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Preeklampsi Olgularında Ortalama Trombosit Hacmi ve Trombosit Düzeylerinin İncelenmesi

Predictive Value of Mean Platelet Volume and Platelet Levels for Preeclampsia

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Öz

Giriş ve Amaç: Preeklampsi; hipertansiyon, proteinüri ve/veya organ hasarı ile seyreden gebeliğe özgü bir hastalıktır. Bu çalışmada, gebelikte rutin takiplerin yapıldığı birinci basamakta bazı hematolojik parametrelere göre preeklampsinin öngörülebilir olup olmadığının araştırılması amaçlanmıştır.
Gereç ve Yöntemler: Bu retrospektif çalışmaya 58 preeklampsili gebe ve 116 sağlıklı gebe dahil edildi. Preeklampsi grubunda tanı anına ve tanıdan 2-6 hafta öncesine ait iki farklı hemogram sonucu; kontrol grubu için doğum zamanı ve doğumdan 2-6 hafta öncesine ait iki farklı hemogram sonucu çalışmaya dahil edildi.
Bulgular: Preeklampsi grubunun ikinci hemogram sonuçlarında trombosit sayısı, NLR ve PLR düzeyleri ilk hemogram sonuçlarına göre daha düşük, MPV düzeyleri daha yüksek olarak bulundu. ROC analizi sonucu, MPV'nin 8.95 (fL) kabul edildiği cut-off değerinde preeklampsiyi öngörmedeki duyarlılığı %75,9 ve özgüllüğü %33,3 olarak saptandı.
Sonuç: Çalışmamızın sonuçlarını literatürle karşılaştırdığımızda MPV, NLR ve PLR verilerinin preeklampsi tanılı hastaları öngörmede kullanılabilir olduğu değerlendirildi. MPV'de yükselme, NLR ve PLR'de düşme eğiliminin preeklampsiyi öngörmede kullanılabilmesi için daha fazla hasta sayılı ve uzun süreli çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Hipertansiyon, Ortalama Trombosit Hacmi, Preeklampsi.

Abstract

Objective: Preeclampsia is a pregnancy-specific disease with hypertension, proteinuria, and/or organ damage. This study aimed to investigate whether preeclampsia is predictable or not based on some hematological parameters at primary care units step where routine follow-ups are made during the pregnancy.
Materials and methods: In this retrospective study, 58 pregnant women with preeclampsia and 116 healthy pregnant women were included. Two different hemogram results belonging to the time of diagnosis and 2-6 weeks before diagnosis in the preeclampsia group; and two different hemogram results belonging to the time of delivery and 2-6 weeks before delivery for the control group were included in the study.
Results: It was determined that MPV levels were higher; platelet count, NLR, and PLR levels were lower in the second hemogram results compared with the first hemogram results of the preeclampsia group. The ROC analysis result, it was revealed that the sensitivity and specificity of MPV for predicting preeclampsia were 75,9% and 33,3%, respectively, when the cut-off value of MPV was accepted as 8,95 (fL).
Conclusion: When we compared the results of our study with the literature, it was evaluated that MPV, NLR, and PLR data could be used for the prediction of preeclampsia patients. It has been required for a long duration of studies

that need a large number of patients to use the tendency in an increase of MPV and the decrease of NLR and PLR for prediction of preeclampsia.

Keywords: Hypertension, Mean Platelet Volume, Preeclampsia**.**

1. Introduction

Hypertension (HT) is seen in approximately 10% of all pregnancies and the most common non-obstetric complication [1]. The incidence of preeclampsia (PE), which is characterized by HT, proteinuria, and/or organ damage, varies between 2-10% [2-4]. Placental ischemia, increase in oxidative and endoplasmic reticulum stress, production of strong pro-inflammatory mediators and anti-angiogenic factors have been suggested as the main causes of PE [5].

Risk factors for PE include nulliparity, multifetal pregnancies, history of PE, obesity, diabetes mellitus, connective tissue diseases such as systemic lupus erythematosus and anti-phospholipid antibody syndrome, first gestational age above 35, smoking, and African American race [6]. Early diagnosis and management of PE, which is an important cause of mortality and morbidity in pregnancy, is of great importance. Some parameters that can be used in primary health care and predict PE are needed to determine the pregnant women at risk [7].

Recently, the issue that inflammatory markers in hemogram evaluation can be used to determine the risk of PE has come to the fore. However, studies have been conducted to determine whether the predictivity of changes in mean platelet volume (MPV) levels in PE, which can progress with thrombocytopenia, is more significant than the decrease in the number of platelets (PLT). However, the results obtained from the studies are contradictory [8,9].

This study aims to investigate whether PE, which is an important complication of hypertensive diseases during pregnancy, is a predictable condition based on some hematological parameters.

2. Material and methods

2.1.Study design

Hospital admission files of pregnant women who gave birth between January 2012 and October 2017 in the University Hospital Gynecology and Obstetrics Service were retrospectively reviewed. Two different groups were formed, namely the pregnant group diagnosed with PE and the healthy pregnant (control) group. In addition to HT that develops after the 20th week of pregnancy; PE was diagnosed with the presence of proteinuria, thrombocytopenia, liver dysfunction, renal failure, pulmonary edema, and any of the cerebral or visual symptoms according to the report of the American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy [10].

Two separate hemograms, taken 2-6 weeks apart, were obtained from the PE group and the control group. The comparison of the hemogram results of PE and the control group between groups was also made in addition to the comparison of the two hemogram results of the PE group in our study. The original aspect of our study is that there are few studies conducted with this algorithm in the literature.

2.2.Inclusion of samples / Data sources

One of the hemogram results obtained for the PE group was selected for the period of diagnosis, the other for the period 2-6 weeks before the PE diagnosis when clinical findings of PE did not appear. The time difference between the two hemograms in our study was determined as 2-6 weeks, in the light of studies reporting 2-8 weeks [11], 4 weeks [12], and 6 weeks [13] in the literature.

Blood and urine tests of all patients included in the study were studied in the hospital's hematology and biochemistry laboratory. The tests performed in the external center laboratory were not included in the study. From the parameters obtained from the hemogram results; neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) were calculated.

2.3.Patient selection

All singleton pregnant women were included in the PE group having hemogram values registered in the hospital information system at the date of diagnosis and 2-6 weeks before this date, with sociodemographic data and blood pressure records in hospital admission files, without the chronic disease (such as hypertension, rheumatic disease, chronic liver and/or kidney disease), or pregnancy with a congenital fetal anomaly.

The control group was formed from pregnant women who were randomly selected among singleton all pregnancies who have no additional disease (such as hypertension, diabetes mellitus, rheumatic disease, chronic liver and/or kidney disease) or medication use, hemogram values in the hospital information system belonging to the date of birth and 2-6 weeks before this date, sociodemographic data, and blood pressure records in hospitalization files, no pregnancy with a fetal anomaly. In addition, the number of pregnant women in the control group was arranged to be twice the number of pregnant women in the PE group for each same year.

2.4.Statistical analysis

The data were evaluated with the SPSS.15 program. In statistical analysis, when descriptive statistics were provided for normal distribution conditions, the Student T-test (Mann Whitney U test when normal distribution conditions were not provided) was used to compare continuous data of two independent groups, and the chi-square test was used to compare categorical data. Statistical significance level was taken as $p < 0,05$ for all data. ROC curves were created to estimate the use of each parameter as a tool to estimate the severity of PE.

2.5.Ethical issue

Approval was obtained from the local University Health Sciences Ethics Committee dated 25.10.2017 and numbered 20.478.486.

3.Results and Discussion

3.1.Descriptive Features

333 preeclampsia and 3960 healthy pregnant women were determined by scanning the hospitalization files of 5496 pregnant women in total. 58 pregnant women who met the inclusion criteria of 333 preeclampsia pregnant women were included in the study. From 3960 healthy pregnant women; 116 pregnant women who were selected with random sampling and who met the inclusion criteria, taking into account the number distribution and gestational weeks by years were included in the study. Descriptive characteristics of the pregnant women included in the study are summarized in Table 1.

Table 1. Descriptive characteristics of pregnant women in preeclampsia and control groups

	Preeclampsia (n=58)	**Controls (n=116)**	**p**
Maternalage (years)	28,81 ± 6,19	28,48 ± 4,46	,721
Nulliparous, n (%)	23(39,6%)	41 (35,3%)	,578
Smoking, n (%)	5 (8,6%)	10 (8,6%)	1,000
Gestational age at delivery (weeks)	37,04 ± 3,07	39,43 ± 1,32	<001
Gravidity, n	2,48 ± 1,47	2,42 ± 1,39	,796
Parity, n	1,14 ± 1,29	1,02 ± 0,97	,532
Neonatal birth weight (g)	2713 ± 779	3316 ± 388	<001
Systolic BP* (mmHg)	152,16 ± 15,56	107,24 ± 10,70	<001
Diastolic BP (mmHg)	95,95 ± 7,86	67,46 ± 7,87	<001

*BP: Blood pressure

3.2.Evaluation of the hemogram data of the preeclampsia group

The PLT values in the second hemogram results of the PE group were significantly lower than the PLT values in the first hemogram results; MPV values were found to be significantly higher (p <0,05). NLR and PLR values were significantly lower in the second hemogram than the first hemogram (p <0,05) (Table 2).

Table 2. Comparison of the first and second hemogram results in the preeclampsia groups

Preeclampsia (n=58)	**First hemogram**	**Second hemogram**	**p**
Hemoglobin (g/dL)	11,83± 1,08	11,82 ± 1,20	,945
Thrombocytes (×10^9/L)	233,87±69,88	209,41±75,92	<001
MPV* (fL)	9,45 ± 1,56	10,01 ± 1,79	<001
Neutrophils (×10^9/L)	8,20 ± 2,77	8,15 ± 2,36	,882
Lymphocytes (×10^9/L)	1,92 ± 0,47	2,00 ± 5,61	,165
NLR**	4,49 ± 1,70	4,35 ± 1,78	<001
PLR***	126,11±39,98	108,63±42,87	<001

***MPV:** *Mean Platelet Volume,* ****NLR:** *Neutrophil/Lymphocyte Ratio,* *****PLR:** *Platelet/Lymphocyte Ratio*

3.3.Comparison of the first hemogram data of the preeclampsia group and the control group

Hemoglobin levels in the first hemogram results of the PE group were found to be significantly higher than the control group (p <0,05). No significant difference was found between the two groups in terms of platelet count, neutrophil count, lymphocyte count, MPV, NLR, and PLR values (Table 3).

Table 3. Comparison of the first hemogram data of the preeclampsia and the control groups

	Preeclampsia (n=58)	**Controls (n=116)**	**p**
Hemoglobin (g/dL)	11,83 ± 1,08	11,28 ± 1,24	,003
Thrombocytes (×10^9/L)	233,87 ± 69,88	233,25 ± 58,28	,954
MPV* (fL)	9,45 ± 1,56	9,07 ± 1,31	,109
Neutrophils (×10^9/L)	8,20 ± 2,77	7,82 ± 2,19	,356
Lymphocytes (×10^9/L)	1,92 ± 0,47	1,86± 0,54	,450
NLR**	4,49 ± 1,70	4,60 ± 2,21	,733
PLR***	126,11 ± 39,98	135,26 ± 51,36	,237

***MPV:** *Mean Platelet Volume*, ****NLR:** *Neutrophil/Lymphocyte Ratio*, *****PLR:** *Platelet/Lymphocyte Ratio*

3.*4.Comparison of the second hemogram data of the preeclampsia group and the control group*

There was no significant difference between the two groups in terms of hemoglobin, platelet, neutrophil, lymphocyte count, NLR, and PLR values. MPV values in the second hemogram results were found to be significantly higher in the PE group compared to the control group (p <0,05) (Table 4).

Table 4. Comparison of the second hemogram values of the groups

	Preeclampsia(n=58)	**Controls (n=116)**	**pValue**
Hemoglobin (g/dL)	11,82 ± 1,20	11,72 ± 1,32	,626
Thrombocytes(×10^9/L)	209,41 ± 75,92	229,92 ± 54,77	,070
MPV* (fL)	10,01 ± 1,79	9,38 ± 1,30	,019
Neutrophils (×10^9/L)	8,15 ± 2,36	8,61 ± 2,62	,243
Lymphocytes (×10^9/L)	2,00 ± 5,61	2,09 ± 6,54	,354
NLR**	4,35 ± 1,78	4,47 ± 2,03	,697
PLR***	108,63 ± 42,87	118,00 ± 40,36	,159

***MPV:** *Mean Platelet Volume*, ****NLR:** *Neutrophil/Lymphocyte Ratio*, *****PLR:** *Platelet/Lymphocyte Ratio*

As a result of the ROC analysis performed in our study (AUC: 0,617, 95% CI: 0,523-0,711), the sensitivity in predicting PE at the cut-off value where MPV was considered to be 8,95 (fL) was found to be 75,9 % and its specificity 33,3 % (Figure 1).

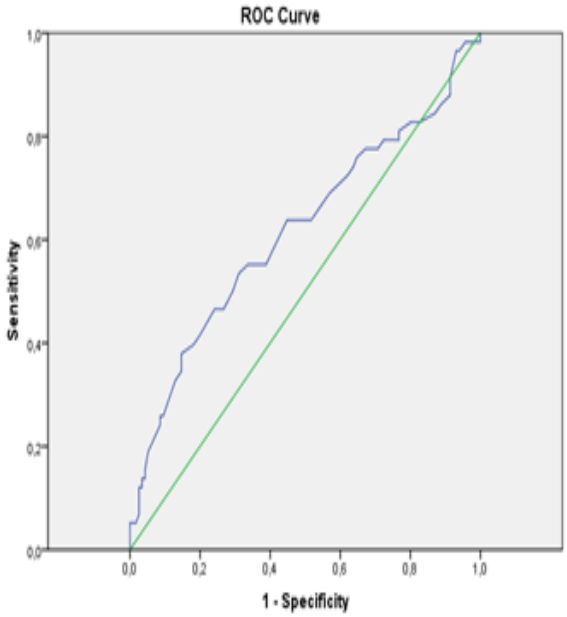

Figure 1. ROC curve for MPV levels in the second hemogram results of the preeclampsia and the control groups

3.4. Discussion

In recent years, it has been raised that inflammatory markers and platelet activation indicators in hemogram evaluation can be used to determine the risk of PE [14]. The incidence of PE in our study was 6% and was found to be similar to the general population. No significant difference was found between the PE group and the control group in terms of mean age, gravida, parity, consanguineous marriage, and smoking.

3.4.1.Evaluation of Hemogram Data of Preeclampsia Group

In two different studies conducted on pregnant women with a diagnosis of PE, it was reported that the number of platelets in the post-diagnosis hemogram results in the PE group was significantly lower than the hemogram results before diagnosis [12,15]. Similarly, the mean platelet count in the second hemogram results of the PE group was found to be significantly lower than the first hemogram values in our study (p <0,05). Even if the platelet count is within normal values, a decrease compared to the previous values can be considered as a stimulant in terms of PE development.

A study from China reported that MPV levels measured at the third trimester in pregnant women with preeclampsia were significantly higher than the values in the first trimester, and an increase was observed in MPV levels during pregnancy in both preeclampsia and control groups [15]. In our case, MPV levels in the second hemogram results in the PE group were significantly higher than the first hemogram values; both NLR and PLR values were significantly lower (p <0,05).

3.4.2.Comparison of the First Hemogram Results of the Preeclampsia and the Control Groups

It has been reported that there is a significant difference in the number of platelets between the groups, in case of comparing the hemogram results of the PE group before the diagnosis with the healthy pregnant group [7,16]. In a study investigating the platelet count and MPV level in the hemogram results obtained before the 20th gestational week, platelet count and MPV level were found to be significantly higher in the PE group compared to the control group [7].

A study of Turkey reported that platelet levels at 11-14 gestational weeks were significantly lower in the PE group compared to the control group, and MPV levels also were higher [16]. When we examined the platelet count and MPV levels in the first hemogram results, we found no statistically significant difference between the PE group and the healthy pregnant group. The difference seen in our results with other studies maybe since the first hemogram test evaluated in our study was 30,78 ± 3,32 gestational week on average and before the 20th gestational week in other studies.

3.4.3.Comparison of Second Hemogram Results of Preeclampsia Group and Control Group

In some of the studies comparing the post-diagnosis hemogram results of the preeclampsia group with the prenatal hemogram results of the healthy pregnant group, MPV levels were found to be high in the preeclampsia group [17-19]; however, some studies reported that there was no significant difference in MPV values between the two groups [20-22]. In a study in Ethiopia, MPV levels in pregnant women with severe PE were found to be significantly higher than healthy pregnant women [17]. In the literature, some studies reporting that MPV levels in the hemogram results taken just before birth are significantly higher in the PE group compared to the control group [7,12,17,18]. MPV levels in pregnant women diagnosed with severe PE, healthy pregnant women, and healthy non-pregnant women were compared and it was reported that there was no statistically significant difference between the groups in another study in Turkey [20]. MPV levels in the second hemogram results evaluated in our study were found to be significantly higher in the PE group compared to the control group.

When the hemograms of healthy pregnant women with PE diagnosis at 11-14 weeks of gestation were examined; the sensitivity of MPV in predicting PE at 10,5fL and above has been reported as 66,7% and its specificity was 63,8% [18]. Another study reported that the sensitivity of MPV in predicting PE at 8,95 fL and above was 93% and the specificity was 22% [15]. In Egypt, it was reported that the sensitivity of MPV measured at 24-28 gestational weeks to be 9,5fL and above in predicting PE as 92,6% and specificity as 87,0% [11]. Analyzes of a study in Austria revealed a cut-off point of MPV as 10,85 fl (sensitivity 65,6%, specificity 26,2%) for the prediction of preeclampsia [12]. In our study, for predicting PE at a

cut-off value of 8,95 (fL) of MPV measured at an average of 34 weeks of gestation its sensitivity was 75,9% and its specificity was 33,3%.

In the examination of the hemogram samples of 3 different groups: PE with severe features, PE without severe features, and healthy pregnant women; the mean platelet count was within normal limits in all groups except PE, which showed severe features. However, as the gestational weeks progressed, it was observed that the average number of platelets decreased in all 3 groups. This decrease was reported to be more in the PE group with severe characteristics, in the PE group without severe characteristics, and in the healthy pregnant group, respectively [11].

In two different studies, it was found that the average platelet count in the PE group was significantly lower than the mean platelet count of healthy pregnant women and one of them has been reported that pregnant women with a platelet count of 248K (×109/ L) or less are at high risk for PE, but this result has low predictivity [21,22]. There was no significant difference observed between healthy and diagnosed with PE pregnants in terms of mean platelet count in our country [23]. The mean number of platelets in the second hemogram results examined in our study was found to be significantly lower in the PE group compared to the control group, similar to some studies in the literature.

Limitations

Since we have a retrospective study, deficiencies in patient data are the most important limitation of this study. However, the fact that the inclusion criteria are organized according to current national and international guidelines and that these criteria are strictly adhered to in the file scanning are the strengths of this study.

4. Conclusion

With our study, we aimed to investigate whether PE is a predictable situation through some parameters in the hemogram, which is an examination that can be studied in many institutions and laboratories. Even if the blood pressure follow-ups of pregnant women continue in a normal course, a closer follow-up can be recommended to the pregnant women who are found to have any of the following conditions in the hemogram results;

- Increase in MPV levels,
- A decrease in the number of platelets,
- A decrease in NLR values,
- The tendency to decrease in PLR values.

5.Acknowledgements and Disclosures

The authors decline no conflict of interest

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