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The utility of albumin-bilirubin score as a prognostic marker in preeclampsia

Albümin-bilirubin skorunun preeklampside prognostik değerinin araştırılması

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ABSTRACT

Aims: To evaluate the utility of the albumin bilirubin (ALBI) score as a liver function test and prognostic marker in patients with preeclampsia.

Materials and Methods: A total of 374 patients were enrolled in the study (148 preeclampsia without severe features, 112 preeclampsia with severe features, 114 controls). The study compared clinical and demographic features, laboratory findings and ALBI scores between the three groups. Also, receiver operating curve (ROC) analysis was used for the estimation of the predictive value of the ALBI score for the severity of preeclampsia and maternal/neonatal poor prognosis.

Results: The median ALBI score of the severe preeclampsia group was significantly higher than mild preeclampsia and control groups (p<0.001 and p<0.001 respectively). Also mild preeclampsia group had a higher ALBI score than the control group (p=0.039). The ROC curve analysis for the predictive value of ALBI score for maternal poor prognosis in preeclamptic patients showed an area under the curve (AUC) of 0.774 (95% CI 0.671 – 0.776, p<0.001). In the ROC curve analysis performed to investigate the value of ALBI score in neonatal poor prognosis prediction, the AUC was calculated as 0.55 (95% CI 0.48 – 0.62, p=0.164). For the prediction of preeclampsia with severe features in all preeclampsia cases, the AUC was 0.751 (95% CI 0.691-0.812, p<0.001)

Conclusion: The ALBI score could be a useful, cost-effective and practical liver function test and prognostic marker for patients with preeclampsia. However, the predictive performance for neonatal poor prognosis was not sufficient.

Keywords: Preeclampsia, albumin-bilirubin score, ALBI score

ÖZ

Amaç: Preeklampsili hastalarda albümin bilirubin (ALBI) skorunun bir karaciğer fonksiyon testi ve prognostik belirteç olarak kullanılabilirliğini değerlendirmek.

Gereç ve Yöntemler: Çalışmaya toplam 374 hasta dahil edildi (148 preeklampsi, 112 şiddetli bulguların eşlik ettiği preeklampsi, 114 kontrol). Üç grup arasında klinik ve demografik özellikler, laboratuvar bulguları ve ALBI skorları karşılaştırıldı. Ayrıca, preeklampsinin şiddeti ve maternal/neonatal kötü prognoz için ALBI skorunun prediktif değerinin tahmini için ROC eğrisi analizi yapıldı.

Bulgular: Şiddetli bulguların eşlik ettiği preeklampsi grubunun median ALBI skoru preeklampsi ve kontrol gruplarından anlamlı derecede yüksekti (sırasıyla p<0.001 ve p<0.001). Ayrıca, preeklampsi grubu kontrol grubundan daha yüksek ALBI skoruna sahipti (p=0.039). Preeklamptik hastalarda maternal kötü prognoz için ALBI skorunun prediktif değeri için yapılan ROC eğrisi analizinde eğri altında kalan alan (EAA) 0,774 (%95 CI 0,671 - 0,776, p<0,001) olarak bulundu. ALBI skorunun yenidoğan kötü prognoz tahminindeki değerini araştırmak için yapılan ROC eğrisi analizinde EAA 0,55 (%95 CI 0,48 - 0,62, p=0,164) olarak hesaplandı. Tüm preeklampsi olgularında şiddetli bulguların eşlik ettiği preeklampsi öngörüsü için EAA 0,751 (%95 GA 0,691-0,812, p<0,001) idi.

Sonuç: ALBI skoru preeklampsili hastalar için yararlı, uygun maliyetli ve pratik bir karaciğer fonksiyon testi ve prognostik belirteç olabilir. Ancak, neonatal kötü prognoz öngörüsündeki performansı yeterli değildir.

Anahtar Kelimeler: Preeklampsi, Albumin-bilirubin skoru, ALBI skoru

INTRODUCTION

Preeclampsia is described as a new onset of hypertension in the second half of the pregnancy or early postpartum period with the presence of proteinuria or end-organ damage (1). The prevalence of preeclampsia is 2-8% worldwide and it is one of the most important causes of morbidity and mortality in the pregnant population (2).

When decreased platelet (PLT) levels, impaired liver or kidney function, severe hypertension, neurological symptoms, or pulmonary edema are accompanied, the diagnosis becomes preeclampsia with severe features(1).

The ALBI score, which is based on the patient's albumin and total bilirubin levels, was first developed as a simple scoring system for

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the evaluation of disease severity in patients with hepatocellular carcinoma (HCC)(3). It defines worsening liver impairment across three grades (1 to 3). Also, its prognostic value for HCC patients treated by different methods (surgical resection, ablative treatment, transarterial or surgical therapies) has been shown by many studies (4). Afterward, its utility was evaluated in non-malignant liver diseases such as primary biliary cholangitis, chronic viral hepatitis B and C and autoimmune hepatitis and data has indicated that ALBI score/grade could serve a role as a prognostic marker in these conditions (5–11).

Furthermore, the prognostic value of ALBI score in non-liver diseases such as acute or chronic heart failure and acute pancreatitis was investigated and a higher ALBI score/grade was found to be associated with poor prognosis in these non-hepatic conditions (12–15).

Since impaired liver function is an important indicator of preeclampsia with severe features, we aimed to evaluate the ALBI score in patients with preeclampsia and its relation with disease severity, maternal and neonatal poor prognosis.

MATERIALS AND METHODS

The present study is a retrospective case-control study that includes data from pregnant women who followed up for preeclampsia and delivered in our hospital between May 2019 and December 2023, as well as healthy pregnant women who were followed up and delivered in our hospital on similar dates. The data of patients demographics and laboratory results were obtained from the delivery room, inpatient ward, operating room registry books and the hospital's electronic registration system. The study received approval from the local ethics committee with approval number E2-24-6195.

All consecutive preeclampsia cases who met the inclusion criteria were included and compared to a control group consisting of low-risk pregnant women at similar gestational ages. Multiple gestations, patients with additional chronic inflammatory conditions, malignancy, renal disease, liver disease, cardiac disease, or diabetes were excluded.

Preeclampsia cases were grouped based on the ACOG guidelines. Patients with a systolic blood pressure of ≥140 mmHg and a diastolic blood pressure of ≥90 mmHg, recorded at least twice with a minimum interval at least 4 hours, accompanied by at least 2+ proteinuria measured by dipstick or 300 mg proteinuria within 24 hours, but without accompanying prodromal symptoms, pulmonary edema, seizures, impaired liver or kidney functions, and without thrombocytopenia, are classified as the preeclampsia group without severe features (1).

Patients with a systolic blood pressure of 160 mmHg or higher and/or a diastolic blood pressure of 110 mmHg or higher on two occasions at least 4 hours apart, accompanied by severe persistent right upper quadrant or epigastric pain, severe analgesic-resistant headache, visual symptoms, pulmonary edema, impaired liver or kidney function, or thrombocytopenia are classified as preeclampsia with severe features (1).

Maternal poor prognosis is described as at least one of the following: Development of hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome, eclampsia, admission to intensive care unit, or death. Neonatal poor prognosis is described as at least one of the following: first or fifth minute APGAR score < 5, admission to neonatal intensive care unit, birthweight < 2500 grams, delivery before 34 weeks, fetal or neonatal death.

The study only included data from patients who provided follow-up blood test results between weeks 30 and 34. Patients who did not provide blood test results during this time frame were excluded.

Gestational ages of the patients were determined using first-trimester crown-rump length measurements, typically taken between the 11th and 14th gestational weeks. The study compared demographic and clinical features such as maternal age, gravidity, parity, birth weights, gestational age at birth, APGAR scores, laboratory findings [hemoglobin level, white blood cell count (WBC), neutrophil count, lymphocyte count, monocyte count, platelet count (PLT), urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST)], total bilirubin, albumin, ALBI scores between the three groups. ALBI scores were calculated using the formula (log10 bilirubinx0,66)+(albumin x -0,085) (3).

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS, version 22, IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.). The Shapiro-Wilk test was employed to assess normality. As the data did not follow a normal distribution, non-parametric tests were utilized, and median values with interquartile ranges were reported for descriptive statistics. To compare data between groups, the Kruskal-Wallis and Mann Whitney U tests was performed. Receiver operating curve (ROC) analysis was employed to estimate the predictive value of the ALBI score for the severity of preeclampsia and maternal/neonatal poor prognosis. A p-value less than 0.05 was considered statistically significant.

RESULTS

The study included a total of 374 patients, with 148 patients categorized into the preeclampsia without severe features group, 112 patients in the preeclampsia with severe features group, and 114 cases enrolled in the control group. Among the preeclampsia group (comprising both cases with and without severe features), sixteen patients met at least one of the maternal poor prognosis criteria. Additionally, 132 neonates born to preeclamptic patients exhibited at least one of the neonatal poor prognostic factors.

Among the three groups, there was no statistically significant difference in gravidity, parity, hemoglobin level, lymphocyte count, monocyte count, platelet count and 5st minute APGAR scores.

The median age of the control group was significantly lower than both preeclampsia groups (p=0.023 and p=0.017 respectively). AST levels were significantly lower in the control group than in the preeclampsia and preeclampsia with severe features groups (p=0.002 and p<0.001 respectively), also the AST level of the preeclampsia with severe features group was significantly higher than the preeclampsia group (p<0.001). The ALT level of the control group was significantly lower than both preeclampsia groups (p=0.006 and p<0.001 respectively). The severe preeclampsia group had higher ALT levels than the preeclampsia group (p=0.037). The total bilirubin level was higher in the severe preeclampsia group than in the mild preeclampsia and control groups (p=0.016 and p=0.002 respectively). The albumin level of the control group was significantly higher than preeclampsia groups (p<0.001 and p<0.001 respectively), also the albumin level of the preeclampsia with severe features group was significantly lower than preeclampsia group (p<0.001).

The median ALBI score of the preeclampsia with severe features group was significantly higher than preeclampsia and control groups (p<0.001 and p<0.001 respectively). Also preeclampsia group had a higher ALBI score than the control group (p=0.039).

Gestational age at birth and birthweight of the preeclampsia with severe features group were significantly lower than preeclampsia and control groups (p=0.004, p=0.003; p<0.001, p<0.001 respectively). Also preeclampsia group had lower gestational age at birth and birthweight than control group (p<0.001 and p<0.001 respectively). 1st minute APGAR score of the control group was significantly higher than both preeclampsia groups (p<0.001 and p<0.001 respectively).

The comparison of demographic data, laboratory results, and neonatal outcomes between preeclampsia, preeclampsia with severe features and control groups are shown in Table 1.

The ROC curve analysis conducted to assess the predictive value of the ALBI score for maternal poor prognosis in preeclamptic patients yielded an area under the curve (AUC) of 0.774 (95% CI 0.671 – 0.776, p<0.001). Similarly, in the ROC curve analysis aimed at evaluating the predictive value of the ALBI score for neonatal poor prognosis, the AUC was determined to be 0.55 (95% CI 0.48 – 0.62, p=0.164). Subsequently, the optimal cutoff value for maximal sensitivity and specificity was calculated as -2.4, resulting in 81% sensitivity and 66% specificity for maternal poor prognosis, while achieving 50% sensitivity and 50% specificity for neonatal poor prognosis.

Furthermore, in predicting preeclampsia with severe features within all preeclampsia cases, the AUC was calculated as 0.751 (95% CI 0.691-0.812, p<0.001), with an observed sensitivity of 71% and specificity of 67% at a cutoff value of -2.5.

The results of ROC curve analyses are shown in Table 2, Figure 1-3.

DISCUSSION

Defective trophoblast invasion and placental ischemia are the mainstream of the pathophysiology of preeclampsia(16). As a result of placental ischemia, circulating levels of various factors and proinflammatory cytokines increase (16). These factors lead to maternal vascular remodeling, endothelial dysfunction and exaggerated inflammation; and these changes cause vascular narrowing, end-organ ischemia, platelet dysfunction and multiorgan damage, especially in the liver, kidneys and brain (2,17–19).

Periportal hemorrhage, ischemic changes and fibrinogen deposition were histologically demonstrated in liver examinations of patients with preeclampsia (20). A prospective study showed increased hepatic fibrosis in preeclamptic patients by using fibroscan performed in the postpartum first week (21). In a study that reports the histopathological findings of three autopsy cases of maternal deaths due to HELLP syndrome, periportal hepatocellular necrosis was the hallmark finding in the livers of the patients (22). As a result of hepatic injury, an increase in liver function tests such as AST and ALT is an important laboratory finding in patients with severe preeclampsia and its more life-threatening complication, HELLP syndrome.

In the current study, both the preeclampsia and preeclampsia with severe features groups exhibited elevated AST and ALT levels in comparison to the control group. In addition, within the preeclampsia cohorts, the severe features group demonstrated even higher AST levels than the mild group. Given that elevated

Table 1. Comparison of demographic data, laboratory results and neonatal outcomes between mild preeclampsia, severe preeclampsia and control groups

	Preeclampsia without severe features (n=148) (median, IQR)	Preeclampsia with severe features (n=112) (median, IQR)	Control group (n=114) (median, IQR)	p value
Age (years)	32 (11)	32 (13)	30 (7)	[a] 0.717 [b] **0.023** [c] **0.017**
Gravidity	2 (2)	2 (2)	2 (1)	0.442
Parity	0 (2)	1 (2)	1 (1)	0.146
Hemoglobin (g/dL)	11.9 (1.9)	12.2 (2.3)	11.8 (2.1)	0.056
WBC (x10^9/L)	10.49 (3.52)	11.35 (4.3)	9.87 (4.09)	[a] **0.003** [b] 0.374 [c] **0.008**
Neutrophil count (x10^9/L)	7,54 (3,42)	8.40 (4.4)	7.19 (3.55)	[a] 0.063 [b] 0.455 [c] 0.046
Lymphocyte count (x10^9/L)	1.99 (0.89)	1.92 (1.02)	1.75 (0.62)	0.076
Monocyte count (x10^9/L)	0.50 (0.24)	0.50 (0.24)	0.47 (0.20)	0.519
Platelet count (x10^9/L)	247 (102.25)	230 (111.5)	248 (104.3)	0.317
Urea (mg/dL)	20 (9)	24 (11)	17 (6)	[a] **0.003** [b] **<0.001** [c] **<0.001**
Creatinine (mg/dL)	0.55 (0.16)	0,62 (0.21)	0.49 (0.15)	[a] **0.007** [b] **0.006** [c] **<0.001**
AST (U/L)	21 (11)	29 (37)	17 (9)	[a] **<0.001** [b] **0.002** [c] **<0.001**
ALT (U/L)	14 (8)	16 (33)	12 (7)	[a] **0.037** [b] **0.006** [c] **<0.001**
Total bilirubin (mg/dL)	0.3 (0.2)	0.4 (0.3)	0.3 (0.2)	[a] **0.016** [b] 0.057 [c] **0.002**
Albumin (g/L)	37 (4)	33 (6)	38 (3)	[a] **<0.001** [b] **<0.001** [c] **<0.001**
Gestational age at birth (weeks)	37 (4)	34 (6)	39 (1)	[a] **0.004** [b] **<0.001** [c] **<0.001**
Birth weigth (grams)	2610 (975)	2065 (1546)	3220 (688)	[a] **0.003** [b] **<0.001** [c] **<0.001**
1st minute APGAR score	7 (1)	6 (1)	8 (1)	[a] 0.398 [b] **<0.001** [c] **<0.001**
5th minute APGAR score	9 (1)	8 (1)	9 (0)	0.515
ALBI score	-2.55 (0.32)	-2.20 (0.51)	-2.65 (0.25)	[a] **<0.001** [b] **0.039** [c] **<0.001**

[a]: Comparison between preeclampsia without severe features and preeclampsia with severe features
[b]: Comparison between preeclampsia without severe features and control groups
[c]: Comparison between preeclampsia with severe features and control groups
p<0.05 accepted as statistically significant. WBC: white blood cell count, AST: aspartate aminotransferase, ALT: alanine aminotransfesase, BUN: blood urea nitrogen

liver enzymes serve as a diagnostic criterion for preeclampsia, our findings are consistent with the literature (1).

In preeclamptic patients, the timing of the delivery is an important issue. International guidelines recommend delivery at 37 $^{0/7}$ weeks in patients with preeclampsia without severe features and delivery between 34 $^{0/7}$ and 36 $^{6/7}$ weeks in patients with severe features. When maternal hemodynamic stability could not be achieved, earlier delivery should be considered (1,23). In our clinical practice, we plan our patients' deliveries in accordance with the guidelines.

Table 2. Reciever operating curve analysis results of predictive value of ALBI score for disease severity, maternal and neonatal poor prognosis*

Outcome	Cut-off	AUC	p	95%CI	Sensitivity	Specificity
Preeclampsia with severe features	-2.5	0.751	<0.001	0.691-0.812	71%	67%
Maternal poor prognosis	-2.4	0.774	<0.001	0.671-0.876	87%	62%
Neonatal poor prognosis	-2.4	0.550	0.164	0.480-0.620	50%	50%

p<0.05 accepted as statistically significant.
AUC: area under the curve, CI: confidence interval.
* Maternal poor prognosis described as at least one of the followings: Developement of HELLP syndrome, eclampsia or admission to intensive care unit. Neonatal poor prognosis described as at least one of the followings: first or fifth minute APGAR score < 5, admission to neonatal intensive care unit, birthweight < 2500 grams, delivery before 34 weeks, fetal or neonatal death.

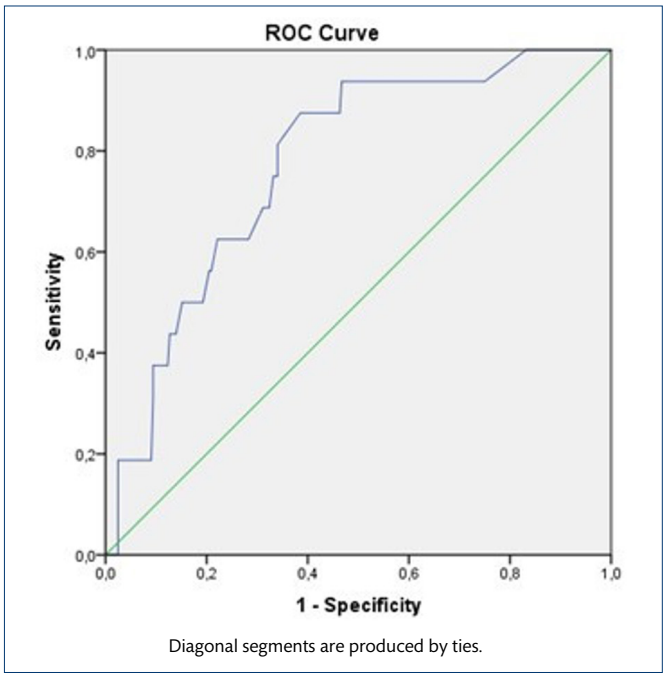

Figure 1. The ROC curve analysis for predictive performance of the ALBI score for maternal poor prognosis.

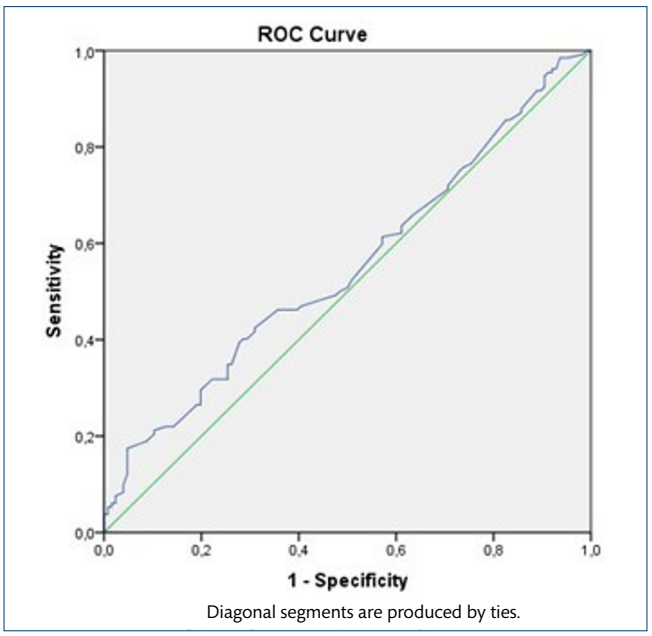

Figure 2. The ROC curve analysis for predictive performance of the ALBI score for neonatal poor prognosis.

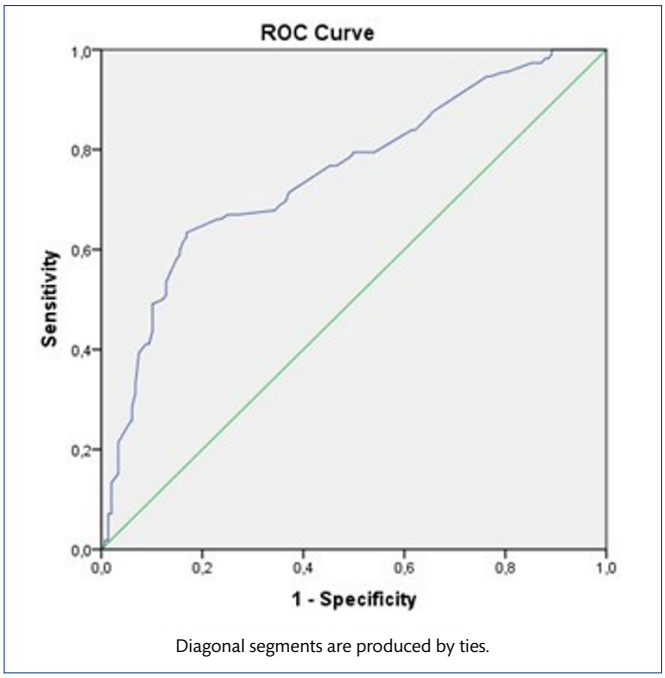

Figure 3. The ROC curve analysis for predictive performance of the ALBI score for severe preeclampsia.

Thus, our study showed lower gestational age at birth in both preeclampsia groups. As a result, we observed lower 1st minute APGAR scores in these groups.

Albumin synthesis is an important function of the liver. Thus, hypoalbuminemia reflects progressive hepatic damage in patients who diagnosed with liver disease (24). In our study, the group with the lowest albumin levels was the preeclampsia with severe features group, followed by the preeclampsia group and the highest albumin levels were observed in the control group and the difference between the three groups was statistically significant. These findings could indicate that hepatic damage may be present in all preeclamptic patients, and the severity of the disease may affect the synthesis function of the liver.

ALBI score was first described by Johnson et al. as a tool for assessment of disease severity in patients with HCC(3). Then they tested the model in several geographic regions and variable clinical

scenarios (patients undergoing resection, sorafenib treatment for advanced HCC and chronic liver disease but without HCC), and reported that the ALBI score provides a simple, objective, and discriminatory method of evaluating liver function in HCC. Its advantage to the classic Child-Pugh (CP) score is subjective findings such as encephalopathy and ascites are not required.

In a study involving 1242 patients, the predictive efficacy of the ALBI score for postoperative liver failure and long-term survival was assessed. The authors concluded that the ALBI score demonstrated superior performance compared to the CP grade in predicting these outcomes (25). Another retrospective study examined the association between the ALBI score and patient survival in live donor liver transplant recipients. The findings indicated that the ALBI score exhibited better performance than the Model for End-Stage Liver Disease (MELD) score for patient survival (26).

A prospective study that followed up 398 chronic hepatitis B-related liver cirrhosis over a median follow-up period of 33.9 months demonstrated that the ALBI score effectively forecasts both severity and long-term prognosis, surpassing the predictive accuracy the MELD score (6). Moreover, its prognostic reliability has been corroborated in patients with chronic hepatitis C infection and primary biliary chirrosis (8,9).

After these studies, the usefulness of the ALBI score in non-liver diseases became a field of investigation. In a multicenter, prospective study which enrolled 1190 patients with acute heart failure, higher ALBI scores was found to be associated with fluid overload and increased mortality (13). Similarly, another study reported a relationship between higher ALBI scores and inpatient mortality of patients with acute heart failure (14). In heart failure patients who required intensive care unit admission, short and long-term mortality rates were higher when the patients had higher ALBI scores (12). As well as, in a retrospective study that included the data of 284 patients who were admitted to the intensive care unit for severe acute pancreatitis, the ALBI score showed significant predictive performance for in hospital mortality and the authors reported that the performance of the ALBI score was superior to previously used scoring systems such as SOFA, SAPS-II, APACHE scores (15). Furthermore, higher ALBI scores were observed in patients with intrahepatic cholestasis of pregnancy in first trimester and at the time of the diagnosis, in a retrospective study (27).

In the present study, both the preeclampsia and preeclampsia with severe features groups had higher ALBI scores than the control group. Additionally, we observed a higher ALBI score in the preeclampsia with severe features group than in the preeclampsia group. As mentioned earlier, preeclampsia is associated with endothelial dysfunction and altered inflammation which results in end organ damage such as the liver, brain and kidneys. The increase in the ALBI score could be an indicator of the hepatic damage in patients with preeclampsia. Also the ROC curve analysis showed that the ALBI score has significant performance for prediction of the disease severity and maternal poor prognosis in patients with preeclampsia. Although, the predictive performance for neonatal poor prognosis was not sufficient.

This study's primary strength lies in its introduction of the ALBI score as a novel prognostic tool in preeclampsia, supported by a well-characterized patient cohort. However, the retrospective design may limit generalizability, and further prospective studies are needed to validate these findings. Despite this, the results provide a foundation for integrating liver function markers into clinical practice for improved maternal care.

CONCLUSION

The ALBI score represents a promising, cost-effective tool for evaluating liver function and predicting maternal outcomes in preeclampsia. Its simplicity and practicality make it a valuable addition to clinical practice, particularly in resource-constrained settings. However, the score's limited predictive value for neonatal outcomes highlights the need for further research to refine its applicability and explore potential combinations with other biomarkers. Future prospective and multicenter studies are essential to validate these findings and establish the ALBI score as a standard prognostic tool in preeclampsia management, thereby enhancing maternal and fetal healthcare outcomes globally.

Author Contributions

O.O.Ö.: Conception and design of the study; analysis and interpretation of the data and writing-review. D.S.: Conception and design of the study; analysis and interpretation of the data and writing-review.

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None

Conflict of Interest

The authors declare no conflict of interest.

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