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ORIGINAL RESEARCH

Association of Systemic Inflammatory Biomarkers (NLR, MLR, PLR, SII, SIRI) with Preeclampsia-Related Kidney Injury: A Retrospective Observational Study

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Background: Approximately 7–13% of pregnant women with preeclampsia (PE) develop acute kidney injury (AKI), which is one of the most serious complications of PE and is linked to long-term chronic kidney disease. This retrospective observational study investigated the association between inflammation indices and PE-related acute kidney injury (PE-AKI).

Methods: This retrospective study analyzed 4071 PE patients admitted between 2013 and 2023. Inflammatory indices, including neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), were derived from complete blood counts. Multivariate logistic regression assessed associations with PE-AKI risk, with nonlinear relationships characterized using restricted cubic spline models.

Results: Among 4071 patients with PE, 290 (7.13%) developed AKI. Multivariate analysis (Model 3) revealed significant positive associations between $\log_2$-transformed inflammatory indices and PE-AKI risk, with the highest odds ratios observed for MLR (OR = 6.02, 95% CI: 4.68–7.73; $P < 0.0001$) and NLR (OR = 3.93, 95% CI: 3.09–5.01; $P < 0.0001$). MLR demonstrated the strongest independent correlation with PE-AKI (highest tertile OR = 7.24, 95% CI: 4.75–11.02), followed by SIRI (OR = 5.78, 95% CI: 3.89–8.59). All indices (NLR, MLR, PLR, SII, SIRI) exhibited linear dose-response relationships with PE-AKI risk (P-overall <0.001 for each). Subgroup analyses further identified elevated MLR as a prominent risk factor in early-onset PE (gestational age ≤32 weeks; OR = 8.81, 95% CI: 4.91–17.10) and patients with complications (OR = 7.28, 95% CI: 5.23–10.32).

Conclusion: MLR and SIRI are positively associated with PE-AKI risk, particularly in early-onset and complicated cases. This first comprehensive assessment of five biomarkers supports clinical utility. Prospective validation is required, with focus on monocyte-mediated inflammatory mechanisms.

Keywords: preeclampsia, acute kidney injury, inflammation index, biomarkers

Introduction

Preeclampsia (PE), a hypertensive disorder unique to pregnancy, is responsible for nearly 14% of maternal mortality worldwide.[1] Acute kidney injury (AKI), a severe complication of PE, occurs in up to 15% of cases and is associated with adverse outcomes including prolonged renal dysfunction, chronic kidney disease (CKD), and elevated perinatal mortality.[2] The pathophysiology of PE-related AKI ((PE-AKI)) involves a complex interplay between hemodynamic alterations and inflammatory processes.[3] Notably, both systolic and diastolic blood pressure elevations contribute to renal injury through distinct mechanisms: sustained systolic hypertension induces glomerular endothelial stress, while elevated diastolic pressure compromises renal perfusion, particularly in the context of preexisting vascular dysfunction.[4] These hemodynamic changes coincide with systemic inflammation, creating a vicious cycle of renal impairment.[5] Despite mechanistic advances, early identification of high-risk patients remains challenging, underscoring the need for reliable biomarkers to predict and mitigate this complication.

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Current diagnostic approaches rely heavily on angiogenic markers – soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF) – and serum creatinine, which have several limitations.[6,7] While the sFlt-1/PlGF ratio shows good predictive value for PE onset, its utility for AKI prediction is limited by several factors: (1) delayed elevation following renal damage, (2) significant inter-assay variability, and (3) limited availability in resource-constrained settings.[8] In contrast, inflammatory biomarkers, including neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), offer distinct advantages: (1) they reflect upstream pathogenic processes preceding overt renal injury, (2) can be derived from routine complete blood counts without additional costs, and (3) demonstrate dynamic changes correlating with disease progression.[9] Particularly, the platelet-derived indices (PLR, SII) may provide unique insights into the thromboinflammatory component of PE-AKI, a dimension not captured by angiogenic markers alone.[10,11]

Emerging evidence underscores the clinical relevance of inflammatory indices across multiple disease states.[12,13] Elevated SII, NLR, and lymphocyte-to-monocyte ratio (LMR) exhibit linear associations with non-alcoholic fatty liver disease (NAFLD) risk, whereas PLR demonstrates nonlinear correlations.[14] Similarly, NLR outperforms other indices in predicting stroke-associated pneumonia and intensive care unit (ICU) admission in intracerebral hemorrhage patients.[15] These findings suggest that inflammatory markers may play a critical role in PE-related multi-organ injury, including AKI.

This pioneering hospital-based retrospective observational study investigates associations between systemic inflammatory biomarkers (NLR, MLR, PLR, SII, SIRI) and concurrent AKI in PE patients at Gansu Provincial Maternity and Child Health Care Hospital (2013–2023). Admission biomarker levels were analyzed to reflect real-world clinical decision points, addressing a key knowledge gap in the relationship between routine inflammatory indices and PE-AKI status.

The study's significance lies in its potential to identify accessible AKI screening tools for resource-limited settings. By establishing baseline biomarker AKI correlations, these findings may inform future development of rapid risk-stratification protocols. While retrospective observational designs cannot infer causality, this work provides essential preliminary data for mechanistic studies and prospective validation of inflammatory biomarkers in PE-AKI pathogenesis.

Methods

Design and Patients

This retrospective observational study examined hospitalized patients with PE who were admitted to the Department of Obstetrics and Gynecology between March 2013 and January 2023. Initially, 10,081 potential subjects were identified through the hospital's electronic medical records. Following an extensive search and application of strict inclusion/exclusion criteria, 4071 patients with confirmed PE diagnoses were ultimately included in our analysis (Figure 1). Patients were stratified based on the occurrence of acute kidney injury within 48 hours of admission, as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. The clinical baseline characteristics showed no significant differences between the study population and excluded PE patients, except for the prevalence of complications (Table S1).

The inclusion criteria were as follows: 1. The diagnosis of preeclampsia was made according to the American College of Obstetricians and Gynecologists (ACOG) clinical criteria.[16] According to these criteria, preeclampsia was diagnosed after the 20th week of pregnancy when blood pressure of ≥140 mmHg systolic and/or ≥90 mmHg diastolic at least in two measurements made 4h apart accompanied by one or more of the following: (1). Proteinuria; (2). Maternal organ dysfunction including: Renal insufficiency (serum creatinine concentrations ≥ 97 μmol/L); Impaired liver function (ALT or AST ≥ 70 U/L); pulmonary edema, microvascular disease, thrombocytopenia, impaired liver function, and peripheral severe organ involvement (visual impairment and headache). 2. the diagnosis of AKI,[17] defined by the Kidney Disease Improving Global Outcomes clinical practice guideline as an increase in serum creatinine levels of 26.5μmol/L within 48 hours, or 1.5 times from baseline within 48 hours within 7 days, or an accumulated 6-hour urine volume of 0.5mL/kg/h.

The exclusion criteria were as follows: (1) There were no other comorbidities or complications, such as multiple pregnancy, gestational diabetes mellitus, intrahepatic cholestasis of pregnancy, chronic kidney disease, renal dysfunction, chronic hypertension with PE, hematological disorders, thyroid disease, immune system diseases; (2) History of blood transfusion, transplantation, immunotherapy; (3) Alcohol, smoking and other adverse life history. (4) COVID-19 or another infectious diseases; (5) at the time of admission, there was insufficient clinical and laboratory data.

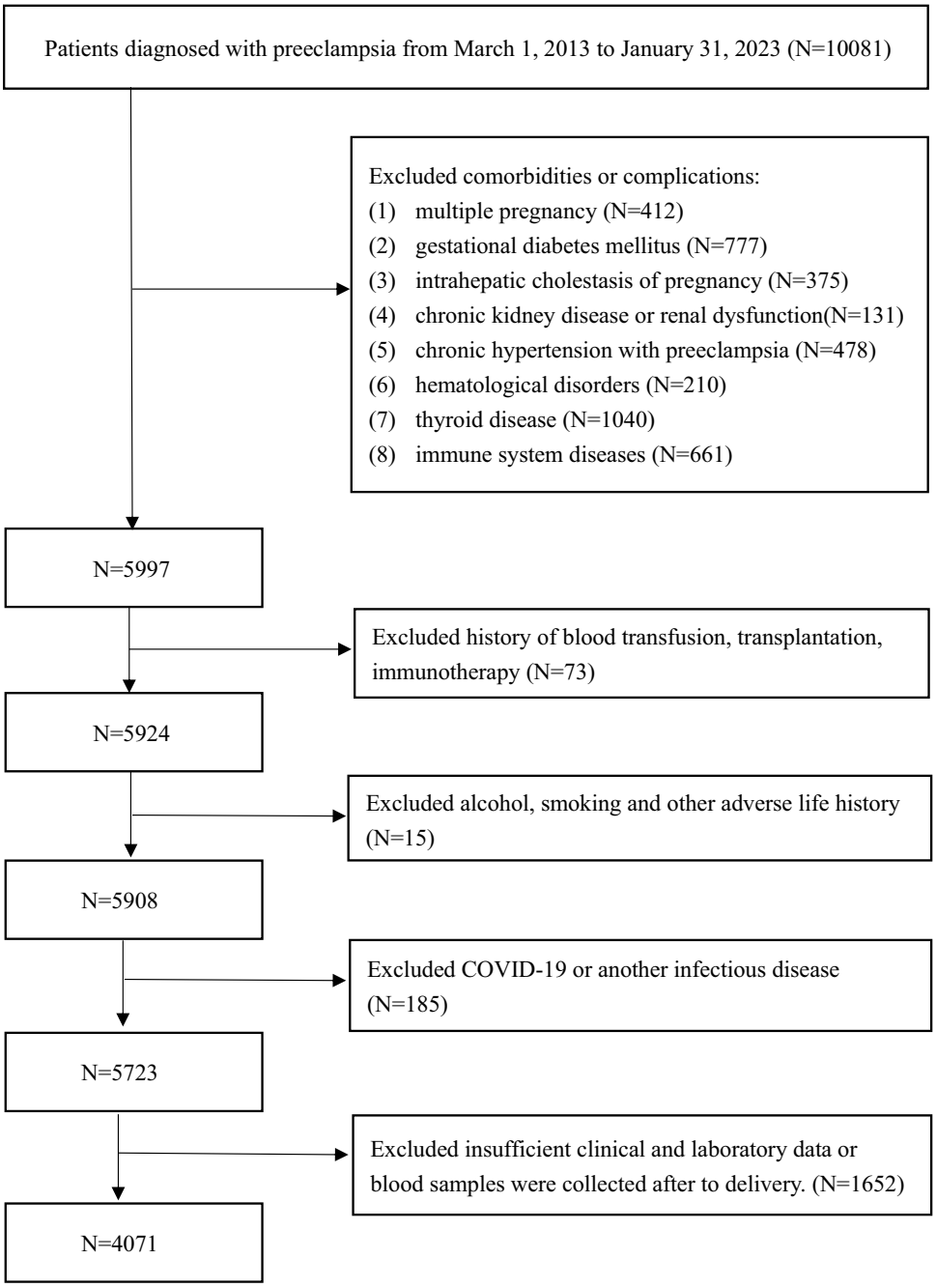

Figure 1 A flow diagram of patient enrollment.

Data Collection

Patient data were obtained from the electronic medical record system of Gansu Provincial Maternity and Child Care Hospital. All the peripheral blood samples used for clinical tests were collected within 24 hours after the patient's admission and before delivery. The comprehensive dataset encompassed: (1) demographic and clinical parameters, including age, body mass index (BMI), gestational age, gravida, parity, systolic blood pressure (SBP), diastolic blood pressure (DBP); (2) laboratory measurements including proteinuria, White blood cell (WBC), Platelet (PLT) count, neutrophil (Neu) count, lymphocyte (Lym) count, monocyte (Mon) counts, albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (Cr), blood urea nitrogen (BUN) and uric acid (UA) were collected. (3) the main maternal and fetal complications were as follows: HELLP (ie, hemolysis, elevated liver-enzyme level, and

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low platelet count), disseminated intravascular coagulation (DIC), eclampsia, left ventricular dysfunction, pulmonary edema, and placental abruption; oligohydramnios (ie, amniotic fluid index (AFI) <5 cm and 2-diameter pocket) and preterm birth (ie, delivery before 37 weeks of gestation).

Detection of Blood Markers

Blood cell counts (monocytes, lymphocytes, platelets, and neutrophils) were quantified using the SYSMEX-XN9000 automated hematology analyzer (Sysmex Corporation, Japan). Serum biochemical parameters (ALB, ALT, AST, Cr, BUN, and UA) were measured using the SYSMEX HISCL-5000 automated immunoassay system (Sysmex Corporation, Japan), with all assays undergoing daily quality control using manufacturer-provided calibrators and controls traceable to international standards.

Novel Inflammation Index

Five inflammatory indices were derived from complete blood count (CBC) results using standardized formulas: NLR, neutrophil-to-lymphocyte ratio (NLR = Neu/Lym), MLR, monocyte-to-lymphocyte ratio (MLR = Mon/Lym), PLR, platelet-to-lymphocyte ratio (PLR = PLT/Lym), SII, systemic immune-inflammation index (SII = [PLT × Neu]/Lym), and SIRI, systemic inflammatory response index (SIRI = [Neu × Mon]/Lym). This structured approach ensured consistent evaluation of both clinical and immunological parameters in the study cohort.

Statistical Analysis

All analyses were performed using R software (version 4.2.3; The R Foundation, http://www.R-project.org). Continuous variables were expressed as mean ± standard deviation or median (25th–75th percentiles), while categorical variables were presented as frequencies (n) and percentages (%). Continuous variables of inflammatory indices (NLR, MLR, PLR, SII, SIRI) were log2-transformed for linear regression analyses, while categorical analyses were performed using untransformed values categorized into tertiles (T1-T3). For continuous analyses, the base-2 logarithmic transformation[18] was implemented to: (1) normalize distributions of indices exhibiting wide numerical ranges (eg, platelet-to-lymphocyte ratio: 92.8–137.6; systemic immune-inflammation index: 587.8–941.2); (2) enable clinically interpretable effect estimates expressed as odds ratios (ORs) per doubling of biomarker levels; and (3) prevent attenuation of effect sizes inherent in raw-scale analyses of variables spanning multiple orders of magnitude. We employed multivariable logistic regression to evaluate the associations between inflammatory biomarkers (NLR, MLR, PLR, SII, SIRI) and PE-AKI risk. For sensitivity analyses, the biomarkers were analyzed as categorical variables using their original-scale values divided into tertiles (T1-T3), with the lowest tertile group (T1) serving as the reference category. Results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs), and trend tests were performed across tertiles. Three progressively adjusted models were constructed: a crude (unadjusted) model; Model 1, adjusted for age and BMI; Model 2, additionally adjusted for SBP and DBP; and Model 3, further adjusted for proteinuria, ALT, AST, ALB, and preterm birth status.

Nonlinear relationships were evaluated using restricted cubic spline (RCS) regression with 3 knots implemented via the "rms" package (version 6.2–0) in R software (v4.2.3), with visualization generated using "ggplot2" (version 3.3.5). The likelihood ratio test assessed nonlinearity (α=0.05), and when present, threshold effects were quantified through two-stage segmented regression analysis at statistically identified inflection points. The likelihood ratio test assessed nonlinearity, and when present, threshold effects were analyzed using two-stage segmented regression at inflection points. Interaction and subgroup analyses were conducted to evaluate effect modification by maternal characteristics (age, BMI), pregnancy factors (gestational age, parity), and clinical outcomes (preterm birth, complications). Biomarkers were analyzed both as continuous and categorical (tertiles) variables in these analyses. The robustness of findings was verified through sensitivity analyses, and a two-tailed *P*-value <0.05 was considered statistically significant.

Results

Participants Characteristics at Baseline

The patient enrollment flow diagram is illustrated in Figure 1. The study included 4071 patients with PE, of whom 290 (7.12%) developed AKI. Compared to the non-AKI group, patients with AKI exhibited significantly higher BMI (26.54 ± 2.04 vs 24.95 ± 2.89 kg/m², $P < 0.0001$), systolic blood pressure (SBP: 166.70 ± 11.70 vs 156.79 ± 6.35 mmHg, $P < 0.0001$), diastolic blood pressure (DBP: 104.80 ± 7.18 vs 100.18 ± 5.02 mmHg, $P < 0.0001$), and proteinuria levels (3.37 [2.11–4.90] vs 0.90 [0.42–1.86] g/24h, $P < 0.0001$). Notably, the AKI group demonstrated pronounced systemic inflammation, evidenced by elevated monocyte counts (0.59 ± 0.24 vs 0.49 ± 0.20 × 10^9/L, $P < 0.0001$), neutrophil counts (7.48 ± 2.42 vs 6.95 ± 2.29 × 10^9/L, $P < 0.001$), and reduced lymphocyte counts (1.31 ± 0.48 vs 1.70 ± 0.57 × 10^9/L, $P < 0.0001$). Consequently, all inflammatory indices (NLR, MLR, PLR, SII, SIRI) were significantly higher in the AKI group (all $P < 0.0001$) (Table 1 and Figure S1).

Table 1 Characteristics of Patients According to Non-AKI and AKI

Variable	Total (n=4071)	Non-AKI (n=3781)	AKI (n=290)	*p*-value
Age (years)	31.31 ± 5.01	31.34 ± 5.02	30.94 ± 4.91	0.19
BMI (kg/m^2)	25.06 ± 2.86	24.95 ± 2.89	26.54 ± 2.04	<0.0001
Gestational age (weeks)	35.62 ± 3.26	35.59 ± 3.27	35.94 ± 3.15	0.07
Gravida (times)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 2.5)	0.22
Parity (times)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.78
SBP (mmHg)	157.50 ± 7.33	156.79 ± 6.35	166.70 ± 11.70	<0.0001
DBP (mmHg)	100.51 ± 5.33	100.18 ± 5.02	104.80 ± 7.18	<0.0001
Proteinuria (g/24h)	0.91(0.44, 2.52)	0.90(0.42, 1.86)	3.37(2.11, 4.90)	<0.0001
WBC (×109/L)	10.58 ± 2.91	10.57 ± 2.91	10.72 ± 2.95	0.40
PLT (×109/L)	185.91 ± 68.73	186.72 ± 69.16	175.35 ± 61.92	<0.01
Mon (×109/L)	0.50 ± 0.20	0.49 ± 0.20	0.59 ± 0.24	<0.0001
Nue (×109/L)	6.99 ± 2.31	6.95 ± 2.29	7.48 ± 2.42	<0.001
Lym (×109/L)	1.67 ± 0.57	1.70 ± 0.57	1.31 ± 0.48	<0.0001
ALT (U/L)	15.00(10.10, 26.55)	15.00(10.10, 26.60)	14.65(9.70, 24.93)	0.52
AST (U/L)	23.20(17.70, 33.90)	23.10(17.60, 33.53)	23.30(18.03, 36.90)	0.97
ALB (g/L)	31.53 ± 5.60	31.52 ± 5.60	31.66 ± 5.55	0.69
Cr (μmol/L)	56.00(47.00, 67.00)	55.00(47.00, 64.00)	104.00(94.00, 134.00)	<0.0001
UA (μmol/L)	378.50 ± 101.72	378.52 ± 101.73	378.27 ± 101.78	0.97
BUN (mmol/L)	5.00 ± 2.32	4.99 ± 2.28	5.08 ± 2.70	0.56
NLR	4.60 ± 2.05	4.46 ± 1.88	6.43 ± 3.05	<0.0001
MLR	0.32 ± 0.15	0.31 ± 0.13	0.51 ± 0.28	<0.0001
PLR	122.22 ± 58.04	120.09 ± 55.79	150.01 ± 76.80	<0.0001
SII	746.22(512.91, 1066.66)	735.42(502.12, 1038.22)	947.19(651.11, 1458.72)	<0.0001
SIRI	1.94(1.28, 2.93)	1.88(1.26, 2.82)	3.14(2.12, 4.82)	<0.0001
Complication, n (%)				0.12
No	1668(40.97)	1536(40.62)	132(45.52)	
Yes	2403(59.03)	2245(59.38)	158(54.48)	
Eclampsia, n (%)				0.57
No	3958(97.22)	3674(97.17)	284(97.93)	
Yes	113(2.78)	107(2.83)	6(2.07)	
Placental abruption, n (%)				0.35
No	3926(96.44)	3643(96.35)	283(97.59)	
Yes	145(3.56)	138(3.65)	7(2.41)	
DIC, n (%)				0.12
No	3921(96.32)	3647(96.46)	274(94.48)	
Yes	150(3.68)	134(3.54)	16(5.52)	

(*Continued*)

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Table 1 (Continued).

Variable	Total (n=4071)	Non-AKI (n=3781)	AKI (n=290)	*p*-value
HELLP, n (%)				0.56
No	3934(96.63)	3656(96.69)	278(95.86)	
Yes	137(3.37)	125(3.31)	12(4.14)	
Pulmonary edema, n (%)				0.62
No	4040(99.24)	3751(99.21)	289(99.66)	
Yes	31(0.76)	30(0.79)	1(0.34)	
Left ventricular dysfunction, n (%)				0.80
No	3839(94.30)	3567(94.34)	272(93.79)	
Yes	232(5.70)	214(5.66)	18(6.21)	
Oligohydramnios, n (%)				0.78
No	3840(94.33)	3568(94.37)	272(93.79)	
Yes	231(5.67)	213(5.63)	18(6.21)	
Preterm birth, n (%)				0.02
No	1948(47.85)	1790(47.34)	158(54.48)	
Yes	2123(52.15)	1991(52.66)	132(45.52)	

Abbreviations: AKI, acute kidney injury; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, White blood cell; Mon, monocyte; Neu, neutrophil; Lym, lymphocyte; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; Cr, creatinine; UA, uric acid; BUN, blood urea nitrogen; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, Systemic Immune Inflammatory Index; SIRI, Systemic Inflammatory Response Index; HELLP, Hemolysis, Elevated Liver enzymes, Low Platelet; DIC, disseminated intravascular coagulation.

While most complications (eg, eclampsia, DIC, and HELLP syndrome) showed no significant intergroup differences, preterm birth rates were notably lower in AKI patients (45.52% vs 52.66%, p=0.02) (Table 1 and Figure S2), suggesting that the observed systemic inflammatory markers (NLR, MLR, PLR, SII, and SIRI) are strongly associated with AKI development in PE and may serve as valuable predictors for early risk stratification.

Association of Inflammation Index (NLR, MLR, PLR, SII, SIRI) with PE-AKI Risk

Table 2 and Figure S3 present the relationship between NLR, MLR, PLR, SII, SIRI and risk of PE-AKI. We constructed three models by adjusting for different confounding variables to evaluate the relationship between NLR, MLR, PLR, SII, SIRI and PE-AKI risk. Multivariable logistic regression analyses revealed significant associations between systemic inflammatory biomarkers and PE-AKI risk across progressively adjusted models.

Table 2 The Relationship Between NLR, MLR, PLR, SII, SIRI and the Risk of PE-AKI

Inflammation Indices	Crude Model		Model 1		Model 2		Model 3	
	95% CI	P	95% CI	P	95% CI	P	95% CI	P
NLR (log_2-NLR)	4.08(3.29, 5.05)	<0.0001	4.10(3.30, 5.10)	<0.0001	3.98(3.13, 5.05)	<0.0001	3.93(3.09, 5.01)	<0.0001
NLR (Tertile)								
T1≤ 3.48	Reference		Reference		Reference		Reference	
T2 (3.48, 5.05)	2.15(1.45, 3.20)	<0.001	2.13(1.43, 3.16)	<0.001	2.04(1.32, 3.14)	0.001	2.09(1.35, 3.24)	<0.001
T3 > 5.05	5.09(3.55, 7.29)	<0.0001	5.04(3.51, 7.24)	<0.0001	5.02(3.38, 7.45)	<0.0001	5.10(3.42, 7.61)	<0.0001
p for trend		<0.0001		<0.0001		<0.0001		<0.0001
MLR (log_2-NLR)	6.06(4.85, 7.57)	<0.0001	6.09(4.86, 7.64)	<0.0001	6.08(4.75, 7.79)	<0.0001	6.02(4.68, 7.73)	<0.0001
MLR (Tertile)								
T1 ≤ 0.25	Reference		Reference		Reference		Reference	
T2 (0.25, 0.35)	2.48(1.62, 3.79)	<0.0001	2.41(1.57, 3.70)	<0.0001	2.45(1.54, 3.90)	<0.001	2.34(1.47, 3.72)	<0.001
T3 > 0.35	6.98(4.76, 10.24)	<0.0001	7.12(4.84, 10.47)	<0.0001	7.53(4.95, 11.47)	<0.0001	7.24(4.75, 11.02)	<0.0001
p for trend		<0.0001		<0.0001		<0.0001		<0.0001

(*Continued*)

Table 2 (Continued).

Inflammation Indices	Crude Model		Model 1		Model 2		Model 3	
	95% CI	P	95% CI	P	95% CI	P	95% CI	P
PLR (log_2-NLR)	1.92(1.59, 2.31)	<0.0001	1.90(1.58, 2.30)	<0.0001	2.16(1.76, 2.66)	<0.0001	2.32(1.87, 2.87)	<0.0001
PLR (Tertile)								
T1 ≤ 92.82	Reference		Reference		Reference		Reference	
T2 (92.82, 137.64)	1.23(0.88, 1.72)	0.230	1.28(0.91, 1.80)	0.150	1.44(0.98, 2.11)	0.06	1.55(1.05, 2.29)	0.030
T3 > 137.64	2.40(1.77, 3.25)	<0.0001	2.38(1.75, 3.23)	<0.0001	2.90(2.05, 4.09)	<0.0001	3.25(2.27, 4.65)	<0.0001
p for trend		<0.0001		<0.0001		<0.0001		<0.0001
SII (log_2-NLR)	1.90(1.62, 2.22)	<0.0001	1.90(1.62, 2.23)	<0.0001	2.02(1.70, 2.41)	<0.0001	2.10(1.76, 2.51)	<0.0001
SII (Tertile)								
T1 ≤ 587.77	Reference		Reference		Reference		Reference	
T2 (587.77, 941.16)	1.52(1.08, 2.15)	0.020	1.53(1.08, 2.17)	0.020	1.72(1.17, 2.53)	0.01	1.87(1.27, 2.78)	0.002
T3 > 941.16	2.79(2.04, 3.83)	<0.0001	2.83(2.06, 3.89)	<0.0001	3.35(2.34, 4.78)	<0.0001	3.67(2.54, 5.31)	<0.0001
p for trend		<0.0001		<0.0001		<0.0001		<0.0001
SIRI (log_2-NLR)	2.83(2.44, 3.29)	<0.0001	2.87(2.46, 3.34)	<0.0001	2.89(2.44, 3.42)	<0.0001	2.86(2.41, 3.40)	<0.0001
SIRI (Tertile)								
T1 ≤ 1.48	Reference		Reference		Reference		Reference	
T2 (1.48, 2.52)	1.62(1.07, 2.46)	0.020	1.60(1.06, 2.43)	0.030	1.59(1.01, 2.50)	0.05	1.50(0.95, 2.37)	0.080
T3 > 2.52	5.72(4.00, 8.17)	<0.0001	5.77(4.03, 8.27)	<0.0001	6.01(4.05, 8.91)	<0.0001	5.78(3.89, 8.59)	<0.0001
p for trend		<0.0001		<0.0001		<0.0001		<0.0001

Notes: Crude model: Unadjusted; Model 1: age, BMI; model 2: age, BMI, SBP, DBP; model 3: age, BMI, SBP, DBP, proteinuria, ALT, AST, ALB, preterm birth.
Abbreviations: OR, Odd ratio; 95% CI, 95% confidence interval; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, Systemic Immune Inflammatory Index; SIRI, Systemic Inflammatory Response Index.

The NLR demonstrated a strong positive association with PE-AKI risk. In the fully adjusted model (Model 3), each log_2-unit increase in NLR was associated with a 3.93-fold elevation in PE-AKI risk (OR = 3.93, 95% CI: 3.09–5.01, $P < 0.0001$). When analyzed categorically by tertiles in the sensitivity analysis, the highest NLR tertile (T3) showed a 5.10-fold increased risk compared to the lowest tertile (T1) (OR = 5.10, 95% CI: 3.42–7.61, $P < 0.0001$). Similarly, MLR exhibited a relatively stronger association compared to other biomarkers. Log_2-transformed MLR values were associated with a 6.02-fold risk increase (OR = 6.02, 95% CI: 4.68–7.73, $P < 0.0001$), with the highest tertile demonstrating a 7.24-fold elevated risk versus the lowest (OR = 7.24, 95% CI: 4.75–11.02, $P < 0.0001$), highlighting MLR's potential as a screening tool for early ICU referral. PLR also showed significant associations, with the highest tertile having a 3.25-fold increased risk (OR = 3.25, 95% CI: 2.27–4.65, $P < 0.0001$). Among composite indices, both SII (T3 OR = 3.67, 95% CI: 2.54–5.31) and SIRI (T3 OR = 5.78, 95% CI: 3.89–8.59) demonstrated robust associations with PE-AKI risk (both $P < 0.0001$).

These associations remained statistically significant after adjustment for age, body mass index, blood pressure, proteinuria, ALT, AST, ALB and preterm birth status. Notably, MLR and NLR emerged as the strongest predictive biomarkers (P trend < 0.0001).

Dose-Response of Inflammation Index (NLR, MLR, PLR, SII, SIRI) and PE-AKI Risk

To validate the robustness of our findings, we examined potential nonlinear associations between systemic inflammatory biomarkers (NLR, MLR, PLR, SII, and SIRI) and PE-AKI risk using restricted cubic spline (RCS) analyses. The RCS regression analysis revealed significant linear dose-response relationships between all evaluated inflammatory biomarkers (NLR, MLR, PLR, SII, and SIRI) and PE-AKI risk in the fully adjusted model (Model3) (all P-overall <0.001; Figure 2). While visual inspection suggested potential nonlinear patterns at higher values of PLR (200–600) and other indices, formal testing confirmed predominantly linear associations (P-nonlinear=0.758 for NLR, 0.394 for PLR, 0.4476 for MLR, 0.198 for SII, and 0.231 for SIRI). These findings demonstrate progressive increases in PE-AKI risk across biomarker concentrations without evidence of threshold effects or biological plateaus, supporting their use as continuous predictors in risk stratification models. Relatively strong linear gradients were observed for NLR and SIRI, suggesting their potential value for clinical risk assessment.

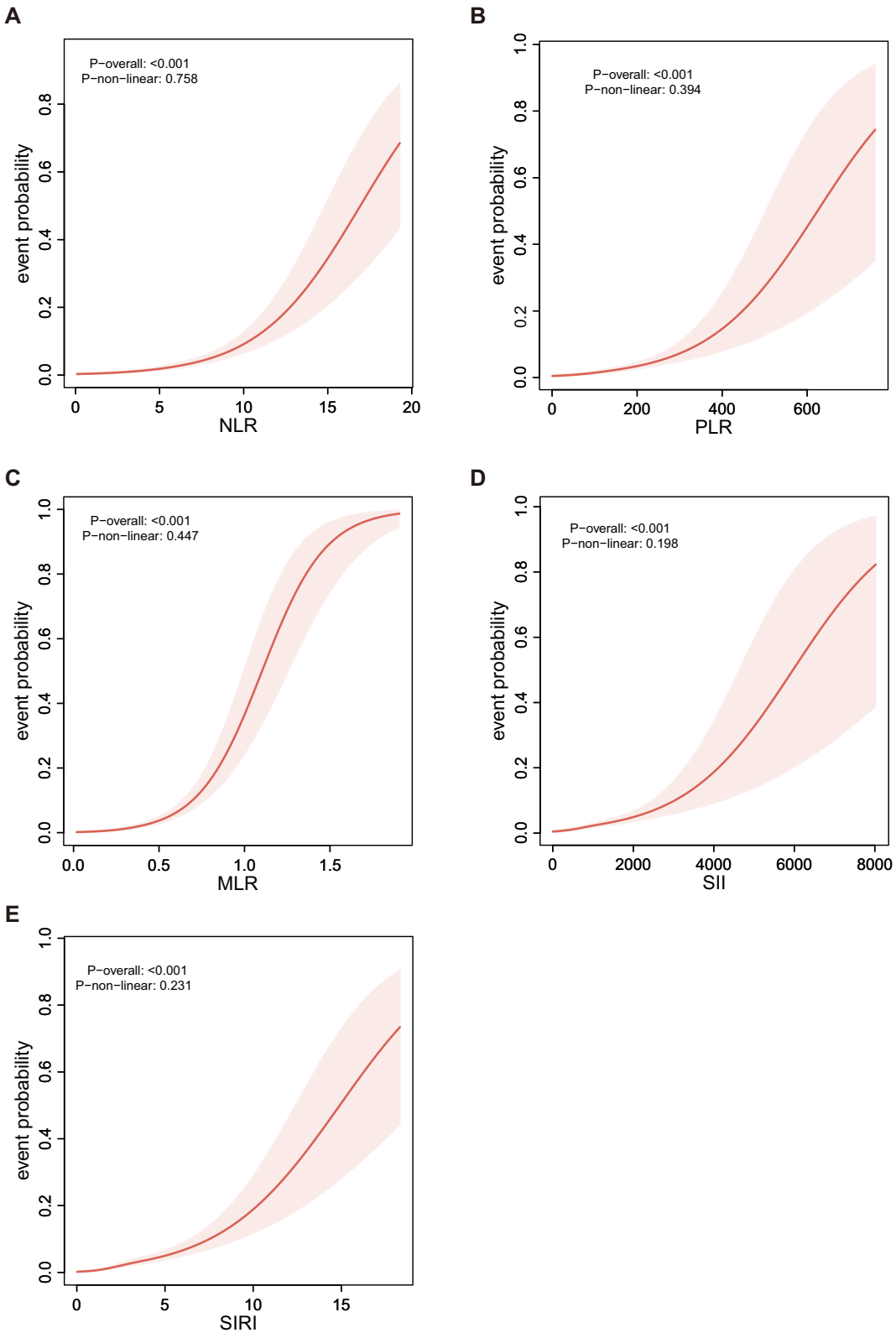

Figure 2 Dose-response of systemic inflammatory biomarkers (NLR, MLR, PLR, SII, SIRI) and PE-AKI risk. (**A**) Dose-response of NLR and PE-AKI. (**B**) Dose-response of MLR and PE-AKI. (**C**) Dose-response of PLR and PE-AKI. (**D**) Dose-response of SII and PE-AKI. (**E**) Dose-response of SIRI and PE-AKI.
Notes: adjusted (model 3): age, BMI, SBP, DBP, proteinuria, ALT, AST, ALB, preterm birth.
Abbreviations: NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, Systemic Immune Inflammatory Index; SIRI, Systemic Inflammatory Response Index.

Association of Inflammation Index (NLR, MLR, PLR, SII, SIRI) with PE-AKI Risk in Subgroup

The subgroup analyses in Table 3 revealed significant associations between systemic inflammatory biomarkers (NLR, MLR, PLR, SII, and SIRI) and PE-AKI risk, with notable variations across demographic and clinical subgroups. In women with preterm birth (≤32 weeks), inflammatory indices showed markedly stronger associations, with MLR demonstrating an 8.8-fold increased PE-AKI risk (OR 8.81, 95% CI 4.90–17.10) and SIRI showing a 4.7-fold risk elevation (OR 4.70, 95% CI 3.00–7.77), suggesting preterm PE-AKI may represent a distinct inflammatory endotype with monocyte-dominated pathogenesis. Similarly, women with obstetric complications exhibited nearly doubled MLR association magnitude (OR 7.27 vs 4.50 in uncomplicated cases) and 45% greater SIRI predictive capacity (OR 3.29 vs 2.27), implying inflammatory kidney injury may drive multiorgan dysfunction in severe PE. Notably, younger women (≤30 years) displayed heightened inflammatory susceptibility, with NLR and MLR showing 5.4- and 7.4-fold risk increases, respectively, challenging assumptions about age-related risk profiles. In contrast, associations remained stable across gravidity, parity and normal BMI subgroups. These findings demonstrate that PE-AKI comprises biologically distinct subsets with varying inflammatory contributions, where MLR/SIRI may optimize early detection in high-risk preterm cases, younger women require intensified inflammatory monitoring despite lower baseline risk, and complicated PE cases could benefit most from targeted anti-inflammatory strategies.

Discussion

This study investigated the association between systemic inflammatory biomarkers (NLR, MLR, PLR, SII, and SIRI) and PE-AKI. Following $\log_2$ transformation of inflammatory indices, significant positive correlations were observed between elevated biomarker levels and increased PE-AKI risk, with particularly robust associations noted for NLR, MLR, and SIRI. Restricted cubic spline analysis revealed clear linear dose-response relationships between these inflammatory indices and AKI risk. Notably, effect modification by disease severity was demonstrated, with substantially strengthened associations in preterm PE cases (gestational age ≤32 weeks). The odds ratio for NLR increased from 3.61 to 5.86 (P-interaction=0.048) in this subgroup, suggesting that these biomarkers reflect both renal injury risk and overall disease severity. These findings support recent proposals to incorporate inflammatory markers into PE subclassification systems.[19,20] In conclusion, our findings suggest that NLR, MLR, PLR, SII, and SIRI are strongly associated with PE-AKI risk. To our knowledge, this represents the first comprehensive evaluation of systemic inflammatory indices in PE-AKI.

The systemic inflammatory response of the maternal body plays a key role in the pathogenesis and progression of PE-AKI,[21,22] a pathological and physiological association that has also been observed in our study. Our findings not only confirm the initial hypothesis that systemic inflammatory markers such as NLR, MLR, PLR, SII, and SIRI are significantly positively correlated with PE-AKI. Among these biomarkers, MLR demonstrated the strongest predictive capacity, followed by SIRI, NLR, PLR, and SII in descending order. These findings corroborate the work of Nagashima et al regarding the crucial involvement of monocytes in placental inflammation,[23] suggesting that monocyte-mediated immune responses may constitute a central mechanism in PE-AKI.[24] Stratified analyses revealed significant clinical heterogeneity. Notably, early-onset PE cases (≤32 weeks of gestation) exhibited significantly higher odds ratios for all inflammatory markers compared to late-onset cases, consistent with Mahmoud et al's characterization of early-onset PE as having more pronounced inflammatory features.[25] Of particular clinical relevance, MLR showed enhanced predictive performance in complicated cases, while SIRI demonstrated stronger associations in obese subgroups. These differential patterns suggest that distinct inflammatory markers may reflect varying pathophysiological subtypes of PE-AKI, thereby providing a scientific foundation for developing personalized risk assessment strategies.

Dose-response analyses further validated the clinical utility of these inflammatory markers. Nonlinear tests revealed approximately linear relationships between NLR, MLR, PLR, SII, and SIRI and PE-AKI risk, suggesting their potential suitability as continuous variables in risk prediction models. Tertile analysis revealed consistent dose-response relationships, with MLR-T3 exhibiting a markedly strong risk association, followed by SIRI-T3, NLR-T3, SII-T3, and PLR-T3. These findings align with Zeynep et al's research on the predictive value of inflammatory markers.[26] Importantly, our study extends current knowledge by providing the first systematic evaluation of these biomarkers' predictive

Table 3 The Relationship Between NLR, MLR, PLR, SII, SIRI and PE-AKI Risk in Different Subgroups

Characteristic	NLR		MLR		PLR		SII		SIRI	
	OR (95% CI)	*p-int.*	OR (95% CI)	*p-int*	OR (95% CI)	*p-int*	OR (95% CI)	*p-int*	OR (95% CI)	*p-int*
Age, n (%)		0.059		0.218		0.313		0.200		0.173
≤30	5.41(3.72, 8.01)		7.40(5.11, 10.97)		2.81(2.06, 3.89)		2.54(1.95, 3.36)		3.37(2.61, 4.41)	
>30	3.21(2.36, 4.43)		5.28(3.80, 7.44)		2.05(1.55, 2.75)		1.87(1.48, 2.38)		2.58(2.06, 3.26)	
BMI, n (%)		0.178		0.143		0.570		0.275		0.047
≤24	2.46(1.35, 4.61)		3.70(1.95, 7.17)		1.76(1.00, 3.22)		1.52(0.95, 2.47)		1.87(1.23, 2.87)	
>24	4.17(3.17, 5.54)		6.25(4.69, 8.44)		2.23(1.77, 2.83)		2.11(1.73, 2.59)		3.05(2.50, 3.74)	
Gestational age, n (%)		0.048		0.069		0.012		0.003		0.004
≤32	5.85(3.21, 11.33)		8.81(4.90, 17.10)		3.78(2.15, 7.06)		3.48(2.17, 5.82)		4.70(3.00, 7.77)	
>32	3.61(2.78, 4.71)		5.45(4.16, 7.22)		2.14(1.71, 2.71)		1.93(1.60, 2.35)		2.60(2.17, 3.14)	
Gravida, n (%)		0.920		0.877		0.312		0.7		0.79
≤2	4.03(3.07, 5.32)		6.03(4.57, 8.05)		2.25(1.78, 2.86)		2.10(1.72, 2.58)		2.91(2.40, 3.56)	
>2	3.75(2.28, 6.30)		6.24(3.70, 11.00)		2.83(1.79, 4.61)		2.21(1.53, 3.24)		2.75(1.94, 3.97)	
Parity, n (%)		0.513		0.846		0.413		0.237		0.972
≤2	3.88(3.04, 5.01)		6.07(4.70, 7.91)		2.31(1.86, 2.89)		2.07(1.72, 2.49)		2.86(2.40, 3.43)	
>2	5.13(2.17, 13.72)		5.55(2.25, 15.62)		4.25(1.92, 10.37)		3.63(1.89, 7.63)		2.80(1.57, 5.36)	
Preterm birth, n (%)		0.125		0.01		0.023		0.034		0.027
No	3.15(2.25, 4.48)		4.46(3.16, 6.37)		1.92(1.44, 2.59)		1.78(1.39, 2.29)		2.37(1.87, 3.03)	
Yes	4.50(3.20, 6.44)		8.24(5.74, 12.12)		2.76(2.02, 3.82)		2.41(1.86, 3.16)		3.40(2.66, 4.40)	
Complication, n (%)		0.126		0.049		0.029		0.014		0.037
No	3.03(2.10, 4.44)		4.50(3.08, 6.67)		1.77(1.28, 2.48)		1.58(1.21, 2.09)		2.27(1.75, 2.97)	
Yes	4.48(3.26, 6.24)		7.27(5.23, 10.32)		2.63(1.99, 3.52)		2.42(1.91, 3.09)		3.29(2.62, 4.17)	

Notes: adjusted for age, BMI, SBP, DBP, proteinuria, ALT, AST, ALB, preterm birth.

Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval; *P*-int, P-value for interaction; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, Systemic Immune Inflammatory Index; SIRI, Systemic Inflammatory Response Index.

performance and clinical applicability specifically in the PE-AKI population, through comprehensive multi-model adjustments and stratified analyses.

Our comprehensive analyses revealed significant differences in the strength of association between various inflammatory biomarkers and PE-AKI risk. A clear hierarchical pattern of association strengths was observed in the highest tertile (T3): MLR demonstrated markedly strong associations, followed by SIRI and NLR, then SII and PLR. Notably, among all biomarkers examined, MLR exhibited particularly robust associations, especially in high-risk clinical subgroups including preterm deliveries and complicated cases. These strong associations remained consistent across multiple adjusted models and displayed clear dose-response relationships. While SIRI and NLR also showed substantial associations with PE-AKI risk, their effect sizes were slightly less pronounced than MLR. In contrast, the platelet-incorporating indices (SII and PLR) demonstrated relatively weaker, yet still statistically significant, associations.

These differential strengths of association likely reflect distinct underlying pathophysiological mechanisms. The superior predictive performance of MLR may stem from its unique pathophysiological significance. As key effector cells of innate immunity, monocytes can differentiate into pro-inflammatory M1 macrophages that directly damage glomerular endothelium while simultaneously activating the NOD-like receptor family, pyrin domain containing 3 (NLRP3) inflammasome through cytokines like Interleukin-1 beta (IL-1β).[27] Our findings support this dual mechanism: MLR showed significant interactions with both preterm birth and complications, reflecting its close association with placental inflammation. Notably, MLR remained highly significant after adjusting for blood pressure and proteinuria, suggesting its potential direct involvement in renal injury independent of traditional risk factors. Meanwhile, SIRI's predictive advantage stems from its comprehensive assessment of systemic inflammation, incorporating neutrophil, monocyte, and lymphocyte counts to reflect both innate immune activation and regulatory dysfunction.[28,29] This systemic inflammation may induce renal injury through multiple pathways: (1) activated neutrophils release reactive oxygen species (ROS) and proteolytic enzymes that directly damage glomerular endothelial cells;[30] (2) monocyte-derived macrophages infiltrate renal tissue, secreting pro-fibrotic factors (eg, Transforming Growth Factor-beta [TGF-β]) that promote pathological changes.[31,32] These findings raise new scientific questions. First, while PLR showed weaker overall associations, its OR increased significantly in the ≤32 weeks gestation subgroup, suggesting platelet activation may play a distinct role in early-onset PE-AKI. Second, SIRI demonstrated enhanced predictive accuracy in younger patients (≤30 years), potentially reflecting age-related immunomodulatory differences that warrant further investigation.

Our results demonstrate certain discrepancies with previous reports. For instance, Dominique et al[33] and Betül et al[34] identified NLR and PLR as superior predictors for PE. Several factors may account for these differences: (1) population heterogeneity, including racial variations, gestational age distributions, and disease severity spectra; (2) variations in biomarker measurement timing; and (3) most importantly, PE-AKI represents a specific target organ injury whose pathogenesis likely differs from generalized preeclampsia, involving more pronounced local renal inflammation, microcirculatory disturbances, and endothelial dysfunction.[24] These findings emphasize that clinical evaluation of inflammatory markers' predictive value must carefully consider specific clinical phenotypes and target organ injury characteristics. For clinical translation, we recommend developing a weighted risk-stratification algorithm integrating MLR, SIRI, and key clinical parameters (eg, gestational age, BMI). This integrated approach may enhance predictive accuracy while preserving clinical utility across varied healthcare environments. Future studies should establish population-specific thresholds and validate the model's performance in prospective cohorts, with particular attention to high-risk subgroups identified in our study (eg, early-onset PE, obese patients).

Building on our findings, we propose developing an integrated PE-AKI risk prediction model combining MLR – given its strong predictive performance and cost-effectiveness - with clinical parameters (eg, blood pressure, proteinuria) and established biomarkers (eg, PlGF) to enhance early risk stratification. The differential biomarker performance across subgroups suggests potential for tailored approaches: MLR-based monitoring for preterm delivery risk, SIRI-focused assessment for obese populations, and combined NLR/angiogenic marker evaluation for hypertensive patients. Notably, the association between elevated MLR and inflammatory pathways supports exploring targeted surveillance protocols for patients with persistent MLR elevation, including potential use of anti-inflammatory agents (eg, low-dose heparin)[27] in high-risk cases and dynamic monitoring strategies guided by biomarker trend. These applications leverage MLR's

advantages as a routinely available biomarker while addressing the need for personalized risk assessment, with initial validation recommended in high-volume obstetric centers prior to adaptation for resource-limited settings.

This study has several limitations: (1) The retrospective single-center design inherently limits causal inference and generalizability, as institutional-specific practices and unmeasured residual confounding factors (including comorbidities, dietary patterns, and other lifestyle factors) may influence results; (2) Some subgroup analyses were constrained by small sample sizes, potentially reducing the statistical power of interaction tests; (3) The absence of specific inflammatory cytokine measurements and renal tissue analyses restricted mechanistic interpretation of the observed associations; and (4) The lack of external validation in diverse populations raises questions about broader applicability. Future multicenter prospective cohort studies with standardized protocols are needed to validate these inflammatory markers' predictive value across different clinical settings, while incorporating advanced techniques like single-cell sequencing and multiplex cytokine profiling to elucidate the molecular pathways linking systemic inflammation with renal injury in PE.

Conclusion

In summary, this study demonstrates significant associations between inflammatory biomarkers (NLR, MLR, PLR, SII, and SIRI) and PE-AKI risk. Elevated MLR and SIRI were identified as particularly strong predictors of increased PE-AKI risk. Furthermore, all inflammatory indices exhibited significant linear dose-response relationships, supporting their utility as continuous variables in risk stratification models. Importantly, we identified key population-specific variations, with MLR showing enhanced strengths of association in preterm and complicated pregnancies. While these findings demonstrate robust associations, residual confounding by unmeasured comorbidities and the single-center design necessitate validation through multicenter prospective studies. Future research should: (1) establish optimal intervention thresholds, (2) elucidate monocyte-mediated pathogenic mechanisms, and (3) evaluate these biomarkers' performance in diverse populations.

Data Sharing Statement

The data presented in this study are available from the corresponding author on request.

Ethics Approval and Consent to Participate

Informed consent was waived due to the retrospective property of the study. All patient data were confidential and handled in compliance with ethical guidelines. Ethical approval was obtained from the ethics committee of Gansu provincial maternity and child-care Hospital (approval number: [2023] GSFY Ethics Review No. (5)).

Author Contributions

All authors significantly contributed to the conception, study design, execution, data acquisition, analysis and interpretation; drafted, revised or critically reviewed the article; approved the version to be published; agreed on the journal for submission of the article; and are accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

References

1. Shibin C, Wendy N, Satyan K, Sukanta J, Lauren RR, Surendra S. Evidence for complement activation in preeclampsia placenta and its presence in circulation. *Am J Reprod Immunol*. 2025;93(5):e70076. doi:10.1111/aji.70076
2. Yawovi MT, Latame KA, Ayoko K, et al. Associated factors of acute kidney injury during severe pre-eclampsia in Togo from 2019 to 2022: a case series study. *Nephrol Ther*. 2025;20(7):632–639.

3. Marie H, Marion DI, Vincent L, Olivier M. A systematic review on the determinants of long-term kidney sequelae after hypertensive diseases of pregnancy. *Acta Obstet Gynecol Scand*. 2025;104(7):1254–1273. doi:10.1111/aogs.15127
4. Ting-Wei K, Chin-Chou H. Blood pressure management and renal protection: revisiting hypertensive nephropathy. *J Chin Med Assoc*. 2021;84 (10):911–916. doi:10.1097/JCMA.0000000000000600
5. Ghada A, Duaa MB, Abdullah A, Reem A, Raghad A, Nedaa B. Incidence and clinical outcomes of pregnancy-related acute kidney injury (PrAKI) in preeclampsia-complicated pregnancies in Saudi Arabia: a single-center experience. *J Nephrol*. 2025;38(3):1093–1100. doi:10.1007/s40620-025-02258-w
6. Fernanda BR, Carlos MK. Acute kidney injury requiring dialysis in pregnancy and postpartum: case series and literature review. *Eur J Obstet Gynecol Reprod Biol*. 2024;302(11):33–37. doi:10.1016/j.ejogrb.2024.08.033
7. Marianna D, Roisin CT, Clare LG, Jiamiao H, Kamlesh K, Bee Kang T. Blood biomarkers to predict the onset of pre-eclampsia: a systematic review and meta-analysis. *Heliyon*. 2022;8(11):e11226. doi:10.1016/j.heliyon.2022.e11226
8. Jamie S, Shauna-Kay S, Ashley G, et al. Acute kidney injury during pregnancy leads to increased sFlt-1 and sEng and decreased renal T regulatory cells in pregnant rats with HELLP syndrome. *Biol Sex Differ*. 2020;11(1):54. doi:10.1186/s13293-020-00331-6
9. Qitong G, Meiling C, Yihang Y, et al. Causal association of metabolic syndrome with chronic kidney disease progression: a Mendelian randomization study. *Pediatr Discov*. 2025;2(4):e93.
10. Yasin Alper Y. Effectiveness of systemic inflammation response index (SIRI) neutrophil-lymphocyte ratio (NLR), derived neutrophil-lymphocyte ratio (dNLR), and systemic immune inflammation index (SII) for predicting prognosis of acute diverticulitis. *Updates Surg*. 2025:1–7.
11. Songfeng Z, Hongyi L, Hailong Z, Yongkai Q, Jiayue D, Aihua L. Systemic inflammation mediates the association between blood trihalomethane concentrations and cardiovascular disease in U.S. individuals over 45: insights from NHANES 2005-2012. *Cardiovasc Toxicol*. 2025;25 (7):1055–1066. doi:10.1007/s12012-025-10008-4
12. Elise L, Maxime D, Véronique D, et al. Comparing neutrophil-to-lymphocyte ratio (NLR), absolute neutrophil count (ANC) and derived NLR as predictive biomarkers in first-line immunotherapy for non-small cell lung cancer: a retrospective study. *Transl Lung Cancer Res*. 2025;14 (4):1212–1230. doi:10.21037/tlcr-24-808
13. Mao T, Zhao X, Jiang K, et al. Preoperative SII can predict postoperative recurrence and serious complications in patients with hepatolithiasis. *J Inflamm Res*. 2025;18:3321–3331. doi:10.2147/JIR.S506442
14. Yunyi Y, Xiaoli H, Shufa T, et al. The association between immunoinflammatory biomarkers NLR, PLR, LMR and nonalcoholic fatty liver disease: a systematic review and meta-analysis. *Clin Exp Med*. 2025;25(1):39. doi:10.1007/s10238-024-01539-1
15. Lixia G, Xudong C, Luyao C, Huandong L. Neutrophil-to-lymphocyte ratio as a predictor of prognosis in patients with spontaneous intracerebral hemorrhage: a systematic review and meta-analysis. *Front Neurol*. 2025;16:1553263. doi:10.3389/fneur.2025.1553263
16. Anisha RB, Johannes JD. Evaluation of the clinical impact of the revised ISSHP and ACOG definitions on preeclampsia. *Pregnancy Hypertens*. 2019;19:206–211. doi:10.1016/j.preghy.2019.11.011
17. Adeera L, Sofia BA, Juan Jesus C, et al. Executive summary of the KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease: known knowns and known unknowns. *Kidney Int*. 2024;105(4):684–701. doi:10.1016/j.kint.2023.10.016
18. Jesse F, Rikje R, Marlies M, et al. The systemic immune-inflammation index is associated with an increased risk of incident cancer-A population-based cohort study. *Int J Cancer*. 2019;146(3):692–698. doi:10.1002/ijc.32303
19. Tifeng X, Liping H, Ruiting Y, et al. Maternal neutrophil inflammation markers predict bronchopulmonary dysplasia in preeclamptic pregnancies. *Am J Reprod Immunol*. 2025;93(5):e70078. doi:10.1111/aji.70078
20. Rayan Abdelraheem M, Ibrahim Abdelrhim A. Role of neutrophil / lymphocyte ratio, uric acid / albumin ratio and uric acid / creatinine ratio as predictors to severity of preeclampsia. *BMC Pregnancy Childbirth*. 2023;23(1):763. doi:10.1186/s12884-023-06083-6
21. Gisoo J, Majid A, Ladan K, et al. Metabolic syndrome mediates proinflammatory responses of inflammatory cells in preeclampsia. *Am J Reprod Immunol*. 2019;81(3):e13086. doi:10.1111/aji.13086
22. Kedziora S, Kräker K, Markó L, et al. Kidney injury caused by preeclamptic pregnancy recovers postpartum in a transgenic rat model. *Int J Mol Sci*. 2021;22(7):3762. doi:10.3390/ijms22073762
23. Nagashima M, Takeda Y, Saitoh S, et al. A loss of tuning of both pro-coagulant and inflammatory responses in monocytes in patients with preeclampsia. *J Reprod Immunol*. 2024;166:104334. doi:10.1016/j.jri.2024.104334
24. Koumei S, Tadayoshi K, Masafumi T. Role of the NLRP3 inflammasome in preeclampsia. *Front Endocrinol*. 2020;11:80. doi:10.3389/fendo.2020.00080
25. Mahmoud AO, Eman RB, Ahmed MAS, Asmaa SS, Sayed AM. Effect of 17-hydroxyprogesterone caproate on interleukin-6 and tumor necrosis factor-alpha in expectantly managed early-onset preeclampsia. *Egypt J Immunol*. 2023;30(2):109–118. doi:10.55133/eji.300210
26. Zeynep S, Burak B, Onur baran B, et al. The role of first trimester serum inflammatory indexes (NLR, PLR, MLR, SII, SIRI, and PIV) and the β-hCG to PAPP-A ratio in predicting preeclampsia. *J Reprod Immunol*. 2024;162:104190. doi:10.1016/j.jri.2023.104190
27. Kunal Kumar S, Anubhuti G, Désirée F, et al. LMWH prevents thromboinflammation in the placenta via HBEGF-AKT signaling. *Blood Adv*. 2024;8(18):4756–4766. doi:10.1182/bloodadvances.2023011895
28. Levent Ö, Burcu Ö, Savaş G, Esra Arslan A, Ahmet Cemal P. Can systemic inflammatory markers be used in pulmonary embolism risk assessment in patients with acute pulmonary thromboembolism? *J Inflamm Res*. 2025;18:5969–5977. doi:10.2147/JIR.S514111
29. Wang G, Wu Y, Chen A, et al. Association between depressive symptoms and mortality in patients with cardiovascular-kidney-metabolic syndrome: the mediating role of inflammatory biomarkers. *J Affective Disorders*. 2025;386:119429. doi:10.1016/j.jad.2025.119429
30. Xiaowan L, Lan C, Hongyang X. Association between systemic inflammation response index and chronic kidney disease: a population-based study. *Front Endocrinol*. 2024;15:1329256. doi:10.3389/fendo.2024.1329256
31. Ellen M, Leilani LS, Wei Z, et al. IL11 activates the placental inflammasome to drive preeclampsia. *Front Immunol*. 2023;14:1175926. doi:10.3389/fimmu.2023.1175926
32. Ehnold L, Melderis S, Hagenstein J, et al. Treg derived Amphiregulin protects from murine lupus nephritis via tissue reparative effects. *Sci Rep*. 2025;15(1):7776. doi:10.1038/s41598-025-91636-2
33. Dominique M, Suzanne H, Chania DC, Claartje M, Charlotte L, Yves J. Are neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and/or mean platelet volume (MPV) clinically useful as predictive parameters for preeclampsia? *J Matern Fetal Neonatal Med*. 2017;32(9):2289–2301.
34. Betül TÇ, Gizem A, Gülşan K, et al. Evaluation of platelet indices and inflammation markers in preeclampsia. *J Clin Med*. 2025;14(5):1406. doi:10.3390/jcm14051406