The importance of visceral fat mass in obese pregnant women and relation with pregnancy outcomes

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Abstract

Background: Maternal obesity is a well established risk factor for gestational diabetes but it is not known if the pattern of maternal fat distribution predicts adverse pregnancy outcomes.

Methods: Body composition was assessed by bioimpedance using Inbody 720® in 302 consecutive obese pregnant women attending a weight management clinic. The relation of visceral fat mass and total percentage body fat with the development of gestational diabetes and perinatal outcomes was evaluated.

Results: Women developing gestational diabetes (Group 1; $n = 72$) were older, had higher body mass indices and greater central obesity (waist:hip ratio, visceral fat mass) compared with those remaining normoglycaemic. Visceral fat mass, but not percentage body fat, correlated with fasting glucose in all patients ($r = 0.2$, $p < 0.001$) and particularly those in Group 1 ($r = 0.35$, $p = 0.002$). Visceral fat mass, but not percentage body fat, also correlated strongly with glycaemia, particularly in Group 1 ($r = 0.47$, $p < 0.0001$). Visceral fat mass also showed a weak but significant correlation with baby weight ($r = 0.17$, $p = 0.01$).

Discussion: Central obesity, as assessed by early pregnancy waist:hip ratio and particularly by visceral fat mass, is a predictor of gestational diabetes in addition to classical risk factors and may help identify those obese patients at increased risk of complications.

Keywords

Gestational diabetes, obesity, visceral fat mass, total percentage body fat, bioimpedance

Introduction

There is substantial evidence that obesity in pregnancy contributes to increased complications including mortality for both mother and baby. The Confidential Enquiry into Maternal and Child Health (2007) reported that 35% of women who had died had a recorded body mass index (BMI) of 30 or more and furthermore 30% of the mothers who had experienced a stillbirth or neonatal death were obese.¹

Obese women are also at increased risk of gestational diabetes (GDM). In a prospective study of more than 16,000 patients with BMI 30–40, the odds ratio (OR) for GDM were 2.6 (95% confidence interval (CI) 2.4–6.0) compared with women with BMI <30.² More recently, a meta analysis of 70 studies found the OR for GDM was 3.01 (95% CI 2.34–3.87) for moderate obesity and 5.55 (95% CI 4.27–7.21) for women with morbid obesity (BMI >40) compared with normal weight women.³ Similar results were reported by Chu et al.⁴

Despite these consistent results, there is still uncertainty regarding the relative importance of the distribution of the fat and the risk of GDM. While central obesity and by implication, visceral fat mass (VFM), is well established as a risk factor for type 2 diabetes and the metabolic syndrome, there are no published data on the possible association of VFM in pregnancy and risk of GDM. We investigated the relation of fat distribution (total percentage fat, VFM and waist:hip ratio (WHR)) and risk of GDM in a cohort of obese women with no known diabetes attending a weight management clinic.

Methods

Subjects

We enrolled 302 consecutive obese pregnant women with no known diabetes attending the weight management clinic at St Helier Hospital, Carshalton, Surrey, UK. The median age of these women was 31 years (range, 26–34 years) and the median BMI was 38.2 kg/m² (range, 36.1–41.4); 74.5% of these women were Caucasians. All women received

standardised dietary and exercise advice. Maternal baseline characteristics are shown in Table 1.

Gestational diabetes

All women underwent a 75 g oral glucose tolerance test at around 28 weeks gestation; GDM was defined by WHO criteria.⁵ Seventy-two of the 302 enrolled patients subsequently developed GDM (23.8%) and were medically managed in the joint antenatal obstetric and diabetic clinic by a standard protocol. They performed home glucose monitoring four times daily and if three or more tests were outside target range (<5.6 mmol/l (fasting), <8 mmol/l (1 h post-prandial) and <7 mmol/l (2 h post-prandial)), they were commenced on metformin. Additional insulin was prescribed if tests remained suboptimal despite maximal metformin.

Fat distribution

All women underwent body composition analysis at booking (median gestation = 15 weeks; range, 14–17 weeks) using Inbody 720® bioimpedance. The instrument performs body composition analysis using Direct Segmental Multi-frequency Bioelectrical Impedance Analysis Method (DSM-BIA Method). It measures weight, BMI, WHR, lean

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Table 1. Maternal baseline characteristics.

	Group 1 (GDM) (n = 72)	Group 2 (non-GDM) (n = 230)	p Value
Age (mean $\pm$ SD)	32.1 $\pm$ 5.5	29.6 $\pm$ 5.8	<0.01*
Ethnicity n (%)			
White	60 (83.3)	165 (71.7)	NS
Asian	7 (9.7)	30 (13)	NS
Blacks	3 (4.2)	27 (11.7)	
Others	2 (2.8)	8 (3.5)	
History of PCOS, n (%)	15 (20.8)	16 (7)	$\leq$ 0.01*
Family history of diabetes, n (%)	41 (56.9)	79 (34.3)	$\leq$ 0.001*
Previous GDM, n (%)	12 (16.8)	0	<0.0001*
Smokers, n (%)	4 (5.6)	16 (7)	NS

GDM: gestational diabetes; PCOS: polycystic ovary syndrome. * $p < 0.05$.

body mass, total percentage body fat (PBF) and VFM. It is a validated tool correlating well with intraabdominal fat area assessed by computed tomography (CT)⁶ and dual-energy X-ray absorptiometry (DEXA).⁷ It has also been used in patients with obesity.^{8,9} It has been shown to be safe in the second and third trimesters of pregnancy and validated against deuterium and hydrodensitometry techniques for body composition analysis.^{10,11} DSM-BIA is also an accurate technique for assessing body water distribution, which changes during pregnancy.¹² There is no evidence that the physiological alterations in body water are different in pregnancies complicated by GDM. In this study, Inbody^R assessment was repeated at 36 weeks gestation in Group 1 patients to assess changes during pregnancy on treatment.

Statistical analysis

The maternal baseline characteristics, pregnancy and neonatal outcome in patients developing GDM (Group 1, $n = 72$) were compared with those with normal glucose tolerance (Group 2, $n = 230$). Group data were compared by $\chi^2 2 \times 2$ contingency tables and by unpaired t -tests; significance was taken as $p < 0.05$. Results are expressed as mean (SD) or median (range) if non-parametric distribution. Pearson's correlation coefficient was used to compare continuous variables.

Results

Women developing GDM (Group 1) were significantly older, more likely to have a history of previous GDM, or a family history of diabetes, or a past history of polycystic ovaries when compared with those remaining normoglycaemic (Group 2) (see Table 1). Group 1 women had significantly higher mean fasting glucose (5.04 ± 2.01) compared with Group 2 (4.57 ± 0.83) and higher mean 2-h glucose values (6.32 ± 2.91 versus 5.44 ± 1.29); $p < 0.01$. Group 1 women also had higher mean BMI, greater WHR and significantly greater VFM compared with those in Group 2 (see Table 2). However, total PBF was very similar in both groups.

The maternal and neonatal outcomes were not significantly different in the two groups except for neonatal hypoglycaemia, which was significantly higher in the diabetic group (see Tables 3 and 4).

VFM but not total PBF correlated with fasting glucose values in the whole cohort ($r = 0.21$, $p < 0.001$) and particularly in Group 1 ($r = 0.35$; $p < 0.002$). There was no significant correlation between VFM and 2 h glucose values in the whole cohort or in the two groups.

There was a significant correlation between glycaemia (HbA1c) and maternal BMI ($r = 0.39$, $p < 0.001$), and between HbA1c and

Table 2. InBody 720[®] body composition data at booking.

	Group 1 (GDM) (n = 72)	Group 2 (non-GDM) (n = 230)	p Value
BMI (kg/m ²) (mean $\pm$ SD)	40.2 $\pm$ 4.6	38.5 $\pm$ 3.9	$\leq$ 0.01*
Waist:hip ratio (mean $\pm$ SD)	1.02 $\pm$ 0.07	0.99 $\pm$ 0.05	$\leq$ 0.01*
Total percentage body fat (mean $\pm$ SD)	49.8 $\pm$ 3.5	49.2 $\pm$ 3.6	NS
Visceral fat mass ^a (units) (mean $\pm$ SD)	199.2 $\pm$ 40.5	183.8 $\pm$ 31.5	$\leq$ 0.01*

GDM: gestational diabetes; BMI: body mass index.

^aNormal value <100 units. * $p < 0.05$.

Table 3. Maternal outcomes.

	Group 1 (GDM) (n = 72)	Group 2 (non-GDM) (n = 230)	p Value
Hypertension, ^a n (%)	8 (11.1)	21 (9.1)	NS
Pre-eclampsia, n (%)	1 (1.4)	2 (0.9)	NS
Mode of delivery, n (%)			
Vaginal	34 (47.2)	122 (53)	NS
Instrumental	3 (4.2)	23 (10)	NS
Elective c/section	13 (18.1)	32 (13.9)	NS
Emergency c/section	22 (30.6)	53 (23)	NS
DVT/PE, n (%)	0	1 (0.4)	NS

GDM: gestational diabetes; NS: not significant; DVT: deep vein thrombosis; PE: pulmonary embolism; BP: blood pressure.

^aBP >150/100 requiring treatment or incremental rise in BP from booking >30/20.

Table 4. Neonatal outcomes.

	Group 1 (GDM) (n = 72)	Group 2 (non-GDM) (n = 230)	p value
Birth weight (mean $\pm$ SD)	3452.8 $\pm$ 626.3	3506.7 $\pm$ 564.1	NS
Large for gestational age, n (%)	13 (18.3)	42 (18.1)	NS
Admissions to neonatal unit, n (%)	8 (11.2)	22 (9.6)	NS
Major malformations, n (%)	0	0	NS
Neonatal hypoglycaemia, ^a n (%)	3 (4.2)	1 (0.4)	<0.05*
Neonatal jaundice, n (%)	3 (4.2)	2 (0.8)	NS
Shoulder dystocia, n (%)	0	1 (0.4)	NS

GDM: gestational diabetes.

^aCapillary glucose <2.6 mmol/l.

VFM ($r = 0.47$, $p < 0.0001$) (see Figure 1). No significant correlation was found between HbA1c and total PBF ($r = 0.16$, $p = \text{NS}$).

We also studied possible associations with baby birth weight (BW). Maternal BMI ($r = 0.14$; $p = 0.02$), VFM ($r = 0.17$; $p = 0.002$) but not PBF for the whole cohort and particularly in Group 2 ($r = 0.21$; $p = 0.001$) had weak but significant correlations with baby weight.

Figure 1. Visceral fat mass versus HbA1c in Group 1 patients. HbA1c: glycaemia

Although the expected increase in mean VFM at 36 weeks was reduced by metformin compared with those in Group 1 on dietary measures alone, the difference was not statistically significant ($3.76 \pm 3.1(\text{SEM})$ versus $8.24 \pm 2.6(\text{SEM})$; NS).

Discussion

To our knowledge, this is the first article to examine the possible role of directly measured VFM in relation to pregnancy outcomes. The novel finding in our study is that in addition to well-established predictors of GDM (maternal age, BMI, family history of GDM, history of polycystic ovary syndrome), visceral fat (and not total fat) assessed at antenatal booking is another risk factor for GDM.¹³ VFM correlated with fasting glucose in all patients, particularly those developing GDM, as well as long-term measures of HbA1c. Proxy measures of visceral fat, such as waist circumference and WHR showed the expected correlation.

Although obese patients will be expected to have higher VFM, we found no correlation between total PBF and indices of HbA1c (fasting or 2 h glucose), suggesting that non-visceral fat (e.g. subcutaneous fat) does not have the same metabolic implications. This is in keeping with concept of the metabolic syndrome and the proposal as long ago as 1997 that GDM should be considered a component of the metabolic syndrome.^{14,15}

A strong association between measures of abdominal obesity (waist circumference, WHR and CT-assessed intra-abdominal fat area) and the development of type 2 diabetes is well established: a meta-analysis of 15 cohorts from 10 longitudinal studies gave a pooled OR for the incidence of diabetes of 2.14 (95% CI: 1.70–2.71)¹⁶ compared with controls. Visceral fat assessed by CT remained a significant predictor of incident diabetes even after adjustment for BMI, total body fat and subcutaneous fat. In a large prospective study of obese non-diabetic subjects, baseline VFM measured by DEXA and magnetic resonance imaging but not general adiposity was independently associated with risk of development of prediabetes and diabetes.¹⁷ These studies point to an important role for visceral fat accumulation in the development of glucose intolerance.

In agreement with a recently published study, Asians developing GDM had lower BMI, lower WHR and lower VFM compared with Caucasians.¹⁸ However, among the Asian cohort, those developing GDM had higher VFM and markers of central obesity. Despite only small numbers in this study, these observations are in keeping with the suggestion that Asians are particularly susceptible to diabetes even at lower BMIs.

The pathogenic mechanism linking visceral fat and the onset of diabetes is likely to be through the development of insulin resistance although we cannot completely exclude the possibility of an effect on insulin secretion. In patients with established type 2 diabetes, visceral fat accumulation has a significant negative impact on glycaemic control through decreased insulin sensitivity.¹⁹

Visceral adipocytes release a variety of inflammatory cytokines that are able to induce insulin resistance such as interleukin-1, interleukin-6, tumour necrosis factor and resistin as well as others such as adiponectin, which improves insulin sensitivity.^{19,20} Adiponectin is down-regulated in obesity and plasma levels are lower in obese subjects compared with controls.²¹ Future studies need to examine the concentration of these substances in normal pregnancies and those complicated by obesity and GDM.

A major concern in pregnancies complicated by GDM or obesity is the increased risk of fetal macrosomia. The risk associated with obesity is increased two- to three fold and appears to correlate with the degree of obesity.²² We noted a positive correlation between maternal BMI and baby BW and between VFM (but not PBF) and BW. On further analysis, these correlations were not found in Group 1 women, reflecting the influence of treatment (metformin and insulin) on perinatal outcomes. We have previously shown a favourable effect of metformin on the incidence of macrosomia in GDM women.²³ Furthermore, we found no significant difference between BWs in the two groups in this study, which is likely to reflect the beneficial effect of metformin in GDM babies. In addition, a reduction in the expected increase in VFM was demonstrated in metformin-treated women, although this observation needs confirmation with larger numbers of patients.

Strengths of this study are direct measurement of fat distribution in vivo in early pregnancy in ambulant women attending a single centre with standardised dietary and exercise advice. There was complete data on all 302 women.

Limitations are the lack of a normal weight cohort of women to act as controls to allow calculation of OR for VFM. We were not able to measure cytokines such as adiponectin or inflammatory markers such as C-reactive protein, which might have added useful information regarding the metabolic syndrome. Also insulin sensitivity and secretion were not measured in this study. Future research will address this issue.

Conclusions

The results of this study add to the growing evidence of the importance of central obesity and in particular VFM in the development of GDM.

While BMI is a convenient measure of obesity, routine measurement of waist circumference or WHR in early pregnancy ideally complemented by VFM assessments may help identify those patients at increased risk.

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Conflicts of interest

None declared.

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Ethical approval

The study was considered by the ethics committee and considered an audit rather than research, and therefore not requiring ethical approval. Patients receiving metformin were given an information sheet detailing its use in pregnancy and the fact that although approved for use in pregnancy, it wasn't licensed for use in pregnancy.

Guarantor

N/A.

Contributorship

JB: Collecting data, analysis of results, initial draft manuscript; SH: Supervision of project, revising manuscript; AJ: Help with data collection, discussion; HS: Conceived idea for project, final version of manuscript.

References

- Lewis G (ed). Confidential enquiry into maternal and child health (CEMACH). Saving mothers' lives: reviewing maternal deaths to make motherhood safer - 2003–2005. In: *The 7th report of the confidential enquiries into maternal deaths in the United Kingdom*. London: CEMACH.
- FASTER Research Consortium. Obesity, obstetric complications and caesarean delivery rate – a population-based screening study. *Am J Obstet Gynecol* 2004; 190(4): 1091–1097.
- Torloni MR, Betran AP, Horta BL, et al. Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis. *Obesity Rev* 2009; 10(2): 194–203.
- Chu SY, Callaghan WM, Kim SY, et al. Maternal obesity and risk of gestational diabetes mellitus. *Diabetes Care* 2007; 30(8): 2070–2076.
- World Health Organization Department of Noncommunicable Disease Surveillance. *Definition, diagnosis and classification of diabetes mellitus and its complications*. Report of a WHO consultation. Geneva: WHO, 1999.
- Ogawa H, Fujitani K, Tsujinaka T, et al. InBody 720 as a new method of evaluating visceral obesity. *Hepato-gastroenterology* 2011; 58(105): 42–44.
- Malavolti M, Mussi C, Poli M, et al. Cross-calibration of eight-polar bioelectrical impedance analysis versus dual-energy X-ray absorptiometry for the assessment of total and appendicular body composition in healthy subjects aged 21–82 years. *Ann Human Biol* 2003; 30(4): 380–391.
- Antal M, Biró L, Regöly-Mérei A, et al. Methods for the assessment of adolescent obesity in epidemiological studies-using InBody. *Orvosi Hetilap* 2008; 149(2): 51–57.
- Sartorio A, Malavolti M, Agosti F, et al. Body water distribution in severe obesity and its assessment from eight-polar bioelectrical impedance analysis. *Eur J Clin Nutr* 2005; 59(2): 155–160.
- Van Loan MD, Kopp LE, King JC, et al. Fluid changes during pregnancy: use of bioimpedance spectroscopy. *J Appl Physiol* 1995; 78(3): 1037–1042.
- McCarthy EA, Strauss BJ, Walker SP, et al. Determination of maternal body composition in pregnancy and its relevance to perinatal outcomes. *Obstet Gynecol Surv* 2004; 59(10): 731–742. (quiz 745–746).
- Martin A, Brown MA and O'Sullivan AJ. Body composition and energy metabolism in pregnancy. *Aust N Z J Obstet Gynaecol* 2001; 41(2): 217–223.
- Savvidou M, Nelson SM, Makgoba M, et al. First-trimester prediction of gestational diabetes mellitus: examining the potential of combining maternal characteristics and laboratory measures. *Diabetes* 2010; 59(12): 3017–3022.
- Clark CM Jr, Qiu C, Amerman B, et al. Gestational diabetes: should it be added to the syndrome of insulin resistance? *Diabetes Care* 1997; 20(5): 867–871.
- Ford ES, Li C and Sattar N. Metabolic syndrome and incident diabetes: current state of the evidence. *Diabetes Care* 2008; 31(9): 1898–1904.
- Freemantle N, Holmes J, Hockey A, et al. How strong is the association between abdominal obesity and the incidence of type 2 diabetes? *Int J Clin Pract* 2008; 62(9): 1391–1396.
- Neeland IJ, Turer AT, Ayers CR, et al. Dysfunctional adiposity and the risk of prediabetes and type 2 diabetes in obese adults. *J Am Med Assoc* 2012; 308(11): 1150–1159.
- Hedderon M, Ehrlich S, Sridhar S, et al. Racial/ethnic disparities in the prevalence of gestational diabetes mellitus by BMI. *Diabetes Care* 2012; 35(7): 1492–1498.
- Gastaldelli A, Miyazaki Y, Pettiti M, et al. Metabolic effects of visceral fat accumulation in type 2 diabetes. *J Clin Endocrinol Metab* 2002; 87(11): 5098–5103.
- Bergman RN, Kim SP, Catalano KJ, et al. Why visceral fat is bad: mechanisms of the metabolic syndrome. *Obesity* 2006; 14(Suppl 1): 16S–19S.
- Weyer C, Funahashi T, Tanaka S, et al. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. *J Clin Endocrinol Metab* 2001; 86(5): 1930–1935.
- Ehrenberg HM, Mercer BM and Catalano PM. The influence of obesity and diabetes on the prevalence of macrosomia. *Am J Obstet Gynecol* 2004; 191(3): 964–968.
- Balani J, Hyer SL, Rodin DA, et al. Pregnancy outcomes in women with gestational diabetes treated with metformin or insulin: a case-control study. *Diabetic Med* 2009; 26(8): 798–802.