

Diagnostic Value of the Third-Trimester Fibrinogen-to-Albumin Ratio for Predicting PE and Small-for-Gestational-Age Neonates: A Retrospective Study

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ABSTRACT

Objective: To evaluate whether the fibrinogen-to-albumin ratio (FAR), measured mainly in the third trimester, is associated with and can predict preeclampsia (PE) and small-for-gestational-age (SGA) neonates in pregnant women.

Methods: In this retrospective study involving 30 patients (PE group) and 330 controls, the FAR was calculated, and its role in predicting PE and SGA was investigated. Additionally, gestational age at delivery, birth weight, percentile values, hemogram parameters, and biochemical variables were compared between the groups.

Results: FAR did not demonstrate sufficient diagnostic power to predict PE [receiver operating characteristic, area under the curve (AUC)= 0.527]; however, decreased serum albumin level was significantly associated with increased risk of PE [odds ratio (OR)= 0.768]. Albumin was identified as an independent predictor of PE (multivariate OR= 0.768, 95% confidence interval: 0.662-0.891, $p < 0.001$). Furthermore, no significant association was found between FAR and birth weight, SGA, or birth weight percentile values.

Conclusion: FAR alone does not possess sufficient diagnostic power (AUC= 0.527). Albumin emerged as a consistent predictor across all analyses (univariate OR= 0.768; multivariate OR= 0.768). Urea and alanine aminotransferase were also identified as independent predictors in the multivariate model. No significant association was detected between FAR and birth weight or SGA.

Keywords: Fibrinogen, albumin, PE, fibrinogen-to-albumin ratio

INTRODUCTION

Preeclampsia (PE), affecting approximately 5-10% of pregnant women, is a pregnancy complication characterized by hypertension and proteinuria occurring after the 20th week of gestation.^{1,2} PE, a multifactorial disorder characterized by hypertension and organ dysfunction, is associated with maternal and neonatal mortality and morbidity worldwide.²

An increasing incidence of PE has been observed in the United States in recent years. This trend has been attributed to a higher prevalence of known risk factors such as obesity and advanced maternal age.³

Although the etiology of PE has not been fully elucidated, clinical and pathological studies indicate that systemic inflammatory response, immune dysfunction, abnormalities in the coagulation and fibrinolytic systems, and aberrant placentation play central roles in the pathogenesis of the disease.² Moreover, a more pronounced hypercoagulable state has been reported in preeclamptic pregnancies compared with normotensive pregnancies, and alterations in the coagulation system are considered to contribute to the disease process.⁴

Early prediction and recognition of PE are among the primary objectives of obstetric care, as appropriate clinical surveillance and timely intervention can prevent serious maternal and



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perinatal complications. To this end, various biomarkers and imaging parameters, including soluble fms-like tyrosine kinase-1, placental growth factor, and uterine artery Doppler indices, have been extensively investigated for their potential in predicting PE.²

In recent years, a growing number of studies have evaluated the clinical utility of the fibrinogen-to-albumin ratio (FAR), derived from routine laboratory parameters and reflecting systemic inflammation and coagulation activity, in predicting the presence and severity of PE. However, the diagnostic and prognostic value of FAR for PE has not yet been conclusively established.

Fibrinogen (Factor I) is one of the major proteins in plasma, present in high concentrations, and plays a central role in the coagulation cascade. As the principal structural component of clot formation, fibrinogen is an indispensable element of the coagulation process; effective clot formation cannot occur in the absence of fibrinogen, even when other coagulation factors are present at normal levels.⁵ Synthesized in hepatic parenchymal cells, fibrinogen is a hexameric glycoprotein with a molecular weight of approximately 340 kDa. Its normal plasma concentration ranges from 200 to 400 mg/dL, with a half-life of approximately 3 to 5 days.⁶

Albumin, another important plasma protein synthesized in the liver, possesses antioxidant, anti-inflammatory, and tissue-repair-supporting properties. Albumin, the most abundant protein in plasma, tends to decrease in conditions such as chronic inflammation, malnutrition, and liver disease.⁷⁻⁹ During pregnancy, serum albumin levels decline due to physiological plasma volume expansion and hemodilution; mild hypoalbuminemia is frequently regarded as a normal finding.⁹

The FAR, calculated from serum fibrinogen and albumin levels, has attracted attention as a novel composite biomarker that simultaneously reflects inflammatory and coagulation processes. FAR has been shown to be useful in predicting clinical outcomes in various cardiovascular diseases and malignancies.^{10,11} In obstetrics, its prognostic value has been

investigated in threatened miscarriage, recurrent pregnancy loss, and several obstetric complications, and promising results have been reported.¹²

During inflammatory processes, FAR increases as a consequence of rising fibrinogen levels and declining albumin levels. Consequently, FAR is regarded as a composite indicator of the degree of systemic inflammation. Recent studies have suggested that FAR may be an important marker for evaluating numerous inflammation-associated conditions and predicting clinical outcomes.^{10,11}

MATERIALS AND METHODS

This retrospective cohort study was conducted in the Department of Obstetrics and Gynecology at Erzincan Binali Yıldırım University Mengücek Gazi Training and Research Hospital. Pregnant women with a gestational age ≥ 20 weeks who were followed at our clinic between January 2023 and June 2024 and who had serum fibrinogen and albumin levels measured were included in the study.

Ethical approval was obtained from the Erzincan Binali Yıldırım University Non-Interventional Clinical Research Ethics Committee (decision no.: 485828, date: 29.09.2025). All procedures were conducted in accordance with the principles of the Declaration of Helsinki. The study was retrospective; therefore, informed consent was not required, as only anonymized data from routine clinical records and patient files were analyzed and no intervention was performed on the patients.

The study population comprised 360 pregnant women, classified into the PE group ($n=30$) and the control group ($n=330$). PE was diagnosed based on the clinical assessment recorded at admission, according to the diagnostic criteria of the Ministry of Health of the Republic of Türkiye, including admission blood pressure ($\geq 140/90$ mmHg). Because individual blood pressure values could not be retrieved retrospectively from the electronic records, severity subclassification could not be performed.

Exclusion criteria included platelet (PLT) count $< 100,000/\text{mm}^3$ for other than PE (either pre-existing or occurring during pregnancy), nephropathy, elevated liver enzymes attributable to causes other than PE, active bleeding, and intrahepatic cholestasis of pregnancy.

The study included pregnant women aged 18 years or older who were hospitalized for the following indications: decreased fetal movement, threatened preterm labor, trauma, hypertension, membrane rupture, uterine contractions, or other obstetric reasons. Demographic characteristics, gestational age at delivery, mode of delivery, birth weight, and neonatal percentile values were obtained from patients' files.

Advanced maternal age was defined as ≥ 35 years. Small for gestational age (SGA) was defined as a birth weight below the 10th percentile for gestational age. The FAR was calculated by dividing serum fibrinogen (mg/dL) by serum albumin (g/L) and reported as a unitless ratio. Levels of fibrinogen, albumin, hemoglobin, PLT, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, urea, and calcium were

MAIN POINTS

- The fibrinogen-to-albumin ratio (FAR), measured mainly in the third trimester, did not show sufficient diagnostic power for predicting preeclampsia (PE) (area under the curve= 0.527), and combining it with other laboratory parameters did not significantly improve discrimination.
- Lower serum albumin was the strongest independent predictor of PE (multivariate odds ratio= 0.768, 95% confidence interval: 0.662-0.891; $p < 0.001$), followed by urea and alanine aminotransferase.
- FAR was not associated with birth weight, small-for-gestational-age status, birth weight percentile, or maternal age.
- Serum albumin, a low-cost routine test, deserves further evaluation as a PE biomarker in larger prospective multicenter studies.

obtained from routine laboratory assessments performed at the time of hospitalization or approximately 3-4 weeks before delivery.

The primary analysis compared FAR and other laboratory parameters between the PE and control groups. The secondary analysis evaluated the association between FAR and birth weight, gestational age at delivery, and neonatal percentile values across the entire study population.

Statistical Analysis

The normality of the data was assessed using the Shapiro-Wilk test. Normally distributed continuous variables are presented as mean ± standard deviation and compared between groups using the independent samples t-test. Non-normally distributed continuous variables were expressed as medians [interquartile range (Q1-Q3)] and analyzed using the Mann-Whitney U test. Categorical variables were presented as frequencies and percentages and were compared using Fisher’s Exact Test.

The diagnostic performance of FAR for predicting PE was evaluated using receiver operating characteristic (ROC) curve analysis. The 95% confidence intervals (CIs) for the area under the curve (AUC) were calculated using the bootstrap method with 2,000 iterations. The optimal cut-off point was determined based on the Youden Index. The DeLong test was used for comparisons between ROC curves. Associations between variables were assessed using Spearman’s correlation analysis. Multivariate logistic regression analysis was performed to identify independent predictors of PE. In the multivariate model, FAR was included a priori as the marker of interest, and albumin, urea, and ALT were included based on their univariate association with PE.

AST was not entered because of its strong correlation with ALT (Spearman $r = 0.609$) to avoid collinearity. Model fit was assessed using the Nagelkerke R-squared and the Hosmer-Lemeshow test. A two-sided P value of <0.05 was considered statistically significant. ROC analyses, bootstrap CIs (2,000 iterations), DeLong comparisons were performed using Python; figures were generated using Python; the remaining analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Comparison of Clinical and Laboratory Characteristics

The clinical, demographic, and laboratory characteristics of all 360 pregnant women included in the study are presented in Table 1. The group-specific distributions of key laboratory parameters are illustrated in Figure 1 using box plots.

Serum albumin levels were significantly lower in the PE group compared with the control group (31.67 ± 4.19 g/L vs. 33.66 ± 2.27 g/L; $P < 0.001$). This difference is also reflected in Figure 1, where box plots demonstrate a marked separation between the two groups.

FAR did not differ significantly between the two groups (control: 10.98 ± 3.01 ; PE: 11.51 ± 3.54 ; $P = 0.365$; Table 1). The expected increase in fibrinogen was limited in this sample.

Urea was significantly elevated in the PE group [15.00 ($12.00-18.00$) vs. 17.50 ($14.25-21.75$) mg/dL; $P = 0.008$; Table 1), consistent with other studies in the literature.¹³ Gestational age at delivery was significantly shorter in the PE group [38.00 ($37.00-39.00$) vs. 37.00 ($36.50-38.00$) weeks; $P = 0.008$].

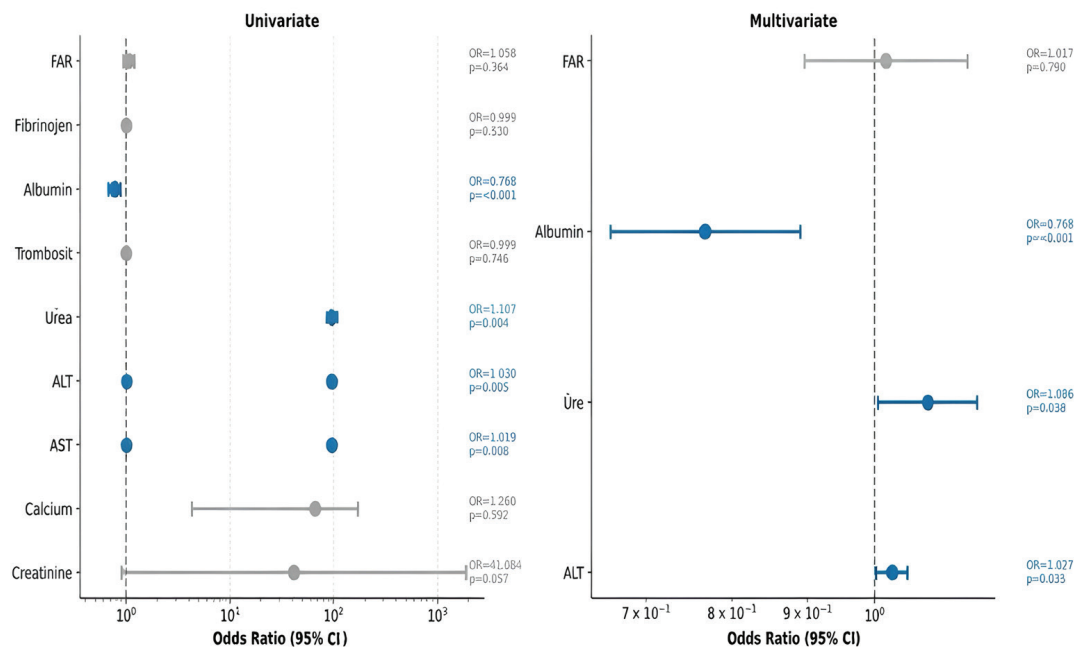


Figure 1. Box plots of FAR, albumin, fibrinogen, platelet count, urea and ALT according to the control (blue) and PE (gray) groups. Albumin ($P < 0.001$) and urea ($P = 0.008$) differed significantly between the groups. P values shown in gray indicate statistical significance.

FAR, fibrinogen-to-albumin ratio; ALT, alanine aminotransferase; PE, preeclampsia; CI, confidence interval; OR, odds ratio.

ALT, AST, PLT count, creatinine, calcium, and birth weight did not differ significantly between the groups (all $p > 0.05$; Table 1).

Correlation Analysis Between FAR and Clinical Parameters

Spearman correlation results between FAR and eight clinical parameters are presented in Table 2. A statistically significant negative correlation was identified between FAR and AST ($r = -0.170$; $P = 0.001$). No significant correlations were found with other parameters (PLT, urea, ALT, calcium, creatinine, birth weight, or percentile).

ROC Analysis of FAR and Combined Models

The standalone diagnostic accuracy of FAR and that of the combined models are presented in Table 3, and the corresponding ROC curves are shown in Figure 2.

The AUC value for FAR alone was 0.527 (95% CI: 0.420-0.633). That the CI encompasses the 0.500 reference value indicates that FAR does not significantly exceed the chance level (Table 3). The optimal threshold determined by the Youden index was 12.60, yielding a sensitivity of 43.3%, a specificity of 69.1%, and

an negative predictive value of 93.1%.

The ROC performance of models combining FAR with six parameters is also presented in Table 3. None of the FAR-combined models provided a statistically significant improvement over FAR alone.

Univariate and Multivariate Logistic Regression

Univariate and multivariate logistic regression results are presented in Table 4, and comparative forest plots are presented in Figure 3. In univariate analysis, albumin was the strongest predictor [odds ratio (OR)= 0.768; 95% CI: 0.670-0.880; $P < 0.001$; Table 4]. An OR below 1 indicates that each 1 g/L increase in albumin level is associated with a 23.2% reduction in the odds of PE. Urea (OR= 1.107; $P = 0.004$), ALT (OR= 1.030; $P = 0.005$), and AST (OR= 1.019; $P = 0.008$) also demonstrated significant associations. FAR did not yield a significant result (OR= 1.058; $P = 0.364$). In the multivariate model, albumin (OR= 0.768; $P < 0.001$), urea (OR= 1.086; $P = 0.038$), and ALT (OR= 1.027; $P = 0.035$) were identified as independent predictors (Table 4). FAR lost its independent predictive significance (OR= 1.017; $P = 0.790$). The model

Table 1. Comparison of Demographic and Clinical Parameters Between Control and PE Groups

Variable	n (C/PE)	Control (n=330)	PE (n=30)	P value	Test
Age (years)	330/30	28.35 ± 5.52	29.80 ± 6.41	0.176	t-test
FAR	330/30	10.98 ± 3.01	11.51 ± 3.54	0.365	t-test
Fibrinogen (mg/dL)	330/30	368.40 ± 99.39	356.58 ± 93.29	0.531	t-test
Albumin (g/L)	330/30	33.66 ± 2.27	31.67 ± 4.19	<0.001*	t-test
Hemoglobin (g/dL)	330/30	11.74 ± 1.39	11.77 ± 1.47	0.908	t-test
Platelet (x10 ³ /uL)	330/30	214.00 (183.00-252.00)	229.00 (199.75-244.75)	0.561	MWU
Creatinine (mg/dL)	330/30	0.60 (0.50-0.60)	0.60 (0.50-0.67)	0.113	MWU
Urea (mg/dL)	330/30	15.00 (12.00-18.00)	17.50 (14.25-21.75)	0.008*	MWU
Calcium (mg/dL)	330/30	8.77 ± 0.43	8.82 ± 0.60	0.593	t-test
ALT (U/L)	330/30	10.00 (8.00-13.00)	12.00 (9.00-16.75)	0.074	MWU
AST (U/L)	330/30	19.00 (15.25-22.00)	20.00 (15.25-24.00)	0.459	MWU
Gestational age (weeks)	318/19	38.00 (37.00-39.00)	37.00 (36.50-38.00)	0.008*	MWU
Birth weight (g)	308/18	3105.20 ± 516.30	2915.28 ± 513.52	0.130	t-test

Mean ± SD, normally distributed; median (Q1-Q3), non-normally distributed variables. * $P < 0.05$.

C/PE, control/PE patient count; MWU, Mann-Whitney U; SD, standard deviation; FAR, fibrinogen-to-albumin ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 2. Spearman Correlation Analysis Between FAR and Clinical Parameters

Parameter	Spearman r	P value	n	Interpretation
Platelet	0.077	0.147	360	Not significant
Urea	-0.025	0.643	360	Not significant
ALT	-0.097	0.067	360	Not significant
AST	-0.170	0.001*	360	Weak negative
Calcium	-0.020	0.712	360	Not significant
Creatinine	0.078	0.141	360	Not significant
Birth weight	0.046	0.408	326	Not significant
Birth weight Percentile	-0.029	0.603	328	Not significant

r, spearman coefficient. * $P < 0.05$. Strength: $|r| > 0.70$ = Strong; 0.40-0.70 = Moderate; 0.20-0.40 = Weak.

ALT, alanine aminotransferase; AST, aspartate aminotransferase.

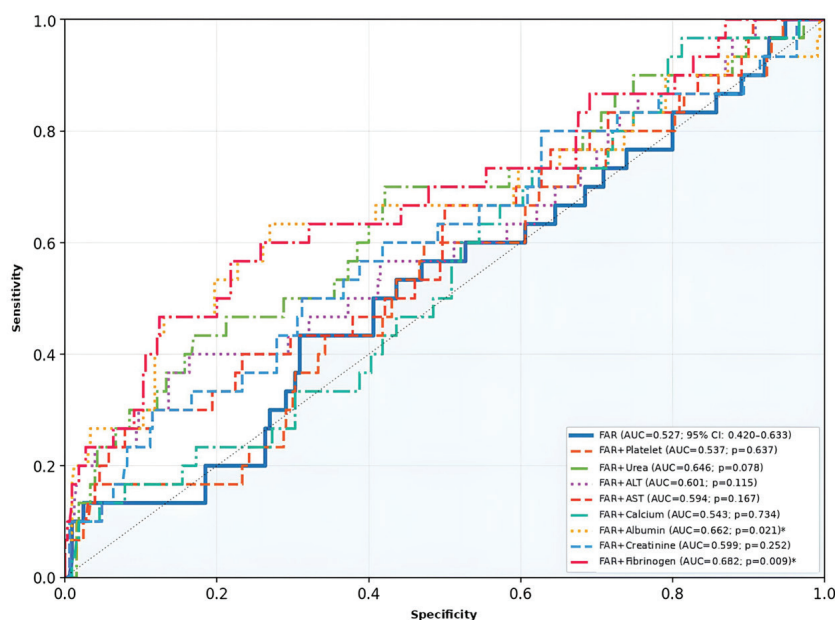


Figure 2. Comparison of ROC curves for FAR alone (thick blue line) and the combined models (coloured dashed lines). None of the combined models provided a statistically significant improvement over FAR alone on the DeLong test (Table 3). The dashed black line represents the chance-level reference line.

FAR, fibrinogen-to-albumin ratio; ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 3. ROC Analysis and DeLong Comparison of FAR Alone and Combined Models

Model	AUC	95% CI	Sensitivity (%)	Specificity (%)	DeLong P
FAR (reference)	0.527	0.420-0.633	43.3	69.1	-
FAR+platelet	0.537	0.434-0.642	16.7	96.1	0.637
FAR+urea	0.646	0.538-0.753	70.0	57.9	0.078
FAR+ALT	0.601	0.482-0.716	40.0	83.6	0.115
FAR+AST	0.594	0.480-0.706	26.7	92.1	0.167
FAR+calcium	0.543	0.440-0.646	96.7	18.8	0.734
FAR+creatinine	0.599	0.487-0.710	50.0	68.8	0.252

FAR alone, negative predictive value 93.1%; Youden threshold 12.60. Combined AUCs derived from logistic regression probability scores. DeLong p: comparison against FAR alone.

AUC, area under the curve; CI, confidence interval (bootstrap, n = 2,000); FAR, fibrinogen-to-albumin ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 4. Univariate and Multivariate Logistic Regression Results

Variable	Univariate OR (95% CI)	Univariate P	Multivariate OR (95% CI)	Multivariate P
FAR	1.058 (0.937-1.194)	0.364	1.017 (0.896-1.155)	0.790
Albumin	0.768 (0.670-0.880)	<0.001	0.768 (0.662-0.891)	<0.001
Urea	1.107 (1.032-1.186)	0.004	1.086 (1.005-1.173)	0.038
ALT	1.030 (1.009-1.051)	0.005	1.027 (1.002-1.052)	0.035
AST	1.019 (1.005-1.033)	0.008	Not included	-
Fibrinogen	0.999 (0.995-1.003)	0.530	Not included	-
Platelet	0.999 (0.992-1.005)	0.746	Not included	-
Calcium	1.260 (0.541-2.933)	0.592	Not included	-
Creatinine	41.084 (0.897-1881.870)	0.057	Not included	-

The multivariate model included FAR, albumin, urea, and ALT. Model fit: Nagelkerke R-squared = 0.178; Hosmer-Lemeshow p = 0.085.

OR, odds ratio; CI, confidence interval; FAR, fibrinogen-to-albumin ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

showed an acceptable fit (Nagelkerke R-squared =0.178; Hosmer-Lemeshow $P = 0.085$).

Association of FAR with Birth Weight and SGA

No significant correlation was found between FAR and birth weight among the 326 patients with available birth weight data (Spearman $r = 0.046$; $P = 0.408$; $n=326$). FAR did not differ significantly between 32 SGA and 296 non-SGA infants (median: 11.95 vs. 11.04; $P = 0.118$). The ROC AUC for FAR in predicting SGA was 0.584, which is close to chance level. The correlation between FAR and birth weight percentile was also non-significant ($r = -0.029$; $P = 0.603$). These results are summarized in Table 5.

Association Between Maternal Age, FAR and SGA

No statistically significant correlation was identified between age and FAR across all patients (Spearman $r = -0.007$; $P = 0.894$;

$n=360$; Table 6). This finding is supported by the scatter plot, in which the nearly horizontal regression line indicates that age has no deterministic effect on FAR.

No significant correlation was found in either the control group ($r = -0.023$; $P = 0.683$) or the PE group ($r = 0.102$; $P = 0.592$) when the groups were analyzed separately (Table 6). When the advanced maternal age (≥ 35 years, $n=63$ in the whole sample) and normal-age (<35 years, $n=297$) groups were compared, no significant difference in FAR values was observed [advanced-age median: 10.84 (9.64-12.83) vs. normal-age median: 11.05 (8.76-13.05); $P = 0.492$], indicating that FAR is independent of maternal age.

Regarding SGA, no statistically significant difference was found in maternal age when comparing mothers of 32 SGA infants and 296 non-SGA infants (26.0 vs. 28.0 years; $P = 0.149$; Table 6). Age

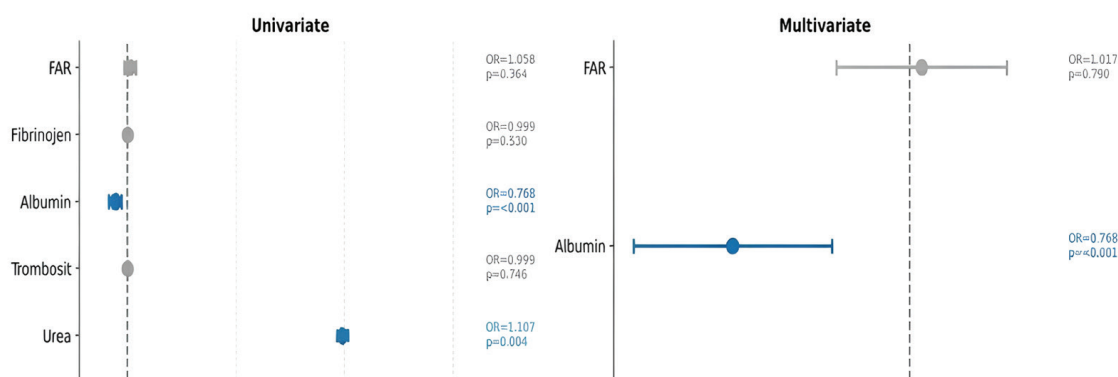


Figure 3. Univariate (left panel) and multivariate (right panel) logistic regression forest plot. Blue dots indicate variables with $P<0.05$, and gray dots indicate non-significant variables. Albumin stands out as the strongest predictor in both analyses.

Table 5. Association Between FAR and SGA

Analysis	P value	Interpretation
FAR, SGA ($n=32$) vs. non-SGA ($n=296$), median	11.95 vs. 11.04; $P = 0.118$ (MWU)	Not significant
FAR $\geq$ SGA (ROC AUC)	0.584	Close to chance level

FAR correlations with birth weight and birth-weight percentile are presented in Table 2.

MWU, Mann-Whitney U test; AUC, area under the curve; FAR, fibrinogen-to-albumin ratio; SGA, small for gestational age; ROC, receiver operating characteristic.

Table 6. Association of Maternal Age with FAR and SGA

Analysis	Value/statistic	P value	Interpretation
Age-FAR (all patients)	$r = -0.007$ ($n=360$)	0.894	Not significant
Age-FAR (control group)	$r = -0.023$ ($n=330$)	0.683	Not significant
Age-FAR (PE group)	$r = 0.102$ ($n=30$)	0.592	Not significant
Age-birth weight percentile	$r = 0.041$ ($n=328$)	0.457	Not significant
Age, SGA vs. non-SGA (median, MWU)	26.0 vs. 28.0 years	0.149	Not significant
Age $\geq$ SGA (logistic regression)	OR = 0.954 (0.891-1.023)	0.185	Not significant
Age $\geq$ SGA (ROC AUC)	0.423	-	Inverse association (AUC < 0.5)
Advanced age (≥ 35) vs. SGA (Fisher)	2/56 (3.6%) vs. 30/272 (11.0%)	0.134	Not significant

Correlations by Spearman; MWU, Mann-Whitney U; Fisher, Fisher's Exact test. Advanced-age counts in the SGA rows refer to the birth-weight-available subset ($n=328$); in the whole sample ($n=360$) the ≥ 35 -year group was $n=63$.

SGA, small for gestational age; FAR, fibrinogen-to-albumin ratio; PE, preeclampsia; ROC, receiver operating characteristic; AUC, area under the curve; OR, odds ratio.

was not an independent predictor of SGA (OR= 0.954; 95% CI: 0.891-1.023; $P = 0.185$). ROC analysis showed that age had no clinical utility in predicting SGA (AUC= 0.423; an AUC below 0.5 indicates an inverse association). No significant correlation was found between age and birth weight percentile ($r = 0.041$; $P = 0.457$), and SGA prevalence did not differ between the advanced age and normal age groups (3.6% vs. 11.0%; Fisher $P = 0.134$).

DISCUSSION

In this study, the diagnostic value of FAR for predicting PE was examined using rigorous statistical methods, and the effect of maternal age on FAR and SGA was evaluated in additional analyses.

FAR alone did not demonstrate sufficient diagnostic power (AUC= 0.527; Table 3). The limited performance of FAR is primarily attributable to the absence of a significant difference in fibrinogen levels between the two groups.

Albumin emerged as a consistent predictor across all analyses (univariate OR= 0.768, multivariate OR= 0.768; Table 4). Urea and ALT were also identified as independent predictors in the multivariate model. No significant association was found between FAR and birth weight or SGA (Table 2, Figure 3).

In a retrospective cohort study encompassing 3,249 pregnancies, patients were classified into control, mild, and severe PE groups. The investigators reported that FAR was independently associated with PE and could be a useful biomarker for clinical risk stratification. FAR could also contribute to the planning of delivery management and perinatal care, although the need for larger, prospective, multicenter studies to validate these findings was emphasized.³ One study reported that FAR demonstrated superior diagnostic performance for predicting PE severity compared with other routine laboratory indicators. Because fibrinogen and albumin levels are readily obtained as part of routine biochemical workup, FAR may serve as a practical and cost-effective biomarker in clinical practice.¹ Although FAR levels were slightly higher in the PE group in our study, the difference was not statistically significant ($P = 0.365$), and discriminatory power in ROC analysis limited. These discrepancies may be attributable to differences in patient populations, sample sizes, and study designs.

Studies evaluating FAR for the early prediction of PE, its disease severity, and its association with adverse perinatal outcomes have reported FAR as a promising biomarker. Given its low cost, ease of access, and strong predictive potential, it has been proposed that FAR could be integrated into first-trimester screening protocols alongside existing biomarkers.²

In contrast, our study assessed FAR during the second and third trimesters and investigated the association between FAR measured at more advanced gestational weeks and PE. This represents a different timing compared with previous studies, which predominantly focus on early pregnancy. While our findings suggest that FAR may be associated with PE even at advanced gestational ages, they demonstrate that it does not exhibit strong standalone diagnostic performance. This discrepancy may be explained by temporal variability in FAR throughout pregnancy and by variation in the pathophysiology

of PE across trimesters.

In a study evaluating the diagnostic performance of FAR for predicting PE, which comprised 131 PE cases and 131 control cases, the combination of second-trimester FAR and PLT distribution width (PDW) demonstrated better diagnostic performance than FAR alone. Nevertheless, the investigators emphasized the need for prospective studies to validate these findings.¹⁴ In our study, PDW was not included in the analysis and only FAR was evaluated. The possibility that adding PDW to the model might improve diagnostic performance is consistent with the literature, but this could not be confirmed with our current data and remains an area for investigation in future multivariate prospective studies.

Serum albumin level in cases of PE has been reported to reflect disease severity and to serve as a useful biomarker for determining the timing of delivery.¹⁵ Studies examining the association between serum albumin levels and PE have reported that hypoalbuminemia is associated with increased vascular permeability, systemic inflammation, and endothelial dysfunction; consequently, low albumin levels may correlate with the presence and severity of PE. It has been further emphasized that albumin, a negative acute-phase reactant, decreases during the inflammatory response and may have clinical implications, particularly in hypertensive disorders of pregnancy.^{16,17} In our study, serum albumin levels were significantly lower in the PE group compared with the control group, and albumin was identified as the strongest independent predictor of PE in multivariate analysis (OR= 0.768; $P < 0.001$). These results are consistent with findings reported in the literature and support the notion that albumin is not merely a nutritional indicator but also a potent biomarker reflecting the systemic inflammatory burden and endothelial damage in PE.

In a study evaluating the role of first-trimester Hemoglobin, Albumin, Lymphocyte, PLT (HALP) score and FAR in predicting PE, FAR levels were significantly higher in both severe and non-severe PE cases than in healthy pregnant women.¹⁷ In our study, FAR values were also numerically higher in the PE group than in the control group, although the difference was not statistically significant. However, FAR alone did not demonstrate sufficient discriminatory power in ROC analysis, suggesting that while FAR may be associated with PE, it may not serve as a robust standalone diagnostic marker.

Significantly elevated serum urea levels have been reported in preeclamptic pregnancies compared with normotensive pregnancies.¹⁸ Similarly, in our study, serum urea levels were significantly higher in the PE group than the control group. This finding is consistent with impaired renal function and reduced glomerular filtration rate in PE, which lead to accumulation of nitrogenous waste products; this interpretation is supported by the literature.

In a study evaluating 62 fetal growth restriction (FGR) cases and 62 control cases, first-trimester C-reactive protein, fibrinogen, and FAR levels were significantly higher in the FGR group.¹² In our study, however, no statistically significant association was found between SGA and FAR. This discrepancy may be related to the small number of SGA cases ($n=32$) and the study's overall

limited sample size. Larger multicenter prospective studies are needed to elucidate more clearly the relationship between FAR and SGA.

FAR has been reported as a prognostic marker in hepatocellular carcinoma, where its prognostic value varied according to AST level.¹⁰ Because both fibrinogen and albumin are synthesized in the liver, hepatic dysfunction can affect both proteins and, thereby, the FAR. In our study, the FAR-AST correlation was weak ($r = -0.170$). Although statistically significant, it was of limited clinical relevance and was not in the same direction as the strong positive correlation reported in hepatocellular carcinoma.

Because the number of PE cases in our study was limited and the majority were classified as non-severe, patients were evaluated as an overall PE group. In this context, FAR levels in non-severe PE cases were similar to those in the control group.

Furthermore, in our study, FAR and other laboratory parameters were evaluated primarily during the third trimester, approximately one month prior to delivery, whereas many studies have measured these parameters during the first and second trimesters. This difference in timing may be an important factor explaining the heterogeneity observed across study results.

Study Limitations

The imbalance between the PE group ($n=30$) and the control group ($n=330$) limited the statistical power for FAR analyses. The retrospective study design and the absence of data on the precise timing of measurements represent major limitations. The SGA group ($n=32$) should be interpreted with caution, given the small sample size. Severity classification for PE could not be directly applied because blood pressure data were unavailable; most patients in the PE group had non-severe disease. Because of the small number of events (30 events; approximately 7.5 events per variable), the multivariate model is at risk of overfitting, and the AUCs for the combined model were derived in-sample and are therefore optimistic. The creatinine OR, with its very wide CI, and the ALT discrepancy between the Mann-Whitney and regression analyses reflect the narrow measurement range, possible outliers, and the small number of events, and both should be interpreted with caution. Severe PE cases below 34 weeks of gestation were referred for delivery to a tertiary university hospital with a neonatal intensive care unit, according to the regional referral chain; therefore, gestational age at delivery was unavailable for 11 and birth weight for 12 of the 30 patients in the PE group, resulting in missing delivery data. In addition, the control group included women hospitalized for various obstetric indications (e.g., preterm premature rupture of membranes, trauma, threatened preterm labor), which may themselves affect fibrinogen and albumin levels and thus FAR.

CONCLUSION

The FAR demonstrated limited diagnostic performance as a standalone marker for predicting PE, with an AUC of 0.527 on ROC analysis (Table 3). In contrast, albumin was identified as the strongest independent predictor of PE in all analyses (multivariate OR= 0.768; $P < 0.001$; Table 4), a finding that is consistent with the existing literature.¹⁵

No statistically significant association was found between FAR and birth weight, SGA, maternal age, or birth weight percentile (Tables 2, 5 and 6). Moreover, advanced maternal age (≥ 35 years) had no significant effect on either FAR or SGA (Table 6).

FAR measurements in our study were predominantly obtained during the third trimester or within 3-4 weeks before delivery. This constitutes an important difference from studies in the literature that rely on first- and second-trimester FAR measurements. In light of these findings, it is necessary to compare the clinical value of FAR in predicting PE across pregnancy trimesters. Prospective, multicenter studies comparing second-trimester FAR measurements with peripartum data are particularly recommended.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Erzincan Binali Yıldırım University Non-Interventional Clinical Research Ethics Committee (decision no.: 485828, date: 29.09.2025).

Informed Consent: Informed consent was waived due to the retrospective nature of the study. Permission to use patient data was obtained from the hospital management.

Footnotes

Author Contributions

Concept Design – Z.G., B.K.; Data Collection or Processing – Z.G.; Analysis or Interpretation – O.A.; Literature Review – Z.G., B.K., O.A.; Writing, Reviewing and Editing – Z.G., B.K.

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REFERENCES

- Ren H, Liu W, Niu A, Zhao X. Fibrinogen to albumin ratio, a novel serum indicator for evaluating the severity of preeclampsia: a single-center retrospective study. *Medicine (Baltimore)*. 2023;102(13):e33419. [CrossRef]
- Zorlu U, Özkavak OO, Şerbetçi H, et al. Unraveling preeclampsia: is the fibrinogen-to-albumin ratio the key to early risk assessment? *Int J Gynaecol Obstet*. 2026;172(3):1553-1560. [CrossRef]
- Shang L, Echevarria G, Ouyang Y, Beilin Y, Katz D. Relationship between fibrinogen-to-albumin ratio and pre-eclampsia: a retrospective cohort study. *Pregnancy Hypertens*. 2026;43:101413. [CrossRef]
- Pieters M, Wolberg AS. Fibrinogen and fibrin: an illustrated review. *Res Pract Thromb Haemost*. 2019;3(2):161-172. [CrossRef]
- Mosesson MW. Fibrinogen and fibrin structure and functions. *J Thromb Haemost*. 2005;3(8):1894-1904. [CrossRef]
- Turkish Haemophilia Society. National diagnosis and treatment guide for rare factor deficiencies. 2023. [CrossRef]
- Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: pathogenesis and clinical significance. *JPEN J Parenter Enteral Nutr*. 2019;43(2):181-193. [CrossRef]

8. Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: a reference table for clinicians. *Obstet Gynecol*. 2009;114(6):1326-1331. [\[CrossRef\]](#)
9. Ağaoglu Z, Tanaçan A, Toptaş GR, et al. Role of fibrinogen-albumin ratio in predicting fetal and maternal outcomes in pregnancies complicated by placental abruption. *Osmangazi J Med*. 2025;48(1):68-74. [\[CrossRef\]](#)
10. Sun H, Ma J, Lu J, et al. Fibrinogen-to-albumin ratio predicts overall survival of hepatocellular carcinoma. *World J Gastrointest Oncol*. 2023;15(9):1662-1672. [\[CrossRef\]](#)
11. Huang R, Dai Q, Chang L, et al. The association between fibrinogen-to-albumin ratio (FAR) and adverse prognosis in patients with acute decompensated heart failure at different glucose metabolic states. *Cardiovasc Diabetol*. 2022;21(1):241. [\[CrossRef\]](#)
12. Özkavak OO, Şahin D. The predictive value of first trimester fibrinogen-albumin ratio for late onset fetal growth restriction. *Osmangazi Journal of Med*. 2025;47(2):316-323. [\[CrossRef\]](#)
13. Abdelrahman RM, Zaroog MS, Abdalla BE, Hamza MA, Mohamed ME. Renal function in preeclampsia versus normal pregnant women. *J Biosci Med*. 2022;10:169-178. [\[CrossRef\]](#)
14. Bulbul CB, Yakistiran B. Second-trimester fibrinogen-to-albumin ratio and platelet activation markers compared with the HALP score for predicting preeclampsia. *Diagnostics (Basel)*. 2026;16(4):613. [\[CrossRef\]](#)
15. Al Ghazali B, Al-Taie AAH, Hameed RJ. Study of the clinical significance of serum albumin level in preeclampsia and in the detection of its severity. *Am J BioMed*. 2014;2(8):964-974. [\[CrossRef\]](#)
16. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Preeclampsia. *Lancet*. 2010;376(9741):631-644. [\[CrossRef\]](#)
17. Polat M, Sapmaz MA, Erbey S, Kindan A, Ruzgar MS, Kahyaoglu İ. Use of first trimester hemoglobin albumin lymphocyte platelet score and fibrinogen to albumin ratio in the prediction of preeclampsia. *Medicine (Baltimore)*. 2025;104(30):e43423. [\[CrossRef\]](#)
18. Tesfa E, Munshea A, Nibret E, Mekonnen D, Sinishaw MA, Gizaw ST. Maternal serum uric acid, creatinine and blood urea levels in the prediction of pre-eclampsia among pregnant women attending ANC and delivery services at Bahir Dar city public hospitals, northwest Ethiopia: a case-control study. *Heliyon*. 2022;8(10):e11098. [\[CrossRef\]](#)