Role of Mean Platelet Volume to Predict Gestational Diabetes in the First Trimester

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Abstract

Background and Objective. *Gestational Diabetes Mellitus (GDM) is defined as glucose intolerance detected for the first time in pregnancy or identified during pregnancy. Mean platelet volume (MPV) is a marker of activation and function of platelet. Several studies investigated the relation between MPV and GDM. Purpose of the present study is to predict GDM in the first trimester by using MPV value.* ***Methods***. *A retrospective case control of 200 pregnant women with GDM and 200 normal pregnant women were enrolled in the study. The first trimester MPV values of GDM and control groups were compared to predict GDM in the first trimester. The study conducted in a university hospital from March 2020 to February 2021.Computed receiver operating characteristic used SPSS statistic program version 21 while adjusting for confounding by Libyan nationality and no chronic illness.* ***Results***. *Women with GDM had higher MPV value compared with the control group (p<.001). The area under the receiver-operator curve was 0.70 for MPV. The cut off value of MPVwas7.38 fl with 70% sensitivity and 60% specificity; According to the ages, MPV value was higher in GDM group in the individuals who were above 28-year-old (p <.001).* ***Conclusion***. *MPV can be used to predict GDM in the first trimester.*

Keywords: Gestational Diabetes Mellitus, Pregnancy, Mean Platelet Volume, Trimester.

Introduction

Diabetes mellitus was previously considered as a disease of minor significance to human health but lately considered one of the main threats to human health. The global epidemic of people with type 2 DM is largely due to many parameters such as population growth, aging, urbanization, and the scourge of obesity and physical inactivity. General, the total number of people worldwide with type 2 diabetes was expected to increase from 171 million in 2000 to 366 million in 2030 [1]. According to the international Diabetes Federation (IDF) the prevalence worldwide reached to 366 million in 2011and estimated on the global level could well extended to 530 million people in 2030 [2].

Diabetes mellitus is one of the most common medical complications of pregnancy and it generates a significant risk to the fetus and the mother. Congenital malformations and perinatal morbidity remain commonly happen when compared with the offspring of non diabetic pregnancies. Diabetic mothers are always at risk of progression of microvascular diabetic complications as well as early pregnancy loss, pre-eclampsia, polyhydramnios and premature labour.

Prediction of GDM in early pregnancy has become the purpose of a great deal of research [3]. Therefore, several methods have been reported in the literature to evaluate insulin resistance (IR) in first trimester of pregnancy [4]. We speculated that mean platelet volume (MPV) which is a marker of activation and function of the platelet may be one of these methods because GDM is a mixed pathophysiological situation. The basic problem is dysfunction of pancreatic beta cells which cause IR especially after the first trimester of pregnancy [5]. Recent studies showed that chronic low-grade inflammation has a central role on IR syndrome associated with GDM and chronic low-grade inflammation induces vascular damage and dysfunction and as a result of these, it stimulates a platelet activation and

aggregation. As a result, elevated MPV is associated with increased thromboxane A2 and beta thrombomodulin release and increased expression of receptors of adhesion molecules such as glycoprotein IIb/IIIa and glycoprotein Ib [6].

In several studies, it is showed that an increase in the MPV value is related to IR in metabolic syndrome, obesity, impaired fasting glucose, diabetes mellitus (DM), and hypertension [7] and some of the previous studies investigated the relation between MPV and GDM; however, to the best of our knowledge, there is no study on whether the first trimester MPV measurement predicts GDM in the literature. The aim of this study to predict GDM in the first trimester by using MPV value, as well as to determine whether there is a threshold below which there is no association between MPV and the GDM.

Methods
Study design
Retrospective case control study conducted at the Department of Obstetrics and Gynecology in University Hospital, Tripoli, Libya, during the period between March 2020 and February 2021. Study included 200 GDM patients and 200 women who had healthy pregnancies were assigned as controls. The participants with the following characteristics are included in the study; single pregnancy with first prenatal visit in outpatient department of obstetrics and gynecology at University Hospital before 13 gestational weeks. The participants with Preeclampsia, eclampsia, pregnancy-related hyper- tension, hypertension history, or blood pressure above 140/90mmHg. Also GDM history or DM before pregnancy or first-visit fasting blood glucose above 92mg/dl. Myeloproliferative disorders, malignancy, auto-immune disease, chronic inflammatory disease, heart failure, acute/chronic infection, polycystic ovary syndrome, hepatic, or renal disorders were excluded from the study.

Maternal blood samples are taken from all pregnant women who are followed in our hospital at the time of first trimester of the gestation for assessing complete blood count. Two milliliters of blood samples taken from all the pregnant women's ante-cubital veins were put into the ethylene diamine tetra acetic tubes with EDTA. The samples were rapidly processed or the purpose of preventing platelets well in the test tubes.

MPV levels were measured using AbbottCell-Dyn3700 auto- mated CBC analyzer. In our laboratory, the normal range for MPV is taken as7–12 femtoliters (fl). Women who had a 1-h140-mg/dl glucose level or more were advised to take 100 g OGTT. Women with two or more abnormal values in test results were considered as GDM. Patients with one or more abnormal glucose level with 75 g OGTT are considered as GDM. We compared the first-trimester MPV values between GDM and control groups to understand if it was possible to predict GDM in the first trimester using MPV values.

Statistical analysis
Statistical analyses were performed with the SPSS (22.0) for Windows (SPSS, Chicago, IL). The data that were distributed normally were tested by using the Shapiro–Wilk test. The Mann–Whitney U-test was employed for the purpose of comparing the MPV value between GDM and control groups. The mean±SD was used for parameters that were distributed normally. Receiver-operating characteristic (ROC) curve analysis was employed for determining the MPV cutoff value in order to predict GDM in the first trimester. Variables between two groups like age, MPV, and weight were analyzed with logistic regression method by using the Enter Method. $p < .05$ was taken to be significant at a statistical level.

Results
A total of 400 cases met the criteria for the study. The control group had 200 patients with a mean age of 29.00 ± 7.5, whereas the study group included 200 patients with an average age of 34.00 ± 6.0 ($p < .001$). No significant differences were detected between the groups in the gestational weeks of screening glucose tolerance test, as well as there was no statistically significant difference between groups in hemoglobin level and platelet count. While there was statistical difference in maternal weight at screening time $p < .001$. Table 1

Table 1. Distribution of patient according to age and demographic parameters

Variables	Patients	Control	p value
Age	34.00 ± 6.0 years	29.00 ± 7.5 years	p<.001
The gestational weeks of screening glucose tolerance test(weeks)	26.66±2.16	26.52±2.48	N
Maternal weight at screening time(kg)	75.23±14.10	73.80±12.00	p<.001
Hemoglobin(g/dl)	11.62±1.30	11.52±1.45	NS
Platelet count	203.05±59.35	212.20±60.30	NS

Significant differences were detected between the groups in MPV levels (p <.001). Mean MPV level in GDM group was8.00±1.70fl, whereas in the control group, the mean MPV level was 7.00±1.47 fl(p<.001). MPV levels were also evaluated according to patients' ages Figure 1.
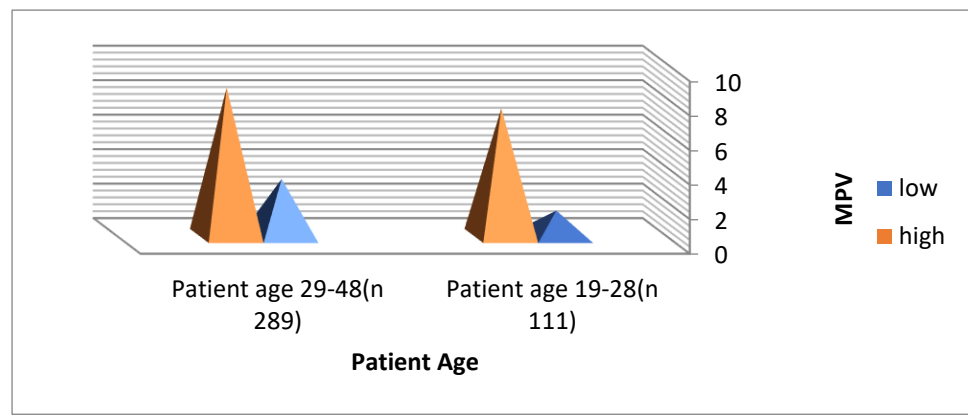

Figure 1. MPV levels according to patients' ages

Age and maternal weights of the study group and the control group were significantly different (p <.001). With logistic regression analyze, we found that maternal weight does not predict the GDM presence (p ¼ .561) but age and MPV so do with 1210/ 1811odds ratio, respectively (p<.001) (Table 2).

Table 2. Variables analyzed in multiple logistic regression model

Variables	B±SE	SE	P Value	Odds ratio	Lower	Upper
Age	0.191±0.03	0.026	<.001	1.210	1.149	1.274
MPV	0.589±0.11	0.108	<.001	1.811	1.463	2.241
Weight	0.005±0,1	0.009	.561	1.005	0.988	1.023
Constant	-10.951±1.4	1.410	<.001			

ROC analysis was employed to determine diagnostic MPV for the prediction of GDM in the first trimester (Figure 2)
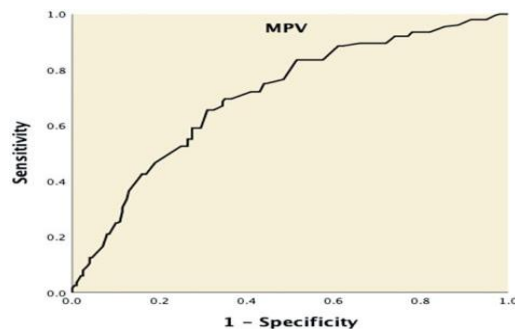
Figure 2: ROC curve of MPV

MPV cutoff value was 7.38 fl with 69.5% sensitivityand65%specificityforthestudy.AUCvalue was 0.704 (p ¼.001) When we analyze the MPV values according to the age groups: MPV value cutoff is 7.38 fl with 71.5% sensitivity and 63.2% specificity (AUC value ¼0.710) (p<.001)in the28-year-old or above group (Figure3); however, in the younger group ,MPV value cut off 7.15flwith71.4%sensitivityand59%specificity(AUC ¼ 0.657) (p ¼ .013) (Figure 4).

According to these variables, when the predictive rates of the model was analyzed, GDM was computed as 74%, control was computed as 76% and general accuracy rate was computed as75%.
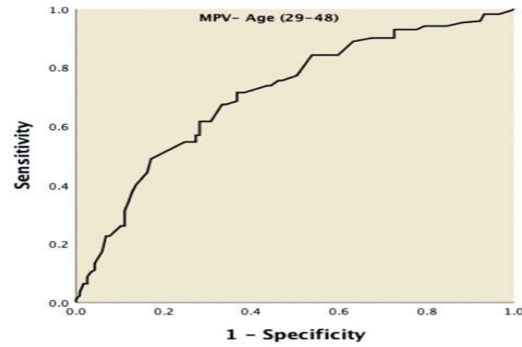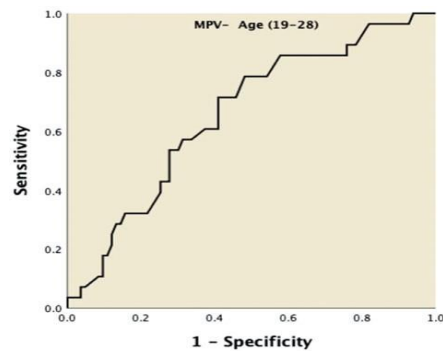

Figure 3. ROC curve of MPV-age (29–48)**.**

Figure 4. ROC curve of MPV-age (19–28).

Discussion

In this study, we evaluated the Power of first trimester MPV value to predict GDM. As the first study on this subject, it is valuable, because, as a result of our data, we speculated that MPV may be used for prediction of GDM in the first trimester. Investigating MPV levels in GDM is derived from studies showing increased platelet activity in DM. High MPV levels were reported in DM patients, and MPV was reported to be independently related to diabetes [8]. A relation between MPV and severity of DM were also found. There are also several studies about Mean Platelet Volume (MPV) to predict GDM. Bozkurt et al. claimed high MPV levels in patients with GDM compared with women who had healthy pregnancies [9]. A similar study was conducted by Erikc et al., and they showed lower platelet count but higher MPV in GDM group in their study [10]. The number of patients in the studies was less and the MPV value was examined in the third trimester of pregnancy. Our aim was to investigate whether there was a significant difference in the MPV values seen in first trimester. Saigo et al., conducted a study on 22diabetic cases whom MPV values were decreased when their blood glucose levels were reduced [11].

In current study, elevated MPV levels were found in the first trimester in which the patients are going to develop GDM. It means real prediction GDM before the negative metabolic effects occur. The strength of this study was to predict GDM in the first trimester, which is a very early time of pregnancy. Furthermore, the patient count was higher in our study than most of the previous studies. In our study, MPV cutoff levels were higher in the older GDM patients. This is a result that goes parallel with the increase in the tendency to diabetes and cardiovascular diseases that increase with further age. Because of these complications, MPV seems to be an important prediction marker in GDM.

Conclusion and Recommendations:: MPV can be used to predict GDM in the first trimester. very large cohorts are required to assess such specific associations, as each of these adverse

outcomes are highly recommended. The next step of our study may be comparing perinatal outcomes of patients with a control group with a close follow-up according to the MPV cutoff values in the first trimester, which we defined in this present study.

References

1. World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Part 1: Diagnosis and Classification of Diabetes Mellitus. WHO/NCD/NCS/99.2 ed. Geneva, World Health Organization, 1999.
2. Jaeggi ET, Fouron JC, Proulx F. Fetal cardiac performance in uncomplicated and well-controlled maternal type I diabetes. Ultrasound Obstet Gynecol 2001; 17: 311–315.
3. Navneet M, Chauhan M. Pregnancy in Type 1 Diabetes Mellitus: How Special are Special Issues? N Am J Med Sci 2012; 4: 250–256.
4. Barker DJ, Winter PD, Osmond C, Margetts B, Simmonds SJ. Weight in infancy and death from ischaemic heart disease. Lancet 2019; 2: 577–580.
5. Barker DJ, Hales CN, Fall CH, Osmond C, Phipps K, Clark PM. Type 2 (noninsulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (syndrome X): relation to reduced fetal growth. Diabetologia. 2020; 36:62–67.
6. Roseboom TJ, van der Meulen JH, Ravelli AC, Osmond C, Barker DJ, Bleker OP.Effects of prenatal exposure to the Dutch famine on adult disease in later life: an overview. Twin Res. 2001; 4:293-2938.
7. Sherer DM, Divon MY. Prenatal ultrasonographic assessment of the ductus arteriosus: a review. Obstet Gynecol. 1996;87:630–637.
8. Madsen H, Ditzel J. Blood-oxygen transport in first trimester of diabetic pregnancy. Acta Obstet Gynecol Scand. 2014;63:317–320.
9. Bozkurt J, Mazurek M. Transcription factors having impact on vascular endothelial growth factor (VEGF) gene expression in angiogenesis. Med Sci Monit. 2004;10:RA89–RA98.
10. Erikc¸i SM, DeVol JM, Wedgwood S. Regulation of fibroblast growth factor-2 expression in pulmonary arterial smooth muscle cells involves increased reactive oxygen species generation. Am J Physiol Cell Physiol. 2008;294:C345–C354.
11. Saigoet E, Radaelli T, Rossi G, Nobile de Santis MS, Bulfamante GP, Avagliano L, Cetin I. Effects of gestational diabetes on fetal oxygen and glucose levels in vivo. BJOG. 2009;116:1729–1735.