Abdominal visceral adiposity in the first trimester predicts glucose intolerance in later pregnancy

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**Background:** We assessed whether abdominal adiposity in early pregnancy is associated with a higher risk of glucose intolerance at a later gestational age.

**Methods:** Subcutaneous and visceral fat were measured by ultrasonography at about 12 weeks’ gestation. A 50-g glucose challenge test (GCT) was performed between 24 and 28 weeks. The risk of having a positive GCT (≥ 7.8 mmol/L) was determined in association with subcutaneous and visceral adipose tissue depths above their respective upper quartile values, relative to their bottom three quartile values.

**Results:** There were 62 women who underwent a GCT. A visceral adipose tissue depth above the upper quartile was significantly associated with a positive GCT in later pregnancy (adjusted OR 16.9, 95% CI 1.5 to 194.6). No association was seen for subcutaneous adipose tissue.

**Conclusions:** Measurement of visceral adipose tissue depth in early pregnancy may be associated with glucose intolerance later in pregnancy.
Maternal obesity is associated with a higher risk of gestational diabetes mellitus (GDM)(1) and adverse perinatal outcomes(2,3). Visceral adiposity(4) may better predict the onset of type 2 DM, independently of body mass index (BMI). Since GDM and type 2 DM share the same risk factors(1), and GDM predates the onset of type 2 DM(5), it is logical to question whether high maternal visceral adiposity is associated with GDM.

We determined the reliability of first trimester ultrasonography for measuring subcutaneous and visceral adipose tissue in pregnancy, and whether either is predictive of a positive glucose challenge test (GCT), a commonly used test to screen for GDM later in pregnancy.

RESEARCH DESIGN AND METHODS

We completed a prospective cohort study at a single outpatient ultrasound clinic at St. Michael's Hospital in Toronto, Ontario, between January and May 2008. Women with a singleton pregnancy were eligible to be enrolled at 11 to 14 weeks’ gestation. Those with type 1 or 2 DM prior to pregnancy or a previous history of GDM were excluded. Written informed consent was obtained and the study was approved by the Hospital Research Ethics Board.

We used the technique of Armellini et al to measure subcutaneous and visceral abdominal adipose tissue(6). A total of 62 patients were scanned on a Phillips IU22 ultrasound machine using either a 5-2MHz or 9 MHz probe. Subcutaneous fat depth was measured from the subcutaneous fat layer to the outer border of the rectus abdominus muscle at the level of the linea alba (Figure). Visceral fat depth was measured from the inner border of the rectus abdominus muscle, at the level of the linea alba, to the anterior wall of the abdominal aorta.

Two sonographers -- one a perinatal obstetrician and the other an experienced ultrasound technologist -- each performed three measurements of the subcutaneous and visceral fat depths. Each rater was masked to the others’ assessment, and the measurements were recorded on separate data collection sheets.

Intra-rater reliability of ultrasonography was determined for each rater using three images of subcutaneous and three images of visceral adipose tissue depth per participant, respectively. Inter-observer reliability was separately calculated for subcutaneous adiposity and for visceral adiposity.

Mean subcutaneous and mean visceral adipose tissue depths were determined for each participant, pooling the measures of both sonographers. The upper quartile value for each was defined as "elevated", and the three lowest quartiles as the referent. All participants underwent a 50-g GCT at 24 to 28 weeks’ gestation. An abnormal 50-g GCT was defined at a conventional cut-point ≥ 7.8 mmol/L. Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI) expressed the risk of an abnormal GCT in association with an elevated subcutaneous and an elevated visceral adipose tissue depth, respectively.

All p-values were two-sided, and significance was set at a value of 0.05. Statistical analyses were performed using SAS Version 9 (SAS Institute Inc., Cary, North Carolina).

RESULTS

There were 62 women recruited in total, at a mean +/- SD of 12.4 +/- 0.60 weeks’ gestation and an age of 31.7 +/- 5.0 years. The median gravidity was 2.0, and 31
(50.0%) were of non-white ethnicity. The mean (SD) pre-pregnancy body mass index was 23.9 +/- 5.2 kg/m². Mean (range) subcutaneous and visceral adiposity depths by ultrasonography were 1.8 +/- 0.72 (0.63-3.7) and 4.0 +/- 1.4 (1.3-8.2) cm, respectively. The 50-g GCT was completed at 27.4 +/- 1.4 weeks gestation.

Reliability measures were based on all 62 women. The intraclass correlation coefficient for intra-observer agreement of visceral adiposity measurement was 0.94 (95% CI 0.91-0.96) for the physician and 0.97 (95% CI 0.95-0.98) for the technologist. Similar results were seen for subcutaneous adiposity measurement. The Lin’s concordance correlation coefficient for inter-observer reliability (between physician vs. technologist) was 0.79 (95% CI 0.69-0.88) for subcutaneous adiposity and 0.87 (95% CI 0.82-0.93) for visceral adiposity.

Fifty-eight women formed the sample used to analyze the relationship between adiposity and subsequent GCT positivity. No significant association was observed between the upper quartile subcutaneous adipose tissue depth and a positive GCT (Table). However, an elevated visceral adipose tissue depth was significantly associated with a positive GCT (unadjusted OR 17.3, 95% CI 1.8-163.8). Even after adjusting for maternal age and pre-pregnancy BMI, the association remained significant (OR 16.9, 95% CI 1.5-194.6).

CONCLUSIONS

Since we only included 62 women, our risk estimates were imprecise. We used a 50-g GCT as an indicator of glucose intolerance later in pregnancy, rather than a more definitive 2-hour 75g oral glucose tolerance test. However, a positive GCT is a reasonable predictor of GDM-related adverse perinatal outcomes(7). As strength, this cohort study prospectively assessed abdominal adiposity at around the same gestational age, using a standardized protocol. All sonographers were masked to one another’s measurements, and the GCTs were carried out without knowledge of the abdominal depth.

Visceral adiposity predicts insulin resistance(8) and DM(4) independently of BMI, so it was logical for us to use ultrasonography to measure visceral fat in relation to glucose intolerance in pregnancy. Outside of pregnancy, ultrasound has a correlation coefficient of between 0.55(9) and 0.81(10), and a diagnostic concordance of 74% with computed tomography(9), in the assessment of visceral adiposity.

Maternal obesity, routinely defined as an elevated pre-pregnancy BMI, is associated with adverse pregnancy outcomes(1-3, 11). BMI may not accurately differentiate between the contributions of muscle and fat to body weight, or that of subcutaneous and visceral abdominal fat. Epidemiological and metabolic studies have found that the adverse metabolic consequences of excess fat depend largely on the location of that fat(12,13), with centrally located visceral fat being more pathogenic than subcutaneous adipose tissue(14). Our results are consistent with this concept.

Measurement of visceral adiposity at the time of a routine 11 to 14 week ultrasound might improve the performance of screening for GDM (15). Moreover, identifying women at high risk for GDM because of elevated visceral adiposity could lead to either earlier screening or earlier dietary and lifestyle modification. Clearly, this opens up a new avenue for research.
REFERENCES
Table. Elevated subcutaneous and visceral abdominal adipose tissue in the first trimester of pregnancy and associated risk of an elevated glucose challenge test in the second trimester of pregnancy. Complete data are presented for 58 participants.

<table>
<thead>
<tr>
<th>Abdominal ultrasound measurement of adipose tissue depth</th>
<th>Abnormal glucose challenge test: ≥ 7.8 mmol/L (n = 6)</th>
<th>Unadjusted OR</th>
<th>Adjusted OR*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td><strong>Cut-points</strong></td>
<td><strong>No. (%)</strong></td>
<td><strong>(95% CI)</strong></td>
</tr>
<tr>
<td>Subcutaneous adipose tissue</td>
<td>Bottom three quartiles: &lt; 2.18 cm (n = 42)</td>
<td>3 (7.1)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Subcutaneous adipose tissue</td>
<td>Upper quartile: ≥ 2.18 cm (n = 16)</td>
<td>3 (18.8)</td>
<td>3.1 (0.55 to 17.4)</td>
</tr>
<tr>
<td>Visceral adipose tissue</td>
<td>Bottom three quartiles: &lt; 4.74 cm (n = 42)</td>
<td>1 (2.4)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Visceral adipose tissue</td>
<td>Upper quartile: ≥ 4.74 cm (n = 16)</td>
<td>5 (31.2)</td>
<td>17.3 (1.8 to 163.8)</td>
</tr>
</tbody>
</table>

*Adjusted for maternal age (continuous, years) and pre-pregnancy body mass index (continuous, kg/m²)
Figure. Cross-sectional representation of the abdominal wall and subcutaneous and visceral fat compartments measured by ultrasound.

From reference 6.