

Systemic Inflammation and Early Pregnancy Loss: Evaluating Platelet-to-Albumin Ratio in First Trimester Threatened Abortion

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What is already known on this topic?

- Threatened abortion (TA) is a common early pregnancy complication that increases the risk of early pregnancy loss (EPL) and adverse obstetric outcomes.
- Systemic inflammation has been implicated in the pathophysiology of TA and EPL.
- Biomarkers like the systemic immune-inflammation index have shown predictive value, but the platelet-to-albumin ratio (PAR) has not been studied in this context.

What does this study add to the existing knowledge?

- This study is the first to evaluate the clinical relevance of PAR in first-trimester pregnancies with TA.
- It demonstrates that lower PAR values are significantly associated with higher EPL risk and worse perinatal outcomes.
- The study introduces PAR as a simple, cost-effective tool that may aid in early risk stratification in pregnancies complicated by TA.

Abstract

Objective: To evaluate the clinical significance of the platelet-to-albumin ratio (PAR) as a predictive marker for early pregnancy loss (EPL) and adverse perinatal outcomes in first-trimester pregnancies complicated by threatened abortion (TA).

Methods: This retrospective case-control study included 60 pregnant women hospitalized for TA and 60 matched healthy controls with term pregnancies, evaluated at Ankara Bilkent City Hospital between September 2024 and March 2025. First-trimester laboratory parameters, including PAR (calculated as platelet count divided by albumin level), were compared between groups. Demographic data, pregnancy outcomes, and perinatal complications were also analyzed. Receiver operating characteristic (ROC) analysis was performed to assess the predictive value of PAR for EPL.

Results: The PAR was significantly lower in the TA group (5.15 ± 1.45) compared to controls ($P < .001$). Early pregnancy loss occurred in 30% of the TA cases, with a median diagnosis at 8 weeks' gestation. The PAR cut-off value of 4.96 predicted EPL with 66.7% sensitivity and 67.7% specificity (area under the curve = 0.697, $P = .008$). Patients with TA also had significantly higher white blood cell counts and adverse perinatal outcomes, including lower birth weights, higher neonatal intensive care unit admissions, and increased C-section rates. Subgroup analysis based on gestational age at TA diagnosis revealed elevated inflammation markers in later first-trimester cases but no significant differences in EPL rates.

Conclusion: Lower PAR values are associated with TA and may serve as a cost-effective, accessible marker to predict EPL and adverse perinatal outcomes. Although its predictive capacity is moderate, PAR could aid in early risk assessment when combined with other clinical parameters. Further large-scale, prospective studies are needed to validate these findings and establish PAR's role in obstetric care.

Keywords: Abortus imminence, early pregnancy loss, perinatal outcomes, platelet-to-albumin ratio, systemic inflammation, threatened abortion

Introduction

Threatened abortion (TA), also called abortus imminence, is defined as vaginal bleeding or spotting with uterine cramping before the 20th week of pregnancy, without cervical dilation. It often occurs during the first trimester, and the fetus is not yet viable.¹ This affects approximately one-quarter of first-trimester pregnancies, and in half of these cases, early pregnancy loss (EPL) occurs.² In TA, vaginal bleeding is usually mild to moderate; heavier bleeding than usual menstrual bleeding indicates an increased risk of EPL. Additional symptoms may include suprapubic pain, lower abdominal pressure, or back pain.^{1,2}

Studies show that TA is associated with adverse obstetric and perinatal outcomes (e.g., EPL, preterm birth, low birth weight [LBW], placental abruption, preterm premature rupture of membranes) in the later weeks of pregnancy.³⁻⁵ These risks are thought to result from progressive inflammatory processes. Threatened abortion cases complicated by pregnancy loss have been shown to exhibit an

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increased Th1-mediated immune response, a feature also observed in preterm birth.⁶ Similarly, elevated systemic immune-inflammation index (SII) values in early pregnancy have been associated with a higher risk of EPL in women with TA.⁷

The platelet-to-albumin ratio (PAR) is a commonly used clinical biomarker derived from routine laboratory tests that reflects systemic inflammation and nutritional status.⁸ Numerous studies have reported that it can predict different multisystemic and vascular conditions.⁸⁻¹² However, to the best of the authors' knowledge, there are no studies in the literature evaluating the relationship between PAR and obstetric pathologies. This study aimed to evaluate the PAR in pregnancies with TA during the first trimester and to assess its association with adverse pregnancy outcomes.

Methods

This retrospective study was conducted at the Perinatology Clinic of Ankara Bilkent City Hospital. Institutional review board approval was obtained from the Ethics Committee of the Ankara Bilkent City Hospital (Approval no: TABED 2-25-1115; Date: 30.04.2025). All stages of the study adhered to the principles of the Declaration of Helsinki. Due to the retrospective design of the research, informed consent could not be obtained from the study population.

The study population includes women aged 18-45 between September 2024 and March 2025. The case group consisted of 60 pregnant women in their first trimester who were hospitalized due to TA during the study period. The control group consisted of 60 low-risk pregnant women who gave birth at term in the hospital. The gestational age at the time of blood sampling during the first-trimester outpatient visit in the control group was matched with

that in the case group (Figure 1). The diagnosis of TA was based on vaginal spotting or bleeding without cervical dilation. Other symptoms (e.g., pelvic pain or pressure, lower back pain) could also be present in these cases.¹ Multiple gestations, multisystem disorders (malignancies, hepatobiliary, rheumatological, or cardiovascular disorders, etc.), active viral or bacterial infections, and congenital anomalies were excluded from the study. If medication or medical intervention was planned for the study population, these procedures were performed after blood sampling.

The researchers obtained the medical records of the study groups from the hospital database retrospectively. The recorded data included the following: maternal age; body mass index (BMI), calculated by dividing weight in kilograms by the square of height in meters; gravidity; parity; abortion history; first trimester hematocrit (HCT [%]), hemoglobin (Hgb [g/dL]), white blood cell count (WBC [$10^9/L$]), platelet count (PLT [$10^9/L$]), albumin (mg/dL), creatinine (mg/dL), and PAR values; and perinatal outcomes. The gestational week at which TA was diagnosed, the length of hospital stays, and EPL rates were recorded as adverse pregnancy outcomes in the case group. The following perinatal outcomes were documented: mode of delivery, birth week and weight, 1- and 5-minute APGAR (Appearance, Pulse, Grimace, Activity [muscle tone], and Respiration) scores, preterm birth, and LBW rates, as well as neonatal intensive care unit (NICU) admission. The PAR value was calculated by dividing the PLT count by the albumin level. The EPL was defined as loss of pregnancy before 20 weeks of gestation or when the estimated fetal weight was less than 500 grams.¹³ While births occurring before the 37th week of pregnancy are considered preterm,¹⁴ births weighing less than 2500 grams are considered LBW.¹⁵ When calculating rates associated with perinatal outcomes

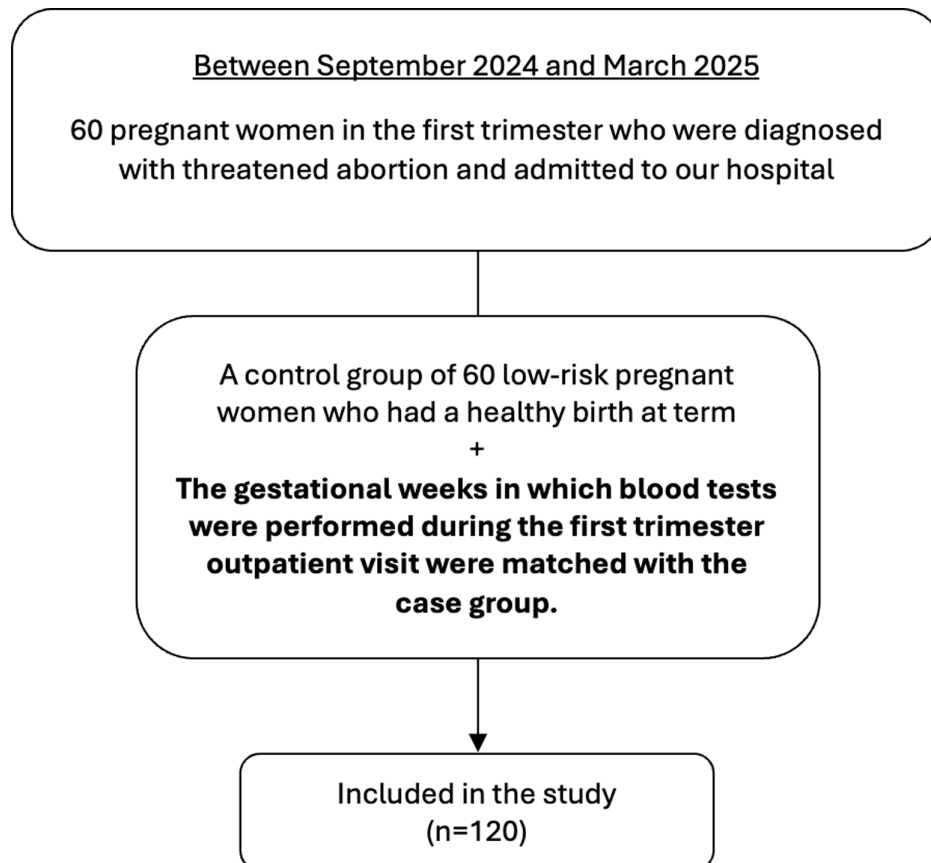


Figure 1. Flowchart of the study population.

in cases, those with EPL were excluded. The TA and control groups were compared in terms of their clinical and demographic characteristics, first-trimester PAR, and perinatal outcomes.

Cases diagnosed with TA were divided into 2 groups according to gestational age at diagnosis: less than 10 weeks and 10-14 weeks. The clinical and demographic characteristics, laboratory parameters, PAR values, EPL rates, and perinatal characteristics of these groups were compared.

Statistical Analysis

The study's sample size was calculated using G Power software (version 3.1 [Software: G*Power 3.1.9.6 for Mac OS X 13(Statistical Power Analyses for Mac and Windows) (Link for download: <https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower>); Heinrich-Heine-Universität Düsseldorf). The effect size of 0.80 was determined with a *P*-value of .05 and a power of 95%, and a minimum of 40 cases was planned for each group. SPSS version 26.0 was utilized for data analysis. Median (interquartile range [IQR]) or mean $\pm$ SD represented continuous variables, while counts (percentages) measured categorical variables. The study assessed the normal distribution of variables through the Kolmogorov-Smirnov test. Two groups' normally distributed continuous variables were compared using the independent *t*-test, while the Mann-Whitney *U* test was used for non-normally distributed variables. Pearson's chi-square or Fisher's exact test was used to compare categorical variables. Receiver operating characteristic (ROC) curve analysis was performed to estimate optimal cut-off values, maximizing sensitivity and specificity according to the Youden index. The performance of the PAR in predicting EPL was evaluated using ROC analysis.

Results

The median gestational age at diagnosis of TA was 8 weeks, and a history of abortion was more common in the medical history (*n* = 17, 28.3%). The HCT, Hgb, and PLT values were significantly lower in the TA group (*P* < .001, all). Conversely, the WBC, albumin, and creatinine values were significantly higher in the same group (*P* < .001, all). The PAR value was calculated as 5.15 ± 1.45 in the TA group, reflecting these differences; it was found to be significantly lower compared to the controls (*P* < .001). The EPL rate was 30% (18/60) in pregnancies diagnosed with TA, and the median gestational age at onset was 8 weeks. The incidence of EPL and C-section rates was higher in the case group, and all perinatal outcomes were found to be significantly adversely affected (*P* < .05, all). Detailed data on the comparison of the clinical-demographic characteristics, laboratory parameters, and perinatal outcomes of the study groups are presented in Table 1.

When TA cases were grouped according to gestational age at diagnosis, no significant differences were found between all demographic data except BMI (*P* = .009). There were no significant differences between these groups in terms of cesarean section rates, length of hospital stays, and EPL incidence (*P* > .05, all). The WBC values were significantly higher in cases diagnosed with TA between 10 and 14 weeks of gestation (*P* = .014). No significant differences were found in other laboratory parameters and PAR values (*P* > .05, all). In cases diagnosed with TA between the 10th and 14th weeks of pregnancy, the median gestational age at delivery was 35 weeks, which was significantly lower than in cases diagnosed before the 10th week (*P* = .014). No significant differences were found between the groups in terms of perinatal

Table 1. Comparison of Clinical-Demographic Characteristics, Laboratory Parameters, and Perinatal Outcomes of Study Groups

	TA Group (n = 60)	Controls (n = 60)	<i>P</i> ^a
Age (years)	28.72 $\pm$ 6.41	28.32 $\pm$ 4.50	.693 ^a
BMI (kg/m ²)	27.86 $\pm$ 2.37	28.86 $\pm$ 3.70	.083 ^a
Gravidity	2 (1)	2 (1)	.209 ^b
Parity	0 (1)	1 (1)	.004^b
Abortion history	17 (28.3%)	5 (8.3%)	.008^c
GA at diagnosis (weeks)*	8 (4)	7 (2) [#]	.072 ^b
Length of hospital stay (day)	2 $\pm$ 1.10	–	–
EPL (n [%]; weeks)	18 (30%); 8 (3.25)	–	<.001^c
First trimester blood parameters			
HCT (%)	34.59 $\pm$ 4.05	37.73 $\pm$ 2.89	<.001^a
Hgb (g/dL)	11.37 $\pm$ 1.41	12.47 $\pm$ 0.99	<.001^a
WBC (10 ⁹ /L)	9.86 $\pm$ 3.02	7.96 $\pm$ 1.26	<.001^a
PLT (10 ⁹ /L)	216.9 $\pm$ 57.1	258.35 $\pm$ 60.89	<.001^a
Albumin (mg/dL)	42.35 $\pm$ 2.88	39.67 $\pm$ 3.98	<.001^a
Creatinine (g/dL)	0.56 $\pm$ 0.07	0.47 $\pm$ 0.10	<.001^a
PAR	5.15 $\pm$ 1.45	6.59 $\pm$ 1.78	<.001^a
Perinatal outcomes			
C-section rates	13 (31%)	8 (13.3%)	.045^c
GA at delivery (weeks)	37 (3)	38 (2)	<.001^b
Preterm birth	11 (26.2%)	–	<.001^c
Low birth weight (<2500 g)	6 (14.3%)	–	.004^c
Birth weight (g)	2872 $\pm$ 286.2	3229.1 $\pm$ 365.8	<.001^a
APGAR score (1st minute)	7 (1)	7 (1)	<.001^b
APGAR score (5th minute)	8 (1)	9 (0)	<.001^b
NICU admission	9 (21.4%)	2 (3.3%)	.007^c

Values are presented as mean $\pm$ SD and median (IQR), or as number (percentage). *P* < .05 was considered statistically significant. Statistically significant data are indicated in bold.

BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); EPL, early pregnancy loss; GA, gestational age; HCT, hematocrit; Hgb, hemoglobin; NICU, neonatal intensive care unit; PAR, platelet-albumin ratio; PLT, platelet; TA, threatened abortion; WBC, white blood cell.

*The GA at which the cases were diagnosed with TA was matched with the week of blood sampling during the first trimester outpatient visit in the control group.

^a*P*-values calculated using: ^aIndependent *t*-test; ^bMann-Whitney *U* test; ^cFisher's exact test.

outcomes, except for differences in gestational age at delivery ($P > .05$, all). Detailed data on the clinical characteristics, laboratory parameters, and perinatal outcomes of TA cases according to gestational age at diagnosis are presented in Table 2.

The summary of the ROC analysis showing the optimal cut-off value of PAR for predicting EPL in the study population is presented in Table 3. According to this analysis, the optimal cut-off value for PAR was determined to be 4.96 (66.7% sensitivity, 67.7% specificity, area under the curve [AUC] 0.697, $P = .008$). The ROC curve for this analysis is shown in Figure 2.

Discussion

Threatened abortion is not merely a benign early pregnancy event; it has been repeatedly associated with complications such as miscarriage, preterm delivery, and LBW in later trimesters.^{4,16} The underlying mechanisms are believed to involve early placental dysfunction and systemic inflammation, which may compromise fetal development and pregnancy continuation.^{6,7} This study evaluated the clinical utility of the PAR, a composite biomarker of inflammation status, in first-trimester pregnancies complicated by TA. The results suggest that PAR is significantly lower in patients with TA and may be associated with an increased risk of EPL and adverse perinatal outcomes.

Some studies have associated pro-inflammatory cytokines and altered immune responses with EPL and preterm birth.¹⁷⁻¹⁹ In this context, the PAR is a practical tool that combines PLT count, a marker of inflammation and thrombopoietic activity,²⁰ with serum albumin, a negative acute-phase reactant affected by nutritional status and inflammatory stress.²¹ While previous studies have demonstrated an association between lower PAR levels and poor outcomes in malignancy, cardiovascular disease, and systemic infections, limited data exist in the obstetric field.²²⁻²⁴

Systemic inflammation plays a central role in the pathophysiology of many obstetric complications. Elevated inflammatory indices, including the SII, have been linked to higher miscarriage risk, as demonstrated by Turgut et al,⁷ who showed that SII could serve as a significant predictor of EPL. Complementing this, Hakeem et al²⁵ recently reported significantly higher maternal serum levels of pro-inflammatory cytokines, such as IL-2 and interferon- γ , in women with TA compared to those with normal pregnancies, suggesting a shift toward a pro-inflammatory immune environment. This study extends this concept by evaluating PAR, which similarly integrates hematologic and nutritional parameters, and finds a significant association between lower PAR and poor pregnancy outcomes. To assess the predictive capacity of PAR for EPL, ROC curve analysis was performed. The results showed that a PAR cut-off value of 4.96 offered a reasonable diagnostic balance, with moderate sensitivity and specificity. Although the AUC was below 0.70, suggesting limited discriminative power, the result was statistically significant and clinically relevant in the context of an easily obtainable, low-cost biomarker. This indicates that PAR may not replace established clinical assessments but could enhance early risk stratification when used alongside other clinical and laboratory parameters.

Subgroup analysis according to gestational age at TA diagnosis revealed subtle differences. Women diagnosed between 10 and 14 weeks of gestation exhibited more inflammatory activity with elevated WBC and tended to deliver earlier than those diagnosed before 10 weeks, although most outcomes were similar between the groups. This supports the idea that inflammatory burden may persist throughout the first trimester and influence later obstetric events.

Table 2. Comparison of Clinical Characteristics, Laboratory Parameters, and Perinatal Outcomes of Threatened Abortion Cases According to Gestational Age at Diagnosis

		GA at Diagnosis of TA		<i>P</i> ^a
		<10 Weeks (n = 37)	10-14 Weeks (n = 23)	
Age (years)		28.5 ± 6.94	28 (5)	.502 ^b
BMI (kg/m ²)		27.89 ± 3.21	30.42 ± 3.96	.009^a
Gravidity		1 (2)	2 (1)	.792 ^b
Parity		0 (1)	0 (1)	.922 ^b
Abortion history		12 (32.4%)	5 (21.7%)	.557 ^c
Length of hospital stay (day)		2 (1)	2 (2)	.583 ^b
EPL (n [%]; weeks)		13 (35.1%); 7 (1)	5 (21.7%); 13 (8.5)	.387 ^c
Laboratory parameters	HCT (%)	35.2 ± 3.79	33.6 ± 4.33	.139 ^a
	Hgb (g/dL)	11.55 ± 1.31	11.06 ± 1.54	.198 ^a
	WBC (10 ⁹ /L)	9.12 ± 2.6	11.06 ± 3.31	.014^a
	PLT (10 ⁹ /L)	210.3 ± 57.25	227.6 ± 56.6	.256 ^a
	Albumin (mg/dL)	42.9 ± 2.35	41.5 ± 3.45	.064 ^a
	Creatinine (g/dL)	0.58 ± 0.07	0.54 ± 0.07	.103 ^a
Perinatal outcomes	PAR	4.89 ± 1.29	5.55 ± 1.62	.088 ^a
	C-section rates	9 (37.5%)	4 (22.2%)	.333 ^c
	GA at delivery (weeks)	38 (2.75)	35 (2.5)	.014^b
	Preterm birth	6 (25%)	5 (27.8%)	1.000 ^c
	Low birth weight (<2500 g)	3 (12.5%)	3 (16.7%)	1.000 ^c
	Birth weight (g)	2914 ± 244.7	2670 (652.5)	.347 ^b
	APGAR score (1st minute)	7 (1)	7 (1)	.828 ^b
	APGAR score (5th minute)	8 (1)	8 (1)	.633 ^b
	NICU admission	3 (12.5%)	6 (33.3%)	.139 ^c

Values are presented as mean ± SD and median (IQR), or as number (percentage). $P < .05$ was considered statistically significant. Statistically significant data are indicated in bold.

BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); EPL, early pregnancy loss; GA, gestational age; HCT, hematocrit; Hgb, hemoglobin; NICU, neonatal intensive care unit; PAR, platelet-albumin ratio; PLT, platelet; TA, threatened abortion; WBC, white blood cell.

**P*-values calculated using: ^aIndependent *t*-test, ^bMann-Whitney *U* test, ^cFisher's exact test.

Table 3. Receiver Operating Characteristic Analysis Table Evaluating the Predictive Performance of Platelet-to-Albumin Ratio for Early Pregnancy Loss in the Study Population

Variable	Outcome	AUC	Std. Error	Sensitivity	Specificity	Asymp. Sig*	95% CI		Cut-Off Value
							Lower	Upper	
PAR	EPL	0.697	0.069	66.7%	66.7%	0.008	0.561	0.833	4.96

AUC, area under curve; CI, confidence interval; EPL, early pregnancy loss; PAR, platelet-albumin ratio.

* $P < .05$ was considered statistically significant.

The EPL rate in the TA group was found to be 30%, which is consistent with previous reports indicating that approximately one-third to one-half of pregnancies complicated by TA may end in miscarriage.^{1,16} This substantial risk reinforces the importance of early identification and monitoring of women with TA, especially in the presence of additional clinical or biochemical risk factors. Notably, the subgroup analysis did not reveal a statistically significant difference in EPL rates between those diagnosed before and after 10 weeks of gestation, although a numerically higher loss was observed in the earlier group. This finding suggests that the timing of TA diagnosis alone may not be the sole determinant of pregnancy outcome. Instead, the underlying inflammatory environment, reflected in lower PAR values, may play a more critical role in predicting EPL.

This study has limitations, including its retrospective, single-center design and limited sample size, which may affect generalizability. Moreover, PAR was assessed at a single time point; future research should investigate its dynamic changes across gestation. Additional markers such as C-reactive protein or interleukin-6 could further strengthen the understanding of the inflammatory pathways involved. The strengths of this study include its

focus on a previously underexplored biomarker in obstetric care. By evaluating PAR, a cost-effective and routinely available laboratory parameter, the study offers a practical tool that could be easily integrated into early pregnancy evaluations. Moreover, the inclusion of a well-matched control group and detailed perinatal outcomes provides a comprehensive view of the implications of early inflammatory status on pregnancy progression. The subgroup analysis by gestational age adds an additional layer of granularity, enriching the clinical relevance of the findings.

This study demonstrated that the PAR, a readily accessible and cost-effective inflammatory biomarker, is significantly lower in pregnancies complicated by TA and is associated with an increased risk of EPL and adverse perinatal outcomes. The findings support the role of systemic inflammation in the pathophysiology of TA and highlight PAR as a potential adjunct tool for early risk assessment. While its predictive value is moderate, PAR may offer clinical utility when combined with other diagnostic parameters. Prospective, multicenter studies are warranted to validate these results and further investigate the integration of PAR into obstetric risk stratification models.

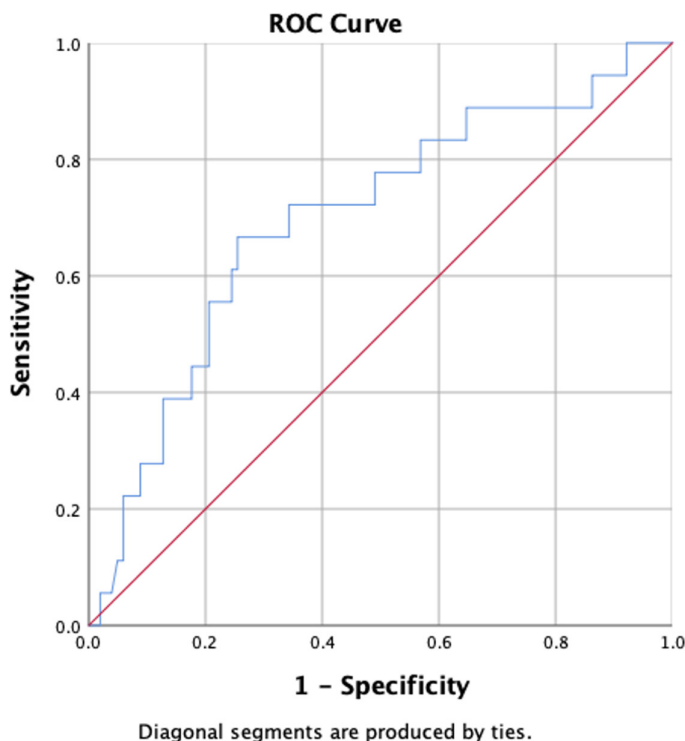


Figure 2. The ROC curve of PAR in predicting EPL in the study population. EPL, early pregnancy loss; PAR, platelet-to-albumin Ratio; ROC, receiver operating characteristic.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Ankara Bilkent City Hospital (Approval no: TABED 2-25-1115; Date: 30.04.2025)

Informed Consent: Due to the retrospective design of the research, informed consent could not be obtained.

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Declaration of Interests: The authors declare that they have no competing interests.

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