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Haemodynamic differences amongst women who were screened for gestational diabetes in comparison to healthy controls

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A B S T R A C T

Aim: To assess the changes in haemodynamics amongst pregnant women who were screened for gestational diabetes mellitus (GDM) in comparison to low-risk healthy pregnant controls.

Methodology: A total of 120 pregnant women of mean (standard deviation) age 31.03 (5.41) years who attended their oral glucose tolerance test as part of the national screening for GDM (study), and 60 low-risk healthy pregnant women (control) of mean age 29.71 (5.33) years, were invited to participate in this study. All women included in the study booked at the University Hospitals of Leicester NHS Trust and fulfilled the relevant inclusion criteria. Non-invasive assessment of arterial stiffness and cardiac output were undertaken on participants between 26 and 28 weeks of pregnancy. The mean difference between GDM and low-risk group for each of the arterial stiffness and cardiac output measurements was assessed by a two-sample unpaired *t*-test.

Results: Significant differences were found between the study and control groups for brachial (-64.5 vs. -69.5, $p < 0.04$) and aortic augmentation indices (5.2 vs. 2.7, $p = 0.04$), though there was no significant difference for PWV (8.3 vs. 8.1, $p = 0.49$). Cardiac output (7.6 vs. 7.0, $p = 0.011$), stroke volume (84.4 vs. 76.9, $p = 0.013$) and central mean arterial pressure (71 vs. 58, < 0.001) were also significantly different between groups. However, no significant differences were reported for heart rate, systolic and diastolic blood pressure, or total peripheral resistance.

Conclusion: Pregnant women at risk of GDM between gestational weeks 26 and 28 had significantly increased measures of arterial stiffness, as assessed by brachial and aortic augmentation indices, compared with low-risk healthy controls. Whether these women are at greater long-term cardiovascular disease risk warrants further investigation.

1. Introduction

Diabetes is the most common metabolic disorder in pregnancy and affects up to 5% of pregnancies within the United Kingdom [1]. The majority (87.5%) have gestational diabtetes mellitus (GDM), whilst 7.5% of this total have type 1 and only 5% have type 2 diabetes mellitus [1]. There is a significant burden associated with the maternal and foetal complications of diabetes, including adverse effects on organs, pre eclampsia [2], operative deliveries, birth trauma, and increased long-term risk of type 2 diabetes mellitus and cardiovascular disease [3]. In view of these adverse consequences, screening programmes have been implemented for the early detection of diabetes mellitus in pregnancy. GDM is diagnosed by means of a screening test performed in women during pregnancy. The International Association of Diabetes and Pregnancy Study Group Consensus Panel recommend that all pregnant women have a 75-gram oral glucose tolerance test (OGTT) between 24 and 28 weeks [4]. However, in the UK, after a cost-benefit analysis, the National Institute for Health and Care excellence (NICE) has recommended testing for GDM in women who have certain risk factors rather than blanket testing of all pregnant women [1].

Whilst pregnancy is associated with significant cardiovascular changes, any link between arterial stiffness and GDM is unclear. There have been few case-controlled studies investigating arterial stiffness in women with GDM, and only three undertaking assessments in late pregnancy [5–7] and one in the immediate postpartum period [8]. These studies report increased arterial stiffness in women with GDM or pre-existing T2DM compared with non-diabetic controls. However, there may be predictive value in evaluating arterial stiffness throughout

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pregnancy, as women who develop GDM may have increased arterial stiffness from the first trimester [9]. Importantly, there is also growing evidence that GDM is associated with chronic effects on vascular stiffness and longer-term outcomes. For example, it has been reported that women with a history of GDM display evidence of endothelial dysfunction, and are at increased risk of vascular complications independent of known risk factors [10,11].

Therefore, the aim of this cross sectional study was to assess, non-invasively, changes in arterial stiffness and cardiac output parameters among women being screened for GDM in comparison to low-risk, healthy pregnant women in order to determine if maternal haemodynamics are altered in women at risk of GDM.

2. Methods

One hundred and twenty consecutive pregnant women attending their routine screening for GDM and a further 60 low-risk healthy pregnant women, with no medical conditions, booked at the University Hospitals of Leicester NHS Trust, and fulfilling the relevant inclusion criteria were invited to participate in this study. Inclusion into the study group required women to be classified as being at risk of GDM (requiring an OGTT) as per NICE guidance [1], with no restriction on BMI. Participants were excluded if they had: multiple pregnancy, foetal anomalies, previous pregnancy complications, pre-pregnancy or pregnancy-induced hypertension, pre-eclampsia at inclusion in the present study, thyroid disease requiring medication, renal disease, known diabetes mellitus, taking any medication that could affect the cardiovascular system or were current smokers. In addition, participants with a BMI > 25 at booking were excluded from the healthy control group.

Following informed written consent (Stanmore National Research Ethics Committee, Reference 12/LO/0810), maternal characteristics, including medical history, were obtained.

Participants were assessed at 26–28 weeks of pregnancy, in a temperature-controlled room (22 °C) in a semi recumbent position. Participants were rested for a minimum of ten minutes, and were free from distraction, including speaking and moving, during the assessments. Assessments were not carried out following a large meal or caffeine intake. Non-invasive arterial stiffness measurements, pulse wave velocity (PWV) and augmentation index (AIx), were obtained with an Arteriograph® (Tensiomed Ltd, Hungary), which has previously been validated against invasive and non-invasive measurements [12,13] in a non-pregnant population. The Arteriograph® cuff was applied to the right arm over the brachial artery for an estimation of central systolic blood pressure (SBP), aortic PWV and AIx, as previously described [12]. Cardiac output (CO) was assessed using a non-invasive monitor (NICOM®, Cheetah medical, Portland, Oregon). After initial calibration, continuous values of stroke volume (SV), CO and total peripheral resistance (TPR) were measured.

All recordings were made by one observer (MWO), who received appropriate training in the use of the Arteriograph® and NICOM® devices.

2.1. Statistical analysis

To account for the increased variability with the mean, data on central SBP and diastolic BP (DBP) and mean arterial pressure (MAP) were logarithmically transformed. Mean difference between the study and control groups for arterial stiffness and CO measurements were assessed by a two-sample unpaired *t*-test. All statistical tests were two-sided with type 1 error rate (p-value) of 0.05 to determine the statistical significance.

3. Results

The study group comprised 120 women of mean (standard deviation) age 31.03 (5.41) years, and the control group 60 women of mean age 29.71 (5.33) years. Baseline characteristics are described in Table 1. Women within the study population had a significantly higher mean age, weight and BMI, and were more likely to be of non-Caucasian descent (Table 1).

Table 1
Baseline characteristics, in mean (SD), of the control and study groups at 26–28 weeks of gestation.

		Control group (n = 60)	Study group (n = 120)	P value
Age (years)		29.7 (5.3)	31.0 (5.4)	0.14
Height (cm)		163.9 (7.4)	160.8 (16.0)	0.08
Weight (kg)		61.1 (7.9)	76.7 (19.6)	< 0.001
BMI (kg/m$^{2)}$		22.25 (2.1)	29.20 (7.6)	< 0.001
OGTT				Normal value
Fasting (mmol/L)			4.57 (0.66)	< 5.6
2 h (mmol/L)			7.00 (1.77)	< 7.8
Parity	P0	27 (45%)	50 (41.7%)	
	P1	26 (43.3%)	43 (35.8%)	
	P2	6 (10%)	15 (12.5%)	
	P3	0	4 (3.3%)	
	P4	1 (1.6%)	4 (3.3%)	
	P5	0	3 (2.5%)	
	P6	0	1 (0.8%)	
Ethnicity	Asian	2 (3.3%)	35 (29.2%)	
	Caucasian	53 (88.3%)	53 (44.2%)	
	African	4 (6.7%)	18 (15%)	
	Far east	0	8 (6.6%)	
	Middle East	1 (1.7%)	6 (5%)	

4. Maternal haemodynamics

Significant differences were found between the study and control group in brachial (−64.5 vs. −69.5, p < 0.04) and aortic AIx (5.2 vs. 2.7, p = 0.04), though there was no significant difference for PWV (8.3 vs. 8.1, p = 0.49), (Table 2, Fig. 1). CO (7.6 vs. 7.0, p = 0.011), SV (84.4 vs. 76.9, p = 0.013) and CMAP (71 vs. 58, < 0.001) were also significantly different between groups, however, no differences in other central haemodynamic parameters such as heart rate, systolic and diastolic BP, or TPR were observed (Table 2, Fig. 2).

Upon sub-group analysis of the study population, participants were divided into GDM+ (n = 60) and GDM− (n = 60) depending on the OGTT result (Table 3). GDM+ being women diagnosed with GDM from an above normal OGTT value as per NICE(1). It was found that women who went on to develop GDM, had a statistically significant difference in both the brachial and aortic AIx (p < 0.001), Table 4. Additionally, the GDM group had higher blood pressures in comparison to the women who did not develop GDM, p < 0.01. CO, SV and TPR did not demonstrate any difference between the two groups within the sub-group analysis.

5. Discussion

This study has demonstrated that pregnant women at risk of GDM have significant alterations in haemodynamics compared to low-risk healthy women, when assessed at 26–28 weeks of gestation. In particular, measures of arterial stiffness (brachial and aortic AIx), CO, SV and MAP were all significantly higher.

Savidou et al. [7] found that patients with GDM had significantly increased arterial stiffness compared to low-risk healthy pregnancy, as assessed by mean AIx. Our study, also found a significant difference in AIx values in women at risk of GDM in comparison to normal pregnant women; brachial AIx, (p = 0.039) and aortic Aix (p = 0.040). Comparable to Savidou et al. [7], this study, also reported no significant differences in PWV. This apparent incongruity between measures of arterial stiffness may reflect that AIx, as a measure of arterial wave