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Maternal vascular indices and hemodynamic parameters at 36 weeks' gestation in gestational and pre-existing diabetes mellitus

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KEYWORDS: arterial stiffness; augmentation index; cardiac output; central blood pressure; heart rate; pulse-wave velocity; stroke volume; third-trimester screening; total peripheral resistance

CONTRIBUTION

What are the novel findings of this work?
At 35–37 weeks' gestation, women with gestational diabetes mellitus (GDM) and those with pre-existing diabetes mellitus (DM), compared to those without GDM or pre-existing DM, have higher central systolic and diastolic blood pressure and aortic pulse-wave velocity. There was no significant difference between the groups in stroke volume or total peripheral resistance. Vascular indices and central hemodynamics in women with GDM generally did not differ according to GDM treatment type.

What are the clinical implications of this work?
Women with GDM and those with pre-existing DM exhibit similar hemodynamic adaptations during pregnancy. They both have increased aortic stiffness and increased central blood pressure compared to women without hyperglycemia, and these changes may contribute to their increased long-term cardiovascular risk.

ABSTRACT

Objective *To compare maternal vascular indices and hemodynamic parameters at 35–37 weeks' gestation in pregnancies complicated by gestational diabetes mellitus (GDM), those with pre-existing diabetes mellitus (DM) and those without GDM or pre-existing DM.*

Methods *This was a prospective observational study in women with a singleton pregnancy attending for a routine hospital visit at 35 + 0 to 36 + 6 weeks' gestation. The visit included recording of maternal demographic characteristics and medical history, and measurement of vascular indices and hemodynamic parameters using a non-invasive operator-independent device. These included carotid-to-femoral pulse-wave velocity, augmentation index, cardiac output, stroke volume, central systolic and diastolic blood pressure, total peripheral resistance and heart rate. The values in the GDM and pre-existing DM groups were compared to those in the unaffected group.*

Results *We examined 6746 women, of whom 396 were excluded because they had chronic hypertension or developed pre-eclampsia or gestational hypertension. The study population of 6350 pregnancies contained 99 (1.6%) with pre-existing Type-I or Type-II DM and 617 (9.7%) that developed GDM, including 261 (42.3%) that were treated with diet alone, 239 (38.7%) treated with metformin alone and 117 (19.0%) treated with insulin with or without metformin. Among women with GDM and those with pre-existing DM, compared to those without GDM or pre-existing DM, there was a higher median cardiac output and heart rate, central systolic and diastolic blood pressure and pulse-wave velocity, but there was no significant difference in stroke volume or total peripheral resistance. There were no significant differences within the GDM group according to treatment type, except for higher heart rate in women treated with metformin alone compared to the group treated with diet alone.*

Conclusion *Women with GDM and those with pre-existing DM have evidence of early vascular disease in the third trimester, and this may contribute to their increased long-term cardiovascular risk.* © *2024 International Society of Ultrasound in Obstetrics and Gynecology.*

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INTRODUCTION

Epidemiological studies have shown that women with gestational diabetes mellitus (GDM), compared to those without GDM, have a 2-fold higher risk of developing premature cardiovascular disease, such as myocardial infarction and stroke, within the first decade after pregnancy, and this association could be explained by the development of Type-II diabetes mellitus (DM)[1,2]. Our group has also reported that, in women with GDM, compared to those without GDM, there is increased aortic stiffness, augmentation index and central blood pressure[3].

Assessment of early vascular changes can be performed using a variety of techniques for characterization of functional and structural changes in central and peripheral arteries[4]. Among various methods, aortic stiffness has gained considerable scientific interest, as it provides prognostic information about future cardiovascular risk[3]. Greater aortic stiffness results in increased transmission of pulsatile pressure into the microcirculation, increasing cardiovascular disease risk[4,5]. Measurements of aortic stiffness can be obtained easily, are accurate and reproducible, and demonstrate little change during normal pregnancy. Using this methodology, in a previous screening study at 35–37 weeks' gestation involving 2018 women with a singleton pregnancy, of whom 218 (10.8%) developed GDM, we found that there was significantly higher carotid-to-femoral pulse-wave velocity (PWV) in the GDM group compared with the non-GDM group[6].

The objectives of this extended study of 6350 pregnancies were: first, to examine further the vascular phenotype of women with *vs* those without GDM; second, to explore potential differences according to GDM treatment strategy; and third, to compare the phenotype of pregnancies with GDM to that of pregnancies with pre-existing DM.

METHODS

Study design and participants

This was a prospective observational study of women attending for a routine hospital visit at 35 + 0 to 36 + 6 weeks' gestation at King's College Hospital, London, UK, between December 2021 and February 2023. In our hospital, all women attending for pregnancy care undergo three routine ultrasound examinations, at around 12, 20 and 36 weeks' gestation. The 36-week visit included: first, recording of maternal demographic characteristics and medical history; second, ultrasound examination for fetal anatomy and growth; and third, measurement of maternal vascular indices and hemodynamic parameters for assessment of cardiac output, stroke volume, heart rate, total peripheral resistance, central systolic and diastolic blood pressure, PWV and augmentation index. Gestational age was determined by the measurement of fetal crown–rump length at 11–13 weeks or fetal head circumference at 19–24 weeks[7,8]. Women gave written informed consent to participate in the Advanced Cardiovascular Assessment in Pregnancy study (REC No.: 18/NI/0013, IRAS ID: 237936), which was approved by the NHS Research Ethics Committee.

Patient characteristics recorded included: maternal age, weight and height (which were measured at the time of screening); self-reported ethnicity (white, black, South Asian, East Asian or mixed); method of conception (natural or assisted by *in-vitro* fertilization or use of ovulation drugs); history of chronic hypertension, DM, systemic lupus erythematosus and/or antiphospholipid syndrome; family history of DM or pre-eclampsia (first- or second-degree relative); smoking status; and obstetric history, including parity (parous or nulliparous if no previous pregnancy at ≥ 24 weeks) and previous pregnancy with GDM or pre-eclampsia.

The inclusion criteria for this study were singleton pregnancy delivering a non-malformed liveborn or stillborn infant. We excluded pregnancies with aneuploidy or major fetal abnormality, those with chronic hypertension and those that developed a hypertensive disorder of pregnancy.

Maternal vascular indices and hemodynamic parameters

Participants were studied in the supine position after resting for approximately 5 min. Aortic stiffness was assessed by measuring carotid-to-femoral PWV. Measurements were performed using the Vicorder device (Skidmore Medical Limited, Bristol, UK)[9]. This device measures simultaneous pressure waveforms by a volume displacement technique using blood-pressure cuffs placed around the neck to pick up the carotid pulse wave and the right upper thigh to measure the femoral pulse wave in real time over at least 10 heartbeats. Both cuffs are automatically inflated and the corresponding oscillometric signal is analyzed to accurately measure in real time the pulse time delay and the consequent PWV. To calculate transit time, the Vicorder software automatically marks the pulse wave's steepest ascending part (maximum systolic upstroke) and uses a definite timeframe to detect the wave's nadir. The shift in time between the marked areas on the carotid and femoral pulse waves, which is the transit time, is detected by cross-correlation. The distance from the carotid to femoral pressure cuffs was measured using a tape. To account for differences in abdominal circumference, due to the pregnancy, and reduce variability and error in distance assessment, all measurements were performed from the suprasternal notch to the right shoulder and from there to the midpoint of the blood pressure cuff on the thigh. PWV was expressed in m/s.

The waveform of brachial artery pulse was also obtained oscillometrically and analyzed. By applying brachial-to-aortic generalized transfer function, the aortic waveform was generated. Analysis of the aortic waveform enables calculation of parameters that describe characteristics of the arterial system, including central aortic systolic and diastolic blood pressure, cardiac output, stroke volume and total peripheral resistance. Augmentation pressure was obtained, and augmentation index was expressed as a percentage of central pulse pressure and adjusted for a heart rate of 75 bpm.

Screening, diagnosis and management of gestational diabetes mellitus

The diagnosis of GDM in our hospital is based on the results of the oral glucose tolerance test (OGTT) following administration of 75 g of glucose; the diagnosis is made if the fasting plasma glucose level is ≥ 5.6 mmol/L and/or 2-h plasma glucose level is ≥ 7.8 mmol/L[10]. The OGTT was carried out in three groups of women. First, women with at least one risk factor (body mass index > 30 kg/m^2, previous birth of a macrosomic baby weighing > 4.5 kg, previous GDM, first-degree relative with DM or persistent glycosuria) were offered measurement of glycosylated hemoglobin at the first visit and, if the value was ≥ 5.7%, they underwent OGTT, usually at 12 weeks' gestation. Second, in all women at 26–28 weeks' gestation, plasma glucose level was measured 1–2 h after eating ≥ 50 g of carbohydrate and, if the concentration was ≥ 6.7 mmol/L, OGTT was carried out. Third, after 28 weeks' gestation, OGTT was performed if there was polyhydramnios or the fetus was macrosomic. Women with a diagnosis of GDM were given dietary and exercise advice and were encouraged to test their capillary blood glucose before and 1 h after each meal. If, during a period of 1–2 weeks, the pre-meal blood glucose level was ≥ 5.5 mmol/L or the 1-h post-meal blood glucose level was > 7 mmol/L, women were treated with metformin and/or insulin.

Statistical analysis

Data were expressed as median (interquartile range) for continuous variables and *n* (%) for categorical variables. The Mann–Whitney *U*-test and the chi-square test or Fisher's exact test were used for comparing outcome groups for continuous and categorical data, respectively. Box-and-whiskers plots were produced to visually depict cardiovascular indices in pregnancies with GDM, those with pre-existing DM and unaffected pregnancies.

We fitted multivariable regression models to describe the association of maternal vascular and hemodynamic variables with GDM, including the type of treatment, adjusting for confounding effects from maternal factors, obstetric and medical history and glycemic status. The process for model construction was carried out as follows. Initially, we explored the distributional properties of the dependent variables. We factored in a prespecified set of confounders, including maternal age, weight, height and ethnicity, method of conception, medical history of chronic hypertension, DM, systemic lupus erythematosus and/or antiphospholipid syndrome, parity, gestational age at delivery in a previous pregnancy, previous birth-weight centile, interpregnancy interval, previous GDM, previous pre-eclampsia, family history of DM or pre-eclampsia, smoking status and glycemic status. Backward elimination was used for variable selection in the regression models. Collinearity among independent variables was further assessed by correlational analyses and by calculating the variance inflation factor. We checked for significant interactions and the final models were chosen on the basis of parsimony. Residual diagnostics were used to examine model fitting and refine the parameter inferences.

The statistical software package R was used for statistical analysis[11]. $P < 0.05$ was considered statistically significant.

RESULTS

Study participants

We examined 6746 women, of whom 396 were excluded because they had chronic hypertension or developed pre-eclampsia or gestational hypertension. The study population of 6350 pregnancies included 99 (1.6%) with pre-existing Type-I or Type-II DM and 617 (9.7%) that developed GDM, of whom 261 (42.3%) were treated with diet alone, 239 (38.7%) were treated with metformin alone and 117 (19.0%) were treated with insulin with or without metformin.

Baseline demographic and clinical characteristics of the study participants are shown in Table 1. In the GDM group, compared to those without GDM or pre-existing DM, there was higher median maternal age, weight and body mass index, higher birth-weight centile, longer interpregnancy interval, earlier gestational age at delivery and higher frequency of black, South Asian and East Asian ethnicity, first- or second-degree relative with DM, conception by *in-vitro* fertilization and previous pregnancy complicated by GDM. Among pregnancies with pre-existing DM, compared to those without GDM or pre-existing DM, there was higher median maternal weight and body mass index, longer interpregnancy interval, earlier gestational age at delivery and higher frequency of black and South Asian ethnicity, first- or second-degree relative with DM and previous pregnancy complicated by GDM.

Maternal vascular indices and hemodynamic parameters

The distributions of the vascular indices and hemodynamic parameters in the GDM, pre-existing DM and unaffected groups are shown in Table 2 and Figure 1. In the GDM group, compared to the unaffected group, there was higher median cardiac output, heart rate, central systolic and diastolic blood pressure, PWV and augmentation index, but there were no significant differences in stroke volume or total peripheral resistance. Among those with pre-existing DM, compared to the unaffected group, there was a higher median cardiac output, heart rate, central systolic and diastolic blood pressure and PWV, but there were no significant differences in stroke volume, total peripheral resistance or augmentation index. In the GDM group, compared to those with pre-existing DM, heart rate and central diastolic blood pressure were significantly lower.

On multivariable analysis, the association between maternal vascular indices and hemodynamic parameters and GDM remained, with the exception of augmentation index (Table S1).

Table 1 Maternal and pregnancy characteristics of study population ($n = 6350$)

Characteristic	*No GDM or pre-existing DM* (n = *5634*)	*GDM* (n = *617*)	P	*Pre-existing DM* (n = *99*)	P
Maternal age (years)	33.8 (30.4–36.7)	34.4 (31.5–37.8)	< 0.0001	34.7 (31.0–37.3)	0.055
Maternal weight (kg)	77.7 (70.0–87.2)	81.4 (73.0–94.7)	< 0.0001	86.9 (75.3–98.7)	< 0.0001
Maternal height (cm)	166 (161–170)	164 (160–168)	< 0.0001	165 (160–169)	0.044
Maternal BMI (kg/m^2)	28.3 (25.7–31.6)	30.7 (27.2–35.0)	< 0.0001	32.3 (28.5–36.7)	< 0.0001
GA at screening (weeks)	35.6 (35.3–35.9)	35.6 (35.3–35.9)	0.532	35.7 (35.4–36.0)	0.084
Ethnicity					
White	4099 (72.8)	347 (56.2)	< 0.0001	40 (40.4)	< 0.0001
Black	810 (14.4)	129 (20.9)	< 0.0001	29 (29.3)	0.0002
South Asian	386 (6.9)	87 (14.1)	< 0.0001	20 (20.2)	< 0.0001
East Asian	115 (2.0)	30 (4.9)	< 0.0001	2 (2.0)	0.998
Mixed	224 (4.0)	24 (3.9)	0.936	8 (8.1)	0.071
Smoker	84 (1.5)	6 (1.0)	0.404	1 (1.0)	0.998
Family history of DM*	1027 (18.2)	160 (26.4)	< 0.0001	40 (40.4)	< 0.0001
Method of conception					
Natural	5224 (92.7)	543 (88.0)	< 0.0001	91 (91.9)	0.998
In-vitro fertilization	381 (6.8)	69 (11.2)	< 0.0001	8 (8.1)	0.888
Use of ovulation drugs	29 (0.5)	5 (0.8)	0.487	0 (0.0)	—
Parity					
Nulliparous	2813 (49.9)	277 (44.9)	0.025	38 (38.4)	0.038
Parous, no previous GDM	2747 (48.8)	262 (42.5)	0.004	45 (45.5)	0.668
Parous, previous GDM	74 (1.3)	78 (12.6)	< 0.0001	16 (16.2)	< 0.0001
Interpregnancy interval (years)	2.4 (1.6–4.2)	2.8 (1.8–5.5)	0.0002	3.3 (1.8–7.0)	0.009
GA at delivery (weeks)	39.7 (39.0–40.6)	39.0 (38.4–39.7)	< 0.0001	38.4 (37.6–39.1)	< 0.0001
Birth-weight centile	48.1 (23.9–72.5)	52.8 (22.5–78.3)	0.043	47.9 (20.5–71.5)	0.775

Data are given as median (interquartile range) or *n* (%). Comparisons between outcome groups were conducted using chi-square test or Fisher's exact test for categorical variables and Mann–Whitney *U*-test for continuous variables. *First- or second-degree relative. BMI, body mass index; DM, diabetes mellitus; GA, gestational age; GDM, gestational diabetes mellitus.

Table 2 Maternal vascular indices and hemodynamic parameters in pregnancies with gestational diabetes mellitus (GDM), those with pre-existing diabetes mellitus (DM) and those without GDM or DM

			GDM (n = *617*)			
				Treatment		
Measurement	*No GDM or pre-existing DM* (n = *5634*)	*Pre-existing DM* (n = *99*)	*All* (n = *617*)	*Diet only* (n = *261*)	*Metformin only* (n = *239*)	*Insulin** (n = *117*)
CO (L/min)	6.86 (6.01–7.82)	7.31 (6.05–8.41)†	6.99 (6.08–8.00)†	6.91 (6.02–7.77)	7.04 (6.19–8.07)	7.24 (6.07–8.27)
Heart rate (bpm)	89 (80–99)	96 (87–105)†	93 (83–101)†‡	91 (81–99)	94 (85–103)§	92 (85–100)
Stroke volume (mL)	78 (68–88)	77 (63–89)	77 (67–87)	76 (67–87)	76 (67–87)	79 (70–89)
TPR (mmHg × min/L)	0.76 (0.66–0.86)	0.74 (0.66–0.89)	0.76 (0.66–0.89)	0.78 (0.67–0.89)	0.75 (0.66–0.89)	0.74 (0.65–0.87)
SBP (mmHg)	113 (107–120)	118 (107–126)†	116 (109–124)†	115 (109–123)	117 (109–124)	117 (109–125)
DBP (mmHg)	63 (59–68)	67 (63–71)†	64 (60–70)†‡	64 (61–70)	65 (60–70)	64 (60–70)
PWV (m/s)	8.2 (7.5–9.0)	8.8 (8.0–9.5)†	8.5 (7.7–9.4)†	8.4 (7.6–9.3)	8.7 (7.8–9.5)	8.7 (7.7–9.6)
AIx@75 (%)	24.5 (14.2–34.7)	23.4 (14.9–34.7)	25.4 (16.8–35.8)†	23.9 (15.0–33.4)	26.3 (17.8–37.1)	26.5 (17.2–36.0)

Data are given as median (interquartile range). Comparisons between outcome groups were conducted using Mann–Whitney *U*-test. *With or without metformin. †Significant difference ($P < 0.05$) compared to those without GDM or pre-existing DM. ‡Significant difference ($P < 0.05$) compared to those with pre-existing DM. §Significant difference compared to diet group after adjustment for multiple comparisons by Bonferroni correction. AIx@75, augmentation index adjusted for a heart rate of 75 bpm; CO, cardiac output; DBP, central diastolic blood pressure; PWV, pulse-wave velocity; SBP, central systolic blood pressure; TPR, total peripheral resistance.

DISCUSSION

Main findings

In this large screening study at 35–37 weeks' gestation, we confirmed that women who develop GDM, compared to those who do not, have a variety of adverse cardiovascular risk factors. These women were older and heavier, had a higher incidence of family history of DM and exhibited altered hemodynamics. In the GDM group, cardiac output was increased, but this was mostly attributed to an increase in heart rate rather than stroke volume, and central blood pressure, aortic PWV and

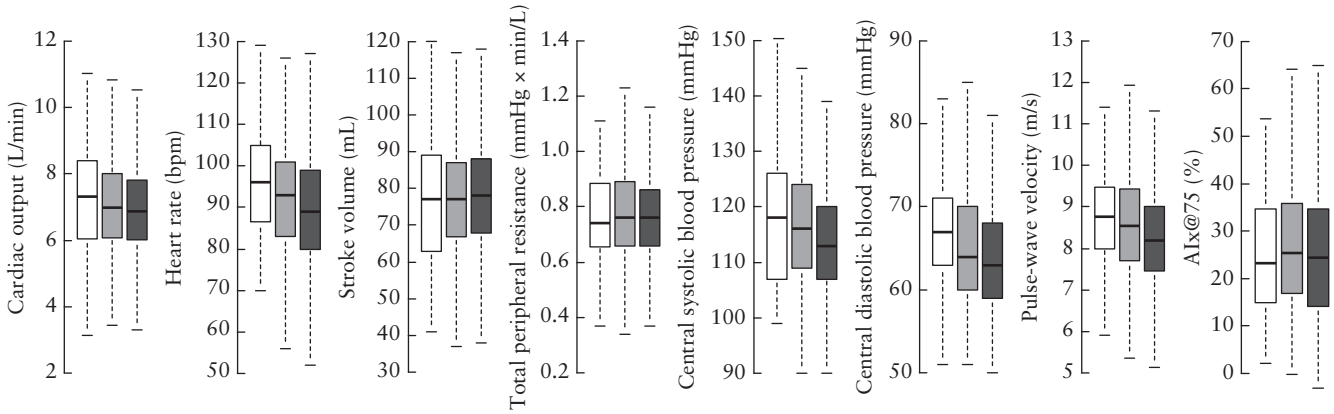

Figure 1 Box-and-whiskers plots showing maternal cardiovascular indices and hemodynamic parameters in pregnancies with pre-existing diabetes mellitus (□), those with gestational diabetes mellitus (■) and unaffected pregnancies (■). AIx@75, augmentation index adjusted for a heart rate of 75 bpm.

augmentation index were increased. Within the GDM group, vascular indices and central hemodynamics did not differ according to GDM treatment, with the exception of higher heart rate in women treated with metformin alone compared to those treated with diet alone. The cardiac output and total peripheral resistance of women with GDM were similar to that of women with pre-existing DM.

These findings suggest that women who develop GDM during pregnancy follow the same pattern of hemodynamic adaptation as women with pre-existing DM and demonstrate similar changes in their vasculature. It is therefore reasonable to postulate that women with GDM may have similar cardiovascular risk to women with pre-existing DM, provided that arterial changes persist beyond pregnancy.

Interpretation of findings and comparison with literature

A number of studies have demonstrated that GDM puts women at increased risk for development of both Type-II diabetes and premature cardiovascular disease within 10 years postpartum[1,2]. Similarly, findings from the Coronary Artery Risk Development in Young Adults (CARDIA) study suggest that GDM is a distinct diabetes-related hazard to cardiovascular health in women[12]. This risk may be attributable to the effects of placental hormones or increased release of inflammatory cytokines during pregnancy that increase insulin resistance and may promote atherogenesis[13]. However, some women may have a high-risk cardiovascular phenotype that is present before pregnancy, but which may only be first identified during routine screening for GDM[14]. In the current study, we showed, consistent with previous reports, that women with GDM have increased body mass index and are more likely to be of non-white ethnicity, have a first- or second-degree relative with DM and have a previous pregnancy complicated by GDM. All these risk factors have been associated consistently with premature development of atherosclerosis and vascular disease, which further increase the risk for adverse cardiovascular events later in life[15]. In addition, the risk-factor profile of women with GDM was similar to that in women with established DM.

To assess the cardiovascular status of our participants, we used well-established operator-independent techniques, which provide information on aortic function and structure[9,16]. By using these techniques, we showed, in the largest reported screening study at 35–37 weeks' gestation, that women with GDM have a worse central hemodynamic profile compared to women without GDM but similar to that in women with pre-existing DM. These results extend our findings from a previous study[6] in a subgroup of the same cohort, in which no difference in augmentation index was identified in women with GDM compared to those without GDM. Our results complement but also contradict findings from other groups. For instance, in a study of 53 pregnant women, Salmi *et al.*[13] found no difference in augmentation index between women with GDM ($n = 22$) and those without GDM ($n = 31$) in the third trimester but documented increased proinflammatory status in the former group. In contrast, Savvidou *et al.*[3] reported a higher augmentation index in the third trimester in 34 women with GDM compared with 34 controls, and this finding aligns with the study of Osman *et al.*[17] in 120 women who were screened for GDM at 26–28 weeks' gestation. The structural component of aortic stiffness, as measured by the carotid-to-femoral PWV, varies also among studies. Salmi *et al.*[13] and Bulzico *et al.*[18] did not find any difference in aortic stiffness in women with GDM compared to controls. However, in these studies[13,18], women with GDM did not differ from controls in maternal characteristics, including body mass index, blood pressure and ethnicity. In contrast, Osman *et al.*[17] reported a higher PWV in 120 women with GDM compared to 60 low-risk healthy pregnant women. The differences in reported findings between groups reflect mostly differences in power and maternal risk-factor profile.

An additional important finding of our study is that aortic stiffness was higher in women with GDM, compared to those without GDM, and we found no difference according to the type of treatment for GDM. Previous studies have shown that metformin may be

associated with improved hemodynamics in the third trimester, although another study did not confirm this finding[6,19,20]. Considering that our study is cross-sectional and women were already on GDM treatment at the time of recruitment, we were unable to identify the independent effect of GDM treatment; however, the lack of differences between groups would argue against a harmful effect of a specific treatment.

Among the hemodynamic parameters, cardiac output was increased in women with GDM compared to the unaffected group, and this was mostly related to an increase in heart rate rather than stroke volume. Although increased heart rate has been considered as an adverse risk factor for long-term cardiovascular risk, we cannot determine whether this finding simply reflects maladaptation to the volume of pregnancy in women with GDM[21,22]. Interestingly, peripheral vascular resistance was not altered in these women. This finding was unexpected considering that vascular indices were increased, but it may also suggest lack of placental insufficiency in this group of women.

In established DM, aortic stiffness has been shown to predict progression of complications of DM, including nephropathy, retinopathy and neuropathy[23]. The common vascular findings identified in women with GDM and those with pre-existing DM confirms previous reports that arterial stiffness may be increased in young people with metabolic syndrome before the clinical onset of overt DM[24]. Postpartum studies are needed to confirm whether aortic stiffness and hemodynamic changes during pregnancy can predict the development of DM and whether interventions targeting aortic stiffness can delay the onset of DM.

Clinical implications

This study demonstrates that women with GDM, compared to those without, have higher central blood pressure and aortic stiffness in the third trimester and these findings are not attributed to differences in maternal risk-factor profile, with the exception of augmentation index. Vascular and hemodynamic changes were comparable to those seen in women with established DM. Considering that previous epidemiological studies have shown that an increase in aortic PWV by 1 m/s in the general population corresponds to an age-, sex- and risk-factor-adjusted risk increase of 15% in cardiovascular mortality within a decade, our findings suggest that these women might benefit from postnatal cardiovascular assessment. Such an approach would clarify whether women with GDM are at risk of accelerated vascular aging similar to that seen in women with DM, or whether the observed vascular and hemodynamic changes are transient and do not contribute to long-term cardiovascular risk.

Strengths and limitations

The study documented central hemodynamics and aortic stiffness in a large cohort of unselected pregnant women at 36 weeks' gestation. We used non-invasive and reproducible vascular techniques, which have been shown to offer information for prediction of future cardiovascular risk in the general population. We found no material differences in vascular phenotype according to GDM treatment type but, due to the cross-sectional study design, we were unable to document the independent effect of GDM treatment. In addition, we cannot draw conclusions as to whether women with GDM have pre-existing vasculopathy or whether the noted vascular changes are transient. However, the fact that their vascular and hemodynamic responses were similar to those in women with pre-existing DM may explain the reported cardiovascular risk in these women.

A limitation of the study is that the OGTT was not carried out in all women, and it is possible that some of the pregnancies we classified as being unaffected by GDM or pre-existing DM could have been affected by GDM. However, such underestimation of the diagnosis of GDM, as well as the observed cardiovascular effects, would not affect our findings or conclusions.

Women with GDM and pre-existing DM were followed up in diabetic clinics and were reported to have well-controlled glucose levels. In this respect, it is not surprising that the birth-weight centiles of the DM and GDM groups were similar to those of unaffected pregnancies. Consequently, our results may not be reflective of poorly controlled diabetics.

Conclusions

At 36 weeks' gestation, women with GDM, compared to those without, have increased central hemodynamics and aortic stiffness, and their hemodynamic responses are comparable to those in women with pre-existing DM. Postnatal assessment is necessary to clarify whether these changes are transient or whether they persist and contribute to long-term cardiovascular risk.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Multivariable regression models for maternal vascular and hemodynamic variables, adjusted for maternal factors, obstetric and medical history and glycemic status