Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Women with a history of gestational diabetes on long-term follow up have normal vascular function despite more dysglycemia, dyslipidemia and adiposity

Olubukola Ajala [a,*], *Louise A. Jensen* [b], *Edmond Ryan* [a], *Constance Chik* [a]

[a] *Division of Endocrinology and Metabolism, Department of Medicine, 9th Floor, Clinical Sciences Building, University of Alberta, Edmonton, Alberta T6G 2G3, Canada*

[b] *Faculty of Nursing Level 3 Edmonton Clinic Health Academy, University of Alberta, Edmonton, Alberta T6G 1C9, Canada*

ARTICLE INFO

Article history:
Received 20 May 2015
Received in revised form
17 September 2015
Accepted 1 October 2015
Available online 9 October 2015

Keywords:
Gestational diabetes
Vascular function
Dyslipidemia
Adiposity

ABSTRACT

Aims: Previous gestational diabetes (GDM) is a risk factor for type 2 diabetes and increased metabolic risk, but the link with vascular dysfunction is not clear. This study examined vascular function in women 4–10 years after a diagnosis of GDM who had a normal oral glucose tolerance test (OGTT) in the first postpartum year.

Methods: We studied 90 women with a history of GDM and 59 age-matched controls, examining differences in insulin resistance as measured by the Homeostatic Model Assessment (HOMA-IR) and glucose responses during an OGTT, adiposity, lipid profile and C-reactive protein (CRP). Using pulse wave analysis, we also measured cardiac function, vascular compliance, and systemic vascular resistance.

Results: Women with a history of GDM had higher measures of adiposity (body mass index 28.9 ± 6.5 vs. 26.6 ± 6.9 kg/m^2, $P = 0.04$, waist–hip ratio 0.85 ± 0.06 vs. 0.79 ± 0.07, $P < 0.001$), dyslipidemia (LDL cholesterol 2.78 ± 0.64 vs. 2.41 ± 0.56 mmol/L, $P < 0.001$, total cholesterol: HDL cholesterol 3.93 ± 1.2 vs. 3.21 ± 0.82 mmol/L, $P < 0.001$) and abnormal glucose metabolism (50% vs. 12%, $P < 0.001$). However, there was no difference in CRP, HOMA-IR, or measures of cardiovascular function including pulse rate, pulse pressure, mean arterial pressure, cardiac output, systemic vascular resistance, small and large artery elasticity index. After controlling for adiposity, blood pressure, lipids and CRP, glycemic status did not contribute to vascular function.

Conclusion: Despite a higher incidence of adiposity, dyslipidemia, and impaired glycemia, women with a history of GDM who had a normal postpartum OGTT did not have impaired vascular function 4–10 years postpartum, when compared to healthy controls.

* Corresponding author. Tel.: +1 780 4923626; fax: +1 780 4926444.
E-mail address: olubaniy@ualberta.ca (O. Ajala).

http://dx.doi.org/10.1016/j.diabres.2015.10.004
0168-8227/

1. Introduction

Gestational diabetes mellitus (GDM) affects up to 14% of pregnant women depending on the population studied [1]. Women with GDM are at a significant risk of developing type 2 diabetes [2] and dyslipidemia [3], both of which accelerate the development of atherosclerosis [4] and explain the increased incidence of cardiovascular disease over a decade after the diagnosis of GDM [5].

Arterial endothelial dysfunction precedes the structural changes that characterize atherosclerosis, is one of the earliest markers of atherogenesis [6], and can be measured accurately by several non-invasive techniques: large artery function can be detected through flow mediated dilatation (FMD) which relies on ultrasonography, whereas structural changes can be measured by carotid-intima media thickness (CIMT). Arterial circulation and vascular compliance can be assessed by peripheral arterial tonometry using pulse wave analysis [7,8] which measures pulsatile volume changes before and after occlusion of brachial flow via plethysmographic cuffs [9]. Measuring vascular function using peripherally acquired waveforms (pulse wave velocity) is validated, reproducible and easy to perform in an outpatient setting [10–12].

A history of GDM is associated with an increase in C-reactive protein (CRP), a marker of low grade inflammation, particularly in the setting of obesity [13]. CRP is also an independent predictor of cardiovascular disease [14,15], and due to its advantage of being stable over time, is recommended over other markers of inflammation for clinical use [16].

Several studies of women with a history of GDM have shown reduced FMD [17–21] and increased CIMT [22], consistent with impaired large artery function and structure respectively. However, most included few subjects [18–20,22] and some were studied within the first year postpartum [17,18,20].

The aim of our study was to examine differences in CRP and other demographic and clinical risk factors, vascular compliance and cardiac function in a cohort of parous women with and without a history of GDM, 4–10 years postpartum. To ensure a homogeneous cohort, we investigated subjects who had a normal 75-g oral glucose tolerance test (OGTT) with fasting glucose <6.1 mmol/L and 2-h plasma glucose <7.8 mmol/L within the first year of delivery.

2. Research design and methods

1084 women with a history of GDM were screened using records from a database of 2 large clinics in Edmonton, Alberta, Canada. Women with a pre-existing history of hypertension, vascular disease, pre-eclampsia, use of blood pressure lowering medication in the previous three months, non-gestational diabetes, abnormal postpartum OGTT, and current pregnancy or pregnancy within four years prior to recruitment were excluded. Participant characteristics were obtained using questionnaires as was information about smoking habits, time spent exercising, and family history of hypertension, heart disease, diabetes, and stroke. During the pregnancy, GDM was diagnosed following a 50 g gestational diabetes screen (GDS) and/or 2-h 75 g OGTT as recommended by the Canadian Diabetes Association [23]. Ninety women with previous GDM participated in the study (pGDM group) and were matched based on age with 59 healthy controls (CG). The study was approved by the Research Ethics Board of the University of Alberta.

2.1. *Physical and laboratory measurements*

All participants were studied after a 12 h overnight fast and underwent measurements of body mass index (BMI), waist circumference (WC), and waist–hip ratio (WHR). BMI was derived from direct measurement of height and weight (health o meter digital scale; Sunbeam, USA) performed between 0800 and 0900 h, while waist circumference was measured by a trained nurse by metal tape midway between the lower rib margin and iliac crest. CRP, fasting plasma glucose (FPG), plasma lipids: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc) and thyroid stimulating hormone (TSH) through standard techniques with the Beckman Coulter DxC800. Serum insulin levels were measured by a chemiluminescent method using an automatic immunoanalyzer. Homeostasis model assessment (HOMA-IR) derived insulin resistance was calculated as fasting serum insulin (mU/L) $\times$ fasting plasma glucose (mmol/L)/22.5 and a 75-g OGTT was performed.

2.2. *Vascular studies*

Vascular function was determined using the HDI/Pulse wave CR-2000 (Hypertension Diagnostics, Inc. Minnesota, USA) following the manufacturer's guidelines. The studies were performed in the follicular phase of the menstrual cycle. Large artery (LAEI mL/mmHg) and small artery (SAEI mL/mmHg) elasticity index were measured after a 10 min supine rest period; the radial arterial pressure waveform of the right arm was acquired using the applanation device in conjunction with an automated blood pressure on the left arm. Systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), systemic vascular resistance (SVR mmHg/min mL^{-1}), pulse rate, pulse pressure, cardiac ejection time (min), stroke volume (mL) and cardiac output (mL/min) were also measured with this device. The inter-observer variability coefficients for the vascular measures were 0.89–0.99, while intra-observer variability coefficients were 0.60–0.89.

2.3. *Statistical analysis*

Statistical analyses were performed using SPSS (statistical package of social science) version 21. Continuous variables were tested for normality of distribution, Student's *t*-test was applied for comparison of groups and categorical variables were compared using the *Chi*-square test. The study participants were divided into 2 groups based on their glycemic status in pregnancy: pGDM and CG, and further into 3 groups based on their glycemic status postpartum: normal glycemic, impaired glucose tolerance and diabetes. Analysis of variance was performed to investigate differences in the three measures of vascular function (LAEI, SAEI, SVR) between the groups with statistical significance defined as