

ORIGINAL RESEARCH ARTICLE

Diagnostic and clinical value of the HALP (hemoglobin, albumin, lymphocyte, and platelet) score in preeclampsia

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Abstract

Preeclampsia (PE) is a leading cause of maternal morbidity, linked to systemic inflammation and nutritional imbalance. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score, an immune-nutritional index, was assessed in PE. A retrospective case-control study included non-pregnant healthy women (NonP), healthy pregnant women (HP), and women with PE. HALP was calculated and compared across groups. Correlations, principal component analysis (PCA), regression, and ROC analysis were performed. HALP was significantly lower in PE than HP and NonP ($p < 0.001$), with the steepest decline in women >36 years. HALP correlated positively with lymphocytes, albumin, and hemoglobin, but negatively with neutrophils and WBCs. PCA highlighted albumin and lymphocytes, while regression identified WBCs as an independent predictor. ROC analysis showed good discrimination for NonP vs PE (AUC = 0.764). HALP is reduced in PE and may serve as a simple, accessible biomarker for risk stratification. (*Afr J Reprod Health* 2026; 30 [20]:59-70).

Keywords: Preeclampsia, HALP score, hemoglobin, albumin, lymphocytes, biom

Résumé

La prééclampsie (PE) est une cause majeure de morbidité maternelle, associée à une inflammation systémique et à un déséquilibre nutritionnel. Le score HALP (hémoglobine, albumine, lymphocytes et plaquettes) — un indice immuno-nutritionnel — a été évalué dans le contexte de la PE. Une étude cas-témoins rétrospective a inclus des femmes non enceintes en bonne santé (groupe NonP), des femmes enceintes en bonne santé (groupe HP) et des femmes atteintes de PE. Le score HALP a été calculé et comparé entre les groupes. Des analyses de corrélation, une analyse en composantes principales (ACP), des analyses de régression et une analyse par courbe ROC ont été réalisées. Le score HALP était significativement plus faible chez les femmes atteintes de PE que chez celles des groupes HP et NonP ($p < 0,001$), la baisse la plus marquée étant observée chez les femmes de plus de 36 ans. Le score HALP présentait une corrélation positive avec les lymphocytes, l'albumine et l'hémoglobine, mais une corrélation négative avec les neutrophiles et les globules blancs. L'ACP a mis en évidence le rôle de l'albumine et des lymphocytes, tandis que l'analyse de régression a identifié les globules blancs comme un facteur prédictif indépendant. L'analyse par courbe ROC a montré une bonne capacité de discrimination entre les groupes NonP et PE (AUC = 0,764). Le score HALP est diminué en cas de PE et pourrait constituer un biomarqueur simple et accessible pour la stratification du risque. (*Afr J Reprod Health* 2026; 30 [20]: 59-70).

Mots-clés: Prééclampsie, score HALP, hémoglobine, albumine, lymphocytes, biom

Introduction

Preeclampsia (PE) is a multisystem hypertensive disorder of pregnancy, typically defined by the onset of hypertension and proteinuria after 20 weeks of gestation. It remains one of the leading causes of maternal and perinatal morbidity and mortality worldwide, accounting for an estimated 10–15% of maternal deaths in low- and middle-income countries¹⁻². Despite decades of research, the exact pathophysiology of preeclampsia is incompletely understood, but it is

widely accepted that abnormal placentation, maternal endothelial dysfunction, systemic inflammation, and oxidative stress play central roles in disease development³⁻⁵. Early identification of women at risk of preeclampsia is crucial to improving maternal and fetal outcomes, yet reliable biomarkers are still lacking.

Several hematological and biochemical alterations accompany preeclampsia, including hypoalbuminemia, hemoconcentration, lymphopenia, and heightened systemic inflammation^{6,7}. These changes reflect the complex

interplay between nutritional status, immune dysregulation, and vascular injury in pregnancy complications. Traditional inflammatory ratios such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been extensively studied as predictors of preeclampsia, with meta-analyses confirming their diagnostic and prognostic value^{8,9}. However, these indices capture only limited aspects of the disease process and do not fully integrate the nutritional component that may also contribute to maternal and fetal outcomes.

The hemoglobin, albumin, lymphocyte, and platelet (HALP) score was first introduced as a composite immune-nutritional biomarker in oncology. Chen *et al.* demonstrated that preoperative HALP score was strongly associated with survival in gastric carcinoma patients, suggesting its ability to reflect the host's nutritional and inflammatory status simultaneously¹⁰. Since then, HALP has been validated in various malignancies, including bladder cancer,¹¹ metastatic renal cell carcinoma,¹² and non-small cell lung cancer¹³. A recent meta-analysis further confirmed its prognostic utility across multiple solid tumors, linking higher HALP scores to better overall, progression-free, and cancer-specific survival¹⁴. These findings highlight the versatility of HALP as an integrative marker bridging nutritional and inflammatory pathways.

In obstetrics, the application of HALP score remains relatively novel but is gaining attention. Sert *et al.* reported that a low HALP score was predictive of preeclampsia with severe features, with sensitivity and specificity exceeding 70%¹⁵. Dal *et al.* similarly showed that HALP scores were significantly reduced in preeclamptic women compared with normotensive pregnant controls, although they cautioned against its use as a standalone diagnostic test¹⁶. These emerging data suggest that HALP may provide additional value beyond traditional ratios such as NLR and PLR by incorporating albumin and hemoglobin, both of which are altered in preeclampsia due to vascular leakage, proteinuria, and systemic inflammation.

Given the global burden of preeclampsia and the ongoing need for accessible biomarkers, further investigation of HALP in this context is warranted. Unlike advanced molecular markers, HALP is easily calculated from routine laboratory

parameters—hemoglobin, albumin, lymphocyte count, and platelet count—that are widely available and inexpensive. This makes HALP a particularly attractive candidate for clinical practice, especially in resource-limited settings¹⁷. Therefore, the aim of this study was to evaluate the role of the HALP score in women with preeclampsia compared to healthy pregnant and non-pregnant women, and to assess its association with hematological and biochemical parameters, age-related variations, and its discriminatory ability using ROC curve analysis. By integrating inflammatory and nutritional indices, this study seeks to provide novel insights into the utility of HALP as a composite biomarker in the context of preeclampsia.

Methods

Study design and participants

This retrospective case-control study was conducted at Abha Maternity and Children's Hospital using clinical and laboratory data collected between January 2022 and December 2023. Participants were recruited from the outpatient and inpatient services of the Department of Obstetrics and Gynecology in Abha, Aseer, Saudi Arabia. The study population included 236 women diagnosed with preeclampsia (PE), 260 women with uncomplicated pregnancies (normotensive pregnancy group), and 100 non-pregnant women who served as the reference group. Age was included as a covariate in all multivariable regression analyses to control for potential confounding, and no significant effect of age on the studied biomarkers was observed after adjustment.

Diagnostic and exclusion criteria for preeclampsia

Women were classified into groups based on medical record review. Preeclampsia was diagnosed in accordance with the American College of Obstetricians and Gynecologists (ACOG) guidelines, which define the condition as a systolic blood pressure (SBP) ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 mmHg after 20 weeks of gestation (18). Patients with concomitant HELLP syndrome, (19) chronic or

essential hypertension, acute or chronic infections, premature rupture of membranes, or other internal medical or surgical conditions were excluded.

Laboratory and biochemical parameters

Data collection included clinical vital signs and biochemical parameters such as complete blood count (CBC), albumin (ALB), total protein (TP). HALP score was calculated according to the following formula: hemoglobin (g/L) $\times$ albumin (g/L) $\times$ lymphocytes (/L)} / platelets (/L). (17)

Statistical analysis

All statistical analyses were performed using GraphPad Prism version 10.1.0 (GraphPad Software, San Diego, CA, USA). A p-value <0.05 was considered statistically significant. Continuous variables, including blood pressure, CBC, and biochemical markers, were expressed as mean and standard deviation. Group differences were evaluated using unpaired two-tailed Student's t-tests for two-group comparisons, and one-way ANOVA for comparisons among more than two groups. Correlations between variables were assessed using Pearson's correlation coefficient. Receiver operating characteristic (ROC) curve analysis was conducted to determine the diagnostic performance of HALP score in distinguishing between groups.

Ethical considerations

The study was done in conformity with the Helsinki Declaration of 1964, as revised in 2013. Ethical approval was obtained from the Regional Committee for Research Ethics, Directorate of Health Affairs, Asir Region (approval number REC-13-1-2024), and the King Khalid University Research Ethics Committee (ECM#2024-215).

Results

Baseline characteristics of the study population

The baseline demographic and laboratory findings of the study groups, which included non-pregnant healthy women (NonP), healthy pregnant women

(HP), and women with preeclampsia (PE), are summarized in Table 1. The mean age showed a significant difference between groups ($p < 0.0001$), with women in the preeclampsia group being slightly older (34.32 ± 5.98 years) compared with the pregnant group (30.56 ± 5.75 years) and the non-pregnant group (32.65 ± 6.48 years).

Red blood cell counts differed marginally across groups ($p = 0.049$), with slightly lower values in preeclamptic women ($4.46 \pm 0.68 \times 10^6/\mu\text{L}$) compared to the other two groups. Hemoglobin levels, however, were significantly higher in preeclamptic women (12.01 ± 2.90 g/dL) than in healthy pregnant (11.43 ± 1.72 g/dL) and non-pregnant women (11.71 ± 1.65 g/dL) ($p = 0.017$). In contrast, white blood cell counts were progressively elevated across groups, reaching their highest levels among preeclamptic women ($11.44 \pm 4.48 \times 10^3/\mu\text{L}$), followed by the healthy pregnant ($10.24 \pm 3.61 \times 10^3/\mu\text{L}$) and non-pregnant groups ($8.98 \pm 3.09 \times 10^3/\mu\text{L}$) ($p < 0.0001$).

Differential leukocyte analysis revealed significant alterations among the study groups. Neutrophil percentages were higher in preeclamptic women ($69.34 \pm 14.24\%$) compared with other groups ($p = 0.0078$), whereas lymphocyte counts were lowest in preeclampsia ($22.11 \pm 11.94\%$) compared to non-pregnant women ($25.86 \pm 9.07\%$) ($p = 0.0062$). Monocyte percentages demonstrated a distinct trend, being highest in pregnant women ($9.73 \pm 6.98\%$) but lowest in preeclampsia ($6.95 \pm 2.50\%$), with highly significant differences between groups ($p < 0.0001$). Platelet counts, however, did not differ significantly among the groups ($p = 0.7583$).

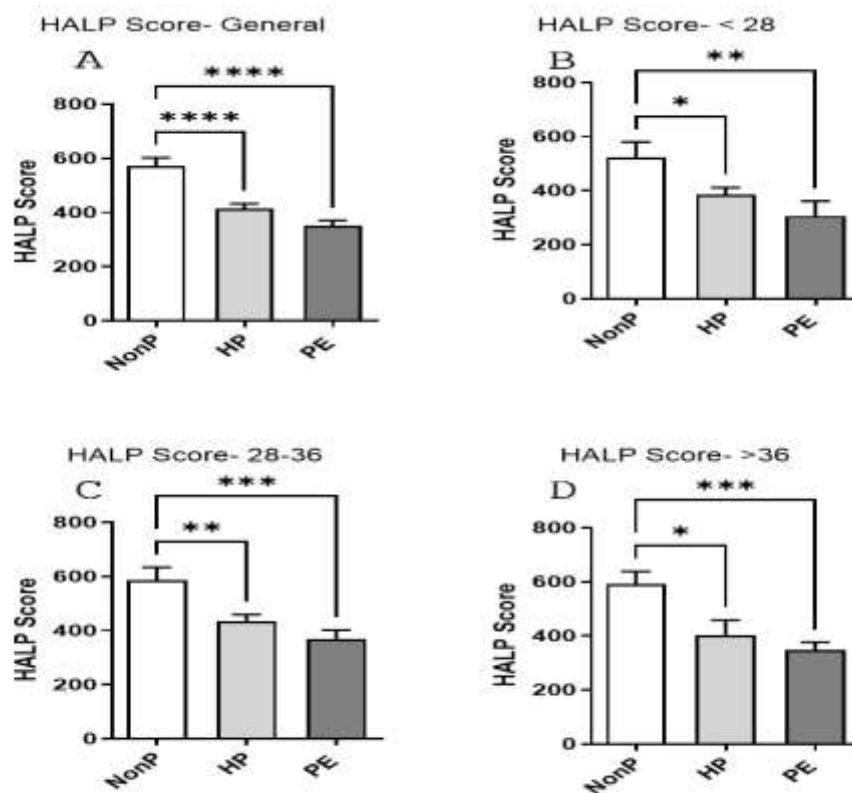
Serum albumin concentrations showed one of the most striking differences. Women with preeclampsia had markedly reduced levels (2.36 ± 0.77 g/dL) compared with both pregnant (3.16 ± 0.50 g/dL) and non-pregnant controls (3.59 ± 0.46 g/dL), with a highly significant p-value (< 0.0001).

HALP score distribution among study groups

In the overall analysis (Figure 1A), HALP scores were significantly lower in preeclamptic women compared with both healthy pregnant and non-pregnant women ($p < 0.001$). When stratified by

Table 1: Baseline demographic, hematological, and biochemical characteristics of non-pregnant, healthy pregnant, and preeclamptic women

	NonP	HP	PE	P value
Age	32.65±6.48	30.56±5.75	34.32±5.98	<0.0001
RBCs	4.48±0.63	4.48±0.53	4.46±0.68	0.049
HBG	11.71±1.65	11.43±1.72	12.01±2.90	0.017
WBCs	8.98±3.09	10.24±3.61	11.44±4.48	<0.0001
NEU	65.28±9.99	69.65±11.32	69.34±14.24	0.0078
LYM	25.86±9.07	22.19±9.74	22.11±11.94	0.0062
MON	7.27±2.011	9.73±6.98	6.95±2.50	<0.0001
PLT	246.9±64.67	240.6±74.1	244.5±91.52	0.75
Albumin	3.59±0.45	3.16±0.50	2.35±0.77	<0.0001
HALP Score	572.5±297.2	414.6±287.2	350.7±314.6	<0.0001

**Figure 1:** Distribution of HALP scores across study groups stratified by age.

(A) Overall population. (B) < 28 years. (C) 28–36 years. (D) > 36 years. HALP scores were highest in NonP women and lowest in PE women across all age groups. The decline was most pronounced in women > 36 years. *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$ vs NonP.

age, the same pattern persisted. Among women younger than 28 years (Figure 1B), HALP scores were reduced in preeclamptic women compared with non-pregnant controls ($p < 0.01$). In the 28–36

years age group (Figure 1C), preeclamptic women demonstrated a marked decline compared with both pregnant and non-pregnant groups ($p < 0.001$). In women older than 36 years (Figure 1D), the

reduction was most pronounced, with preeclamptic women exhibiting the lowest HALP scores across all categories ($p < 0.001$).

Diagnostic performance of HALP Score

Receiver operating characteristic (ROC) curve analysis was performed to assess the discriminatory ability of the HALP score between the study groups (Figure 2). In the comparison between non-pregnant and healthy pregnant women (Figure 2A), the HALP score showed a modest diagnostic value with an area under the curve (AUC) of 0.6758 ($p < 0.0001$). When comparing non-pregnant and preeclamptic women (Figure 2B), the HALP score demonstrated stronger discriminatory performance, yielding an AUC of 0.7640 ($p < 0.0001$). In the comparison between healthy pregnant and preeclamptic women (Figure 2C), the HALP score retained moderate diagnostic accuracy with an AUC of 0.6131 ($p < 0.0001$).

Overall, these results indicate that the HALP score has the highest diagnostic utility in differentiating preeclamptic women from non-pregnant controls, while its ability to discriminate preeclampsia from healthy pregnancy is modest but statistically significant.

Association of HALP score with clinical parameters

Correlation analysis was conducted to examine the association between HALP score and hematological/biochemical parameters (Table 2). The HALP score showed a strong positive correlation with lymphocyte count ($r = 0.724$, $p < 0.0001$), followed by moderate positive correlations with albumin ($r = 0.466$, $p < 0.0001$), hemoglobin ($r = 0.425$, $p < 0.0001$), and monocytes ($r = 0.372$, $p < 0.0001$). In contrast, HALP score was negatively correlated with neutrophils ($r = -0.721$, $p < 0.0001$), white blood cell count ($r = -0.495$, $p < 0.0001$), and platelet count ($r = -0.389$, $p < 0.0001$). No significant association was observed with red blood cell count ($r = 0.052$, $p = 0.209$).

Taken together, these results demonstrate that lymphocytes and albumin are the strongest positive contributors to HALP, whereas neutrophilia and leukocytosis drive its reduction in

preeclampsia. This highlights HALP's ability to integrate nutritional (albumin, hemoglobin) and inflammatory (lymphocytes, neutrophils, WBCs, platelets) elements into a single predictive index for disease severity.

Multivariable and dimensionality reduction analyses

To further explore interrelationships among laboratory parameters, a Spearman correlation heatmap was constructed (Figure 3A). The analysis demonstrated strong positive correlations between HALP score and lymphocyte count, albumin, and hemoglobin, while significant inverse correlations were observed with neutrophils, total white blood cell count, and platelets. These findings reinforce the dual contribution of nutritional and inflammatory parameters to HALP score variability.

Principal component analysis (PCA) was then applied to reduce dimensionality and identify the major contributors to variation among study groups (Figures 3B–D). The scree plot (Figure 3B) indicated that the first two principal components explained the majority of variance. The loading plot (Figure 3C) highlighted albumin, lymphocytes, and hemoglobin as the strongest positive contributors, while neutrophils and total leukocyte count contributed negatively. The score plot (Figure 3D) demonstrated a distinct clustering pattern, with preeclamptic women separating clearly from both pregnant and non-pregnant groups, driven primarily by low albumin and lymphocyte counts alongside elevated inflammatory markers.

Together, these multivariable analyses confirm that the HALP score is underpinned by integrated relationships among inflammatory and nutritional parameters, and that PCA can effectively differentiate preeclamptic women from other groups based on these profiles.

Multiple linear regression analysis

A multiple linear regression model was performed to evaluate the independent associations of clinical and hematological parameters with the HALP score (Table 3). The overall model demonstrated modest explanatory power ($R^2 = 0.462$, adjusted $R^2 = 0.315$), suggesting that only a small proportion of

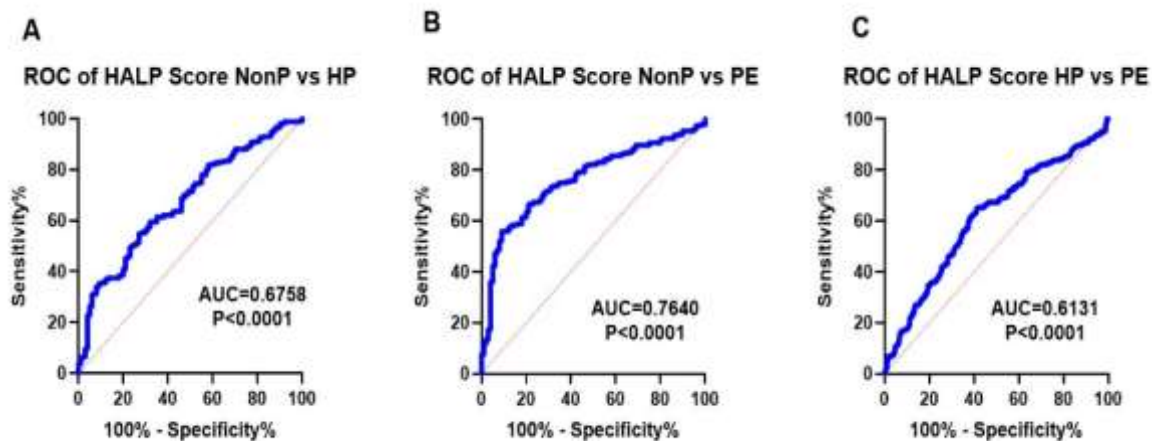


Figure 2: Receiver operating characteristic (ROC) analysis of HALP score among study groups. (A) NonP vs. HP women (AUC = 0.6758, $p < 0.0001$). (B) NonP vs. PE women (AUC = 0.7640, $p < 0.0001$). (C) HP vs. PE women (AUC = 0.6131, $p < 0.0001$). HALP score showed the strongest discriminatory ability between NonP and PE groups, while discrimination between HP and PE was modest but statistically significant

Table 2: Correlation of HALP score with hematological and biochemical parameters in the study groups

	r	95% confidence interval	P value
HALP Score vs. RBCs	0.052	-0.03130 to 0.1338	0.209
HALP Score vs. Hemoglobin	0.4249	0.3546 to 0.4904	<0.0001
HALP Score vs. WBCs count	-0.495	-0.5552 to -0.4300	<0.0001
HALP Score vs. Neutrophils	-0.721	-0.7586 to -0.6789	<0.0001
HALP Score vs. Lymphocytes	0.724	0.6819 to 0.7609	<0.0001
HALP Score vs. Monocytes	0.372	0.2983 to 0.4411	<0.0001
HALP Score vs. Plts count	-0.389	-0.4574 to -0.3169	<0.0001
HALP Score vs. Albumin	0.466	0.3987 to 0.5284	<0.0001

HALP score variability could be explained by the included predictors.

Among the variables, white blood cell count (WBCs) emerged as a significant independent predictor of HALP score (Estimate = 5.42, 95% CI: 1.374–9.484, $p = 0.0088$). Red blood cell count (RBCs) showed a borderline association (Estimate = 37.99, $p = 0.0569$), whereas other variables including systolic and diastolic blood pressure, fasting glucose, creatinine, hemoglobin, hematocrit, and platelet count did not demonstrate significant independent associations (all $p > 0.05$).

These findings indicate that elevated leukocyte counts contribute significantly to the variability in HALP score, even after adjusting for multiple clinical and biochemical parameters. The modest R^2 values suggest that other unmeasured

factors, including inflammatory and nutritional pathways, likely play an important role in determining HALP levels in preeclampsia.

Women with preeclampsia showed marked reductions in albumin and lymphocytes, elevations in WBCs and neutrophils, and consequently lower HALP scores compared with non-pregnant and healthy pregnant women. The decline was consistent across all age groups, most pronounced in older women. HALP demonstrated modest but significant discriminatory ability, while correlation, PCA, and regression analyses confirmed that both inflammatory and nutritional factors drive its variability, with WBCs emerging as an independent predictor. These findings support HALP as a simple integrative marker of inflammation and nutrition in preeclampsia.

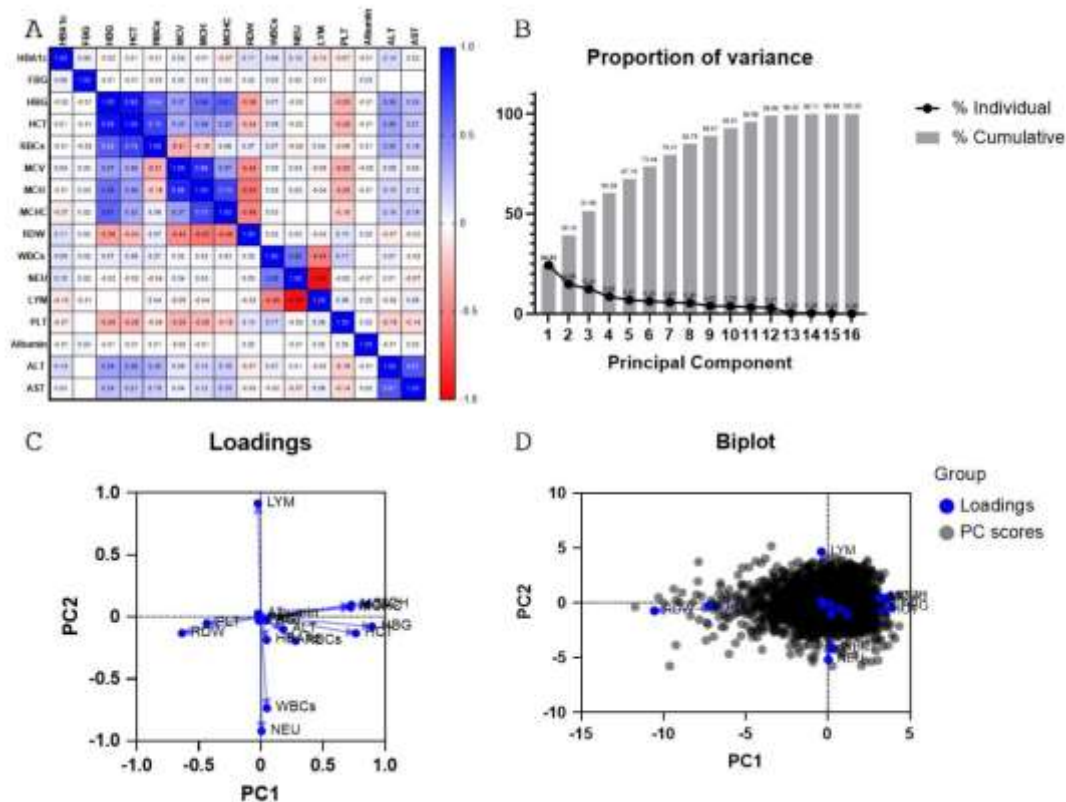


Figure 3: Correlation heatmap and principal component analysis (PCA) of hematological and biochemical parameters. (A) Spearman correlation heatmap showing positive associations of HALP score with lymphocytes, albumin, and hemoglobin, and inverse associations with neutrophils, white blood cell count, and platelets. (B) Scree plot of explained variance indicating the contribution of principal components. (C) Loading plot showing variable contributions, with albumin, lymphocytes, and hemoglobin as the strongest positive contributors, and neutrophils and WBCs as negative contributors. (D) PCA score plot demonstrating distinct clustering of PE women compared with HP and NonP groups

Table 3: Multiple linear regression analysis of clinical and hematological predictors of HALP score.

Variable	Estimate	95% CI (profile likelihood)	t	P value
Intercept	222.8	33.08 to 412.6	2.306	0.0214
SBP (90-140mmHg)	-0.3949	-1.039 to 0.2488	1.205	0.2287
DBP (60-90 mmHg)	-1.166	-3.148 to 0.8165	1.155	0.2486
Glucose fasting	-0.4774	-1.199 to 0.2440	1.3	0.1942
Creatinine	-20.47	-62.18 to 21.25	0.9636	0.3357
HB	-9.261	-41.09 to 22.57	0.5714	0.5679
HCT	0.8336	-12.31 to 13.97	0.1246	0.9009
RBCs	37.99	-1.118 to 77.11	1.908	0.0569
WBCs	5.42	1.374 to 9.484	2.629	0.0088
PLT	-0.04569	-0.1963 to 0.1871	0.04682	0.9627
Degrees of Freedom	585			
Multiple R	0.215			
R squared	0.4622			
Adjusted R squared	0.3154			

Discussion

The observed reduction in HALP scores among women with preeclampsia provides important insight into the underlying pathophysiology of the disorder, reflecting the interplay between nutritional status, immune response, and hematological alterations. The decrease in albumin likely results from increased vascular permeability and its role as a negative acute-phase reactant, indicating systemic inflammation, while lymphopenia suggests immune dysregulation characterized by an imbalance in inflammatory pathways. The concurrent elevation in leukocyte counts further supports an activated inflammatory state, often associated with oxidative stress and endothelial dysfunction. In addition, changes in hemoglobin and platelet parameters may reflect hemoconcentration, platelet activation, and a prothrombotic state, all of which are well-recognized features of preeclampsia. Collectively, these findings highlight the value of the HALP score as an integrative biomarker that captures multiple pathophysiological processes simultaneously, offering advantages over single markers in complex conditions such as preeclampsia. Despite its clinical relevance, the modest discriminatory ability between preeclampsia and healthy pregnancy suggests that HALP should be considered a supportive tool within a broader diagnostic framework, with future studies needed to evaluate its predictive value, longitudinal changes during pregnancy, and potential integration with other biomarkers.

The decline in albumin observed in the preeclamptic group can be explained by impaired hepatic synthetic function, increased vascular permeability, and proteinuria, which are characteristic of the disease and contribute to endothelial dysfunction^{20,21}. Furthermore, the significant decrease in lymphocytes, accompanied by elevated neutrophil and total WBC counts, is consistent with systemic inflammatory activation and immune dysregulation previously described in preeclampsia^{6,7}. These combined alterations directly impact HALP, explaining the substantially lower values observed among affected women. Our ROC curve analysis confirmed the discriminatory value of HALP, with the strongest

performance seen in distinguishing preeclamptic women from non-pregnant controls. The diagnostic power in differentiating preeclampsia from healthy pregnancy was modest but statistically significant, suggesting that HALP could serve as a supportive biomarker rather than a standalone diagnostic test. Similar findings have been reported in recent literature: Sert *et al.* demonstrated that a low HALP score was predictive of severe preeclampsia with an AUC of 0.72, while Dal *et al.* showed reduced HALP scores in preeclamptic women compared with normotensive pregnancies, though with moderate sensitivity and specificity^{15,16}.

Other immune-nutritional indices such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have also been investigated, with meta-analyses supporting their predictive value in preeclampsia²². However, HALP may offer an advantage by integrating not only inflammatory markers but also nutritional status through hemoglobin and albumin. This broader scope likely explains its consistent decline in preeclampsia across different age strata in our cohort. Beyond obstetrics, HALP has been validated as a prognostic marker in various malignancies,^{10-12,14} further supporting its robustness as a composite index. The application of HALP in preeclampsia is still emerging, but our findings, together with recent studies, suggest that it holds promise as an accessible and cost-effective biomarker that can be derived from routine laboratory tests.

Taken together, these findings indicate that the HALP score effectively captures both the inflammatory burden and the nutritional disturbances characteristic of preeclampsia. Although its ability to discriminate between preeclampsia and healthy pregnancy is modest, HALP may have greater clinical value as an adjunctive biomarker when used alongside established predictors and clinical parameters. Further prospective, multicenter investigations are required to validate its utility, determine optimal cut-off values, and assess its potential integration into comprehensive risk assessment models for preeclampsia.

Our multivariate analyses provide additional insight into the mechanisms underlying HALP score reduction in preeclampsia. The

correlation heatmap and PCA demonstrated that albumin and lymphocytes contributed positively to HALP, whereas neutrophils, WBCs, and platelets loaded negatively. These axes of variation effectively distinguished preeclamptic women from both healthy pregnant and non-pregnant controls. Similar PCA-based studies in obstetrics have reported that inflammatory and metabolic pathways are the main drivers of variance in PE datasets, separating patients from controls on the basis of innate immune activation and nutritional status²³⁻²⁶. Moreover, recent metabolomics and multi-omics approaches confirmed that principal components enriched for inflammatory markers, vascular dysfunction, and hypoalbuminemia are central to preeclampsia pathophysiology²⁷⁻²⁹. Collectively, these findings reinforce that HALP reflects the same fundamental biological axes—nutritional depletion and inflammation—that repeatedly emerge in unbiased multivariate models of PE.

The multiple linear regression model further highlighted WBC count as an independent determinant of HALP score. This aligns with large-scale cohort studies showing that leukocytosis is associated with higher risk of developing preeclampsia and adverse pregnancy outcomes^{30,31}. Elevated WBCs and neutrophils, together with lymphopenia, are consistent with the systemic inflammatory response and immune dysregulation reported in preeclampsia⁷. Meta-analyses evaluating NLR and PLR confirm the contribution of neutrophil-predominant inflammation to both the occurrence and severity of PE^{22,32}. Concurrently, hypoalbuminemia has been linked to increased vascular permeability, proteinuria, and disease severity in PE^{33,34}. Altered platelet counts and coagulation abnormalities have also been reported as markers of progression in PE^{35,36}. These results explain why HALP, which integrates hemoglobin, albumin, lymphocytes, and platelets into a single index, is significantly reduced in preeclampsia. Our regression findings therefore confirm that leukocytosis independently suppresses HALP, while reduced albumin and lymphocyte counts further accentuate this effect, supporting HALP as a robust composite indicator of the inflammatory and nutritional imbalance characteristic of preeclampsia.

Strengths and limitations

The present study has several strengths. First, it is one of the few to investigate the HALP score in preeclampsia using a case-control design that included both pregnant and non-pregnant reference groups, allowing a clearer understanding of baseline variations across different physiological states. Second, the relatively large sample size enhanced the reliability of the comparisons, while age-stratified analyses provided additional insight into the interaction between maternal age and HALP score. Third, the study employed multiple complementary statistical approaches—including correlation mapping, principal component analysis, and regression modeling—which strengthened the interpretation by demonstrating consistent findings across different analytic methods.

Nonetheless, some limitations should be acknowledged. The retrospective design restricts causal inference, and the study was conducted at a single tertiary center, which may limit generalizability to broader populations. Certain potentially relevant variables, such as dietary intake, body mass index (BMI), and detailed inflammatory cytokine profiles, were not available, which may have further clarified the mechanisms linking HALP score to preeclampsia. Additionally, while the HALP score demonstrated discriminatory value, especially when distinguishing preeclampsia from non-pregnant women, its diagnostic accuracy between preeclampsia and healthy pregnancy was modest. This suggests that HALP is best considered as a supportive biomarker rather than a standalone diagnostic tool. Finally, prospective, multicenter studies are needed to validate these findings, establish cut-off values for clinical use, and evaluate the predictive potential of HALP in early pregnancy before the onset of preeclampsia.

Implications for clinical practice and policy

The findings of this study have several relevant implications. From a clinical perspective, the HALP score represents a simple, cost-effective, and readily available biomarker derived from routine laboratory parameters (hemoglobin, albumin, lymphocyte count, and platelet count). Its integration into clinical assessment may support the early identification and risk stratification of women

with preeclampsia, particularly in resource-limited settings where advanced biomarkers are not readily accessible. However, given its modest discriminatory performance between preeclampsia and healthy pregnancy, HALP should be used as a complementary tool alongside established clinical and laboratory parameters, rather than as a standalone diagnostic marker.

From a policy standpoint, the use of such composite indices may contribute to optimizing maternal health screening programs, especially in regions with a high burden of hypertensive disorders of pregnancy. Incorporating HALP into routine antenatal care protocols could enhance cost-efficiency and accessibility of screening, provided that its clinical utility is further validated. Additionally, these findings highlight the importance of integrating nutritional and inflammatory status into maternal health strategies, which may inform preventive approaches and targeted interventions.

Nevertheless, before widespread clinical or policy implementation, prospective, multicenter validation studies are essential to confirm reproducibility, establish standardized cut-off values, and assess its predictive value in early pregnancy.

Conclusion

This study provides novel insights into the clinical value of the HALP score in preeclampsia. Unlike previous research that primarily compared normotensive and preeclamptic pregnancies, our analysis included three groups—non-pregnant women, healthy pregnancies, and preeclampsia—allowing us to clearly delineate changes in HALP across physiological and pathological states. Age-stratified analyses further demonstrated that the reduction in HALP among preeclamptic women was consistent across all age categories and most pronounced in older women, an observation not emphasized in earlier studies. By combining correlation analysis, PCA, and regression modeling, we were able to identify the specific component contributions of albumin, lymphocytes, and neutrophils as key drivers of HALP score variation, thereby supporting a mechanistic rather than solely descriptive interpretation. Finally, ROC

curve analyses across multiple group comparisons confirmed that HALP has discriminatory utility, particularly in distinguishing preeclampsia from non-pregnant and normotensive pregnant women. Collectively, these findings suggest that HALP is a simple, accessible, and integrative biomarker that reflects both nutritional and inflammatory alterations in preeclampsia, with potential value for risk assessment in clinical practice.

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Ethics approval statement

This study was approved by the Directorate Health Affairs-Asir Region Research Ethics Committee (Approval Number REC-13-1-2024). It was also approved by the King Khalid University Research Ethics Committee (ECM#2024-215).

Authors contributions

Conceptualization, methodology, validation, formal analysis, writing, and funding acquisition by A.A.D. The author has agreed to finalize and publish this version of the manuscript. I agree to take responsibility for all aspects of the research to ensure that challenges relating to the accuracy or integrity of any part of the paper are properly investigated and resolved.

Consent to participate and publish

The author accepts responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interest

The authors declare that they have no conflicts of interest.

Data availability

All data used in this manuscript are available from the author and will be provided upon reasonable request for noncommercial purposes.

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