

Increased MPV Is Not a Significant Predictor for Preeclampsia During Pregnancy

Sibel Altınbas,* Cihan Toğrul, Anil Orhan, Munihe Yücel, and Nuri Danışman
Zekai Tahir Burak Women Health Research and Education Hospital, Ankara, Turkey

Background: Preeclampsia, defined as the presence of hypertension and proteinuria, is usually related with maternal and neonatal adverse effects. However, the exact predictor of preeclampsia is still lacking. Even though there are some conflicting data, mean platelet value or MPV, that is, platelet ratio with or without Doppler velocimetry was determined as highly sensitive markers for preeclampsia. We aimed to investigate the utility of MPV in prediction of preeclampsia. **Methods:** Seventy-four preeclamptic pregnant women (21 in mild, 53 in severe preeclampsia groups) were included in the study. To assess the difference of MPV between preeclamptic, normal pregnant, and healthy control rather than mild and severe preeclamptic pregnant women, we included in the analysis 31 healthy pregnant women and 35 healthy nonpregnant women. **Results:** Mean age of the preeclamptic pa-

Key words: MPV; preeclampsia

tients was 25.3 (17–38) years. Platelet levels were higher in mild preeclampsia (group 1) than severe preeclampsia (group 2), whereas alanine aminotransferase (AST), hemoglobin, and hematocrit level was higher in group 2. MPV levels were found to be similar in groups 1 and 2, MPV level increased from healthy control to preeclamptic women ($P = 0.003$). MPV:platelet ratio was similar according to the severity of preeclampsia ($P = 0.123$). Doppler velocimetry did not add an additional benefit to predict preeclampsia or its severity. **Conclusion:** Our results showed that MPV level was higher in the pregnant than the control group. However, MPV did not differ both between mild and severe preeclampsia, and preeclampsia and non-preeclamptic pregnant women. *J. Clin. Lab. Anal.* 26:403–406, 2012. © 2012 Wiley Periodicals, Inc.

INTRODUCTION

Preeclampsia, defined as the presence of hypertension and proteinuria during pregnancy, is a serious disorder that cannot be cured without delivery. Preeclampsia is usually related with maternal and neonatal morbidity and mortality. Preterm delivery and growth retardation are the most common adverse effects of preeclampsia (1). On the other hand, preeclampsia may progress to severe preeclampsia or eclampsia, which is attributed to higher rate of stillbirth (2). Besides the well-known risk factors as advanced age, presence of hypertension before pregnancy or diabetes mellitus or overweight, positive self-history or family history of preeclampsia, nulliparity was also declared as a significantly risk factor for preeclampsia (3). Despite of the articles focussing on preeclampsia and its pathogenesis, the exact pathogenetic mechanism and a novel treatment method preventing preeclampsia are still unknown. Because of the higher mortality and morbidity rates seen in severe preeclampsia than mild form, predict-

ing the severity of the ongoing disease is important for both maternal and neonatal complications (2, 3).

Mean platelet volume (MPV) is a marker of platelet function provided by complete blood count analysis. However, in a daily practice most of the physicians take into consideration the platelet count while ignoring MPV values (4). It is widely accepted that a small increase in platelet aggregation seen in normal pregnancies is compensated with increased platelet synthesis, and MPV is more sensitive marker than platelet counts to define this early changes (5, 6).

In the recent years, it has been shown that MPV increase reflects the increase of severe inflammatory process, such

*Correspondence to: Sibel Altınbas, Emrah mah. Goksel Sok 27/8, İncirli, Ankara, Turkey. E-mail: drsibela@yahoo.com.tr

Received 8 May 2012; Accepted 23 June 2012

DOI 10.1002/jcla.21542

Published online in Wiley Online Library (wileyonlinelibrary.com).

as Crohn's disease, rheumatoid arthritis, chronic hepatitis B, metabolic syndrome, and myocardial infarction (7, 8). There are conflicting data on the importance of MPV predicting preeclampsia (9–12). On the other hand, prediction of the severity of preeclampsia is also necessary due to high morbidity and mortality rates (2). So, we aimed to investigate the risk factors of preeclampsia and the possible role of MPV predicting preeclampsia and its severity.

MATERIAL AND METHODS

Between January 1 and December 31, 2006, among 26,090 pregnancies, all the preeclamptic pregnant women admitted to Zekai Tahir Burak Women Health Hospital were included in the study. For the diagnosis of preeclampsia, the criteria were as follows: Arterial blood tension higher than 140/90 (via two separated measurement in 6 hr) and proteinuria (higher than 100 mg/dL in spot analysis twice, or higher than 300 mg in 24 hr collecting urine) (13). All the demographic data and laboratory analysis of the patients were collected retrospectively from the digital database of the hospital. To assess the difference of MPV between preeclamptic, normal pregnant, and healthy control rather than mild and severe preeclamptic pregnant women, we included in the analysis 74 primigravid preeclamptic women, 31 healthy pregnant women and 35 healthy nonpregnant women.

Definition of severity criterion of preeclampsia (with presence of at least one parameter) (13) is as follows:

- Mean arterial blood pressure higher than 126 mmHg.
- Proteinuria (5 g/24 hr).
- Oliguria (500 mL/24 hr).
- Cerebral or visual symptoms.
- Pulmonary edema or cyanosis.
- Epigastric or right upper quadrant pain.
- Elevated liver function tests (twofold greater than the normal ranges).
- Thrombocytopenia ($<100,000/\text{mm}^3$).
- Fetal growth retardation.

The statistical analyses were performed with SPSS 15 computer-based program (Chicago, IL). Data were expressed as mean \pm standard deviation (SD). Kruskal–Wallis and Mann–Whitney *U* tests were used for group comparisons. Statistical significance was accepted at a *P*-value of less than 0.05. The calculated statistical power was 0.72.

RESULTS

Seventy-four primigravid women were diagnosed for preeclampsia. The patients included in the study were

divided into two groups according to the severity of preeclampsia. Group 1 consisted of mild preeclampsia ($N = 21$), and group 2 consisted of severe preeclampsia ($N = 53$) (Table 1).

Mean ages of the preeclamptic patients were 23.8 ± 5.4 and 24.5 ± 4.9 years in groups 1 and 2, respectively (*P*-value 0.577). Body mass index values before the pregnancy and the amount of gaining weight during the pregnancy did not differ between the two groups (*P* values 0.72 and 0.36, respectively). Severe preeclampsia was seen almost 2 weeks earlier than mild preeclampsia ($P < 0.001$). The laboratory analysis of both groups was shown in Table 1. Platelet levels were higher in group 1 than group 2, whereas alanine aminotransferase (AST), hemoglobin, and hematocrit levels were higher in group 2. MPV levels were found to be similar in groups 1 and 2, however, MPV level increased from healthy control to preeclamptic women ($P = 0.003$). In MPV, platelet ratio was similar according to the severity of preeclampsia ($P = 0.123$).

We also used Doppler velocimetry to assess the role of altered values in predicting severity of preeclampsia in 35 preeclamptic patients. A total of 71.4% of the mild preeclamptic patients had normal Doppler velocimetry profiles; in contrast, 60.7% of the severe group had altered Doppler velocimetry (*P*-value 0.207). MPV values reached significance between the normal and abnormal Doppler profiles (*P*-value 0.024) (Table 2).

DISCUSSION

Even though there are some conflicting data, the importance of MPV count predicting preeclampsia was already shown (9, 10, 14). On the other hand, von Dadelszen et al. found that MPV: platelet ratio is more sensitive than MPV alone in predicting preeclampsia-related adverse maternal outcome (11). The increase in MPV occurs before any change in platelet count (14). Moreover, Dundar et al. showed that MPV increase during pregnancy, but it is more prominent in cases developing preeclampsia (9). Investigators described two different cutoff values, one was 8.5 fL (with a sensitivity of 78% and specificity of 86%) to determine risk of preeclampsia and the other was 10 fL (femtolitre) (with a sensitivity of 45% and specificity of 89.7%) to define the chance of unfavorable neonatal outcome (the necessity of severe oxygen support) (9, 15). A combination of reduced platelet count and elevated MPV has a sensitivity of 90% and specificity of 83.3% in predicting preeclampsia (16). On the other hand, Ceyhan et al. claimed that the importance of MPV predicting preeclampsia may be due to some methodological mistakes (12). Our study revealed that both MPV:platelet ratio and MPV alone were not criterion to predict severity of preeclampsia or the risk ratio of preeclampsia. But

TABLE 1. Baseline Characteristics, Laboratory Analyses, and Adverse Effects of the Primigravide Preeclamptic Patients

	Group 1 (mild preeclampsia)	Group 2 (severe preeclampsia)	P-value ^a
Mean ages \pm SD	24 \pm 4	24 \pm 5	0.30
BMI, before the pregnancy (kg/m ²)	24 \pm 4.21	23.9 \pm 4.2	0.72
Week of the pregnancy at the diagnosis	37.2 \pm 3.4	35.1 \pm 4	<0.001
Amount of the gaining weight during the pregnancy (kg)	14.8 \pm 5.7	14.3 \pm 5.5	0.36
Hemoglobin (mean mg/dL \pm SD)	11.8 \pm 1.9	12.7 \pm 1.7	<0.001
Hematocrit (mean % \pm SD)	35.9 \pm 5.5	38.1 \pm 5.6	<0.001
Platelet (mean /mm ³ \pm SD)	228,000 \pm 72,600	197,000 \pm 103,000	<0.001
MPV (mean fL \pm SD)	9.5 \pm 1.0	9.3 \pm 1.22	0.688
PTZ (mean ms \pm SD)	11.8 \pm 0.8	12.1 \pm 5.8	0.62
Fibrinogen (mean g/L \pm SD)	506 \pm 120	491 \pm 138	0.28
LDH (mean U/L \pm SD)	611 \pm 252	867 \pm 520	0.18
AST (mean U/L \pm SD)	25 \pm 9.7	91.2 \pm 8.7	<0.001
Blood urea nitrogen (mean \pm SD)	26 \pm 9.8	32 \pm 15	<0.001
Maternal complications, ^b N (%)	8 (6.4)	83 (29.8)	<0.001
Neonatal complications, ^c N (%)	35 (28.6)	164 (55.5)	<0.001

^aStatistically significance accepted as <0.05.

^bMaternal complications consist of HELLP, eclampsia, acute renal failure, abruption placenta, and atonia.

^cNeonatal complications consist of prematurity, meconium aspiration, increased hematocrit value, and exitus.

TABLE 2. The Relation Between Doppler Velocimetry Alterations According to the Severity of Preeclampsia

	Normal Doppler velocimetry, N (%)	Abnormal Doppler velocimetry, N (%)	P-value*
Mild preeclampsia	5 (71.4)	2 (28.6)	0.207
Severe preeclampsia	11 (39.3)	17 (60.7)	
MPV (mean fL \pm SD)	8.95 \pm 0.94	9.81 \pm 1.05	0.024

*Statistically significance accepted as <0.05.

our results showed that MPV level increases during the pregnancy.

A group from Italy determined that Doppler velocimetry alterations are correlated with MPV changing in two consecutive studies (15, 17). We also checked out the utility of Doppler velocimetry to predict severity of preeclampsia. We determined that most of the severe preeclamptic patients had abnormal Doppler velocimetry, whereas mild preeclamptic patients had normal profile. However, this difference did not reach significance (*P*-value 0.207) (Table 2). The same investigators also showed that MPV values were higher in preeclamptic patients compared with normal group. Even though MPV values were similar in both group, our study showed an unexpected results with higher MPV values in mild preeclamptic group rather than severe one (Table 2).

Similar to the literature, our study showed a higher cesarean, maternal, and neonatal morbidity and mortality rates in severe preeclampsia than mild form (2, 3). Therefore, not only predicting preeclampsia, but also the severity of preeclampsia should be important. Our study added new data to the literature as mentioned above that MPV

value may play a role in predicting high preeclampsia risk, whereas it has no role in distinguishing between mild and severe preeclampsia.

Even though the recent studies claimed that MPV increase is usually followed by a decline in platelet, in our study platelet decreasing reached to significance between two groups, in contrast to MPV and MPV; platelet ratio remained similar in both groups (11).

Because our center is a referral hospital, most of our patients were included in the severe preeclamptic group. A total of 72.7% of the patients in group 1 were referred from abroad, whereas only 28.3% in group 2. Because of this, the ratio of severe-to-mild preeclampsia did not give epidemiological data of our country. The other limitation of our study was the less number of the patients for the analysis of MPV. The ideal way is to calculate MPV soon after taking the blood sample; however, because of a retrospective design of our study, we were not able to standardize this issue. On the other hand, although our study was performed retrospectively, its results can be more useful for the physicians. And of course, the anticoagulant agents used in the collecting tubes may have effect on MPV value.

In conclusion, our results showed that MPV level increased during the pregnancy. However, it has no role in distinguishing between mild and severe preeclampsia or does not have a chance of potential predictor for preeclampsia progression.

REFERENCES

1. Saftlas AF, Olson DR, Franks AL, Atrash HK, Pokras R. Epidemiology of preeclampsia and eclampsia in the United States, 1979–1986. *Am J Obstet Gynecol* 1990;163(2):460–465.

2. Fonseca EB, Celik E, Parra M, Singh M, Nicolaides KH; Fetal Medicine Foundation Second Trimester Screening Group. Progesterone and the risk of preterm birth among women with a short cervix. *N Engl J Med* 2007;357(5):462–469.
3. Pennington KA, Schlitt JM, Jackson DL, Schulz LC, Schust DJ. Preeclampsia: Multiple approaches for a multifactorial disease. *Dis Model Mech* 2012;5(1):9–18.
4. Bath PM, Butterworth RJ. Platelet size: Measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis* 1996;7(2):157–161.
5. Stubbs TM, Lazarchick J, Van Dorsten JP, Cox J, Loadholt CB. Evidence of accelerated platelet production and consumption in nonthrombocytopenic preeclampsia. *Am J Obstet Gynecol* 1986;155(2):263–265.
6. Tygart SG, McRoyan DK, Spinnato JA, McRoyan CJ, Kitay DZ. Longitudinal study of platelet indices during normal pregnancy. *Am J Obstet Gynecol* 1986;154(4):883–887.
7. Ekiz F, Yüksel O, Koçak E, et al. Mean platelet volume as a fibrosis marker in patients with chronic hepatitis B. *J Clin Lab Anal* 2011;25(3):162–165, doi: 10.1002/jcla.20450.
8. Yüksel O, Helvacı K, Başar O, et al. An overlooked indicator of disease activity in ulcerative colitis: Mean platelet volume. *Platelets* 2009;20(4):277–281.
9. Dunder O, Yoruk P, Tutuncu L, et al. Longitudinal study of platelet size changes in gestation and predictive power of elevated MPV in development of pre-eclampsia. *Prenat Diagn* 2008;28(11):1052–1056.
10. Järemo P, Lindahl TL, Lennmarken C, Forsgren H. The use of platelet density and volume measurements to estimate the severity of pre-eclampsia. *Eur J Clin Invest* 2000;30(12):1113–1118.
11. von Dadelszen P, Magee LA, Devarakonda RM, et al. The prediction of adverse maternal outcomes in preeclampsia. *J Obstet Gynaecol Can* 2004;26(10):871–879 [Article in English, French].
12. Ceyhan T, Beyan C, Başer I, Kaptan K, Güngör S, Ifran A. The effect of pre-eclampsia on complete blood count, platelet count and mean platelet volume. *Ann Hematol* 2006;85(5):320–322.
13. ACOG Committee on Obstetric Practice. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet* 2002;77(1):67–75.
14. Boriboonhirunsarn D, Atisook R, Taveethamsathit T. Mean platelet volume of normal pregnant women and severe preeclamptic women in Siriraj Hospital. *J Med Assoc Thai* 1995;78(11):586–589.
15. Gioia S, Piazzè J, Anceschi MM, et al. Mean platelet volume: Association with adverse neonatal outcome. *Platelets* 2007;18(4):284–288.
16. Howarth S, Marshall LR, Barr AL, Evans S, Pontre M, Ryan N. Platelet indices during normal pregnancy and pre-eclampsia. *Br J Biomed Sci* 1999;56(1):20–22.
17. Piazzè J, Gioia S, Cerekja A, et al. Doppler velocimetry alterations related to platelet changes in third trimester pregnancies. *Platelets* 2007;18(1):11–15.