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The Role of the Fibrinogen-Albumin Ratio in Predicting Fetal and Maternal Outcomes in Pregnancies Complicated by Placental Abruption

Ablasyo Plasenta ile Komplike Olan Gebeliklerde Fetal ve Maternal Sonuçların Tahmininde Fibrinojen-Albümin Oranının Rolü

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Abstract: To investigate the role of the fibrinogen-albumin ratio (FAR.) in predicting fetal and maternal outcomes in patients with placental abruption (PA). This study was retrospectively designed at a single tertiary care center between June 2019 and June 2023. A total of 190 patients with PA were included. The patients were divided into two groups based on the degree of PA. There were 54 patients in the total PA group and 136 patients in the partial PA group. Fibrinogen levels were found to be statistically significantly lower in the total PA group compared to partial PA group ($p<0.001$). There was also a statistically significant difference in FAR results ($p<0.001$). Gestational age at diagnosis, gestational age at delivery, and birth weight were lower in the total PA group ($p<0.001$). Intrauterine fetal loss was more frequent in the total PA group ($p<0.001$). The rate of maternal admission to the intensive care unit was also higher in the total PA group ($p<0.001$). Receiver operating characteristic analysis revealed that FAR had an optimal cut-off value of 0.07, at which it predicted maternal intensive care unit admission with 82% sensitivity and 73% specificity (area under the curve=0.855; $p<0.001$). As the degree of PA increases, fetal and maternal outcomes worsen. FAR was found to be lower in patients with total PA, and it demonstrated high sensitivity in predicting adverse maternal outcomes. Being a simple and feasible measure, FAR could assist clinicians in managing cases of PA.

Keywords: albumin, fibrinogen, fibrinogen-albumin ratio, placental abruption

Ethics Committee Approval: The study was approved by Ankara Bilkent City Hospital Clinical Research Ethical Committee (Decision no: E2-23-5174, Date: 11.10.2023

Informed Consent: The authors declared that informed consent was not required as the study was based on retrospective data analysis.

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[GRT, MÖA, Gİ, EB] assisted in statistical analysis, data interpretation, and manuscript revisions.[HŞ, DŞ] contributed to the design of the study, supervision of the project, and final manuscript approval.

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Özet: Plasenta dekolmanı (PA) olan hastalarda fetal ve maternal sonuçları öngörmede fibrinojen-albümin oranının (FAR) rolünü araştırmak. Bu çalışma, Haziran 2019 ile Haziran 2023 tarihleri arasında tek bir üçüncü basamak sağlık merkezinde retrospektif olarak tasarlanmıştır. Çalışmaya PA'lı toplam 190 hasta dahil edilmiştir. Hastalar PA derecesine göre iki gruba ayrılmıştır. Toplam PA grubunda 54 hasta ve kısmi PA grubunda 136 hasta bulunmaktadır. Fibrinojen düzeylerinin, kısmi PA grubuna kıyasla toplam PA grubunda istatistiksel olarak anlamlı derecede düşük olduğu bulunmuştur ($p<0,001$). FAR sonuçlarında da istatistiksel olarak anlamlı bir fark bulunmuştur ($p<0,001$). Tanı anındaki gebelik yaşı, doğum anındaki gebelik yaşı ve doğum ağırlığı, toplam PA grubunda daha düşük bulunmuştur ($p<0,001$). İntrauterin fetal kayıp, toplam PA grubunda daha sık görülmüştür ($p<0,001$). Yoğun bakım ünitesine anne yatışı oranı toplam PA grubunda daha yüksekti ($p<0,001$). Alıcı çalışma karakteristiği analizi, FAR'ın 0,07'lik optimum bir kesme değerine sahip olduğunu ve bu değerde %82 duyarlılık ve %73 özgüllükle anne yoğun bakım ünitesine yatışını öngördüğünü ortaya koydu (eğri altında kalan alan = 0,855; $p<0,001$). PA derecesi arttıkça fetal ve maternal sonuçlar kötüleşmektedir. FAR'ın toplam PA'lı hastalarda daha düşük olduğu ve olumsuz maternal sonuçları öngörmede yüksek duyarlılık gösterdiği bulundu. Basit ve uygulanabilir bir ölçüm olan FAR, klinisyenlerin PA vakalarını yönetmesine yardımcı olabilir..

Anahtar Kelimeler: albümin, fibrinojen, fibrinojen-albümin oranı, ablasyo plasenta

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1. Introduction

Placental abruption (PA) is generally defined as the partial or complete separation of the placenta from the placental bed before delivery 1. It is estimated that approximately 0.5–1% of all deliveries are complicated by PA (1,2). Although risk factors for PA include hypertensive disorders during pregnancy, low pre-pregnancy body mass index, maternal smoking and cocaine use, assisted reproductive techniques and uterine fibroids, the exact cause and pathophysiology of PA remain unclear (3).

Clinically, PA commonly presents with sudden onset vaginal bleeding, often accompanied by abdominal pain and uterine contractions (4). It is associated with severe adverse fetal and maternal outcomes such as fetal hypoxia and intrauterine fetal death, disseminated intravascular coagulation, hypovolemic shock, hysterectomy (5, 6). The degree of placental separation (partial or total) determines the severity of PA and the spectrum of adverse outcomes (6).

Identifying a potential blood marker or index that could predict adverse fetal and maternal outcomes associated with PA has become a focus of interest (7-9). Just as adverse outcomes vary with the severity of PA, a potential blood marker or index should also exhibit variability in maternal blood depending on the severity of the disease. Previous studies have demonstrated that liver function tests, renal function tests, and blood coagulation components in maternal blood can vary widely depending on the severity of PA (9). One study showed that levels of D-dimer, fibrinogen, and fibrinogen degradation products in maternal blood were significantly affected by the severity of PA (9).

The fibrinogen-albumin ratio (FAR.) derived from serum fibrinogen and albumin levels, has previously been shown to successfully predict outcomes in various cardiovascular diseases and several cancer types (10-12). In obstetric practice, FAR has been used in cases of threatened abortion and recurrent pregnancy loss, where it was observed to have a high predictive value (13, 14).

Given that fibrinogen and fibrinogen-derived products, D-dimer, and other coagulation factors are affected by the severity of PA (9), we hypothesized that FAR could predict the severity of this condition prenatally. To the best of our knowledge, no study has yet examined the role of FAR in predicting adverse fetal and maternal outcomes in patients with PA. The current study aimed to investigate the predictive ability of FAR for fetal and maternal outcomes influenced by the severity of PA.

2. Materials and Methods

This study was designed retrospectively at a tertiary care hospital. It included patients diagnosed with PA at 24–40 weeks of gestation, who were followed up and treated at the High-Risk Pregnancy Department of Ankara City Hospital between June 2019 and June 2023. Ethical approval for the study was obtained from the Ethics Committee of Ankara City Hospital (approval number: E2-23-5174). All procedures throughout the study adhered to the principles of the Declaration of Helsinki.

Patients diagnosed with PA included in the study were classified into two groups. The first group consisted of patients with confirmed total PA, where the placenta had completely separated before delivery. The second group included patients with confirmed partial PA, where only a partial separation of the placenta was observed before delivery. Diagnostic confirmation and group classification were undertaken retrospectively by comparing ultrasonographic findings obtained at the time of diagnosis with the records of PA observed during delivery (either vaginal or cesarean section), as documented by the surgeon or midwife.

The gestational age of the patients was retrospectively correlated based on the crown-rump length measurements taken during the first-trimester ultrasound. For each patient included in the study, clinical and demographic data, such as age, parity, gravidity, body mass index (BMI), gestational age at PA diagnosis, extensive liver function tests, complete blood count, spot urine test results, fibrinogen and albumin levels, gestational age at delivery, birth weight, neonatal information, umbilical artery pH and base excess (BE), intrauterine fetal loss rates, maternal intensive care unit (ICU) admission rates, and neonatal ICU (NICU) admission rates, were collected retrospectively from the hospital database. FAR was calculated by dividing fibrinogen by albumin.

Patients with multiple pregnancies, those with known major fetal chromosomal or structural anomalies, and those with incomplete or inaccessible data were excluded from the study.

Data analysis was performed using SPSS v. 22.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality of data distribution. Student's t-test and the Mann-Whitney U-test were used to compare normally and non-normally distributed variables, respectively. Descriptive analyses for non-normally distributed variables were presented using median and minimum–maximum values. The chi-square test was conducted to compare categorical variables. The receiver operating characteristic curve was utilized to determine the cut-off value of FAR in predicting maternal ICU admission. All statistical analyses were two-tailed, and a p-value of <0.05 was considered statistically significant.

3. Results

The study included a total of 190 patients with PA. Based on the degree of PA, the patients were divided into two groups. There were 54 patients in the total PA group and 136 patients in the partial PA group. Table 1 presents the clinical-demographic characteristic, laboratory results, obstetric outcome and FAR values of the study groups.

No significant differences were found between the groups in terms of age, gravidity, parity, abortion rates, or BMI. Creatinine levels were higher in total PA group (p = 0.003).

During hospitalization, there was a statistically significant difference between the hemoglobin levels of the two groups (p = 0.025). The pH values of umbilical cord arterial blood were statistically significantly lower in the total PA group (p = 0.008). The rate of NICU admission was higher in the total PA group (p < 0.001). Intrauterine fetal loss was more frequent in the total PA group, which was statistically significant (p < 0.001) (Table 1).

Fibrinogen levels statistically significantly differed between the total and partial PA groups (p < 0.001). Gestational age at diagnosis, gestational age at delivery, and birth weight were lower in the total PA group (p < 0.001). There was also a statistically significant difference between the FAR values of the groups (p < 0.001). Concerning maternal ICU admission rates, the total PA group had a higher rate of maternal ICU admission (p < 0.001) (Table 1).

Table 1. Obstetric, clinical, and laboratory analysis results of patients with placental abruption

Variables	Total placental abruption (n = 54)	Partial placental abruption (n = 136)	*p*-value
Age (n)	27.1 (16–42)	28.05 (17–44)	0.595
Gravida (n)	2.39 (1–6)	2.21 (1–6)	0.780
Parity (n)	0.86 (0–3)	0.96 (0–4)	0.895
Miscarriage (n)	0.50 (0–4)	0.27 (0–5)	0.823
BMI (kg/m^2)	31.12 (22.6–45.4)	30.16 (20.9–44.3)	0.316
Gestational week at delivery	29.58 (22.6–36.6)	34.34 (21.0–39.3)	<0.001
Albumin (g/dL)	35.39 (21.0–46.0)	36.36 (26.0–46.0)	0.126
Fibrinogen (mg/dL)	3.42 (0.6–7.6)	4.32 (2.3–8.1)	<0.001
Hemoglobin (g/dL)	9.8 (5.1–13.8)	11.1 (6.0–14.9)	0.025
Platelet count ($x10^9/L$)	244.8 (22.0–687.0)	261.0 (129.0–494.0)	0.051
Aspartate aminotransferase (U/L)	23.5 (11.0–115.5)	20.0 (7.0–62.0)	0.053
Alanine aminotransferase (U/L)	16.0 (6.0–101.0)	14.0 (7.0–123.0)	0.709
Total bilirubin (mg/dL)	0.4 (0.0–2.3)	0.4 (0.2–63.0)	0.654
Direct bilirubin (mg/dL)	0.1 (0.1–1.0)	0.1 (0.0–0.6)	0.695

Creatinine (mg/dL)	0.53 (0.2–21.0)	0.49 (0.3–0.87)	0.003
First-minute Apgar score	0.0 (0.0–6.0)	6.0 (1.0–8.0)	<0.001
Fifth-minute Apgar score	0.0 (0.0–8.0)	8.0 (3.0–9.0)	<0.001
Birth week	29.58 (22.6–36.6)	34.34 (21.0–39.3)	<0.001
Birth weight (g)	1350 (410–3070)	2150 (660–4040)	<0.001
UA pH	6.8 (5.6–7.41)	7.1 (6.5–7.45)	0.008
UA BE (mmol/L)	8.0 (2.5–26.5)	4.8 (0.4–34.5)	0.210
NICU	68.5% (37/54)	44.9% (61/136)	<0.001
Intrauterine fetal loss	33 (61.1%)	19 (0.13%)	<0.001
FAR	0.08 (0.02–0.15)	0.10 (0.02–0.20)	<0.001
Maternal ICU	17 (31.5)	5 (3.7%)	<0.001

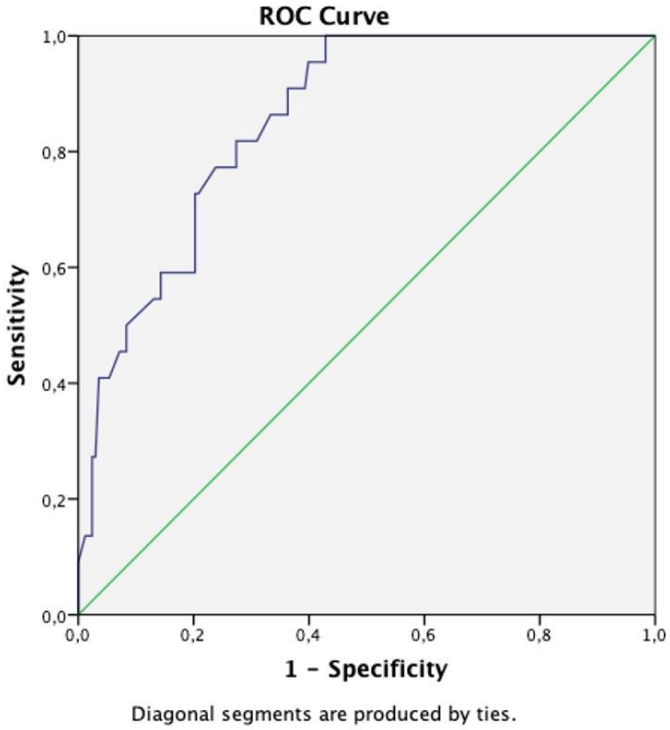
BMI: Body mass index, BE: base excess, FAR: Fibrinogen-Albumin Ratio, NICU: neonatal intensive care unit, UA: umbilical artery

Upon analyzing the distribution of cases by trimester, it was determined that 81.1% (154/190) of the PA cases occurred in the third trimester, while 18.9% (36/190) occurred in the second trimester ($p < 0.001$). In addition, of the total PA cases, 59.3% (32/54) occurred in the third trimester and 40.7% (22/54) in the second trimester ($p < 0.001$) (Table 2).

Table 2. Distribution of patients by the degree of placental abruption and trimester

	Trimester			
Degree of placental abruption	**Second**	**Third**	**Total**	***p*-value**
Total	22	32	54	
	40.7%	59.3%	100.0%	<0.001
Partial	14	122	136	
	10.3%	89.7%	100.0%	
Total	36	154	190	
	18.9%	81.1%	100.0%	

ROC analysis revealed that the optimal cut-off value of FAR 0.07 for predicting maternal ICU admission was 0.07, at which it had 82% sensitivity and 73% specificity (area under the curve = 0.855; $p < 0.001$) (Figure 1).



4. Discussion

In this study, we investigated the role of FAR in predicting adverse fetal and maternal outcomes in patients with PA. We evaluated adverse outcomes by dividing all patients into two groups: total PA and partial PA. The results showed that fetal and maternal outcomes were worse in the total PA group compared to the partial PA group. In other words, as the extent of PA increased, the likelihood of adverse fetal and maternal outcomes also increased. We determined that fibrinogen levels were lower in the total PA group, which resulted in lower FAR values compared to the partial PA group. We found that FAR predicted maternal ICU admission with a sensitivity of 82% and a specificity of 73%.

PA is an obstetric emergency that develops suddenly and is associated with severe fetal and maternal outcomes (15). The extent of placental separation has been directly linked to fetal and maternal outcomes (5, 16). Ultrasonographic examination is commonly used in the diagnosis of PA and in predicting the extent of abruption (17). However, challenges arise when placental location and periplacental hemorrhage appear similar to the placenta in the early stages, making diagnosis and estimation difficult (17, 18).

Various blood parameters have been investigated to predict adverse fetal and maternal outcomes in patients with PA. We consider that markers that change in response to the extent of PA might be more sensitive in predicting adverse outcomes. Su et al. demonstrated that fibrinogen levels decreased with increasing PA severity, while albumin levels were also affected (9). In another study, Wang et al. found that pre-delivery fibrinogen levels successfully predicted adverse maternal and neonatal outcomes in patients with PA (7). Similarly, a recent study demonstrated the predictive ability of pre-delivery fibrinogen levels for the severity of this condition (8). In the current study, as the degree of PA increased, fibrinogen levels decreased, which is consistent with the findings of Koroglu et al. (8). The primary determinant of clinical severity in PA and a direct indicator of adverse fetal and maternal outcomes is the degree of PA and the resulting hemorrhage (19).

Fibrinogen levels and FAR values have been used to predict disease severity and adverse outcomes in various diseases where both fibrinogen and albumin levels are affected (8, 9). FAR has been used and proven to have predictive value for disease severity or adverse outcomes in many types of cancer, cardiovascular diseases, autoimmune diseases, and neurological conditions (11, 12, 20, 21). The use of FAR has also become more widespread in obstetric practice. Ren et al. retrospectively used FAR to predict the severity of preeclampsia and found it to be effective (22). A recent study examined the ability of FAR to predict recurrent pregnancy loss, and authors reported it can predict recurrent

pregnancy loss with 79.5% sensitivity and 88.3% specificity (14). Our study is the first in the literature to examine the use of FAR in predicting adverse fetal and maternal outcomes in patients with PA. Similar to the studies mentioned above, FAR in our study showed high sensitivity and specificity in predicting adverse maternal outcomes and predicted maternal ICU admission with 83% sensitivity.

Another finding of our study was that as the degree of PA increased, FAR values decreased, which was related to the decrease in fibrinogen levels. This finding is consistent with the literature that prenatal fibrinogen level is a predictor of the severity of placental abruption(8). In cases of PA, the impact on the fetus ranges in a wide spectrum from fetal distress to fetal death. Fetal hypoxia, low umbilical artery pH values, low Apgar scores, and increased NICU admission rates are common. Tikkanen et al. demonstrated PA as one of the leading causes of perinatal death. Despite improvements in obstetric care over the years, adverse outcomes in PA remain significant (23). Su et al. presented fetal outcomes in patients with PA based on the degree of abruption and reported that as the degree of abruption increased, the rates of stillbirth and low first- and fifth-minute Apgar scores increased, but no differences were found in birth weight or NICU admission rates based on the degree of abruption (9). The adverse fetal outcomes observed in the current study were similar to those in the studies mentioned above. However, unlike Su et al., we found that NICU admission rates increased with the degree of abruption, while fetal weight was lower in total PA cases.

The limitations of this study include its retrospective and single-center design and the limited number of patients in each group. Another limitation is that placental pathology results of patients with PA were not included in the study. We plan to conduct another study that includes placental pathology results to evaluate diagnostic correlations.

This study showed that patients with total PA had lower FAR values due to decreased fibrinogen levels. We also determined that FAR successfully predicted adverse maternal outcomes with high sensitivity. Future prospective studies involving larger patient cohorts will help confirm these findings and support the routine use of FAR in clinical practice.

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