Original Article

Alterations in Red Blood Cell Indices in Preeclampsia and Their Potential Clinical and Translational Implications

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Abstract

Background: Preeclampsia is a pregnancy-specific disorder characterized by multisystem involvement and significant maternal–fetal morbidity. Emerging evidence suggests that hematological indices may reflect underlying pathophysiological mechanisms, including inflammation, oxidative stress, and impaired erythropoiesis.

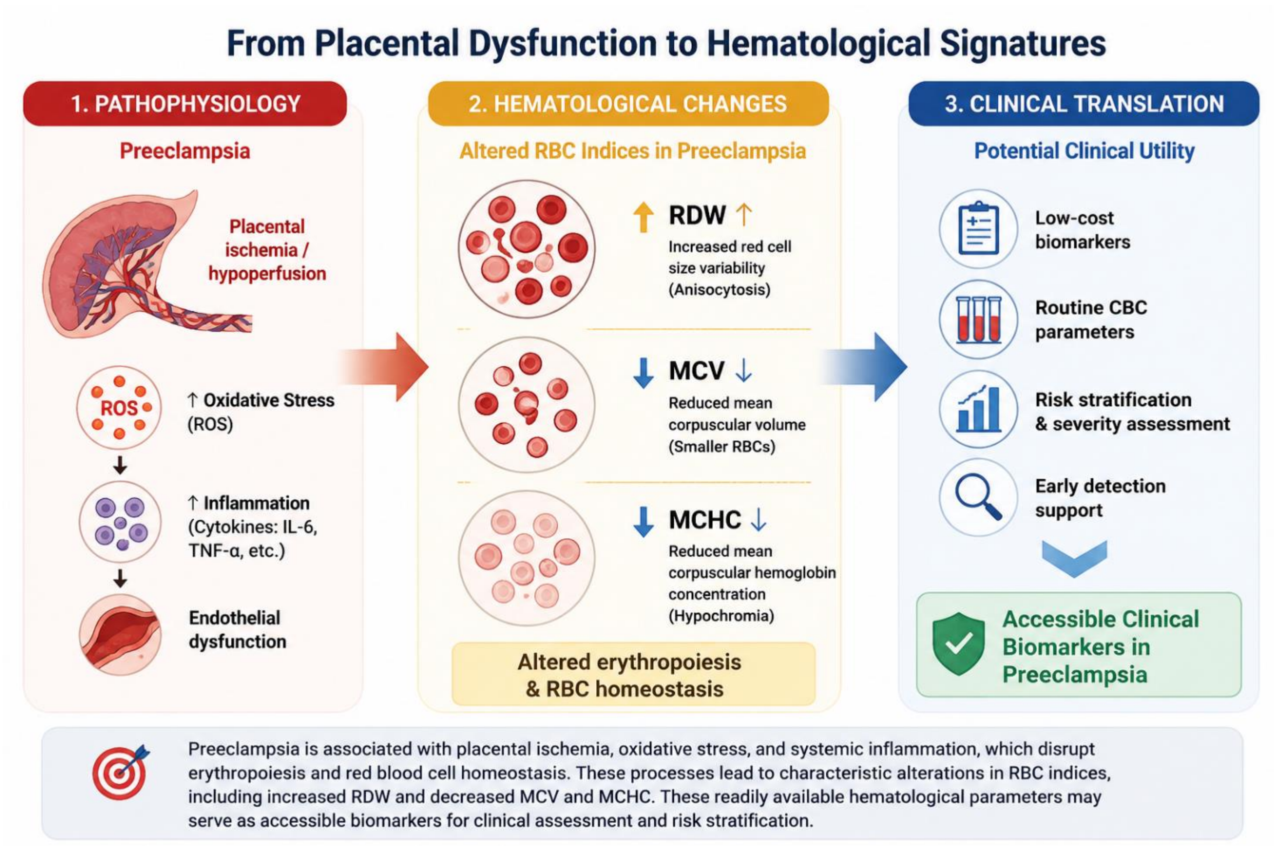
Methods: This case–control study was conducted on 130 pregnant women (65 cases and 65 controls) referred to Shahid Rahimi Hospital between 2023 and 2024. Participants were matched based on maternal age and gestational age. Demographic characteristics and hematological parameters, including hemoglobin (Hb), hematocrit (HCT), red blood cell (RBC) count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW), were extracted from medical records. Independent t-tests and analysis of covariance (ANCOVA) were used for statistical analysis, adjusting for age, body mass index (BMI), education level, and parity.

Results: Significant differences were observed in MCV, MCHC, and RDW between the two groups. MCV and MCHC were significantly lower in the preeclampsia group, while RDW was significantly higher (P = 0.001 for all). These associations remained statistically significant after adjustment for confounding variables. No significant differences were observed in Hb, HCT, RBC count, or MCH.

Conclusion: Alterations in RBC indices, particularly RDW, MCV, and MCHC, are associated with preeclampsia and may reflect underlying biological processes such as oxidative stress, inflammation, and impaired erythropoiesis. These routinely available hematological parameters may have potential translational value as accessible biomarkers for clinical assessment and risk stratification in preeclampsia, although further mechanistic and prospective studies are warranted.

Mechanistic and Translational Relevance: These hematological indices may reflect underlying inflammation, oxidative stress, and impaired erythropoiesis in preeclampsia. They may serve as accessible, low-cost biomarkers of systemic involvement and could support adjunctive clinical assessment and risk stratification, particularly in resource-limited settings.

Keywords: Preeclampsia; Red Blood Cell Indices; RDW; MCV; Oxidative Stress and Inflammation.



Graphical Abstract. Hematological Signatures of Preeclampsia: Linking Placental Stress to RBC Index Alterations. The figure illustrates the mechanistic link between placental dysfunction and hematological alterations in preeclampsia. Placental ischemia induces oxidative stress and systemic inflammation, leading to impaired erythropoiesis and altered red blood cell indices. The observed increase in RDW and reduction in MCV and MCHC may represent downstream hematological signatures of systemic disease burden, highlighting their potential utility as accessible biomarkers for clinical risk assessment.

Introduction

Preeclampsia remains a leading cause of maternal and perinatal morbidity and mortality worldwide, characterized by new-onset hypertension and multisystem involvement after mid-gestation (1). Although extensively studied, its pathophysiology remains incompletely understood and is generally considered a complex disorder driven by abnormal placentation, endothelial dysfunction, and systemic inflammatory activation (2). A key concept in current models is placental hypoperfusion, which triggers a cascade of maternal vascular and immune responses (3). This process is associated with an imbalance in angiogenic factors, increased oxidative stress, and progressive endothelial injury, which collectively contribute to disease development and progression (4).

Beyond classical vascular alterations, emerging evidence suggests that hematological changes may reflect systemic pathophysiological disturbances in preeclampsia (5). Hematological indices, including red blood cell (RBC) parameters such as red cell distribution width (RDW), are increasingly recognized as accessible surrogate markers of systemic inflammatory and thromboinflammatory activity in preeclampsia (6). In a meta-analysis including 951 preeclamptic women and 2024 controls, red cell distribution width (RDW) was significantly higher in preeclamptic women compared to controls, and even higher in severe cases compared to mild preeclampsia (7). RDW is consistently reported to be altered in preeclampsia and reflects systemic inflammation, oxidative stress, and impaired erythropoiesis, whereas evidence regarding mean corpuscular volume (MCV) is less consistent across studies (8). This variability may reflect differences in study design and disease severity. It may also be influenced by underlying hemorheological alterations. Accordingly, MCV has been reported to show variable alterations in preeclampsia, potentially reflecting changes in erythrocyte size distribution and blood rheology, while mean corpuscular hemoglobin concentration (MCHC) generally shows no consistent or clinically significant alterations in this condition (9). Despite growing evidence on hematological alterations in preeclampsia, the independent association of RBC indices after adjustment for key confounders and their integration into a coherent mechanistic framework remain insufficiently characterized. Therefore, this study aimed to systematically evaluate the association between RBC indices and preeclampsia in a case–control design and to explore their potential as accessible biomarkers reflecting underlying pathophysiological processes, including erythropoietic disruption and systemic inflammatory–oxidative stress burden. We hypothesized that preeclampsia is independently associated with significant alterations in RBC indices, reflecting inflammation- and oxidative stress–related mechanisms.

Methods

Study Design and Setting

This case–control study was conducted among third-trimester pregnant women referred to Shahid Rahimi Hospital between 2023 and 2024 to evaluate the association between red blood cell (RBC) indices and preeclampsia. The study design and reporting were conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (10). The study was based on medical record data and was performed in accordance with institutional regulations. The study protocol was approved by the institutional ethics committee (Approval No.: IR.LUMS.REC.1404.214). All data were handled confidentially, and no personally identifiable information was disclosed.

Study Population

The study population consisted of pregnant women attending the above-mentioned hospital during the study period. Participants were classified into two groups: a case group including pregnant women diagnosed with preeclampsia based on standard clinical criteria, and a control group consisting of healthy pregnant women without preeclampsia selected from the same source population. The control group was matched to the case group based on maternal age (±2 years) and gestational age (±2 weeks). Inclusion and exclusion criteria were applied to ensure comparability between groups.

Sampling Method and Sample Size

A convenience sampling method was applied, and medical records of all eligible pregnant women were reviewed. Cases were consecutively selected from hospital records until the required sample size was achieved, while controls were selected from healthy pregnant women and matched to cases accordingly. The sample size was calculated based on the comparison of proportions of normal RBC indices between the two groups, using α = 0.05 (Z = 1.96), power = 80% (Z = 0.84), an expected proportion of 0.70 in the case group, and 0.90 in the control group, with a 1:1 case-to-control ratio. The calculated sample size was 59 participants per group, which was increased by 10% to account for potential data loss, resulting in 65 participants per group (total n = 130). The final sample size provided adequate statistical power to detect clinically meaningful differences between groups.

Data Collection

Data were extracted from medical records using a researcher-designed checklist. Demographic variables included maternal age, parity, body mass index (BMI), gestational age at delivery, and history of abortion. Hematological parameters included hemoglobin (Hb), hematocrit (Hct), red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW). All hematological measurements were obtained using standardized laboratory methods as part of routine clinical assessment.

Definition of Preeclampsia

Preeclampsia was defined according to standard clinical criteria as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg occurring after 20 weeks of gestation, accompanied by proteinuria or relevant clinical findings (11).

Statistical Analysis

Data analysis was performed using SPSS version 30 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic and clinical characteristics. Quantitative variables were expressed as mean ± standard deviation. Normality of data distribution was assessed using the Shapiro–Wilk test. Comparisons between case and control groups were performed using appropriate statistical tests. Independent t-tests were used for normally distributed variables. Analysis of covariance (ANCOVA) was performed to adjust for potential confounding variables, including age, body mass index (BMI), education level, and parity. A two-tailed p-value < 0.05 was considered statistically significant.

Results

4.1. Baseline demographic and clinical characteristics of the study population.

A total of 130 pregnant women were included in the study. Baseline demographic and obstetric characteristics are presented in Table 1. The mean age of participants was 27.80 ± 3.34 years, and the mean body mass index (BMI) was 22.01 ± 3.05 kg/m². The mean parity and number of abortions were 1.52 ± 0.55 and 0.35 ± 0.55, respectively, while the mean gestational age was 27.67 ± 2.97 weeks. No extreme values or implausible distributions were observed.

Variable	Mean	Standard Deviation
Age (years)	27.80	3.34
BMI (kg/m²)	22.01	3.05
Parity	1.52	0.55
Number of abortions	0.35	0.55
Gestational age (weeks)	27.67	2.97

Table 1. Baseline demographic and clinical characteristics of the study population. Data are presented as mean ± Standard Deviation

4.2. Distribution of Demographic and Background Variables

The distribution of demographic and background variables is presented in Table 2. Half of the participants (50.0%) had a university education, followed by 27.7% with upper secondary education, 16.2% with lower secondary education, and 6.2% with primary education. No participants were illiterate. Most participants (79.2%) were housewives, while 13.8% were classified as having other occupations and 6.9% were employed. Regarding obstetric history, 68.5% of participants had no previous history of abortion, whereas 31.5% reported at least one abortion.

Variable	Category	Frequency	Percentage
Education	Illiterate	0	0.0%
	Primary	8	6.2%
	Lower secondary	21	16.2%
	Upper secondary	36	27.7%
	University	65	50.0%
Occupation	Housewife	103	79.2%
	Employed	9	6.9%
	Other	18	13.8%
History of abortion	No	89	68.5%
	Yes	41	31.5%

Table 2. Distribution of demographic and background variables in the study population. Data are presented as frequency (percentage).

4.3. Hematological Indices of the Study Population

The hematological indices of the study participants are presented in Table 3. The mean hemoglobin (Hb) level was 12.26 ± 0.95 g/dL, and the mean hematocrit (HCT) was 36.57 ± 2.05%. The mean red blood cell (RBC) count was 4.03 ± 0.30 $\times 10^6$/µL. The mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) were 86.52 ± 5.44 fL, 28.46 ± 5.49 pg, and 31.37 ± 1.96 g/dL, respectively. The red cell distribution width (RDW) was 13.51 ± 1.70%.

Parameter	Mean	Standard Deviation
Hb (g/dL)	12.26	0.95
HCT (%)	36.57	2.05
RBC Count ($\times 10^6$/µL)	4.03	0.30
MCV (fL)	86.52	5.44
MCH (pg)	28.46	5.49
MCHC (g/dL)	31.37	1.96
RDW (%)	13.51	1.70

Table 3. Hematological indices of the study population. Data are presented as mean ± standard deviation.

4.4. Comparison of the Case and Control Groups in Terms of Demographic and Background Variables

The comparison between the case and control groups for quantitative demographic and background variables is presented in Table 4. The mean age was 27.05 ± 3.27 years in the control group and 28.55 ± 3.27 years in the preeclampsia group (P = 0.01). The mean body mass index (BMI) was 20.69 ± 2.31 and 23.34 ± 3.15 in the control and case groups, respectively (P = 0.001). The mean number of deliveries was 1.63 ± 0.57 in the control group and 1.40 ± 0.49 in the case group (P = 0.015). No significant differences were observed in the number of abortions (0.29 ± 0.55 vs. 0.42 ± 0.56, P = 0.207) or gestational age (28.09 ± 2.67 vs. 27.25 ± 3.21 weeks, P = 0.105).

Variable	Healthy Group (Mean ± SD)	Preeclampsia Group (Mean ± SD)	P-value
Age (years)	27.05 ± 3.27	28.55 ± 3.27	0.01
BMI (kg/m²)	20.69 ± 2.31	23.34 ± 3.15	0.001
Number of deliveries	1.63 ± 0.57	1.40 ± 0.49	0.015
Number of abortions	0.29 ± 0.55	0.42 ± 0.56	0.207
Gestational age (weeks)	28.09 ± 2.67	27.25 ± 3.21	0.105

Table 4. Comparison of demographic and background variables between case and control groups. Data are presented as mean ± standard deviation; P-values were obtained using independent t-tests.

4.5. Comparison of Categorical Demographic and Background Variables Between Case and Control Groups

The comparison of categorical demographic and background variables between the two groups is presented in Table 5. Regarding educational level, 36.9% of the control group had a university degree, compared to 63.1% in the preeclampsia group. Other categories included upper secondary education (32.3% vs. 23.1%), lower secondary education (21.5% vs. 10.8%), and primary education (9.2% vs. 3.1%). No participants were illiterate in either group. Educational level differed significantly between groups (P = 0.021).

No significant differences were observed in occupational status between groups (P = 0.126), with most participants being housewives (73.8% vs. 84.6%). Similarly, no significant difference was observed in abortion history (P = 0.131), with 75.4% of the control group and 61.5% of the case group reporting no previous abortion.

Variable	Category	Healthy Group n (%)	Preeclampsia Group n (%)	P-value
Education	Illiterate	0 (0.0)	0 (0.0)	0.021
	Primary	6 (9.2)	2 (3.1)	
	Lower secondary	14 (21.5)	7 (10.8)	
	Upper secondary	21 (32.3)	15 (23.1)	
	University	24 (36.9)	41 (63.1)	
Occupation	Housewife	48 (73.8)	55 (84.6)	0.126
	Employed	4 (6.2)	5 (7.7)	
	Other	13 (20.0)	5 (7.7)	
History of abortion	No	49 (75.4)	40 (61.5)	0.131
	Yes	16 (24.6)	25 (38.5)	

Table 5. Comparison of categorical demographic and background variables between study groups. Data are presented as frequency (percentage); P-values were obtained using chi-square tests.

4.6. Comparison of Hematological Indices Between Case and Control Groups

The comparison of hematological indices between the healthy and preeclampsia groups is presented in Table 6. No significant differences were observed in hemoglobin (Hb), hematocrit (HCT), or red blood cell (RBC) count between the two groups (all P > 0.05). In contrast, significant differences were identified in key red cell indices.

A distinct pattern of alteration was observed in red cell indices. Specifically, mean corpuscular volume (MCV) was significantly lower in the preeclampsia group compared with the healthy group (83.10 ± 4.31 vs. 89.95 ± 4.14 fL, P = 0.001). Similarly, mean corpuscular hemoglobin concentration (MCHC) was significantly reduced in the preeclampsia group (30.44 ± 2.03 vs. 32.29 ± 1.38 g/dL, P = 0.001). In addition, red cell distribution width (RDW) was significantly higher in the preeclampsia group (14.18 ± 2.11 vs. 12.84 ± 0.68%, P = 0.001). No significant difference was observed in mean corpuscular hemoglobin (MCH) between groups (P = 0.384).

Variable	Healthy Group (Mean ± SD)	Preeclampsia Group (Mean ± SD)	P-value
Hb (g/dL)	12.30 ± 0.54	12.21 ± 1.23	0.6
HCT (%)	36.64 ± 1.59	36.49 ± 2.43	0.676
RBC count (million/µL)	4.01 ± 0.29	4.05 ± 0.32	0.422
MCV (fL)	89.95 ± 4.14	83.10 ± 4.31	0.001
MCH (pg)	28.88 ± 2.33	28.04 ± 7.41	0.384
MCHC (g/dL)	32.29 ± 1.38	30.44 ± 2.03	0.001
RDW (%)	12.84 ± 0.68	14.18 ± 2.11	0.001

Table 6. Comparison of hematological indices between case and control groups. Data are presented as mean ± standard deviation; P-values were obtained using independent t-tests.

4.7. Comparison of Hematological Indices Between Case and Control Groups After Adjustment for Demographic and Background Variables

The results of the analysis of covariance (ANCOVA), adjusted for age, education level, body mass index (BMI), and parity, are presented in Table 7. After adjustment for these variables, significant differences between the preeclampsia and control groups remained for mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW) (all P = 0.001). None of the adjusted covariates were significantly associated with MCV, MCHC, or RDW (all P > 0.05). Group status remained a significant independent predictor of all evaluated red cell indices after adjustment for confounding variables.

DISCUSSION

In this case–control study, we found that red blood cell (RBC) indices were significantly altered in women with preeclampsia compared with healthy controls. Specifically, MCV and MCHC were decreased, while RDW was increased in the case group. These findings suggest that routine hematological parameters may reflect underlying systemic pathophysiological changes associated with preeclampsia (12). Importantly, these associations remained statistically significant after adjustment for potential confounding variables, including age, education level, body mass index

(BMI), and parity, supporting an independent association between altered RBC indices and preeclampsia.

In the present study, the most prominent finding was the increase in RDW among women with preeclampsia. RDW reflects heterogeneity in erythrocyte size and is associated with inflammatory processes (13).

Independent Variable	Dependent Variable	F-value	P-value
Group	MCV	76.424	0.001
	MCHC	25.858	0.001
	RDW	25.319	0.001
Age	MCV	3.062	0.083
	MCHC	0.480	0.490
	RDW	1.297	0.257
Education	MCV	0.410	0.523
	MCHC	0.042	0.838
	RDW	1.622	0.205
BMI	MCV	1.053	0.307
	MCHC	0.138	0.711
	RDW	0.537	0.465
Parity	MCV	0.011	0.916
	MCHC	0.009	0.925
	RDW	0.358	0.551

Table 7. Comparison of hematological indices between case and control groups after adjustment for confounding variables. Data are presented as adjusted mean estimates; P-values were obtained using analysis of covariance (ANCOVA).

This increase in RDW may reflect impaired erythrocyte maturation and reduced erythroid cell survival under hypoxic conditions, as mediated by dysregulation of erythropoietin-dependent erythropoiesis (14). Placental ischemia, a key feature of preeclampsia, may promote oxidative stress and inflammatory activation, which can disrupt erythropoiesis and lead to the release of immature erythrocytes into circulation (2). Inflammatory mediators such as interleukin-6 regulate hepcidin expression through the JAK/STAT signaling pathway, thereby affecting systemic iron metabolism and erythropoiesis (15). Similar associations between elevated RDW and inflammatory or oxidative stress–related states have been reported in previous studies (16).

We observed a significant increase in MCV in the preeclampsia group. This finding may reflect altered erythrocyte dynamics in response to the inflammatory and angiogenic imbalance associated with placental insufficiency. Changes in erythrocyte indices may represent downstream hematologic adaptations to the systemic inflammatory and vascular dysfunction observed in preeclampsia (17). Comparable findings have been described in studies evaluating hematological changes in inflammatory and pregnancy-related conditions (18). In addition, MCHC was significantly lower in women with preeclampsia. This may reflect changes in erythrocyte hemoglobin concentration and membrane-related properties (19). Oxidative stress and lipid peroxidation may impair red cell structure and deformability, which may reduce oxygen-carrying efficiency (20). Similar mechanisms have been proposed in previous studies investigating oxidative damage in preeclampsia (21).

Overall, the pattern of changes in RBC indices observed in this study may reflect altered erythropoiesis occurring in a setting of hypoxia, inflammation, and oxidative stress. Although causal relationships cannot be established in this study, these findings are in line with previously proposed biological mechanisms in preeclampsia (22, 23). From a translational perspective, RDW, MCV, and MCHC are inexpensive and routinely available laboratory parameters. The significant differences observed in this study suggest that these indices may serve as non-specific but potentially useful adjunct markers of systemic alterations in preeclampsia and may support adjunctive clinical risk assessment, particularly in resource-limited settings. However, their clinical applicability requires confirmation in larger prospective studies.

Limitations

The present study has several limitations. Its case–control design limits causal inference, and residual confounding cannot be completely excluded despite statistical adjustment. In addition, inflammatory and oxidative stress biomarkers were not directly measured, which limits mechanistic confirmation. Future prospective studies with integrated molecular and functional biomarkers are needed to better clarify these pathways.

Conclusion

Preeclampsia was associated with significant alterations in RBC indices, particularly increased RDW and decreased MCV and MCHC. These findings support a potential association between altered erythrocyte homeostasis and the inflammatory–oxidative stress milieu observed in preeclampsia. Routine hematological parameters may therefore represent accessible adjunctive indicators of systemic disease-related alterations, although further prospective and mechanistic studies are required to confirm their clinical utility.

Mechanistic and Translational Relevance

The observed alterations in red blood cell indices, notably RDW, MCV, and MCHC, likely represent integrated pathophysiological responses encompassing inflammation, oxidative stress, and dysregulated erythropoiesis in preeclampsia. Mechanistically, inflammatory mediators and oxidative damage may impair erythroid maturation and disrupt red cell homeostasis, leading to heterogeneous erythrocyte populations with altered size and hemoglobin content. These hematologic perturbations may thus serve as downstream signatures of placental hypoperfusion and endothelial dysfunction, central elements in the pathogenesis of preeclampsia.

From a translational perspective, RDW, MCV, and MCHC are readily measurable, cost-effective parameters that can complement conventional clinical and laboratory assessments. While inherently non-specific, these indices may provide early insight into systemic inflammatory and hematologic dysregulation, particularly in settings where advanced biomarker profiling is not feasible. Their integration into routine obstetric evaluation could enhance risk stratification, guide closer monitoring, and inform timely interventions.

Future prospective studies are warranted to validate their predictive performance, define clinically meaningful thresholds, and establish their role within multimodal models for preeclampsia risk assessment and disease stratification. Such investigations may facilitate the translation of simple hematologic indices into practical tools for personalized maternal care.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

All authors contributed to the conception and design of the study, literature search, data interpretation, drafting of the manuscript, and critical revision of the article. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Ethics Statement

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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