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Platelet Lymphocyte Ratio as a Novel Inflammatory Marker for Preterm Premature Rupture of Membrane

Dr. Nasrin Akhter[1]*, Dr. Sonia Alam[2], Dr. Umme Aysha Kashfee[3], Dr. Jinia Afroz[4]

[1]Medical Officer, Department of Obstetrics and Gynaecology, Sir Solimullah Medical College Mitford Hospital, Dhaka, Bangladesh
[2]Assistant Professor, Department of Obstetrics and Gynaecology, Ad-Din Momin Medical College Hospital, Dhaka, Bangladesh.
[3]Medical Officer, Department of Obstetrics and Gynaecology, Dhaka Medical College, Dhaka, Bangladesh.
[4]Assistant Professor, Department of Obstetrics and Gynaecology, Monno Medical College, Manikganj, Bangladesh

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***Corresponding author:** Dr. Nasrin Akhter
Medical Officer, Department of Obstetrics and Gynaecology, Sir Solimullah Medical College Mitford Hospital, Dhaka, Bangladesh

Abstract

Background: Premature rupture of membranes (PROM) is the rupture of fetal membranes before labour. When it occurs before 37 weeks, it is termed preterm prelabour rupture of membranes (PPROM), which is associated with increased maternal and perinatal morbidity and mortality. The early identification of at-risk cases is crucial. The platelet–lymphocyte ratio (PLR) from routine blood counts has emerged as a low-cost inflammatory biomarker for obstetric conditions. This study evaluated the association between maternal PLR and PPROM and explored its predictive value. ***Methods:*** This cross-sectional analytical study was conducted at the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, from June 2022 to May 2023. Sixty pregnant women between 28 and 36+6 weeks of gestation were included: 30 with PPROM (Group A) and 30 healthy controls (Group B). Complete blood counts were performed and the PLR was calculated as the ratio of the platelet to lymphocyte count. Data were analyzed using SPSS version 26.0. ***Results:*** The mean age did not differ significantly between the groups (27.57±5.14 vs. 28.33±5.02 years; p=0.56). The platelet count was significantly higher in the PPROM group (269.63±63.4 vs. 207.43±46.5 $\times 10^3/mm^3$; p<0.001), whereas the lymphocyte counts were comparable (p>0.05). The mean PLR was significantly higher in PPROM cases than in those with intact membranes (123.15±27.73 vs. 104.48±26.09; p=0.009). ***Conclusion:*** Elevated maternal PLR is significantly associated with PPROM and may serve as a simple, cost-effective inflammatory marker for risk identification in pregnancies. Larger multicenter studies are needed to confirm its clinical utility.

Keywords: Platelet–lymphocyte ratio, PPROM, inflammatory markers.

INTRODUCTION

Premature rupture of membrane (PROM) refers to the spontaneous rupture of fetal membranes before the onset of labour. When this event occurs before 37 completed weeks of gestation, the condition is specifically designated as preterm prelabour rupture of membranes (PPROM), a clinical entity that carries substantial implications for both the mother and the neonate.[1] PPROM complicates approximately 3% of all pregnancies and accounts for 30 to 40% of preterm births worldwide. [2] In referral centers, more than 50% of all PROM cases may occur in preterm pregnancies, underscoring its clinical burden in tertiary obstetric settings.[3]

The adverse consequences of PPROM extend across both the maternal and neonatal spectrums. From the maternal perspective, PPROM significantly increases the risk of chorioamnionitis, endometritis, postpartum haemorrhage and caesarean delivery. For the neonate, it is a critical risk factor for prematurity, neonatal infection, neonatal sepsis, hypoxia and neonatal jaundice.[4] PPROM is the presenting symptom in approximately 20% of all women who develop spontaneous preterm labour, further highlighting its central role in preterm birth pathophysiology.[5] Although PPROM accounts for only 3 to 5% of all PROM cases due to the relative infrequency of preterm deliveries, its disproportionate contribution to neonatal morbidity makes early diagnosis a clinical priority.[6]

The etiology of PPROM remains incompletely understood. While several risk factors have been identified, including lower socioeconomic status, cigarette smoking, urinary tract and sexually transmitted infections, low maternal body mass index, uterine distension, amniocentesis, prior preterm rupture of membranes and vaginal bleeding during pregnancy, the precise trigger for membrane weakening and rupture has not been fully elucidated.[7] A prevailing hypothesis implicates chronic sterile intra-amniotic inflammation as a key pathogenic mechanism. Through processes such as membrane stretching, local degradation and impaired maternal resistance to ascending bacterial colonization, inflammation is thought to weaken fetal membranes and precipitate their premature rupture.[7]

Platelets and lymphocytes are known to share regulatory roles in the pathophysiology of inflammation, immunity, thrombosis and atherosclerosis. Platelets influence lymphocyte function via direct cellular contact and through soluble mediators, including P-selectin and L-selectin, thereby enhancing lymphocyte adhesion and migration in a complex and interdependent manner.[8] In chronic inflammatory states, the megakaryocytic series undergoes proliferation, resulting in increased platelet counts, while lymphocyte counts tend to decline through apoptosis.[9] This reciprocal dynamic underpins the rationale for examining the platelet lymphocyte ratio (PLR) as a marker of systemic inflammation.

The PLR, calculated by dividing the absolute platelet count by the absolute lymphocyte count from a standard complete blood count, is a widely available, inexpensive and simple parameter that requires no additional laboratory resources. It has been proposed as a predictive and prognostic marker in a range of conditions, including cardiovascular disease and malignancies. [10,11] In obstetrics, the PLR has been previously explored as a novel inflammatory marker for conditions such as preeclampsia and preterm labour. [12,13] Its potential association with PPROM has attracted growing research interest, with some studies demonstrating a significant elevation of PLR in PPROM patients, while others have reported inconsistent results. [14,15]

Given the limited and conflicting evidence, particularly from low- and middle-income country settings where routine access to advanced biomarkers may be restricted, there is a clear need for studies evaluating the association between PLR and PPROM in the local clinical context. The present study was therefore conducted to evaluate the relationship between maternal PLR and PPROM at a major tertiary referral center in Bangladesh, to determine whether PLR can be considered a useful novel inflammatory marker for predicting this condition.

MATERIALS & METHODS

This was a cross-sectional analytical study conducted at the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh. The study was carried out over a period of twelve months, from June 2022 to May 2023. The study population comprised pregnant women attending the department who were between 28 and 36+6 weeks of gestation. A total of 60 participants were enrolled: 30 women diagnosed with PPROM (Group A) and 30 healthy pregnant women without PPROM (Group B), each group selected according to the defined inclusion and exclusion criteria.

Sample Selection

Inclusion Criteria:

- All pregnant women between 28 and 36+6 weeks of gestation.
- Mothers who were willing to participate and provided written informed consent.

Exclusion Criteria:

- Unwillingness to participate.
- Multiple gestations.
- Hematologic disorders.
- Malignancies.
- Hepatic disease.
- History of autoimmune disease.
- Any inflammatory disease of pregnancy, including gestational diabetes mellitus and preeclampsia.
- Any acute or chronic infectious or inflammatory diseases.
- Pregnancies with fetal chromosomal anomalies.

Data Collection Procedure

Before initiating the study, formal ethical approval was obtained from the Ethical Review Committee (ERC) of Dhaka Medical College Hospital and the protocol was subsequently submitted to the Bangladesh College of Physicians and Surgeons (BCPS). All pregnant women admitted to the department were approached for participation. Following a thorough explanation of the study aim, purpose and procedure, written informed consent was obtained from each participant or, where necessary, from their caregiver. Thirty mothers diagnosed with PPROM were enrolled in Group A and 30 full-term healthy pregnant women were enrolled in Group B. A semi-structured questionnaire was developed and administered through face-to-face interviews. Detailed clinical history, physical examination findings, co-morbidities and laboratory investigations including a complete blood count, were recorded for each participant. PLR was calculated as the absolute platelet count divided by the absolute lymphocyte count. Data were recorded by the researcher in a separate case record form and subsequently entered into SPSS version 26.0 for analysis.

Ethical Considerations

The study was conducted in accordance with established ethical principles. Before commencement, ethical clearance was obtained from the ERC of Dhaka Medical College Hospital. Written informed consent was obtained from each participant or their caregiver in both Bangla and English. Participants were explicitly informed that their involvement was entirely voluntary, that their confidentiality would be strictly maintained, that there was no financial benefit associated with participation and that they could withdraw from the study at any time without any effect on their clinical care. No invasive procedure was performed as part of the study protocol.

Statistical Analysis

All collected data were verified for consistency, coded and entered into SPSS version 26.0 for analysis. Continuous variables were expressed as mean and standard deviation and categorical variables were expressed as frequency and percentage. Between-group comparisons of continuous variables were performed using the independent sample t-test. Associations between categorical variables were evaluated using the chi-square test or Fisher's exact test, as appropriate. Statistical significance was set at a 95% confidence level with an acceptable error level of 5%, corresponding to a p-value of less than 0.05.

RESULTS

This cross-sectional analytical study enrolled 60 pregnant women attending the Department of Obstetrics and Gynaecology at Dhaka Medical College Hospital. Among them, 30 women diagnosed with PPROM at 28 to 36+6 weeks of gestation were allocated to Group A and 30 healthy non-PPROM pregnant women in the same gestational age range were allocated to Group B.

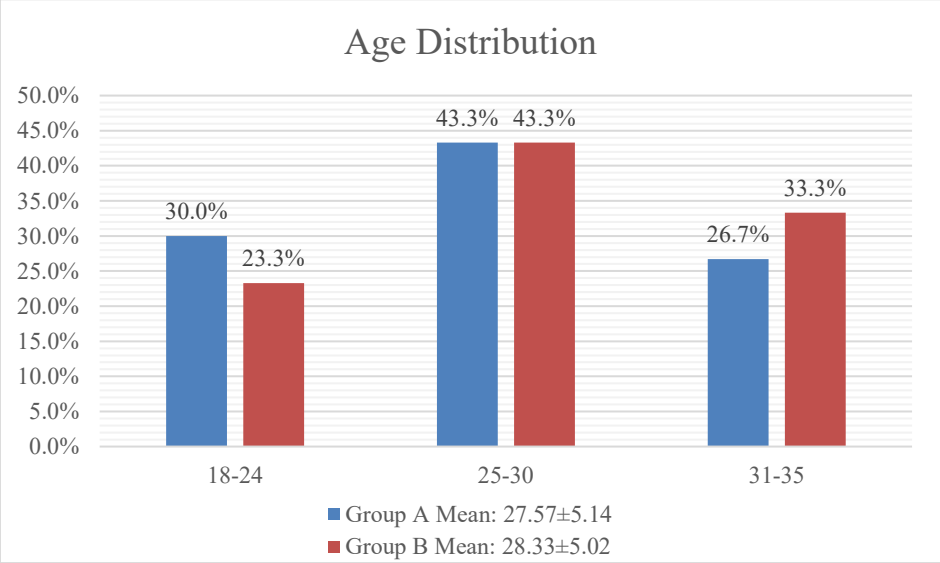

Figure 1: Distribution of age groups of respondents (n=60)

The majority of respondents in both groups belonged to the 25 to 30 years age category (43.3% each). The mean age of age group A and group B respondents were 27.57±5.14 years and 28.33±5.02 years.

Table 1: Distribution of educational status, occupational status, family income and BMI of respondents (n=60)

Variables		PPROM Group A n=30 n (%)	Non-PPROM Group B n=30 n (%)	p value
Educational status of respondents	Illiterate	2 (6.7)	2 (6.7)	0.06
	Primary	12 (40.0)	3 (10.0)	
	SSC	9 (30.0)	10 (33.3)	
	HSC	5 (16.7)	9 (30.0)	
	Graduate and above	2 (6.7)	6 (20.0)	
Occupation of respondents	Housewife	24 (80.0)	17 (56.7)	0.116
	Service holder	5 (16.7)	12 (40.0)	
	Business	1 (3.3)	1 (3.3)	
Monthly family income (BDT)	<20,000	14 (46.7)	7 (23.3)	0.059
	20,000 to 50,000	9 (30.0)	18 (60.0)	
	>50,000	7 (23.3)	5 (16.7)	

Variables		PPROM Group A n=30 n (%)	Non-PPROM Group B n=30 n (%)	p value
BMI (kg/m²)	<18.5	3 (10.0)	6 (20.0)	0.554
	18.5 to 24.9	18 (60.0)	14 (46.7)	
	25.0 to 30.0	7 (23.3)	6 (20.0)	
	>30.0	2 (6.7)	4 (13.3)	

Table 1 presents the distribution of educational status, occupation, family income and BMI across both groups. Regarding educational level, the majority of women in Group A had completed primary education (40.0%), whereas most women in Group B had attained SSC level (33.3%). The difference in educational status between the two groups approached but did not reach statistical significance (p=0.060). In terms of occupation, the majority of respondents in both groups were housewives (80.0% in Group A and 56.7% in Group B) and this difference was not statistically significant (p=0.116). However, a statistically significant difference was observed in monthly family income between the two groups (p=0.059): 46.7% of Group A women had a monthly family income of less than 20,000 BDT, compared to 23.3% in Group B, while 60.0% of Group B women had income between 20,000 and 50,000 BDT. With respect to BMI, the majority of respondents in both groups fell within the normal range of 18.5 to 24.9 kg/m² (60.0% in Group A and 46.7% in Group B) and no statistically significant association was found between BMI and group allocation (p=0.554).

Table 2: Distribution of parity and antenatal care (ANC) history of respondents (n=60)

Variables		Group A n=30 n (%)	Group B n=30 n (%)	p value
Parity	0	6 (20.0)	8 (26.7)	0.435
	1	15 (50.0)	13 (43.3)	
	2	8 (26.7)	5 (16.7)	
	3	1 (3.3)	4 (13.3)	
ANC visit	Irregular	23 (76.7)	19 (63.3)	0.399
	Regular	7 (23.3)	11 (36.7)	

Table 2 describes the parity and antenatal care (ANC) visit history of the study respondents. Parity 1 was the most common in both groups, accounting for 50.0% of Group A and 43.3% of Group B. Nulliparity (parity 0) was noted in 20.0% of Group A and 26.7% of Group B, while parity 2 was observed in 26.7% and 16.7%, respectively. No statistically significant difference in parity distribution was identified between the two groups (p=0.435). Additionally, the mean gestational age was significantly lower in Group A compared to Group B (32.27 ± 2.5 weeks vs. 36.7 ± 1.62 weeks), which is consistent with the preterm nature of PPROM. Regarding ANC attendance, irregular antenatal visits were more prevalent in Group A (76.7%) compared to Group B (63.3%), though this difference was not statistically significant (p=0.399).

Table 3: Distribution of haematological investigation profile of respondents (n=60)

Variables	Group A (PPROM) Mean±SD	Group B (Non-PPROM) Mean±SD	p value
Platelet count (x 10^3/mm^3)	269.633±63.4	207.43±46.5	<0.001
Lymphocyte count (/mm^3)	2253.98±588.02	2022.7±326.42	0.065
Platelet Lymphocyte Ratio (PLR)	123.15±27.73	104.48±26.09	0.009

Table 3 presents the haematological parameters of the two study groups. The mean platelet count was significantly higher in Group A (PPROM) compared to Group B (non-PPROM) [269.633 ± 63.4 vs. 207.43 ± 46.5 x 10^3/mm^3; p<0.001]. The mean lymphocyte count was 2253.98 ± 588.02 per mm^3 in Group A and 2022.7 ± 326.42 per mm^3 in Group B, with no statistically significant difference between the two groups (p=0.065). The mean PLR was significantly higher in Group A compared to Group B (123.15 ± 27.73 vs. 104.48 ± 26.09; p=0.009), indicating a significant association between elevated PLR and the occurrence of PPROM.

DISCUSSION

Preterm premature rupture of membranes exerts a profound influence on pregnancy prognosis and constitutes a major public health concern due to its well-established association with preterm birth and its sequelae.[4] The search for simple, cost-effective and routinely available biomarkers to identify women at risk of PPROM has prompted interest in haematological indices, among which the platelet-to-lymphocyte ratio has emerged as a candidate of considerable interest. The present study was undertaken with the objective of evaluating the association between maternal PLR and PPROM in a tertiary care setting in Bangladesh.

With respect to the demographic characteristics of the study population, the mean age of the PPROM group and the non-PPROM group were 27.57 ± 5.14 years and 28.33 ± 5.02 years, respectively. This difference was not statistically significant (p=0.9), suggesting that both groups were well-matched for age. These findings are consistent with those reported by Toprak *et al.,* who found that the mean age in the PPROM group was 28.7 ± 5.1 years compared to 29.4 ± 5.0 years in the control group (p=0.56). [14] Similarly, Husuni *et al.,* reported a mean age of 28.2 ± 5.6 years in the PPROM group and 30.4 ± 6.5 years in the non-PPROM group, findings that are in close agreement with the present study.[16]

Regarding parity, the most common obstetric profile in both groups was primiparity, accounting for 50.0% of Group A and 43.3% of Group B and this distribution was not statistically significantly different between the two groups (p=0.435). These results align with observations from Husuni *et al.,* who reported that primipara women developed PPROM in 71% of cases, a finding that was also not statistically significant.[16] Jaffar and Faissal Rabie similarly found no significant association between parity and preterm birth in their control comparison (p=0.9).[17] The consistency of parity findings across studies suggests that parity alone does not independently predict PPROM risk and therefore, its non-significant association in the present study is both expected and reproducible.

The mean gestational age of participants in Group A was 32.27 ± 2.5 weeks, which was lower than that of Group B (36.7 ± 1.62 weeks), consistent with the preterm nature of PPROM. This difference is clinically expected, as PPROM by definition occurs before 37 completed weeks of gestation and is associated with 30 to 40% of all preterm births.[14] The gestational age profile observed in Group A is also consistent with the broader epidemiological characterization of PPROM, in which the majority of affected pregnancies deliver before 34 weeks in referral settings.[2] Toprak *et al.,* in their study evaluating PLR in PPROM, similarly enrolled patients within the preterm gestational window, further affirming that the gestational age distribution in the present study reflects a representative PPROM population.[14]

The socioeconomic profile of the two groups revealed notable differences in monthly family income. The majority of women in Group A (46.7%) had a monthly family income of less than 20,000 BDT, while most women in Group B (60.0%) reported income between 20,000 and 50,000 BDT. This difference approached statistical significance (p=0.059), highlighting the potential role of socioeconomic disadvantage in PPROM risk. These findings resonate with those of Yeasmin *et al.,* who found that the majority (60.6%) of PROM cases occurred among women of low socioeconomic status.[18] Addisu *et al.,* similarly reported that PPROM respondents were predominantly from lower economic backgrounds.[19] The broader literature also supports this association, as Sarkar *et al.,* found that PROM commonly occurred in those of lower socioeconomic status, accounting for 73.39% of their cases. [20]

The central finding of this study relates to the hematological inflammatory profile, specifically the comparison of PLR between the PPROM and non-PPROM groups. The mean platelet count was significantly higher in Group A than in Group B (269.633 ± 63.4 vs. 207.43 ± 46.5 x 10^3/mm^3; p<0.001), while lymphocyte counts were comparable between the two groups (p=0.065). Consequently, the mean PLR was significantly elevated in the PPROM group (123.15 ± 27.73 vs. 104.48 ± 26.09; p=0.009). This finding confirms the study hypothesis that raised maternal PLR is associated with PPROM and it is consistent with the biological rationale that PPROM is underpinned, at least in part, by a chronic inflammatory process that alters the platelet-to-lymphocyte balance.

The observed elevation in PLR among PPROM patients is corroborated by several published studies. A similar investigation by Eric Horasanli *et al.,* demonstrated that PLR values were higher in the PPROM group compared to controls (146.26 ± 74.17 vs. 130.07 ± 57.05; p=0.076), though the difference did not reach statistical significance.[15] Sharami *et al.,* employing the Mann-Whitney U test, found PLR to be significantly higher in the PPROM group (160.8 ± 34.3) than in controls (226 ± 52.2; p=0.0001).[9] Toprak *et al.,* also reported a statistically significant elevation in PLR in PPROM patients.[15] Collectively, these studies provide a consistent body of evidence supporting the association between elevated PLR and PPROM, with the present study adding further data from a South Asian, low-resource hospital setting where such routine haematological parameters are particularly valuable.

From a pathophysiological standpoint, these findings are mechanistically plausible. In chronic inflammatory conditions, the megakaryocytic series undergoes proliferation, increasing platelet production, while lymphocytes are subject to apoptosis-mediated reduction in count [9]. The net effect is an elevation in the PLR, which reflects a state of systemic immune activation. Since PPROM is increasingly recognized as an inflammatory condition, potentially triggered by chronic sterile intra-amniotic inflammation, the PLR may serve as a peripheral blood surrogate of this underlying inflammatory milieu. PLR is advantageous as a marker because it is derived from a standard complete blood count, is inexpensive, requires no additional laboratory infrastructure and is available in virtually all clinical settings.

CONCLUSION

The findings of this study demonstrate that maternal platelet lymphocyte ratio is significantly elevated in women with preterm prelabour rupture of membranes compared to healthy non-PPROM pregnant controls. As an easily calculable, cost-effective and routinely available haematological parameter, PLR holds considerable promise as a novel inflammatory marker for identifying women at increased risk of PPROM. The significantly higher PLR observed in the PPROM group supports the hypothesis that raised maternal PLR is associated with this condition.

Conflicts of Interest: There are no conflicts of interest.

Ethical Approval: This study approved by the institutional ethical review committee.

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