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OPEN RESEARCH ARTICLE

Evaluation of Hematologic Inflammatory Markers in Missed Abortus: A Retrospective Case-Control Study

Missed Abortus Olgularında Hematolojik İnflamatuvar Belirteçlerin Değerlendirilmesi: Retrospektif Bir Vaka Kontrol Çalışması

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ABSTRACT
Objective: This study aims to evaluate the relationship between hematological inflammatory markers neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and systemic immune-inflammatory index (SII) and missed abortion, as well as to investigate their potential predictive roles.
Materials and Methods: In this retrospective cross-sectional study, the missed group included 150 pregnant women diagnosed with missed abortion between the ages of 18 and 40. This group was compared to a control group of 150 pregnant women with healthy singleton pregnancies, matched according to gestational week. Demographic data and laboratory results for all cases were collected retrospectively from the hospital automation system. Exclusion criteria included multiple pregnancy, recurrent pregnancy loss, chronic illness, history of malignancy, smoking or alcohol use, hereditary thrombophilia, and a history of anhydramnios.
Results: The demographic characteristics of the groups were similar (p>0.05). Mean lymphocyte levels were higher in the missed abortion group compared to the control group (p=0.037). The median NLR value was 2.88 (2.26–3.66) in the control group and 2.62 (1.81–3.44) in the missed abortion group, showing a significant difference (p=0.018). No significant differences were observed between the groups in other hematological parameters (WBC, neutrophil count, RBC, platelet count, HCT, MCV, MPV, PDW, RDW, INR, and hemoglobin) or in inflammatory indices such as PLR (p=0.057) and SII (p=0.073). In the subgroup analysis of pregnancies under 12 weeks, WBC and lymphocyte levels were higher in the missed abortion group, whereas PLR was higher in the control group (p<0.05).
Conclusion: The etiology of missed abortion remains unexplained in most cases. This study suggests that NLR and lymphocyte levels may have predictive value in the diagnosis of missed abortion. Particularly in early pregnancy, careful evaluation of these parameters may contribute to the identification of high-risk cases.

Keywords: Missed abortion, inflammatory markers, NLR, PLR, SII

ÖZET
Amaç: Bu çalışmanın amacı, hematolojik inflamatuar belirteçler olan Nötrofil/Lenfosit Oranı (NLR), Trombosit/Lenfosit Oranı (PLR) ve Sistemik İmmün-İnflamatuar İndeks (SII) ile missed abortus arasındaki ilişkiyi değerlendirmek ve bu belirteçlerin öngörüdeki potansiyel rollerini araştırmaktır.
Gereç ve Yöntemler: Bu retrospektif kesitsel çalışmada, 18–40 yaş aralığında missed abortus tanısı alan 150 gebeden oluşan missed grubu ile gebelik haftasına göre eşleştirilmiş, sağlıklı tekil gebelikleri bulunan 150 gebeden oluşan kontrol grubu karşılaştırılmıştır. Çalışmaya dahil edilen tüm olguların demografik verileri ve laboratuvar sonuçları, hastane otomasyon sisteminden retrospektif olarak elde edilmiştir. Çoğul gebelik, tekrarlayan gebelik kaybı, kronik hastalık, kanser öyküsü, sigara/alkol kullanımı, kalıtsal trombofili ve anhidroamniyoz öyküsü olanlar çalışma dışı bırakılmıştır.
Bulgular: Grupların demografik özellikleri benzerdi (p>0,05). Missed abortus grubunda ortalama lenfosit düzeyleri kontrol grubuna göre daha yüksekti (p=0,037). NLR medyan değeri de kontrol grubunda 2,88 (2,26–3,66) iken, missed grubunda 2,62 (1,81–3,44) olarak saptandı ve bu fark anlamlıydı (p=0,018). Diğer hematolojik parametreler (WBC, nötrofil sayısı, RBC, trombosit sayısı, HCT, MCV, MPV, PDW, RDW, INR ve hemoglobin) ile inflamatuvar belirteçlerden PLR (p=0,057) ve SII (p=0,073) açısından gruplar arasında belirgin fark izlenmedi. Alt grup analizinde (gebelik <12 hafta), missed abortus grubunda WBC ve lenfosit düzeyleri daha yüksek, PLR ise kontrol grubunda daha yüksek bulundu (p<0,05).
Sonuç: Missed abortus etiyolojisi çoğu vakada açıklanamamaktadır. Bu çalışma, NLR ve lenfosit düzeylerinin missed abortus tanısında prediktif değer taşıyabileceğini göstermektedir. Özellikle gebeliğin erken döneminde bu parametrelerin dikkatle değerlendirilmesi, riskli olguların belirlenmesine katkı sağlayabilir.

Anahtar Kelimeler: Missed abortus, inflamatuar belirteçler, NLR, PLR, SII

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INTRODUCTION

Missed abortion is defined as the intrauterine retention of a nonviable fetus before the 20th week of gestation (1). Miscarriage occurs in nearly 15% of clinically identified pregnancies (2). Loss of pregnancy without medical intervention is frequently observed and represents a significant health issue among women of reproductive age, with about 25% of women experiencing at least one miscarriage during their lifetime (3). Abortions are categorized as threatened, inevitable, complete, incomplete, septic, missed, or anembryonic types. In missed abortion cases, the precise moment of fetal demise is generally unknown (4). It is one of the most frequent complications in early pregnancy (5). The etiopathogenesis of missed abortion includes several factors such as chromosomal anomalies, advanced maternal age, previous pregnancy losses, endocrine disorders, obesity, diabetes, thyroid disorders, inherited thrombophilia, drug and substance use, infections, cervical insufficiency, and uterine structural abnormalities (e.g., fibroids, polyps, septum, or intrauterine adhesions (2,6). However, in nearly 50% of cases, no underlying cause can be identified.

Although inflammation is recognized as a normal physiological process during early pregnancy, pathological examinations of curettage specimens often show inflammation as the most common histopathological finding (7,8). The exact timing and mechanism by which inflammation leads to miscarriage remain unclear (9). Inflammatory markers, such as the values of PLR and NLR, are obtained through complete blood counts that include lymphocyte, neutrophil, and platelet counts. These markers are commonly used to evaluate systemic immune response and infection. Recently, these ratios have been linked to chronic inflammatory diseases, cardiovascular conditions, and malignancies (10–12). In this context, the Systemic Immune-Inflammation Index (SII), calculated as (neutrophil count × platelet count) divided by lymphocyte count, is seen as a more comprehensive parameter that indicates both systemic inflammation and immune response.

These parameters may help clarify inflammatory processes involved in diseases with unknown causes. Since the cause remains unclear in nearly half of missed abortion cases, this study aimed to assess the relationship between hematological inflammatory markers and missed abortion and to explore their potential as predictive indicators.

MATERIALS AND METHODS

The study was conducted at the Obstetrics and Gynecology Clinic of a tertiary hospital from January to June 2023. It used a retrospective case-control design. The case group included 150 pregnant women aged 18-40 who met the inclusion criteria and were diagnosed with missed abortion before 20 weeks. The control group consisted of 150 pregnant women with healthy singleton pregnancies, matched for gestational age at the time of diagnosis in the missed abortion group. All control group participants had routine outpatient follow-up records confirming uncomplicated pregnancies that extended beyond the 20th week of gestation. Inclusion criteria included being between 18 and 40 years old, having a singleton pregnancy of less than 20 weeks, newly diagnosed pregnant women in whom the fetal heartbeat has been detected as absent in the case group, and healthy pregnant women at the same gestational weeks in the control group. Exclusion criteria included multiple pregnancies, a history of recurrent miscarriage, chronic illnesses (such as hypertension, diabetes mellitus, thyroid, and rheumatologic diseases), history of malignancy, alcohol consumption, smoking, hereditary thrombophilia, and anhydramnios.

Demographic data and laboratory results were retrospectively collected from the hospital's electronic database. For the missed abortion group, laboratory values were recorded at the time of diagnosis and hospital admission. For the control group, laboratory data were obtained from the same gestational week as their matched cases, specifically from routine outpatient visits during scheduled antenatal check-ups. This method ensured that both groups were compared using laboratory values taken during the same gestational period and under standardized clinical conditions.

This retrospective case-control study was approved by the local Ethics Committee with an assigned approval number (22.09.2023/ 17/15)

Statistical Analysis

The sample size was calculated using G*Power software. Assuming a moderate effect size (0.5), $\alpha = 0.05$, and a power of 95%, the minimum required sample size was determined to be 210 participants, with at least 105 in each group. Data analysis was performed using IBM SPSS Statistics version 27. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequency and percentage. For comparisons of categorical variables, Pearson's Chi-square test was used when expected frequencies were sufficient; otherwise, Fisher–Freeman–Halton test was applied. For continuous variables, independent t-test was used for normally distributed data and Mann–Whitney U test for non-normally distributed data. Receiver Operating Characteristic (ROC) curve analysis was performed to assess the discriminatory power of markers.A p-value <0.05 was considered statistically significant.

RESULTS

The study comprised a total of 300 participants — 150 with missed abortion and 150 healthy controls. The groups were found to be demographically similar, with no statistically significant differences ($p>0.05$). Table 1 shows the demographic characteristics. Except for lymphocyte count, there were no significant differences between the control and missed abortion groups across routine hematologic indices. The lymphocyte count was higher in the missed abortion group (2.18 ± 0.70 vs. $2.02 \pm 0.61 \times 10^3/\mu L$), and this difference was statistically significant ($p=0.037$; mean difference −0.158, 95% CI −0.306 to −0.010; effect size −0.242). Table 2 presents a comparison of laboratory parameters between the groups.

When comparing inflammatory markers, the control group showed a higher median NLR than the missed group (2.88 [2.26–3.66] vs. 2.62 [1.81–3.44]); this difference was statistically

Table 1. Descriptive Characteristics of Pregnant Women

Variable	Control Group (N=150)	Missed Group (N=150)	t/χ^2	p
Age (years)	26.80 ± 5.36	26.66 ± 5.75	0.218	0.827
Height (cm)	160.82 ± 5.26	161.73 ± 4.00	-1.679	0.094
Weight (kg)	63.50 ± 10.79	64.40 ± 8.41	-0.806	0.421
BMI (kg/m^2)	24.56 ± 4.09	24.55 ± 3.04	0.034	0.973
Gravida	2.15 ± 1.10	2.33 ± 1.33	-1.321	0.187
Parity	1.15 ± 1.10	1.31 ± 1.33	-1.137	0.257
Living Children	1.15 ± 1.10	1.30 ± 1.32	-1.090	0.277
Nationality (Turkish/Syrian)	135 (90.0%) / 15 (10.0%)	126 (84.0%) / 24 (16.0%)	2.387	0.169
Education Level	Various	Various	0.877	0.825
Employment (Yes/No)	76 (50.7%) / 74 (49.3%)	72 (48.0%) / 78 (52.0%)	0.213	0.729
Gestational Age (<12 / ≥12 weeks)	100 / 50	101 / 49	0.015	1.000

Table 2. Comparison of Laboratory Parameters Between Groups (N=300)

Laboratory Parameter	Control Group	Missed Abortion Group	95% confidence intervals (95% CI)	Effect Size	p-value (t/U)
Hemoglobin (g/dL)	12.50 ± 1.03	12.44 ± 1.30	0.053 (−0.214 to 0.319)	0.045	0.698
Platelet (10^3/μL)	258.67 ± 58.28	260.92 ± 66.80	−2.255 (−16.499 to 11.989)	−0.036	0.756
Lymphocyte (10^3/μL)	2.02 ± 0.61	2.18 ± 0.70	−0.158 (−0.306 to −0.010)	−0.242	0.037
Hematocrit (%)	37.35 ± 2.70	37.68 ± 3.49	−0.332 (−1.040 to 0.376)	−0.107	0.357
MCV (fL)	84.05 ± 5.22	83.94 ± 5.41	0.114 (−1.094 to 1.322)	0.022	0.853
INR	1.07 ± 0.08	1.07 ± 0.08	0.003 (−0.014 to 0.021)	0.046	0.694
WBC (10^3/μL)	8.59 (7.24–9.82)	8.55 (7.08–10.3)	−0.130 (−0.650 to 0.390)	0.030	0.650
Neutrophil (10^3/μL)	5.71 (4.60–6.97)	5.58 (4.39–6.84)	0.100 (−0.340 to 0.520)	−0.031	0.644
RBC (×10^6/μL)	4.44 (4.19–4.73)	4.51 (4.23–4.73)	−0.060 (−0.160 to 0.030)	0.092	0.167
MPV (fL)	10.4 (9.9–11.1)	10.4 (9.8–11.1)	≈0.000 (−0.200 to 0.200)	0.005	0.944
PDW (fL)	11.80 (10.6–13.3)	11.90 (10.5–13.3)	≈0.000 (−0.500 to 0.400)	≈ 0.000	0.998
RDW (%)	13.4 (12.6–14.4)	13.1 (12.6–14.6)	0.100 (−0.200 to 0.300)	−0.035	0.603

MPV: mean platelet volume; PDW: platelet distribution width; RDW-SD: red blood cell distribution width; WBC: white blood cell, RBC:red blood count

significant (p=0.018; mean/median difference=0.320, 95% CI 0.063–0.564) with a small effect size (−0.158). PLR was numerically higher in controls (130 [109–163] vs. 120 [94.7–151]); however, the difference did not reach statistical significance (difference=9.295, 95% CI −0.233–18.973; p=0.057; effect size=−0.127). SII showed a similar, non-significant trend favoring controls (733 [562–972] vs. 649 [452–913]; difference=69.112, 95% CI −5.745–146.063; p=0.073; effect size=−0.120). Overall, only NLR differed significantly between groups, and the effect sizes across markers were consistently small. Table 3 presents the distribution of NLR, PLR, and SII values across different groups.

ROC analyses for NLR, PLR, and SII were conducted to assess their ability to predict missed abortion. All parameters had AUC values below 0.5, indicating limited discriminative power. For transparency, ROC curves and AUCs with 95% confidence intervals are shown in Table 4 and Figure 1. Due to the non-significant AUC results, these findings lack clinical predictive value. In the subgroup analysis for pregnancies less than 12 weeks, the missed group exhibited a higher median WBC count compared to controls (8.54 [7.27–10.4] vs. 7.93 [6.71–9.30] ×10^3/μL), with statistical significance (p=0.020; effect size=0.16). The mean lymphocyte count was also higher in the missed group (2.29±0.73 vs. 1.99±0.58 ×10^3/μL), indicating a strong difference (p=0.001; effect size=0.46). Conversely, the median PLR was higher in the control group (132 [111–167] vs. 119 [92.9–148]), and this difference was statistically

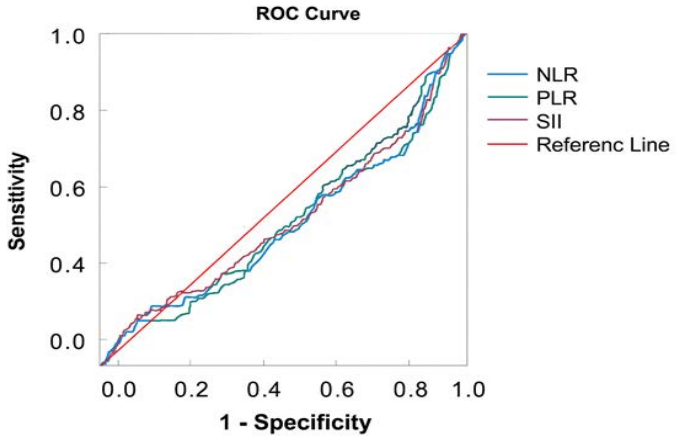

Figure 1. ROC Curve of NLR, PLR, and SII for Predicting Missed Abortion.

Table 3. Distribution of NLR, PLR, and SII Values by Group

Inflammatory Marker	Control Group (N=150)	Missed Group (N=150)	95% confidence intervals (95% CI)	Effect Size	P value
NLR	2.88 (2.26–3.66)	2.62 (1.81–3.44)	0.320 (0.063 to 0.564)	−0.158	0.018
PLR	130 (109–163)	120 (94.7–151)	9.295 (−0.233 to 18.973)	−0.127	0.057
SII	733 (562–972)	649 (452–913)	69.112 (−5.745 to 146.063)	−0.120	0.073

NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio; SII: Systemic Immune-Inflammation Index
The Mann-Whitney U test was used. Values are given as median (25th–75th percentile). Differences are presented as Missed – Control with 95% confidence intervals. Effect sizes are given rank biserial correlation (r) for Mann–Whitney U. p-values indicate statistical significance ($p < 0.05$).

Table 4. ROC Analysis Results for Determining the Predictive Value of NLR, PLR, and SII in Pregnant Women According to Group

Laboratory Parameters	Area Under the Curve(AUC)	Standard Error	p	95% Confidence Interval	
				Lower	Upper
NLR	0.421	0.033	0.018	0.355	0.486
PLR	0.436	0.033	0.057	0.371	0.501
SII	0.440	0.033	0.073	0.375	0.506

NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio; SII: Systemic Immune-Inflammation Index

Table 5. Laboratory Parameters and Inflammatory Markers in Pregnancies Under 12 Weeks Weeks by Group (N=20)

Parameter		Control Group (N=100)	Missed Group (N=101)	95% confidence intervals CI	Effect Size	p-value (t/U)
WBC (10^3/μL)	Med. (25-75th)	7.93 (6.71–9.30)	8.54 (7.27–10.4)	0.017–0.024	0.16	0.020
Hemoglobin(g/dL)	$\bar{x}$±SS	12.64 ± 1.06	12.46 ± 1.26	-0.15–0.50	0.15	0.278
Neutrophil (10^3/μL)	Med. (25-75th)	5.22 (4.33–6.23)	5.58 (4.47–7.04)	0.178–0.198	0.09	0.188
Platelet(10^3/μL).	$\bar{x}$±SS	259.33 ± 52.50	265.16 ± 70.73	-23.15–11.49	0.09	0.507
Lymphocyte(10^3/μL).	$\bar{x}$±SS	1.99 ± 0.58	2.29 ± 0.73	-0.49–-0.12	0.46	0.001
RBC (×10^6/μL)	Med. (25-75th)	4.50 (4.30–4.74)	4.55 (4.32–4.74)	0.404–0.429	0.06	0.414
Hematocrit(%)	$\bar{x}$±SS	37.79 ± 2.51	38.02 ± 3.25	-1.03–0.58	0.08	0.582
MCV(fL)	$\bar{x}$±SS	83.86 ± 4.75	83.79 ± 5.45	-1.35–1.50	0.02	0.916
MPV (fL)	Med. (25-75th)	10.40 (9.90–11.0)	10.50 (9.90–11.2)	0.624–0.649	0.03	0.632
PDW (fL)	Med. (25-75th)	11.80 (10.6–13.3)	11.90 (10.6–13.7)	0.692–0.715	0.03	0.702
RDW(%)	Med. (25-75th)	13.5 (12.6–14.4)	13.1 (12.7–14.4)	0.595–0.620	0.04	0.600
INR	$\bar{x}$±SS	1.07 ± 0.08	1.07 ± 0.08	-0.02–0.02	0.02	0.895
NLR	Med. (25-75th)	2.68 (2.22–3.50)	2.52 (1.84–3.23)	0.081–0.095	0.12	0.089
PLR	Med. (25-75th)	132 (111–167)	119 (92.9–148)	0.005–0.010	0.18	0.009
SII	Med. (25-75th)	683 (534–890)	649 (485–893)	0.307–0.331	0.07	0.317

NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio; SII: Systemic Immune-Inflammation Index, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio; SII: Systemic Immune-Inflammation Index
Notes: Normally distributed variables were analyzed with independent samples t-test (reported as mean ± SD); non-normally distributed variables were analyzed with Mann–Whitney U (reported as median [25th–75th percentile]). Differences are presented as Missed – Control with 95% confidence intervals. Effect sizes are given as Cohen's d for t-tests and rank biserial correlation (r) for Mann–Whitney U. Bold p-values indicate statistical significance ($p < 0.05$).

Table 6. ROC Analysis of NLR, PLR, SII and Lymphocyte for Group-wise Prediction in Pregnancies <12 Weeks' Gestation

Laboratory Parameter	Area Under the Curve (AUC)	Standard Error	p	95% Confidence Interval		Cut-off	Sensitivity	Specificity
				Lower	Upper			
NLR	0.430	0.041	0.089	0.351	0.510	-	-	-
PLR	0.394	0.040	0.009	0.316	0.472	131.69	%40	%50
SII	0.459	0.041	0.317	0.379	0.539	-	-	-
Lymphocyte	0.607	0.040	0.009	0.529	0.685	2.09	%51	%58

NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio; SII: Systemic Immune-Inflammation Index

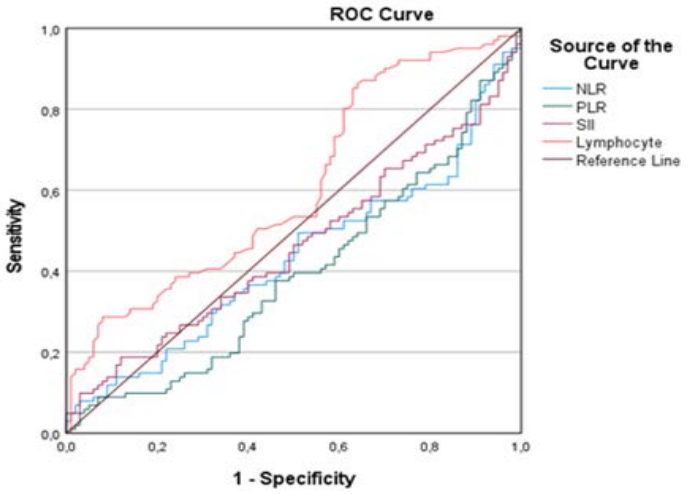

Figure 2. ROC Curve of NLR, PLR, and SII for Predicting Missed Abortion.

significant (p=0.009; effect size=0.18). Other hematologic indices did not differ significantly between groups; NLR showed a nonsignificant increasing trend in controls, and SII remained similar. Table 5 shows the laboratory parameters and inflammatory markers in pregnancies under 12 weeks, categorized by group.

In the study, the predictive capability of NLR, PLR, SII, and lymphocyte levels in different groups during pregnancies of less than 12 weeks was evaluated using ROC curves. The AUC for lymphocytes was 0.607 (SE=0.040; p=0.009; 95% CI: 0.529–0.685), indicating limited discriminative ability; at a cutoff of 2.09, sensitivity was 51%, and specificity was 58%. For PLR, the AUC was 0.394 (SE=0.040; p=0.009; 95% CI: 0.316–0.472), which is below 0.5 and statistically significant; this suggests weak discrimination and an opposite trend (higher PLR may be associated with the control group). At a cutoff of 131.69, sensitivity was 40%, and specificity was 50%. NLR (AUC 0.430; SE=0.041; p=0.089; 95% CI: 0.351–0.510) and SII (AUC 0.459; SE=0.041; p=0.317; 95% CI: 0.379–0.539) did not show significant discriminative ability; cutoff values were not reported for either marker. Table 6 and Figure 2 show the ROC analysis results evaluating the predictive value of NLR, PLR, SII, and lymphocyte levels for pregnancies under 12 weeks of gestation.

DISCUSSION

In this study missed ve control group comparisons showed a significantly higher lymphocyte count in the missed abortion group and lower NLR values. These findings imply a possible change in the immune response linked to early pregnancy loss. Increased lymphocyte levels may indicate a shift from innate immunity, which is neutrophil-driven, to adaptive immune responses fueled by lymphocytes, possibly reflecting an immune regulation imbalance. Prior research also supports this link, suggesting that altered lymphocyte-mediated immunity and maternal-fetal tolerance could be involved in missed abortions (13). Although PLR and SII values did not achieve statistical significance in the overall population, their borderline p-values (p=0.057 and p=0.073, respectively) suggest possible biological relevance. SII, which combines neutrophils, lymphocytes, and platelets, is considered a comprehensive inflammatory marker (14). While our results did not show significant differences, the slight downward trends in PLR and SII in the missed abortion group are notable.

Previous studies, reported higher SII levels in cases of threatened or missed abortion (15-16), which may reflect temporal or population differ. Th1/Th2 balance is directly related to lymphocytes because this balance is one of the main mechanisms that determines how the immune system works during pregnancy. A Th2-dominant immune response is essential for successful pregnancy maintenance, while a shift toward Th1-type cytokine profile has been associated with pregnancy loss. Alterations in circulating lymphocyte populations may reflect this imbalance (17). In the subgroup analysis of pregnancies <12 weeks (n=201), WBC and lymphocyte levels were significantly higher in the missed abortion group (p=0.020 and p=0.001, respectively), while PLR was significantly lower (p=0.009). This suggests that immune dysregulation may be more prominent in very early gestational losses. The elevated lymphocyte levels may reflect a Th1-skewed immune response, associated with cytotoxic T-cell activation and fetal rejection mechanisms (18). In contrast, the decrease in PLR might indicate impaired platelet-mediated immune signaling, which may impact placental development.

Interestingly, in the <12-week subgroup, the ROC analysis demonstrated that lymphocyte count had a modest predictive value (AUC = 0.607; p=0.009), while PLR also showed fair discriminative ability (AUC = 0.394; p=0.009). These results support the hypothesis that inflammatory markers, especially lymphocyte-driven indices, may provide valuable insights into early pregnancy failure. A lower PLR may reflect diminished platelet-mediated immune and paracrine signaling at the maternal–fetal interface (e.g., reduced P-selectin/CD40L interactions and growth-factor release), processes that support trophoblast invasion and spiral-artery remodeling. Consistent with this mechanism, human studies have reported lower mean platelet volume (a surrogate of platelet activation) in miscarriage cohorts, aligning with the notion of blunted platelet activity (19--21). Taken together, a decrease in PLR could plausibly contribute to impaired placental development through attenuated platelet–trophoblast and platelet–immune cross-talk (22-23). Previous studies show mixed results: Liu et al. reported no significant differences in NLR or PLR values between groups, while another study found elevated SII in missed abortion (14,24). These inconsistencies may stem from sample size, gestational age differences, or inclusion/exclusion criteria, using a self-controlled design, found no difference in SII between pregnancy and abortion periods, further emphasizing individual variability (25). The gestational age-specific nature of immune modulation is essential. Our study found that immune marker patterns differ between early (<12

weeks) and later gestation (≥12 weeks), showing a dynamic shift in maternal immune tolerance as pregnancy advances. This aligns with longitudinal studies demonstrating that NLR increases with gestational age, while PLR may decrease (18).

In our study, the missed abortion group showed a lower NLR and higher lymphocyte count compared to healthy controls. Although elevated NLR has been widely associated with adverse pregnancy outcomes, our findings may reflect early gestational immune modulation or a compensatory Th2-shift following fetal demise. Similar immunological alterations have been suggested in rheumatic pregnancies and early pregnancy complications, where altered NLR and lymphocyte activity indicate systemic immune imbalance (26).

Study Limitaitons

The study was conducted at a single tertiary center, which might limit how well the findings apply to different populations or healthcare settings. The research focused on basic hematologic indices (e.g., NLR, PLR, SII) and did not include cytokine levels, T-cell subsets, or hormonal measurements, which could provide more detailed insights into the immune mechanisms. Although laboratory data for the missed abortion group were collected at the time of hospital admission and gestational age matching was used, a limitation remains because the exact timing of fetal demise could not be determined. This uncertainty may have caused slight physiological variations in inflammatory markers between the groups.

CONCLUSION

This study found higher lymphocyte counts and lower NLR in missed abortion cases, especially before 12 weeks of gestation, indicating a Th1-dominant immune response and reduced maternal-fetal tolerance. Although PLR and SII did not significantly differ overall, their patterns in early pregnancy suggest they could serve as early biomarkers. Further multicenter studies with matched gestational ages are necessary to confirm these findings and determine whether such hematological changes cause or result from early pregnancy loss.

DECLARATIONS

Conflict of Interest: *The authors declare that there is no conflict of interest.*

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