

# Thrombocyte Alterations in Pregnant Women with Gestational Diabetes Mellitus

Senol SENTURK<sup>1</sup>, Mehmet KAGITCI<sup>2</sup>, Emine Seda GUVENDAG GUVEN<sup>3</sup>

Rize, Turkey

## ABSTRACT

**OBJECTIVE:** Inflammation and its complications might develop in patients diagnosed with diabetes mellitus. It is shown that number, shape and functions of thrombocytes are important for development and prediction of inflammatory process. We aimed to show the changes of number, morphology and functions of platelets in the patients with gestational diabetes mellitus.

**STUDY DESIGN:** In a retrospective study, 928 cases in 24-28<sup>th</sup> weeks of gestation followed regularly in the same clinic were included. We performed 75g oral glucose tolerance test to all cases. Mean platelet volume, platelet distribution width and plateletcrit values of the cases with and without gestational diabetes mellitus according to American Diabetes Association criteria were compared to evaluate the platelet count, morphology, functions and activity.

**RESULTS:** Platelet count and plateletcrit values of cases were significantly higher in the patients with gestational diabetes mellitus. No significant differences were found between the cases with and without gestational diabetes mellitus in mean platelet volume and platelet distribution width values.

**CONCLUSION:** There is tendency to inflammation in gestational diabetes mellitus and platelets are part of inflammatory process in human metabolism. Our findings show that, platelets are affected in gestational diabetes mellitus. We believe that further studies in this subject will help understanding of pathophysiology of gestational diabetes mellitus.

**Keywords:** Diabetes mellitus, Pregnancy, Gestational diabetes, Platelet activation

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## Introduction

Many factors including obesity, sedentary lifestyle and environmental factors caused an increase in the frequency of type 2 diabetes mellitus (DM.) in recent years. DM. is an important health problem that might cause vascular problems

<sup>1</sup> Department of Gynecology and Obstetrics Recep Tayyip Erdogan University Medical School, Rize

<sup>2</sup> Department of Gynecology and Obstetrics Mersin State Hospital, Mersin

<sup>3</sup> Department of Obstetrics and Gynecology Karadeniz Technical University School of Medicine, Trabzon

Address of Correspondence: Mehmet Kagitci  
Department of Gynecology and  
Obstetrics, Mersin State Hospital,  
33240 Mersin, Turkey  
mehmetkagitci1@hotmail.com

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and organ damage due to increased risk of atherosclerosis as a result of endothelial damage (1).

It is understood that changes in platelet number, function and activity in presence of diabetes mellitus have an important role in development of endothelial damage and increased risk of cardiovascular disease according to recent studies (2). Efficiency of platelet function and activity changes for prediction of prognosis in inflammatory diseases (e.g. Crohn's disease, myocardial infarction, DM.) is investigated in recent years (3,4). It has been shown in some studies that mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW) which have a role to show the activity and functions of platelets have important roles in prediction of D.M. complications.

No consensus is established for glucose amount that should be used in oral glucose tolerance test (OGTT) for screening of pregnant women. 50gr OGTT is used for screening in low risk pregnancies in many clinics, however, in case of obesity, glycosuria, history of gestational diabetes mellitus (GDM) and macrosomic baby and DM. in the family 100gr oral glucose tolerance test is preferred. GDM develops in the second period of the pregnancy which is called the catabolic period in which the energy need is increased for fetal growth. Hormones that are against insulin such as human placental lactogen, cortisol, estrogen, and prolactin are secreted in this

catabolic period. This state is compensated in normal pregnancies, in pregnancies that it is not compensated carbohydrate metabolism is impaired and gestational diabetes mellitus is seen (5). There are many studies showing that atherosclerotic cardiovascular disease risk is increased in presence of GDM and platelet function and activity might play an important role. It is thought that platelets contribute to development of atherosclerotic complications due to their role in inflammation and endothelial damage development (7,8).

Efficiency of MPV, PDW and PCT, that have role in evaluating platelet function and activity, in prediction of complications of atherosclerotic cardiac diseases in prediabetic and diabetic patients is tried to be show in recent years. In many studies, increase of MPV in presence of D.M. is detected and its relation to development of cardiovascular diseases, nephropathy and retinopathy is reported (9,10). Generally, changes in MPV values are parallel to changes in PDW values. The reason for simultaneous increase of MPV and PDW in cases with GDM is thought to be the same (11).

Mean platelet volume, PDW and PCT values are thought to be important in prediction of prognosis and complications of diseases that have inflammation in ethiopathogenesis and the importance is tried to be shown with studies recently.

The purpose of our study is to show the changes of number, morphology and functions of platelets in presence of GDM comparing to patients that are not diagnosed with GDM. We investigated the changes in MPV, PDW and PCT values in cases that we diagnosed with GDM in our study.

## Material and Method

The study was conducted in Recep Tayyip Erdoğan University Research and Training Hospital Obstetrics and Gynecology Clinic between 31.08.2011 and 31.08.2014 with the permission of ethical committee. 928 cases aged 15-47 at 26-28 weeks of gestations had been included in the study. Each case included in the study was informed about the study and included voluntarily.

Venous blood was collected in appropriate circumstances from all cases included in the study following 8-10 hours of fasting for platelet count and 75gr oral glucose tolerance test was performed afterwards. Cases with previously diagnosed iron deficiency anemia, vitamin B12 deficiency, folic acid deficiency, and acute and chronic inflammation were excluded as platelet count, MPV measurement and PCT values will be affected negatively. Cases with Hemoglobin value below 12gr/dL, known or previous idiopathic thrombocytopenic purpura and thrombocytosis and cases with collagen tissue disease were not included in the study. Cases that had blood glucose levels over 126gr/dL following 8-10hours of fasting from venous blood and over 200gr/dL at any hour of the day were not included as these cases are diagnosed with diabetes melli-

tus according to ADA criteria (12). Patients with history of drugs such as antibiotics, hormone replacement and anti-hypertensive drugs (e.g. thiazides) were not included in the study as these drugs might interfere with OGTT evaluation.

Patients were recommended a diet containing 150gr/day carbohydrates and no restriction of physical activity three days prior to the test for true evaluation of OGTT. Venous blood was collected from all cases to evaluate the fasting blood glucose levels after venous blood collection for platelet count and 10 minutes prior to 75gr OGTT. OGTT was performed while patients were in sitting position and 75gr/100mL glucose solution had been administered to all cases. Blood glucose levels were evaluated with Abbott Architect device using standard methods.

Oral glucose tolerance test were evaluated according to ADA (American Diabetes Association) criteria. Fasting glucose level  $\geq 92$ mg/dL, 1<sup>st</sup> hour blood glucose level  $\geq 180$  mg/dL and 2<sup>nd</sup> hour blood glucose level  $\geq 153$  mg/dL had been accepted as pathological and the patients were diagnosed as GDM in case any pathological value is detected (12).

Venous blood collected from all patients was put in tubes containing EDTA for platelet measurement evaluation and measurements were done in 3 hours without hemolysis. Venous blood is centrifuged around 7-10 minutes and modern hematology analyzer electrical impedance technique is used for correct measurement of MPV, PCT and PDW (Abbot, Cell Dyn Ruby). Normal values were accepted as 100.000 mm<sup>3</sup> /L-300.000 mm<sup>3</sup> /L for platelet count, <0.1ng/mL for PCT, 9-14fl for PDW.

## Statistical Evaluation

NCSS (Number Cruncher Statistical System) 2007& PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, frequency, and ratio, minimum, maximum) were used along with student t test for comparison of two groups of variables with normal distribution for evaluation of quantitative data. Significance was evaluated at  $p < 0.01$  and  $p < 0.05$  values.

## Results

The age of the included cases ranged between 15 to 47 years and the median age was 29.10 $\pm$ 5.74 years. Platelet count ranged between 76 000 $\mu$ m/L and 488 000 $\mu$ m/L and the mean platelet count (Plt) was 237,18 $\pm$ 57,82  $\mu$ m/L. Mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW) were evaluated in all cases. MPV ranged from 4.82 to 13.60fl and mean MPV value was 7.55 $\pm$ 1.31fl; PCT ranged from 0.078 to 0.339fl and the mean PCT was 0.17 $\pm$ 0.04fl; PDW ranged from 17.4 to 24.2ng/L and the mean was 20.01 $\pm$ 1.06 ng/ml. Distribution of definition features shown at table 1.

Table 1: Distribution of Definition Features

		Minimum-Maximum	Mean± SS
Age (year)		15-47	29.10±5.74
Thrombocyte (103 per $\mu$ L)		76-488	237.18±57.82
Mean Platelet Volume (fL)		4.82-13.60	7.55±1.31
Plateletcrit (fL)		0.078-0.339	0.17±0.04
Platelet Distribution Width (ng/mL)		17.4-24.2	20.01±1.06
		<b>n</b>	<b>%</b>
Gestational	Non-diabetes mellitus	737	79.4
Gestational	Diabetes mellitus	191	20.6

In the study group, 79.4% (n=737) of the cases had no GDM and 20.6% (n=191) of the cases were diagnosed as GDM. Distribution of GDM shown at figure 1.

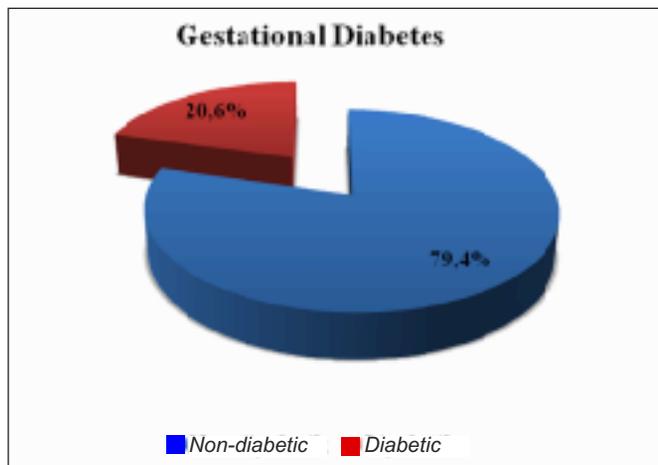


Figure 1: Distribution of gestational diabetes mellitus

The mean age of the cases with GDM had significantly higher than the cases that are not diagnosed with GDM. ( $p=0.001$ ;  $p<0.01$ ). Plt value of cases with gestational diabetes mellitus was significantly higher than the cases without GDM ( $p=0.022$ ;  $p<0.05$ ). Mean MPV and PDW values were not different at a statistically significant level between the cases with GDM and the cases without GDM ( $p>0.05$ ). Mean PCT value of GDM cases were significantly higher than the cases without GDM ( $p=0.001$ ;  $p<0.01$ ). Evaluation of Descriptive Data in Relation to Frequency of GDM shown at table 2.

## Discussion

World Health Organization (WHO) reported that cardiovascular diseases are responsible for 30% of mortality all around the world. Sedentary lifestyle, obesity, increased frequency of DM. is counted among important reasons of increased frequency of cardiovascular diseases (13). Frequency of hypertension and cardiovascular diseases is higher with diabetes mellitus diagnosis compared to the normal population. Hormones are protective for females at reproductive ages; however, cardiovascular disease risk is increased with diseases such as polycystic ovary, GDM developing during these ages (14).

Gestational diabetes mellitus plays an important role in development of especially atherosclerotic cardiovascular diseases by causing DM. type 2 in postpartum period in addition to increased risk of atherosclerosis during pregnancy. It is reported that DM. might develop at a rate of 2.6-70% in postpartum 6 weeks to 28 years' period in GDM cases. GDM is an important health problem as it increases maternal and fetal morbidity and mortality and also the risk of postpartum D.M. development (15,16).

We have aimed to show the influence of platelet function and activity in GDM cases as it is known that insulin resistance and impaired glucose tolerance causes secretion of inflammatory mediators (CRP, visfatin, omentin, IL-6 etc.) and changes in platelet function and activity starts endothelial damage (17).

Table 2: Evaluation of descriptive data in relation to frequency of gestational diabetes mellitus

	Mean ± SS	Mean ± SS	<i>p</i>
	Gestational diabetes mellitus (n=191)	Gestational non-diabetes mellitus (n=737)	
Age (year)	31.75 ± 5.42	28.42 ± 5.62	0.001**
Thrombocyte (103 per $\mu$ L)	245.69 ± 60.42	234.98 ± 56.96	0.022*
Mean Platelet Volume (fl)	7.68 ± 1.33	7.52 ± 1.30	0.132
Plateletcrit (fl)	0.18 ± 0.04	0.17 ± 0.04	0.001**
Platelet Distribution Width (ng/mL)	20.04 ± 1.05	20.00 ± 1.07	0.590

One or two step approach could be use for the diagnosis of the D.M or GDM. In the two step approach, 50 gr glucose is given to the patients and blood glucose is measured after an hour and if it is over 140mg/dL 75 or 100gr OGTT is performed for diagnosis. However, no consensus is established for the diagnosis of GDM and further wider research is recommended. We have diagnosed our cases with GDM following 75gr oral glucose tolerance test.

We have detected that mean maternal age is higher in cases diagnosed with GDM compared to cases that are not diagnosed with GDM in our study. Results obtained from many studies showed that obesity, insulin resistance, and increased maternal age are important risk factors for development of GDM (14). Maternal age could be a risk factor for GDM and therefore contribute to development of atherosclerotic vascular and organ damage according to data obtained from our study.

It was shown that tendency to hypercoagulability and homeostasis disorders during pregnancy could be related to development of atherosclerosis and ischemic cardiovascular diseases (11). High and low levels of platelet count are important causes of coagulation disorders. We have aimed to show the relation between coagulopathy and GDM by evaluation of platelet numbers. Platelet measurements were in between the normal ranges in all cases; however, platelet numbers were insignificantly higher in cases with GDM. We think that higher number of GDM cases included in the study with regard to clinical and demographical characteristics of the patients would cause different results and we would still find platelet count of GDM cases higher.

We have found that MPV value of cases with or without GDM were in between the normal ranges and there was no difference between the groups. MPV is an indicator of platelet functions and also increased number of immature platelets in the bone marrow. Therefore, we concluded that MPV measurements in the normal limits should be parallel to platelet production and count.

Platelet distribution width values were increased in both groups with and without GDM however measurements were not different between the groups in our study. Increased PDW values in our study groups could be related to hypercoagulopathy, inflammation developing during pregnancy and increased atherosclerosis risk. PCT values were increased in both groups, and it was significantly higher in the GDM group compared to the other group. In some studies, it was detected that PCT values were higher in preterm deliveries and repeated abortions and frequency of preeclampsia, GDM and hypertension were increased (18). It was reported that preeclampsia, hypertension and GDM presence are important reasons for atherosclerotic vascular and organ damage and therefore PCT measurements might be helpful for prediction of atherosclerosis. Higher values of PCT for both groups in our study could be explained as the pregnancy itself are a con-

dition that could be related to atherosclerosis, inflammation and coagulopathy. Higher values of PCT in GDM cases could be explained by they are a group with higher risk for atherosclerosis.

In summary, the place of platelets for prediction of diagnosis or prognosis of atherosclerosis and inflammation for the diseases with and ethiopathogenesis of atherosclerosis. Data obtained from many studies had shown that platelet function and activity might be meaningful for diagnosis and prognosis prediction. However, general idea is that the role of MPV, PDW and PCT measurements should be investigated with wider studies including more patients with regard to demographical and clinical characteristics of the patients.

## Conclusion

There is tendency to inflammation in GDM and platelets are part of inflamatuary process in human metabolism. In addition, evaluation of platelet number, function and activity could be helpful for prediction of atherosclerotic vascular and organ damage in cases diagnosed with gestational diabetes mellitus. Our findings show that, platelets are affected in GDM. We believe that further prospective studies with large sample size in this subject will help understanding of pathophysiology of platelet alterations in GDM.

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