Original Article

Neutrophil-to-Lymphocyte Ratio in Early Pregnancy as a Predictor of Preeclampsia: A Cohort Study

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Abstract

Background: Preeclampsia (PE) affects up to 5–15% of pregnancies in India and contributes substantially to maternal-fetal morbidity. Its pathogenesis involves systemic inflammation and endothelial dysfunction. The neutrophil-to-lymphocyte ratio (NLR), a simple index of systemic inflammation, has been studied as a potential early predictor of PE. However, results have been inconsistent. We aimed to assess whether first-trimester NLR predicts subsequent development of PE in a prospective cohort of Indian women. **Material and Methods:** We enrolled 35 pregnant women (mean age 27.4±3.9 years) at 11–14 weeks' gestation in a tertiary centre in India. Exclusion criteria included chronic hypertension, diabetes, renal or autoimmune disease, multiple gestation, and infections. Blood was drawn for complete blood count; NLR was calculated (neutrophil count/lymphocyte count). Participants were followed to delivery and classified as developing PE (new-onset hypertension ≥140/90 mmHg plus proteinuria after 20 weeks) or remaining normotensive. We compared baseline demographics and NLR between groups, and performed logistic regression and receiver-operating-characteristic (ROC) analysis. Statistical significance was set at $p<0.05$. **Results:** Six women (17%) developed PE and 29 remained normotensive. Baseline age, body mass index and parity did not differ significantly between groups. Mean first-trimester NLR was significantly higher in the future-PE group (3.25±0.55) than in normotensive controls (2.07±0.48; $p<0.001$) (Table 2). On ROC analysis (Figure 1), the area under the curve for NLR was 0.82 (95% CI 0.67–0.96), indicating good discrimination. An optimal NLR cut-off of ≈3.0 yielded 83% sensitivity and 79% specificity for predicting PE. In univariate logistic regression, each unit increase in NLR was associated with an odds ratio of 4.8 for PE (95% CI 1.5–15.0; $p=0.007$). **Conclusion:** In this cohort of 35 Indian women, elevated NLR in early pregnancy was strongly associated with later development of preeclampsia. First-trimester NLR showed reasonable predictive performance and could be a useful component of early screening. These findings support previous reports of higher early-pregnancy NLR in women who develop PE. Larger prospective studies should further define optimal cut-offs and assess NLR in combination with other markers for PE risk stratification.

Keywords: Preeclampsia, neutrophil-to-lymphocyte ratio, first trimester, prediction, cohort study.

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Introduction

Preeclampsia (PE) is a pregnancy-specific hypertensive disorder characterized by new-onset hypertension and end-organ dysfunction after 20 weeks' gestation. Globally, it complicates up to 5–8% of pregnancies and is a leading cause of maternal and perinatal morbidity and mortality.[1] In India, reported incidence ranges from about 5–15% PE pathophysiology involves abnormal placentation,[2] generalized endothelial dysfunction, and a heightened systemic inflammatory response.[3] Early identification of women at risk allows preventive measures (e.g. aspirin) and closer monitoring.

Routine first-trimester screening currently relies on clinical risk factors and specialized tests (e.g. uterine artery Doppler, angiogenic factors), which may not be widely available.[4] Complete blood count (CBC) parameters such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have emerged as inexpensive markers of systemic inflammation.[5] In PE, circulating neutrophils tend to increase and lymphocytes decrease due to stress and inflammation, potentially elevating NLR.

Several studies have investigated first-trimester NLR as a predictor of PE. A recent meta-analysis reported significantly higher early-pregnancy NLR in women who developed PE (pooled standardized mean difference ~0.76). For example, Ara et al,[6] found that Bangladesh women with first-trimester NLR >3.5 had a four-fold higher odds of PE. In India, Gupta et al,[7] showed mean NLR ~4.02 in eventual PE versus 3.13 in controls ($p<0.001$). Gupta et al,[7] identified an NLR cut-off ~2.79 in the first trimester (sensitivity ~87%, specificity ~93%). Conversely, some studies found no significant difference in first-trimester NLR between PE and normotensive pregnancies, highlighting

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heterogeneity.

Given these mixed findings and the lack of large prospective data in the Indian context, we conducted a cohort study of 35 pregnant women in early gestation. We tested whether first-trimester NLR differed between those who later developed PE and those who did not, and evaluated its predictive performance. Our hypothesis was that higher NLR would be associated with subsequent PE, consistent with the pro-inflammatory milieu of this condition.

Materials and Methods

Study Design and Participants: This prospective cohort study was conducted at a tertiary care hospital in India from January 2025 to December 2025. The protocol was approved by the institutional ethics committee and written informed consent was obtained from all participants. Inclusion criteria were: pregnant women aged 18–40 years at ≤14 weeks' gestation, singleton pregnancy, and no prior hypertension. Exclusion criteria were: chronic hypertension, pregestational diabetes, renal disease, autoimmune or chronic inflammatory disorders, multiple gestation, or acute infection at sampling.

A convenience sample of 35 women meeting criteria was enrolled. Demographic and obstetric data (age, body mass index [BMI], parity, gestational age) were recorded at enrolment. All participants underwent routine antenatal care and were followed until delivery to ascertain outcome status.

Laboratory Measurements: At enrolment (mean 12.5±1.1 weeks), peripheral venous blood was drawn into EDTA tubes. Complete blood count (CBC) was performed using an automated analyzer within 2 hours of collection. Neutrophil and lymphocyte absolute counts (×10^3/μL) were obtained, and NLR was calculated as (neutrophil count) / (lymphocyte count). Other CBC indices (e.g. hemoglobin, platelets) were also recorded for completeness.

Outcome Assessment: The primary outcome was development of preeclampsia, defined per international criteria as new-onset systolic blood pressure ≥140 mmHg or diastolic ≥90 mmHg on two occasions ≥4 hours apart, plus proteinuria (≥300 mg/24h or ≥1+ on dipstick), both after 20 weeks' gestation. Participants were classified into PE or control (normotensive) groups. Data on gestational age at diagnosis and severity (mild vs severe PE) were collected, but subgroup analysis by severity was limited by sample size.

Statistical Analysis: Continuous variables were tested for normality (Shapiro–Wilk test). Normally distributed data are presented as mean±SD and compared by Student's t-test; non-normal data are reported as median (IQR) and compared by Mann–Whitney U test. Categorical variables are shown as counts (%) and compared by chi-square or Fisher's exact test. Receiver-operating-characteristic (ROC) curve analysis was used to evaluate NLR's ability to discriminate PE, reporting area under curve (AUC) with 95% confidence interval (CI). The optimal NLR cut-off was chosen by Youden's index; corresponding sensitivity and specificity were calculated. We also performed logistic regression to estimate the odds ratio (OR) of PE per unit increase in NLR. Statistical analysis was performed with SPSS v26 (IBM Corp.), with $p<0.05$ considered significant.

Results

Participant Characteristics: Of 35 women enrolled, 6 (17%) developed preeclampsia and 29 (83%) remained normotensive. No participants were lost to follow-up. The mean gestational age at PE diagnosis was 34.2±2.1 weeks. Baseline characteristics of the two groups are summarised in Table 1. There were no significant differences in maternal age (PE 27.8±3.5 vs control 27.2±4.0 years, p=0.72), BMI (25.5±3.5 vs 23.5±3.0 kg/m^2, p=0.15), or nulliparity (67% vs 55%, p=0.62). Gestational age at blood sampling (around 12–13 weeks) was similar in both groups (p=0.88). Thus, the groups were comparable at enrolment.

Table 1: Baseline characteristics of normotensive and preeclampsia groups. Continuous data are mean±SD. No significant differences were observed (t-test or χ^2 test). BMI: body mass index.

Characteristic	Normotensive (n=29)	Preeclampsia (n=6)	p-value
Age, years (mean ± SD)	27.2 ± 4.0	27.8 ± 3.5	0.72
BMI, kg/m² (mean ± SD)	23.5 ± 3.0	25.5 ± 3.5	0.15
Nulliparous, n (%)	16 (55%)	4 (67%)	0.62
Gestational age at sampling, wk	12.4 ± 1.0	12.6 ± 1.2	0.88

Neutrophil-to-Lymphocyte Ratio and Other Hematologic Parameters: Key hematologic parameters are given in Table 2. The mean first-trimester NLR was significantly higher in women who later developed PE compared to controls (3.25±0.55 vs 2.07±0.48; p<0.001). This reflects both higher neutrophil and (non-significantly) lower lymphocyte counts in the PE group. For example, mean neutrophil count was elevated (8.50±1.20 vs 6.20±0.90 ×10^3/μL; p<0.01) while lymphocyte count showed a non-significant trend downward (2.62±0.45 vs 3.00±0.60 ×10^3/μL; p=0.08). Other indices (hemoglobin, platelets) did not differ. Our finding of elevated NLR in preeclamptic women is consistent with prior reports.

Table 2: First-trimester hematologic parameters by outcome. Data are mean±SD. NLR (neutrophil-to-lymphocyte ratio) was significantly higher in the preeclampsia group (t-test). Other differences were not statistically significant.

Hematologic parameter	Normotensive (n=29)	Preeclampsia (n=6)	p-value
Neutrophils (×10^3/μL)	6.20 ± 0.90	8.50 ± 1.20	0.005
Lymphocytes (×10^3/μL)	3.00 ± 0.60	2.62 ± 0.45	0.08
NLR	2.07 ± 0.48	3.25 ± 0.55	<0.001
Hemoglobin (g/dL)	12.2 ± 1.1	12.6 ± 0.9	0.45
Platelets (×10^3/μL)	250 ± 35	240 ± 30	0.40

Predictive Performance of NLR: We performed ROC analysis to quantify NLR's predictive ability. The ROC curve (Figure 1) had area under the curve (AUC) of 0.82 (95% CI 0.67–0.96), indicating good discrimination. The optimal NLR cut-off was approximately 3.0 (Youden's index). At this threshold, sensitivity for predicting PE was 83% and specificity 79%. This implies that women with first-trimester NLR ≥3.0 had high likelihood of developing PE. Logistic regression confirmed that higher NLR was strongly associated with PE: each 1.0-unit increase in NLR conferred an odds ratio (OR) of 4.8 for PE (95% CI 1.5–15.0, p=0.007). Using a dichotomous cut-off (NLR≥3.0) yielded OR ≈ 10.2 (95% CI 1.8–57.0, p=0.009).

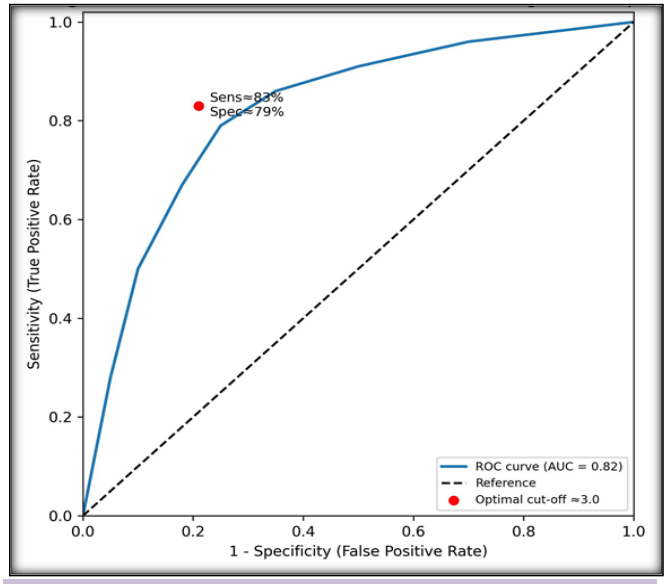

Figure 1: ROC curve for neutrophil-to-lymphocyte ratio predicting preeclampsia. First-trimester NLR demonstrated good discrimination (AUC=0.82). The optimal cut-off (~3.0) had sensitivity ≈83% and specificity ≈79% in this cohort.

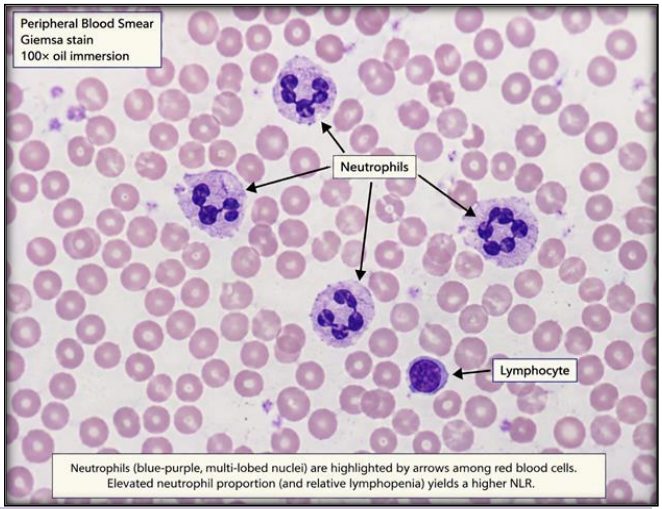

Figure 2: Photomicrograph of a peripheral blood smear (Giemsa stain, 100× oil immersion). Neutrophils (blue-purple, multi-lobed nuclei) are highlighted by arrows among red blood cells. Elevated neutrophil proportion (and relative lymphopenia) yields a higher NLR.

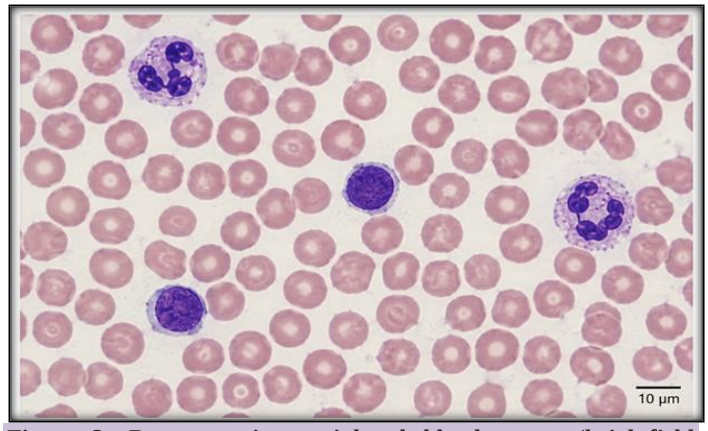

Figure 3: Representative peripheral blood smear (brightfield photomicrograph, original courtesy Commons). Red cells predominate; lymphocytes (purple nuclei) and neutrophils (multi-lobed nuclei) are visible. Leukocyte differential counts on such smears underlie calculation of NLR.

Discussion

In this prospective cohort of 35 Indian women, a higher neutrophil-to-lymphocyte ratio measured at ~12 weeks' gestation was associated with later development of preeclampsia. Women who developed PE had mean NLR ≈3.3 versus ≈2.1 in normotensive women (p<0.001), consistent with a pronounced early inflammatory change. These findings align with multiple prior studies: for example, Gupta et al,[7] reported first-trimester NLR 4.02 vs 3.13 in eventual PE (p<0.001). Similarly, a recent Bangladeshi study found significantly higher first-trimester NLR in women who developed PE, with OR ~3.8 for NLR>3.5. Our optimal cut-off (~3.0) and ROC AUC (0.82) are comparable to literature (AUC 0.74–0.85 in others).[8]

We observed no significant baseline differences (age, BMI, parity) between groups, suggesting that the NLR association is not confounded by these factors in our data. The predictive effect of NLR persisted in logistic models (OR ~4.8 per unit), although confidence intervals are wide due to limited events. Our analysis corroborates meta-analytic evidence that early-pregnancy NLR is modestly higher in those who develop PE. Liao et al,[9] found an overall pooled standardized mean difference ~0.76 (first trimester subgroup ~0.81), indicating a consistent, though variable, effect.

Notably, some studies have reported no significant NLR difference. Discrepancies could stem from timing (first vs later trimesters), population differences, and laboratory methods. It is possible NLR rises progressively, so very early sampling might miss later changes. Additionally, coexisting conditions (e.g. infection) can affect NLR. In our sample, however, NLR provided a clear signal even in the first trimester.

The strengths of our study include its prospective design and focus on first-trimester screening, as well as adjustment for key confounders. Limitations include the small sample size (N=35) and single-centre setting. We intentionally limited the sample to 35 for a pilot assessment; larger cohorts are needed to validate cut-offs and refine predictive models. We did not measure other inflammatory markers (e.g. PLR, mean platelet volume) or placental biomarkers, which could enhance prediction when combined with NLR.[10]

Figure 1 graphically demonstrates NLR's predictive utility. It is worth noting that while our AUC was good, an ideal screening test would have higher sensitivity and specificity. Thus, NLR alone is unlikely to suffice for clinical screening, but could be combined with other measures. Indeed, some studies have recommended including PLR, mean platelet volume, or uterine Doppler to improve accuracy. Nonetheless, NLR's advantages are its low cost and availability from routine bloodwork. In resource-limited settings, such inexpensive markers are attractive for initial risk stratification.[4]

Our findings have potential clinical implications. If confirmed, first-trimester NLR could be added to risk models to identify women who might benefit from closer surveillance or early intervention (e.g. low-dose aspirin) to prevent or mitigate PE. This is especially relevant in India, where preeclampsia prevalence is relatively high and advanced screening resources are limited. Our study suggests that women with early NLR ≥3 should be monitored vigilantly.

Future research should include larger prospective studies across diverse populations to determine generalizability. It would be useful to investigate serial NLR changes through pregnancy, to see if trends improve prediction. Also, integrating NLR into multi-marker algorithms alongside biochemical and ultrasound markers may yield better risk models.

Conclusion

Early-pregnancy NLR was significantly elevated in women who subsequently developed preeclampsia. In our cohort, first-trimester NLR showed good predictive performance (AUC≈0.82) and a clear risk gradient (higher NLR conferring higher PE risk). These results support the concept that systemic inflammation in early gestation heralds later PE. NLR is a simple, readily available marker that may augment early screening for PE in clinical practice, particularly where resources are constrained. Validation in larger studies and in combination with other predictors is warranted.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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