RANZCOG WOMEN'S HEALTH FOUNDATION RESEARCH SCHOLARSHIPS

NORMAN BEISCHER CLINICAL RESEARCH SCHOLARSHIP, 2018 - 2019

PROGRESS REPORT

Recipient: **Dr Amanda Poprzeczny**
Project Title: *'Maternal Overweight and Obesity and Gestational Diabetes: Effect on Fetal Growth and Adiposity'.*

Introduction/Background

The burden of overweight and obesity

Obesity, defined as a BMI >30.0kg/m2, represents a significant public health burden globally. Data from the most recent Pregnancy Outcome in South Australia report suggest that approximately 50% of women entering pregnancy in South Australia are overweight or obese (Schiel, 2013). The long term health risks of overweight and obesity include a greatly increased risk of cardiovascular disease, type 2 diabetes mellitus and several cancers, all of which result in reduced life expectancy and increased health-care expenditure.

Obesity and Fetal and Neonatal Growth

Infant birth weight is associated with many factors including gestational age at birth, infant birth order, smoking, pre-eclampsia and multiple pregnancy. Maternal pre-pregnancy weight and infant macrosoma during pregnancy are important factors in prediction of macrosomia (Dodd JM, 2011) (Cedergren, 2004).

Newborns of overweight and obese women have been shown to have significantly greater percentage of fat mass and total mass, and significantly less fat-free mass, when compared to those of normal weight women (Hull HR, 2008) (Sewell MF, 2006). This increase in fat mass may be an important mediator of later health, including childhood and adolescent obesity and metabolic syndrome. To date, however, ultrasound assessment of fetal growth, particularly two-dimensional measures of skeletal growth, have been poorly correlated with neonatal measures of body composition and body fat, regardless of how soon prior to delivery these ultrasound measures were obtained (Khoury F, 2009) (Lee W, 2009) (Moyer-Mileur LJ, 2009).

Ultrasound measures of fetal fat mass have been developed and normal ranges validated (Bernstein IM, 1991) (Gardeil F, 1999) (Higgins MF, 2008) (Hill LM, 1992) (Larciprete G, 2008). Fetal body composition measures most frequently examined to date include subscapular fat mass (SSFM), abdominal wall fat mass (fetal abdominal fat layer) (AFM), mid-thigh total mass (MTTM), mid-thigh lean mass (MTLM) and mid-thigh fat mass (MTFM) (Bernstein IM, 1991) (Gardeil F, 1999) (Higgins MF, 2008) (Hill LM, 1992) (Larciprete G, 2008). However, there is little published data regarding the effect of maternal BMI and gestational weight gain on fetal body composition.

Hure et al, in an Australian population, performed a prospective study investigating the effect of pre-pregnancy BMI and gestational weight gain on fetal growth parameters and fetal markers of adiposity (Hure AJ, 2011). While the methodology used is not directly comparable to that being used by our group, they showed that, independent of pre-pregnancy BMI, excessive gestational weight gain was associated with a larger fetus, predominantly as a result of an increase in lean abdominal mass, but not abdominal fat mass. A larger study performed by our group looked at fetal growth and markers of adiposity in overweight and obese women exposed to a diet and lifestyle intervention to limit gestational weight gain (Grivell RM, 2016), suggested a greater mid thigh fat mass and a slower rate of subscapular adipose tissue deposition among women exposed to the intervention. This suggests that the effects of maternal overweight and obesity on fetal fat mass can potentially be ameliorated by antenatal intervention.

Current fetal growth parameters and growth trajectories have been derived from healthy women, but have rarely considered the potential impact of maternal body mass index, using ultrasound assessment of femur length, abdominal circumference and in some circumstances, biparietal diameter and head circumference measurements. My proposal will involve performing an ultrasound examination for women participating in randomised trials of antenatal lifestyle interventions across the maternal BMI spectrum (The GRoW and OPTIMISE trials) at 28 and 36 weeks gestation to assess standard fetal growth parameters, and measures of adiposity. Ultrasonographic information related to fetal growth trajectories over time will allow the evaluation of the effect of the dietary and lifestyle intervention on in-utero fetal growth in a dynamic fashion.

Research from Professor Dodd's group has demonstrated that among overweight and obese pregnant women, provision of a dietary and lifestyle intervention is associated with a significant 18% relative risk reduction in the chance of an infant being born with weight above 4kg (Dodd BMJ 2014), and a 44% relative risk reduction in weight above 4.5kg (BMC Medicine 2014). Furthermore, the provision of the intervention generated modest but significant

improvements in maternal diet and physical activity (Dodd BMC Medicine 2014), which appear to persist to at least 6 months after birth (Dodd, unpublished data).

An important, but unanswered question arising from this work is how these observed changes among overweight and obese pregnant women compare with women of normal BMI, and specifically, whether an antenatal dietary maternal dietary change changes maternal diet among women of normal BMI, and the potential impact of such changes on fetal and neonatal growth.

I have been involved in performing fetal ultrasound at 28 and 36 weeks' gestation for women recruited to the GRoW and Optimise randomised trials, and collecting data on the ultrasound fetal biometry and adiposity measures. I have also been involved in data analysis and publication, and am currently working on writing up and publishing results of fetal biometry and adiposity measures gathered in the GRoW randomized trial.

Progress/Update

We have performed analysis of the mediating effects of gestational diabetes on fetal growth and adiposity in the LIMIT randomized trial cohort of women, and this has recently been published in the British Journal of Obstetrics and Gynaecology (attached). This work has shown that fetal growth and adiposity is not mediated by the diagnosis and treatment of gestational diabetes in this cohort of women who were overweight or obese in early pregnancy.

We have analysed data from the GRoW randomized trial, investigating the effect of a combined intervention of antenatal dietary and lifestyle advice and oral metformin on fetal biometry and adiposity measures among women who are overweight or obese in early pregnancy. I am currently in the process of writing up these results and submitting it for publication.

We have recently completed data collection for the Optimise randomized trial, investigating the effect of an antenatal dietary and lifestyle intervention on fetal growth and infant birthweight among women who have a normal BMI in early pregnancy. This cohort of women will represent the normal BMI comparator group, allowing us to perform analysis investigating the effect of maternal BMI, across the BMI spectrum, on fetal growth and adiposity. This data is in the process of being cleaned and analysed.

Conclusions

Thus far, my work has shown an important association between increased maternal BMI fetal growth, which is not mediated by treated gestational diabetes. We did not find an association between increased maternal BMI and fetal adiposity measures. We also did not find that this relationship was mediated by treated gestational diabetes. Future work will investigate whether a combined intervention of antenatal diet and lifestyle advice and oral metformin has an effect on fetal growth and adiposity, and will investigate the effect of maternal BMI, across the BMI spectrum, on fetal growth and adiposity.

Publication and/or Presentation of Results

Poprzeczny AJ, Louise J, Deussen AR, Dodd JM. The mediating effects of gestational diabetes on fetal growth and adiposity in women who are overweight and obese: secondary analysis of the LIMIT randomized trial. BJOG 2018 Nov;125(12):1558-1566

Budget

My budget remains the same as that proposed in my scholarship application, providing salary supplementation and statistical support – 70% of the scholarship funding I have received has gone towards salary supplementation for myself, as I am working clinically part-time. The remainder of the scholarship funding (30%) has contributed to statistical analysis and data entry.