First-Trimester Maternal Abdominal Adiposity Predicts Dysglycemia and Gestational Diabetes Mellitus in Midpregnancy

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OBJECTIVE

This study assessed the association between first-trimester abdominal adiposity and dysglycemia and gestational diabetes mellitus (GDM) in midpregnancy.

RESEARCH DESIGN AND METHODS

In a prospective cohort of 485 women, we measured subcutaneous (SAT), visceral (VAT), and total (TAT) adipose tissue depth, using ultrasound at 11–14 weeks' gestation. Logistic regression analysis assessed the relation between quartiles of SAT, VAT, or TAT depth and the composite outcome of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or GDM, based on a 75-g oral glucose tolerance test at 24–28 weeks.

RESULTS

Adjusting for maternal age, ethnicity, family history of diabetes, and BMI, quartile 4 versus quartile 1 VAT (adjusted odds ratio [aOR] 3.1, 95% CI 1.1–9.5) and TAT (aOR 2.7, 95% CI 1.1–7.8) were significantly associated with the composite outcome, but SAT was not (aOR 1.8, 95% CI 0.70–4.8). The same was seen for GDM alone.

CONCLUSIONS

Elevated first-trimester VAT and TAT depth independently predicted the risk of dysglycemia later in pregnancy.

Maternal obesity affects 40% of pregnancies (1,2) and is a major risk factor for gestational diabetes mellitus (GDM), associated adverse pregnancy outcomes, and the long-term risk of developing type 2 DM (3,4).

Elevated central adiposity in early pregnancy is a modifiable risk factor for abnormal glucose homeostasis in the second trimester of pregnancy, as detailed within a few small-sample studies (5–9). We showed that ultrasound-measured visceral adipose tissue (VAT) depth in early pregnancy was strongly associated with a positive glucose challenge test in later pregnancy and was independent of BMI (5). We also observed that first-trimester VAT and total adipose tissue (TAT) depth was associated with insulin resistance in early pregnancy (6).

In this study we investigated the relation between early pregnancy maternal central adipose tissue depth and the development of dysglycemia and GDM at 24–28 weeks' gestation.

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RESEARCH DESIGN AND METHODS

This was a prospective cohort study within the general Obstetrics Outpatient Clinic at St. Michael's Hospital in Toronto, ON, Canada, between 2012 and 2014. The study was approved by the St. Michael's Hospital Research Ethics Board, and participants provided written informed consent.

Women aged 18 years and older were eligible for study entry if they had a viable singleton pregnancy at 11–14 weeks' gestation. We excluded women with known pre-GDM or a prior pregnancy affected by GDM.

At 11–14 weeks' gestation, abdominal adipose tissue depth was measured by a trained ultrasound technician, as previously described (5). Subcutaneous adipose tissue (SAT) depth was measured from the outer border of the rectus abdominus muscle to the skin surface, at the intersection of the linea alba and the umbilicus. VAT depth was measured from the inner border of the rectus abdominus muscle to the anterior wall of the abdominal aorta. TAT depth was measured from the SAT layer surface to the anterior wall of the abdominal aorta, along the same plane as above. Depth and zoom settings were standardized, such that the aorta was at the bottom of the screen and the vertebral bodies were just visible. This technique has an interobserver reliability of 0.79 (95% CI 0.69–0.88) for SAT and 0.87 (95% CI 0.82–0.93) for VAT (5). Measurements were taken using a Phillips IU22 or GE E8 ultrasound machine with a 5–2-MHz or 9-MHz probe.

At 11–14 weeks, participants completed a self-administered questionnaire detailing information about ethnicity, self-reported pregestational height and weight, and family history of type 2 DM. Weight at 11–14 weeks was directly measured using a calibrated scale.

Data Analysis

Logistic regression analysis assessed the association between the respective quartiles of SAT, VAT, or TAT depth and the development of the composite outcome of impaired fasting glucose (IFG), gestational impaired glucose tolerance (GIGT), or GDM, based on the 75-g oral glucose tolerance test (OGTT) at 24–28 weeks' gestation. IFG was defined as a fasting glucose $\geq$5.3 mmol/L, in isolation; GIGT was based on a glucose value at 1 h $\geq$10.6 mmol/L or at 2 h $\geq$8.9 mmol/L, in isolation; and GDM was defined as two or more abnormal serum glucose values (i.e., fasting $\geq$5.3 mmol/L, 1 h $\geq$10.6 mmol/L and/or 2 h $\geq$8.9 mmol/L) (10). We examined the outcome of GDM alone using the latter traditional criteria (10) as well as the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria (11). Odds ratios were adjusted (aOR) for maternal age (continuous in years), ethnicity (Caucasian vs. non-Caucasian), family history of type 2 DM, measured BMI at 11–14 weeks' gestation (continuous in kg/m^2), and change in BMI from 11–14 weeks' to 24–28 weeks' gestation. Quartile 1 served as the referent in each model. Including gestational age at the time of the OGTT in the logistic regression models did not alter the effect sizes, so it was excluded from all models. Statistical analyses were performed using SAS 9.1.3 software (SAS Institute Inc., Cary, NC).

RESULTS

All study measures were completed by 485 of 501 women at a mean (SD) age of 32.9 (4.8) years. BMI at 11–14 weeks' gestation ranged from 27.0 to 49.9 kg/m^2, with a mean of 25.1 (5.1) kg/m^2. VAT depth ranged from 1.1 to 11.4 cm, with a mean of 4.1 (1.7) cm; SAT depth ranged from 0.56 to 5.1 cm, with a mean of 1.9 (0.80) cm; and TAT depth ranged from 2.0 to 14.2 cm, with a mean of 5.9 (2.1) cm.

The composite of GDM, IFG, or GIGT developed in 52 of 485 women, a rate of 10.7% (95% CI 8.1–13.8), of which 45 (9.3%, 95% CI 7.0–12.2) met the traditional criteria for GDM (10). Relative to the bottom quartile, the highest quartile of SAT was significantly associated with a higher risk for the composite outcome (unadjusted OR 3.4, 95% CI 1.5–8.3), but not after adjusting for the covariates (aOR 1.8, 95% CI 0.70–4.8) (Table 1). The highest quartile of VAT depth (aOR 3.1, 95% CI 1.1–9.5) and TAT depth (aOR 2.7, 95% CI 1.1–7.8) were each associated with the composite outcome (Table 1).

Limiting the outcome to GDM using traditional criteria (10), a slightly more pronounced effect was seen for the highest quartiles of VAT (aOR 4.2, 95% CI 1.4–14.2) and TAT (aOR 3.0, 95% CI 1.1–8.9) (Table 1). Using the IADPSG criteria for GDM (11), the association remained significant, albeit less pronounced.

CONCLUSIONS

Elevated TAT and VAT were each associated with dysglycemia and GDM at 24–28 weeks' gestation. The associations were independent of maternal age, parity, ethnicity, family, history of type 2 DM, and BMI.

A strength of the current study was its large sample size, derived from a multiethnic population, and use of a standardized ultrasound protocol that measures abdominal adiposity, coinciding with the time at which prenatal measurement of fetal nuchal translucency is performed. VAT and TAT measurement is relatively simple to learn, is cost-effective, and could be applied within clinical practice, if further validated by others. As a limitation, 16 of 501 women did not have complete capture of all study variables, including the requisite 75-g OGTT.

GDM unmasks a latent tendency for the metabolic syndrome: 20–50% of affected women go on to develop type 2 DM within 5 years (4,12). In nonpregnant populations, visceral adiposity has emerged as an independent predictor of insulin resistance (IR), the metabolic syndrome, and type 2 DM (4). Proposed mechanisms underlying the pathological association between VAT and IR include free fatty acid release into the hepatic portal circulation (13,14).

A few small studies have examined the association between ultrasound-measured VAT and glucose homeostasis in pregnancy (5–9). In a small pilot study, we showed that higher VAT depth but not SAT depth in early pregnancy was associated with a positive glucose challenge test later in pregnancy (5). In a follow-up study, we found that first-trimester VAT and TAT depth explained 42% and 46%, respectively, of the variance in IR at 16 weeks' gestation (6).

In this study we demonstrated that TAT, and especially VAT, appear to be important pathogenic markers of abnormal glucose homeostasis and GDM in pregnancy. SAT alone appeared less important, however. SAT has a heterogeneous histology, with two distinct deep and

Table 1—Association between SAT, VAT, and TAT and GDM

Adipose tissue assessed	Quartile	Sample size (*n*)	Depth (cm)	Composite outcome of IFG, GIGT, or GDM at 24–28 weeks: *N* (%)	OR (95% CI): Unadjusted	OR (95% CI): Adjusted
SAT	Q1	124	≤1.3	8 (6.5)	1.0 (Ref.)	1.0 (Ref.)
	Q2	118	1.4–1.7	9 (7.6)	2.0 (0.44–3.3)	1.0 (0.36–2.8)
	Q3	121	1.8–2.3	12 (9.9)	1.6 (0.64–4.2)	1.2 (0.45–3.3)
	Q4	122	>2.3	23 (18.9)	3.4 (1.5–8.3)	1.8 (0.70–4.8)
VAT	Q1	120	≤3.0	6 (5.0)	1.0 (Ref.)	1.0 (Ref.)
	Q2	122	3.1–3.8	9 (7.5)	1.5 (0.53–4.6)	1.3 (0.45–4.0)
	Q3	121	3.9–4.8	8 (6.6)	1.3 (0.45–4.2)	1.1 (0.35–3.4)
	Q4	122	>4.8	29 (23.4)	5.9 (2.5–16.4)	3.1 (1.1–9.5)
TAT	Q1	121	≤4.5	8 (6.6)	1.0 (Ref.)	1.0 (Ref.)
	Q2	122	4.6–5.5	4 (3.3)	0.48 (0.13–1.6)	1.0 (0.12–1.5)
	Q3	120	6.6–7.0	10 (8.3)	1.3 (0.49–3.5)	1.0 (0.39–2.9)
	Q4	122	>7.0	30 (24.2)	4.6 (2.1–11.2)	2.7 (1.1–7.8)
				GDM at 24–28 weeks using the CDA criteria (10)		
SAT	Q1	124	≤1.3	7 (5.7)	1.0 (Ref.)	1.0 (Ref.)
	Q2	118	1.4–1.7	9 (7.6)	1.4 (0.50–4.0)	1.2 (0.42–3.4)
	Q3	121	1.8–2.3	12 (9.9)	1.8 (0.71–5.1)	1.4 (0.53–4.2)
	Q4	122	>2.3	17 (14.0)	2.7 (1.1–7.2)	1.5 (0.56–4.5)
VAT	Q1	120	≤3.0	5 (4.2)	1.0 (Ref.)	1.0 (Ref.)
	Q2	122	3.1–3.8	8 (6.6)	1.6 (0.52–5.5)	1.4 (0.46–4.9)
	Q3	121	3.9–4.8	6 (5.0)	1.2 (0.35–4.3)	1.0 (0.30–3.7)
	Q4	122	>4.8	26 (21.3)	6.2 (2.5–19.0)	4.2 (1.4–14.2)
TAT	Q1	121	≤4.5	7 (5.8)	1.0 (Ref.)	1.0 (Ref.)
	Q2	122	4.6–5.5	4 (3.3)	1.0 (0.14–1.9)	1.0 (0.13–1.8)
	Q3	120	6.6–7.0	9 (7.5)	1.3 (0.48–3.8)	1.1 (0.39–3.3)
	Q4	122	>7.0	25 (20.5)	4.2 (1.8–10.9)	3.0 (1.1–8.9)
				GDM at 24–28 weeks using the IADPSG criteria (11)		
SAT	Q1	124	≤1.3	14 (11.3)	1.0 (Ref.)	1.0 (Ref.)
	Q2	118	1.4–1.7	17 (14.4)	1.3 (0.62–2.9)	1.2 (0.56–2.7)
	Q3	121	1.8–2.3	22 (18.2)	1.8 (0.86–3.7)	1.5 (0.73–3.3)
	Q4	122	>2.3	32 (26.2)	2.8 (1.4–5.7)	2.0 (0.95–4.5)
VAT	Q1	120	≤3.0	12 (10.0)	1.0 (Ref.)	1.0 (Ref.)
	Q2	122	3.1–3.8	18 (14.8)	1.6 (0.72–3.5)	1.5 (0.67–3.3)
	Q3	121	3.9–4.8	16 (13.2)	1.4 (0.62–3.1)	1.3 (0.57–2.9)
	Q4	122	>4.8	39 (32.0)	4.2 (2.1–8.9)	3.4 (1.5–8.0)
TAT	Q1	121	≤4.5	15 (12.4)	1.0 (Ref.)	1.0 (Ref.)
	Q2	122	4.6–5.5	10 (8.2)	1.0 (0.30–1.5)	1.0 (0.26–1.5)
	Q3	120	6.6–7.0	19 (15.8)	1.3 (0.64–2.8)	1.3 (0.60–2.7)
	Q4	122	>7.0	41 (33.6)	3.6 (1.9–7.1)	3.4 (1.6–7.7)

Adipose tissue depth was measured at 11–14 weeks' gestation, and the subsequent risk of the composite outcome of IFG, GIGT, or GDM at 24–28 weeks' gestation was assessed among 485 pregnant women. ORs were adjusted for maternal age, ethnicity, family history of type 2 DM, BMI at 11–14 weeks' gestation, and change in BMI between 11–14 weeks' gestation and 24–28 weeks' gestation. CDA, Canadian Diabetes Association.

superficial layers (14), of which the former exhibits metabolic activity like that of VAT (14). Certainly, future work should attempt to distinguish deep and superficial SAT layers.

Ultrasound measurement of maternal abdominal adiposity affords the opportunity to overcome some of the limitations posed by using BMI. Our proposed screening approach uses a practical and validated ultrasound-based first-trimester screening tool. Using this tool and identifying women with high VAT or TAT might enable a practitioner to mitigate the onset of GDM through the upstream management of risk factors. This approach can be compared with our current downstream approach of screening and treating GDM in the second trimester of pregnancy.

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in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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