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Original Article

The neutrophil-to-lymphocyte ratio as an inflammatory marker in preeclampsia: a retrospective cohort study from Saudi Arabia

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Abstract

Preeclampsia (PE) is a major hypertensive disorder of pregnancy, with systemic inflammation being a key component of its pathogenesis. The neutrophil-to-lymphocyte ratio (NLR) has been investigated as an inflammatory biomarker for PE; however, its levels are rarely compared directly to both healthy pregnant and non-pregnant controls. This study aimed to evaluate the role of NLR in PE by comparing its levels across these three distinct groups. This retrospective study analyzed medical records from Abha Maternity and Children's Hospital (2022–2023), including 236 PE cases, 260 healthy pregnancies, and 100 non-pregnant controls. Biochemical and hematological parameters were assessed, as well as Receiver Operating Characteristic (ROC) analysis, which evaluated NLR's discriminatory power. Women with PE exhibited significantly elevated NLR compared to both the HP and NP groups ($p < 0.001$). ROC analysis showed that NLR could distinguish NP from PE with an AUC of 0.643 ($p<0.0001$) and NP from HP with an AUC of 0.623 ($p=0.0003$). An elevated NLR was associated with a 40.7% increased relative risk (RR=1.41, $p<0.0001$) and nearly threefold higher odds (OR=3.08, $p<0.0001$) of developing PE. It is concluded that NLR is significantly elevated in PE and demonstrates a significant association with increased risk of the disorder. These findings support its potential utility as an accessible, cost-effective inflammatory biomarker for aiding in the risk stratification of pregnant women. Further prospective studies are warranted to validate its clinical diagnostic value.

Keywords: Preeclampsia (PE), Neutrophil-to-Lymphocyte Ratio (NLR), Systemic inflammation, Hypertensive disorders of pregnancy, Biomarkers in pregnancy.

1. Introduction

Preeclampsia (PE) is a complex condition characterized by the sudden onset of hypertension, typically occurring after 20 weeks of gestation, along with at least one additional complication such as proteinuria or uteroplacental dysfunction (e.g., fetal growth restriction, maternal organ dysfunction, or angiogenic imbalance) [1]. It remains a leading cause of maternal and perinatal morbidity and mortality globally, affecting approximately 4 million women annually and contributing to more than 70,000 maternal deaths and 500,000 neonatal fatalities [2]. Beyond pregnancy, PE poses long-term health risks, including cardiovascular disease, stroke, and diabetes in mothers, while offspring are at increased risk of preterm birth, developmental delay, and chronic health complications [3-6].

The International Society for the Study of Hypertension in Pregnancy (ISSHP) classifies PE into preterm (<37 weeks), term (≥37 weeks), and postpartum forms. Although the early- and late-onset classifications were initially proposed for research stratification, emerging evidence suggests they are clinically relevant, especially in tailoring management and predicting outcomes [1, 5]. For instance, while aspirin prophylaxis and early screening show promise in preventing preterm PE, they have limited impact on term cases. Furthermore, using gestational age alone to define PE can be imprecise due to interindividual variation in disease progression and hospital presentation [6, 7]. Currently, effective predictive strategies for PE are not well defined. Consequently, investigating laboratory markers, including hematological parameters, that may assist in predicting PE and assessing its severity is extremely valuable.

Systemic inflammation is increasingly recognized as central to PE pathogenesis, driven by endothelial dysfunction, placental ischemia, and maternal immune dysregulation [8-10]. In this context, complete blood count (CBC)-derived inflammatory indices, such as the neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR), have gained attention due to their accessibility, cost-effectiveness, and capacity to reflect immune status [11-14]. Neutrophil and lymphocyte activity, in particular, has been implicated in the immunological imbalance observed in PE [11]. While several studies report elevated NLR in PE patients [15-19], others have found no significant difference compared to normotensive pregnancies [14, 15], highlighting inconsistencies in the literature.

Importantly, immune responses fluctuate throughout gestation, transitioning from a pro-inflammatory phase

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in the first trimester to an anti-inflammatory state in the second, and returning to a pro-inflammatory profile in the third trimester [20, 21]. However, most studies comparing NLR levels are limited to pregnant cohorts. Understanding baseline NLR values in non-pregnant women could provide further insight into inflammation-related susceptibility to PE.

Therefore, the present retrospective case-control study was designed to evaluate the diagnostic potential of NLR in women with PE compared to both normotensive pregnant and non-pregnant controls. Our primary aim was to determine whether NLR levels are significantly elevated in PE within a Saudi cohort. Furthermore, we sought to assess its discriminatory power using ROC analysis, its correlation with other clinical parameters, and its associated risk for developing PE.

2. Materials and Methods

2.1. Study design and participant groups

This retrospective study was conducted at Abha Maternity and Children's Hospital, utilizing data collected from January 2022 to December 2023. Approval for the study was granted by the Regional Committee for Research Ethics in the Directorate of Health Affairs, Asir Region (approval number REC-13-1-2024)**,** as well as by the King Khalid University Research Ethics Committee (ECM#2024-215)**.** All participants were drawn from the local community in Abha, Aseer, Saudi Arabia, and were selected from the outpatient and inpatient Departments of Obstetrics and Gynecology. Medical records indicated that 236 pregnant women met the criteria for PE, while 260 women with normal pregnancies and no complications were also included as "normotensive pregnancy group" and 100 non-pregnant women were selected as non-pregnant reference group. Gestational age at the time of blood sampling and maternal age were documented for all participants. Although formal matching between groups was not performed, these variables were compared statistically and are reported to allow assessment of their potential confounding effects.

2.2. Diagnostic and exclusion criteria for preeclampsia

The dataset comprised healthy pregnant women, as well as those diagnosed with PE, particularly those at increased risk, including those with hypertension. PE diagnoses adhered to the clinical criteria established by the American Congress of Obstetricians and Gynecologists (ACOG), specifically requiring a systolic blood pressure (SBP) of ≥140 mm Hg and/or a diastolic blood pressure (DBP) of ≥90 mm Hg [17]. All participants were classified strictly in accordance with these diagnostic standards. Exclusion criteria were applied to ensure a homogeneous cohort. The following cases were excluded: PE patients with HELLP syndrome [18], Women with essential (chronic) hypertension, Individuals with recent acute or chronic infections, Cases of premature rupture of membranes, and Patients with internal surgical conditions or other comorbidities that could influence inflammatory markers.

Biochemical parameters were collected, from the first blood draw following the diagnosis of PE, including vital signs, complete blood count (CBC), blood urea nitrogen (BUN), creatinine (CREA), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin (ALB), total protein (TP), total bilirubin (TBIL), direct bilirubin (DBIL), uric acid (UA), prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (APTT). Additionally, NLRs were calculated by dividing the absolute neutrophil count ($\times 10^9$/L) by the absolute lymphocyte count ($\times 10^9$/L) for each participant, with values ranging from 1 to 3 considered to be within the normal range [19].

2.3. Statistical analysis

Data analysis was conducted using GraphPad Prism version 10.1.0 (GraphPad Software, Inc., San Diego, CA, USA), with statistical significance defined as a p-value of <0.05. Blood pressure, CBC, and parameters related to liver, kidney were presented as the medians ± 95% CI. For group comparisons, data were first assessed for normality and were found to be non-normally distributed. Accordingly, non-parametric tests were applied: the Mann–Whitney U test was used for analyses involving two independent groups, while the Kruskal–Wallis test was employed for comparisons across multiple groups. Pearson's correlation coefficient was used to assess the strength and significance of correlations among variables. Furthermore, ROC curve analysis was performed to evaluate the diagnostic predictive power of the NLR.

3.Results

The data revealed significant differences among non-pregnant (NP), healthy pregnant (HP), and PE women. Specifically, PE is associated with advanced maternal age, notable hypertension, systemic inflammation (indicated by elevated white blood cell counts (WBCs)), and mild hepatic stress (characterized by increased AST and ALT), as detailed in Table 1. Hematological changes in PE include hemoconcentration (evidenced by higher hematocrit and lower MCHC) and slight variations in red blood cell (RBC) indices, suggesting vascular dysfunction. Platelet counts remained stable across all groups, indicating the absence of considerable coagulopathy or disturbances in glucose metabolism within this cohort. Elevated ALP levels in HP and PE women indicated normal physiological changes during pregnancy. In contrast, the increase in WBCs and mild elevations in liver enzymes observed in PE suggested inflammation and hepatic involvement, aligning with the endothelial dysfunction characteristic of PE. These findings underscore the established pathophysiological features of PE and offer valuable insights into potential diagnostic markers.

3.1. NLR significantly increased in preeclamptic women

Figure 1 illustrates age-specific NLRs in NP women, HP women, and women with PE. Women with PE exhibited significantly elevated NLR levels in comparison to both HP and NP women across all age groups, indicating heightened inflammation. HP women showed a moderate increase in NLR relative to NP women, reflecting the normal immune changes associated with pregnancy (Figure 1A). Among younger women with PE, the NLR was at its highest, while HP women demonstrated a slight increase over their NP counterparts. Elevated NLR levels were consistently found in women with PE, with HP women showing a moderate rise compared to NP participants (Figure 1B). Elevated NLR levels were consistently observed in women with PE, while healthy pregnant women

Table 1. Characteristics of study subjects.

Variable	NP *vs.* HP[a]	NP *vs.* PE[b]	HP *vs.* PE [c]
Age (years)	32.0 (31.36-33.94)	30.0 (29.86-31.27)	35.0 (33.55-35.08)
SBP (mmHg)	116.5 (115.2-120.3)	116.0 (115.0-118.4)	181.0 (181.2-189.9)
DBP (mmHg)	74.0 (72.17-76.03)	79.0 (77.92-80.06)	97.0 (97.33-99.43)
FBG (mg/dl)	90.0 (87.75-95.60)	89.0 (88.35-94.15)	92.21 (93.49-100.6)
RBCs (million/µl)	4.52 (4.35-4.60)	4.47 (4.41-4.55)	4.39 (4.38-4.55)
Hematocrit (%)	34.65 (34.16-36.01)	33.90 (33.80-34.87)	35.05 (35.58-37.61)
Hemoglobin (g/dl)	11.65 (11.38-12.04)	11.30 (11.22-11.64)	11.50 (11.63-12.38)
MCH (pg)	26.75 (25.65-27.16)	25.90 (25.21-26.11)	26.80 (26.34-27.53)
MCHC (g/dl)	33.30 (33.09-33.65)	33.20 (32.87-33.28)	32.90 (32.42-32.91)
MCV (fL)	80.30 (77.11-80.74)	77.20 (76.06-78.16)	81.85 (80.47-83.38)
RDW-CV (	15.70 (16.06-17.44)	16.10 (16.30-17.10)	15.95 (16.25-17.17)
WBCs (x10^3/µl)	8.71 (8.36-9.59)	9.65 (9.79-10.68)[a]	10.65 (10.87-12.02)
Platelets (x10^3/µl)	247.0 (234.1-259.7)	237.0 (232.1-252.7)	244.5 (232.8-256.2)
Neutrophils	65.28 (60.9-69.66)	69.65 (65.27-74.03	69.34 (64.96-73.72)
Lymphocytes	25.86 (22.18-29.45)	22.19 (18.25-25.87	22.11 (18.43-25.79)
MPV (fL)	10.10 (9.69-10.15)	10.20 (10.10-10.39)	10.15 (10.05-10.36)
ALT (U/L)	11.15 (12.07-18.18)	11.10 (12.23-15.17)[a]	13.10 (18.74-30.83)
AST (U/L)	20.85 (20.74-26.33)	20.0 (21.71-25.67)[a]	23.40 (28.55-38.96)
ALP (U/L)	76.0 (69.26-130.8)	131.0 (108.0-163.5)	126.9 (125.9-145.3)

Data are shown as medians ± 95% CI. [a]NP *vs*. HP; [b]NP *vs*. PE; [c]HP *vs*. PE.

showed a moderate increase compared to non-pregnant participants within the 28–36 age range (Figure 1C). Preeclampsia consistently exhibited the highest NLR values, whereas healthy pregnancy showed a modest increase in NLR among women older than 36 years (Figure 1D).

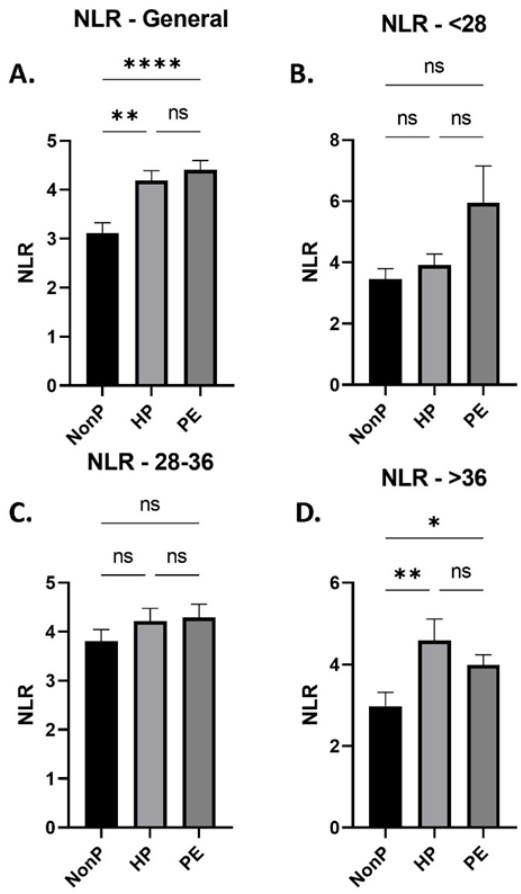


Fig. 1. NLR ratio increased in preeclamptic women (mean±SD) of three groups (A), in participants aged less than28 (B), in participants aged 28-36 (C), in participants aged more than 36 (D).

3.2. NLR displays moderate diagnostic accuracy for PE

Receiver Operating Characteristic (ROC) curve analysis was conducted to assess the diagnostic performance of the NLR in distinguishing between groups, as illustrated in Figures 2A–C. The result showed a fair significant discrimination for NLR between NP women and those with PE (AUC=0.643, p<0.0001), as well as between NP women and HP women (AUC=0.623, p=0.0003). However, there was no significant and fair discrimination between HP women and those with PE (AUC=0.533, p=0.2009).

3.3. Comparison and Association of NLR and CBC parameters among study groups

Figure 3 illustrates the relationship between the NLR and CBC parameters across the three groups: NP women, HP women, and women with PE. The heatmap highlights correlations between NLR and immune-related CBC parameters. Notably, NLR shows a positive correlation with WBCs (0.61) and monocytes (0.44), suggesting immune changes, particularly in cases of PE. Conversely, NLR exhibits negative correlations with basophils (−0.47) and eosinophils (−0.64), indicating specific immune responses associated with pregnancy or PE. Additionally, weak associations were observed between NLR and parameters such

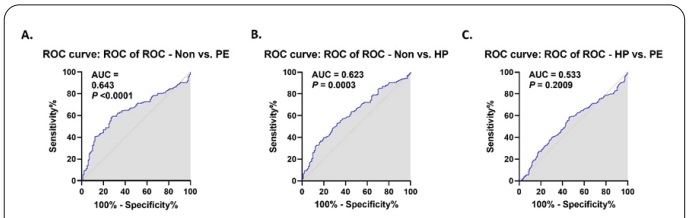


Fig. 2. ROC curves of the subjects to discriminate (A) Non-Pregnant vs. Preeclampsia, (B) Non-Pregnant vs. Healthy Pregnancy, and (C) Healthy Pregnancy vs. Preeclampsia.

as hemoglobin and platelets (Figure 3A).

The variance plot demonstrates that the first two principal components (PC1 and PC2) account for approximately 45% of the data variance, highlighting significant differences in CBC profiles. By PC6, the cumulative variance reaches 87%, encompassing most of the variability across the groups (Figure 3B). The loadings plot reveals that PC1 is primarily influenced by red cell indices, such as hemoglobin and RBC counts, likely reflecting hematological differences related to pregnancy states. In addition, PC2 focuses on the NLR and WBC counts, capturing immune variations, especially in cases of PE (Figure 3C). The PCA scores plot indicates clustering patterns, showing that elevated NLR values, represented by larger points, are concentrated in specific areas, particularly among women with PE, thus indicating distinctive inflammatory profiles (Figure 3D). Overall, the distinct clustering observed in the PCA scores plot indicates variations in inflammation among the groups, with PE exhibiting unique patterns for the CBC and NLR. This analysis enhances our understanding of how pregnancy and PE affect inflammatory markers and CBC parameters.

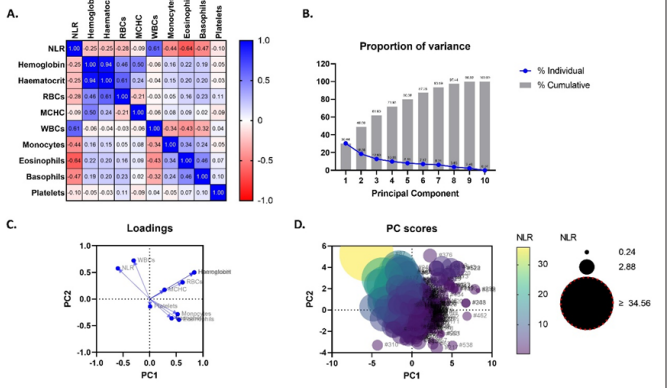


Fig. 3. Multivariate analysis of CBC parameters across three groups: (A) Panel A displays the correlation matrix, illustrating relationships among CBC variables; (B) Panel B presents a scree plot, indicating that the first two principal components account for the majority of the variance; (C) Panel C shows a PCA biplot, demonstrating how samples cluster based on CBC features; and (D) Panel D features a bubble plot highlighting variable distribution and density, along with a loading plot identifying the CBC parameters that contribute most to group separation.

3.4. Comparison and association of NLR and liver function test parameters among study groups

Figure 4 illustrates a multivariate statistical evaluation of the relationship between the NLR and various LFT parameters. Panel A features a Pearson correlation heatmap, which reveals moderate positive correlations between the NLR and several LFT markers, such as AST ($r = 0.46$), ALT ($r = 0.40$), total bilirubin ($r = 0.45$), direct bilirubin ($r = 0.38$), and ALP ($r = 0.30$). Conversely, the NLR shows a negative correlation with albumin ($r = -0.41$) and total protein ($r = -0.36$), indicating an inverse relationship between systemic inflammation and hepatic synthetic capacity (Figure 4A). Panel B, the PCA scree plot, demonstrates that the first two principal components (PC1 and PC2) account for 43.16% and 20.79% of the total variance, respectively, resulting in a cumulative variance of 63.95%, thereby supporting the use of PCA for dimensionality reduction (Figure 4B). Panel C presents the PCA loading plot, which indicates that markers such as AST, ALT, and bilirubin load positively on PC1, while albumin and total protein load negatively, highlighting a biologically significant contrast between markers of hepatocellular injury and synthetic function (Figure 4C). Panel D features the PCA bubble plot, which illustrates the distribution of individual subjects along PC1 and PC2. Samples with a higher NLR and elevated liver enzymes cluster toward the positive axis of PC1, while those with normal profiles are primarily situated in the opposite direction (Figure 4D). This multivariate analysis underscores the significant association between the NLR and disturbances in liver function, suggesting that it may serve as a composite marker for both systemic inflammation and hepatic dysfunction, especially in conditions such as PE.

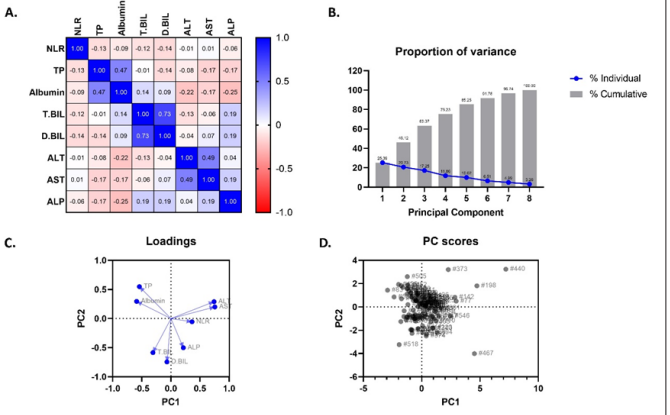


Fig. 4. Multivariate analysis of liver function tests across three groups: (A) Panel A displays the correlation matrix, showing relationships among liver function test variables; (B) Panel B presents a scree plot, indicating that the first two principal components account for the majority of the variance; (C) Panel C features a PCA biplot, illustrating how samples cluster based on liver function test features; and (D) Panel D shows a bubble plot highlighting variable distribution and density, along with a loading plot that identifies the liver function test parameters contributing most to group separation.

3.5. Correlation between NLR and systolic and diastolic blood pressure

The linear regression analyses of the NLR in relation to systolic and diastolic blood pressure (BP) across various study groups reveal weak and inconsistent associations. In the overall study population, the NLR showed weak but statistically significant positive correlations with systolic ($r = 0.082$, $p < 0.05$) and diastolic BP ($r = 0.081$, $p < 0.05$) (Figure 5A), indicating a minor correlation between systemic inflammation and BP regulation. However, subgroup analyses presented diverging trends. In the cohort of HP women, no significant correlation was found between NLR and systolic BP ($r = 0.0$, $p = 0.99$), while a weak inverse relationship was noted with diastolic BP ($r = -0.135$, $p = 0.029$) (Figure 5B). This suggests a possible physiological adaptation during normal pregnancy. In contrast, within the PE group, NLR showed no significant correlations with either systolic ($r = 0.018$, $p = 0.782$) or diastolic BP ($r = 0.075$, $p = 0.25$) (Figure 5C), indicating that inflammatory markers like the NLR do not play a considerable role in BP variations among women with PE. These findings imply that while the NLR may have a minor association with BP in the general population, its predictive value for

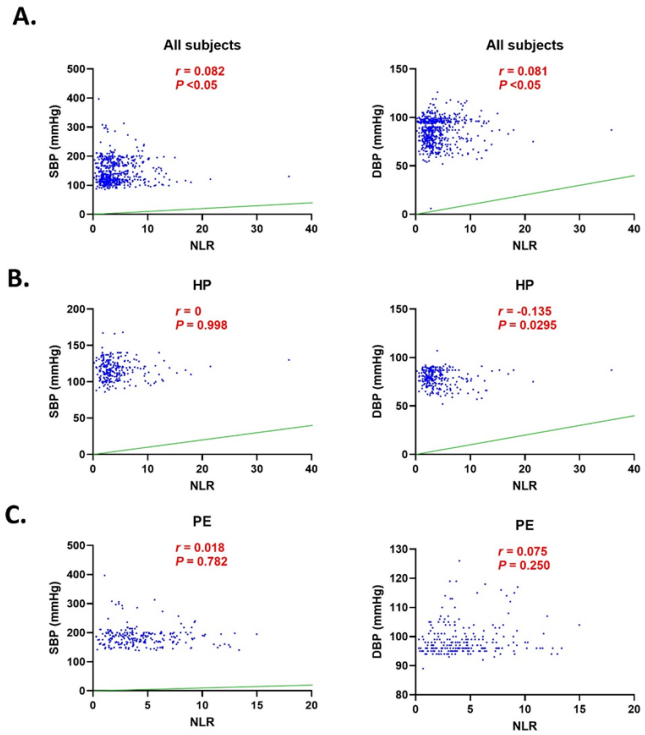


Fig. 5. Scatterplot of the association between NLR and SBP-DBP (A) in all subjects (B) in HP and (C) in PE.

BP regulation in both healthy pregnant women and pregnant women with PE is limited.

3.6. Elevated NLR carries a greater risk for PE

The analysis revealed a significant correlation between elevated NLR and an increased risk of PE showed in Table 2. A relative risk (RR) of 1.41, accompanied by a 95% confidence interval (CI) of 1.2 to 1.65, indicates that individuals with elevated NLR face a 40.74% higher risk of developing PE compared to those with normal NLR levels. The z-statistic of 4.275 and p-value of less than 0.0001 further confirmed the statistical strength of this association. These findings clarify the potential of NLR as an early clinical marker for evaluating the risk of developing PE.

The odds ratio (OR) for NLR levels among NP women, HP women, and those with PE is 3.08, with a 95% CI ranging from 1.89 to 5.01. This OR suggests that individuals with elevated NLR levels have nearly three times the odds of developing PE compared to those with normal NLR levels. The z-statistic of 4.54 and a significance level of $p < 0.0001$ further confirm the statistical significance of this association, indicating a robust and reliable link between elevated NLR and the risk of PE. This finding suggests NLR could be used as a potential risk indicator for PE, deserving further attention in clinical risk assessments.

3.7. Multivariable regression analysis of NLR with RBC indices

A multivariable linear regression analysis was conducted to evaluate the relationship between NLR and various RBC indices. The overall regression model was statistically significant ($p < 0.0001$), with an F-statistic of 5.67 and an adjusted R^2 of 0.59, indicating that approximately 59% of the variance in the outcome variable could be explained by the included predictors, as shown in Table 3. However, none of the individual RBC parameters demonstrated statistically significant associations with NLR after controlling for other variables. The parameter estimates (β) and

Table 2. Risk assessment of elevated NLR.

		Score	95% CI	z Statistic	Significance Level
Non-P ver PE	PR	1.41	1.20 to 1.65	4.28	P < 0.0001
	OR	3.08	1.89 to 5.00	4.54	P < 0.0001
Non-P ver HP	PR	1.25	1.09 to 1.43	3.28	P = 0.0011
	OR	2.23	1.39 to 3.59	3.32	P = 0.0009
HP ver PE	PR	1.19	0.97 to 1.44	1.70	P = 0.08
	OR	1.38	0.96 to 1.98	1.74	P = 0.08

Table 3. Multivariable regression analysis of NLR with RBC indices.

	β	SE	95% CI	|t|	*P* value
NLR	12.18	8.83	-5.15 to 29.52	1.38	0.17
Hemoglobin	-0.45	0.59	-1.62 to 0.72	0.75	0.45
Hematocrit	0.12	0.23	-0.31 to 0.57	0.58	0.57
RBCs count	-1.09	1.22	-3.48 to 1.29	0.90	0.37
MCV	-0.014	0.10	-0.22 to 0.19	0.14	0.89
MCH	0.031	0.2513	-0.46 to 0.52	0.12	0.90
MCHC	-0.057	0.1724	-0.39 to 0.28	0.33	0.74
RDW-CV	-0.0097	0.04243	-0.09 to 0.073	0.2293	0.81
Model	–	–	–	–	**<0.0001**
Residual	8.82	–	–	–	–
F statistic	5.67	–	–	–	–
Adjusted R^2	0.59	–	–	–	–

β, parameter estimate coefficient; SE, standard error; CI, confidence interval; RBC, red blood cells; MCV, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW-CV, red cell distribution width-coefficient of variation.

corresponding P values were as follows: hemoglobin (β = −0.45, P = 0.45), hematocrit (β = 0.12, P = 0.57), RBC count (β = −1.09, P = 0.37), MCV (β = −0.014, P = 0.89), MCH (β = 0.031, P = 0.90), MCHC (β = −0.057, P = 0.74), and RDW-CV (β = −0.0097, P = 0.81). Although the NLR had a positive β coefficient of 12.18, it was not statistically significant (p = 0.17). These results indicate that while the RBC indices collectively enhance the model's explanatory power, no individual parameter independently predicted the NLR with statistical significance in this cohort.

4. Discussion

PE remains a complex obstetric disorder with incompletely understood pathophysiology, where inflammation and hypertension play central roles. Current treatments primarily target blood pressure control and, in severe cases, early delivery. In this context, the present study retrospectively evaluated the NLR as a potential inflammatory biomarker by comparing its levels among NP, HP, and PE women. ROC curve analysis was used to assess the diagnostic performance of NLR, while correlations with hematological and biochemical markers were analyzed to elucidate its clinical relevance. This approach aligns with previous studies highlighting NLR's association with systemic inflammation in PE [22] and supports its utility in predicting adverse maternal outcomes [23,24].

The findings of this study demonstrate that PE is significantly associated with elevated NLR levels across all age groups. When NP women were compared to those with PE, as well as to HP women, NLR levels were consistently higher in the PE group. This elevation reflects enhanced systemic inflammatory activity, aligning with the well-established role of immune dysregulation and inflammation in the pathophysiology of PE [9]. Interestingly, HP women also exhibited a moderate but statistically significant increase in NLR compared to NP women, which may reflect the physiological immune adaptations necessary for maternal–fetal tolerance during normal gestation [23].

ROC curve analysis confirmed the diagnostic utility of NLR, with the AUC indicating that it reliably a fair discriminates between NP, HP, and PE groups. This supports prior findings suggesting that NLR may serve as a cost-effective, readily available biomarker for the early identification of PE [13, 24]. Moreover, correlation analyses in this study revealed a positive association between NLR and WBC count, monocyte levels, and ALT, suggesting the involvement of both inflammatory and hepatic components in the disease process. Conversely, a negative correlation between NLR and basophil count, eosinophils, and serum albumin levels may indicate broader immune imbalance and altered protein metabolism in PE [25]. Although the overall multivariable regression model examining the association between NLR and RBC indices was statistically significant, individual predictors did not reach significance. This pattern may reflect multicollinearity among the RBC parameters, whereby intercorrelations reduce the apparent independent contribution of each variable, despite the model as a whole explaining a meaningful proportion of variance.

Importantly, women with elevated NLR values were found to have a 40.74% increased risk of developing PE, with nearly threefold higher odds compared to those with normal NLR levels. These findings align with previous research reporting elevated NLR as a predictive factor for adverse maternal outcomes [26-28]. Collectively, these results highlight the potential of NLR as a clinically relevant, non-invasive biomarker for risk stratification and early diagnosis of PE.

Future investigations incorporating larger, multicenter cohorts and prospective study designs are warranted to validate the utility of NLR and other composite hematological indices, such as the platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), in the routine screening and monitoring of preeclampsia [29-33].

In recent years, the NLR has emerged as a crucial biomarker of systemic inflammation, with increased NLRs associated with worse clinical outcomes in various pathological conditions, including cardiovascular [34, 35]. This ratio represents an easily accessible and cost-effective indicator of inflammation, capturing the dynamic equilibrium between Neu-driven innate immune responses and Lym-mediated adaptive immunity.

In the context of PE, a growing body of research has offered compelling evidence that the NLR is closely linked to the condition's pathophysiology, highlighting its potential as both a diagnostic and prognostic marker [16, 17, 24]. Numerous studies have shown that patients with PE present considerably elevated NLRs, with severe cases typically exhibiting even higher levels, thereby underscoring the role of systemic inflammation in the progression of the disease.

Consistent with prior research, our study demonstrated a significant elevation in NLR levels among PE women, driven by increased neutrophil and decreased lymphocyte counts, reflecting a shift toward a pro-inflammatory immune profile. Even HP women showed moderately elevated NLRs compared to NP women, likely due to physiological immune adaptations during gestation. These findings reinforce the role of systemic inflammation in the pathogenesis of PE and support NLR as a sensitive marker of immune dysregulation. Altered leukocyte dynamics underscore the immunological complexity of maternal–fetal interactions in PE. Supporting evidence from studies by Kurtoglu et al. and Serin et al. similarly identified significantly higher NLRs in women with PE and severe PE, emphasizing its potential utility in clinical monitoring [15, 35].

In contrast to our findings, Yavuzcan et al. reported a statistically significant increase in the NLR in women with severe PE compared to healthy NP women [36]. In PE, immune dysregulation is marked by a shift from anti-inflammatory Tregs to pro-inflammatory Th17 cells, contributing to systemic inflammation, endothelial dysfunction, and placental pathology. This imbalance supports NLR as a marker of disrupted immune tolerance in PE [37]. Our findings further support the inflammatory basis of PE, evidenced by reduced lymphocyte counts and elevated NLR, reflecting impaired immune regulation and heightened neutrophil-driven inflammation. Although NLR correlated significantly with both systolic and diastolic blood pressure, the associations were weak, indicating that while inflammation contributes to hypertensive changes in PE, other mechanisms, such as endothelial dysfunction, oxidative stress, and placental ischemia, may play more dominant roles in blood pressure regulation [18, 28].

This study underscores the potential role of the neutro-

phil-to-lymphocyte ratio (NLR) as an inflammatory biomarker in PE. Women with PE exhibited. This study underscores the potential of the NLR as an inflammatory biomarker in PE. Women with PE showed significantly higher NLRs compared to both HP and NP women, indicating an amplified inflammatory response in PE. The ability of the NLR to effectively distinguish between non-pregnant and pregnant states, as demonstrated by ROC analysis, further supports its clinical relevance. Moreover, women with elevated NLRs faced a substantially increased risk of developing PE, reinforcing the link between systemic inflammation and PE pathogenesis. Based on these findings, the NLR may suggest that NLR could be a useful, low-cost adjunct for risk stratification in pregnant women. However, further prospective studies are warranted to validate its diagnostic utility and to explore its integration into predictive models for PE management.

Limitations

The retrospective design of the study may limit the ability to establish temporal relationships. Moreover, the analysis was conducted at a single center with a relatively small sample size, which could impact the generalizability of the findings. To confirm the clinical relevance of the NLR in PE, further prospective, multicenter studies with larger cohorts are recommended. The groups were not matched for gestational age or maternal age, both of which may influence NLR values. Although these variables were recorded and compared, residual confounding cannot be excluded.

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Ethics approval statement

This study was approved by the Directorate of 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.

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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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