Original Research Article

The role of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in determining the severity of pre-eclampsia in antenatal women: A case control study

Madhurya Nagesh[1]*, Rathnamma P[1], Thonangi Aashritha[1], Kalyani Raju[2]

[1]Dept. of Obstetrics and Gynaecology, Sri Devaraj Urs Medical College, Kolar, Karnataka, India
[2]Dept. of Pathology, Sri Devaraj Urs Medical College, Kolar, Karnataka, India

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ABSTRACT

Background: Pre-eclampsia (PE) remains a significant global health concern, affecting 2-8% of pregnancies and contributing to maternal and perinatal morbidity and mortality. Characterized by hypertension and proteinuria after 20 weeks of gestation, PE often involves systemic inflammation and endothelial dysfunction. Its exact etiology is multifactorial, involving immune dysregulation and vascular abnormalities. Early identification of high-risk pregnant women is crucial to mitigate adverse outcomes. In India, PE affects 8-10% of pregnancies.

Inflammatory markers such as the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) have emerged as potential indicators of systemic inflammation. Elevated NLR and PLR levels in PE suggest a role in the disorder's pathophysiology, reflecting immune responses to placental ischemia and pro-inflammatory cytokine release.

This study aims to compare NLR and PLR levels between PE patients and normotensive pregnant women, evaluate their association with PE severity, and discuss their potential as predictive biomarkers.

Materials and Methods: A case-control study was conducted with 84 participants, following eligibility criteria via convenient sampling. Demographic characteristics, obstetric history, and CBC-derived biomarkers were assessed.

Results: Among 84 pregnant women, 42 had preeclampsia (PE) and 42 were normotensive. The PE group had significantly higher Neutrophil-to-Lymphocyte Ratios (5.11 ± 2.88 vs. 2.74 ± 0.78) and Platelet-to-Lymphocyte Ratios (108 ± 46.7 vs. 85.4 ± 29.4) compared to controls. PE incidence peaked between 34-38 weeks. Higher PLR and NLR values were linked to severe PE. ANC booking was lower in the PE group. Obesity trends were not statistically significant. Significant associations were found between elevated NLR and PLR and PE severity, highlighting their potential clinical utility.

Conclusion: Our findings indicate NLR and PLR as valuable biomarkers for predicting and managing PE. Integration of these markers into routine prenatal care could enhance clinical management and improve maternal and fetal outcomes.

1. Introduction

Preeclampsia (PE), a specific hypertensive disorder remains a significant cause of maternal and perinatal morbidity and mortality worldwide, affecting approximately 2-8% of pregnancies globally.[1,2] It is characterized by hypertension and proteinuria after 20 weeks of gestation, often accompanied by systemic inflammation and endothelial dysfunction.[3,4] The exact etiology of PE remains elusive,

* Corresponding author.
E-mail address: madhuryamedico@gmail.com (M. Nagesh).

but it is increasingly recognized as a multifactorial condition involving immune dysregulation and vascular abnormalities.[5] Early identification of pregnant women at high risk for developing preeclampsia or severe forms of the condition is crucial to mitigate adverse pregnancy outcomes.[6] In India, it is estimated to affect 8-10% of pregnant women.[7]

Inflammatory markers such as the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) have emerged as potential indicators of systemic inflammation and stress in various medical conditions.[6,8] In the context of PE, elevated levels of these ratios have been linked to the inflammatory response characteristic of the disorder.[9,10] Neutrophilia and alterations in lymphocyte and platelet counts are common in PE, reflecting the immune system's response to placental ischemia and the release of pro-inflammatory cytokines.[2]

Understanding the role of NLR and PLR in PE could provide valuable insights into its pathophysiology and potentially improve diagnostic and prognostic strategies. Recent studies have suggested that these ratios may not only differentiate between PE and normal pregnancies but also correlate with the severity of PE and predict adverse maternal and fetal outcomes.[7,8]

Therefore, this study aims to comprehensively compare the levels of NLR and PLR in patients with PE and normal pregnant women, evaluate their association with PE severity and discuss their potential clinical utility as predictive biomarkers. This study therefore highlights the significance of NLR and PLR in maternal health care.

2. Materials and Methods

A case-control study was conducted in a tertiary Obstetrics and Gynecology Department after obtaining Internal Ethical Committee approval on [date:11/6/2024] with Ethics Committee clearance number [SDUAHER/KLR/R&D/CEC/S/PG/20/2024-25]. It included all pregnant women with singleton pregnancy attending the outpatient department (OPD) or admitted in the obstetric ward after taking their consent. A Sample Size of 82, (rounded to 84 for similarity) was calculated using formula n= $z^2(SD_1+SD_2)/(m_1-m_2)^2$ with z= 1.96 for 95% CI, m_1= mean of case group (3.52); m_2= mean of control group (3.22); SD_1= mean of case group (1.05) SD_2= mean of control group (0.88); with PE patients grouped into cases and healthy normotensive pregnant women as controls from June 12 2024, to July 12, 2024; following convenient sampling. Patients with gestational hypertension, chronic hypertension, gestational diabetes mellitus, thyroid disorders, tuberculosis, acquired infections during the early stage of pregnancy, pre-existing vascular diseases or malignancy, history of alcohol or tobacco use, premature rupture of membranes, and history of COVID-19 infection were excluded.

Detailed history was taken along with the abdomen examination. Cases were categorized as severe and non-severe PE patients based on American College of Obstetricians and Gynecologists (ACOG) criteria.[11] Obstetric outcomes like gestational age at delivery, mode of delivery, indication for cesarean delivery, antepartum, intra-partum, and postpartum complications, and neonatal outcomes were documented. NLR and PLR were calculated from noting absolute counts of neutrophils, lymphocytes, and platelets

Data was entered into an Excel sheet and analyzed in STATA version 10.1 (StataCorp LLC, College Station, TX) Quantitative variables were summarized by descriptive statistics & categorical variables were summarized as frequency (%). The chi-square test compared attributes in two groups and a p-value of 0.05 or lower was considered statistically significant.

3. Results

A total of eighty four pregnant women were enrolled in the study with 42 having PE and remaining 42 normotensive. Mean age of the participants among PE group and normotensive group were 26.43 ± 4.05 & 25.83 ± 3.63 years respectively. In both groups, the majority of women were in the 25-30 age groups. A higher percentage of women in the PE group lived in rural areas (78.57%) compared to the normotensive group (71.43%), while a higher percentage of women in the normotensive group lived in urban areas (28.57%) compared to the PE group (21.43%).The majority of women in both groups belong to the upper middle (47.62%) followed by lower middle (26.19%) socioeconomic status.

A higher percentage of women in the normotensive group (76.19%) booked antenatal care (ANC) services compared to the PE group (45.24%), indicating that there is an association between ANC booking status and the occurrence of PE. (P< 0.05).

The distribution of obstetric history was fairly similar between two groups with 54.76% primigravida and 42.24% cases showed multigravida while 47.62% primigravida and 52.38% multigravida among controls respectively.

Mean Neutrophil-to-Lymphocyte Ratio (NLR) in the case group and control group was 5.11 ± 2.88 and 2.74 ± 0.78, respectively, with statistically significant results (p<0.05). Additionally, the Platelet-to-Lymphocyte Ratio (PLR) in the case group was 108 ± 46.7, and in the control group, it was 85.4 ± 29.4, having a significant difference between both the groups along with a significant difference in the case group among the severe and non-severe PE. PLR reading above ninety and NLR value greater than 3 showed to have significantly reported severe PE in pregnant women. (P< 0.05) (Figures 1 and 2)

PE incidence peaked between 34 to 38 weeks of gestation and declined thereafter (p < 0.05). (Figure 3)

Mean Body Mass Index (BMI) was 27.80 ± 4.57 in the PE group and 25.97 ± 3.99 in the normotensive group, with obesity showing a trend towards increased PE risk, although statistically insignificant ($p > 0.05$). (Figure 4)

Although statistically insignificant, cases with a higher mean PLR were shown to have IUD. (Table 1)
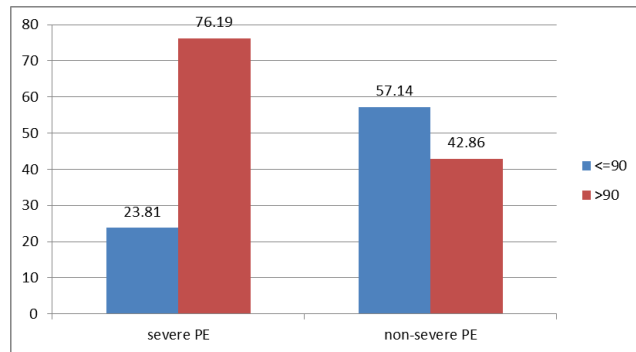

Figure 1: Relationship between the severity of pre-eclampsia and PLR PE: Pre-eclampsia; PLR: Platelet-to-lymphocyte ratio
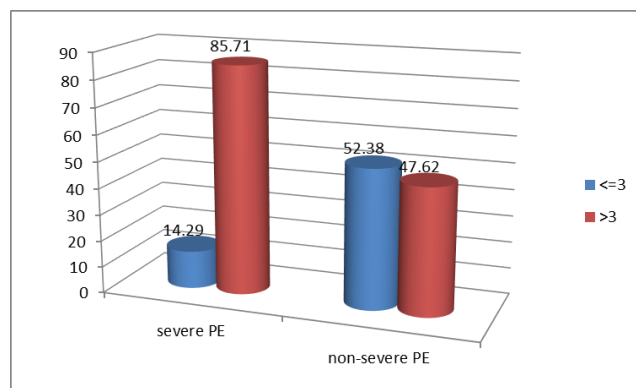

Figure 2: Relation between severity of pre-eclampsia and NLR PE: Pre-eclampsia; NLR: Neutrophil-to-lymphocyte ratio.
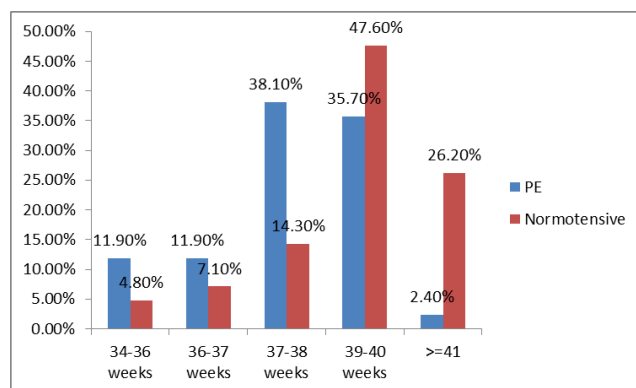

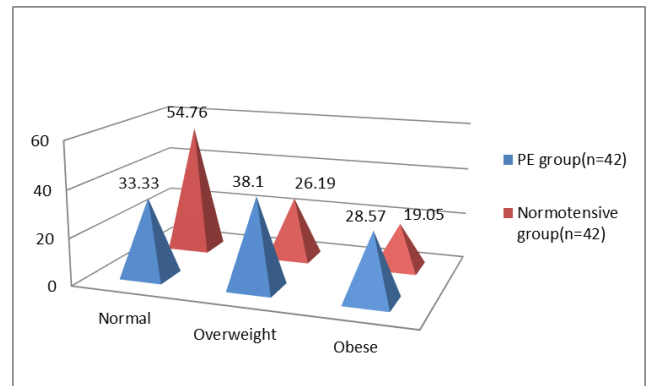**Figure 3:** Relation between gestational age and pre-eclampsia

Figure 4: Relation between BMI category and pre-eclampsia

4. Discussion

In this study, we investigated the NLR and PLR levels in pregnant women with PE compared to normotensive pregnant women, aiming to assess their association with PE severity and explore their potential as predictive biomarkers. The demographic analysis revealed that both groups had similar age distributions, predominantly comprising women aged 25-30 years. However, a higher proportion of women in the PE group resided in rural areas compared to those in the normotensive group, whereas urban residence was more prevalent among normotensive women. Socioeconomic status analysis showed a predominant representation of the upper middle class in both groups, highlighting potential similarities in lifestyle and healthcare access affecting outcomes.

Both groups exhibited comparable distributions in obstetric history, with a slightly higher proportion of primigravida in the PE group. However, significant differences were observed in the rates of booking ANC services, with fewer PE patients booking ANC compared to their normotensive counterparts, where more patients had adequate ANC visits or were booked cases. This finding suggests a potential association between inadequate prenatal care and an increased risk of PE, consistent with previous findings.[1]

Analysis of NLR and PLR revealed significantly elevated levels in the PE group compared to normotensive controls. Elevated NLR and PLR have been associated with systemic inflammation and oxidative stress, which are recognized contributors to the pathogenesis of PE.[3,4,12] Importantly, higher NLR and PLR values correlated with severe cases of PE within our study cohort, indicating their potential utility as predictive markers for disease severity and maternal outcomes.

Our findings support previous studies that underscore NLR and PLR as valuable biomarkers in predicting PE and assessing its severity.[6,8] These biomarkers reflect underlying inflammatory processes and endothelial

Table 1: Relation between NLR, PLR and adverse pregnancy outcomes

| Adverse pregnancy outcome | PE group (n=42) | | | | | | Normotensive group (n=42) |
| | Severe pre-eclampsia(n=21) | | | Non-severe pre-eclampsia(n=21) | | | |
	No.(%)	Mean NLR	Mean PLR	No.(%)	Mean NLR	Mean PLR	
IUD	3(14.29)	6.63	138.98	1(4.76)	7.5	128.4	0
Antepartum Eclampsia	2(9.52)	5.05	132.25	0(0.00)	0	0	0
Abruptio placenta	2(9.52)	5.8	98.3	0(0.00)	0	0	0

dysfunction, which are pivotal in the pathophysiology of PE.[9,10]

Canzoneri et al. highlighted a significant increase in neutrophil numbers contributing to leukocytosis observed in women with PE, suggesting a link between heightened neutrophil activity and the inflammatory milieu characteristic of PE.[13] Studies conducted in antenatal women with PE further reinforced the role of NLR and PLR as potential biomarkers for predicting the onset and severity of PE across diverse populations.[9,14] Cui et al. explored NLR as a marker for liver and coagulation dysfunction in PE patients, indicating its utility in reflecting systemic inflammation and organ-specific complications.[14] Additionally, NLR and PLR were affirmed as prognostic markers in pregnancy, crucial for guiding the clinical management of PE.[15]

5. Conclusion

Our study contributes to the evolving understanding of NLR and PLR as predictive biomarkers for PE onset, severity, and complications. Further validation and integration of these biomarkers into routine prenatal care protocols hold promise for improving maternal and fetal outcomes in pregnancies complicated by PE. These CBC-derived markers offer accessible, predictive insights, enhancing PE management across healthcare settings, especially helpful in low-resource and rural settings.

6. Author Contributions

Authors 1 have drafted the manuscript. Authors 2, 3 and 4 have been a part of conceptualization and final approval of the study.

7. Source of Funding

None declared.

8. Conflicts of Interest

The authors declare no conflicts of interest.

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Author's biography

Madhurya Nagesh, Junior Resident https://orcid.org/0009-0003-2697-425X

Rathnamma P, Professor

Thonangi Aashritha, Assistant Professor

Kalyani Raju, Professor ⓘ https://orcid.org/0000-0003-1090-0558