Internal Medicine: Open Access

Senturk et al., Intern Med 2017, 7:5
DOI: 10.4172/2165-8048.1000254

Research Article OMICS International

Thrombocyte Functions in Pregnant Women with Gestational Diabetes Mellitus

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Received date: January 06, 2016; **Accepted date:** September 27, 2017; **Published date:** September 30, 2017

Abstract

Objective: We have aimed to show the changes of number, morphology and functions of platelets in presence of gestational diabetes mellitus comparing to patients that are not diagnosed with gestational diabetes mellitus in our study.

Methodology: The 928 cases in 24th to 28th weeks of gestation followed regularly in the same clinic were included in the study. Mean platelet volume, platelet distribution width and plateletcrit values of cases that are diagnosed with gestational diabetes mellitus according to American Diabetes Association criteria and that are not diagnosed with gestational diabetes mellitus were compared to evaluate the platelet count, morphology, functions and activity.

Results: Platelet count and plateletcrit values of cases diagnosed with gestational diabetes mellitus were significantly higher than those that were not diagnosed with gestational diabetes mellitus. No difference between mean platelet volume and platelet distribution width values of cases diagnosed with gestational diabetes mellitus and not diagnosed with gestational diabetes mellitus was found.

Conclusion: 75 gm oral glucose tolerance test to prevent false negative results and evaluation of platelet count, function and activity for cases that are diagnosed with gestational diabetes mellitus could contribute importantly to predict and take necessary precautions for possible atherosclerotic vascular and end-organ damage.

Keywords: Diabetes mellitus; Pregnancy; Gestational diabetes; Platelet activation

Introduction

Many factors including obesity, sedentary lifestyle and environmental factors caused an increase in the frequency of type 2 diabetes mellitus in recent years. Diabetes mellitus is an important health problem that might cause vascular problems 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, diabetes mellitus) 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 has a role to show the activity and functions of platelets have important roles in prediction of diabetes mellitus complications. The purpose of our study is to show the changes of number, morphology and functions of platelets in presence of gestational diabetes mellitus comparing to patients that are not diagnosed with gestational diabetes mellitus in our study.

We have aimed to avoid false negative results by performing 75 gm oral glucose tolerance test in 24th to 28th weeks of gestation to diagnose gestational diabetes mellitus for all cases included in our study (Figures 1 and 2).

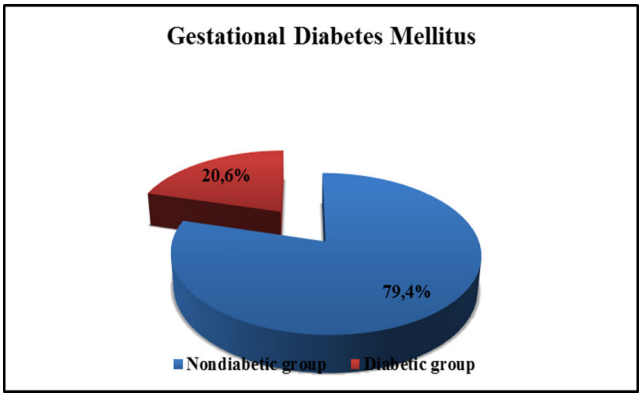

Figure 1: Distribution of gestational diabetes mellitus.

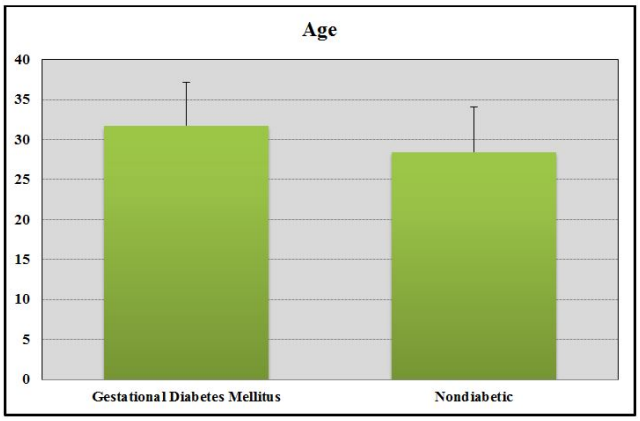

Figure 2: Age distribution of the cases according to presence of gestational diabetes mellitus.

No consensus is established for glucose amount that should be used in oral glucose tolerance test for screening of pregnant women. 50 gm oral glucose tolerance test is used for screening in low risk pregnancies in many clinics, however, in case of obesity, glycosuria, history of gestational diabetes mellitus and macrosomic baby and diabetes mellitus in the family 100 gm oral glucose tolerance test is preferred.

Gestational diabetes mellitus 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 gestational diabetes mellitus and platelet function and activity might play an important role [6]. 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 diabetes mellitus 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 gestational diabetes mellitus is thought to be the same [11].

MPV, PDW and PCT values are thought to be important in prediction of prognosis and complications of diseases that have inflammation in etio-pathogenesis and the importance is tried to be shown with studies recently. We have aimed to show the changes in MPV, PDW and PCT values in cases that we diagnosed with gestational diabetes mellitus in our study.

Materials and Methods

The study was conducted in Recep Tayyip Erdogan 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 2-28 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 hours to 10 hours of fasting for platelet count and 75 gm 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 12 gm/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 126 gm/dL following 8 hours to 10 hours of fasting from venous blood and over 200 gm/dL at any hour of the day were not included as these cases are diagnosed with diabetes mellitus 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 (Figure 3).

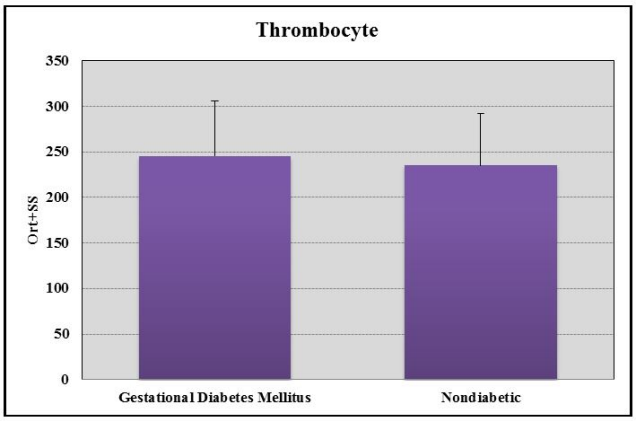

Figure 3: Thrombocyte measurement and distribution according to presence of gestational diabetes mellitus.

Patients were recommended a diet containing 150 gm/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 75 gm OGTT. OGTT was performed while patients were in sitting position and 75 gm/100 ml glucose solution had been administered to all cases. Blood glucose levels were evaluated wit Abbott Architect device using standard methods.

OGTT were evaluated according to ADA (American Diabetes Association) criteria. Fasting glucose level>92 mg/dL, 1st hour blood glucose level>180 mg/dL and 2nd hour blood glucose level>153 mg/dL

had been accepted as pathological and the patients were diagnosed as gestational diabetes mellitus 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 minutes to 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^3/L to 300.000 mm^3/L for platelet count,<0.1 ng/ml for PCT, 9-14 fL for PDW.

Statistical analysis

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 (Tables 1 and 2).

Variables		Minimum-Maximum	Mean ± SS
Age (year)		15-47	29.10 ± 5.74
Thrombocyte (µm/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
-		n	%
Gestational	Non-diabetes Mellitus	737	79.4
	Diabetes Mellitus	191	20.6

Table 1: Distribution of definition features.

Variables	Mean ± SS		P
	Gestational Diabetes Mellitus (n=191)	Gestational Non-Diabetes Mellitus (n=737)	
Age (year)	31.75 ± 5.42	28.42 ± 5.62	0.001**
Thrombocyte (µm/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	0.59

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

Results

The study was conducted in Recep Tayyip Erdogan University Research and Training Hospital Obstetrics and Gynecology Clinic between 31-08-2011 and 31-08-2014 with 928 cases. The age of the included cases ranged between 15 to 47 years and the median age was 29.10 ± 5.74 years. Platelet count ranged between 76.000 µm/L and 488.000 µm/L and the mean platelet count (Plt) was 237.18 ± 57.82 µm/L. Mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW) were evaluated in all cases. MPV ranged from 4.82 to 13.60 fL and mean MPV value was 7.55 ± 1.31 fL; PCT ranged from 0.078 to 0.339 fL and the mean PCT was 0.17 ± 0.04 fL; PDW ranged from 17.4 to 24.2 ng/L and the mean was 20.01 ± 1.06 ng/ml (Figure 4).

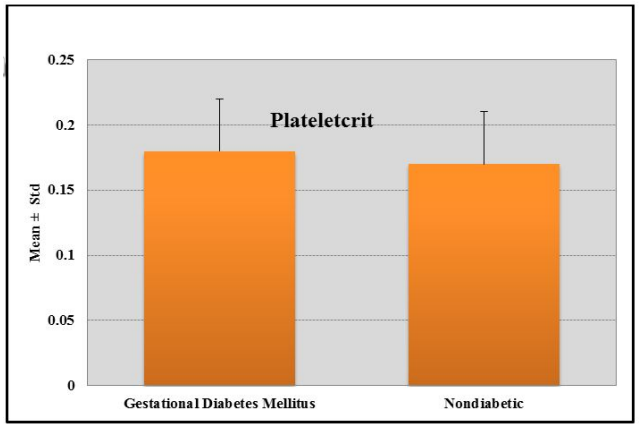

Figure 4: Plateletcrit measurement distribution according to presence of gestational diabetes mellitus.

79.4% (n=737) of the cases had gestational diabetes mellitus.

20.6% (n=191) of the cases were diagnosed with gestational diabetes mellitus.

Cases detected with gestational diabetes mellitus had a mean age significantly higher than the cases that are not diagnosed with gestational diabetes mellitus and all cases ($p=0.001$; $p<0.01$).

Plt value of cases with gestational diabetes mellitus was significantly higher than the cases without gestational diabetes mellitus ($p=0.022$; $p<0.05$).

Mean MPV and PDW values were not different at a statistically significant level between the cases with gestational diabetes mellitus and the cases without gestational diabetes mellitus ($p>0.05$).

Mean PCT value of gestational diabetes mellitus cases were significantly higher than the cases without gestational diabetes mellitus statistically ($p=0.001$; $p<0.01$).

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 diabetes mellitus are 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, gestational diabetes mellitus developing during these ages [14].

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

We have aimed to show the influence of platelet function and activity in gestational diabetes mellitus 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].

We have diagnosed our cases with gestational diabetes mellitus following 75 gm oral glucose tolerance test. General approach recently is to screen high risk pregnancies with 50 gm glucose for the risk of diabetes mellitus development. Blood glucose is measured after an hour and if it is over 140 mg/dL 75 gm or 100 gm OGTT is performed for diagnosis. However, no consensus is established for the diagnosis of gestational diabetes mellitus and further wider research is recommended.

We have detected that mean maternal age is higher in cases diagnosed with gestational diabetes mellitus compared to cases that are not diagnosed with gestational diabetes mellitus in our study. Results obtained from many studies showed that obesity, insulin resistance, and increased maternal age are important risk factors for development of gestational diabetes mellitus (14). Maternal age could be a risk factor for gestational diabetes mellitus 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 hemostasis 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 gestational diabetes mellitus 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 gestational diabetes mellitus. We think that higher number of gestational diabetes mellitus 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 gestational diabetes mellitus cases higher.

We have found that MPV value of cases with or without gestational diabetes mellitus were in between the normal ranges and there were 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.

PDW values were increased in both groups with and without gestational diabetes mellitus however measurements were not different between the groups in our study. Increased PDW values in our study groups could be related to hyper coagulopathy, inflammation developing during pregnancy and increased atherosclerosis risk. PCT values were increased in both groups, and it was significantly higher in the gestational diabetes mellitus 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, gestational diabetes mellitus and hypertension were increased (18). It was reported that preeclampsia, hypertension and gestational diabetes mellitus presence are important reasons for atherosclerotic vascular and organ damage and therefore PCT measurements might be helpful for prediction of atherosclerosis. A higher value of PCT for both groups in our study could be explained as the pregnancy itself is a condition that could be related to atherosclerosis, inflammation and coagulopathy. Higher values of PCT in gestational diabetes mellitus 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 etiopathogenesis 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

Screening with 75 gm oral glucose tolerance test instead of 50 gm could prevent false negative results for diagnosis of gestational diabetes mellitus. It might contribute to prevention of maternal and fetal complications. 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. We think that prevention of false negative results for diagnosis of gestational diabetes mellitus and prediction of possible complications will contribute to decreased fetal-maternal and postpartum morbidity and mortality.

Acknowledgement

We thank you for allowing collection of data Recep Tayyip Erdogan University Research and Training Hospital Ethical Committee.

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