

Elevated Neutrophil-to-Lymphocyte Ratio in First Trimester of Pregnancy – Is a Predictor for Development of Pre-Eclampsia

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ABSTRACT

Background: Pre-eclampsia is a major cause of maternal and perinatal morbidity and mortality, particularly in developing countries. Early identification of high-risk women remains challenging. The neutrophil-to-lymphocyte ratio (NLR), an inexpensive and readily available inflammatory marker derived from routine blood tests, has emerged as a potential predictor of adverse pregnancy outcomes. This study aimed to evaluate the role of first-trimester NLR in predicting the development of pre-eclampsia. **Methods & Materials:** This prospective observational study was conducted in the Department of Obstetrics and Gynaecology at Bangladesh Medical University (BMU), Dhaka, from January to December 2025. A total of 120 pregnant women in their first trimester (≤ 13 weeks) were enrolled consecutively. Socio-demographic and clinical data were recorded and complete blood counts were performed to calculate NLR. Participants were followed until delivery for the development of pre-eclampsia. Statistical analysis was performed using SPSS version 25, with $p < 0.05$ considered significant. **Results:** The mean age of participants was 26.8 ± 4.9 years. Elevated NLR (>3.5) was observed in 33.3% of women. Overall, 31 women (25.8%) developed pre-eclampsia. The incidence increased significantly with rising NLR values, from 11.1% in the <2.5 group to 45.0% in the >3.5 group ($p = 0.002$). Women with elevated NLR had nearly fourfold higher odds of developing pre-eclampsia (OR = 3.82; 95% CI: 1.61–9.05). **Conclusion:** First-trimester NLR is a simple, cost-effective and significant predictor of pre-eclampsia. Incorporating NLR into routine antenatal screening may facilitate early risk stratification

and improve maternal outcomes.

Keywords: Neutrophil-to-lymphocyte ratio, Pre-eclampsia, First trimester, Inflammation, Pregnancy, Predictive marker.

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INTRODUCTION

Pre-eclampsia is a common hypertensive disorder of pregnancy and remains a leading cause of maternal and perinatal morbidity and mortality worldwide, particularly in low- and middle-income countries [1]. It complicates approximately 5–10% of pregnancies and is associated with serious adverse outcomes, including preterm birth, fetal growth restriction, placental abruption, eclampsia and maternal organ dysfunction [2]. Despite advances in antenatal care, early identification of women at risk remains challenging, especially in resource-constrained settings where access to advanced biochemical markers and imaging modalities is limited [3]. Therefore, simple, affordable and readily available predictors are needed to facilitate early risk stratification and timely intervention.

The pathophysiology of pre-eclampsia is complex and multifactorial, involving abnormal placentation, endothelial

dysfunction and an exaggerated systemic inflammatory response [4]. Increasing evidence suggests that inflammation plays a central role in disease development. During normal pregnancy, physiological changes in the immune system occur; however, excessive inflammatory activation may contribute to impaired placental perfusion and vascular dysfunction, ultimately leading to hypertensive complications [5]. Hematological parameters reflecting systemic inflammation have thus gained attention as potential early markers for predicting pre-eclampsia [6].

The neutrophil-to-lymphocyte ratio (NLR), calculated from routine complete blood count parameters, has emerged as a novel and cost-effective indicator of systemic inflammatory status [7]. Elevated neutrophil counts reflect acute inflammatory activation, whereas decreased lymphocyte counts indicate relative immunosuppression or stress and the

combined ratio provides a more stable measure of inflammatory burden [8]. Several studies have demonstrated an association between increased NLR and adverse cardiovascular, metabolic and obstetric outcomes. In pregnancy, higher NLR levels have been linked with gestational hypertension and pre-eclampsia, suggesting its potential utility as an early predictive biomarker [9, 10].

Early detection during the first trimester is particularly important, as it allows closer surveillance, preventive strategies such as low-dose aspirin therapy and improved maternal and fetal outcomes [11]. Because complete blood count testing is routinely performed in antenatal clinics, NLR could serve as a practical screening tool without additional cost or specialized equipment, making it especially suitable for busy tertiary hospitals and developing healthcare systems [12].

Therefore, this study aimed to evaluate the

association between first-trimester neutrophil-to-lymphocyte ratio and the subsequent development of pre-eclampsia and to determine its potential role as an early, simple and reliable predictor among pregnant women attending a tertiary care hospital.

METHODS & MATERIALS

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology at Bangladesh Medical University (BMU), Dhaka, Bangladesh, from January 2025 to December 2025. A total of 120 pregnant women attending the antenatal clinic during the first trimester (≤ 13 weeks of gestation) were enrolled consecutively after obtaining informed written consent. Women aged 18–40 years with singleton pregnancies were included. Exclusion criteria comprised a history of chronic hypertension, pre-existing diabetes mellitus, renal or hepatic disease, autoimmune or inflammatory disorders, hematological diseases, thyroid disorders, acute or chronic infections, multiple gestations, previous pre-eclampsia, current use of corticosteroids or anti-inflammatory

drugs and incomplete follow-up or missing laboratory data, as these conditions could influence inflammatory markers and pregnancy outcomes. Baseline socio-demographic and clinical information, including age, parity, body mass index (BMI), blood pressure and antenatal history, was recorded using a structured questionnaire and clinical examination. Venous blood samples were collected during the first trimester for complete blood count analysis using an automated hematology analyzer. Absolute neutrophil and lymphocyte counts were obtained and the neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the neutrophil count by the lymphocyte count. Participants were followed prospectively through routine antenatal visits until delivery for the development of pre-eclampsia, which was diagnosed according to standard criteria as new-onset hypertension ($\geq 140/90$ mmHg after 20 weeks of gestation) with proteinuria (≥ 300 mg/24 hours or $\geq 1+$ on dipstick). The primary outcome was the association between first-trimester NLR and the subsequent development of pre-eclampsia.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. Continuous variables were expressed as mean \pm standard deviation and categorical variables as frequency and percentage. Group comparisons were performed using the independent t-test and chi-square test and logistic regression analysis was conducted to determine odds ratios with 95% confidence intervals. A p value of <0.05 was considered statistically significant.

RESULTS

Table I presents the socio-demographic characteristics of the 120 enrolled pregnant women. The majority of participants were aged 21–25 years (32.5%), followed by 26–30 years (28.3%), while only 7.5% were older than 35 years. More than half of the women were from urban areas (55.8%). Slightly over half were primigravida (50.8%), with the remainder multigravida (49.2%). Most participants had regular antenatal care visits (60.8%), whereas 39.2% attended irregularly.

Table I
Socio-demographic Characteristics of the Study Participants ($n = 120$).

Variables	Frequency (n)	Percentage (%)
Age group (years)		
<20	17	14.2
21–25	39	32.5
26–30	34	28.3
31–35	21	17.5
>35	9	7.5
Residence		
Urban	67	55.8
Rural	53	44.2
Parity		
Primigravida	61	50.8
Multigravida	59	49.2
Booking status		
Regular ANC	73	60.8
Irregular ANC	47	39.2

Table II shows the baseline clinical and laboratory characteristics of the participants during the first trimester. The mean age was 26.8 ± 4.9 years and the average BMI was 24.6 ± 3.7 kg/m². The mean systolic and diastolic blood pressures

were 112.4 ± 9.6 mmHg and 71.8 ± 7.8 mmHg, respectively. The mean hemoglobin level was 10.9 ± 1.2 g/dL and the total WBC count was $8.7 \pm 2.1 \times 10^9/L$. The mean neutrophil and lymphocyte counts were 6.1 ± 1.8 and 2.3 ± 0.9 ,

respectively. Regarding inflammatory status, 36 women (30.0%) had an NLR <2.5 , 44 (36.7%) had 2.5–3.5 and 40 (33.3%) showed elevated NLR >3.5 .

Table II
Baseline Clinical and Laboratory Characteristics in the First Trimester ($n = 120$).

Variables	Mean \pm SD / n (%)
Age (years)	26.8 ± 4.9
BMI (kg/m ²)	24.6 ± 3.7
Systolic BP (mmHg)	112.4 ± 9.6
Diastolic BP (mmHg)	71.8 ± 7.8
Hemoglobin (g/dL)	10.9 ± 1.2
Total WBC count ($\times 10^9/L$)	8.7 ± 2.1
Neutrophil count	6.1 ± 1.8
Lymphocyte count	2.3 ± 0.9

NLR categories	
<2.5	36 (30.0)
2.5–3.5	44 (36.7)
>3.5	40 (33.3)

Table III illustrates the incidence of pre-eclampsia according to first-trimester NLR categories. Overall, 31 out of 120 women (25.8%) developed pre-eclampsia. The

frequency of pre-eclampsia increased progressively with higher NLR values, occurring in only 11.1% of women with NLR <2.5, 20.5% in the 2.5–3.5 group and

rising markedly to 45.0% among those with NLR >3.5. This trend was statistically significant ($p = 0.002$).

Table III

Incidence of Pre-eclampsia According to First-Trimester NLR Category ($n = 120$).

NLR category	Developed Pre-eclampsia n (%)	No Pre-eclampsia n (%)	Total	p value
<2.5	4 (11.1)	32 (88.9)	36	
2.5–3.5	9 (20.5)	35 (79.5)	44	
>3.5	18 (45.0)	22 (55.0)	40	
Total	31 (25.8)	89 (74.2)	120	0.002*

Table IV demonstrates the association between elevated first-trimester NLR and the development of pre-eclampsia. Women with NLR >3.5 had a significantly higher risk of developing pre-eclampsia, with 18

cases compared to 22 in the non-pre-eclampsia group, yielding nearly fourfold increased odds (OR = 3.82, 95% CI: 1.61–9.05; $p = 0.002$). Although higher BMI (≥ 25 kg/m²), primigravida and age >30

years showed increased odds ratios, these associations were not statistically significant. These findings suggest that elevated NLR is an independent and significant predictor of pre-eclampsia.

Table IV

Association Between Elevated NLR (>3.5) and Development of Pre-eclampsia.

Variables	Pre-eclampsia (n=31)	No Pre-eclampsia (n=89)	Odds Ratio (OR)	95% CI	p value
NLR >3.5	18	22	3.82	1.61–9.05	0.002
BMI ≥ 25 kg/m ²	14	25	2.09	0.91–4.77	0.08
Primigravida	19	42	1.63	0.72–3.69	0.24
Age >30 years	11	19	1.96	0.80–4.82	0.13

DISCUSSION

The present prospective observational study evaluated the role of the first-trimester neutrophil-to-lymphocyte ratio (NLR) as an early predictor of pre-eclampsia among 120 pregnant women. Overall, 25.8% of participants developed pre-eclampsia and the incidence increased progressively with rising NLR values. Women with NLR >3.5 demonstrated a markedly higher occurrence of pre-eclampsia (45.0%) compared with those with NLR 2.5–3.5 (20.5%) and <2.5 (11.1%), with a statistically significant association ($p = 0.002$). Logistic regression further showed nearly fourfold increased odds (OR = 3.82), indicating that elevated NLR is an independent predictor of adverse hypertensive outcomes in pregnancy.

These findings are consistent with the growing evidence linking systemic inflammation to the pathogenesis of pre-eclampsia. Sultana et al. reported a significant association between elevated NLR and pre-eclampsia in a case-control study, emphasizing its usefulness as a simple inflammatory marker [13]. Similarly, Sabry et al. demonstrated higher NLR and platelet indices among pre-eclamptic women, supporting the role of inflammatory hematological parameters in disease prediction [14]. Khan et al. also identified NLR as a reliable marker for both clinical prediction and disease

severity evaluation, which aligns with our observation of increased risk among women with higher NLR levels [15].

Endothelial dysfunction and neutrophil activation are key mechanisms in pre-eclampsia. Wazib et al. found a correlation between neutrophil elastase levels and NLR, suggesting that increased neutrophil activity contributes to vascular injury [16]. Our higher mean neutrophil counts (6.1 ± 1.8) and elevated NLR categories further reinforce this inflammatory basis. Additionally, Liao et al. and Liu et al. reported that peripheral blood parameters, particularly neutrophil-related indices, could predict both occurrence and severity of pre-eclampsia, findings that parallel our results [17,18].

Several studies have emphasized the predictive utility of first-trimester hematological markers. Mensah et al. demonstrated that NLR, along with platelet indices, had good predictive value for pre-eclampsia in a teaching hospital setting, while Srinivasa et al. highlighted NLR as an early, inexpensive screening parameter [19,20]. Tekin et al. also confirmed that first-trimester clinical and laboratory findings, including inflammatory markers, are helpful in early risk stratification [21]. Furthermore, Seyhanli et al. showed that first-trimester inflammatory indexes such

as NLR and PLR were significantly associated with later development of pre-eclampsia, supporting our strategy of early measurement [22].

More recently, Liang et al. developed a comprehensive first-trimester predictive model incorporating multiple indicators, where inflammatory markers improved prediction accuracy [23]. Our findings similarly suggest that NLR could be integrated into routine antenatal screening models, especially in resource-limited settings where advanced biomarkers may not be available. Given that complete blood count testing is routinely performed, NLR offers a cost-effective and easily accessible alternative without additional financial burden.

In summary, the present study corroborates previous evidence that elevated first-trimester NLR reflects systemic inflammation and is significantly associated with the subsequent development of pre-eclampsia. The progressive rise in incidence from 11.1% to 45.0% across NLR categories and the nearly fourfold increased risk highlight its clinical relevance. Therefore, NLR may serve as a simple, affordable and practical early screening tool for identifying high-risk pregnancies and enabling closer

monitoring and timely preventive interventions.

LIMITATIONS

This study has several limitations that should be considered while interpreting the findings. It was conducted at a single tertiary care center with a relatively small sample size of 120 participants, which may limit the generalizability of the results to the wider population. Although efforts were made to exclude confounding conditions, unmeasured factors such as nutritional status, subclinical infections and other inflammatory states might have influenced NLR values. Additionally, NLR was assessed only once during the first trimester and serial measurements could have provided a better understanding of dynamic inflammatory changes throughout pregnancy.

CONCLUSION

In conclusion, the present study demonstrates that an elevated first-trimester neutrophil-to-lymphocyte ratio is significantly associated with the subsequent development of pre-eclampsia. Women with higher NLR values showed a markedly increased risk, suggesting that NLR can serve as a simple, inexpensive and readily available early screening marker. Incorporating NLR into routine antenatal evaluation may help identify high-risk pregnancies for closer monitoring and timely preventive interventions, ultimately improving maternal and fetal outcomes.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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