

Comparison of SIRI and other inflammatory index parameters in patients diagnosed with preterm premature rupture of membranes with healthy pregnant women

Preterm prematür membran rüptürü tanısı alan hastalarda SIRI ve diğer inflammatuar indeks parametrelerinin sağlıklı gebelerle karşılaştırılması

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ABSTRACT

Aim: To investigate the relationship between subclinical inflammatory indices such as Systemic Inflammatory Response Index (SIRI) and Systemic Inflammatory Index (SII), which are known to be closely associated with inflammation and preterm premature rupture of membranes (PPROM).

Materials and Methods: Between November 2022 and November 2023, 150 singleton pregnant women admitted to the Perinatology Clinic with a diagnosis of preterm premature rupture of membranes between 24 and 37 weeks of gestation and 150 healthy singleton pregnant women of similar gestational age admitted to the clinic were included in the study. Laboratory results of the patients at the time of presentation to the clinic were taken as reference. Their records were evaluated retrospectively from the records.

Results: There were no statistically significant differences in maternal age, gravidity, parity ($p: 0.082$; $p: 0.034$; $p: 0.235$ respectively). However abortion rates were different between the case and control groups ($p<0.001$). Body Mass Index (BMI), birth weight, Apgar score at 1 minute, and Apgar score at 5 minutes were lower in the PPRM group than in the control group ($p<0,01$). Primary C/S rate was higher in PPRM group ($p<0.001$). Higher leukocyte, neutrophil, neutrophil to lymphocyte ratio (NLR), Platelet to lymphocyte ratio (PLR), systemic inflammatory response index (SIRI) and Systemic immune-inflammation index (SII) levels were observed in the PPRM group than in the control group ($p<0.005$). There was no differences between Hb values of the groups ($p=0.545$).

Conclusion: According to these findings, SII, SIRI, NLR and PLR screening will be usefull for potential PPRM before membrane rupture occurs.

Keywords: Preterm premature rupture of membranes, inflammatory indices, Systemic Inflammatory Response Index

ÖZ

Amaç: İnflamasyon ile yakından ilişkili olduğu bilinen Sistemik İnflamatuar Yanıt İndeksi (SIRI) ve Sistemik İnflamatuar İndeks (SII) gibi subklinik inflammatuar indeksler ile preterm prematür membran rüptürü arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: Kasım 2022 ile Kasım 2023 tarihleri arasında Perinatoloji Kliniğine başvuran, 24 ila 37. gebelik haftalarında preterm prematür membran rüptürü tanısı alan 150 tekil gebe ve kliniğe başvuran benzer haftalarda sağlıklı 150 tekil gebe çalışmaya dahil edildi. Hastaların kliniğe başvuru zamanına ait laboratuvar sonuçları referans alındı. Kayıtlar retrospektif olarak değerlendirildi.

Bulgular: Maternal yaş, gravide, parite açısından istatistiksel olarak anlamlı bir fark yoktu (sırasıyla $p: 0.082$; $p: 0.034$; $p: 0.235$). Ancak abortus oranları vaka ve kontrol grupları arasında farklıydı ($p<0.001$). VKİ, doğum ağırlığı, 1. dakika Apgar skoru ve 5. dakika Apgar skoru preterm prematür membran rüptürü grubunda kontrol grubuna göre daha düşüktü ($p<0,01$). Primer C/S oranı preterm prematür membran rüptürü grubunda daha yüksekti ($p<0,001$). Preterm prematür membran rüptürü grubunda kontrol grubuna göre daha yüksek lökosit, nötrofil, Nötrofil Lenfosit Oranı (NLR), Platelet Lenfosit Oranı (PLR), Sistemik İnflamatuar Yanıt İndeksi (SIRI) ve Sistemik İmmün-inflamasyon indeksi (SII) düzeyleri gözlemlendi ($p<0,005$). Grupların hemoglobin değerleri arasında fark bulunmamıştır ($p=0,545$).

Sonuç: Bu bulgulara göre, SII, SIRI, NLR ve PLR indeksleri membran rüptürü oluşmadan önce preterm prematür membran rüptürü öngörüsünde yararlı olacaktır.

Anahtar Kelimeler: Preterm prematür membran rüptürü, inflammatuar indeks, Sistemik İnflamatuar Yanıt İndeksi

Cite as: Oguz Y, Sarikaya Kurt D, Agaoglu RT, Hizli B, Ulusoy CO, Vural Yilmaz Z et al. Comparison of SIRI and other inflammatory index parameters in patients diagnosed with preterm premature rupture of membranes with healthy pregnant women. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2024;21(3):227–231.

Geliş/Received: 06.08.2024 • Kabul/Accepted: 17.08.2024

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Cevrimiçi Erişim/Available online at: <https://dergipark.org.tr/pub/jgon>

INTRODUCTION

Premature rupture of membranes (PROM) is the rupture of the fetal membranes at least one hour before the onset of labor. If PROM occurs before 37 weeks of gestation, it is called preterm premature rupture of membranes (PPROM). Although PPRM and PROM are similar in terms of etiology, complications and outcomes, infection in the choriodesidual region is thought to be the main cause of membrane rupture in PPRM. PPRM occurs in approximately 3% of pregnancies (1,2).

Management of PPRM is one of the most controversial issues. Many factors such as correct diagnosis, appropriate management and intervention, correct use of tocolytics, antibiotic prophylaxis and their duration of administration, antenatal corticosteroid administration and timing, testing methods to be used for infection and delivery decision should be managed appropriately and at the right time. The diagnosis of rupture of membranes can be made by direct visualization of the arrival of amniotic fluid or, in suspected cases, after confirmation by placental alpha microglobulin-1 (PAMG-1) testing (3-5).

Once the diagnosis of PPRM is confirmed, maternal or fetal indications for emergency delivery should be sought. The most urgent indications are cord prolapse and bradycardia due to compression and chorioamnionitis. Treatment varies between emergency delivery and follow-up depending on the maternal and fetal condition. Gestational age, concomitant medical and obstetric complications, infection, presence of meconium, positive vaginal culture, non-reactive NST, variable decelerations, cervical maturity and presentation should be considered when deciding on the treatment procedure (6-8).

Although there is an association between preterm labor and infection, these two findings are not always seen together. In the literature, it has been shown that if subclinical infection is detected, these patients are resistant to treatment and will often result in preterm delivery. There are studies showing a significant association between PPRM and various inflammatory factors. There are easily measurable, reproducible, noninvasive, inexpensive and guiding markers for the determination of inflammation by complete blood count (CBC) which is a simple and inexpensive method and contains important parameters used in the diagnosis of many diseases. Inflammatory markers in CBC have been shown to reflect disease activity (9-11).

The aim of this study was to investigate the relationship between subclinical inflammatory factors such as, Systemic Inflammatory Response Index (SIRI) and Systemic Inflammatory Index (SII), which are known to be closely associated with inflammation, and PPRM.

MATERIAL METHOD

This retrospective case-control study was conducted in the Department of Perinatology, Ministry of Health, Etlik City Hospital in Ankara. The protocol of this study was approved by the Ethics Committee of the hospital. The study was conducted based on the universal ethical principles of the Declaration of Helsinki.

Between November 2022 and November 2023, 150 singleton pregnant women admitted to the Perinatology Clinic with a diagnosis of preterm premature rupture of membranes between 24 and 37 weeks of gestation and 150 healthy singleton pregnant women of similar gestational age admitted to the clinic were included in the study. Laboratory results of the patients at the time of presentation to the clinic were taken as reference. Inclusion criteria were being between the ages of 18-45, singleton pregnancy, being diagnosed with PPRM, being in the low risk group in 1st trimester aneuploidy screening and no structural anomaly was detected in the ultrasonographic anomaly scan performed between 18-22 weeks. Study participants with multiple pregnancy, maternal illness, fetal congenital and chromosomal abnormalities, chronic drug use, alcohol and smoking, additional pregnancy complications such as preeclampsia during follow-up and those who have been treated with tocolytics were excluded from the study. Cases whose data could not be accessed, who delivered at another hospital, and who had additional pregnancy complications were also excluded from the study.

PPROM was diagnosed by placental alpha microglobulin-1 (PAMG-1) test or direct amniotic flow in speculum examination. As case group; 150 cases who met the inclusion criteria and as control group 150 age and gestational week matched healthy pregnant women were included in the study.

Data such as maternal age, height, weight, number of pregnancies, history of previous pregnancies, last menstrual period, history of previous operations, history of systemic diseases, and biochemistry parameters in whole blood analyzed at the week of delivery, neonatal intensive care unit admission, 1 and 5. minute Apgar scores, birth weights were taken from the records.

Systemic Inflammatory Index (SII): neutrophil count \times platelet count/lymphocyte count, Systemic Inflammatory Response Index (SIRI): monocyte count \times neutrophil count/lymphocyte count were obtained from the hemogram values, and the indices were calculated according to the formulas.

The study was a retrospective study. The distribution of variables was determined using the Kolmogorov-Smirnov method. Because of continuous variables did not fit the normal distribution, Mann-

Whitney U test was applied. Chi-square test was applied for comparison of proportions. For correlation evaluation, Spearman or Pearson correlation test applied depending on whether it fits the normal distribution or not. Numerical variables were expressed as median (min-max). P value <0.05 was considered statistically significant.

RESULTS

The demographic and clinical characteristics and perinatal outcomes of the study groups are summarized in Table 1. There were no statistically significant differences in maternal age and parity (p: 0.082; p:0.235 respectively). However abortion rates and gravidity were different between the case and control groups

(p<0.001, p: 0.034; respectively). BMI, birth weight, Apgar score at 1 minute, and Apgar score at 5 minutes were lower in the PPROM group than in the control group (p=0.009; p<0.001; p<0.001; p<0.001 respectively).

Comparison of CBC and systemic inflammatory indices between groups is shown in Table 2. Higher leukocyte, neutrophil, NLR, PLR, SIRI and SII levels were observed in the PPROM group than in the control group (p<0.001; p<0.001, p<0.001, p: 0.005; p<0.001, p<0.001 respectively). There was no differences between Hb values of the groups (p=0.545). Therefore, statistically significant differences were also found in the CBC parameters such as count of lymphocytes, monocytes, platelets between the two groups (p<0.001; p: 0.007; p<0.001, p<0.001, p<0.001 respectively).

Table 1. The demographic and clinical characteristics and perinatal outcomes of the study groups

	PPROM Median (Min-Max)	Control Median (Min-Max)	P value
Maternal Age	28 (14-44)	26 (17-42)	0,082
Gravidity	2 (1-8)	2 (1-8)	0,034
Parity	1 (0-5)	1 (0-4)	0,235
Abortion Rates	0 (0-4)	1 (0-5)	<0.001
BMI	29 (19-49)	28 (18-45)	0,009
Birth Weight (gr)	2300 (526-3670)	3240 (1720-4390)	<0,001
Apgar Score 1 min	8 (0-9)	9 (4-9)	<0,001
Apgar Score 5 min	9 (0-10)	10 (6-10)	<0,001

PPROM: preterm premature rupture of membranes, BMI: Body Mass Index, p value <0,05 is statistically significant

Table 2. Comparison of CBC and systemic inflammatory indices between groups

	PPROM	Control	P value
Leukocyte count	9790 (4570-16650)	240 (117-533)	<0.001
neutrophil count	10700 (880-14300)	6945 (610-15020)	<0.001
Lymphocytes count	1260 (860-2470)	1905 (850-8800)	<0.001
monocytes count	635 (39-1460)	3900 (411-27350)	0.007
Platelets count	360000 (237000-475000)	235500 (124000-465000)	<0.001
NLR	3,62 (0,38-17,67)	2,7 (0,56-4,73)	<0.001
PLR	126,7 (20,0-330,1)	100 (90-161)	<0.005
SIRI	2,26(0,97-11,7)	4,39 (1,02-44,8)	<0.001
SII	1900 (406-2900)	846,48 (148-1958)	<0.005
Hb (gr/dl)	11.7 (7-15.9)	11.7 (8-15)	0:545

CBC: Complete Blood Count, NLR: Neutrophil/Lymphosit ratio, PLR: Platelet/Lymphosit ratio, SIRI: Systemic Inflammatory Response Index, SII: Systemic Inflammatory Index, Hb: Hemoglobin, p<0.05 is statistically significant

DISCUSSION

Although various factors have been proposed in the pathogenesis of PPRM, infection or inflammation is an important cause of preterm labor (9-11). Recognizing and eliminating maternal infection is of great importance to reduce preterm deliveries and to prevent neonatal consequences of prematurity. A number of markers have been studied for the investigation and early and non-invasive recognition of maternal infection and inflammatory status. Such as those of soluble intercellular adhesion molecule-1, interleukin-6, matrix metalloproteinase-9, tissue inhibitor of metalloproteinases-1, angiotensin-2, and insulin-like growth factor binding protein-2, which are not used much in routine examinations but can be used to predict chorioamnionitis [4,5]. Therefore, an easy, cheap, and routine early diagnostic test for PPRM is needed.

There are studies on the prognostic and predictive value of inflammation and related biomarkers such as NLR and PLR in many diseases (12-14). In response to inflammation, as neutrophil count increases, lymphocyte count decreases, thus NLR can be used as a marker of inflammation. High NLR values have been reported in pregnancy-related intrahepatic cholestasis, hyperemesis gravidarum and preeclampsia (15-17). Although NLR is useful, it is a nonspecific parameter. It may increase in many pregnancy-related conditions. In inflammatory conditions, activation in platelets is accompanied by a decrease in lymphocyte count (18,19). Accordingly, it has been reported that increased PLR values may be used in the recognition of the disease and prediction of prognosis in many inflammation-related diseases (20-22). Ekin et al. (23) reported an increase in first trimester platelet count and a decrease in MPV levels in patients with PPRM. SII index is a parameter indicating inflammation and immune status calculated by using neutrophil/lymphocyte as well as platelet values. Tanaçan et al. reported that SII and platelet counts were associated with adverse maternal and neonatal events in PPRM cases. They emphasized that platelets play a role in immune regulation and have extra importance compared to neutrophils by playing a role in placental remodelling especially in pregnant women (20). In our study, SII indices, platelet counts and PLR and NLR ratios were found to be higher compared to the control group. However in some studies, no correlation was found between PLR and PPRM.

CONCLUSION

According to these findings, SII, SIRI, NLR and PLR screening will be useful for potential PPRM before membrane rupture occurs. Predicting PPRM and possible complications may provide opportunities for early intervention and treatment options.

In addition, although the place of these and similar indexes in the literature is not clear, this study is expected to contribute to this point. The results should be supported by other prospective, multicenter and large sample studies.

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