Preeclampsia and Preterm Birth Associated With Visceral Adiposity in Early Pregnancy

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Abstract

Objective: To determine if an increasing amount of visceral adipose tissue, measured by ultrasound in early pregnancy, is associated with a higher risk of preeclampsia and preterm birth (PTB).

Methods: We completed a prospective cohort study of 463 pregnant women. Maternal visceral adiposity tissue (VAT) depth was measured by ultrasound at 11 to 14 weeks' gestation. Relative risks (RR) were adjusted for age, parity, chronic hypertension, pre-pregnancy BMI, and use of acetylsalicylic acid.

Results: The rate of preeclampsia was much higher at quintile (Q) 5 of VAT depth (9.8%) than at Q1 to Q4 (1.6%) but not significantly so in the adjusted model (RR 3.39, 95% CI 0.86 to 13.39). The adjusted RR of PTB was significantly elevated at Q5 VAT depth (6.53, 95% CI 1.47 to 6.53), as was preeclampsia with PTB (16.91, 95% CI 1.24 to 231.07).

Conclusion: Higher amounts of VAT in pregnancy may play a direct role in the pathogenesis of preeclampsia, including early onset preeclampsia necessitating preterm delivery.

Résumé

Objectif : Déterminer si l'augmentation de la quantité de tissu adipeux viscéral, mesurée par échographie en début de grossesse, est associée à un risque plus élevé de prééclampsie et d'accouchement avant terme.

Méthodologie : Nous avons mené une étude de cohorte prospective auprès de 463 femmes enceintes. La profondeur du *tissu adipeux viscéral* (TAV) maternel a été mesurée par échographie entre 11 et 14 semaines de grossesse. Les risques relatifs (RR) ont été corrigés selon l'âge, la parité, l'hypertension chronique, l'IMC avant la grossesse et la prise d'acide acétylsalicylique.

Résultats : Le taux de prééclampsie était beaucoup plus élevé chez les femmes dont la profondeur du TAV était dans le cinquième quintile (9,8 %) que chez celles des quatre autres quintiles (1,6 %), mais la différence n'était pas significative dans le modèle corrigé (RR : 3,39; IC à 95 % : 0,86-13,39). Le RR corrigé d'accouchement avant terme était significativement élevé pour le cinquième quintile (6,53; IC à 95 % : 1,47-6,53), tout comme celui de prééclampsie avec accouchement avant terme (16,91; IC à 95 % : 1,24-231,07).

Conclusion : L'augmentation de la quantité de TAV pendant la grossesse peut jouer un rôle direct dans la pathogenèse de la prééclampsie, ce qui comprend la prééclampsie d'apparition précoce nécessitant un accouchement avant terme.

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Key Words: Visceral adiposity, pregnancy, preeclampsia, obesity, hypertension

Conflicting interests: None declared.

Received on August 15, 2016

Accepted on October 18, 2016

http://dx.doi.org/10.1016/j.jogc.2016.10.007

J Obstet Gynaecol Can 2016;■(■):1-4

INTRODUCTION

High maternal BMI predisposes to chronic hypertension.[1] Both pre-pregnancy BMI and blood pressure are linearly related to adverse pregnancy outcomes, including preeclampsia[2] and both provider-initiated and spontaneous preterm birth[3]; that is, to conditions in which maternal or fetal health is jeopardized and delivery is necessary.

The prognostic value of BMI is limited by the fact that it does not distinguish between excess fat, muscle, or bone mass, nor does it reveal the distribution of adipose tissue. Visceral adipose tissue may better reflect cardio-metabolic risk than BMI. For example, VAT is related to blood pressure, independent of BMI, in non-pregnant women.[4] In a sample of 3363 randomly selected Danish adults (mean age 49 years and 56% women), the odds of chronic hypertension linearly increased with higher sex-specific VAT quartiles.[4] Including BMI in a multivariable model, the odds ratio of prevalent hypertension was 1.38 (95% CI

1.22 to 1.55) for each one standard deviation increase in ultrasound-measured VAT.[5]

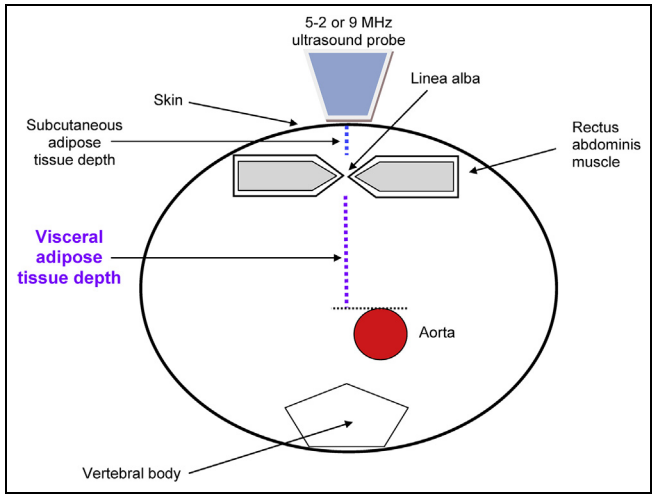
As the measurement of VAT in pregnancy can be limited by the fact that using CT or MRI introduces either radiation or high complexity and cost, little is known about the relationship between VAT and adverse outcomes. Ultrasound measurement of intra-abdominal adipose tissue correlates quite well with the amount of intra-abdominal adipose tissue on CT,[6] with correlation coefficients of 0.68 to 0.74.[7] A simple straight-line vertical measurement of VAT depth on ultrasound, from the anterior abdominal wall to the aorta also, correlates well with CT and serves as a proxy measure of visceral fat and other measures of the metabolic syndrome.[7] Thus, since VAT can be efficiently measured by ultrasound in early pregnancy, we evaluated its relation to preeclampsia and PTB.

METHODS

We completed a prospective cohort study at St. Michael's Hospital in Toronto, Ontario, a large urban hospital. The current cohort was formed for our main study on the risk of gestational diabetes mellitus in relation to VAT,[8] and both preeclampsia and PTB were protocol-described secondary study outcomes. Women were recruited between August 2012 and May 2015, and all participants provided written informed consent.

We included women with a viable singleton pregnancy and no known diabetes mellitus within or outside pregnancy. At 11 to 14 weeks' gestation, at the time of sonographic assessment of fetal nuchal translucency, maternal VAT depth was determined using a reproducible and standardized method described by Armellini et al.[6,9] VAT was measured using a Philips IU22 ultrasound machine (Philips North America Corp., Andover, MA) and a 5-2 or 9 MHz probe, from the inner border of the rectus abdominus muscle, at the level of the linea alba, to the anterior wall of the abdominal aorta (Figure 1). Depth and zoom settings were standardized, such that the aorta was at the bottom of the screen and the vertebral bodies were just visible. VAT depth was measured in triplicate, and then averaged. This technique has an inter-observer reliability of 0.87 (95% CI 0.82 to 0.93).[9] VAT was only measured at 11 to 14 weeks of pregnancy.

Figure 1. Representation of the method for sonographic measurement of visceral adipose tissue depth. Shown is a cross-sectional representation of the patient in a supine position.



We initially modelled VAT by quintiles, comparing each higher Q to Q1. However, the outcome event rates were too low in Q1 and Q2, so we created a single threshold point at Q5, and collapsed Q1 to Q4 together to form the reference group. We examined the relationship between VAT depth Q5 versus Q1 to Q4, and the subsequent development of (1) preeclampsia, an eclamptic seizure, or the HELLP syndrome[10]; (2) PTB before 37 weeks' gestation; or (3) preeclampsia with PTB before 37 weeks. Preeclampsia was defined by the onset in pregnancy of elevated blood pressure (usually a systolic blood pressure $>$ 140 mm Hg and/or a diastolic blood pressure $>$ 90 mm Hg) and proteinuria of $\geq$ 1+ on dipstick or $>$ 300 mg in a 24-hour urine collection. Relative risks were generated using modified Poisson regression adjusted for maternal age, parity, history of chronic hypertension, pre-pregnancy BMI, and use of acetylsalicylic acid in pregnancy. Analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

The Research Ethics Board at St. Michael's Hospital approved the study.

ABBREVATIONS

ASA	acetylsalicylic acid
PTB	preterm birth
Q	quintile
RR	relative risk
SD	standard deviation
VAT	visceral adiposity tissue

RESULTS

We included 463 women, after excluding 23 women without complete exposure, covariate, and/or outcome data. The mean (standard deviation) age was 32.9 (4.7)

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