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Original Research Article

Association of maternal neutrophil-lymphocyte ratio with adverse perinatal outcomes in preterm premature rupture of membranes: a case-control study

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ABSTRACT

Background: Preterm premature rupture of membranes (PPROM) is a significant contributor to preterm birth and is associated with both maternal and perinatal complications. Neutrophil lymphocyte ratio (NLR) is an emerging marker of systemic inflammation. This study was conducted to evaluate the association of maternal NLR with adverse maternal and perinatal outcomes in PPROM cases.
Methods: This prospective case-control study was conducted among 60 pregnant women (30 PPROM cases with elevated NLR and 30 controls with normal NLR). Maternal NLR was calculated using complete blood count reports. Participants were grouped based on NLR levels and their association with maternal and perinatal outcomes were study.
Results: The incidence of neonatal intensive care unit (NICU) admission was significantly higher among newborns in the case group (70%) compared to the control group (36.66%). Similarly, perinatal mortality was markedly elevated in the case group (70%) relative to the control group (13.33%), indicating an overall poorer perinatal outcome in the case group.
Conclusion: Elevated maternal NLR is significantly associated with adverse maternal and perinatal outcomes in PPROM. It can serve as a simple and cost-effective inflammatory marker for risk stratification and early intervention.

Keywords: PPROM, Neutrophil-lymphocyte ratio, Perinatal outcomes

INTRODUCTION

Preterm premature rupture of membranes (PPROM) refers to spontaneous rupture of fetal membranes before 37 weeks of gestation and prior to the onset of labor.[1] It complicates approximately 3% of all pregnancies and is a leading cause of preterm births globally.[2,3] PPROM is associated with significant maternal and neonatal risks, including chorioamnionitis, puerperal pyrexia, puerperal sepsis, urinary tract infection, postpartum hemorrhage neonatal intensive care unit (NICU) admissions, low birth weight, low appearance, pulse, grimace, activity, and respiration (APGAR) score.[3]

Many etiological factors may be taken into consideration like prior preterm birth, sexually transmitted infections, cervical surgery (past or present), low socioeconomic level, low maternal body mass index, amniocentesis that can cause preterm premature rupture of membrane.[4]

The pathogenesis of PPROM is multifactorial, with inflammation playing a central role in the weakening of fetal membranes.[4] Several inflammatory markers, including the neutrophil lymphocyte ratio (NLR), have emerged as potential tools in identifying systemic inflammation.[5,6]

NLR is an inexpensive and widely accessible marker derived from complete blood count, offering diagnostic and prognostic insight into various inflammatory and obstetric conditions.[7] Despite growing interest, limited research has evaluated the role of maternal NLR in predicting adverse perinatal outcomes in PPROM, particularly in the Indian population.[1] The present study was conducted to assess the association between maternal NLR and perinatal outcomes in women with PPROM.

METHODS

This prospective case-control study was conducted in the Department of Obstetrics and Gynaecology at SMS Medical College, Jaipur. A total of 60 antenatal women with gestational age 24 weeks and 36+6 weeks with PPROM were included: 30 with abnormal NLR (cases) and 30 with normal NLR (controls) between July 2023 to June 2024. The inclusion criteria for cases and controls were women with singleton, live pregnancy with gestational age 24 weeks to 36 weeks+6 day with Abnormal/Normal neutrophil lymphocyte ratio with PPROM group. The exclusion criteria included preeclampsia, diabetes mellitus, fetal anomalies, and known autoimmune/infectious conditions.

On admission blood sample of all women was taken for complete blood count before administration of steroid and antibiotic prophylactics. Absolute neutrophil count to absolute lymphocyte count was calculated and maternal neutrophil to lymphocyte ratio was assessed. All women were followed till delivery and discharge from hospital, fetal outcome was studied with regard to need for admission to NICU, birth weight and APGAR score. Data was collected and compiled; statistical analysis was done.

The calculation of results and statistical analysis were carried out using Microsoft Excel (MS Office 2010 Microsoft Corp., Redmond, WA, USA) and appropriate statistical tools.

RESULTS

The study examined various demographic, socio-economic, and clinical factors among two groups: cases and controls, each consisting of 30 individuals. The study found no significant difference between age groups, gestational age at birth, parity and socio- economic status among cases and controls.

Out of 30 cases, 13 were primigravidas while 17 were multiparous women. Out of 30 cases 22 had normal vaginal deliveries (NVD), while caesarean sections (CS) were 8 (Table 1).

There was no difference between demographic and obstetric data between two groups.

In the present study, various perinatal outcomes were compared between cases and controls. The mean birth weight in the case group was 1.87±0.83 kg, which was lower than that in the control group (2.15±0.75 kg), with a p value of 0.06, indicating a statistically non-significant difference. NICU admission was required in 70% of cases (21 out of 30) compared to 36.66% of controls (11 out of 30). Resuscitation at birth was needed in 53.33% of cases and 30.00% of controls, though the difference was not statistically significant (p=0.116). The proportion of newborns with an Apgar score ≥7 at 1 minute was 33.33% in cases and 60.00% in controls. However, at 5 minutes, 46.66% of cases and 80.00% of controls had an APGAR score ≥7, which was statistically significant (p=0.024). These findings suggest a trend toward poorer perinatal outcomes in the case group compared to controls (Table 2).

Table 1: Demographical parameters in cases and controls.

Parameters	Case (n=30)	Control (n=30)	P value
Mean age (years)	27±2.45	25.9±4.5	0.387
Mean gestational age at birth (weeks)	33.60±2.47	34.26±1.91	0.070

Table 2: Perinatal outcome in cases and controls.

Parameter	Case	Control	P value
Birth weight (kg)	1.87±0.83	2.15±0.75	0.06
NICU admission (%)	21 (70.00)	11 (36.66)	0.010
Resuscitation at birth (%)	16 (53.33)	9 (30.00)	0.116
APGAR score at 1 minute ≥7 (%)	10 (33.33)	18 (60.00)	0.116
APGAR score at 5 minutes ≥7 (%)	14 (46.66)	24 (80.00)	0.024

Table 3 shows maternal outcomes. The case group showed a higher prevalence of maternal complications compared to the control group. Chorioamnionitis (6.7%), puerperal pyrexia (13.3%), puerperal sepsis (6.7%), and postpartum hemorrhage (10%) were more common among cases. Puerperal pyresia was the most common maternal complication in the case group. Although urinary tract infections were slightly more frequent in the control group (6.7% versus 3.3%), the overall findings suggest an increased risk of adverse maternal outcomes in the case group.

The mean NLR was significantly higher in the case group (6.00±2.53) compared to the control group (3.03±0.37), with a highly significant p value (<0.001). The overall mean NLR among all participants was 4.515±1.81. These findings suggest that elevated NLR may be a useful inflammatory marker for identifying women at risk of PPROM (Table 4).

Table 3: Maternal outcome in cases and controls.

Maternal outcome	Case (n=30)		Control (n=30)	
	N	%	N	%
Chorioamnionitis	2	6.7	1	3.3
Puerperal pyrexia	4	13.3	3	10.0
Puerperal sepsis	2	6.7	1	3.3
Urinary tract infection	1	3.3	2	6.7
Postpartum hemorrhage	3	10.0	2	6.7

Table 4: Parameters of NLR with 95% of confidence level among cases and controls.

Parameters	Value (95% CI)
Cutoff (p value)	≥3.57 (<0.001)
AUROC	0.840 (0.729-0.951)
Sensitivity	77%
Specificity	96.5%
PPV	84.60%
NPV	94.40%
Positive likelihood ratio (LR+)	2.2
Negative likelihood ratio (LR-)	0.238
Diagnostic odds ratio	9.24

Sensitivity is 77% and specificity is 96.5%, suggesting high accuracy in identifying true positives and true negatives (Figure 1).

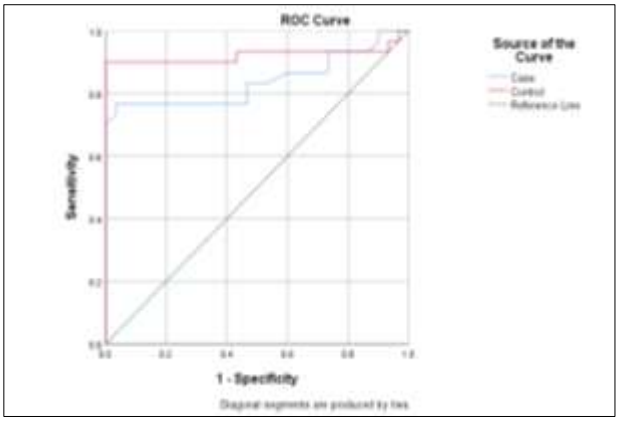

Figure 1: The ROC analysis for neutrophil-to-lymphocyte ratio reveals a significant diagnostic capability in distinguishing between cases and controls. With a cutoff value of 3.57 (p<0.001), the AUROC is 0.840 (95% CI: 0.729–0.951), indicating good discrimination.

DISCUSSION

PPROM has been established as significant risk factor for various morbidities in the newborns. However, there is no single reliable predictor of PPROM, which makes clinical management challenging.[1] The primary aim of the study was to evaluate the association between maternal neutrophil-to-lymphocytes ratio and adverse maternal and perinatal outcomes in PPROM cases.[2]

This study was conducted among pregnant women with PPROM aged above 18 years. The majority of women in both case and control groups belonged to the age group of 25 to 27 years. There was no significant difference in obstetric history, gestational age, birth weight, or mode of delivery between PPROM cases and controls.[3] Analysis of laboratory parameters revealed that the mean values of total neutrophil count, lymphocyte counts and neutrophil to lymphocyte ratio were elevated among cases compared to controls. The observed difference in the mean values of NLR between the groups was statistically significant.[4]

Similar findings were reported by Lakshmi et al, where women with PPROM showed elevated NLR and platelet-to-lymphocyte ratio compared to controls. Another study done by Ozel et al also reported similar results, demonstrating elevated NLR among PPROM cases.[3]

Maternal outcomes such as chorioamnionitis (6.7%), puerperal pyrexia (13.3%), puerperal sepsis (6.7%), and postpartum hemorrhage (10%) were more common among cases.

The incidence of adverse neonatal outcomes was also higher among cases compared to controls. High rate of NICU admissions was observed in newborns of case group (70%) compared to control group (36.66%) in controls. Apgar score at 5 minutes were significantly lower in cases. Perinatal mortality was higher in case group (70%) compared to control group (13.33%). Although there was an Increased incidence of low birth weight and need for resuscitation at birth in case group, these differences were not statistically significant.

A similar study by Dhannapaneni et al also effectively outlined the maternal and neonatal outcomes of PPROM, with findings consistent with the present study.

The study demonstrated that elevated maternal NLR was a significant predictor of adverse maternal and perinatal outcomes in PPROM. NLR showed good discriminative ability, with an AUROC value supporting its effectiveness. It had a sensitivity of 77% and specificity of 96.5%, accurately identifying both true positives and negatives. The positive predictive value (84.6%) and negative predictive value (94.4%) indicated strong reliability. A positive likelihood ratio of 2.2 and a negative likelihood ratio of 0.238 reflected moderate diagnostic strength. The diagnostic odds ratio of 9.2 suggested that women with a high NLR were approximately nine times more likely to experience adverse outcomes.[7]

A study conducted by Ozel et al also used ROC curve analysis to assess the predictive value of NLR and PLR in PPROM. The area under the curve was 0.717, and the best cutoff value for NLR was 5.14, with a sensitivity of 70% and specificity of 72%.[1]

Limitations

Small sample size

The study was conducted on a limited number of participants (30 cases and 30 controls), which may reduce the power and generalizability of the findings.

Single-center study

The research was conducted at a single tertiary care hospital (SMS Medical College, Jaipur), which may not reflect the broader population or outcomes in different health-care settings.

Short duration of study

The study was conducted over a one-year period, potentially limiting the observation of long-term maternal and neonatal outcomes.

Exclusion of comorbid conditions

Patients with common conditions like pre-eclampsia, diabetes, autoimmune disorders, or hepatic disease were excluded, which may affect the real-world applicability where such comorbidities often coexist with PPROM.

No long-term neonatal follow-up

The study did not assess long-term neuro-developmental or health outcomes in neonates, which are crucial in evaluating the full impact of adverse perinatal outcomes.

CONCLUSION

This case-control study evaluated the role of NLR as a potential marker in predicting adverse maternal and perinatal outcomes among women with PPROM. A cutoff value of NLR ≥3.57 demonstrated high diagnostic accuracy, with sensitivity of 77% and specificity of 96.5%, as evidenced by the AUROC of 0.840. Adverse perinatal outcomes including prematurity, low birth weight, neonatal sepsis, respiratory distress syndrome, and low Apgar scores were more prevalent in cases with elevated NLR. Increased NLR was significantly associated with maternal complications such as chorioamnionitis, puerperal pyrexia, and postpartum hemorrhage.

These findings suggest that NLR can serve as a simple, inexpensive, and effective early biomarker for identifying women at risk and poor perinatal outcomes in PPROM. Its integration into routine clinical evaluation could enhance early risk stratification and guide timely intervention, ultimately improving maternal and neonatal prognosis.

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