Mean platelet volume as a risk factor in pregnant diabetic women

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Background
Diabetes is an established risk factor for cardiovascular disease (CVD); therefore, the subset of women with gestational diabetes mellitus (GDM) who develop type 2 diabetes mellitus is at an increased risk for developing CVD in the future.
Objectives
To assess the platelet count and mean platelet volume (MPV) of pregnant women with GDM and gestational impaired glucose tolerance (GIGT) to determine whether GDM and GIGT are risk factors for future development of CVD.
Patients and methods
A 50 g oral glucose load (OGL) was administered to all participants (400 pregnant women), and routine hematologic parameters and MPV were studied at 24–28 gestational weeks using a Beckman/Coulter MAXM Hematology Analyzer.
When a plasma glucose level of at least 140 mg/dl was measured after administering OGL, a 100 g 3-h oral glucose tolerance test was performed. Of these women, 296 (74%) had normal oral glucose tolerance, 48 (12%) had GIGT, and 65 (14%) had GDM. The mean platelet counts were higher in the normal OGL group than in the GIGT group, and higher in the GIGT group than in the GDM group, with no statistically significant differences among the three groups. However, MPV was significantly higher in the GDM group than in the normal glucose level group ($P<0.05$). Also, women with high MPV values had lower platelet counts.
Results
A significant difference was observed for MPV values between the GDM and normal OGL groups.
Conclusion
Presence of a high MPV in cases of GDM could indicate an increased risk for current and future thrombotic complications.

Keywords:
cardiovascular risk factors, diabetes mellitus, gestational diabetes mellitus, gestational impaired glucose tolerance, mean platelet volume, pregnancy, thrombotic complications

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Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy, and it affects 1.2–14.3% of pregnant women [1]. Gestational impaired glucose tolerance (GIGT) is a glycemic disorder and is considered a prediabetic state [2]. Considering the GDM consequences on increased perinatal and maternal morbidity and mortality, in addition to long-term complications, its accurate identification and treatment is of utmost importance [3,4]. More than 50% of GDM women will develop type 2 diabetes mellitus (DM) in the future, and women with a history of GIGT also have an increased risk for developing diabetes [5]. Diabetes is an established risk factor for cardiovascular disease (CVD); therefore, the subset of women with GDM who develop type 2 DM is at an increased risk for developing CVD in the future [6]. Altered platelet morphology and function have been reported in patients with metabolic syndrome, stroke, and DM [7–10]. Mean platelet volume (MPV) is a new and independent risk factor for myocardial infarction (MI), cerebral infarction, and transient ischemic attacks [7–11]. MPV is an important, simple, effortless, and cost-effective measure that should be used for predicting the possibility of impending acute events such as MI and cerebrovascular events [2,11,12]. Patients with large platelet counts can be identified easily during routine hematological examination and could possibly benefit from preventive treatment [13].

In this study, we aimed to assess the platelet count and MPV values of pregnant women with GDM and GIGT to ascertain whether GDM and GIGT are risk factors for future development of cardiovascular disorders.

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Materials and methods

This research was conducted in Bakhsh Hospital-Makkah (Saudi Arabia), in the Departments of Obstetrics & Gynaecology and Internal Medicine, between January 2009 and December 2011. Patients with anemia, hemoglobinopathy, chronic inflammatory bowel disease, renal failure, cyanotic congenital heart disease, pre-existing DM, other chronic diseases, and pre-eclampsia were excluded from the study. Informed consent was obtained from all selected patients.

A 50 g oral glucose load (OGL) was administered at 24–28 gestational weeks to all participants. When plasma glucose of at least 140 mg/dl was measured 2 h after the OGL, a 100 g 3-h oral glucose tolerance test (OGTT) was performed. A fasting peripheral venous blood sample was obtained from all participants at the same time as the OGTT. GDM was diagnosed when two or more abnormal plasma glucose levels were obtained during the OGTT according to the NDDG criteria ($\geq$105 mg/dl fasting, $\geq$190 mg/dl at 1 h, $\geq$165 mg/dl at 2 h, or $\geq$145 mg/dl at 3 h) [14]. Only one abnormal value was considered for GIGT. For all cases the following hematological parameters were evaluated: hemoglobin, hematocrit, red blood cell and platelet counts, MPV, red cell distribution width, and platelet distribution width. Samples were taken by means of antecubital vein puncture into tubes containing tripotassium EDTA. All samples were analyzed on a Beckman/Coulter MAXM Hematology Analyzer (Beckman Coulter, California, USA) 1–2 h after collection to minimize changes in platelet size. MPV reference range was determined as 7.8–11 fl. Data were analyzed with SPSS software version 13.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Mean ± SD was calculated for age and MPV for all these groups separately. Differences between the mean age and MPV values between groups and within groups were calculated by analysis of variance. *P*-values and 95% confidence intervals were also calculated. A *P*-value 0.05 or less was considered statistically significant. The relationships between two continuous variables, platelet count, and MPV were assessed by linear regression analysis. All tests were two-sided with a 0.05 significance level.

Results

A total of 400 pregnant women fulfilling the selection criteria were selected and divided into three groups according to the OGL and OGTT result: 296 (74%) women with a normal OGL, 48 (12%) with GIGT, and 56 (14%) with GDM. Mean age, gravity, parity, and gestational age were similar, as shown in Table 1. The mean OGL results were 115.9, 148.7, and 171.3 mg/dl for the nondiabetic, GIGT, and GDM groups, respectively. There were significant differences between the three groups with respect to the OGL test results ($P<0.002$ for GDM vs. GIGT and GDM vs. normal OGL, GDM vs. GIGT and GIGT vs. normal OGL).

With regard to the hematological parameters, red blood cell count, hemoglobin, hematocrit, red cell distribution width, and platelet distribution width values were similar among the three groups (Table 1). The mean platelet counts were higher in the normal OGL group than in the GIGT group and higher in the GIGT group than in the GDM group, with no statistically significant differences among the three groups. With regard to the mean MPV values there was a significant difference between the GDM group and the group with normal OGL ($P<0.05$) (Table 1). In linear regression analysis, an inverse relationship between platelet count and MPV levels was observed ($P<0.001$, $r=0.105$). Patients with high MPV values had lower platelet counts (Table 1).

Discussion

GDM leads to significant health problems in mothers later in life. Women with a history of GDM have a 20–50% risk of developing type 2 DM within 5 years of pregnancy [15,16]. Although the risk for type 2 DM is well established among women with GDM, there have been few studies on this issue in women with lower degrees of glucose intolerance during pregnancy [14,17–20]. Research by Carr *et al.* [21] on this subject showed that women with a history of GIGT have an increased risk for developing diabetes. A recent study by Vambergue *et al.* [22] reported that GIGT was independently associated with glucose intolerance at 6.75 years postpartum, and cases with GIGT had a 4.57-fold increased risk compared with normal pregnant women.

Diabetes is an established risk factor for CVD; therefore, the subset of women with GDM who develop type 2 DM is at an increased risk for developing CVD in the future [6]. It is uncertain, however, whether normoglycemic women with a history of GDM or GIGT who do not develop type 2 DM later are also at increased risk for future CVD. Women with a history of GDM, although normoglycemic after pregnancy, have an increased risk for insulin resistance and decreased endothelium-dependent vasodilatation [23,24]. Such data suggest that GDM may represent the transient unmasking of a latent metabolic

Table 1 Demographic characteristics. Hematological and biochemical results of the group

	Normal OGL	GIGT	GDM
N (%)	296 (74%)	48 (12%)	56 (14%)
Age (years)	29.3 ± 3.9	31.1 ± 5.2	31.8 ± 6.2
Gravidity (*n*)	2.6 ± 1.2	2.3 ± 1.4	2.4 ± 1.5
Gestational age (weeks)	25.2 ± 1.3	25.7 ± 1.2	25.7 ± 1.4
OGL (mg/dl)	115.9 ± 23.3	148.7 ± 19.9	171.8 ± 28.1
RBC (million)	4.21 ± 0.61	4.22 ± 0.42	4.31 ± 0.38
Hemoglobin (g/dl)	11.92 ± 1.3	12.6 ± 1.10	12.3 ± 1.6
Hematocrit (%)	35.5 ± 4.1	35.4 ± 2.9	35.1 ± 2.2
RDW (%)	13.91 ± 3.1	13.7 ± 1.2	13.5 ± 1.1
Platelet (*n*)	251.0 ± 64.8	240.12 ± 44	233.8 ± 54.2
MPV (fl)	8.21 ± 0.69	8.22 ± 0.93	8.71 ± 1.50*
PDW (%)	15.9 ± 1.3	16.1 ± 1.4	16.0 ± 2.1

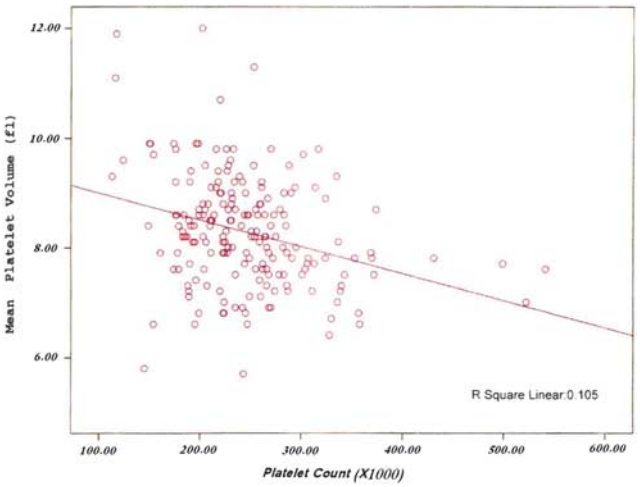
GDM, gestational diabetes mellitus; GIGT, gestational impaired glucose tolerance; MPV, mean platelet volume; OGL, oral glucose load; PDW, platelet distribution width; RBC, red blood cell; RDW, red cell distribution width.
*$P<0.05$: between the normal OGL and GDM groups.

syndrome that may become clinically apparent later in life as CVD. Vascular dysfunction is another independent risk factor for CVD and women with prior GDM may have impaired vascular function [25,26]. In their study, Anastasiou *et al.* [24] concluded that women with a history of GDM have impaired endothelium function as assessed by flow-mediated dilatation. Another study on this issue [26] showed that women with prior GDM have impaired acetylcholine-induced skin vasodilatation after the postpartum period (2–4 years), as assessed by laser Doppler flow, when compared with normal controls. The changed balance between prostacyclin and thromboxane observed in vessels of diabetic patients might serve as an explanation for the vascular modifications mentioned above [27]. This imbalance between prostacyclin and thromboxane is responsible for the hypercoagulability in diabetic women and could result in fetal loss – one of the most important complications of GDM. Hypercoagulability and vascular dysfunction cause microthrombosis in placental bed vessels and placental infarctions. Consequently, this generates an impairment in the fetomaternal circulatory system, which results in low placental perfusion and finally in fetal loss [28].

Platelets play an important role in the integrity of normal homeostasis, and MPV is the indicator for their function [29]. Large platelets contain more dense granules, are more potent than smaller ones, and are hence more thrombogenic [30,31]. An increase in MPV has been documented in patients with metabolic syndrome, stroke, and DM [31]. Increased MPV is now emerging as an independent risk factor for thromboembolism and MI [10,32,33]. Bozkurt *et al.* [34] demonstrated that the MPV in their GDM group was significantly higher than the MPV of healthy pregnant women, but no statistically significant difference was observed in the platelet count between the women in the GDM group and normal pregnant women. In addition, an inverse relationship was observed between platelet number and MPV. Our study showed results similar to those of Bozkurt *et al.* [34] and Kosus *et al.* [35]. GDM cases had a lower platelet count and a higher MPV. There was no difference between groups in terms of platelet count, but the MPV of our GDM group was significantly higher than that of the healthy group. An inverse relationship between platelet count and MPV levels was also observed (Fig. 1). This knowledge may be important for the prevention of thrombotic complications related to increased MPV in patients with GDM that can result in impairment in the fetomaternal circulatory system. Anticoagulant therapy such as low-dose aspirin may improve pregnancy outcome by blocking the action of cyclooxygenase synthesis and preventing thrombosis of the placental vasculature.

In one study, De Pablos [36] showed that patients with GIGT had a higher prevalence of certain cardiovascular risk factors compared with patients with normal glucose tolerance in the white population. In our study MPV was found to be increased in the GIGT group. Although this increase was not statistically significant, it may be an early sign of risk for future CVD.

Figure 1



Correlation between platelet count and mean platelet volume.

Conclusion

Glucose intolerance during pregnancy may be an early sign of metabolic disease later in life. Pregnancy helps women to assess their metabolic state. Because pregnancy itself contains excessive metabolic changes, women who tolerate these changes successfully can be considered as having a lower CVD risk in the future if no other risk factors are present. Women with GDM would be expected to be at higher risk for future CVD. Our results suggest that GDM may serve as a marker of increased risk for future CVD. Another important finding in our study was the presence of higher MPV in GIGT women than in normal women. This means that GIGT may be a risk factor for CVD also. However, future studies with a larger series and long-term follow-up of such cases are needed to confirm this evidence. Such evidence might lead women to take preventive measures now and in the future, such as lifestyle changes or prophylactic pharmacological interventions.

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Conflicts of interest

There are no conflicts of interest.

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الأهميه الإكلينيكه لتقدير متوسط حجم الصفائح الدمويه في النساء الحوامل ذوات السكرى الحملى

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أجرى هذا البحث لتقدير ما اذا كان عدد او حجم الصفائح الدمويه فى النساء الحوامل ذوات السكرى الحملى له أهميه فى تقدير توقع الأصابه بأمراض القلب و الأوعيه الدمويه .إشتمل هذا البحث على 400 إمرأه حامل تنطبق عليهن شروط البحث. 296(74%) إمرأه ذوات مستوى سكر طبيعى و 48(12%) ذوات إعتلال فى مستوى السكرى بالدم ,و 56(14%) ذوات السكرى الحملى. وقد وجد أن هناك اختلاف هام ذو دلاله احصائيه عاليه فى حجم الصفائح الدمويه بين النساء ذوات السكرى الحملى والنساء الحوامل الغير مصابات بالسكرى الحملي مما يرجح إرتفاع إحتمالية تعرضهن لخطورة ألاصابه بأمراض القلب و الأوعيه الدمويه