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ORIGINAL ARTICLE

Evaluation of the Relationship between Fibrinogen-to-Albumin Ratio and Disease Severity in Preeclamptic and Healthy Pregnant Women

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ABSTRACT

Background: **The aim of this study was to determine the predictive value of fibrinogen-to-albumin ratio (FAR) and blood urea nitrogen-to-albumin ratio (BAR) in pregnancies complicated by preeclampsia in the first trimester. Furthermore, the study evaluated their relationship with disease severity and composite perinatal adverse outcomes (CAPO).**

Methods: **The present retrospective cross-sectional study comprised 144 pregnant women with gestational ages between 20 and 39 weeks, who were divided into three groups: mild preeclampsia (n = 48), severe preeclampsia (n = 48), and a normotensive healthy control group (n = 48). The first trimester blood samples were utilized to calculate the FAR and BAR values. Comparisons were made between the groups, and the relationship of these indices with disease severity and CAPO was evaluated.**

Results: **FAR and BAR values were considerably elevated in both the mild and severe preeclampsia cohorts in comparison to the control group ($p < 0.001$). However, there were no statistically significant differences in FAR and BAR values between the mild and severe preeclampsia subgroups ($p > 0.05$). ROC analysis yielded moderate to high diagnostic performance for both markers in the detection of preeclampsia. Nevertheless, both FAR and BAR exhibited a lack of statistical significance in relation to the occurrence of composite perinatal adverse outcomes (CAPO), with $p > 0.05$.**

Conclusions: **FAR and BAR have been identified as biomarkers that may facilitate the timely diagnosis of preeclampsia in the first trimester of pregnancy. However, since these markers do not demonstrate significant benefits in predicting the severity of the disease or adverse perinatal outcomes, further research is required in larger prospective cohorts.**

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KEYWORDS

preeclampsia, fibrinogen, serum albumin, biomarkers, inflammation

INTRODUCTION

Preeclampsia is a systemic inflammatory disease characterized by endothelial dysfunction and reduced placental perfusion [1,2]. Even with the expansion of pathophysiological knowledge, the precise triggers remain poorly understood. Impaired adaptive mechanisms contribute to oxidative stress and inflammation, creating a microenvironment that promotes the development and

progression of complications [3]. Inflammation is strongly associated with vascular dysfunction and plays a critical role in the onset of systemic complications. Furthermore, an imbalance between anti-inflammatory and pro-inflammatory pathways may have detrimental effects on the developing fetus [3,4]. The multifactorial etiology and complex pathophysiology of preeclampsia make its underlying mechanisms unclear and its risk difficult to predict with high accuracy [5,6]. Reliable prediction is crucial for implementing timely preventive and therapeutic strategies, such as monitoring maternal blood pressure, administering antihypertensive medications, or planning early delivery to mitigate maternal and fetal complications. Although the literature on prediction methods is abundant, there is no universally defined approach. In addition to Doppler studies and placental hormones for prediction, the search for cost-effective maternal plasma markers that are clinically applicable continues. The evaluation of biomarkers for preeclampsia has been extensively studied and holds promise for early detection, potentially even in the first trimester, before hypertension develops.

In recent years, various blood-based inflammatory markers have been extensively investigated as indicators of inflammation across multiple diseases. In the field of obstetrics, these markers may indicate an imbalance associated with the systemic inflammatory burden observed in preeclampsia. There is an urgent need for the development of practical laboratory markers that can improve the early detection of PE and the prognosis of its severity [7,8].

Based on this, in our study, we investigated the potential use of the fibrinogen-to-albumin ratio (FAR) and blood urea nitrogen-to-serum albumin ratio (BAR) in predicting preeclampsia and their association with neonatal outcomes.

MATERIALS AND METHODS

This retrospective cross-sectional study was conducted in the perinatology clinic of Ankara, Etlik City Hospital, between January 01, 2023, and February 01, 2024. The Ethics Committee of our center approved the study protocol (protocol ID: AEŞH-BADEK-2024-196), and the study was conducted in accordance with the universal ethical standards of the Declaration of Helsinki. The required data were obtained from the electronic database and patient records of the hospital's records department.

Preeclampsia is defined as the presence of new-onset hypertension and proteinuria or other end-organ damage after 20 weeks of gestation, while eclampsia is defined as the development of grand mal seizures in a woman with preeclampsia.

The diagnosis of PE is made by the presence of at least one of the following criteria in addition to newly developed hypertension (140/90 mmHg measured at least 4 hours apart) after the 20th week of gestation: ≥ 300 mg proteinuria in 24-hour urine or +1 proteinuria with a urine swab in spot urine; more than 2-fold increase in liver function tests (AST, ALT); platelet count below 100,000/μL; *creatinine ≥ 1,1 mg/dL.

Severe PE is defined as PE in which any of the following characteristics are present: blood pressure ≥ 160/110 mmHg in two separate conditions; platelet count < 100,000 per microliter; liver dysfunction evidenced by elevation of liver enzymes to twice the normal concentration or severe, persistent right upper quadrant or epigastric pain; a serum creatinine level of > 1,1 mg/dL or a doubling of the serum creatinine level in the patient with renal insufficiency, pulmonary edema, or new onset cerebral or visual disturbances.

A patient who applied to the Perinatology outpatient clinic of Etlik City Hospital and was admitted to the perinatology service and patients diagnosed with preeclampsia between January 01, 2023, and February 01, 2024, whose maternal ages were between 18 - 45 years and whose gestational week ranges were between 20 - 39 weeks, were included. In addition to newly developed hypertension (blood pressure ≥ 140/90 mmHg measured at least 4 hours apart) after the gestational week of 20, proteinuria of ≥ 300 mg in 24-hour urine or +1 proteinuria with a urine swab in spot urine, more than 2-fold increase in liver function tests (AST, ALT), platelet count below 100,000/μL, creatinine ≥ 1.1 mg/dL, and preeclampsia patients who did not have fetal congenital and chromosomal abnormalities, who did not have signs and diagnoses of systemic maternal diseases, who did not have chronic drug use, and who did not receive tocolytic therapy during pregnancy were included. A control group was established by matching for maternal age and gestational age at delivery. To minimize confounding factors affecting neonatal outcomes, patients with fetal comorbidities, congenital anomalies, or chromosomal aneuploidies were excluded from all three groups. The study comprised patients who had undergone a complete blood count assessment. In addition, albumin, fibrinogen, and blood urea nitrogen measurements were taken during the procedure. Patients with conditions that could affect these parameters, such as active infections, chronic liver or kidney disease, hematological disorders, or malignancies, were excluded from the study. Consequently, patients with pre-existing conditions that might have affected these parameters were excluded from participation.

For neonatal outcomes, birthweight, gestational age at delivery (weeks), neonatal intensive care unit (NICU) admission, umbilical cord blood pH (< 7.0), Apgar score < 7 (at any time during the first 10 minutes), and respiratory problems were recorded. The presence of at least one of these parameters was defined as a composite adverse outcome.

The FAR ratio and BAR ratio were calculated using third-trimester measurements of hemoglobin, lymphocytes, platelets, albumin, fibrinogen, and blood urea nitrogen. The formulas were as follows: FAR ratio = fibrinogen (mg/dL)/albumin (g/dL); BAR ratio = blood

Table 1. Comparison of maternal characteristics and neonatal outcomes among pregnancies complicated by mild preeclampsia, severe preeclampsia, and control groups.

Variables	m-PE (n = 48)	s-PE (n = 48)	Control group (n = 48)	p-value
Maternal age (years)	30 (28 - 34)	29 (25 - 33)	28 (24 - 32)	0.180 [a]
Gravidity (n)	2 (1 - 3)	2 (1 - 3)	1 (0 - 2)	0.276 [a]
Parity (n)	1 (0 - 2)	1 (0 - 2)	1 (0 - 2)	0.559 [a]
BMI (kg/m^2)	30.40 ± 4.8	30.34 ± 3.58	28.96 ± 2.28	0.101 [b]
GW at delivery (weeks)	37 (35-39) [1]	37 (35 - 38) [2]	39 (38 - 40) [1, 2]	< 0.001 [a]
Birthweight (g)	2,648 (2,240 - 3,375) [1]	2,740 (2,215 - 3,230) [2]	3,235 (3,010 - 3,640) [1, 2]	< 0.001 [a]
Neonatal outcome				
NICU admission (n, %)	10 (20.8%)	12 (25.0%)	4 (8.3%)	0.087 [c]
Apgar score ≤ 7 at 5th minute (n, %)	7 (14.5%)	8 (16.6%) [1]	1 (2.0%) [1]	0.049 [c]
Respiratory problems (n, %)	3 (6.2%)	6 (12.5%)	2 (4.1%)	0.384 [c]
CAPO (n, %)	14 (29.1%)	16 (33.3%) [1]	5 (10.4%) [1]	0.020 [c]

[a] The Kruskal-Wallis test was used. Results are presented as median (25th - 75th percentile).
[b] One-way ANOVA test was used. Results are presented as mean ± standard deviation (SD).
[c] Pearson's chi-squared test or Fisher's exact test was used for the analysis of categorical variables, as appropriate.
Superscript numbers indicate statistically significant pairwise comparisons after Bonferroni correction.
1: Significant difference between the mild preeclampsia and control groups.
2: Significant difference between the severe preeclampsia and control groups.
PE: preeclampsia, m-PE: mild preeclampsia, s-PE: severe preeclampsia, BMI: body mass index, GW: gestational week, NICU: neonatal intensive care unit, CAPO: composite adverse perinatal outcome.

Table 2. Distribution of first trimester hematological, biochemical, and inflammatory parameters among mild preeclampsia, severe preeclampsia, and control groups.

Variables	m-PE (n = 48)	s-PE (n = 48)	Control group (n = 48)	p-value
Hemoglobin (g/dL)	11.3 ± 1.4	11.7 ± 1.4	11.3 ± 1.6	0.290[a]
Albumin (g/L)	39.1 ± 3.1 [1]	39.9 ± 3.2 [2]	42.3 ± 1.5 [1, 2]	< 0.001 [a]
Platelet (10^9/L)	240 ± 69	250 ± 63	250 ± 60	0.675 [a]
Fibrinogen (mg/dL)	410.7 ± 70.4 [1]	403.4 ± 80.5 [2]	372.3 ± 30.0 [1, 2]	0.023 [a]
BUN (mg/dL)	19.7 (15.9 - 27.7) [1]	20.4 (13.1 - 28.4) [2]	13.9 (11.9 - 17.1) [1, 2]	< 0.001 [b]
FAR	10.518 ± 1.713 [1]	10.193 ± 2.214 [2]	8.792 ± 0.625 [1, 2]	< 0.001 [a]
BAR	4.99 (3.95 - 7.32) [1]	5.06 (3.25 - 7.37) [2]	3.22 (2.73 - 4.05) [1, 2]	< 0.001 [b]

[a] One-way ANOVA was used for group comparisons. Results are presented as mean ± standard deviation.
[b] The Kruskal-Wallis test was used. Results are presented as median (25th - 75th percentile).
Superscript numbers indicate statistically significant pairwise comparisons based on post hoc analysis (Bonferroni or Games-Howell, as appropriate).
1: Significant difference between the mild preeclampsia and control groups.
2: Significant difference between the severe preeclampsia and control groups.
PE: preeclampsia, m-PE: mild preeclampsia, s-PE: severe preeclampsia, BUN: blood urea nitrogen, FAR: fibrinogen-to-albumin ratio, BAR: BUN-to-albumin ratio.

urea nitrogen (mg/dL)/albumin (g/dL).

Visual and quantitative analyses were performed to assess the normality of data distribution. As the data did not follow a normal distribution, quantitative variables were presented as median values with minimum and maximum ranges. The Mann-Whitney U test was used for comparing independent continuous variables, while the Friedman test was used for non-parametric dependent variables. All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) software for Windows (version 23). A p-value of < 0.05 was considered statistically significant.

Table 3. Comparison of maternal and laboratory characteristics between preeclamptic pregnancies with and without composite adverse perinatal outcomes.

Variables	CAPO (n = 30)	Non-CAPO (n = 66)	p-value
Maternal age	29.3 ± 4.7	29.9 ± 5.1	0.550 [a]
BMI	30.68 ± 3.94	30.23 ± 4.35	0.627 [a]
Gestational age at delivery	37 (29 - 39)	37 (36 - 39)	0.145 [b]
Birth weight	2,262 ± 1,175	2,787 ± 775	0.031 [a]
Hemoglobin (g/dL)	11.3 ± 1.1	11.6 ± 1.5	0.230 [a]
Albumin (g/L)	39.9 ± 3.6	39.3 ± 3.0	0.388 [a]
Platelet (10^9/L)	267 ± 70	235 ± 62	0.028 [a]
Fibrinogen (mg/dL)	419 ± 84	402 ± 71	0.291 [a]
BUN (mg/dL)	23.09 ± 9.46	21.21 ± 9.13	0.357 [a]
FAR	10.603 ± 2.350	10.243 ± 1.789	0.411 [a]
BAR	5.386 (3.721 - 6.957)	4.851 (3.401 - 7.380)	0.425 [b]

[a] Independent samples *t*-test was used for comparisons between groups. Data are presented as mean ± standard deviation.
[b] The Mann-Whitney U test was used for comparisons between groups. Data are presented as median (interquartile range).
CAPO: composite adverse perinatal outcome, BMI: body mass index, BUN: blood urea nitrogen, FAR: fibrinogen-to-albumin ratio, BAR: blood urea nitrogen-to-albumin ratio.

Table 4. Correlation analysis of first trimester biochemical parameters, FAR, and BAR scores with the development of preeclampsia.

Variables	r	p-value
Albumin	-0.340	< 0.001
Fibrinogen	0.180	0.031
BUN	0.304	< 0.001
FAR	0.403	< 0.001
BAR	0.436	< 0.001

Spearman correlation analysis was performed.
BUN: blood urea nitrogen, FAR: fibrinogen-to-albumin ratio, BAR: BUN-to-albumin ratio, r: Spearman correlation coefficient.

Table 5. Receiver operating characteristic (ROC) curve analysis of first trimester FAR and BAR scores in predicting the development of preeclampsia.

Variables	Cutoff	AUC	95% CI	Sensitivity (%)	Specificity (%)	+LR	-LR	p-value
FAR	> 9.677	0.747	0.668 - 0.815	61.5	95.8	14.75	0.40	< 0.001
BAR	> 4.275	0.767	0.690 - 0.833	63.5	83.3	3.81	0.44	< 0.001

FAR: fibrinogen-to-albumin ratio, BAR: BUN-to-albumin ratio, AUC: area under the curve, CI: confidence interval, LR: likelihood ratio.

RESULTS

The study comprised 144 pregnant women: 48 with mild preeclampsia, 48 with severe preeclampsia, and 48 in the healthy control group. The comparison of demographic and neonatal outcomes among the groups is shown in Table 1. No statistically significant differences were observed between the groups regarding maternal

Table 6. Univariate and multivariate logistic regression analysis of first trimester FAR and BAR scores in predicting pre-eclampsia.

Variables	Univariate				Multivariate			
	B	OR	(95% CI)	p-value	B	aOR	(95% CI)	p-value
FAR	0.688	1.990	1.467 - 2.700	< 0.001	0.879	2.409	1.589 - 3.654	< 0.001
BAR	0.703	2.020	1.480 - 2.757	< 0.001	0.929	2.533	1.699 - 3.775	< 0.001

Multivariate analysis was adjusted for maternal age, gravidity, parity, and body mass index (BMI) to control for potential confounding effects. FAR: fibrinogen-to-albumin ratio, BAR: blood urea nitrogen-to-albumin ratio, B: regression coefficient, aOR: adjusted odds ratio, CI: confidence interval.

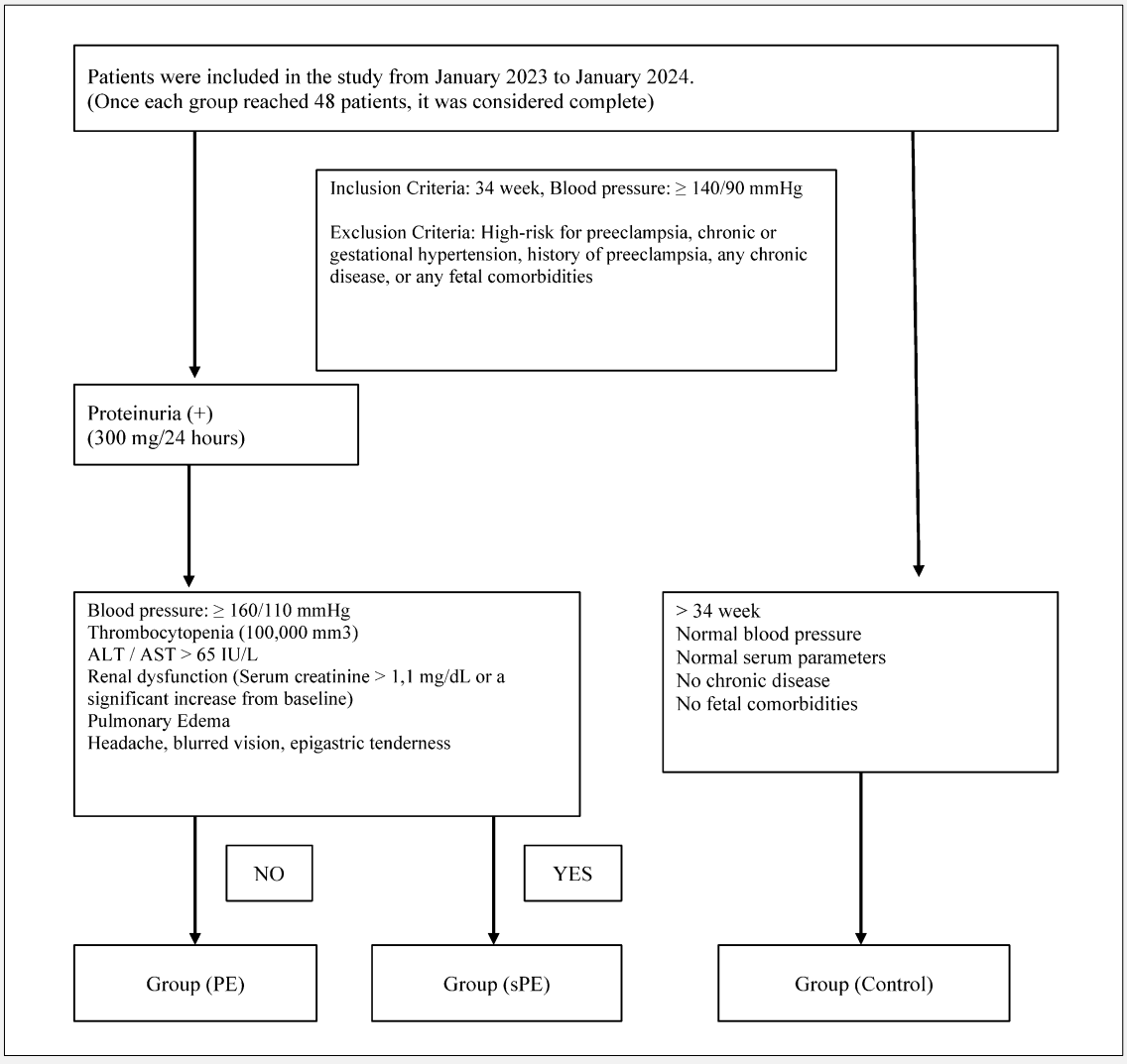

Figure 1. Flowchart of patient selection, inclusion and exclusion criteria, and group allocation.

Patients were screened based on clinical and laboratory criteria for preeclampsia and severe preeclampsia, with control cases matched for gestational age and absence of comorbidities.

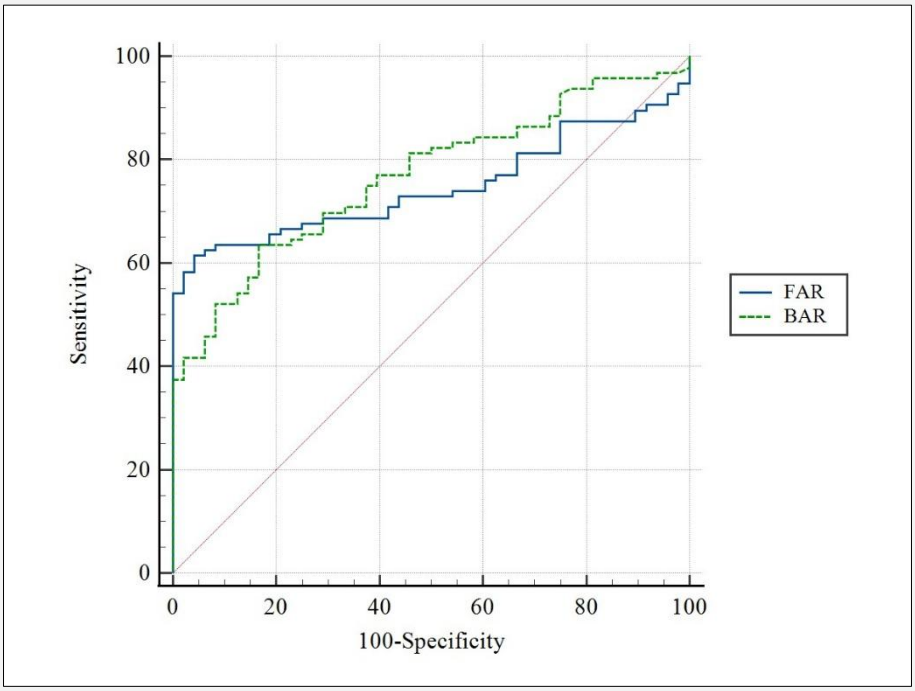

Figure 2. Receiver operating characteristic (ROC) curves for the diagnostic performance of fibrinogen-to-albumin ratio (FAR) and blood urea nitrogen-to-albumin ratio (BAR) in predicting preeclampsia.

Area under the curve (AUC) values indicate the potential utility of both biomarkers in differentiating preeclamptic patients from healthy controls.

age, gravidity, parity, and body mass index (BMI) ($p > 0.05$). A notable disparity was observed between the groups regarding the incidence of neonates with a 5-minute Apgar score ≤ 7 ($p = 0.049$) and the occurrence of CAPO ($p = 0.020$). Following the Bonferroni correction, it was demonstrated that the incidence of newborns with a 5-minute Apgar score ≤ 7 was significantly higher in the severe preeclampsia cohort relative to the control group ($p = 0.015$). Similarly, the CAPO rate was significantly higher in the severe preeclampsia group than in the control group ($p = 0.007$).

The comparison of the hematological, biochemical, and inflammatory parameters in the first trimester between the groups is shown in Table 2. A significant difference was found in albumin levels between the groups ($p < 0.001$). Both the mild preeclampsia (39.1 ± 3.1) and severe preeclampsia (39.9 ± 3.2) groups had significantly lower albumin levels than the control group (42.3 ± 1.5), as determined by the Games-Howell post hoc test ($p < 0.001$ for both comparisons). Significant differences between the groups were also observed for fibrinogen, BUN, FAR, and BAR values ($p = 0.023$, $p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). After Games-Howell correction for multiple comparisons, the control group had significantly lower fibrinogen and FAR values than the mild preeclampsia and severe preeclampsia groups ($p = 0.003$ and $p < 0.001$, respectively). However, no statistically significant difference in FAR levels was observed between the mild and severe preeclampsia groups ($p = 0.702$). Bonferroni correction was applied for BUN and BAR; both parameters were significantly lower in the control group than in the mild preeclampsia and severe preeclampsia groups ($p < 0.001$ for each comparison). However, after Bonferroni correction, there was no significant difference in BAR levels between mild and severe preeclampsia groups ($p = 0.392$).

Among the 96 preeclamptic pregnant women included in the analysis, 30 (31.3%) developed composite adverse perinatal outcomes (CAPO), while 66 (68.7%) did not. There were no statistically significant differences between the CAPO and non-CAPO groups in terms of maternal age (29.3 ± 4.7 vs. 29.9 ± 5.1 years, $p = 0.550$) and BMI (30.68 ± 3.94 vs. 30.23 ± 4.35, $p = 0.627$). The median gestational age at delivery did not differ significantly between groups (37 [29 - 39] vs. 37 [36 - 39] weeks, $p = 0.145$). However, birth weight was significantly lower in the CAPO group (2,262 ± 1,175 g) com-

pared to the non-CAPO group (2,787 ± 775 g, p = 0.031). Among laboratory parameters, platelet counts were significantly higher in the CAPO group (267 ± 70 vs. 235 ± 62 × 10⁹/L, p = 0.028). No statistically significant differences were observed between the groups regarding hemoglobin, albumin, fibrinogen, BUN, FAR, or BAR levels (all p > 0.05).

The correlation analysis revealed a moderately significant positive correlation between first-trimester FAR and BAR scores and the development of preeclampsia (FAR: r = 0.403, p < 0.001; BAR: r = 0.436, p < 0.001) (Table 4).

The diagnostic accuracy of FAR and BAR scores in the first trimester in predicting the development of preeclampsia was assessed using ROC analysis (Table 5). The cutoff value for FAR was set at > 9.677. At this value, the AUC was calculated as 0.747 (95% CI: 0.668 - 0.815), the sensitivity was 61.5%, the specificity was 95.8%, the positive likelihood ratio (+LR) was 14.75, and the negative likelihood ratio (-LR) was 0.40 (p < 0.001).

The cutoff value determined for BAR is > 4.275. At this threshold, the AUC is 0.767 (95% CI: 0.690 - 0.833), the sensitivity is 63.5%, the specificity is 83.3%, the +LR is 3.81, and the -LR is 0.44 (p < 0.001). Table 6 shows the results of the univariate and multivariate logistic regression studies performed to assess the relationship between first-trimester FAR and BAR scores and preeclampsia. In the univariate analysis, the odds ratio (OR) for FAR was 1.990 (95% CI: 1.467 - 2.700) and for BAR was 2.020 (95% CI: 1.480 - 2.757) (both p < 0.001). In the multivariable analysis, after adjusting for potential confounders such as maternal age, gravidity, parity and body mass index (BMI), the adjusted odds ratio (aOR) for FAR was 2.409 (95% CI: 1.589 - 3.654) and for BAR was 2.533 (95% CI: 1.699 - 3.775) (both p < 0.001). Consequently, both variables continued to serve as independent predictors for developing preeclampsia.

DISCUSSION

In this study, fibrinogen-to-albumin ratio (FAR) and blood urea nitrogen-to-albumin ratio (BAR) values were significantly higher in the first trimester in both the mild and severe preeclampsia groups compared to the healthy controls. However, there was no statistically significant difference in FAR and BAR values between the mild and severe preeclampsia groups. ROC analysis showed moderate to high differentiating power in predicting preeclampsia for both markers, and multivariate logistic regression analysis confirmed FAR as an independent predictor of preeclampsia. Preeclampsia is an important cause of maternal and perinatal morbidity and mortality worldwide [6,9].

The ability to predict the disease before the onset of clinical symptoms would be a very useful approach for the patient and the physician. Preeclampsia is a complex disease with multiple etiologic factors, including abnormal placentation, systemic endothelial dysfunction, immune system dysfunction, and excessive maternal inflammation [3,10,11]. The elucidation of the underlying pathophysiological processes of preeclampsia has directed scientific research towards angiogenic and inflammatory mediators, in particular placental growth factor (PlGF) and soluble Fms-like tyrosine kinase-1 (sFlt-1), both of which have shown promise as early biomarkers. These molecules could facilitate the prediction of preeclampsia before the first clinical manifestations occur [3,12-14]. In parallel, maternal demographic variables, uterine artery Doppler velocimetry and maternal hemodynamic parameters have been studied as complementary predictors [15]. Given the systemic and multifactorial nature of the disease, laboratory indicators such as serum uric acid, creatinine, hepatic transaminases, and platelet indices have been shown to be indirect indicators of endothelial dysfunction and renal damage [15-18]. Among these indicators, the fibrinogen-to-albumin ratio (FAR) has attracted particular attention due to its cost-effectiveness, ease of assessment, and mechanistic relevance to inflammatory and vascular disorders implicated in the pathogenesis of preeclampsia [7,19,20].

Fibrinogen, a glycoprotein synthesized in the liver, exhibits both pro-angiogenic and immunomodulatory functions. Although traditionally viewed as a key element of the coagulation cascade, mounting evidence highlights its clinical relevance as an indirect indicator of systemic inflammatory activity [19-22]. In pregnancies complicated by preeclampsia, elevated fibrinogen levels are commonly regarded as a reflection of endothelial dysfunction and the activation of coagulation pathways - two interrelated processes central to the disorder's vascular pathology [7,18,19]. In contrast, albumin acts as a negative acute phase reactant, meaning that its levels tend to decrease in response to inflammation and increased vascular permeability. As a potent antioxidant, albumin contributes significantly to vascular homeostasis and endothelial cell protection [22-24]. Therefore, decreased serum albumin may indicate inflammation as well as early-stage renal dysfunction.

Several recent studies point to a growing understanding of how inflammation and endothelial dysfunction are involved in both the development and severity of preeclampsia. Fibrinogen levels, for instance, have been reported to rise in women affected by both mild and severe forms of the condition, which may reflect its dual role in inflammation and coagulation. Interestingly, some data also suggest that higher fibrinogen concentrations might be related to elevated mean arterial pressure, hinting at a link between circulatory stress and the inflammatory process in this context [7,19].

Uric acid has emerged as a relevant laboratory marker in the evaluation of preeclampsia, primarily because of its connection to renal impairment and oxidative stress. Clinical observations suggest that when levels surpass 7 mg/dL, the risk of more severe disease progression, ear-

lier delivery, and NICU admission increases noticeably [16]. Rather than looking at uric acid alone, some researchers have proposed that the uric acid-to-creatinine ratio (SUA/Cr) may offer better predictive insight. Elevated SUA/Cr values during gestation have been linked to both the onset of preeclampsia and greater maternal and neonatal complications [15]. In some cases, blood tests from the second trimester have shown higher BUN and creatinine levels, even when proteinuria is not yet detectable. Taken together, these findings suggest that early changes in renal function might be useful for identifying women at higher risk for preeclampsia [17,25].
In this study, we examined whether two biochemical ratios, fibrinogen-to-albumin (FAR) and blood urea nitrogen-to-albumin (BAR), might assist in identifying preeclampsia and gauging its severity. FAR incorporates higher fibrinogen levels and lower albumin, a combination often seen in inflammatory and prothrombotic states. BAR, meanwhile, reflects kidney dysfunction by combining elevated urea with hypoalbuminemia. Since these two ratios touch on overlapping areas such as vascular stress, inflammation, and renal compromise, they could offer added value in spotting patients who are at higher risk for more severe disease forms [7,19].
The fibrinogen-to-albumin ratio (FAR) can be calculated using routine biochemical and coagulation parameters, which makes it readily accessible in clinical settings [7,26]. Elevated FAR levels have been observed across a broad spectrum of inflammatory conditions, including early pregnancy loss [26], systemic lupus erythematosus [27], acute coronary syndrome [28], rheumatoid arthritis [29], and ankylosing spondylitis [30]. These associations reflect the ratio's sensitivity to systemic inflammatory activity. In a recent study by Ren et al. (2023), patients with severe preeclampsia exhibited significantly higher FAR values, suggesting that this index may function as an independent indicator of disease severity [7].
Between 2015 and 2019, Sudjai and Satho analyzed records from 400 women with preeclampsia at Rajavithi Hospital in Thailand. Among them, 331 (82.7%) were diagnosed with the severe form of the condition. Many of these patients had notably elevated serum uric acid, especially those whose levels exceeded 7 mg/dL. This group experienced more kidney-related complications and showed signs of more advanced clinical involvement. Similar trends have been reported elsewhere, with uric acid levels between 5 and 7 mg/dL - and especially above 7 mg/dL - linked to earlier births, respiratory distress in newborns, and higher NICU admission rates. These patterns point to hyperuricemia as a potentially useful marker for identifying individuals at greater risk for severe preeclampsia [16].
Piani et al. observed 269 pregnant women over a multiyear period to assess outcomes related to hypertensive disorders of pregnancy. Participants were classified into three groups based on their clinical presentation: normotensive, gestational hypertension, and preeclampsia. The data revealed that higher third-trimester serum uric acid-to-creatinine (SUA/Cr) ratios were more frequently seen in cases of preeclampsia, often accompanied by preterm delivery and neonatal complications. After adjusting for confounding factors such as maternal age, body mass index, and antihypertensive treatment, the SUA/Cr ratio remained a strong independent predictor [15].
In addition to SUA/Cr, the blood urea nitrogen-to-albumin (BAR) ratio has been examined as another potential marker. Elevated BUN levels in combination with hypoalbuminemia are commonly found in pregnancies with impaired renal perfusion, a condition that can lead to decreased glomerular filtration and reflect underlying inflammation [17,31]. Although research on BAR is still developing, findings from Gafurri et al. (2012) showed significantly elevated BUN-to-creatinine ratios in women with preeclampsia, suggesting a possible link with disease severity [32]. In addition, studies by Zhou and Pan (2025) and Shi et al. (2024) have associated elevated BAR levels with worsening clinical condition, including organ dysfunction and increased mortality in various patient groups [31,33]. The present results suggest that BAR plays a role beyond the context of preeclampsia and may be relevant in inflammation and renal disease.
In our study, both FAR and BAR were significantly higher in the preeclamptic (PE) and severe preeclamptic (sPE) groups compared to the control group ($p < 0.001$). These findings are consistent with previous literature. Several studies have associated increased FAR with increased severity and adverse maternal outcomes, including mortality [7]. Although the number of studies investigating BAR is limited, the available data also suggest a possible association between higher BAR values and disease severity or mortality risk [31,34]. Based on ROC analysis, both indices had moderate to high diagnostic performance for the prediction of preeclampsia. In particular, the positive likelihood ratio for FAR was remarkably high (14.75), indicating a strong ability to rule out disease when tested positive and reflecting a low false-positive rate. However, in our study, we did not detect a relationship between FAR and BAR with capo prediction and severity of disease, although it was significant in predicting preeclampsia.
Numerous investigations have evidenced a robust correlation between preeclampsia and composite adverse perinatal outcomes (CAPOs), including preterm birth, fetal growth restriction, and admission to the neonatal intensive care unit [16,17,26]. It is widely accepted amongst the relevant scientific community that this relationship is primarily attributable to the existence of underlying placental insufficiency and systemic endothelial dysfunction. These two phenomena are characteristic of severe preeclampsia. For instance, the research conducted by Piani et al. revealed a significantly higher prevalence of adverse outcomes in newborns in pregnancies complicated by preeclampsia in comparison with the normotensive control group [15]. Furthermore, the research by Gul et al. indicated that the likeli-

hood of perinatal morbidity and mortality was considerably elevated in pregnancies complicated by severe cases of preeclampsia and eclampsia, particularly when HELLP syndrome was present [35].

However, the present study found no statistically significant differences between the CAPO and non-CAPO groups in terms of inflammatory markers. These included the fibrinogen-to-albumin ratio (FAR) and the blood urea nitrogen-to-albumin ratio (BAR). One potential explanation for this finding is that the relatively limited sample size may have reduced the ability to detect subtle variations in biomarkers. Furthermore, given that the laboratory parameters were derived from first-trimester blood samples, pathophysiological changes which give rise to perinatal outcomes, in particular those linked with endothelial dysfunction and systemic inflammation, may not have fully manifested at this early pregnancy stage.

A major strength of this study is the assessment of FAR and BAR in the first trimester of pregnancy, which suggests that these markers may have a predictive value prior to the clinical onset of preeclampsia. This highlights their potential role not only in the diagnosis of preeclampsia but also in the early risk stratification and planning of preventive care. These parameters can be derived from routine, inexpensive laboratory testing, making them accessible in different clinical settings.

The limitations of our study include its single-center design and the relatively small size of the sample. In addition, we were not able to assess longitudinal changes in FAR and BAR over time, as this was a cross-sectional study. Nevertheless, the robustness of the statistical analyses, the well-matched group comparisons, and the consistency of the results from the ROC and logistic regression models strengthen the credibility of our findings. One of the limitations of this study is that important biomarkers such as placental growth factor (PlGF) and soluble Fms-like tyrosine kinase-1 (sFlt-1), which have an established role in the early prediction of preeclampsia, are not routinely assessed during the first trimester in our clinical setting. Therefore, these parameters were not included in our analysis. Furthermore, a standardized model for scoring the risk of preeclampsia was not applied to the study population, which may have limited the ability to stratify the participants' baseline risk.

In conclusion, this study shows that early pregnancy FAR and BAR scores may help to predict preeclampsia. In this study, we aimed to emphasize the importance of the first trimester FAR and BAR ratio in predicting the progression to preeclampsia. The incorporation of Doppler findings, maternal characteristics, and novel biomarkers such as FAR and BAR into prediction models has the potential to enhance the identification of patients at risk for preeclampsia. This multimodal approach may offer a more comprehensive reflection of both hemodynamic disturbances and underlying vascular and organ-level involvement. This situation will be clarified in future studies with the addition of large series FAR and BAR values to prediction models.

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Availability of Data and Materials:
The datasets of the current study are available upon reasonable request.

Declaration of Interest:
The authors declare no conflicts of interest.

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