The Value of Mean Platelet Volume in Predicting The Severity of Preeclampsia and of Hellp Syndrome

Pınar KUMRU[1], **Nurettin AKA**[1], **Gültekin KOSE**[1], **Özgür KARTAL**[1], **Sacide ATALAY**[2]
İstanbul- Turkey

OBJECTIVE: Assessing the value of MPV in predicting the severity of preeclampsia, and HELLP syndrome.
STUDY DESIGN:12 women with HELLP syndrome,57 severely preeclamptic,30 mildly preeclamptic, 170 healthy pregnant women were included in this study and their MPV are recorded.
RESULTS: The calculated sensitivity was 53% for mild preeclampsia,77% for severe preeclampsia, and 83% for HELLP syndrome.
CONCLUSION: The measurement of MPV is not enough for diagnosis but can be useful with other sensitive tests.
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Key Words: Preeclampsia, HELLP syndrome, Mean Platelet Volume (MPV), Platelets

Preeclampsia is defined as hypertension, proteinuria, and/or edema after the 20th gestational week[1]. It occurs in 7-10% of all pregnancies, and is one of the leading causes of maternal mortality and morbidity[2]. Although its etiology is not entirely known, immunological interactions, and especially, endothelial cell damage and -dysfunction are thought to play a major role.[3] HELLP syndrome, on the other hand, is a syndrome manifested by hemolysis, an increase in liver enzymes, as well as a drop in platelet count, and occurs in 4-12% of severe preeclampsia cases, and in 0.1-0.6% of all pregnancies.[4]

Platelets play a major role in the pathophysiology and clinical follow-up of preeclampsia.[5] In spite of progressive platelet breakdown, thrombocytopenia is a delayed finding of preeclampsia.[6] Several publications report that in spite of the increased formation of platelets in the maternal circulation, the platelet count in preeclamptic pregnancies is lower than normal pregnancies due to enhanced activation.[7]

An inversely proportional relationship was shown between the platelet count and the mean platelet volume (MPV) in healthy individuals. A lower platelet count and wider thrombocytes were observed in preeclampsia.[8] Based on these findings, we aim to investigate the value of mean platelet volume measurements in predicting the severity of preeclampsia and of HELLP syndrome.

[1]*Haydarpaşa Numune Education and Research Hospital, Department of Gynecology and Obstetrics, İstanbul, Turkey*

[2]*Haydarpaşa Numune Education and Research Hospital, Department of Clinical Biochemistry, İstanbul, Turkey*

Address of Correspondence *Nurettin AKA*
Feneryolu Mah. Hüseyinpaşa Sk. 32/7
A Blok Kaptan Apt.
34724 Kadıköy, İstanbul, Turkey

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Materials and Method

Our study was a prospectively controlled trial performed after obtaining consent from the ethical committee of the Haydarpasa Numune Training and Research Hospital.

12 HELLP syndrome, 57 severely preeclamptic, 30 mildly preeclamptic, and 170 normal pregnant women who applied to and were treated at the Haydarpaşa Numune Training and Research Hospital were included in this study. The first group consisted of normal pregnant women, the second group of mildly preeclamptic women with a blood pressure (BP) between 140/90 and 160/110 mmHg, proteinuria (0.3-5 g/24 h), and/or edema, and the third group of severely preeclamptic patients with ≥160/100 mmHg blood pressure, proteinuria over 5 g/24h, and/or edema findings. The fourth group, which was composed of pregnant women with HELLP syndrome, was characterized by an abnormal blood picture indicating hemolysis, an increase in plasma LDH (>600 U/L), and bilirubin level (>1.2 g/dL), thrombocytopenia (<100,000/L), an increase in serum amino transferase level (≥70 U/L). Individuals with chronic hypertension, Diabetes Mellitus, autoimmune disorders, and hematological problems were excluded.

4 cc venous blood was obtained from the antecubital veins to be used for the whole blood count. In order to minimize any variation in platelet size and count, all samples were analyzed within 2-4 hours. Platelet count and MPV measurements were carried out using Coulter STKS system (Manufactured by Coulter Co., Miami, US). The normal interval for MPV was defined as 7-10,5 fl. The age, gravidity, parity, number of abortions, gestational week, platelet counts, and MPV values were recorded. Statistical analysis of the data was performed using SPSS for Windows, v. 11.5. Continuous parameters were expressed as mean ± SS. Kruskal Wallis nonparametric test was used to analyze the groups with a homogenous distri-

bution. AP - value <0,05 was considered significant. Comparison between data - pairs was performed using Bonferroni approach, and Mann-Whitney U-test. For the comparison between the four groups, P<0.008 was considered significant.

Results

No significant difference was found between the groups with regard to mother's age, gravidity, parity, number of abortions, and gestational weeks **(Table 1).**

pregnancies (p=0,655). There was a statistically significant difference, however, between mildly preeclamptic pregnancies and severely preeclamptic pregnancies (p=0,001), mildly preeclamptic pregnancies and HELLP syndrome patients (p=0,001), severely preeclamptic pregnancies and normal pregnancies (p=0,001), and finally between HELLP syndrome patients and healthy pregnant women **(Table 2)**. The difference between the MPV values of HELLP syndrome patients and women with preeclampsia was highly significant (p=0,0001).

Table 1. Demographic characteristics, platelet counts, and MPV, expressed as mean±SS

	Normal pregnancy	*Mild PE*	*Severe PE*	*HELLP Synd*	P
	n:170	*n:30*	*n:57*	*n:12*	
Age	27.06±5.38	27.47±7.64	28.84±7.32	26.83±6.12	0.293
Gravidity	2.49±1.48	2.43±1.13	2.98±2.34	2.62±1.72	0.202
Parity	1.12±1.61	1.00±0.94	1.46±1.92	2.00±2.52	0.80
# of Abortions	0.48±0.83	0.43±0.67	0.53±1.05	0.08±0.28	0.43
Gest. weeks	33.72±5.06	36.6±1.94	33.91±4.68	32.92±5.01	0.18
Platelet count	246659±72378	212000±105873	161925±46066	87416±41307	0.03
MPV	8.08±1.24	8.95±1.66	8.78±2.16	9.81±1.52	0.0001

The mean MPV values were 8,08±1,24 fl in normal pregnancies, 8,95±1,66 fl in mildly preeclamptic pregnancies, 8,78±2,16 fl in severely preeclamptic pregnancies, and 9,81±1,52 fl in women with HELLP syndrome **(Figure 1)**.

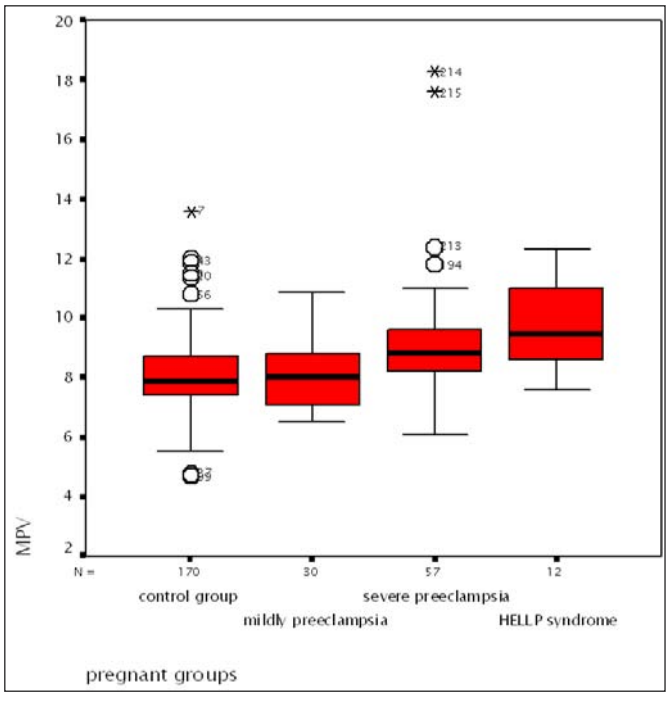

Figure 1. MPV values in pregnancy groups, mean±SS

When we compared the MPV values between the groups; no significant differences were found between severely preeclamptic pregnancies and HELLP syndrome patients (p=0,121), and mildly preeclamptic pregnancies and normal

Table 2. Comparison between the groups with regard to MPV values. p<0,008 was considered significant. (nd: no statistically significant difference was found)

Comparison between the groups	P
Normal&Mildly preeclamptic	0.655 NS
Normal&Severely preeclamptic	0.001
Normal&HELLP syndrome	0.0001
Mildly&Severely preeclamptic	0.001
Mildly preeclamptic&HELLP syndrome	0.001
Severely preeclamptic&HELLP syndrome	0.121 nd

The platelet count was 246659±72378 in normal pregnancies, 212000±105873 in mildly preeclamptic pregnancies, 161925±46066 in severe preeclampsia, and 87416±41307 in HELLP syndrome patients. When we compared the groups with regard to platelet count, no significant difference could be shown between normal pregnancies and mildly preeclamptic pregnancies (p=0,16), as well as between mildly preeclamptic and severely preeclamptic pregnancies (p=0,062). A statistically significant difference, however, existed between normal pregnancies and severely preeclamptic pregnancies (p=0,0001), normal pregnancies and HELLP syndrome patients (p=0,0001), mildly preeclamptic and HELLP syndrome patients (p=0,0001), and severely preeclamptic and HELLP syndrome patients (p=0,0001) **(Table 3).**

Table 3. Comparison between the groups with regard to platelet counts. P<0,008 was considered significant. (nd: no statistically significant difference was found).

Comparison between the groups with the regard to platelet counts	P
Normal&Mildly preeclamptic	0.16 NS
Normal&Severely preeclamptic	0.0001
Normal&HELLP syndrome	0.0001
Mildly&Severely preeclamptic	0.062 NS
Mildly preeclamptic&HELLP syndrome	0.0001
Severely preeclamptic&HELLP syndrome	0.0001

The distribution of MPV values was extrapolated from the ROC curve for preeclamptic and normal pregnancies **(Figures 2, 3, and 4)**.

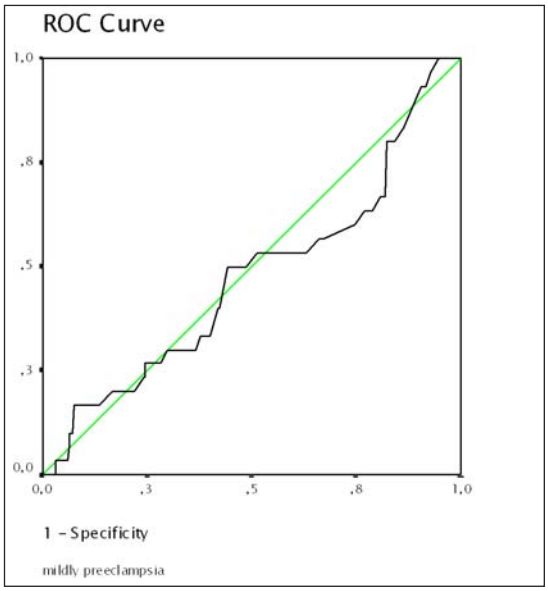

Figure 2. ROC curve for mildly preeclampsia; Sensitivity: 53%, Specifity: 51% (Cut-off:

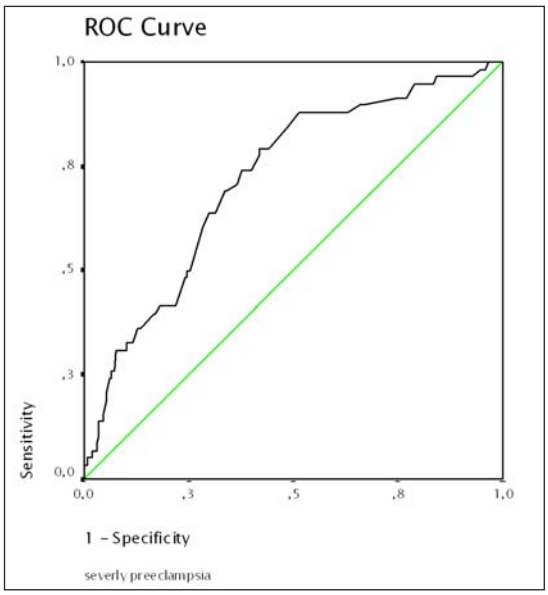

Figure 3. ROC curve for severe preeclampsia Sensitivity: 77%, Specifity: 58% (Cut-off: 8,2)

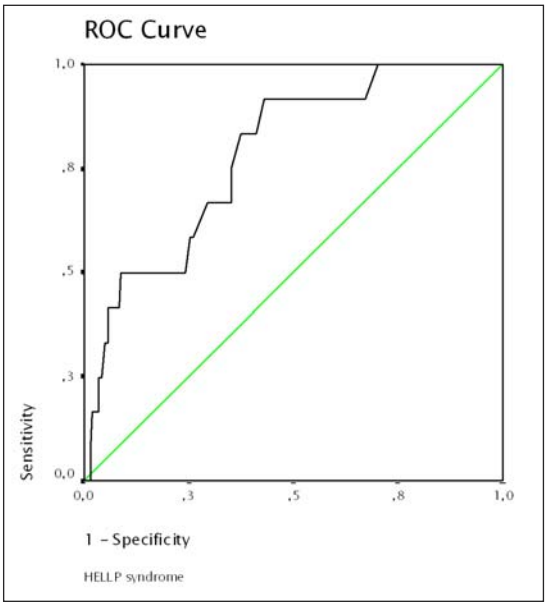

Figure 4. The ROC curve showing the sensitivity and specifity of the MPV measurement for HELLP syndrome patients Sensitivity: 83%, Specifity: 70% (Cut-off : 8,6)

The cut - off and diagnostic values for the highest sensitivity, specifity, positive predictive value, and the negative predictive value for the three clinical conditions (mild preeclampsia, severe preeclampsia, and HELLP syndrome) are shown in Table 4.

Table 4. The cut-off and diagnostic value of MPV for the highest sensitivity, specifity, positive predictive value (PPD), and negative predictive value (NPD)

	Sensitivity (%)	Specifity (%)	PPD (%)	NPD (%)	Diagnostic value (%)	Cut-off value
Mild PE	53	51	16	86	56	7.9
Severe PE	77	58	42	87	64	8.2
HELLP syndrome	83	70	18	98	66	8.6

Discussion

MPV is an indicator of platelet function and activity, and can be used for the diagnosis of thrombomegaly, which is a risk factor for vascular disorders. MPV is reported to increase in certain disorders, such as DM, myocardial infarction, renal artery stenosis, and preeclampsia.[9] The underlying pathology is thought to involve endothelial damage, rather than coagulation, or platelet activation[3]. Deterioration of microcirculation, formation of micro-thrombi, increased platelet turnover, and younger thrombocytes entering the circulation as a result of endothelial damage are reported to increase the MPV level[10]. While the platelet count remains stable throughout the whole gestation in normal pregnancies, the MPV decreases between 20th and 31st weeks, and shows a prominent increase after the 38th week until the 41st week.

Marumato et al.[10] showed that MPV value is increased in cases with severe preeclampsia and IUGR compared to normal pregnancies. Boriboonhirunsarn et al.[11], in their study conducted in 1995, found that MPV value was higher in severely preeclamptic pregnancies compared to normal pregnancies, with platelet count remaining normal in spite of the change in the MPV value, and reported that MPV was more beneficial and more sensitive in indicating the platelet changes in high - risk patients. Jaremo et al.[12] (2000) found that proteinuria and increased blood pressure was related to abnormal platelet distribution and increased platelet volume, and showed that platelet density and volume measurements may be used in predicting the severity of preeclampsia.

Howart et al.[13] found that the sensitivity and specifity of MPV in predicting preeclampsia is 60% and 83.3%, respectively, and reported that MPV may be used in predicting the risk of preeclampsia.

Sullivan et al.[14] (1998) administered antiaggregant therapy to pregnant women under high risk of developing preeclampsia, and adjusted the treatment dose based on longitudinal MPV monitorization. With this method of follow - up, the neonatal death incidence was found lower than previous pregnancies. They also emphasized that monitoring the MPV changes, instead of a single value, might be important in the prognosis and management of this disorder.

We were not able to find any publication on the relationship of HELLP syndrome and MPV.

We found that MPV value, in contrast to platelet count, was increased in preeclamptic pregnancies and HELLP syndrome patients, compared to our control group of normal pregnancies. The severity of this condition appears to be directly related to the increase in MPV value. These findings are compatible with other publications.

We also calculated the sensitivity, specifity, positive predictive value, and negative predictive value of MPV for preeclamptic and normal pregnancies using ROC curves. In contrast to other reports, sensitivity, specifity, and PPV were found to be low for preeclampsia, especially for mild preeclampsia **(Table 5)**, while NPV reached a higher level (mild preeclampsia: 86%, severe preeclampsia: 87%, HELLP syndrome: 98%).

Table 5. The sensitivity, specifity, positive predictive value (PPD), and negative predictive velue at different MPV cut-off values

Cut-off	SENSITIVITY	SPECIFITY	PPD	NPD
8 fl	72	65	48	76
8.5 fl	56	70	49	71
9 fl	35	80	52	68
9.3 fl	30	89	57	67
9.5 fl	28	92	64	65
9.7 fl	20	93	65	53

In summary, platelet count and MPV are simple, rapid, and economic tests available in many hospitals. We concluded that MPV measurements are useful in predicting the severity of preeclampsia and the presence of HELLP syndrome, if used in combination with other more sensitive tests. If no other test is available, it might be indicative to a certain degree. We believe that NPD value may play an important role in predicting the severity of preeclampsia and HELLP syndrome.

Further prospective and multi-centric studies with larger patient populations are necessary to elucidate the predictive factors for the severity of preeclampsia and the presence of HELLP syndrome.

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