

# Can Complete Blood Count Parameters Analyzed in Early Pregnancy Predict Threatened Abortion and Spontaneous Abortion: A Retrospective Study

## Erken Gebelikte Analiz Edilen Tam Kan Sayımı Parametreleri Düşük Tehdidi ve Gebelik Kaybını Öngörebilir mi: Retrospektif Bir Çalışma

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### ABSTRACT

**Background:** To evaluate whether first-trimester complete blood count (CBC) parameters predict the risk of spontaneous abortion and threatened abortion.

**Materials and Methods:** We retrospectively analyzed 90 pregnant women who presented to our hospital in 2024. Participants were equally divided into three groups: spontaneous abortion (n = 30), threatened abortion (n = 30), and healthy controls with no history of bleeding or miscarriage (n = 30). First-trimester CBC parameters assessed included hemoglobin, total white blood cell count (WBC), neutrophil count, and platelet count. Platelet indices (mean platelet volume [MPV], platelet distribution width [PDW]) and inflammatory ratios (MPV/platelet ratio, PDW/platelet ratio, platelet-to-lymphocyte ratio [PLR], neutrophil-to-lymphocyte ratio [NLR], and monocyte-to-lymphocyte ratio [MLR]) were evaluated for their ability to distinguish normal early pregnancies from pathological early pregnancies.

**Results:** Maternal age was comparable across groups; however, gravidity, parity, gestational age at assessment, and body mass index (BMI) differed significantly. In univariate analyses, WBC (p = 0.040), neutrophil count (p = 0.018), NLR (p = 0.045), and MLR (p = 0.032) differed among groups, whereas hemoglobin, platelet count, MPV, PDW, and PLR did not differ significantly (all p > 0.05). After Bonferroni correction, statistical significance remained for only three comparisons: gestational age (spontaneous abortion vs. controls, p = 0.001), neutrophil count (spontaneous abortion vs. threatened abortion, p = 0.015), and BMI (spontaneous abortion vs. controls, p = 0.008). In a multinomial logistic regression model adjusted for gestational age, BMI, and gravidity (reference: controls), neutrophil count (adjusted odds ratio [aOR] = 0.487; 95% confidence interval [CI]: 0.251–0.946; p = 0.034), NLR (aOR = 0.194; 95% CI: 0.041–0.919; p = 0.039), and MLR (aOR = 0.433; 95% CI 0.214–0.875; p = 0.020) were inversely associated with the odds of spontaneous abortion per 1 standard deviation. No independent associations were observed for the other parameters.

**Conclusion:** Neutrophil count and CBC-derived indices (NLR, MLR) may independently predict spontaneous abortion after adjustment; platelet-related parameters were not significant predictors. These markers should not be used in isolation but may complement clinical and sonographic assessments. Larger prospective studies are needed.

**Keywords:** Neutrophil-to-lymphocyte ratio, spontaneous abortion, threatened abortion

### ÖZ

**Amaç:** Birinci trimester tam kan sayımı (TKS) parametrelerinin spontan abortus ve düşük tehdidi riskini öngörmedeki değerini araştırmak.

**Gereç ve Yöntemler:** 2024 yılında hastanemize başvuran 90 gebe kadın retrospektif olarak analiz edildi. Katılımcılar eşit üç gruba ayrıldı: spontan abortus (n = 30), düşük tehdidi (n = 30) ve kanama ya da düşük öyküsü olmayan sağlıklı gebeliğe sahip kontroller (n = 30). Hematolojik değerlendirme için birinci trimester kan sonuçları kullanıldı. Analize hemoglobin, toplam lökosit sayısı (WBC),



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nötrofil sayısı ve trombosit sayısı dâhil edildi. Ortalama trombosit hacmi (MPV) ve trombosit dağılım genişliği (PDW) gibi trombosit indeksleri ile birlikte MPV/trombosit, PDW/trombosit, trombosit/lenfosit oranı (TLO), nötrofil/lenfosit oranı (NLO) ve monosit/lenfosit oranı (MLO) gibi inflamatuvar oranlar incelendi. Bu değişkenler, normal ve patolojik erken gebelikleri ayırt etmedeki ilişkilerini değerlendirmek amacıyla analiz edildi.

**Bulgular:** Maternal yaş grupları arasında benzerdi; ancak gravide, parite, değerlendirme sırasındaki gebelik haftası ve vücut kitle indeksi (VKİ) anlamlı farklıydı. Tek değişkenli analizlerde WBC ( $p = 0,040$ ), nötrofil ( $p = 0,018$ ), NLO ( $p = 0,045$ ) ve MLO ( $p = 0,032$ ) grupları arasında farklılık gösterdi; hemoglobin, trombosit, MPV, PDW ve TLO anlamlı değildi (tümü  $p > 0,05$ ). Bonferroni düzeltmesi sonrası yalnızca üç karşılaştırmada anlamlılık korundu: gebelik haftası (spontan abortus–kontrol,  $p = 0,001$ ), nötrofil (spontan abortus–düşük tehdidi,  $p = 0,015$ ) ve VKİ (spontan abortus–kontrol,  $p = 0,008$ ). Gebelik haftası, VKİ ve gravideye göre düzeltilmiş multinomiyal lojistik regresyonda (referans: kontrol) nötrofil (düzeltilmiş olasılık oranı [aOR] = 0,487; %95 güven aralığı [GA]: 0,251–0,946;  $p = 0,034$ ), NLO (aOR = 0,194; %95 GA 0,041–0,919;  $p = 0,039$ ) ve MLO (aOR = 0,433; %95 GA 0,214–0,875;  $p = 0,020$ ) her 1 standart sapma artış için spontan abortus olasılığıyla ters ilişkili bulundu; diğer parametrelerde bağımsız ilişki yoktu.

**Sonuç:** Nötrofil sayısı ve TKS-türevi indeksler (NLO, MLO), karıştırıcı değişkenler için düzeltme yapıldıktan sonra spontan abortusu öngörmeye bağımsız bir değere sahip olabilirken, trombosit parametreleri ve diğer indeksler anlamlı bulunmadı. Bu bulgular, hematolojik belirteçlerin klinik karar vermede tek başına kullanılmaması, ancak klinik ve ultrasonografik değerlendirmeyi tamamlayıcı nitelikte olabileceğini düşündürmektedir. Daha büyük, prospektif çalışmalar gereklidir.

**Anahtar Kelimeler:** Nötrofil/lenfosit oranı, spontan abortus, düşük tehdidi

## Introduction

First-trimester vaginal bleeding occurs in about 7–27% of pregnancies, and roughly 12% of these cases end in miscarriage (1). During this period, the leading causes of vaginal bleeding include spontaneous abortion, threatened abortion, ectopic pregnancy, and cervical disorders. A thorough medical history, a detailed physical examination, ultrasound, and laboratory tests are used to determine the cause of bleeding during pregnancy.

Spontaneous abortion refers to a nonviable intrauterine pregnancy before 20 weeks of gestation. In clinical practice, it is also termed miscarriage or pregnancy loss. The pathophysiology of spontaneous abortion is complex. In addition, the identified risk factors include a previous miscarriage, young maternal age (<20 years), advanced maternal age (>35 years), uncontrolled diabetes, hypertension, thyroid disease, chromosomal abnormalities, smoking, alcohol use, obesity or extremely low body weight, uterine anomalies (uterine septum, uterus didelphys, etc.), and cervical insufficiency (2). Threatened abortion is a condition occurring before the 20<sup>th</sup> week of gestation, characterized by vaginal bleeding with a closed cervix. Under these conditions, approximately 15–20% of pregnancies may result in miscarriage (3).

The complete blood count (CBC), a simple and widely used test during pregnancy, has been evaluated in numerous studies for its role in predicting spontaneous or threatened abortion. These parameters included the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), investigated for their association with inflammation, platelet distribution width (PDW)/platelet ratio, mean

platelet volume (MPV)/platelet ratio, MPV, and PDW, examined to determine their association with thrombosis. Other biochemical markers that have been examined in some studies to assess the risk of miscarriage (spontaneous abortion) include progesterone, serum beta-human chorionic gonadotropin alpha-fetoprotein, follistatin, and activin A. However reliable biochemical markers that can predict the risk of miscarriage and threatened abortion have not yet been established due to the complexity of the underlying mechanisms.

Pregnancy is inherently prothrombotic, and disturbances in placental vascular hemostasis are considered major contributors to spontaneous abortion. Decreased platelet function has been reported in the patient group (4). In this regard, many studies have examined parameters such as PDW, MPV, PDW/platelet count ratio, and MPV/platelet count ratio to demonstrate this prothrombotic state. Platelets also play an important role in inflammation by increasing the secretion of cytokines.

Bleeding in the first trimester is common; both threatened and spontaneous abortion are significant causes of early pregnancy loss. Currently, reliable biomarkers that can predict which cases of bleeding will result in miscarriage are limited. In recent years, inexpensive hematological indices have received increasing attention. For instance, meta-analyses have demonstrated that the neutrophil-to-lymphocyte ratio (NLR) is significantly higher in women with abortion than in healthy controls (5). Similarly, markers of platelet activation such as MPV and PDW have been associated with spontaneous abortion in systematic reviews (6). However, the evidence is inconsistent because other studies have demonstrated no significant difference

in platelet indices among women with recurrent pregnancy loss (7).

We set out to evaluate the roles of PDW, MPV, PDW/platelet ratio, MPV/platelet ratio, platelet-to-lymphocyte ratio (PLR), NLR, and monocyte-to-lymphocyte ratio (MLR) as predictors of the risk of spontaneous and threatened abortion, and of selected inflammatory and thrombotic markers among CBC indices.

## Materials and Methods

This retrospective analysis included 90 pregnant women admitted to our hospital between January and October 2024. Participants were divided into three equal groups of 30 each: women with threatened abortion, women who experienced spontaneous abortion, and healthy controls without vaginal bleeding. Eligible gestational ages ranged from 6 to 14 weeks. The threatened-abortion group included patients with vaginal bleeding, an intact cervical os, and an ongoing intrauterine pregnancy. The spontaneous abortion group consisted of women diagnosed with pregnancy loss before 14 weeks' gestation. Controls were randomly chosen from women attending the same clinic period with viable first-trimester pregnancies and no bleeding complaints.

Clinical and laboratory data were extracted from archived files and electronic medical records. Demographic variables included maternal age, gravidity, parity, gestational week, and body mass index (BMI). Hematological parameters include hemoglobin, white blood cell (WBC) count, neutrophil, lymphocyte, monocyte, and platelet counts, MPV, and PDW.

Women with systemic conditions likely to influence hematologic indices, including hematologic disorders, multiple pregnancy, smoking, diabetes, chronic hypertension, thyroid dysfunction, autoimmune diseases, or acute or chronic infection were excluded from the study. Ethical approval was obtained from the Non-Interventional Research Ethics Committee of Necmettin Erbakan University (decision number: 2024/5333, dated: 15.11.2024), and the study complied with the principles of the Declaration of Helsinki.

## Statistical Analysis

Data were analyzed using version 22.0 of IBM SPSS Statistics. The normality of continuous variables was first examined using the Shapiro–Wilk test, and the homogeneity of variances was evaluated using Levene's test. Continuous variables that had a normal distribution and equal variances were reported as mean  $\pm$  standard deviation (SD) and compared between groups using one-way analysis of variance (ANOVA). When the assumptions of normality or homogeneity of variances were not met, data were reported

as medians and analyzed using the Kruskal–Wallis test. When overall tests were significant, post hoc pairwise comparisons were conducted using an independent-samples t-test or a Mann–Whitney U test, with the Bonferroni procedure applied to adjust for multiple comparisons.

Effect sizes were also reported to accompany p-values and were expressed as eta squared ( $\eta^2$ ) for ANOVA and  $\epsilon^2$  for Kruskal–Wallis test. Multinomial logistic regression analyses were used to further establish independent associations between hematological measurements and study outcomes. Models were adjusted for potential confounders (gestational age, BMI, and gravidity), and the control group was used as a reference category. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were provided. A two-sided p-value  $<0.05$  was considered statistically significant.

## Power Analysis

Because this was a retrospective study, we included all women who met the inclusion criteria during the study period ( $n = 90$ ; 30 per group). A post-hoc sensitivity analysis using G\*Power (v3.1, one-way ANOVA,  $\alpha = 0.05$ ) indicated approximately 80% power to detect a medium effect size (Cohen's  $f \approx 0.30$ ) and more than 95% power to detect a large effect size (Cohen's  $f \approx 0.40$ ). Accordingly, the study was adequately powered for moderate-to-large effects but may be underpowered for small effects.

## Results

A total of 90 women were evaluated: 30 with spontaneous abortion, 30 with threatened abortion, and 30 healthy controls.

### Demographic Characteristics (Table 1)

There was no significant difference in maternal age among the groups ( $p = 0.730$ ). In contrast, gravidity ( $p = 0.007$ ), parity ( $p = 0.028$ ), BMI ( $p = 0.006$ ), and gestational age at evaluation ( $p = 0.015$ ) differed significantly across groups. Overall, the control group was assessed at a more advanced gestational age and had a lower BMI than the spontaneous abortion group.

### Hematological Parameters (Table 2)

As shown in Table 2, 90 women were evaluated (spontaneous abortion,  $n = 30$ ; threatened abortion,  $n = 30$ ; controls,  $n = 30$ ). WBC levels differed significantly among the groups (medians [interquartile range]: 7.82 [7.05–10.00], 9.77 [8.84–10.39], and 9.65 [7.06–11.56], respectively;  $p = 0.040$ ;  $\eta^2/\epsilon^2 = 0.05$ ). Neutrophil counts also differed significantly across groups (5.25 [4.13–6.62], 6.75 [6.05–7.63], and 6.87 [4.79–8.57], respectively;  $p = 0.018$ ;  $\eta^2/\epsilon^2 =$

0.07). Among inflammatory indices, both NLR (2.55 [1.85–3.35], 3.02 [2.41–4.00], and 3.27 [2.44–4.68], respectively;  $p=0.045$ ,  $\eta^2/\epsilon^2=0.05$ ) and MLR (0.24 [0.21–0.32], 0.28 [0.24–0.34], and 0.29 [0.24–0.40], respectively;  $p=0.032$ ,  $\eta^2/\epsilon^2=0.06$ ) differed significantly among groups. In contrast, no significant between-group differences were observed for hemoglobin ( $p = 0.108$ ), platelet count ( $p = 0.778$ ), MPV ( $p = 0.542$ ), PDW ( $p = 0.574$ ), PLR ( $p = 0.904$ ), or the MPV/platelet ( $p = 0.965$ ) and PDW/platelet ( $p = 0.997$ ) ratios (all  $p > 0.05$ ). Overall, the observed significant differences were associated with small effect sizes ( $\eta^2/\epsilon^2 \approx 0.05–0.07$ ).

### PostHoc Comparisons (Supplementary Table 1)

According to Bonferroni-adjusted analyses using a significance threshold of  $p < 0.017$ , only three comparisons reached statistical significance. Gestational age differed significantly between the spontaneous abortion and control groups ( $p = 0.001$ ), while neutrophil counts differed significantly between the spontaneous abortion and

threatened abortion groups ( $p = 0.015$ ). In addition, BMI differed significantly between the spontaneous abortion and control groups ( $p = 0.008$ ). In contrast, the initially observed differences in gravidity ( $p = 0.027$ ,  $p = 0.019$ ), WBC count ( $p = 0.021$ ), and MLR ( $p = 0.042$ ) did not remain statistically significant after Bonferroni correction.

### Multinomial Logistic Regression (Table 3).

To minimize multicollinearity between leukocyte subtype counts and derived ratios (e.g., NLR and MLR), we fitted separate adjusted multinomial logistic regression models for each CBC-related marker, expressed per 1-SD increase. Models were adjusted for potential confounders (gestational age, BMI, and gravidity), and the control group was used as a reference category. In these models, no marker was significantly associated with threatened abortion compared with controls (all  $p > 0.05$ ). Compared with controls, neutrophil count (aOR = 0.487, 95% CI 0.251–0.946;  $p = 0.034$ ), NLR (aOR = 0.194, 95% CI 0.041–0.919;

**Table 1. Demographic characteristics across groups.**

Variable	Spontaneous abortion (n = 30)	Threatened abortion (n = 30)	Control (n = 30)	p-value	Effect size ( $\eta^2/\epsilon^2$ )
Age (year)	29.60 ± 5.39	28.50 ± 5.26	29.07 ± 5.43	0.730 <sup>a</sup>	0.01
Gravidity	2.00 (2.00–3.00)	1.50 (1.00–2.00)	3.00 (1.25–4.00)	<b>0.007<sup>b</sup></b>	0.09
Parity	1.00 (0.00–2.00)	0.00 (0.00–1.00)	1.00 (0.00–2.00)	<b>0.028<sup>b</sup></b>	0.06
BMI (kg/m <sup>2</sup> )	29.74 (27.01–34.30)	28.19 (25.47–31.45)	24.79 (23.23–29.83)	<b>0.006<sup>b</sup></b>	0.10
Gestational age (week)	10.00 (8.25–10.00)	9.00 (7.00–13.00)	12.00 (10.25–13.00)	<b>0.015<sup>b</sup></b>	0.07

Reporting rule: mean ± SD if normality and homoscedasticity were satisfied; otherwise median (IQR). Test selection based on Shapiro–Wilk and Levene's tests. Effect sizes are  $\eta^2$  (ANOVA) or  $\epsilon^2$  (Kruskal–Wallis). <sup>a</sup>ANOVA test, <sup>b</sup>Kruskal–Wallis test,  $p < 0.05$  was considered statistically significant. ANOVA, analysis of variance; BMI, body mass index; IQR, interquartile range; SD, standard deviation.

**Table 2. CBC parameters across groups.**

Variable	Spontaneous abortion (n = 30)	Threatened abortion (n = 30)	Control (n = 30)	p-value	Effect size ( $\eta^2/\epsilon^2$ )
Hemoglobin	13.20 (12.30–13.57)	12.80 (11.80–13.57)	11.90 (11.27–13.40)	0.108 <sup>b</sup>	0.03
Platelets	277.50 (228.50–331.25)	273.00 (238.25–314.50)	263.00 (227.25–290.75)	0.778 <sup>b</sup>	0.00
WBC	7.82 (7.05–10.00)	9.77 (8.84–10.39)	9.65 (7.06–11.56)	<b>0.040<sup>b</sup></b>	0.05
Neutrophil	5.25 (4.13–6.62)	6.75 (6.05–7.63)	6.87 (4.79–8.57)	<b>0.018<sup>b</sup></b>	0.07
MPV	10.48 ± 0.89	10.36 ± 0.84	10.25 ± 0.71	0.542 <sup>a</sup>	0.01
PDW	11.80 (10.83–13.38)	11.65 (10.50–13.47)	11.55 (10.80–12.57)	0.574 <sup>b</sup>	0.00
PLR	121.75 (94.66–162.31)	125.84 (105.34–144.69)	131.91 (100.36–167.01)	0.904 <sup>b</sup>	0.00
NLR	2.55 (1.85–3.35)	3.02 (2.41–4.00)	3.27 (2.44–4.68)	<b>0.045<sup>b</sup></b>	0.05
MLR	0.24 (0.21–0.32)	0.28 (0.24–0.34)	0.29 (0.24–0.40)	<b>0.032<sup>b</sup></b>	0.06
MPV/platelet	0.04 (0.03–0.05)	0.04 (0.03–0.05)	0.04 (0.03–0.05)	0.965 <sup>b</sup>	0.00
PDW/platelet	0.04 (0.03–0.05)	0.04 (0.04–0.06)	0.05 (0.04–0.05)	0.997 <sup>b</sup>	0.00

<sup>a</sup>ANOVA test, <sup>b</sup>Kruskal–Wallis test,  $p < 0.05$  was considered statistically significant. Negative  $\epsilon^2$  values (which may occur due to sampling variability) were truncated to 0.00 for reporting. ANOVA, analysis of variance; CBC, complete blood count; MLR, monocyte-to-lymphocyte ratio; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PDW, platelet distribution width; PLR, platelet-to-lymphocyte ratio; WBC, white blood cell count.

**Table 3. Adjusted multinomial logistic regression results for CBC-related markers across groups (reference: control).**

Marker (per 1 SD increase)	Threatened abortion vs. control adjusted OR (95% CI)	p-value	Spontaneous abortion vs. control adjusted OR (95% CI)	p-value
Hemoglobin	1.267 (0.737–2.179)	0.393	1.592 (0.882–2.875)	0.123
Platelets	0.876 (0.511–1.501)	0.630	0.871 (0.470–1.617)	0.662
WBC	1.118 (0.631–1.980)	0.702	0.617 (0.334–1.142)	0.125
Neutrophil	1.020 (0.567–1.835)	0.948	<b>0.487 (0.251–0.946)</b>	<b>0.034</b>
MPV	1.076 (0.600–1.929)	0.807	1.221 (0.680–2.192)	0.504
PDW	1.139 (0.620–2.096)	0.674	1.345 (0.731–2.473)	0.341
PLR	0.956 (0.580–1.574)	0.859	0.894 (0.484–1.650)	0.719
NLR	1.155 (0.547–2.438)	0.706	<b>0.194 (0.041–0.919)</b>	<b>0.039</b>
MLR	0.924 (0.531–1.607)	0.780	<b>0.433 (0.214–0.875)</b>	<b>0.020</b>

Each marker was evaluated in a separate adjusted multinomial logistic regression model (per 1-SD increase) to avoid multicollinearity among mathematically related predictors (e.g., leukocyte subtype counts and derived ratios). Models were adjusted for gestational age, BMI, and gravidity. BMI, body mass index; CI, confidence interval; MLR, monocyte-to-lymphocyte ratio; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; OR, odds ratio; PDW, platelet distribution width; PLR, platelet-to-lymphocyte ratio; SD, standard deviation; WBC, white blood cell count.

$p = 0.039$ ), and MLR (aOR = 0.433, 95% CI 0.214–0.875;  $p = 0.020$ ) were inversely associated with spontaneous abortion.

## Discussion

Based on the assumption that prothrombotic events may affect the hemostatic balance in placental vessels and that chronic inflammation may cause spontaneous and threatened abortion, we evaluated various hematologic parameters in our study. PDW, MPV, PDW/platelet ratio, MPV/platelet ratio, PLR, NLR, and MLR were examined in this context.

Many studies have shown that threatened miscarriage is associated with an increased risk of complications later in pregnancy (8). These complications can be avoided if the cause of threatened miscarriage is elucidated. Chronic decidual inflammation with hemorrhage has been proposed in the pathophysiology of threatened abortion (8). Therefore, we analyzed the levels of the inflammatory markers NLR, PLR, and MLR.

Inconsistencies exist among studies examining NLR and PLR values in patients with spontaneous abortion and in those with threatened abortion. In a study of 300 patients that compared threatened abortion, spontaneous abortion, and healthy pregnancies, NLR did not differ between groups, whereas PLR was higher in the threatened abortion and spontaneous abortion groups (9). In another study of 285 patients with spontaneous abortion and healthy pregnant women as the control group, no difference was found between NLR and PLR (10).

Recent evidence from systematic reviews further contextualizes our findings. A 2024 systematic review and meta-analysis evaluating NLR and PLR across early pregnancy loss phenotypes (including threatened abortion,

missed abortion, and RPL) reported that NLR was often higher in early pregnancy loss, whereas PLR did not show a consistent difference, and rated the certainty of evidence as moderate while noting substantial between-study heterogeneity (e.g., variations in definitions, timing of sampling, and populations) (11). In our cohort, NLR (and MLR) varied across groups; however, the direction of association for spontaneous abortion differed from some reports, with lower NLR in spontaneous abortion compared with controls and an inverse association in adjusted analyses. These discrepancies may reflect differences in study populations, gestational age at sampling, and measurement timing.

More recently, additional meta-analyses have suggested that NLR may be higher in some early pregnancy loss phenotypes, while noting heterogeneity and the influence of study design, geographic region, and cut-off selection (5). Conversely, a systematic review and meta-analysis of PLR concluded that PLR does not appear to have reliable predictive value for early miscarriage (12). Taken together, these data suggest that inflammatory ratios, particularly NLR, may reflect a systemic inflammatory milieu associated with early pregnancy loss, but their direction and discriminative performance are likely context-dependent and sensitive to methodological differences.

A notable finding of our study was an inverse association between neutrophil count and spontaneous abortion in adjusted models (per 1-SD increase in neutrophil count). Although inflammation plays an important role in the pathophysiology of early pregnancy loss, peripheral neutrophil levels can be influenced by several factors, including gestational age-related physiological changes, hemodilution, stress response, and the timing of blood sampling relative to symptom onset. In addition,

assessment of the control group at a more advanced gestational age and differences in BMI across groups may have affected baseline leukocyte profiles and, consequently, the direction of the association. In this context, the similarly inverse associations observed for NLR and MLR suggest that CBC-derived indices may reflect context-dependent inflammatory dynamics rather than a uniform inflammatory signature. Therefore, these parameters should not be used in isolation for clinical decision-making; rather, they should be interpreted as supportive markers alongside clinical assessment and ultrasound findings.

In addition to their well-established role in blood clotting, platelets contribute significantly to angiogenesis and cellular proliferation. They release several growth factors, including vascular endothelial growth factor, epidermal growth factor, and basic fibroblast growth factor, which are essential for tissue development. Research has shown that the levels of these molecules are reduced in women who experience pregnancy loss. This reduction suggests that compromised platelet function may hinder the development of decidual blood vessels, interfere with the formation of the uteroplacental unit, and impair trophoblast differentiation. Such disruptions in early placental development can increase the likelihood of miscarriages. Therefore, diminished platelet functionality during pregnancy may serve as a biomarker for miscarriage or threatened miscarriage (4). The key indicators of platelet activity include MPV, PDW, and platelet count.

An increased MPV indicates platelet activation and growth. In addition, MPV is increased in conditions such as myocardial infarction and venous thromboembolism (13). In addition, from an obstetric perspective, MPV has been found to be associated with recurrent pregnancy loss and spontaneous abortion (14–16). For example, another study of 200 patients found no difference in MPV and platelet values between the spontaneous abortion group and the control group (17).

The MPV/platelet ratio has been associated with thrombosis and inflammation in previous studies (18). However, our study found no relationship between the MPV/platelet ratio and the prediction of miscarriage risk. We assessed that this difference was due to a variety of factors predisposing to miscarriage.

The PDW value provides information on the variability in platelet volume. Increased PDW may be an indicator of abnormal thrombus formation. In our study, we did not observe a significant difference in PDW values between the groups. Supporting this, another study found no difference in PDW values between the threatened abortion and control groups (15). In another study of 300 patients, the PDW/platelet and MPV/platelet ratios did not differ between the

spontaneous abortion and threatened abortion groups (19).

Our analysis confirms partial alignment with recent literature. While many univariate comparisons in our study did not reach statistical significance, multinomial logistic regression revealed that neutrophil count, NLR, and MLR remained independent predictors after adjustment for gestational age, BMI, and gravidity. Although several meta-analyses report higher NLR in early pregnancy loss compared with controls (5), our adjusted analyses suggested an inverse association with spontaneous abortion, highlighting that the direction of CBC-derived inflammatory indices may be context-dependent. Conversely, some studies found no significant differences in platelet parameters (MPV, PDW) between patients with recurrent pregnancy loss and controls, suggesting that these indices may have limited predictive value or that their effects are context-dependent (7).

Our findings similarly show limited utility of platelet-derived parameters when considered alongside inflammatory markers. The discrepancy between univariate findings and regression-based outcomes underscores the role of confounding variables. Some differences that seem modest or non-significant on their own become meaningful once gestational age, BMI, or gravidity are controlled for. This implies that hematological indices like NLR and MLR may be masked by clinical variation unless analyzed in multivariable frameworks. Other parameters did not demonstrate significant predictive value, underscoring the need for larger prospective studies to validate these findings and to clarify the clinical utility of hematological indices for predicting early pregnancy outcomes.

Although the retrospective nature of our study was a limitation, a strength of our study was that PDW, MPV, PDW/platelet ratio, MPV/platelet ratio, NLR, PLR, and CBC parameters were evaluated simultaneously. However, because CBC parameters were based on a single measurement obtained in early pregnancy, the timing of sampling relative to symptom onset and physiological gestational age-related hematologic changes may have introduced variability into the results. Moreover, due to the etiologic heterogeneity of early pregnancy loss (e.g., chromosomal or pathological causes) and the lack of consistent availability of certain ultrasound markers (e.g., subchorionic hematoma characteristics), stratified analyses were not feasible. Additionally, gestational age and BMI differed across groups, and these variables are potential confounders that may influence hematological indices. Although statistical adjustments were applied, these differences may still affect the results. Moreover, the balanced three-arm design ( $n=30$  per group) provided sufficient power to detect moderate-to-large effects. However, the total sample size ( $n=90$ ) may be insufficient to reliably detect small effects. Therefore, non-

significant findings should not be interpreted as evidence of no effect. Larger, prospective studies are warranted.

## Conclusion

In this study, we evaluated a wide spectrum of CBC parameters and their derivatives in women with spontaneous abortion, threatened abortion, and healthy pregnancies during the first trimester. Although most indices did not show significant differences across groups, neutrophil count, NLR, and MLR retained independent predictive value for spontaneous abortion after adjustment for gestational age, BMI, and gravidity. These results emphasize that CBC-derived indices cannot serve as standalone diagnostic tools but may provide additional support when interpreted alongside ultrasound findings and clinical assessment.

## Ethics

**Ethics Committee Approval:** Ethical approval was obtained from the Non-Interventional Research Ethics Committee of Necmettin Erbakan University (decision number: 2024/5333, dated: 15.11.2024).

**Informed Consent:** Retrospective study.

## Footnotes

### Authorship Contributions

Concept: O.A., F.Ş., Design: O.A., A.A., P.B., Data Collection or Processing: F.Ş., P.B., Analysis or Interpretation: O.A., D.T., Literature Search: O.A., Writing: O.A., F.Ş., D.T.

**Conflict of Interest:** No conflict of interest was declared by the author(s).

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**Supplementary Table 1. Pairwise post-hoc comparisons (Bonferroni-adjusted).**

Variable	Pairwise comparison	Bonferroni p
Gravidity	Spontaneous abortion vs. threatened abortion	0.027
Gravidity	Spontaneous abortion vs. control	1.000
Gravidity	Threatened abortion vs. control	0.019
Parity	Spontaneous abortion vs. threatened abortion	0.058
Parity	Spontaneous abortion vs. control	1.000
Parity	Threatened abortion vs. control	0.057
BMI	Spontaneous abortion vs. threatened abortion	0.676
BMI	Spontaneous abortion vs. control	<b>0.008</b>
BMI	Threatened abortion vs. control	0.078
Gestational age (week)	Spontaneous abortion vs. threatened abortion	1.000
Gestational age (week)	Spontaneous abortion vs. control	<b>0.001</b>
Gestational age (week)	Threatened abortion vs. control	0.448
WBC	Spontaneous abortion vs. threatened abortion	0.021
WBC	Spontaneous abortion vs. control	0.474
WBC	Threatened abortion vs. control	1.000
Neutrophil	Spontaneous abortion vs. threatened abortion	<b>0.015</b>
Neutrophil	Spontaneous abortion vs. control	0.126
Neutrophil	Threatened abortion vs. control	1.000
NLR	Spontaneous abortion vs. threatened abortion	0.086
NLR	Spontaneous abortion vs. control	0.117
NLR	Threatened abortion vs. control	1.000
MLR	Spontaneous abortion vs. threatened abortion	0.177
MLR	Spontaneous abortion vs. control	0.042
MLR	Threatened abortion vs. control	1.000

Post-hoc pairwise tests (t-test or Mann-Whitney with Bonferroni correction) were performed when the overall tests were significant.  $p < 0.017$  was considered statistically significant. Power context: With total  $n = 90$  ( $n = 30$ /group), achieved power is ~80% for medium effects (Cohen's  $f \approx 0.30$ ;  $\eta^2 \approx 0.08$ ) and >95% for large effects ( $f \approx 0.40$ ) at  $\alpha = 0.05$ .

BMI, body mass index; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; WBC, white blood cell count.