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Can mean platelet volume values predict maternal and fetal outcomes in the third trimester of pregnancy in gestational diabetic patients? A retrospective cohort study

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Abstract

This study aims to determine if mean platelet volume (MPV) can predict maternal and fetal outcomes in pregnant women during their third trimester. A retrospective case-control study was conducted at Medipol Hospital's Obstetrics and Gynecology Clinic, involving 200 women with gestational diabetes mellitus (GDM) and 200 healthy pregnant women. Data collected included age, gestational age, body mass index (BMI), and complete blood count parameters such as hemoglobin, hematocrit, thrombocyte count, and MPV values. The results indicated that the GDM group had significantly higher age, BMI, cesarean rates, and MPV values compared to the healthy group. Maternal complications like preeclampsia, preterm labor, shoulder dystocia, and fetal growth restriction were more frequent in the GDM group. Neonatal complications, including hyperbilirubinemia, hypoglycemia, transient tachypnea of the newborn (TTN), and increased admissions to the neonatal intensive care unit, were also significantly higher. A notable finding was the significant association between elevated maternal MPV values and the occurrence of TTN in newborns (p=0.043). Mothers of infants with TTN had higher third-trimester MPV values. Receiver operating characteristic (ROC) curve analysis established a cut-off MPV value of >11.35 ft for predicting TTN. The study concludes that elevated MPV in women with GDM is strongly associated with an increased risk of TTN in their newborns. MPV, being a simple and cost-effective parameter obtained from routine blood counts, could serve as a predictive marker for TTN. However, due to limitations such as the retrospective design and single-center data, further multi-center cohort studies are recommended to validate these findings and establish MPV as a reliable predictor for adverse neonatal outcomes in GDM pregnancies.

Keywords: Preterm labor, mean platelet volume, platelet count, preeclampsia, diabetes mellitus, gestational

Introduction

Gestational diabetes mellitus (GDM) is a disorder that affects numerous systems in the body and manifests throughout pregnancy as varying degrees of glucose intolerance [1]. It affects 4–25% of pregnant women [2]. The increase in oxidative stress associated with GDM causes a variety of problems [3]. Fetal and neonatal difficulties include newborns being larger than expected for their gestational age (LGA), respiratory difficulty, delivery trauma, low blood sugar after birth (postpartum hypoglycemia), and stillbirth. Furthermore, children born to women with GDM may develop long-term health issues such as metabolic syndrome, obesity, diabetes mellitus (DM), and hypertension [4]. Since most GDM diagnoses are established and treated after 24-28 weeks of GDM screening, it affects the 3rd trimester blood parameters [5]. Platelet morphology and function are affected by hypertriglyceridemia, oxidative stress, absolute or relative insulin insufficiency, hyperglycemia, and inflammation associated with GDM [6]. Mean platelet volume (MPV) is a basic, quick, and easy-to-measure metric used to evaluate platelet function and shape [7]. High MPV values cause vasoconstriction by causing vascular occlusion and a decrease in prostacyclin concentration [8]. There are not many studies in the literature showing the relationship between GDM and MPV [9]. We asked the question of whether 3rd Trimester MPV in GDM patients can be predictive in terms of maternal and fetal outcomes.

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This study has two primary objectives: firstly, to examine MPV in women with GDM during their third trimester with that of healthy pregnant women, and secondly, to assess whether MPV can be used to predict maternal and fetal outcomes.

Material and Methods

The Universe and Sample of the Research

This retrospective case-control study was carried out by evaluating the data of pregnant women who gave birth between January 1, 2019 and March 23, 2021 at Medipol Hospital's Obstetrics and Gynecology Clinic. The pregnant women's data were checked retrospectively for one month in April 2021. The pregnant women participated in the study were grouped as gestational diabetic and healthy.

Patient files of 298 individuals with GDM and 267 individuals with uncomplicated pregnancies were collected retrospectively. Both in the GDM group and the control group, individuals with pre-existing conditions such as chronic inflammatory diseases, autoimmune disorders, pre-pregnancy diabetes mellitus, renal or hepatic disorders, malignancies, and other comorbidities were excluded to ensure a more homogeneous sample and minimize confounding factors. Ninety-eight patients in the GDM group and 67 patients in the uncomplicated group were excluded due to lack of outcome data, non-compliance with follow-up and pre-existing conditions mentioned above. A total of 200 women from both groups were included in the study. Participants with a history of acute or chronic infection, multiple pregnancies, heart failure, hypertension, pre-pregnancy diabetes mellitus, chronic inflammatory disease or autoimmune disease, renal or hepatic disorders, or other known malignancies and myeloproliferative disorders were excluded from the study.

The Medipol University Clinical Research Ethics Committee approved the study on March 4, 2021, and assigned it the number 293.

Data Collection Tools

Our study's variables included age, gestational age, complete blood count (CBC) parameters such as hemoglobin, hematocrit, thrombocyte, and MPV values, as well as body mass index (BMI).

To calculate the gestational age, the first day of the last menstrual period or first trimester obstetric ultrasonography was used. Routine blood counts from venous blood of pregnant women in the last trimester (between 28-40 weeks) were noted.

We retrieved obstetric complications and pregnancy outcomes of patients from their files retrospectively. Complications including fetal growth restriction (FGR), preterm labor, shoulder dystocia, and preeclampsia were recorded in the database. Preeclampsia was defined as blood pressure readings exceeding 130/80 mmHg on two separate occasions after the 20th week of pregnancy, regardless of whether protein was present in the urine [10]. FGR was determined as birth weight less than 10% or more of estimated fetal weight suitable to gestational age [11]. Labor earlier than the 37th week of pregnancy was considered as preterm labor [12]. Vaginal cephalic delivery that needed additional maneuvers to deliver the fetus after the head was born was defined as shoulder dystocia [13].

Hypoglycemia, hyperbilirubinemia, transient tachypnea of newborn (TTN), and newborn unit admission were described as fetal complications. Those who received intravenous glucose therapy were evaluated as having a diagnosis of hypoglycemia [14]. Hyperbilirubinemia was defined as requiring phototherapy after birth or having at least one laboratory report of a bilirubin level greater than 20 mg/dL [15]. TTN was described as a respiratory rate >60/min that started within the first six hours after birth and was evaluated according to the diagnosis made by the pediatricians [16].

Data Analysis

Statistical analyses were carried out using IBM SPSS version 25.0. Continuous variables are expressed as mean±standard deviation (SD), while categorical variables are represented as counts (N) and percentages (%) in the tables. The independent t-test was used to compare continuous variables between groups, and the chi-square test was utilized for comparing categorical variables. A Receiver operating characteristic (ROC) analysis was performed to determine the diagnostic performance of MPV for tachypnea, with the area under the curve (AUC), sensitivity, and specificity values included in the table. Statistical significance was set at a p-value of less than 0.05.

Results

The study was conducted with files of 200 women with GDM and 200 healthy pregnant women. The comparison of sociodemographic characteristics, pregnancy and birth information, and laboratory analysis of both groups are given in Table 1.

Comparison of maternal and fetal complications of groups were shown in Table 2. As a result, all assessed complications were shown to be higher in the group diagnosed with GDM.

Table 3 shows a comparison of maternal and fetal MPV results in pregnant women with GDM. A statistically significant difference was noticed between transient tachypnea in newborns and MPV values (p=0.043). Mothers of TTN newborns had higher last trimester MPV values.

ROC curve has been drawn to calculate a certain cut-off value of MPV in terms of TTN estimation and the area under the ROC curve (AUC) was 0.614 (p=0.015; 95% [CI], 0.528-0.700). For the cut-off value of MPV>11.35(ft), the sensitivity was 68.6% and specificity was 49.3% (Figure 1).

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Table 1. Comparison of the sociodemographic characteristics, pregnancy, birth, newborn information and laboratory analyzes of both groups

	Groups		p value
	Control (n=200)	GDM (n=200)	
	Mean±SD	Mean±SD	
Age (years)*	29.52±5.32	32.71±5.34	**<0.001**
Gastational age (weeks)*	33.50±1.12	33.52±1.11	0.946
BMI (kg/m²)*	28.09±0.98	30.37±1.41	**<0.001**
Birth weight (gr)*	3342.19±452.89	3364.72±524.92	0.647
Form of delivery*			
Vaginal	114 (57.0)	46 (23.0)	**<0.001**
Caesarean	86 (43.0)	154 (77.0)	
Hb (g/dl)*	11.84±1.40	11.74±1.36	0.490
Htc (%)*	34.20±3.48	34.44±3.57	0.500
Plt (mm³)*	202.97±58.65	204.78±55.29	0.751
MPV(ft)*	10.77±0.82	11.47±1.22	**<0.001**

GDM: gestational diabetes mellitus, BMI: body mass index, Hb: hemoglobin, Htc: hematocrit, Plt: platelet, MPV: mean platelet volume; * Independent t test

Table 2. Comparison of maternal and fetal complications of groups

	Groups		p value
	Control n (%)	GDM n (%)	
	Maternal complications		
Preterm labour*			
No	197 (98.5)	197 (98.5)	1.000
Yes	3 (1.5)	3 (1.5)	
Preeclampsia*			
No	197 (98.5)	144 (72.0)	**<0.001**
Yes	3 (1.5)	56 (28.0)	
Shoulder dystocia*			
No	198 (99.0)	178 (89.0)	**<0.001**
Yes	2 (1.0)	22 (11.0)	
FGR*			
No	199 (99.5)	192 (96.0)	**0.018**
Yes	1 (0.5)	8 (4.0)	
	Fetal complications		
Hyperbilirubinemia*			
No	187 (93.5)	116 (58.0)	**<0.001**
Yes	13 (6.5)	84 (42.0)	
TTN*			
No	190 (95.0)	148 (74.0)	**<0.001**
Yes	10 (5.0)	52 (26.0)	
NICU*			
No	192 (96.0)	159 (79.5)	**<0.001**
Yes	8 (4.0)	41 (20.5)	
Hypoglycemia*			
No	190 (95.0)	134 (67.0)	**<0.001**
Yes	10 (5.0)	66 (33.0)	

FGR: fetal growth restriction, NICU: neonatal intensive care unit, TTN: transient tachypnea of newborn; *Chi square test

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Table 3. Comparison of maternal and fetal outcomes and MPV in pregnant women with GDM

	MPV Mean±SD	p value
Preterm labour*		
No (n=168)	11.46±1.28	0.809
Yes (n=32)	11.52±0.86	
Preeclampsia*		
No (n=144)	11.50±1.33	0.660
Yes (n=56)	11.41±0.91	
Shoulder dystocia*		
No (n=178)	11.47±1.27	0.912
Yes (n=22)	11.50±0.80	
FGR*		
No (n=192)	11.46±1.24	0.604
Yes (n=8)	11.71±0.84	
Hyperbilirubinemia*		
No (n=116)	11.41±1.41	0.426
Yes (n=84)	11.55±0.89	
TTN*		
No (n=148)	11.37±1.31	**0.043**
Yes (n=52)	11.77±0.87	
NICU*		
No (n=159)	11.44±1.30	0.489
Yes (n=41)	11.59±0.85	
Hypogycemia*		
No (n=134)	11.46±1.36	0.834
Yes (n=66)	11.50±0.88	

FGR: fetal growth restriction, NICU: neonatal intensive care unit, TTN: transient tachypnea of newborn; *Independent t test

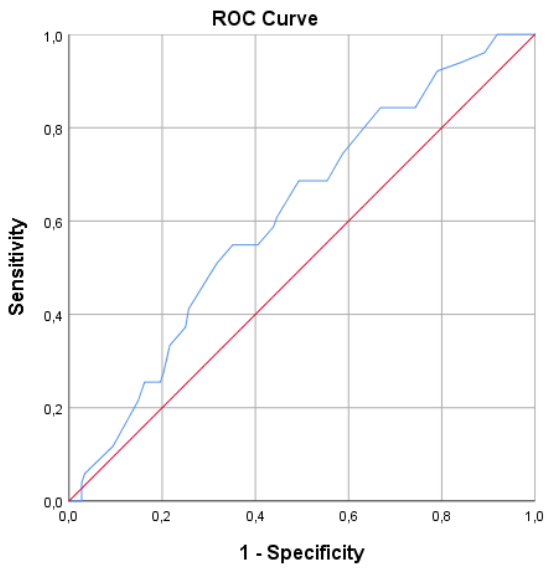

Figure 1. The ROC curve analysis for MPV to predict tachypnea. In the ROC analysis designed to define the sensitivity and specificity of predict tachypnea value, AUC was found to be 0.614 (95% CI: 0.528–0.700 and p=0.015). For the cut-off value of >11.35(ft) , the sensitivity of MPV was 68.6%, and its specificity was 49.3%

Discussion

GDM is characterized as an abnormal tolerance to glucose that appears for the first time during pregnancy and may result in poor obstetric outcomes for both the mother and the fetus [17]. This study revealed that pregnant women with GDM have higher MPV values compared to healthy pregnant women during the third trimester. A significant association was identified between elevated MPV levels and transient tachypnea of the newborn (TTN), with a cut-off MPV value of >11.35 ft providing a sensitivity of 68.6% and a specificity of 49.3% for predicting TTN. Additionally, maternal and neonatal complications, including preeclampsia, preterm birth, shoulder dystocia, fetal growth restriction, hypoglycemia, hyperbilirubinemia, and neonatal intensive care unit admissions, were observed more frequently in the GDM group. These findings highlight the potential role of MPV as a predictive marker for adverse neonatal outcomes, particularly TTN, in pregnancies complicated by GDM.

According to Çolak et al. [18], MPV can be a reliable indication of GDM during early pregnancy. A meta-analysis stated that in the third trimester with GDM patients, MPV increased significantly, whereas no difference was observed in first and

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second [19]. It corresponds with the peak insulin resistance in the third trimester. Consistent with this conclusion, our study demonstrated that the mean 3rd trimester MPV was significantly higher in the GDM group. MPV, a simple and affordable metric obtained from regular blood counts, can be used as an indication of platelet shape and activity [20]. Elevated MPV is associated with platelet activation markers such as increased platelet aggregation, expression of adhesion molecules, thromboxane synthesis, and thromboglobulin release [21].

The exact mechanism responsible for higher MPV in diabetic patients is not yet fully understood. Hyperglycemia enhances platelet activation and aggregation, contributing to a prothrombotic state in diabetes. This phenomenon is linked to increased glucose metabolism within platelets, which amplifies their activation and promotes thrombosis. Furthermore, hyperglycemia-induced endothelial changes, such as elevated prostaglandin E2 synthesis, further stimulate platelet activation. Additionally, hyperglycemia induces platelet hypersensitivity and alters coagulation components, leading to the formation of fibrinolysis-resistant clots [22-24].

GDM increases morbidity and mortality in pregnant women, including congenital malformations in the baby, metabolic problems in the newborn, stillborn births, and the development of diabetic ketoacidosis, retinopathy, neuropathy, and nephropathy in the mother [25]. GDM may cause birth traumas, an increased cesarean rate, preeclampsia, and future development of type 2 DM [26]. In the GDM group of our study, in accordance with the literature, preeclampsia, preterm birth, shoulder dystocia, fetal growth restriction, neonatal hyperbilirubinemia, hypoglycemia, TTN, and admission rates to the neonatal intensive care unit were significantly higher.

In our study, we investigated the relationship between the MPV value measured in the third trimester and the maternal and neonatal outcomes of GDM patients. A statistically significant relationship was found only between TTN occurrence and increased MPV values in pregnant women with GDM, even though MPV averages were found to be high in all adverse maternal and neonatal outcomes. In many studies conducted on acquired diseases, it has been reported that MPV, measured by electronic cell counters, increased significantly compared to healthy subjects, and also high MPV value could predict poor prognosis [27,28].

In our study, a certain cut-off value of MPV in terms of TTN estimation was found as 11.35, with a sensitivity of 68.6% and a specificity of 49.3%. It has been suggested in the literature that MPV may be a diagnostic marker in late-onset neonatal pneumonia and TTN [29,30]. According to our study, the babies of mothers with MPV above the cut-off value may be evaluated as high risk in terms of TTN, and this is valuable in terms of taking prenatal measures such as booking an intensive care unit and allowing rapid intervention.

Limitations

Our study has several limitations that should be addressed to provide a more comprehensive understanding of the findings and their generalizability. Firstly, the retrospective design inherently carries biases, such as incomplete or missing data, reliance on recorded information, and potential misclassification of outcomes. These factors may limit the accuracy and reliability of our conclusions.

Secondly, the study was conducted at a single center, which may not fully represent diverse populations or healthcare practices. Differences in patient demographics, clinical management, and institutional protocols may affect the generalizability of the results to other settings or populations.

Thirdly, although we analyzed a considerable sample size, it may still be insufficient to detect subtle but clinically relevant differences, especially for less common maternal and neonatal outcomes. Larger, multicenter studies could provide more robust and generalizable data.

Additionally, while we established a cut-off MPV value for predicting TTN, the sensitivity and specificity values were moderate. This suggests that MPV alone may not be a definitive predictive marker and should be used in conjunction with other clinical and laboratory parameters. Addressing these limitations in future research through multi-center, prospective cohort studies with larger and more diverse populations is essential. Such studies could validate the utility of MPV as a reliable predictor of neonatal outcomes like TTN in GDM pregnancies and explore its integration with other predictive markers to improve risk assessment and management strategies.

Conclusion

We discovered that GDM patients had higher MPV, which had a strong connection with TTN. However, we believe that multi-center cohort studies should be conducted to use MPV as a predictor in TTN.

Also, our study is valuable in terms of evaluating babies of pregnant women with MPV values above the cut-off value as high-risk in terms of development of TTN, and accordingly, taking measures such as booking an intensive care place for the newborn and providing a chance for rapid intervention.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
Ethical committee approval was obtained from the Medipol University Clinical Research Ethics Committee dated 04.03.2021 and numbered 293.

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