

Mean Platelet Volume as Risk Factor for Pregnant Diabetics

Sayed M. Abel-rahman, Md¹

Essam Saad Badawy, Md²

Ahmad a. Amer, Md³

Dalal Fekry, Md⁴

Assistant Prof. of Internal Medicine, Sohage University¹

Assistant Prof. of Internal Medicine, Minia University²

Prof. of Obstetric and Gynecology, Zagazig University³

Assist. Prof. of Hematology & Clinical Pathology, Ain-Shams University⁴

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Abstract

Background: Diabetes is an established risk factor for CVD; therefore, the subset women with GDM who develop type 2 DM are at an increased risk of developing CVD in the future

Objectives: Assessment of platelet count and mean platelet volume (MPV) of pregnant women with gestational diabetes mellitus (GDM) and gestational impaired glucose tolerance (GIGT) to find out whether GDM or GIGT are risk factors for future development of cardiovascular disease.

Patients & Methods: A 50 gram oral glucose load (OGL) was administered to all participants (400 pregnant women) and routine hematologic parameters and mean platelet volume by using Beckman/Coulter MAXM Hematology Analyzer (Beckman Coulter, CA, USA), were studied at 24 - 28 gestational weeks. When plasma glucose \geq 140 mg/dl was measured following (OGL), a 100 gm-3-h oral glucose tolerance test was undertaken. Of these women, 296 (74%) have normal OGT, 48 (12%) have GIGT and 65 (14%) have GDM. The mean platelet counts were higher in normal OGL group than in GIGT and in GIGT group than in GDM group with no statistically significant differences between the three groups. However, the MPV was significantly higher in GDM group than that in the NGL group $P < 0.05$. also; women with high MPV values had a lower platelet counts.

Results: A significant difference was observed for MPV values between GDM and normal ORL groups.

Conclusion: Presence of a high MPV in GDM could demonstrate an increased risk for current and future thrombotic complications.

Keyword: Diabetes mellitus-Pregnancy-Gestational DM-Mean platelet volume-Cardiovascular risk factors- Thrombotic complications-GIGT.

Introduction

Gestational diabetes mellitus is defined as any degree of glucose intolerance with onset or first recognition during pregnancy and it affects 1.2 to 14.3% of the pregnant women¹. Gestational impaired glucose tolerance is a glycemic disorder and is considered as a pre-diabetic state². Considering the GDM consequences of 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 in their future life and women with a history of GIGT also have an increased risk of developing diabetes⁵. Diabetes is an established risk factor for CVD; therefore, the subset women with GDM who develop type 2 DM are at an increased risk of developing CVD in the future⁶. Altered platelet morphology and function have been reported in patients with metabolic syndrome, stroke, and diabetes mellitus⁷⁻¹⁰. MPV is a new and independent risk factors for MI, cerebral infarction and transient ischemic attacks⁷⁻¹¹. MPV is an important, simple, effortless and cost effective measure that should be used for predicting the possibility of impending acute events like MI and cerebrovascular events^{2,11,12}. Patients with large platelets can easily be identified during routine hematological examination and could possibly benefit from preventive treatment¹³. In this study we aimed to assess the platelet count and MPV values of pregnant women with GDM, GIGT to find out whether GDM and GIGT are considered risk factors for future development of cardiovascular disorders.

Materials and methods

This research was conducted in Bakhsh Hospital-Makkah, SA. Departments of Obstetrics & Gynaecology and Internal Medicine, between January 2009 and December 2011. Exclusion criteria include patients with anemia, hemoglobinopathy, chronic inflammatory bowel disease, renal failure, cyanotic congenital heart disease, pre-existing diabetes mellitus, other chronic diseases, and preeclampsia. Informed consent was obtained from all selected subjects.

A 50-gram oral glucose load was administered at 24- 28 gestational weeks to all participants. When plasma glucose \geq 140 mg/dl was measured 2h following the OGL, a 100 gm-3-h OGTT was done. A fasting peripheral venous blood sample was obtained from all participants at the same time during OGTT. GDM was diagnosed when 2 or more abnormal plasma glucose levels were obtained during

the OGTT according to NDDG criteria (≥ 105 mg/dl fasting, ≥ 190 mg/dl at one hour, ≥ 165 mg/dl at 2 hour, or ≥ 145 mg/dl at 3-hours)(18). Only one abnormal value was considered GIGT.

For all cases the following hematological parameters were performed (hemoglobin, hematocrit, RBC and platelet count, MPV, RDW and PDW). Samples were taken by antecubital vein puncture into tubes containing tripotassium EDTA. All samples were analysed on a Beckman/Coulter MAXM Hematology Analyzer(Beckman Coulter, CA, USA)1-2h after collection to minimize changes in platelet size. MPV reference range is determined as 7.8-11 fl. Data were analysed with SPSS software version 13.0 for Windows (SPSS Inc. Chicago, Illinois, USA) Mean \pm SD were calculated for age and MPV for all these groups separately. Difference between the means of age, MPV between the groups and within the groups were calculated by analysis of variance (ANOVA). P-values and 95% confidence intervals (CI) were also calculated. A p-value of ≤ 0.05 was considered as 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. These include 296(74%) with normal OGL, 48(12%) with GIGT, and 56(14%) with GDM groups. 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 non-diabetic, GIGT and GDM groups respectively. There were significant differences between the three groups regarding the OGL test results ($p < 0.002$ for GDM versus GIGT and GDM versus normal OGL, GDM versus GIGT and GIGT versus normal OGL).

Regarding the hematological parameters; RBC count, hemoglobin, hematocrit, RDW, and PDW values were similar in the three groups (table-1). The mean platelet counts were higher in normal OGL group than in GIGT group and in GIGT group than in the GDM group but with no statistically significant differences between the three groups. Regarding the mean MPV there was significant difference between the GDM group and 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 a lower platelet count (table-1).

Table-1: Demographic. Hematological and Biochemical Results of The group

	Normal OGL	GIGT	GDM
No.	296(74%)	48(12%)	56(14%)
Age(years)	29.3 \pm 3.9	31.1 \pm 5.2	31.8 \pm 6.2
Gravidity(n)	2.6 \pm 1.2	2.3 \pm 1.4	2.4 \pm 1.5
Gestational age(week)	25.2 \pm 1.3	25.7 \pm 1.2	25.7 \pm 1.4
OGL (mg/dl)	115.9 \pm 23.3	148.7 \pm 19.9	171.8 \pm 28.1
RBC (million)	4.21 \pm 0.61	4.22 \pm 0.42	4.31 \pm 0.38
Hemoglobin(gm/dl)	11.92 \pm 1.3	12.6 \pm 1.10	12.3 \pm 1.6
Hematocrit (%)	35.5 \pm 4.1	35.4 \pm 2.9	35.1 \pm 2.2
RDW (%)	13.91 \pm 3.1	13.7 \pm 1.2	13.5 \pm 1.1
Platelet (n)	251.0 \pm 64.8	240.12 \pm 44	233.8 \pm 54.2
MPV (fl)	8.21 \pm 0.69	8.22 \pm 0.93	8.71 \pm 1.50*
PDW (%)	15.9 \pm 1.3	16.1 \pm 1.4	16.0 \pm 2.1

* $p < 0.05$: between normal OGL and GDM group
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.

Discussion

Gestational diabetes mellitus is a significant problem for the future health of the mother. Women with a history of GDM have 20-50% risk of developing type 2 diabetes mellitus within 5 years following pregnancy^{14,15}. Although the risk of type 2 DM is well established for women with GDM, there have been few studies of this issue in women with lesser degrees of glucose intolerance in pregnancy^{16,20}. Research by Carr et al²¹, on this subject showed that women with a

history of GIGT have an increased risk of developing diabetes. In a recent study by Vambergue et al²², reported GIGT was independently associated with glucose intolerance at 6.75 years postpartum, and cases with GIGT had an 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 are at increased risk of developing CVD in the future⁶. It is uncertain, however, whether normoglycemic women with

history of GDM or GIGT who do not develop type 2 DM later are also at increased risk of future CVD. Women with history of GDM, although normoglycemic after pregnancy, have increased risk of insulin resistance and decreased endothelium-dependent vasodilatation^{23,24}. Such data suggest that GDM may represent the transient unmasking of a latent metabolic 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 history of GDM have impaired endothelium function as assessed by flow-mediated dilatation. Another study on this issue²⁶ showed that women with prior GDM have impaired acetylcholine-induced skin vasodilatation after the postpartum period (2-4years), 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 above²⁷. 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 micro thrombosis on placental bed vessels and placental infarctions. Consequently this generates an impairment in the fetomaternal circulatory system that results in low placental perfusion and finally in fetal loss²⁸. Platelets play an important role in the integrity of normal homeostasis, and MPV is the indicator for their function²⁹. The large platelets contain more dense granules, are more potent than the smaller ones and hence more thrombogenic^{30,31}. An increase in MPV has been documented in patients with metabolic syndrome, stroke, and DM³¹. Increased MPV is now emerging as an independent risk factor for thromboembolism and myocardial infarction^{10,33,34}. Bozkurt et al.³⁵, demonstrated that the MPV of 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 GDM and the normal pregnant

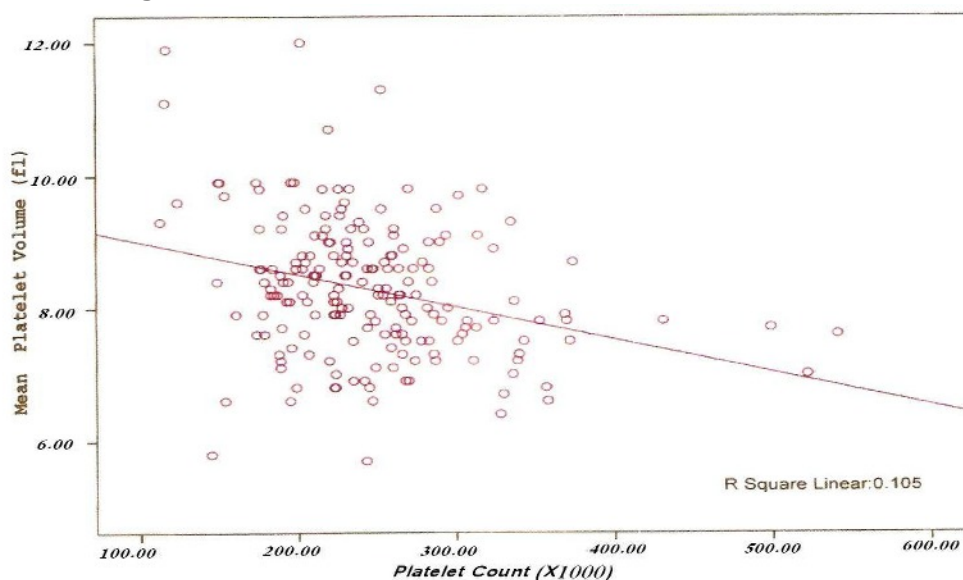
women. Additionally an inverse relationship was observed between platelet number and MPV. Our study showed similar results to Bozkurt et al. and Kosus et al.³⁷, GDM cases had a lower platelet count and a higher MPV. There was no difference between groups in terms of platelet count, but the MPV of our GDM group was significantly higher than the healthy group. An inverse relationship between platelet count and MPV levels was also observed. This knowledge may be important for 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 cyclo-oxygenase synthesis and preventing thrombosis of the placental vasculature.

In one study³⁶, De Pablos showed that patient with GIGT had higher prevalence of certain cardiovascular risk factors than patient with normal glucose tolerance in 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.

Conclusion

glucose intolerance during pregnancy may be an early sign of metabolic disease later in life. Becoming pregnant is good challenge for women to assess their metabolic state. Because pregnancy itself contains excessive metabolic changes, women who tolerate these changes successfully can be accepted as having lower CVD risk for the future if no other risk factors are present. Women with GDM would be expected to be at higher risk of 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 than in normal subjects this means that GIGT may be a risk factor for CVD also. However, further studies with large 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 life style changes or prophylactic pharmacological interventions

Figure-1, Correlation Between Platelet Count and Mean Platelet Volume.



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