Dr. Low has had one of the most influential and productive careers as an academic obstetrician and gynecologist in Canada. He is recognized as a world-renowned expert in the fields of fetal asphyxia, cerebral palsy and female urinary incontinence. With all of these achievements, Dr. Low always identified that his successes have been a part of his role with the Department at Queen's and has always promoted recognition of this university.

Following his retirement from clinical practice in the early 1990s, he embarked on a second career when he established and had been leading and promoting the Museum of Health Care at Kingston until shortly before his passing.

Dr. Low received many awards during his lengthy career including being named a Fellow of the Royal College of Obstetricians and Gynaecologists (United Kingdom), Queen's University Distinguished Service Award, Kingston First Capital Honourable Achievement Award, Queen Elizabeth Diamond Jubilee Medal and this year, just prior to his death, Dr. Low was invested into the Order of Canada, specifically for his work with the Museum of Health Care.

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