Research Article / *Araştırma Makalesi*

Ege Journal of Medicine / *Ege Tıp Dergisi* 2025; 64 (2): 324-329

The role of biochemical markers in predicting pre-eclampsia

Preeklampsiyi öngörmede biyokimyasal belirteçlerin rolü

Ufuk Atlıhan[1] Begüm Ertan[2] Mehmet Emre Peker[1] Can Ata[3]
Onur Yavuz [4] Hüseyin Aytuğ Avşar [5] Alper İleri [6] Tevfik Berk Bildacı[7]
Selçuk Erkılınç[7]

[1]Manisa Merkezefendi State Hospital, Manisa, Türkiye
[2] Sandıklı State Hospital, Afyonkarahisar, Türkiye
[3]Buca Seyfi Demirsoy Training and Research Hospital Izmir, Türkiye
[4]Dokuz Eylul University School of Medicine, Izmir, Türkiye
[5] Tınaztepe Galen University, Izmir, Türkiye
[6] University Of Health Sciences, İzmir Tepecik Health Research Center, Izmir, Türkiye
[7] İzmir Democracy University Faculty of Medicine, Izmir, Türkiye

ABSTRACT

Aim: The aim of our study was to evaluate the role of biochemical markers in predicting preeclampsia.

Materials and Methods: 7240 women whose pregnancy follow-ups and deliveries were carried out by us between March 2018 and March 2024 were retrospectively screened. Patients in the study group consisted of 102 women diagnosed with preeclampsia at <34 weeks of gestation, and patients in the control group consisted of 118 women who gave birth at ≥37 weeks of gestation. Demographic characteristics and obstetric and biochemical outcomes of the two groups were compared with each other.

Results: The body mass index (BMI) value was significantly higher in the preeclampsia group compared with the controls group (p=0.016). The birth weight value was significantly lower in the preeclampsia group compared with the controls group (p<0.001). The gestational week at delivery was significantly lower in the preeclampsia group compared with the controls group (p<0.001). Lymphocyte and platelet counts were significantly lower in the preeclampsia group compared with the controls group (p<0.001 and p<0.001, respectively). NLR and SII value were significantly higher in the preeclampsia group compared with the controls group (p=0.022, p<0.001, respectively).

Conclusion: Our study reveals important clinical and laboratory differences in preeclamptic pregnancies. Increased inflammatory markers were found to be a feature of preeclamptic pregnancies and are consistent with the existing literature. Our findings can be used to determine early diagnosis and comprehensive management strategies to minimize the risks associated with preeclampsia.

Keywords: NLR, PLR, Pregnancy, Preeclampsia, SII, SIRI

ÖZ

Amaç: *Çalışmamızın amacı preeklampsiyi öngörmede biyokimyasal belirteçlerin rolünü değerlendirmektir.*
Gereç ve Yöntem: *Mart 2018-2024 tarihleri arasında gebelik takipleri ve doğumları tarafımızca gerçekleştirilen 7240 kadın retrospektif olarak tarandı.*

Corresponding author: Ufuk Atlıhan
Manisa Merkezefendi State Hospital, Manisa, Türkiye
E-mail: *cfl_ufuk@hotmail.com*
Application date: 27.12.2024 Accepted: 10.03.2025

Çalışma grubundaki hastalar <34 gebelik haftasında preeklampsi tanısı konulan 102 kadından, kontrol grubundaki hastalar ise ≥37 gebelik haftasında doğum yapan 118 kadından oluştu. İki grubun demografik özellikleri, obstetrik ve biyokimyasal sonuçları birbirleriyle karşılaştırıldı.
Bulgular: *Preeklampsi grubunda vücut kitle indeksi kontrol grubuna göre anlamlı yüksek saptandı (p=0.016). Doğum ağırlığı preeklampsi grubunda kontrol grubuna göre anlamlı düşük saptandı (p<0.001). Doğumdaki gebelik haftası preeklampsi grubunda kontrol grubuna göre anlamlı düşük saptandı (p<0.001). Lenfosit ve trombosit sayıları preeklampsi grubunda kontrol grubuna göre anlamlı düşük saptandı (p<0.001 ve p<0.001, sırasıyla). NLR ve SII değeri preeklampsi grubunda kontrol grubuna göre anlamlı yüksek saptandı (p=0.022, p<0.001, sırasıyla).*
Sonuç: *Çalışmamız, preeklamptik gebelerde önemli klinik ve laboratuvar farklılıklarını ortaya koymaktadır. Artmış inflamatuar belirteçlerin preeklamptik gebeliklerin bir özelliği olduğu bulunmuştur ve mevcut literatürle tutarlıdır. Bulgularımız, preeklampsi ile ilişkili riskleri en aza indirmek için erken tanı ve kapsamlı yönetim stratejilerini belirlemek için kullanılabilir.*
Anahtar Sözcükler: *Gebelik, NLR, PLR, Preeklampsi, SII, SIRI*

INTRODUCTION

Preeclampsia is a pregnancy-specific health condition that is observed in approximately 6-8% of women, may recur in the next pregnancy, occurs after the 20th week of gestation and may significantly affect maternal and fetal health (1). Predicting this condition is very important for maternal and fetal health and is still being researched and there is no definitive method yet. Preeclampsia is characterized by widespread endothelial dysfunction in the body, often diagnosed by new-onset hypertension and concomitant disorders of various end organ disorders with or without new-onset proteinuria, and even seizures, and can have fatal consequences (2). The definitive treatment is delivery and if this delivery has to be preterm, it increases prematurity, perinatal mortality and morbidity. The etiology and pathogenesis of pre-eclampsia are considered multifactorial. Major pathophysiological processes include alterations in hemostatic-system, such as the endothelial-cell-damage, platelet activation and enhanced intravascular thrombin generation (3). Hyperactivation of inflammatory and immunologic responses in preeclampsia leads to a marked increase in the number of neutrophils and a change in neutrophils towards superoxide production leading to endothelial damage and dysfunction (4). Recently, there has been increased interest in predictive biomarkers for preeclampsia. An effective predictive test would facilitate early diagnosis and targeted treatment and contribute to the timing of delivery. There are many difficulties in the prevention and management of pre-eclampsia. Research has shown that the neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR), as well as the ratio between blood and blood products, may be promising in diagnosing the prognosis of inflammation of chronic low-level associated diseases and in identifying cell subtypes (5–9). Leukocyte count is higher in pregnant women with PE compared to normal pregnant women, mainly due to an increase in neutrophil count as opposed to a decrease in leukocyte count (10). As a result of these changes, the neutrophil/lymphocyte ratio (NLR) is expected to increase in PE compared to normal pregnancies (10,11). Endothelial dysfunction in preeclampsia leads to increased platelet consumption in the maternal bloodstream and uncontrolled intravascular platelet activation. Some studies have reported a significant decrease in platelet count and an increase in mean platelet volume (MPV) and platelet distribution width (PDW) in pregnant women with preeclampsia (12). Some studies claim that platelet/lymphocyte ratio (PLR) and PDW may predict preeclampsia (13,14). The aim of our study was to evaluate the role of biochemical markers in predicting preeclampsia.

MATERIALS AND METHODS

The present study had a retrospective case-control design following the Principles of the Helsinki Declaration. Informed consent documents were received from all patients. The study received approval from our hospital's Ethics Committee (Date: 25/12/2024, Number: 2024/373). In our study, 7240 women whose pregnancy follow-ups and deliveries were carried out by us between March 2018 and March 2024 were retrospectively screened. The patients in the study group consisted of 102 women aged 18-45 years with a singleton pregnancy who were diagnosed with preeclampsia at <34 weeks of

gestation. The patients in the control group consisted of 118 women aged 18-45 years who had no complications during pregnancy, had a singleton pregnancy, and gave birth at ≥37 weeks of gestation. Women with a history of assisted reproductive technologies, body mass index (BMI) >30kg/m2 at the time of pregnancy diagnosis, birth with chromosomal anomalies, history of preterm birth, history of complicated birth, multiple pregnancy, and history of chronic disease and immunosuppressive treatment for any reason were excluded. For the preeclampsia diagnosis, females having hypertension must also exhibit proteinuria, which is defined as the presence of minimum 300-mg of protein in a 24-hour urine collection. Patients who satisfy the requirements for hypertension associated with preeclampsia but do not exhibit proteinuria or any severe additional complications are diagnosed with GHT (15). Demographic characteristics and obstetric and biochemical outcomes of the two groups were compared with each other. Blood tests of all patients performed at first trimester were evaluated retrospectively. NLR, PLR, MLR, SII, and SIRI values of all patients were analyzed. SII was calculated using the (neutrophil×platelet)/lymphocyte formula, and SIRI was calculated using the (neutrophil×monocyte)/lymphocyte formula (16,17).

Statistical Analysis

Statistical analysis was carried out by employing the-SPSS 26.0 (IBM-Inc-Chicago-IL-USA). The distribution normality was measured with the Kolmogorov Smirnov Test. The quantitative data of the patients were reported as mean ± Standard Deviation (SD) (minimum-maximum). The Mann-Whitney U test was used in the comparison of groups. The results were evaluated at a 95% Confidence-Interval (CI). The p-value, <0.05, was regarded as statistically significant.

RESULTS

The BMI value was significantly higher in the preeclampsia group compared with the controls group (p=0.016). The birth weight value was significantly lower in the preeclampsia group compared with the controls group (p<0.001). The gestational week at delivery was significantly lower in the preeclampsia group compared with the controls group (p<0.001) (Table-1).

Lymphocyte and platelet counts was significantly lower in the preeclampsia group compared with the controls group (p<0.001 and p<0.001, respectively). NLR was significantly higher in the preeclampsia group compared with the controls group (p=0.022). SII was significantly higher in the preeclampsia group compared with the controls group (p<0.001) (Table-2).

Table-1. Comparison of demographic and obstetric data according to the presence of pre-eclampsia

	Preeclampsia n=102	**Controls n=118**	**p***
	Mean±SD		
Age (years)	29.5±3.8	28.6±3.7	0.82
BMI (kg/m^2)	24.2±3.6	23.3±3.5	0.016
Smoking, n (%)	9 (8.8%)	10 (8.4%)	0.68
Gravidity	2 (1-3)	2 (1-4)	0.78
Parity	2 (1-3)	2 (1-3)	0.90
Birth weight (g)	2720±280	3380±430	<0.001
Gestational week	36.4±1.2	39.1±1.1	<0.001

* Mannn-Whitney U test, BMI: Body mass index

Table-2. Comparison of biochemical parameters according to the presence of preeclampsia

	Preeclampsia n=102	Controls n=118	p*
	mean ± SD		
Neutrophil (10^3/μL)	7.1±2.2	6.8±2.1	0.42
Lymphocyte (10^3/μL)	1.82±0.54	2.17±0.66	<0.001
Platelet (10^3/μL)	211.3±52.5	249.4±58.6	<0.001
NLR	3.88±1.16	3.12±1.24	0.022
PLR	116.2±54.4	115.8±53.8	0.76
MLR	0.19±0.04	0.18±0.05	0.68
MPV (fL)	9.2±1.28	9.4±1.22	0.46
SII	832.3±116.4	720.3±108.6	<0.001
SIRI	390.8±66.8	376.6±66.8	0.72

* Mann-Whitney U test, NLR: Neutrophil/lymphocyte-ratio, PLR: Platelet/lymphocyte-ratio, MLR: Monocyte/lymphocyte ratio, MPV: Mean platelet volume, SII: Systemic immuno-inflammation-index, SIRI: Systemic inflammatory response-index

DISCUSSION

Although there are many studies on pre-eclampsia in the literature, diagnostic tests to predict pre-eclampsia are limited. In our study, BMI values were significantly higher in the preeclampsia group compared to the control group, while birth weight and gestational age at birth were significantly lower. In addition, lymphocyte and platelet counts showed a significant lower in the preeclampsia group, while NLR and SII values showed a significant higher.

BMI was significantly higher in the preeclampsia group than in the control group, indicating that increased BMI may be a contributing factor to the development of preeclampsia. In the study conducted by Robillard et al., it was revealed that high BMI showed a linear relationship with late-onset preeclampsia in particular. It was also emphasized that BMI was an independent risk factor (18). The study by Sohlberg et al. showed that high BMI significantly increases the risk of preeclampsia (19). Our study supports previous research emphasizing the relationship between maternal obesity and hypertensive disorders in pregnancy.

In our study, when parameters such as neonatal outcomes, birth weight and gestational age were taken into account, pregnant women in the preeclampsia group were significantly negatively affected. Birth weight and gestational age at birth were significantly lower in the preeclampsia group, revealing the negative effects of preeclampsia on fetal development and timing of birth. In the study conducted by An et al., it was revealed that preeclampsia significantly increases the risk of preterm birth (20). The meta-analysis by Bossung et al. confirmed that preeclampsia increases the risk of preterm birth, especially in cases of severe or early-onset preeclampsia (21). In the study conducted by Gunnarsdottir et al., it was emphasized that babies exposed to preeclampsia generally have lower birth weight and that this has a significant effect regardless of the gestational week (22). These findings highlight the need for careful prenatal care and timely intervention to optimize neonatal outcomes in pregnancies complicated by preeclampsia.

When biochemical parameters were evaluated, lymphocyte and platelet counts were significantly lower in the preeclampsia group. These changes reflect the systemic inflammatory response and endothelial dysfunction specific to preeclampsia. In the study conducted by Walle et al., a decrease in platelet counts was observed in the preeclampsia group and it was stated that this parameter was related to the severity of the diseases (23). In addition, unlike our study, lymphocyte counts were also evaluated but no significant difference was found (23). In the study conducted by Toptas et al., a decrease in PLR levels was detected in patients with preeclampsia. However, no statistical difference was found in lymphocyte levels (24).

In our study, an increase in NLR and SII values were found in the preeclampsia group, indicating an increased inflammatory condition in preeclampsia. In the study conducted by Oğlak et al., it was shown that NLR values in the first trimester were significantly higher in women with preeclampsia compared to healthy pregnant women. It has been stated that NLR may be a potential marker for the prediction of preeclampsia (25). In the study conducted by Zheng et al., it was reported that NLR has a moderate diagnostic value in predicting preeclampsia. It was stated that NLR can be a helpful tool in the diagnosis of preeclampsia because it reflects the inflammatory process (26). In the study conducted by Çallıoğlu et al., they found that SII could be a valuable biomarker in preeclampsia risk groups (27). In the study by Akdulum et al., SII was shown to be significantly higher in patients who developed preeclampsia. This emphasizes the importance of inflammation in the pathogenesis of preeclampsia (28). These markers can be used as potential indicators of the severity and progression of the condition, consistent with previous studies.

Overall, our findings are consistent with current evidence and reinforce the multifactorial pathophysiology of preeclampsia, including contributions from maternal obesity, systemic inflammation, and endothelial dysfunction. These results highlight the importance of early diagnosis and targeted management strategies to reduce adverse maternal and neonatal outcomes associated with this condition. The retrospective design of the study and the small sample size can be shown as limitations. However, the evaluation of many biochemical parameters in terms of two groups can be shown as a strength of the study.

CONCLUSION

Our study reveals important clinical and laboratory differences between preeclamptic and normotensive pregnancies. Increased inflammatory markers have been found to be a feature of pregnancies complicated by preeclampsia and are consistent with existing literature. These findings can be used to determine early diagnosis and comprehensive management strategies to minimize the risks associated with preeclampsia and improve both maternal and neonatal outcomes. However, prospective studies with large sample sizes are needed to evaluate the usefulness of inflammatory markers in the early diagnosis and monitoring of preeclampsia.

Conflicts of interest: Authors declared no conflict of interest.

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