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Predictive value of inflammatory markers (NLR, PLR, MLR, SII, SIRI, PIV, IG, and MII) for latency period in Preterm premature rupture of membranes (PPROM) pregnancies

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Abstract

Background Our study aimed to investigate the value of inflammatory indices in predicting the latency period until birth in patients with preterm premature rupture of membranes (PPROM).

Methods This retrospective study was conducted on PPROM cases between 24 and 34 weeks of gestation at Ankara Etlik City Hospital Perinatology Department from October 2023 to April 2024. A total of 146 participants were divided into two groups: Group 1 included 73 patients who gave birth within 72 hours (h) of PPROM diagnosis, and Group 2 included 73 patients who gave birth after 72 h.

Results This study evaluated the prognostic significance of various inflammatory markers neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), systemic immune inflammation index (SII), systemic inflammatory response index (SIRI), pan-immune inflammation value (PIV), immature granulocytes (IG), multi-inflammatory index (MII)-1, MII-2, and MII-3 in predicting the latency period in patients with PPROM. Only MII-1, MII-2, and MII-3 reliably predicted labor within 72 h. The cut-off value for MII-1 was > 48.3, with a sensitivity of 57.7% and specificity of 57.3% (AUC: 0.598, 95% CI: 0.503–0.692, $p = 0.042$). For MII-2, the cut-off was > 1037.6, with a sensitivity of 57.7% and specificity of 57.3% (AUC: 0.611, 95% CI: 0.516–0.705, $p = 0.021$). MII-3 had a cut-off of > 10919.9, with a sensitivity of 53.5% and specificity of 52% (AUC: 0.595, 95% CI: 0.501–0.690, $p = 0.046$).

Conclusion Our findings show that, among NLR, PLR, MLR, SII, SIRI, PIV, IG, MII-1, MII-2, and MII-3, only MII-1, MII-2, and MII-3 levels are statistically significant in predicting birth timing.

Keywords Preterm premature rupture of membranes, Latency period, Inflammation, Multi-inflammatory index

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Introduction

Preterm premature rupture of membranes (PPROM) refers to the rupture of fetal membranes before the 37th week of gestation [1]. The incidence of PPROM is approximately 3%, and it accounts for about 25–30% of preterm births [2]. This condition is associated with increased perinatal mortality and morbidity. Newborns affected by PPROM often experience prenatal complications such as respiratory distress syndrome (RDS), bronchopulmonary dysplasia, intraventricular hemorrhage, and adverse neonatal outcomes, including neonatal sepsis and fetal loss. Additionally, PPROM increases the risk of maternal complications such as chorioamnionitis, sepsis, placental abruption, and uterine atony [3, 4].

Although the precise etiology of PPROM is not fully understood, several factors have been identified as predisposing to the condition. These factors include infections/inflammation, smoking, substance use, early pregnancy bleeding, low body mass index, and stress [5, 6]. Among these factors, infections/inflammation are particularly emphasized. Recent studies suggest a primarily non-infectious etiology and inflammation as the main underlying pathophysiology [7, 8]. However, it is unclear whether inflammation is a cause or a consequence of PPROM. Systemic inflammation is characterized by changes such as neutrophilia, lymphopenia, thrombocytosis, and elevated C-reactive protein (CRP) [9, 10]. Yet, the sensitivity of isolated changes in these parameters is quite poor. For this reason, various indices have recently been developed that include combinations of parameters. Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), systemic immune inflammation index (SII), systemic inflammatory response index (SIRI), pan-immune inflammation value (PIV), multi-inflammatory index-1 (MII-1), multi-inflammatory index-2 (MII-2), and multi-inflammatory index-3 (MII-3) have been investigated as new inflammatory markers in many diseases [11–15]. Immature granulocytes (IG) are found in the peripheral blood and are a new marker for inflammation [16]. The detection and increase of IG indicate activation of the bone marrow. IG has been associated with severe infections in recent studies [17]. There is not enough literature to examine these indices in PPROM cases.

The interval between membrane rupture and birth correlates with the severity of complications [18]. This period is influenced by factors such as gestational age, type of pregnancy (multiple or singleton), cervical length, maternal age, and infections, but predicting the exact timing of birth remains challenging [19, 20]. Additionally, estimating the time of birth is extremely important for prenatal care and medication management, as well as for organizing the postnatal care environment [19]. In this process, it is particularly important to predict whether birth will occur within the first 72 hours (h). Therefore, new markers that can predict birth are needed. The aim of this study is to investigate the role of inflammatory indices in predicting parturition in pregnants diagnosed with PPROM.

Materials and methods

This retrospective study was conducted at the Perinatology Department of Ankara Etlik City Hospital on PPROM cases that occurred between October 2023 and April 2024. The study adhered to the principles outlined in the Declaration of Helsinki, with ethical approval granted by the Ankara Etlik City Hospital Ethics Committee (approval number: AESH-BADEK-2024-242). In this study, due to its retrospective nature, informed consent was waived with the approval of the Ethics Committee of Ankara Etlik City Hospital. Patient information was retrieved from medical records and the hospital's information management system. The study included a total of 146 participants, who were divided into two groups: Group 1 comprised 73 patients diagnosed with PPROM who gave birth within 72 h, while Group 2 included 73 patients who gave birth more than 72 h after being diagnosed with PPROM.

The study included pregnants who had a diagnosis of PPROM within the gestational age range of 24 to 34 weeks. PPROM was diagnosed by the presence of active amniotic fluid flow during vaginal examination, the accumulation of amniotic fluid on speculum examination, or the presence of placental alpha-microglobulin-1 (PAMG-1) (AmniSure® ROM) in the vaginal discharge, which is a diagnostic test. The gestational age of study participants was determined by calculating it based on the start day of the last menstrual cycle and then verifying this information with ultrasound examinations. Exclusion criteria included chronic maternal diseases (such as diabetes and hypertension), uterine anomalies, placenta previa, placental abruption, multiple pregnancies, signs of active cervicovaginal infection, surgical intervention during the current pregnancy, smoking, alcohol consumption, and congenital anomalies, as well as patients whose medical records were not accessible.

NLR, PLR, MLR, SII, SIRI, PIV, IG, MII-1, MII-2, and MII-3 were determined by laboratory tests at the time of initial presentation. The inflammatory scores were calculated as follows: NLR: neutrophil count/lymphocyte count, PLR: platelet count/lymphocyte count, MLR: monocyte count/lymphocyte count, SII: neutrophil count*platelet count/lymphocyte count, SIRI: neutrophil count*monocyte count/lymphocyte count, PIV: neutrophil count*platelet count*monocyte count/lymphocyte count, MII-1: NLR*CRP, MII-2: PLR*CRP, MII-3: SII*CRP. Each patient diagnosed with PPROM on admission was administered 12 milligram (mg) of

betamethasone intramuscularly twice at 24-hour intervals and tocolytic treatment with nifedipine were applied to reduce perinatal morbidity and mortality. These patients were started on 1 gram (g) orally azithromycin and 4*2 g intravenous (IV) ampicillin as antibiotic therapy for two days. Antibiotic treatment was continued with amoxicillin 3*500 mg orally for five days. Those with penicillin allergy were given cefazolin 3*1 g IV (instead of IV ampicillin) for two days and cephalexin 4*500 mg orally (instead of oral amoxicillin) for five days. Birth was planned after the 34th week of pregnancy.

Statistical analysis

The data analysis was performed using IBM's Statistical Package for the Social Sciences (SPSS) version 26.0 (Armonk, New York, USA). A significance level of $p<0.05$ was used for all statistical analyses. Numerical data were presented as mean ± standard deviation (SD) or median (interquartile range (IQR)), while qualitative data were shown as percentages. The Student's T-test was utilized for normally distributed continuous variables, and the Mann-Whitney U test was applied for non-normally distributed continuous variables. The area under the receiver operating characteristic (ROC) curve (AUC) was used to determine cut-off values, sensitivity, and specificity.

Results

Maternal characteristics and perinatal outcomes of the participants are shown in Table 1. Both groups had similar maternal ages, averaging 28 ± 6 years. BMI during testing and parity were similar between both groups. Gestational age at hospitalization was similar in both groups, but gestational age at delivery was significantly higher in the latency > 72 h group compared to the ≤72 h group (32.4 weeks vs. 30.5 weeks, $p<0.001$). The hospitalization-to-birth interval was significantly longer in the latency > 72 h group, with a median of 8 (5–18) days compared to 1 (0–2) days in the ≤72 h group ($p<0.001$). Birth weights were higher in the latency > 72 h group, averaging 1928 ± 622 g compared to 1691 ± 627 g in the ≤72 h group ($p=0.028$). The rate of cesarean section was similar between the two groups. Neonatal outcomes showed no significant difference in rates of sepsis, hyperbilirubinemia, umbilical cord arterial pH, and umbilical cord arterial pH < 7.35 ($p>0.05$, for all), but there were significant differences in APGAR scores at the 5th minute and the rate of low APGAR scores (<7) ($p=0.012$ and $p=0.020$, respectively). RDS and NICU admissions were similar between groups. (Table 1).

The study analyzed various inflammation parameters in relation to maternal and gestational characteristics for participants with latency ≤ 72 h and > 72 h in Table 2. Hemoglobin levels, white blood cell (WBC) counts, and neutrophil counts were similar between the groups.

Table 1 Maternal characteristics and perinatal outcomes of the participants

	Latency ≤ 72 h *n* = 73	Latency > 72 h *n* = 73	*p*
Maternal age (year) (mean ± SD)	28 ± 6	28 ± 6	0.798
BMI during testing (kg/m^2) (mean ± SD)	28.2 ± 5.6	28.3 ± 5.2	0.809
Parity (n,%)			0.192
Nulliparous	38 (52.1%)	30 (41.1%)	
Multiparous	35 (47.9%)	43 (58.9%)	
Gestational age at hospitalization (week) (mean ± SD)	30.3 ± 3	30.4 ± 2.4	0.998
Gestational age at delivery (week) (mean ± SD)	30.5 ± 3	32.4 ± 2.8	< 0.001
Hospitalization-birth interval (day) median (IQR)	1 (0–2)	8 (5–18)	< 0.001
Birth weight (gram) (mean ± SD)	1691 ± 627	1928 ± 622	0.028
Cesarean section (n,%)	39 (53.4%)	44 (60.2%)	0.271
Neonatal sepsis (n,%)	17 (23.3%)	12 (16.4%)	0.300
Neonatal hyperbilirubinemia (n,%)	6 (8.2%)	12 (16.4%)	0.131
Umbilical cord arterial pH (mean ± SD)	7.31 ± 0.10	7.32 ± 0.08	0.792
Umbilical cord arterial pH < 7.35 (n,%)	35 (64.8%)	31 (57.4%)	0.430
APGAR score at 1st minute (mean ± SD)	7 ± 2	7 ± 2	0.094
APGAR score at 5th minute (mean ± SD)	8 ± 2	9 ± 1	0.012
APGAR score at 5th minute < 7 (n,%)	13 (17.8%)	4 (5.5%)	0.020
RDS (n,%)	52 (73.2%)	51 (68%)	0.586
NICU admission (n,%)	61 (83.6%)	58 (79.5%)	0.522
Composite adverse neonatal outcomes (n,%) *	62 (84.9%)	58 (79.5%)	0.387

BMI: Body mass index, RDS: Respiratory distress syndrome, NICU: Neonatal intensive care unit

* The composite adverse neonatal outcome was defined as the occurrence of at least one of the following situations: Neonatal sepsis, neonatal hyperbilirubinemia, APGAR score at 5th minute < 7, respiratory distress syndrome (RDS), and admission to neonatal intensive care unit (NICU).

Table 2 The relationship between inflammation parameters and maternal-gestational parameters

	Latency ≤ 72 h *n* = 73	Latency > 72 h *n* = 73	*p*
Hemoglobin (g/dL) median (IQR)	11.9 (11.2–12.4)	11.5 (10.9–12.3)	0.123
WBC (*10^3/mm^3) median (IQR)	12.2 (10.4–15.8)	12.3 (10.1–14.8)	0.438
Neutrophil (*10^3/mm^3) median (IQR)	9.39 (7.31–13.45)	9.0 (7.30 ± 11.40)	0.336
Lymphocyte (*10^3/mm^3) (mean ± SD)	2.04 ± 0.93	2.11 ± 0.76	0.496
Monocyte (*10^3/mm^3) (mean ± SD)	0.70 ± 0.44	0.72 ± 0.34	0.729
Immature granulocytes absolute (*10^3/mm^3) median (IQR)	0.1 (0.06–0.15)	0.1 (0.06–0.18)	0.603
Platelet (*10^3/mm^3) (mean ± SD)	264 ± 64	256 ± 63	0.439
CRP (mg/L) median (IQR)	9.4 (4.2–25)	7.9 (3.9–14.2)	0.065
Neutrophil to lymphocyte ratio (NLR) median (IQR)	5.2 (3.08–9.74)	4.25 (3.05–6.71)	0.140
Platelet to lymphocyte ratio (PLR) (mean ± SD)	157.7 ± 79.8	138.4 ± 64.2	0.106
Monocyte to lymphocyte ratio (MLR) median (IQR)	0.327 (0.214–0.396)	0.342 (0.264–0.386)	0.693
Systemic immune inflammation index (SII) median (IQR)	1182.5 (873.1-2569.2)	964.7 (759.7-1974.9)	0.078
Systemic inflammation response index (SIRI) median (IQR)	2.83 (1.92–3.91)	2.72 (2.10–3.94)	0.989
Pan-immune inflammation value (PIV) median (IQR)	734.8 (463.7-1286.9)	663.4 (500.5-1142.3)	0.753
Multi Inflammatory Index-1 (MII-1) median (IQR)	75.6 (17.5-191.1)	31.9 (14.4–75.6)	0.042
Multi Inflammatory Index-2 (MII-2) median (IQR)	2400.9 (515.1-4561.8)	966.9 (450.4-2015.5)	0.021
Multi Inflammatory Index-3 (MII-3) median (IQR)	20290.4 (3466.7-51011.7)	9339.1 (3852.2-22977.4)	0.046

WBC: White blood cell, CRP: C-reactive protein

Table 3 The ROC curve analysis to determine the optimal cut-off levels for NLR, PLR, MLR, SII, SIRI, PIV, IG, MII-1, MII-2, and MII-3 in predicting the latency period

	Cut-off	Sensivity	Specificity	AUC	CI	*P* value
Neutrophil to lymphocyte ratio (NLR)	> 4.3	57.5%	56.2%	0.571	0.477–0.664	0.140
Platelet to lymphocyte ratio (PLR)	> 127.8	54.8%	53.4%	0.581	0.488–0.673	0.106
Monocyte to lymphocyte ratio (MLR)	< 0.328	47.9%	46.6%	0.481	0.386–0.576	0.693
Systemic immune inflammation index (SII)	> 1107.2	59.2%	57.3%	0.584	0.491–0.678	0.078
Systemic inflammation response index (SIRI)	> 2.79	53.5%	52%	0.499	0.405–0.594	0.989
Pan-immune inflammation value (PIV)	> 692.3	54.9%	54.7%	0.515	0.421–0.610	0.753
Immature granulocytes absolute	> 0.09	57.5%	54.8%	0.525	0.430–0.620	0.603
Multi Inflammatory Index-1 (MII-1)	> 48.3	57.7%	57.3%	0.598	0.503–0.692	0.042
Multi Inflammatory Index-2 (MII-2)	> 1037.6	57.7%	57.3%	0.611	0.516–0.705	0.021
Multi Inflammatory Index-3 (MII-3)	> 10919.9	53.5%	52%	0.595	0.501–0.690	0.046

AUC: Area under the curve, CI: Confidence interval

Lymphocyte counts, monocyte counts, and immature granulocyte counts also showed no significant differences. Markers of inflammation, including CRP, NLR, PLR, MLR, SII, SIRI, and PIV, did not show significant differences between the two groups. However, significant differences were observed in the multi inflammatory indexes (MII-1, MII-2, MII-3), with higher values in the latency ≤ 72 h group, suggesting a higher inflammatory state MII-1 [75.6 (17.5-191.1) vs. 31.9 (14.4–75.6), $p=0.042$], MII-2 [2400.9 (515.1-4561.8) vs. 966.9 (450.4-2015.5), $p=0.021$], MII-3 [20290.4 (3466.7-51011.7) vs. 9339.1 (3852.2-22977.4), $p=0.046$]. (Table 2).

The ROC curve analysis was performed to determine the optimal cut-off levels for inflammatory markers in predicting the latency period, as shown in Table 3. Among these parameters, only MII-1, MII-2, and MII-3 demonstrated significant statistical significance. The identified cut-off value for MII-1 was >48.3, yielding a sensitivity of 57.7% and a specificity of 57.3%, with an AUC of 0.598 (95% CI: 0.503–0.692, $p=0.042$). Similarly, the cut-off value for MII-2 was >1037.6, with a sensitivity of 57.7% and a specificity of 57.3%, with an AUC of 0.611 (95% CI: 0.516–0.705, $p=0.021$). The cut-off value for MII-3 was >10919.9, with a sensitivity of 53.5% and a specificity of 52%, with an AUC of 0.595 (95% CI: 0.501–0.690, $p=0.046$). (Table 3; Fig. 1).

Discussion

The correlation between the duration of membrane rupture and the occurrence of complications is well-documented [18]. Accurate prediction of birth timing is crucial for optimizing prenatal care and preparing for potential neonatal intensive care needs. This study aimed to evaluate the prognostic significance of various inflammatory markers—NLR, PLR, MLR, SII, SIRI, PIV, IG, MII-1, MII-2, and, MII-3—in patients with PPROM. Our

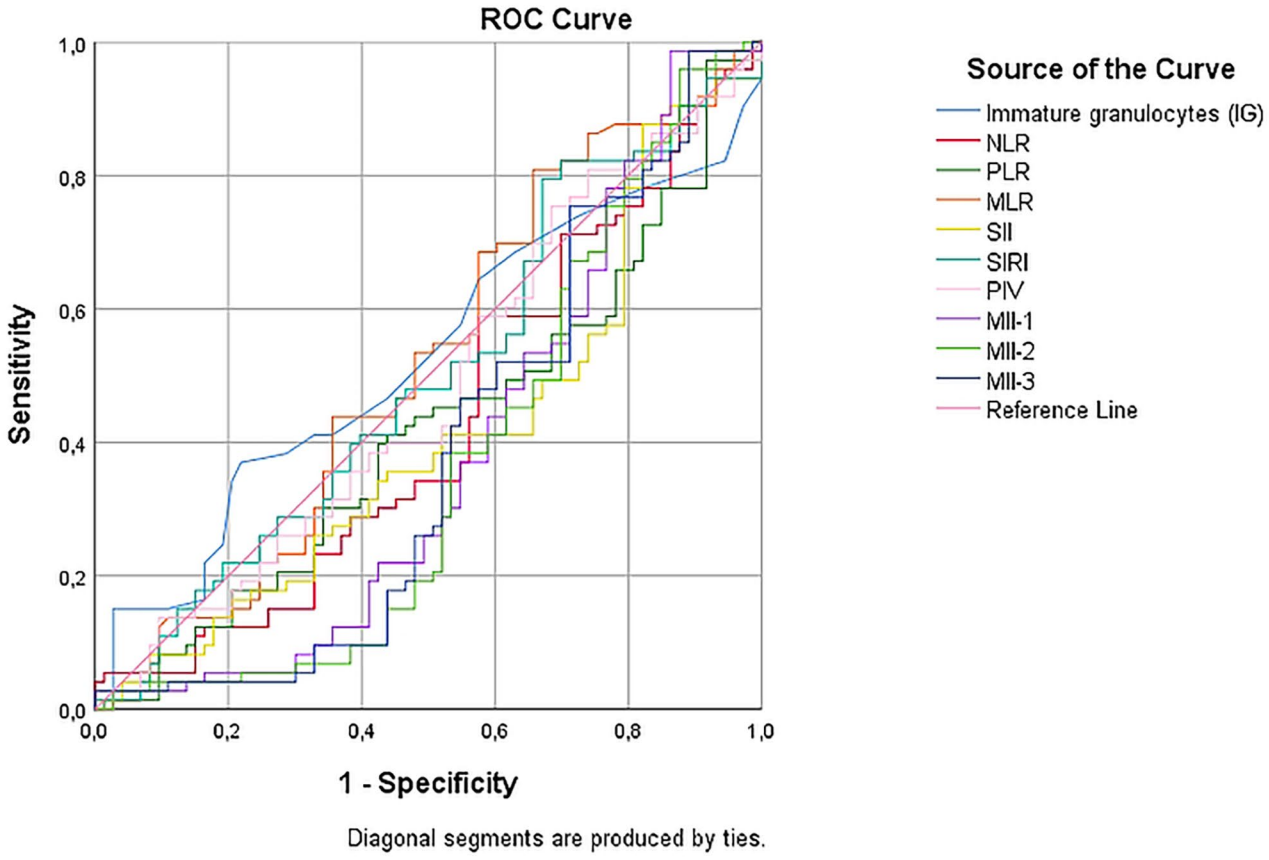

Fig. 1 The ROC curve analysis to evaluate NLR, PLR, MLR, SII, SIRI, PIV, IG, MII-1, MII-2, and MII-3 in predicting the latency period

findings indicate that among these markers, only MII-1, MII-2, and MII-3 could reliably predict the onset of labor within ≤72 h or beyond 72 h. Specifically, MII-1 with a threshold greater than 48.3 showed a sensitivity of 57.7% and a specificity of 57.3% ($p=0.042$). Similarly, MII-2 with a threshold above 1037.6 had a sensitivity of 57.7% and a specificity of 57.3% ($p=0.021$), and MII-3 with a threshold over 10919.9 demonstrated a sensitivity of 53.5% and a specificity of 52% ($p=0.046$). These findings suggest that MII-1, MII-2, and MII-3 are promising markers for predicting the timing of labor in PPROM patients. Their ability to differentiate between labor onset within 72 h or later can significantly aid in clinical decision-making and prenatal care planning.

Although PPROM has a multifaceted etiology, infection and inflammation are frequently highlighted as significant factors. Amniocentesis is a reliable diagnostic procedure for detecting intrauterine infections in PPROM patients [21]. However, the invasiveness of amniocentesis, its associated complications, and the delayed culture results make it less ideal. In a meta-analysis examining the safety of amniocentesis in PPROM patients, the overall complication rate was 0.35% [22]. This has led to the ongoing search for non-invasive prognostic markers that can predict the timing of delivery. Systemic inflammation, characterized by neutrophilia, lymphopenia, thrombocytosis, and elevated CRP levels, can be assessed through simple blood tests. However, these parameters alone have low reliability in recognizing inflammation. For this reason, indices combining multiple inflammation parameters have been developed. In the literature, the number of studies investigating markers to predict the latency period in PPROM cases is very limited. Ekin et al. investigated the prediction of birth within 72 h using NLR and PLR in PPROM cases, including only those below 34 weeks of gestation [23]. Both NLR and PLR failed to predict birth latency. Dagdeviren et al. attempted to predict birth within 72 h using NLR, PLR, and MLR in PPROM cases, including only those below 34 weeks of gestation [24]. They found that NLR was higher in cases where birth occurred within 72 h, while MLR was significantly higher in the >72 h group. However, PLR could not distinguish births within 72 h. In our study, NLR, PLR, and MLR could not predict the time of birth in PPROM cases. These conflicting findings indicate that NLR, PLR, and MLR do not have strong prognostic value in predicting the duration of labor in PPROM cases. Therefore, further research is needed to identify more reliable non-invasive markers for predicting labor timing in these patients.

In recent years, several new inflammatory markers, such as SII, SIRI, and PIV, have been developed to represent the inflammatory state. These indices, which include neutrophil, monocyte, platelet, and lymphocyte counts, have been studied in various contexts. However, their relationship with the latency period in PPROM has not been thoroughly investigated. Tanacan et al. demonstrated a positive relationship between SII levels and adverse neonatal outcomes in pregnant women with PPROM [25]. Kucukbas et al. showed that SIRI was significantly predictive of PPROM diagnosis and negative neonatal outcomes [26]. Fuca et al. were the first to define the PIV index by conducting a study on individuals diagnosed with metastatic colorectal cancer. Their findings revealed a statistically significant relationship between the low inflammation index and survival probability in these patients [27]. Similarly, Baba et al. found that elevated PIV levels negatively correlated with the prognosis of individuals diagnosed with esophageal cancer [14]. An emerging inflammatory signature detected in peripheral blood is an elevated proportion of immature granulocytes, which serves as an early indicator of severe disease and sepsis. IG contains promyelocytic, myelocytic, and metamyelocytic fractions of neutrophils [28]. These fractions reflect the active response of the bone marrow to an infection. Unal et al. were able to predict serious disease in patients with acute cholecystitis using IG levels [16]. In the study by Bhansaly et al. IG were defined as the earliest biomarker of sepsis [29]. However, to our knowledge, IG and PIV have not been studied in PPROM patients. In our study, we evaluated these indices for the first time in PPROM patients and found that they could not predict latency in PPROM. We observed no statistically significant relationship between SII, SIRI, PIV, and IG with the timing of birth within 72 h in PPROM patients. Therefore, these markers cannot be used to predict the timing of delivery in PPROM cases. These findings highlight the complexity of predicting labor timing in PPROM cases and suggest that while some inflammatory markers may provide insights into neonatal outcomes, they may not be effective in predicting the latency period.

After various indices in the literature gave conflicting results, the MII was first developed by Gardini et al. in 2020 and examined in patients with colorectal cancer [15]. This index also includes CRP, an acute-phase reactant. CRP is synthesized in the liver and increases significantly within 48 h after infection, making it a critical parameter in acute inflammation [30]. Specifically, it consists of MII-1 (NLR multiplied by CRP), MII-2 (PLR multiplied by CRP), and MII-3 (SII multiplied by CRP). In Gardini et al.'s study, patients with low levels of MII-1, MII-2, and MII-3 had a better prognosis. Subsequent research has further validated the utility of these indices. For example, a study by Gozdas et al. on COVID-19 patients found that MII was the best predictor of mortality [31]. Demirel et al. examined the relationship between various inflammatory indices and mortality in acute ischemic stroke, concluding that MII-1, MII-2, and MII-3 were the best predictors of mortality [32]. Additionally, Agircan et al. demonstrated that MII could predict the occurrence of acute symptomatic seizures [33]. To the best of our knowledge, our study is the first to evaluate MII levels in pregnant women with PPROM. While the CRP levels in PPROM patients who delivered within 72 h and those who did not were similar, the levels of MII-1, MII-2, and MII-3, which include CRP, were significantly higher in patients who delivered within 72 h. These results suggest that the MII could be a valuable tool for predicting labor timing in PPROM cases, offering significant potential for improving prenatal care and birth planning.

Our study has several limitations. Since our study included single-center and single-population data, the generalizability of our findings to different groups may be limited. To increase the reliability and validity of these findings, further studies involving larger patient cohorts and different populations are necessary. Additionally, due to its retrospective nature, unknown confounding factors may not have been included. Future studies could improve sensitivity and specificity values by including factors related to PPROM etiology in expanded prediction models. One of the strengths of our study is the comprehensive evaluation of multiple inflammatory indices, including novel markers like MII-1, MII-2, and MII-3, in the context of PPROM. This approach provides a broader perspective on the potential utility of these markers in clinical settings. Additionally, the non-invasive nature of the blood tests used to measure these markers enhances their applicability in routine prenatal care.

Conclusions

In our study, we compared various inflammatory markers to predict labor time in PPROM patients. Unlike previous studies, we included a wide range of novel inflammatory parameters. Our findings indicate that the levels of MII-1, MII-2, and MII-3 were statistically significant in predicting the onset of labor. These markers showed potential as reliable predictors for labor within 72 h. The ability to predict the timing of delivery is crucial for birth planning, prenatal care, and preparation. Incorporating these inflammatory markers into clinical practice could improve prenatal management, enhance patient counseling, and optimize resource allocation. Further research with larger cohorts is needed to validate these findings and confirm their clinical utility.

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Author contributions
Gulsan Karabay: Conceptualization, Methodology, Writing – Review & Editing. Burak Bayraktar: Formal Analysis, Writing – Review & Editing. Zeynep Seyhanli: Resources, Writing – Review & Editing. Betul Tokgoz Cakir and Gizem Aktemur: Writing – Review & Editing. Serap Topkara Sucu: Resources, Formal Analysis. Nazan Vanli Tonyali: Supervision. Mevlut Bucak and Hatice Ayhan: Writing – Review & Editing. Gulsah Dagdeviren: Supervision.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study adhered to the principles outlined in the Declaration of Helsinki, with ethical approval granted by the Ankara Etlik City Hospital Ethics Committee (approval number: AESH-BADEK-2024-242). In this study, due to its retrospective nature, informed consent was waived with the approval of the Ethics Committee of Ankara Etlik City Hospital.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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