

## Original Research Article

## Platelets Indices and Glycated hemoglobin (Hb A1C) in Gestational Diabetes Mellitus

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**Abstract:** The relationship between platelets indices and gestational diabetes mellitus (GDM) has not been studied widely. The association between mean platelet volume (MPV) and HbA1c as glycemic control marker has been investigated in few studies. The study aimed to compare the platelets indices in pregnant women with and without GDM, to evaluate the relationship between MPV and HbA1c. Case-control study was conducted on 100 Sudanese pregnant women aged above 17 years with a singleton pregnancy at 16 weeks of gestation or more. They were enrolled when attended Omdurman Maternity Hospital for antenatal care, were divided into two groups: 50 were newly diagnosed gestational diabetes mellitus (GDM) as cases, 50 were normal pregnancies as controls. Platelets indices were performed as part of complete blood count by automated blood cell counter. HbA1C % also was determined by a fully automated procedure. MPV value was found to be significantly higher in the group with GDM, than that of the control group [ $12.1 \pm 1.1$  vs.  $9.1 \pm 2.5$ ;  $P= 0.04$ ]. However, the difference in the platelets distribution width (PDW) was borderline [ $16.1 \pm 6.3$  vs.  $12.5 \pm 7.5$ ;  $P= 0.07$ ]. HbA1c% was significantly higher in the group of GDM [ $7.2 \pm 2.6$  vs.  $5.4 \pm 1.8$ ;  $P= 0.00001$ ]. However, Hemoglobin level and red blood cells (RBCs) indices had no effects on HbA1c values in GDM; since these parameters didn't vary significantly between cases and control,  $P > 0.05$ ). A weak positive correlation was found between MPV and HbA1c ( $r = 0.14$ ,  $P = 0.019$ ). Socio-demographic, clinical, and obstetric data were compared; a maternal age of  $> 25$  years was significantly associated with GDM (p. value : 0.005). We concluded that MPV value was significantly higher in GDM group than normal pregnancies. Moreover, there was a positive correlation between MPV and HbA1c values. Maternal age of  $> 25$  years could be a risk factor for GDM.

**Keywords:** Gestational diabetes, mean platelet volume, platelets indices, HbA1c, pregnancy

### INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as the first onset of glucose intolerance in pregnancy and is seen in approximately 3–10% of all pregnancies [1]. Early detection and adequate treatment are essential to prevent fetomaternal complications. The prevalence rates for GDM are higher for African, Hispanic, Indian, and Asian women than for Caucasian women [2].

Women with GDM have an increased risk of hypertensive disorders during pregnancy, including gestational hypertension, pre-eclampsia, eclampsia, and polyhydramnios. The poor blood glucose control may increase the risk for spontaneous abortion, infection, macrosomia and dystocia and cause ketoacidosis. Other neonatal morbidities that potentially occur more

frequently in infants of women with GDM include hyperbilirubinemia, hypocalcemia, erythematous, and respiratory distress syndrome [3]. To improve the adverse pregnancy outcomes in pregnant women with DM, to strictly control the blood glucose is necessary. HbA1c as an important parameter detection of blood glucose is appropriate to serve as an adjunctive parameter reflecting the blood glucose in pregnancy. It is necessary to include HbA1c as a useful parameter in the clinical examinations in the second trimester [4].

During normal pregnancy, a progressive insulin resistance (IR) is developed by many placenta-secreted adipokines. In addition, the hormonal increasing contributes to a disruption of the glucose - insulin balance [5, 6]. Since IR is a well-known

atherosclerotic risk factor, women with GDM may have increased risk for cardiovascular disease. In addition to insulin resistance, GDM is also associated with altered platelet function [7] and endothelial dysfunction which is an early indicator of atherosclerosis [8].

Platelets play a key role in the initiation of atherosclerosis and formation of coronary thrombus [9, 10]. Active platelets are large in size and have a higher potential thrombotic ability, evaluation of their volume indices as an indicator of their activity [11, 12]. Mean platelet volume (MPV), Platelet distribution width (PDW), and Platelet large cell ratio (P-LCR) are platelet volume measuring indices; which increase during platelet activation. Platelets indices have been recently used in the prediction, diagnosis, and prognosis of many diseases [11, 13-16], being reported as clinically useful biomarkers [17]. An increase in the MPV value has been demonstrated in conditions closely associated with insulin resistance including metabolic syndrome, obesity, impaired fasting glucose, diabetes mellitus, hypertension, and preeclampsia [18, 19-21]. Several studies have investigated the relationship between MPV and GDM. Bozkurt *et al.*; reported significantly increased MPV values in patients with GDM relative to the control group [22] and Erikçi *et al.*; reinforced the findings of Bozkurt *et al.*; [23]. However, few studies have investigated the association/correlation between MPV and HbA1c in GDM. The aim of this study was to find if there is association between platelets volume indices and HbA1c level in GDM, to compare and correlate between MPV and HbA1c in those patients.

## MATERIAL AND METHODS

The research protocol was approved by Review Board at Hematology Department, Faculty of Medical Laboratory Sciences - Khartoum University. Case-control study was conducted in Omdurman Maternity Hospital- Omdurman during the period of February to May 2017. A written informed consent was taken from all participants.

The study population consisted of 100 pregnant women aged above 17 years with a singleton pregnancy at 16 weeks of gestation or more, were enrolled when they attended antenatal care unit and were divided into two groups: GDM (N/50) as cases, normal pregnancies (N/50) as controls. The socio-demographic, obstetric and clinical data of each woman were recorded in a pre- designed a questionnaire. Women with GDM were diagnosed according to the

standard diagnostic criteria in the Hospital. Normal pregnancies were all healthy women, with no history of preeclampsia, chronic hypertension, thrombosis, and cardiovascular diseases.

*Procedure:* EDTA- K3 venous blood sample (3 ml) was collected from each subject was sent immediately after collection for laboratory investigation. Platelets count and platelets indices were performed as part of complete blood count by automated blood cell counter, Sysmex KX-21. HbA1C % also was determined in whole blood by fully automated GLOVER A1C System. The reference values for platelets indices in Sudanese were considered as Awad-Elkareem *et al.*, [21].

## Data analysis:

The results data was analyzed using Microsoft Office and Statistical software Statistical Package for Social Science (SPSS) program. Simple T-test was used to compare the HbA1c and platelets volume indices in the entire study groups. The quantitative variables were presented as mean  $\pm$  (SD) for each group. Fisher test was used to compare socio-demographic, obstetric, and clinical data between cases and controls.

## RESULTS

In this study, we compared the platelets indices and HbA1c in a group of Sudanese pregnant women (N/100) with and without GDM, their ages range was 17-48 years (mean: 30). All women were enrolled at the gestational age of 16 weeks or more (mean: 31 weeks). The correlation between MPV and HbA1c also was analyzed.

MPV value was found to be significantly higher in the group with GDM, than that of the controls group [ $12.1 \pm 1.1$  vs.  $9.1 \pm 2.5$ ;  $P= 0.04$ ]. However, the difference in the platelets distribution width (PDW) was borderline [ $16.1 \pm 6.3$  vs.  $12.5 \pm 7.5$ ;  $P= 0.07$ ]. HbA1c% was significantly higher in the group of GDM [ $7.2 \pm 2.6$  vs.  $5.4 \pm 1.8$ ;  $P= 0.00001$ ]. However, Hemoglobin level and RBCs indices had no effects on HbA1c values in GDM; since these parameters were not varied significantly between the studied groups, ( $P > 0.05$ ). A weak positive correlation was found between MPV and HbA1c ( $r= 0.14$ ,  $P= 0.019$ ). Socio-demographic, obstetric, and clinical data were compared; a maternal age of  $> 25$  years was found to be a risk factor for GDM (p. value: 0.005).

**Table 1: Mean ± SD of laboratory data in GDM and healthy controls.**

Parameter	GDM (n=50)	Controls (n=50)	T-test P-value
HbA1c%	7.2 ± 2.6	5.4 ± 1.8	0.00001
MPV/fl	12.1 ± 1.1	9.1 ± 2.5	0.04
PDW/fl	16.1 ± 6.3	12.5 ± 7.5	0.07
P-LCR%	27.6 ± 64.4	22.5 ± 85.3	0.1
PCT%	0.27 ± 0.04	0.24 ± 0.03	0.39
Platelets x109/L	264 ± 60	266 ± 56	0.1
Hb g/dl	11.9 ± 1.3	12.1 ± 1.2	0.49
MCV/fl	80 ± 31.8	82 ± 39.8	0.15
MCH/Pg	27.8 ± 6.3	28.6 ± 7.2	0.12

**Table 2: Socio-demographic, obstetric, and clinical data in GDM and healthy controls**

Characteristic	GDM	Normal pregnancy	Fisher test P-value
Maternal Age/year			
> 25	46	34	0.005
< 25	4	16	
Parity No.			
≥3	20	19	1.0
≤2	30	31	
Family History of Diabetes			
Yes	26	22	0.54
No	24	28	
History of Miscarriage			
Yes	19	12	0.19
No	31	38	
Contraceptive hormones			
Yes	10	7	0.59
No	40	43	
Chronic Hypertension			
Yes	1	0	1.0
No	49	50	
Thrombosis			
Yes	1	0	1.0
No	49	50	
Cardiovascular Disease			
Yes	1	0	1.0
No	49	50	

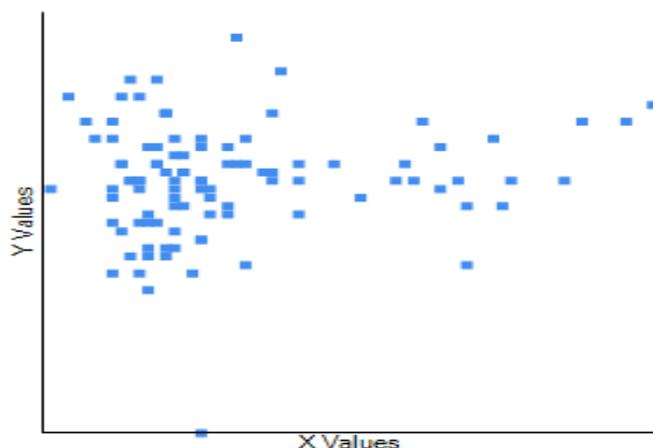


Fig 1: Correlation between HbA1c(X) and MPV (Y).

## DISCUSSION

In the present study, we determine the HbA1c levels platelets indices of MPV, PDW, and P-LCR in a group of Sudanese pregnant women with and without GDM. We examined the association between platelets volume indices; specifically the MPV with HbA1c in the groups of GDM and normal pregnancies.

The present study revealed that MPV values of the GDM patients were significantly higher than those of the normal pregnancies. GDM represents insulin resistance (IR) state that may extend to the postpartum period. Such IR may be linked to some changes in platelet activity in favor of thrombosis [24, 25]. MPV as a marker of platelets activity has been found to be significantly increased in IR states such as diabetes, IFG, obesity and metabolic syndrome [22, 26-28]. Platelet volume or size, which can be measured as MPV, determines platelet function or activity. The higher MPV means larger platelets that contain more granules, thus, they are hemostatically more active than small platelets, and reflect the state of thrombogenesis [29-31]. The study findings suggest that alterations in MPV values were associated with the gestational diabetic state. As an elevated MPV may reflect increased platelet activation and a decrease in the concentration of prostacyclin, resulting in vasoconstriction and a hypercoagulable state. In concordance with our results, it has been reported that MPV values obtained in the second and third trimesters were significantly higher in women with GDM compared to healthy pregnant controls [32]. Previous studies revealed that the MPV was significantly higher in GDM populations [22, 23, 33]. Thus, MPV values can be an effective marker for blood glucose. In a study of 22 diabetic patients reported high MPV values and

significantly reduced MPV values after their blood glucose was reduced [34].

HbA1c is the predominant Hb found in HbA1 fractions [35]; it can maintain in the whole lifespan (120 days) of RBCs. The synthesis rate of HbA1c is positively related to concentration of glucose in RBCs. If there is an increase in the blood glucose level, more HbA1c will be formed. HbA1c as a useful marker in the determination of blood glucose is appropriate to serve as an adjunctive parameter reflecting the blood glucose in pregnancy. O'Shea et al performed a study in 622 patients with GDM diagnosed by OGTT. Their results showed that when the threshold of HbA1c in the second trimester was 5.4%, 46% of pregnant women with GDM could be diagnosed with GDM by HbA1c detection. Thus, they proposed that it is necessary to include HbA1c as a parameter in the clinical examinations in the second trimester [4]. In this study we determined HbA1c as a marker of glucose control in newly diagnosed GDM women and compared it with that of normal pregnancies. HbA1c% was found to be significantly higher in the group of GDM than normal controls ( $7.2 \pm 2.6$  vs.  $5.4 \pm 1$ .) However, adult Hemoglobin (Hb) levels and RBCs indices values had no effects on HbA1c values in GDM; since these parameters were not varied significantly between cases and controls.

Our results also showed that the MPV values were positively correlated with the HbA1c levels in the patients with GDM. We also found a relationship between the MPV and HbA1c values in the controls group. This positive correlation supports the association of increased platelets activation in GDM. Previous studies found that MPV of diabetic patients was

positively correlated with blood glucose and HbA1c levels [23, 36]. Demirtunç *et al.*; noted that MPV increased as the blood glucose level increased and there was a positive correlation between MPV and blood glucose level. In addition, they found that MPV levels increased as HbA1c level increased and positive correlation existed between MPV and HbA1c level [37]. Kurt *et al.*; [38] investigated whether a correlation exists between MPV and HbA1c and FPG changes after treatment. They found that the change in HbA1c level is similar to MPV level change. The effect of insulin therapy on MPV is significant.

Furthermore, we compared the socio-demographic, obstetric, and clinical data between GDM and normal pregnancies; we found that maternal age of > 25 years was significantly associated with GDM (p. value: 0.005). Such finding can indicate that maternal age of > 25 could be one of the risk factors involved in GDM. A study of Terence *et al.*; [39] indicated that the risk of GDM becomes significantly and progressively increased from 25 years onwards. Our study supports their findings and the American Diabetes Association recommendation on the use of age  $\geq 25$  years as the cutoff for screening and the observation that maternal age  $\geq 25$  years is the factor most predictive of GDM [40]. In clinical practice, maternal age of  $\geq 25$  years should be adopted instead of  $\geq 35$  years or 40 years as a risk factor for the development of GDM.

## CONCLUSION

We reached to conclude that MPV as a marker of platelets activity increases in GDM women than normal pregnant women. Moreover, a positive correlation between MPV and HbA1c levels exists. Maternal age of > 25 years could be a risk factor for the development of GDM.

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