Mean Platelet Volume, Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio in Severe Preeclampsia

Średnia objętość płytek krwi, wskaźnik neutrofile/limfocyty oraz wskaźnik płytki krwi/limfocyty w ciężkiej preeklampsji

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Abstract

Objectives: *The aim of the study was to compare the changes in the values of leukocytes, neutrophils, lymphocytes, mean platelet volume (MPV), and systemic inflammatory response (SIR) markers (neutrophil-lymphocyte ratio/ platelet-lymphocyte ratio) in patients with severe preeclampsia (PE) of healthy pregnant and non-pregnant women.*

Material and methods: *Hematological parameters including MPV, and SIR markers [neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR)] were compered between the between three groups comprising of women with severe PE, healthy pregnant women and healthy non-pregnant women.*

Results: *MPV and PLR did not show statistically significant differences between the three groups (p=0.081, p=0.098). NLR showed a statistically significant difference between the three groups (p=0.000). NLR values of patients with severe PE were statistically significantly higher than healthy non-pregnant women (p=0.000). No statistically significant difference was found between patients with severe PE and healthy pregnant women (p=0.721). The cut-off value of the leukocyte number for severe PE was 7.6 x 10^3/ml, with 76.7% sensitivity and 60.6% specificity. The cut-off value of neutrophil number was 6.4 x 10^3/ml for the group with severe PE, with 76.7% sensitivity and 69% specificity.*

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Conclusions: *Our results showed that MPV level did not differ among patients with severe PE, healthy pregnant women and non-pregnant women. NLR cannot be used to identify patients with severe PE. PLR measured before termination of pregnancy is not an effective marker for severe PE, either.*

Key words **leukocytes** / **mean platelet volume** / **neutrophils** / **neutrophil-lymphocyte ratio** / **platelet-lymphocyte ratio** / **preeclampsia** /

Streszczenie

Celem badania było porównanie zmian w ilości leukocytów, neutrofilów, limfocytów, średniej objętości płytek krwi (MPV) a układową odpowiedzią zapalną (SIR)wyrażoną za pomocą markerów (wskaźnik neutrofile/limfocyty oraz wskaźnik płytki krwi/limfocyty) u pacjentek z ciężką preeklampsją (PE), u zdrowych ciężarnych i u niecięzarnych kobiet.

Materiał i metoda: *Parametry hematologiczne oraz MPV i markery SIR (wskaźnik neutrofile/limfocyty NRL oraz wskaźnik płytki krwi/limfocyty PLR) zostały porównane między trzema grupami pacjentek: z ciężką preeklampsją, zdrowymi ciężarnymi i zdrowymi niecięzarnymi kobietami.*

Wyniki: *MPV oraz PLR nie wykazały istotnych różnic pomiędzy porównywanymi grupami (p=0,081, p=0,098). NRL różniło się istotnie w badanych grupach (p=0,000). Wartości NRL były istotnie wyższe w grupie z ciężką PE niż u zdrowych niecięzarnych kobiet (p=0,000). Nie znaleziono istotnej różnicy pomiędzy pacjentkami z ciężką PE a zdrowymi ciężarnymi (p=0,721). Punkt odcięcia liczby leukocytów dla ciężkiej PE wynosił 7,6x10^3/ml, przy 76,7% czułości i 60,6% specyficzności. Punkt odcięcia liczby neutrofili dla ciężkiej PE wynosił 6,4x10^3/ml, przy 76,7% czułości i 69% specyficzności.*

Wnioski: *Nasze wyniki pokazują, że poziom MPV nie różni się pomiędzy pacjentkami z ciężką preeklampsją, zdrowymi ciężarnymi i zdrowymi niecięzarnymi kobietami. NRL nie może być wykorzystany do identyfikacji pacjentek z ciężką PE. Również pomiar PRL przed zakończeniem ciąży nie jest skutecznym markerem ciężkiej PE.*

Słowa kluczowe: **leukocyty** / **średnia objętość płytek krwi** / **neutrofile** / **wskaźnik neutrofile-limfocyty** / **wskaźnik płytki krwi-limfocyty** / **preeklampsja** /

List of abbreviations:

PE, preeclampsia; **MPV,** mean platelet volume; **SIR,** systemic inflammatory response **NLR,** neutrophil-lymphocyte ratio**; PLR,** platelet-lymphocyte ratio; **g/dL,** GramsPerDeciLiter; **fL,** FemtoLiter; **/uL,** PerMicroLiter; **10^3/uL,** ThousandPerMicroLiter; **Hb,** Hemoglobin; **ROC,** Receiver operating characteristic

Introduction

Preeclampsia (PE) is a pregnancy-specific hypertensive disorder which occurs in 3-5% of all gestations. Hypertension and proteinuria are the two basic criteria of the disease, and PE cannot be completely treated before the birth takes place. PE is generally related with maternal and fetal morbidity. According to the ACOG report from 2012, PE has been the leading cause of maternal and infant illness and death in the United States [1].

Balance of angiogenesis and systemic inflammation is believed to play a role in etiopathogenesis of PE [2]. The exact etiology of the disease and ways of distinguishing between preeclamptic and normal pregnancies by using markers associated with these factors remain to be determined. Systemic inflammation increases in normal pregnancies. It is believed that PE develops due to a dysregulation of TH1 and TH2 type inflammatory responses [3]. Ramma et al., reported an exaggerated maternal vascular inflammatory response formed in PE, and an important role of neutrophils in that inflammatory response [4]. Due to systemic inflammation in PE, the neutrophil count is higher in PE subjects as compared to healthy pregnant women. Clark et al., demonstrated a high number of proinflammatory cytokines such as IL 6 in severe PE cases in whom the arterial blood pressure was higher, as well as that fact that the end organ damage was indicated by clinical and laboratory parameters [5].

In the recent years, the neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR), which can be easily obtained from a complete blood count, have been used as SIR markers. NLR has a diagnostic value in pathologies where inflammatory responses occur, i.e. diabetes mellitus, coronary artery disease, ulcerative colitis and inflammatory arthritis [6, 7]. PLR is regarded as a more sensitive marker of inflammation and described as a prognostic factor for breast, ovarian and colorectal cancers [8].

Thrombocytopenia is one of the diagnostic criteria of severe preeclampsia [9]. Turgut et al., reported platelet participation in some processes like endothelial damage, angiogenesis and hypoxia [10]. Mean platelet volume (MPV) demonstrates an increase in low-level inflammatory diseases, including cardio-cerebrovascular diseases characterized by microthrombosis formation. However, in high-level inflammatory responses such as active rheumatoid arthritis, familial Mediterranean fever attacks and chronic obstructive pulmonary disease, the MPV level is low [11].

Objectives

The literature on the relationship between MPV and PE offers controversial and conflicting reports [12, 13]. NLR and PLR values in severe PE remain to be fully elucidated. In this study, we aimed to examine the values of leukocytes, neutrophils, lymphocytes, MPV, NLR and PLR in patients with severe PE and compare them with normal healthy pregnant women and healthy non-pregnant women.

Material and methods

Between February 1, 2011 and February 1, 2013, a total of 1349 patients underwent caesarean sections at the Obstetrics and Gynecology Department, Düzce University. Pregnant women who underwent emergency caesarean section in the 3rd trimester due to severe PE, healthy pregnant women undergoing elective caesarean at term (≥37 weeks), and healthy non-pregnant women having bilateral tubal ligation under elective conditions, were enrolled in the study. As ACOG announced in 2002, patients were diagnosed with severe PE, if they had one or more of the following clinical or laboratory symptoms: i) detection of 160 mmHg or higher level of systolic and 110 mmHg or higher level of diastolic in the two measurements carried out during bed rest with 6-hour intervals, ii) presence of 5gr or more proteinuria in 24-hour urine, or presence of +3 g; proteinuria in two spot urines taken with 4-hour intervals, iii) less than 500 mL urine within 24 hours, iv) cerebral or visual symptoms, v) pulmonary edema or cyanosis, vi) epigastric or right upper quadrant pain, vii) liver dysfunctions, viii) thrombocytopenia, vix) presence of fetal growth retardation [9]. All patients provided their written informed consents before the procedures. Düzce University School of Medicine Ethics Committee for Non-invasive Clinical Researches granted approval for the present study (Decision No.: 2013/390). All demographic data and laboratory analyses were obtained by means of retrospective analysis of medical records of Düzce University Hospital.

All study participants were Caucasian women of reproductive age (16-50 years), and residents of Düzce. Due to exposure potential of hematological parameters the exclusion criteria were: non-reproductive age; borderline ovarian tumor/myoma uteri detected intra-operatively; chronic or acute inflammatory diseases; smoking; autoimmune, infectious, or systemic diseases, hepatitis and intrahepatic cholestasis of pregnancy; use of corticosteroids during pregnancy; diagnosis of gynecological or non-gynecological malignancy. Also, non-vertex presentations, multiple pregnancy, regular contractions, active labor and opened membranes, cervical dilation and effacement were reasons for exclusion. The control group included 35 healthy women undergoing laparoscopic tubal ligation.

A total of 101 patients compliant with the inclusion criteria (30 patients with severe PE, 36 healthy pregnant women without medical complications and 35 healthy non-pregnant women) were included in the study. Neurological symptoms of the patients with convulsions, headaches and vision problems were regarded positive. Gastrointestinal symptoms of the patients with right upper quadrant pain, epigastric pain, epigastric discomfort and nausea/vomiting were considered positive. Patients suffering from cyanosis, dyspnea, pulmonary edema and cardiac failure were regarded to have positive cardiopulmonary complications. Highest systolic and diastolic values were recorded according to the arterial blood pressure values measured twice (at 6-hour intervals) before the caesarean sections both, for patients with severe PE and healthy pregnant women undergoing elective caesarean. As the patients in the severe PE group were urgently taken into caesarean section, 24-hour urine values of 16 patients could not be measured.

In the present study, all of the 101 patients gave 5-7 mL blood samples before the caesarean delivery and the laparoscopic tubal ligation, and samples were filled in sterile EDTA tubes to avoid blood clotting. Hematological parameters were automatically calculated with Abbott CELL DYN 3700 blood count equipment within 30 min. The number of blood elements was denominated in 10^3/uL; the number of leukocytes (10^3/uL), neutrophils (10^3/uL), lymphocytes (10^3/uL), and platelets (10^3/uL) was recorded. NLR and PLR ratio was assessed by using these parameters. Also, hemoglobin (Hb) levels (g/dL) and mean platelet volumes (fL) (MPV) of the patients were determined by means of that analysis. While Hb level was denominated in g/dL, MPV value was denominated in fL.

Statistical method

Average values, standard deviation, and rate and frequency values were used in the descriptive statistics of the data. Distribution of the data was analyzed with the Kolmogorov-Smirnov Test. One-way ANOVA test was used for comparing the quantitative data of the three groups. The Tukey test was used in conjunction with ANOVA to find means that were significantly different from each other. Analyses were performed with the SPSS v19.0 program. $P < 0.05$ was regarded as statistically significant.

Results

In the present study, the average age was 28.00+/-6.28 for patients with severe PE, 29.33+/-4.70 for healthy pregnant women, and 36.29+/-6.68 for non-pregnant controls. No significant difference was documented between the severe PE patients and healthy pregnant women in terms of average age (p=1.000). However, average age of controls was statistically higher than patients with severe PE (p=0.000), and healthy pregnant women (p=0.000). The gestational week at caesarean section was statistically significantly earlier in patients with severe PE (p=0.000). Table I indicates the mean systolic/diastolic arterial blood pressure values, average neonatal birth weight, Apgar scores at 1 and 5 minutes, aspartate transaminase (AST)/alanine transaminase (ALT) levels, protein amount in 24-hour urine and protein positivity in spot urine, as well as age and gestational week.

There were no statistically significant differences in Hb values between the groups of severe PE patients, healthy pregnant women and controls (p=0.490) (Table II). Lymphocyte count in the severe PE group was higher. However, a comparison between patients with severe PE and healthy pregnant and non-pregnant women, revealed the difference to be statistically insignificant (p=0.072) (Table II).

The leukocyte number was reported to differentiate significantly in patients with severe PE, healthy pregnant women and controls (p=0.000) (Table II). The leukocyte number in patients with severe PE was significantly higher than both, of healthy pregnant women (p= 0.012) and controls (p=0.000) (Table III). In addition, the leukocyte number in healthy pregnant

Table I. Patient characteristics.

	Severe preeclampsia (N=30 / 29.7%)	Healthy pregnant women (N=36 / 35.6%)	Controls (N=35 / 34.6%)
Age[q]	28.00+/-6.28	29.33+/-4.70	36.29+/-6.68
Gestational week [q]	33.91+/-2.91	38.11+/-0.54	
Systolic BP. (mmHg) [q]	166.63+/-21.70	113.58+/-12.23	
Diastolic BP. (mmHg) [q]	106.57+/-12.56	70.81+/-10.04	
Birth Weight(gr.) [q]	1987.90+/-664.71	3238.89+/-395.77	
APGAR 1[q]	7.10+/-1.64	8.14+/-0.79	
APGAR 5[q]	8.77+/-1.79	9.36+/-1.35	
AST(iu/ml)[q]	63.16+/-131.10	17.44+/-5.97	
ALT(iu/ml)[q]	53.40+/-114.54	11.27+/-5.98	
Protein in 24hour(gr.) [q]	3.42+/-4.07	Not measured	
Spot urine protein (+)[q]	0.88+/-1.28(+)	0	
SSS symptom (+)	10/9.9	0	
GIS symptom (+)	5/4.9	0	
Cardiopul. Sympt. (+)	1/0.9	0	

q, mean +/-standard deviation; N, number of the patients; BP, blood pressure; AST, Aspartate AminoTransferase; ALT, Alanine AminoTransferase; +, positivity; Cardiopul. Sympt., cardiopulmonary symptoms; mmHg, millimeters of mercury; iu/ml, İnternational Units Per milliliter; gr., gram.

Table II. Comparison of hematological parameters and NLR -PLR values.

	Severe preeclampsia (N=30 / 29.7%)	Healthy pregnant (N=36 / 35.6%)	Controls (N=35 / 34.6%)	P value*
Hb[q]	11.99+/-1.83	11.55+/-1.57	11.97+/-1.78	0.490
WBC[q]	11028.33+/-2939.79	9413.89+/-1708.15	7244.86+/-2001.86	***0.000***
Neutrophil[q]	8.29+/-2.75	6.73+/-1.50	4.44+/-1.54	***0.000***
Lymph. [q]	2.47+/-1.47	1.92+/-0.64	2.24+/-0.67	0.072
Platelet[q]	224570.00+/-86230.29	229222.22+/-57527.68	284171.43+/-66583.201	***0.001***
MPV[q]	9.34+/-1.40	9.04+/-0.87	8.56+/-1.77	0.081
NLR[q]	4.04+/-2.03	3.76+/-1.28	2.10+/-0.85	***0.000***
PLR[q]	109.81+/-54.99	127.41+/-41.17	124.28+/-45.53	0.098

q, mean +/-standard deviation; N, number of patients; Hb, hemoglobin; WBC, white blood cell; Lymph., lymphocyte; MPV, mean platelet volume; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio.
* P < 0.05 value was regarded as statistically significant.

Table III. Bilateral comparison of MPV, NLR and PLR values between the groups.

	Severe preeclampsia (N=30 / 29.7%)	Healthy pregnants (N=36 / 35.6%)	Controls (N=35 / 34.6%)	P value a	P value b	P value c
Hb	11.99+/-1.83	11.55+/-1.57	11.97+/-1.78	0.558	0.562	0.999
WBC	11028.33+/-2939.79	9413.89+/-1708.15	7244.86+/-2001.86	***0.012***	***0.000***	***0.000***
Neutr.	8.29+/-2.75	6.73+/-1.50	4.44+/-1.54	***0.005***	***0.000***	***0.000***
Lymp.	2.47+/-1.47	1.92+/-0.64	2.24+/-0.67	0.061	0.353	0.602
Plt.	224570.00+/-86230.29	229222.22+/-57527.68	284171.43+/-66583.201	0.961	***0.004***	***0.003***
MPV	9.34+/-1.40	9.04+/-0.87	8.56+/-1.77	0.659	0.328	0.070
NLR	4.04+/-2.03	3.76+/-1.28	2.10+/-0.85	0.721	***0.000***	***0.000***
PLR	109.81+/-54.99	127.41+/-41.17	124.28+/-45.53	0.257	0.838	0.092

q, mean +/-standard deviation; N, number of patients; Hb, hemoglobin; WBC, white blood cell; Neutr., Neutrophil; Lymph., lymphocyte; Plt., platelet; MPV, mean platelet volume; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio.
* P < 0.05 value was regarded as statistically significant.
a: Comparison between patients with severe preeclampsia and healthy pregnant women.
b: Comparison between healthy pregnant women and controls.
c: Comparison between patients with severe preeclampsia and controls.

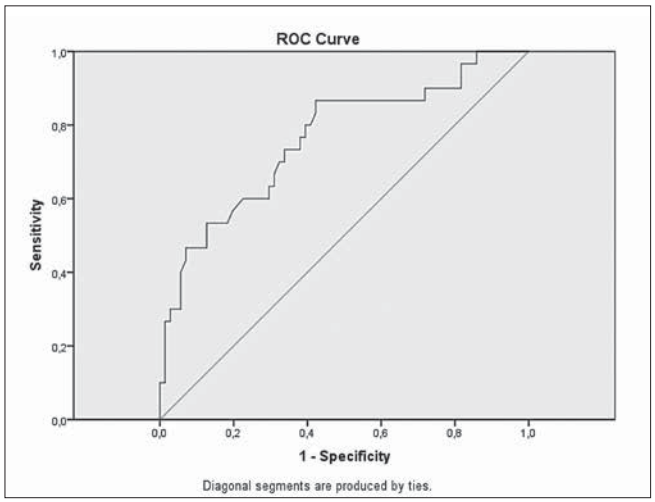

Figure 1. Correlation between leukocyte number and severe PE.

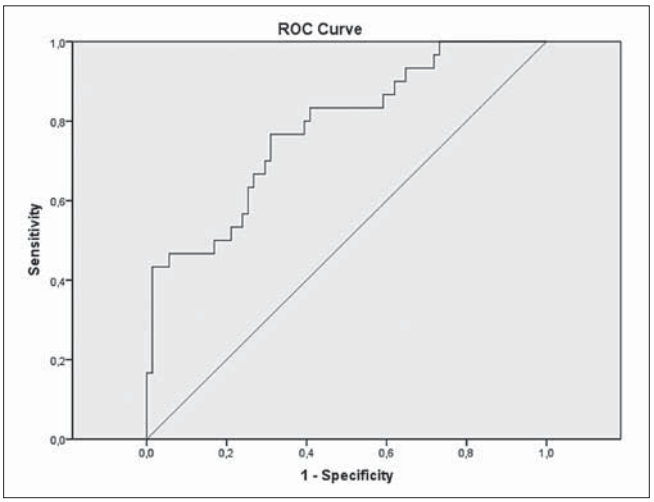

Figure 2. Correlation between neutrophil number and severe PE.

women was statistically higher as compared to control subjects (p=0.000) (Table III).The number of neutrophils showed a statistical alternation in severe PE patients, healthy pregnant women, and controls (p=0.000) (Table II). The paired comparisons of the groups indicated that the neutrophil number was higher in severe PE patients than controls (p=0.005), and the neutrophil number of healthy pregnant women was higher than controls (p=0.000) (Table III). The performance of leukocyte number measurement to identify women with severe PE was shown in the Receiver Operating Characteristic (ROC) curve (Figure 1). The ROC curve revealed that the continuum of sensitivity and specificity encountered as the cutoff point varied. The optimal combination observed at the shoulder of the curve at the top left was sensitivity = 76.7% and specificity = 60.6%, with a cutoff point of 7.6 x 10^3/ml. The performance of neutrophil number to detect women with severe PE was shown in the ROC curve (Figure 2). The ROC curve revealed that the continuum of sensitivity and specificity encountered as the cutoff point varied. The optimal combination observed at the shoulder of the curve at the top left was sensitivity = 76.7% and specificity = 69%, with a cutoff point of 6.4 x 10^3/ml.

A statistically significant difference in platelet number between patients with severe PE, healthy pregnant women, and controls (p=0.001) was observed (Table 2). However, the difference was not statistically significant between patients with severe PE and healthy pregnant women (p=0.961) (Table III). Platelet number was significantly lower in controls as compared to severe PE patients (p=0.004), and also healthy pregnant women (p=0.003) (Table III).

If severe PE patients, healthy pregnant women and controls were analyzed together, the MPV values did not show a statistically significant difference between the three groups (p=0.081) (Table II). Bilateral comparisons were also conducted for these groups. No statistically significant differences in the MPV values between severe PE patients and healthy pregnant women; between severe PE patients and controls; and between healthy pregnant women and controls (p=0.659, p=0.070, p=0.328, respectively) were noted (Table III).

When patients with severe PE were analyzed together with the healthy pregnant women and controls, the NLR values showed a statistically significant difference between the three groups (p=0.000) (Table II). The NLR values of severe PE patients were statistically significantly higher than controls (p=0.000). Likewise, the NLR values were significantly higher in healthy pregnant women as compared to controls (p=0.000) (Table III). However, no statistically significant change was documented in NLR values between severe PE patients and healthy pregnant women (p=0.721) (Table III).

When the PLR values of the three groups were compared, there was no statistically significant difference between the three groups (p=0.098) (Table II). The situation was the same for the paired comparisons. There were no significant differences between patients with severe PE and healthy pregnant women (p=0.257); or between patients with severe PE and controls (p=0,092), or between healthy pregnant women and controls (p=0.838) (Table III).

Discussion

Edelstam et al., reported that the Hb level decreased, leukocyte number increased and the number of platelets reduced during the third trimester in subjects with healthy pregnancy as compared to non-pregnant women [14]. The present study demonstrated that the leukocyte number in healthy pregnant women was higher than in non-pregnant women (p=0.000), and the leukocyte number of patients with severe PE was higher than healthy pregnant women (p=0.012). These results are consistent with the results obtained by Canzoneri et al., in a study carried out in PE patients. In that comprehensive study, the significant difference in leukocyte number resulted from the increase in the number of neutrophils [15]. Our study indicated that the number of neutrophils, like the number of leukocytes, was higher in healthy pregnant than in non-pregnant women (p=0.000), and there were more neutrophils in circulation in patients with severe PE as compared to the normal pregnant women (p=0.005). Järemo et al,. claimed the neutrophil number in PE patients to be similar to neutrophil number in normal pregnant women [16]. However, the present study examined only cases of severe PE, where advanced SIR developed. In this study, the cut-off value of neutrophils for severe PE patients was 6.4 x 10^3/ml ,with 76.7% sensitivity and 69% specificity. The cut-off value of leukocytes

was 7.6 x 10^3/ml, with 76.7% sensitivity and 60.6% specificity.

Ceyhan et al., found no differences in the platelet numbers between women with severe PE and healthy pregnant women [17]. Canzoneri et al., analyzing the hematological parameters of patients with severe PE, concluded that the platelet level was lower and the Hb level was higher in patients with severe PE as compared to normal healthy pregnant women [15]. Many hematological parameters in adults, such as Hb and platelet number, are influenced by geographic location, nutritional properties and racial features [16]. In the present study, the Hb level did not show a difference between the three groups (p=0.490). There was no difference in the platelet number between healthy pregnant women and patients with severe PE (p=0.961). These findings might have resulted from variations of the hematological parameters stated above. The current study included pregnant women with homogenous characteristics; they were Caucasian, residents of the same province and practically age-peers.

Platelet activation increases in normal pregnant women as compared to non-pregnant subjects. Kuşçu et al., and Stubbs et al., demonstrated that deterioration of platelet characteristics is the result of the inflammatory process in PE characterized by primary endothelial damage [19, 20]. MPV is a parameter providing information on platelet activation and velocity. MPV can increase or decrease, depending on the severity of the inflammatory response [11]. Although MPV value is anticipated to be higher in severe PE disease where severe SIR occurred, the present study showed that MPV value was not different in groups of patients with severe PE, healthy pregnants and controls (p=0.081). Previous studies have yielded conflicting results regarding the association between MPV and PE. Some studies report that MPV goes up in PE even before there is a change in the platelet number, and MPV is also a significant indicator in PE [12, 21]. In line with the current study, Altınbaş et al. [13], and Ceyhan et al. [17], indicated that MPV did not change in severe PE. Ceyhan et al., may be right in their claim that such variable results can be due lack of unified blood count equipment and sampling methods for venous blood [17].

Wieczorek et al., demonstrated that changes of neutrophil CD11b and CD62 expression indicate increased activity of these cells in women with pregnancy-induced hypertension in 2001 [22]. Ramma et al., obtained two important results from their recent comprehensive study in 2012. The increased neutrophil activity and the release of antiangiogenic factors occur in severe PE. The antiangiogenic factors not developing in normal pregnancies, such as sFlt-1 and sEng, increase significantly only in patients with severe PE in whom exaggerated SIR occurs [4]. Secretion of alpha-defensins and calprotection is an indicator of neutrophil deregulation in PE. Alfa-defensins and calprotection, the markers of neutrophil activation, have a correlation with the IL-6 level in PE [4]. It can be understood from these results that neutrophil activation, comorbid to severe inflammation in PE, develops simultaneously with the clinical symptoms in a patient [4].

There are several studies on the relation between NLR and PLR values, which are the peripheral markers of severe SIR, and the level of the primary disease in ulcerative colitis, diabetes, pancreatitis, and ischemic processes [6, 7, 23, 24], but NLR and PLR values in severe PE need to be investigated. Lymphocytes provide the initial physiological response to stress, and then mediate the inflammatory process in adults. Neutrophil was discovered to have a role in increased NLR, a marker of SIR in healthy adults, and that the lymphocyte number remained static [24]. The present study and the study of Ramma et al., along with the study of Canzoneri et al., indicated that lymphocyte number did not change significantly in patients with severe PE [4,15]. In normal pregnancies there is a deviation towards Th2 type of the immune response. This deviation protects the fetus from the cytotoxic effects of TH1 type immune response such as interleukin IL-2, IL-12, interferon gamma, and tumor necrosis factor α (TNF). Wegmann et al., reported that TH1 type reactions are dominant in the systemic inflammation of PE [26]. In light of this information, this study explored the variation of NLR values between patients with severe PE, healthy pregnant women and healthy non-pregnant women. NLR value was found to be higher in patients with severe PE as compared to non-pregnant women (p=0.000). No difference was found in terms of NLR values in patients with severe PE and normal healthy pregnant women (p=0.721). Both, this study and the study of Canzoneri et al. [15], found the lymphocyte number to be higher in patients with severe PE than healthy pregnant women, but the difference was not statistically significant. That increment might be reflected in the NLR values of patients with severe PE.

High level secretion of proinflammatory mediators such as IL-1, IL-2 and IL-6 leads to thrombocytosis [26, 27]. The ratio of platelets to lymphocytes (PLR), playing a role in cytokine-dependent immune response, is known to increase in severe ischemia and end-organ damage [23, 28]. The authors of this study expected the PLR ratio to increase in PE due to generalized vasospasm, end-organ damage and severe inflammation. Nevertheless, PLR showed no statistical difference between severe PE patients, healthy pregnant women and controls (p=0.092). That result might have derived from the fact that the platelet and lymphocyte numbers did not show a statistically significant difference between the groups of patients with severe PE, healthy pregnant women and healthy non-pregnant women. Similarly to our findings, Laskin et al., reported that the platelet count should not be used as an isolated factor to guide care because of its poor sensitivity in women with PE and normal healthy pregnant women [29].

Conclusions

Our results showed that neutrophil and leukocyte numbers differ among patients with severe PE, healthy pregnant women and non-pregnant women, but MPV level did not. Elevated NLR was found in patients with severe PE, but there was no difference in terms of NLR between patients with severe PE and healthy pregnant women. NLR cannot be used to identify patients with severe PE. PLR is an excellent marker of SIR in patients with end-organ damage, while PLR measured before termination of pregnancy is not an effective marker for severe PE. More comprehensive studies are needed with homogeneous patient populations in order to determine the possibility of routine use of leukocyte subtypes, MPV, NLR and PLR values as useful and cost-effective markers in patients with severe PE to prove the development of severe inflammation, at either molecular or cellular level.

Authors' Contribution

1. Ali Yavuzcan – study design, methodology, interpretation of results and writing of the text – corressponding author.
2. Mete Çağlar – study design and methodology.
3. Yusuf Üstün – statistical analysis.
4. Serdar Dilbaz – Study design
5. İsmail Özdemir – Scientific control of the text.
6. Elif Yıldız – data collection.
7. Sıtkı Özbilgeç – data collection.
8. Selahattin Kumru – scientific control of the text.

Authors' statement

- This article has not been previously published anywhere. This article is not currently under consideration for publication elsewhere.
- The authors declare no financial interests.
- Any case of scientific unreliability, if detected in this text, the Polish Gynecology will inform our institutions employing us Turkish Ministry of Health and Turkish Society of Obstetrics and Gynecology. We are members of these institutions.
- This agreement has been signed by all of the authors who contributed to this article.

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