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Determination of the relationship between severe preeclampsia and HALP scores

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Abstract

Objective: We conducted our study to investigate the relationships between severity of preeclampsia (PE) and hemoglobin, albumin, lymphocyte, and platelet (HALP) score.

Methods: Our study comprised 115 pregnant women diagnosed with preeclampsia (PE) and 69 with severe PE. Demographic data, complete blood count results, and albumin values comprised the data that was examined.

Results: We found that the HALP scores were significantly greater in severe PE patients than in non-severe PE patients ($p < 0.05$). Receiver operating characteristic (ROC) analysis revealed that this marker had moderate discriminative power (AUC 0.620, 95% CI: 0.0545-0.692). Logistic regression revealed signiŞcantly greater HALP scores (OR 1.141, 95% CI: 1.020–1.276; $p = 0.021$) in the severe PE patients than in PE patient.

Conclusion: The HALP is elevated in pregnant women with severe PE, supporting the pathophysiology of this condition. The HALP score may be useful in predicting the severity of preeclampsia.

Keywords: HALP score, preeclampsia, severe preeclampsia

Introduction

Preeclampsia is a condition defined by significant end-organ dysfunction in a previously normotensive pregnant woman, usually after 20 weeks' gestation or after delivery, with new-onset hypertension and proteinuria or new-onset hypertension with or without proteinuria.[1] Approximately 4.6% of pregnancies worldwide are complicated by preeclampsia (PE).[2,3] Patients with preeclampsia are at an increased risk for life-threatening obstetric or medical complications. Worldwide, 10 to 15 percent of direct maternal deaths are associated with preeclampsia/eclampsia.[4] The pathophysiology of PE is not clearly known. Many theories predict that abnormal placental invasion and trophoblast invasion initiate the disease.[5,6] As a result of abnormal placentation and trophoblast invasion, endothelial dysfunction occurs and an increased systemic inflammatory response occurs.[7] In PE, heightened platelet destruction may occur via immunological processes, aberrant platelet activation, and augmented platelet consumption.[8]

The hemoglobin, albumin, lymphocyte, and platelet (HALP) score, a novel metric established by Chen et al.[9] that integrates the principles of inflammation and nutritional deficiency, has been proposed to offer insights into the prognostic prediction of diverse malignancies, ischemic stroke, and acute heart failure.[9-11] The prognostic significance of HALP score has only been investigated in obstetrics in preterm labor and hyperemesis gravidarum.

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[12,13] HALP may play a diagnostic role in severe PE with increased inflammation, oxidative stress, and endothelial dysfunction. In our study, we also examined the prognostic significance of HALP score in patients with non-severe and severe PE.

Methods

This retrospective study was conducted at a regional hospital from August 2018 to August 2024. In our study, 115 patients were diagnosed with PE and 69 patients with severe PE were selected. The American College of Obstetricians and Gynecologists criteria published in 2020 were used to determine the diagnosis of preeclampsia. For the diagnosis of preeclampsia; systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in two measurements 4 hours apart after the 20th week of pregnancy in a woman without previous hypertension and accompanied by various multisystem disorders with or without new-onset proteinuria (platelet count less than 100,000×109 /L, liver enzymes elevated to twice the upper limit of normal concentration, unexplained severe persistent right upper quadrant or epigastric pain, renal failure (serum creatinine ≥1.1 milligrams per deciliter (mg/dL) or doubling of serum creatinine concentration in the absence of renal disease), pulmonary edema, or new-onset headache unresponsive to acetaminophen and unexplained) were used.[1] Severe features included severe hypertension (systolic blood pressure of 160 mm Hg and/or diastolic blood pressure of 110 mm Hg), thrombocytopenia (platelet count of <100x109/L), impaired liver function as indicated by elevated liver enzymes to more than twice the upper limit of normal or severe persistent right upper quadrant or epigastric pain unresponsive to medications, renal insufficiency defined as serum creatinine concentration of >1.1 mg/dL pulmonary edema, headache unrelieved by medication, or visual disturbances. Patients who had chronic hypertension, gestational diabetes, coronary artery disease, chronic renal failure, autoimmune disease or multiple pregnancy were excluded.

Demographic data, including maternal age, body mass index (BMI), gravida, parity, and abortion history, were documented and as prenatal outcomes, gestational age at delivery of the patients and birth weight, APGAR score at 1. minutes and 5. minutes and neonatal intensive care unit (NIUC) admission were recorded as fetal outcomes. Data such as the white blood cell (WBC) count, neutrophil count (NEU), lymphocyte count (LYM), hemoglobin (Hb), platelet count (PLT), and albumin count (ALB) of patients were retrospectively obtained from hospital records. The timing of routine blood tests was recorded as the time when the patient initially presented to the gynecology and obstetrics outpatient clinic or emergency room with complaints of PE during the diagnostic phase prior to receiving therapies for PE. HALP score was calculated using Hb, ALB, LYM and PLT values (HALP = Hb × ALB × LYM/PLT).

The study was approved by Adana City Training and Research Hospital Scientific Research Ethics Committee (Date: 06.02.2025, Decision No: 349).

We employed the Shapiro-Wilk test to confirm the normality of continuous data distribution. The mean ± standard deviation was employed for normally distributed continuous variables, whereas the median [25%-75%] was utilized for other variables. Numbers and percentages were used to collect categorical data. The Chi-square or Fisher's exact tests were used to compare proportions between groups. If the distribution wasn't normal, the Mann–Whitney U test was used to compare two separate groups. If the distribution was normal, the independent samples t test was used. The receiver operating characteristic (ROC) curve analysis was employed to determine the optimal cut-off values for the HALP to diagnose severe PE with maximal sensitivity and specificity. We considered $p < 0.05$ to indicate statistical significance. Logistic regression analysis was used to investigate the associations between severe PE and clinical factors. The possible risk factors for severe PE identified with univariate analysis ($p < 0.10$) were included in the multiple logistic regression analysis. Odds ratios (ORs) and their 95% confidence intervals were calculated. We considered $p < 0.05$ to indicate statistical significance.

Results

The study comprised 115 individuals diagnosed with PE and 69 with severe PE. Table 1 displays the patients' demographic characteristics. hematological values and HALP scores. No significant differences were observed in age, gravida, parity, abortion, Hb, WBC count, LYM count, NEU count, or ALB values across the groups in the statistical examination. The mean PLT counts of the PE and severe PE groups were 203.91 ± 72.47 and 1.85 179.81 ± 77.98,respectively. The mean HALP scores of the PE and severe PE groups were 3.70 ± 2.37 and 4.88 ± 2.53, respectively. Statistically significant differences were found between the groups with respect to PLT counts and HALP scores.

Fetal outcomes measurements of the study participants were shown in Tables 2. While there were statistically significant differences in terms of fetal outcomes such as birth weight, and NIUC admission requirement,

there was no difference between the groups in terms of Apgar scores.

Table 1. Demographic and laboratory measurements of the study participants

Variables	PE without severe features (n = 115)	PE with severe features (n = 69)	P value
Age (years)	29.64 ± 6.76	30.96 ± 6.77	0.204
BMI (kg/m²)	33.74 ± 5.95	31.51 ± 4.29	0.007
Gravida	2 (1–4)	3 (1–4)	0.342
Parity	1 (0–2)	1 (0–4)	0.205
Abortion	1 (0–1)	0 (0–0)	0.324
Gestational age (weeks)	36.20 ± 3.48	34.88 ± 3.59	0.015
Hb (g/dL)	11.59 ± 1.42	12.02 ± 1.56	0.066
WBC count	10.96 ± 3.12	11.58 ± 3.10	0.193
Platelet count (10^3/µl)	203.91 ± 72.47	179.81 ± 77.98	0.035
Neutrophil count (10^3/µl)	8.01 ± 2.52	8.48 ± 2.89	0.245
Lymphocyte count (10^3/µl)	2.12 ± 0.85	2.22 ± 0.92	0.440
Albumin (g/L)	26.89 ± 2.92	26.31 ± 3.79	0.260
HALP score	3.70 ± 2.37	4.88 ± 2.53	0.008

Abbreviations: PE: preeclampsia; Hb: hemoglobin; g/dL: grams per deciliter; WBC: white blood cell; g/l; grams per liter; HALP: hemoglobin × albumin × lymphocytes/platelets.
Notes:
Continuous data are summarized with the mean ± standard deviation and median (25%–75%).
Independent samples T test was used to compare continuous variables with normal distribution.
Mann–Whitney U test was used for nonnormal variables.

P < 0.05 was consider to indicate statistical significance.

Table 2. Fetal outcomes measurements of the study participants

Variables	PE without severe features (n = 115)	PE with severe features (n = 69)	P value
APGAR score at 1 minutes	8 (8–9)	8 (8–8)	0.185
APGAR score at 5 minutes	10 (9–10)	10 (9–10)	0.049
Birth weight (g)	2619.87 ± 825.48	2241.88 ± 863.76	0.004
NIUC admission			0.035
(+)	21[a] (18.3%)	22[b] (31.9%)	
(-)	94[a] (81.7%)	47[b] (68.1%)	

Abbreviations: PE: preeclampsia; NIUC: neonatal intensive care unit.
Notes: Categorical variables were collected as numbers and percentages. The Chi-square or Fisher's exact tests were used to compare proportions between groups. Different superscripts indicate significant mean differences.
Continuous data are summarized with the mean ± standard deviation and median (25%–75%).
Independent samples T test was used to compare continuous variables with normal distribution.
Mann-Whitney U test was used for nonnormal variables.

P < 0.05 was consider to indicate statistical significance.

ROC analysis was performed using the HALP scores to separate the PE and severe PE groups. The discriminatory power of the HALP between the PE and severe PE groups was intermediate and statistically significant. The AUC value for the HALP was 0.620, 95% CI: 0.0545-0.692 (p<0.007). The HALP cut-off values was 3.2699, with 66.2% sensitivity and 56.8% specificity (Table 3) (Figure 1).

Table 3. Analysis of cut-off points of the HALP value to diagnose severe PE

Variables	Cut off points	AUC	P value	Sensitivity (%)	Specificity (%)
HALP	3.2699	0.620	0.006	66.2	56.8

Abbreviations: AUC: area under the curve; PE: preeclampsia; HALP: hemoglobin × albumin × lymphocytes/platelets.
Notes:
The maximum sensitivity and specificity of severe PE were established using receiver operating characteristic (ROC) curve analysis.

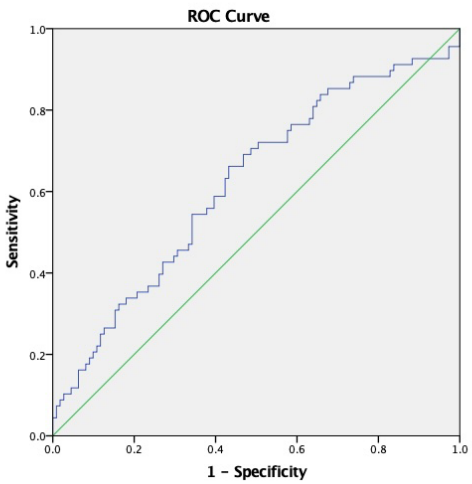

Fig 1. ROC Curve: The AUC value for the HALP was 0.620, 95% CI: 0.0545-0.692 (p<0.007)

In this analysis, logistic regression revealed signiŞcantly greater HALPs (OR 1.141, 95% CI: 1.020–1.276; p = 0.021) and BMI (OR 1.079, 95% CI: 1.013–1.1152; p = 0.018) in the severe PE patients than in PE patients. (Table 4).

Table 4. Multiple logistic regression analysis of factors related to severe PE.

Variable	OR (95% CI)	P value
HALP	1.141 (1.020–1.276)	0.021
BMI	1.079 (1.013–1.152)	0.018

Abbreviations: PE: preeclampsia; BMI: body mass index; HALP: hemoglobin × albumin × lymphocytes/platelets; OR: Odds ratio.
Notes: [a] Variable(s) entered in step 1: HALP, BMI, gestational age. (These factors had a p value lower than 0.10 in the comparison of the PE and severe PE groups in Table 1).
[b] We excluded the gestational age variable because p value was higher than 0.01. This affected the results and confidence intervals.
[c] We used the backwards LR method for the selection of significant factors and the selection of variables was completed in Step 3: BMI.
[d] The goodness of the fit of model was good according to the Hosmer–Lemeshow Test (p = 0.298).

Discussion

PE is a progressive multisystemic disease that is defined by a multifaceted pathophysiological pathway, wherein inflammation is considered a significant factor [14]. The only definitive treatment for PE is delivery. Therefore, it is important to correctly determine the severity of the disease and make a quick decision. In our study, we planned to investigate the relationship between HALP score and PE severity. We found that HALP score was significantly higher in the severe PE group than in the PE group, and HALP score was 1.141 times more predictive of severe PE patients than the remaining patients (OR: 1.141, 95% CI: 1.020–1.276; p = 0.021).

Preeclampsia is considered an inflammatory and anti-angiogenic disorder.[1] Women with preeclampsia exhibit an augmented inflammatory and cellular immune response.[15] Platelet activation is crucial in the etiology of PE and is characterized by a reduced platelet count in PE.[16] Prior research has indicated that as the severity of PE escalates, there is a more pronounced reduction in platelet count.[17] Platelet count may be significantly decreased in preeclamptic women before the development of preeclampsia and during the second trimester of pregnancy, regardless of severity and the presence or absence of concomitant problems. It has been shown that platelet count may serve as a possible biomarker to identify and predict preeclampsia.[18] HALP score, a new biomarker that combines platelet count with other serum values, represents easily obtained and conclusive inflammatory indicators and can also be used in preeclampsia.

When we look at the literature, there are two publications investigating the relationship between HALP score and preeclampsia. In the study conducted by Dal et al., the HALP score was found to be lower in preeclampsia patients compared to the control group and it was concluded that it was an insufficient diagnostic marker in the diagnosis of PE.[19] Another study compared patients with severe and non-severe PE with controls. Higher HALP scores were found in patients with severe and non-severe PE compared with controls and found a significant correlation between HALP score and preeclampsia with severe features. It has been suggested that HALP score may be useful in predicting the severity of preeclampsia.[20] The HALP scores were markedly higher in the severe PE group and correlated with the severity of PE. The ROC curve indicated that HALP scores possess modest discriminative ability in distinguishing severe PE patients from non-severe PE patients. Despite the fact that the sensitivity and specificity values of this marker are insufficient to function as definitive diagnostic tools, they offer valuable insights into the severity status of patients and may be used as adjunctive markers in the clinical evaluation of severe PE.

HALP score has been studied in the literature such as hyperemesis gravidarum, preterm birth and fetal growth restriction in obstetrics. In a study conducted on patients diagnosed with hyperemesis gravidarum using the HALP score, the HALP score was found to be statistically significantly lower in patients diagnosed with hyperemesis gravidarum compared to the control group.[21] Hrubaru et al., found that the highest predictive value for preterm birth was observed to be represented by the HALP score.[22] Another study has shown that the HALP score is a valuable prognostic tool in estimating the risk of fetal growth restriction in the first trimester.[23]

Our study has several limitations. The study's retrospective design and reliance on medical records led to a limited patient cohort and insufficient data, and it was conducted at a single center. Secondly, we omitted patients with comorbidities or drug use that can influence inflammation; hence, we may not have accounted for all variables that could impact Hb, ALB, LYM, and PLT levels. Ultimately, we determined the HALP score by utilizing the blood parameters collected from the patients at the time of their initial diagnosis. We did not investigate the potential fluctuations in the HALP score of these parameters prior to and following the onset of the disease.

Conclusion

In conclusion, our study demonstrated that the HALP is elevated in pregnant women with severe PE, supporting the pathophysiology of this condition. Further studies must be undertaken to clarify the mechanisms behind the development of PE and to examine the benefits of utilizing these markers in its management.

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