

Neutrophil-Lymphocyte Ratio in Pregnancy Induced Hypertension- A Comparative Study

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Abstract:

Introduction: Hypertension is one of the common medical complications of pregnancy that contributes significantly to maternal and perinatal morbidity and mortality. The neutrophil-to-lymphocyte ratio (NLR) is a marker of subclinical inflammation, used to predict hypertension incidence, especially preeclampsia.

Objective: To compare neutrophil-lymphocyte ratio between subjects with pregnancy-induced hypertension and normotensive pregnant subjects.

Materials & Methods: This cross-sectional comparative study was carried out over a period of one year after informed consent and ethical clearance. The study population included 260 antenatal patients of 29-40 weeks of gestation (130 pregnant women with pregnancy-induced hypertension (PIH) and 130 normotensive pregnant women) who were admitted in the department of Obstetrics & Gynaecology, Assam Medical College & Hospital, Dibrugarh, after fulfilment of inclusion and exclusion criteria. The primary outcome was neutrophil-lymphocyte ratio (NLR).

Result: NLR was significantly higher in pregnant women with PIH (3.58 ± 0.79) and normotensive pregnant women (2.38 ± 0.58) ($p < 0.001$).

Conclusion: The study showed that the mean NLR value of pregnant subjects with PIH was noticeably higher than that of normotensive pregnant subjects, suggesting an increased inflammatory response in hypertensive disorder of pregnancy. Unlike many other inflammatory markers, NLR proves to be an inexpensive and readily available biomarkers, obtained from complete blood counts that may be useful for prediction and diagnosis of pre-eclampsia.

Keywords: Neutrophil-lymphocyte ratio (NLR), pregnancy-induced hypertension (PIH).

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Introduction

The hypertension diagnosed after 20 weeks of gestation is known as pregnancy-induced hypertension (PIH). [1]

Prior to the 2000s, hypertension that developed during pregnancy was commonly referred to as "pregnancy-induced hypertension" (PIH). After 2005, the term "hypertensive disorders of pregnancy (HDP)" started to take the place of "pregnancy-induced hypertension" (PIH) and this change was further cemented in 2018 when classifications were standardized. These days, "hypertensive disorders of pregnancy" (HDP) is the preferred term, covering a variety of conditions such as preeclampsia, gestational hypertension, and preeclampsia on top of chronic hypertension. [2,3]

Worldwide, eclampsia and preeclampsia constitute the main causes of maternal death and morbidity which complicate 10% of all pregnancies globally.

[4] According to additional research, preeclampsia affects 2–8% of pregnancies worldwide and accounts for up to 12% of maternal deaths worldwide. [5,6] In India, they are responsible for up to 30% of mortality.

Pregnancy complications caused by hypertension are common (10–14%) and are among the three deadly triads that cause morbidity in mothers and newborns, along with bleeding and infection. [7] Preeclampsia is more common in developing nations like India because of low socioeconomic level, apathy, inadequate health education, and irregular prenatal care. [8] Very few studies have been conducted in India's northeastern state of Assam.

One of the leading causes of maternal morbidity and death is pre-eclampsia. [9] Approximately 2–8% of pregnancies globally are complicated by it. [10,11] Due to the absence of trophoblastic inva-

sion, there is insufficient placentation, which results in placental hypoxia, elevated neutrophil numbers, thrombocyte activation, systemic inflammation, and endothelial dysfunction. [3] Preeclampsia's clinical symptoms are linked to widespread endothelial dysfunction, which results in end-organ ischemia and vasoconstriction. [12,13] Preeclampsia symptoms include excruciating headaches, visual abnormalities blurred vision, excruciating discomfort between the ribcage, vomiting, and facial, hand, or foot edema. [14]

Pregnancy activates circulating maternal leukocytes- including neutrophils, lymphocytes, and monocytes, and PIH activates them much more. [15] The placenta releases lipids that go across the intervillous area and activate leukocytes. These activated leukocytes may be to blame for preeclampsia's vascular dysfunction since they re-enter the maternal systemic circulation. [15]

The neutrophil-lymphocyte ratio (NLR) is a biomarker that combines two components of the immune system- the innate immune response, which is mostly caused by neutrophils, and adaptive immunity, which is bolstered by lymphocytes. [16]

NLR is cheap ratio that can be easily calculated from a basic blood count, is a gauge of endothelial dysfunction and systemic inflammation. The ratio is commonly used as a prognostic factor in many medical disciplines because of how simple it is to calculate and how simply it reflects an inflammatory load. [17] A reliable sign of mild inflammation in several clinical contexts is the neutrophil lymphocyte ratio (NLR). [18] Numerous factors affect NLR, such as age, stress, anemia, medication, chronic illnesses like heart disease, stroke, diabetes, obesity, mental health diagnoses, solid organ cancer, and rice. [19]The neutrophil and lymphocyte counts in particular, which make up the differential white cell count, have been suggested to be clinically useful in disease prediction in recent years.20 Adult NLR normal range is between 1-2, and values above 0.3 and below 0.7 are pathological. [19]

The purpose of this research is to assess the diagnostic precision of NLR in the identification of pregnancy-induced hypertension (PIH) by a quick, affordable, and accessible way. This will help us to manage patients before the develop any complications. [20]

Materials and Methods

This was a comparative cross-sectional study conducted in 260 antenatal patients in 3rd trimester (130 pregnant women with pregnancy-induced hypertension (PIH) and 130 normotensive pregnant women) from October 2023 to September 2024, who were admitted in the department of Obstetrics & Gynaecology, Assam Medical College & Hospital, Dibrugarh, after fulfillment of inclusion and

exclusion criteria. The study was conducted in the department of physiology in collaboration with the department of Obstetrics & Gynaecology, AMCH, and Dibrugarh, Assam.

Study Population: Pregnant women in 3rd trimester (29 to 40 weeks of gestation) with or without pregnancy-induced hypertension (PIH) admitted in Obstetrics & Gynaecology Department, AMCH, and Dibrugarh.

Sample Size: Considering the neutrophil-lymphocyte ratio (NLR) to be 4.01 ± 1.53 and 3.62 ± 0.33 among the pregnant women with pregnancy-induced hypertension (PIH) and normotensive pregnant women respectively,²¹ sample size for the present study was calculated and rounded off to be 130 in each group with 95% confidence and 80% power.

Inclusion Criteria:

- Pregnant women in 3rd trimester (29 and 40 weeks of gestation) with pregnancy-induced hypertension (PIH) [7] who gave consent.
- Normotensive pregnant women in 3rd trimester (29 and 40 weeks of gestation) who gave consent.

Exclusion Criteria:

- Patients with essential hypertension.
- Patients with history of haemorrhagic disorder, epilepsy, diabetes mellitus, on anti-coagulation therapy, hepatic or renal disorder.
- Patients with multifetal gestation.
- Pregnant women in labour.
- Patients with bad obstetric history.
- Those not giving consent.

Case Definition: Pregnant women in 3rd trimester (29 to 42 weeks of gestation) diagnosed as pregnancy-induced hypertension admitted in the Department of Obstetrics & Gynaecology, AMCH, and Dibrugarh.

Informed Consent: Every participant received a description of the study, and prior to their enrolment, their informed written consent was obtained.

Ethical Clearance: This study was commenced after obtaining clearance from the Institutional Ethics Committee (Human), Assam Medical College, Dibrugarh.

Methodology: Pregnant women fulfilling the inclusion criteria were identified. Written consent was taken after proper explanation. A detailed history was taken, general examination and systemic examination including the obstetrical examination.

Pregnancy-induced hypertension (PIH) subjects were identified as per American College of Obstetricians & Gynaecologists (ACOG) guidelines.

Blood sample was collected with all aseptic and

antiseptic measures in purple top vial (EDTA vial). Total and differentials leukocyte counts were measured by an automated hematology analyser SYSMEX XN-550 along with full blood count. Neutrophils and lymphocytes level are measured and neutrophil to lymphocyte ratio in the obtained blood samples are determined. Data were entered in microsoft excel sheet and analysed statistically.

Statistical Analysis: The statistical analysis of data was performed using the computer program, Statistical Package for Social Sciences (SPSS for Win-

dows, version 20.0. Chicago, SPSS Inc.) And Microsoft Excel 2010. Results on continuous measurements are presented as mean \pm standard deviation are compared using student t test. For all analyses, the statistical significance was fixed at 5% level (p value <0.05).

Results

The mean age, gestational age, systolic blood pressure and diastolic blood pressure in cases are decreased compared to matched controls as shown in Table 1.

Table 1: Demographic data of study group and control group

| Parameters | Hypertensive (Cases) | Normotensive (Control) | p-value |
|-----------------------------|----------------------|------------------------|----------|
| Age (years) | 29.95 \pm 5.80 | 28.94 \pm 5.88 | 0.162 |
| Period of gestation (weeks) | 37.07 \pm 2.45 | 34.71 \pm 3.65 | <0.001 |
| SBP (mmHg) | 161.08 \pm 8.38 | 117.04 \pm 11.44 | <0.001 |
| DBP (mmHg) | 106.62 \pm 7.26 | 72.83 \pm 7.12 | <0.001 |

SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 2: Mean NLR Distribution of Study Subjects

| Variable | Hypertensive | | | Normotensive | | | p value* |
|----------|--------------|------|------------|--------------|------|------------|------------|
| | Number | Mean | \pm S.D. | Number | Mean | \pm S.D. | |
| NLR | 130 | 3.58 | 0.79 | 130 | 2.38 | 0.58 | <0.001 * |

*Student t Test; The p-value is significant at 5% level of significance

The above table indicates that, the mean NLR in hypertensive group is 3.58 ± 0.79 and that in normotensive group is 2.38 ± 0.58 , which is statistically significant ($p < 0.001$).

Discussion

Pregnancy-associated intrahepatic cholestasis, endometriosis, hyperemesis gravidarum, gestational diabetes, preeclampsia, ovarian hyperstimulation syndrome, premature ovarian insufficiency, gynaecological malignancies, and other conditions have all been evaluated for NLR in the literature on obstetrics and gynaecology. [22] Maternal and neonatal outcomes have been predicted using NLR as a tool. [23] To avoid complications such as HELLP syndrome and increased maternal and fetal morbidity and death, early evaluation of the severity of pre-eclampsia and eclampsia is essential. It is possible to use maternal NLR to predict preeclampsia and the severity of preeclampsia, although there haven't been many studies on this topic. [15]

By analyzing the NLR in subjects with PIH and normotensive pregnant subjects, we aim to use maternal NLR as a predictor of PIH, which is a leading maternal mortality and morbidity. The current study's findings and observations are compared in view of the data, information, and observations that have been made by other researchers in this topic in their research.

In the present study, the mean age (years) was observed to be 29.95 ± 5.80 and 28.94 ± 5.88 in hyper-

tensive subjects and normotensive subjects respectively. ($p=0.162$) The mean gestational age (weeks) was observed to be 34.71 ± 3.65 in normotensive pregnant subjects, 37.07 ± 2.45 in hypertensive subjects ($p < 0.001$).

The systolic blood pressure (mmHg) was observed to be 117.04 ± 11.44 in normotensive pregnant subjects, 161.08 ± 8.38 in hypertensive subjects ($p < 0.001$).

The diastolic blood pressure (mmHg) was observed to be 72.83 ± 7.12 in normotensive pregnant subjects, 106.62 ± 7.26 in hypertensive subjects ($p < 0.001$).

However, Meena et al. [7], in their study, reported that mean age (years) was 27.60 ± 6.47 in hypertensive pregnant women and 26.98 ± 6.33 in normotensive pregnant women ($p=0.502$); also, mean gestational age (weeks) was 35.3 ± 2.6 in preeclamptic subjects and 37.9 ± 1.3 in normotensive pregnant women ($p < 0.001$). The mean SBP (mmHg) was 156.44 ± 13.8 in preeclamptic subjects and 108.16 ± 11.15 in normotensive pregnant women ($p < 0.001$) the mean DBP (mmHg) was 101.39 ± 9.73 in preeclamptic subjects and 67.54 ± 7.55 in normotensive pregnant women ($p < 0.001$).

Similarly, Sweed et al. [21], in their study, reported that mean age (years) was 29.11 ± 2.90 in hypertensive pregnant women and 28.83 ± 2.56 in normotensive pregnant women ($p=0.66$); but mean gesta-

tional age (weeks) was 36.26 ± 1.46 in preeclamptic subjects which was lower than normotensive pregnant women 37.91 ± 1.36 ($p < 0.001$). The mean SBP (mmHg) was 142.43 ± 12.62 in preeclamptic subjects and 109.71 ± 11.24 in normotensive pregnant women ($p < 0.001$); and the mean DBP (mmHg) was 96 ± 8.98 in preeclamptic subjects and 69.57 ± 7.71 in normotensive pregnant women ($p < 0.001$).

The findings in these studies correlates with the present study showing significant difference between two groups in relation to mean gestational age, systolic and diastolic blood pressure, and insignificant finding in relation to mean age.

Comparison of subjects according to mean NLR

In the present study, the mean NLR was observed to be 3.58 ± 0.79 and 2.38 ± 0.58 in pregnant women with PIH and normotensive pregnant women respectively. ($p < 0.001$)

Singgih et al. [4], in their study, similarly reported that mean NLR was 6.75 ± 4.84 in hypertensive pregnant women and 6.01 ± 5.04 in normotensive pregnant women ($p = 0.004$).

A study done by Yavuzcan et al. [26] reported that mean NLR in severe preeclamptic subjects was 4.04 ± 2.03 and in normotensive subjects was 3.76 ± 1.28 ($p = 0.000$).

Firdaus et al. [24], in their study, reported that mean NLR was 5.911 ± 3.663 in normotensive pregnant women and 3.403 ± 0.975 in preeclamptic subjects ($p < 0.001$).

Singhal et al. [27], in their study, reported that mean NLR was 5.64 ± 1.789 in preeclamptic subjects and 4.19 ± 1.00 in normotensive subjects ($p < 0.001$).

A study by Swetha et al. [20], it was observed that mean NLR was 4.64 ± 1.08 in hypertensive pregnant women and 2.35 ± 0.78 in normotensive pregnant women ($p < 0.05$). Toptas et al. [25], in their study, reported that mean NLR was 7.4 ± 5.2 in preeclamptic subjects and 7.2 ± 3.7 in normotensive subjects ($p = 0.7$).

This study demonstrated that NLR is significantly higher in subjects with PIH than in normotensive pregnant subjects. This may serve as a predictor of PIH. In antenatal follow-up, measurement of NLR periodically may be useful to predict high-risk pregnancies in terms of PIH.

Conclusion

The study found that the mean NLR value of hypertensive subjects was noticeably greater than that of subjects with normotension, suggesting an increased inflammatory response in hypertensive disorder of pregnancy. Despite using a suitable

formula to calculate the sample size, the limitations of a small sample size cannot be completely eliminated because it cannot be more accurately projected in the general population. Nevertheless, extensive prospective research is required to identify the ideal NLR value and its predictive relevance in the diagnosis of PIH and to predict the incidence of hypertension with pregnancy. Maternal NLR obtained from complete blood count can be considered a cost-effective biomarker for predicting the severity of PIH.

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