



# The Association Between Platelets/Lymphocyte Ratio and Premature Rupture of Membranes

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## Abstract

**Objectives:** Premature rupture of membrane (PROM) refers to the spontaneous rupture of fetal membranes prior to delivery and the initiation of the labor. In addition, the early rupture of membranes can lead to several adverse complications for both the mother and the fetus. Therefore, the present study aimed to investigate the association between the platelet-to-lymphocyte ratio (PLR) and the premature rupture of the membrane in pregnant women.

**Materials and Methods:** This retrospective case-control study reviewed the files of 150 women with PROM matched with 150 spontaneous preterm labor (SPL) women at Al-Zahra hospital of Rasht during 2017-2018. Demographic data, complete blood cell count, PLR, maternal age, gestational week, gravida, parity, and birth weight were recorded, and finally, the obtained data were analyzed by SPSS, version 19.

**Results:** Based on the results, there was a statistically significant difference between maternal platelet count and PLR in these two groups ( $P=0.0001$ ). However, no significant difference was observed regarding maternal age, gravida, parity, and maternal lymphocytes count in PROM and control groups ( $P>0.05$ ). According to logistic regression analysis, a negative association was found respecting gestational age and PLR in the PROM group while a positive association was observed in the group without PROM regarding birth weight and PRL. In the receiver-operator curve diagram, the appropriate cut-off point for the PLR index for detecting PROM was determined as 142.2 with a sensitivity of 62.7% and a specificity of 63.3%.

**Conclusions:** In general, a significant association was found between PLR and PROM. Therefore, well-planned cohort studies are welcomed to find any prognostic role for this marker.

**Keywords:** Premature rupture of membranes, Association, Platelet-to-lymphocyte ratio

## Introduction

The premature rupture of membrane (PROM) as a crucial risk factor for prenatal mortality and morbidity occurs in 3% of all pregnancies and is defined as an early fetal membrane rupture before labor initiation (1). In addition, as the main cause of preterm delivery, PROM is accompanied by some adverse effects for both the mother and fetus (2,3). Based on a systemic review conducted by Bond et al, expectant management was preferred when PROM diagnosis was confirmed with the absence of any contraindication for continuing the pregnancy. They further reported that this approach was most beneficial for both the mother and the baby. Accordingly, when this decision is made, close monitoring is highly vital for the fetus (4) since the risk of neonate and mother infection, sudden intrauterine death, neonatal jaundice, hypoxia, sepsis, intra-ventricular hemorrhage, and necrotizing enterocolitis may demonstrate an increase. In these conditions, anesthesiologists inevitably get more involved in neonatal resuscitation (5, 6). Although

some predisposing risk factors such as abnormal vaginal discharge, history of caesarian section, previous PROM history of abortion (7), and temperature changes (8) have been described, the real responsible pathophysiologic mechanism of PROM remains unknown. Due to the significant adverse consequences of PROM, early diagnosis is extremely crucial for choosing an appropriate medical intervention in order to protect the mother and fetus from serious complications (9). Based on the evaluation of different inflammatory markers such as interleukin-6 and mean platelet volume, studies have demonstrated the significant role of inflammation while not always microbial parameters in this process. Based on their findings, sterile intra-amniotic inflammation is more common among women presenting PROM after 24 weeks of gestation (10-12). Furthermore, it has been highly discussed as a simple, inexpensive, and available marker and its prognostic role has been supported in various inflammation conditions. Evidence suggests that in chronic inflammatory conditions, megakaryocytic series

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Key Messages

- ▶ This study highlighted the significant association of platelets to lymphocyte ratio to premature rupture of membranes.
- ▶ Maternal age, gravida and parity were not recognized as related factors associated to premature rupture of membranes.

proliferation tends to increase while lymphocyte count decreases due to the apoptosis phenomenon. Therefore, it is supposed that PLR raises during inflammatory conditions (13). Based on the literature review, limited data are available about the diagnostic role of PLR for the early diagnosis of PROM and have often focused on other conditions.

**Objectives**

Considering the advantages of PLR as an inflammatory marker and inadequate data in this field, this research was planned to investigate whether PLR has any association with PROM.

**Methods**

The protocol of this retrospective case-control study was approved by the Research Ethics Committee of Guilan University of Medical Sciences and was registered as IR.GUMS.REC.1398.038. Additionally, it took place at Al-Zahra hospital, which is a referral and academic center, during 2017-2018. A responsible medical student sorted out the files of 150 women with PROM and matched them with 150 spontaneous preterm labor (SPL) women who were admitted during the above-mentioned period. According to the documented data, a questionnaire was filled out, including data on age, gestational week, gravida, parity, and birth weight, followed by documenting the recorded complete blood count at the admission time. Eventually, PLR was calculated by dividing patients' platelet count to lymphocyte count.

**Inclusion Criteria**

Women with the PROM and SPL admitted during the mentioned study period.

**Exclusion Criteria**

Patients suffering from any acute or chronic inflammatory conditions, hematologic disorders, malignancies, hepatic diseases, autoimmune disease, preeclampsia, any kind of fetal infection, and cases undergoing invasive interventions such as amniocentesis were excluded from the study. Files with incomplete data were excluded as well. Finally, the data between the two groups were compared based on the aim of the study.

**Statistical Analysis**

The data were analyzed by SPSS, version 19. Categorical

variables were presented as frequencies and percentages. A Chi-square test was performed to compare categorical variables between the two groups. In addition, the Mann-Whitney U test or independent sample *t* test was used for comparing normally distributed continuous numeric variables. Eventually, receiver-operator curve (ROC) analysis was utilized to figure out the sensitivity and specificity of PLR values regarding predicting PROM, and  $P \leq 0.05$  was considered statistically significant.

**Results**

In this study, patients were evaluated in two groups including pregnant women with (n=150) and without (n=150) PROMs. Patients' baseline demographic and clinical features are shown in Table 1. Based on the results, there was no significant difference between the two groups in terms of age, gravida, parity, and lymphocyte count ( $P > 0.05$ ). Conversely, a statistically significant difference was observed between these two groups regarding maternal platelet count and the PLR ratio ( $P = 0.0001$ ). The mean of the gestational week and the mean birth weight (gram) were  $33.49 \pm 2.67$  and  $37.98 \pm 1.9$ , as well as  $2305.8 \pm 479$  and  $2912.2 \pm 651$  in pregnant women with PROM and those with SPL, respectively. According to logistic regression analysis, a negative association was found regarding gestational age and PLR in the PROM group (Table 2) whereas a positive association was observed in the group without PROM regarding birth weight and PRL (Table 3). Based on the ROC diagram which was used to detect PROM, the appropriate cut-off point for the PLR index was 142.2 with a sensitivity value of 62.7% and a specificity of 63.3%, which is an acceptable point and represents an association between PLR values and PROM (Figure 1).

**Discussion**

In general, it was mainly found that PLR was significantly linked to a higher risk of PROM, namely, the prenatal rupture of the membrane before the pregnant woman is in the labor. In our research, PLR was remarkably higher in the PROM, indicating a positive association between neonate weight and PLR in the PROM group. Conversely,

**Table 1.** Demographic and Clinical Characters of the Patients

	PROM	Control	P Value
Age (y)	28.38± 6.59	27.82±4.88	0.404 <sup>a</sup>
Gravida (number)	1.87 ±0.88	1.97±0.9	0.333 <sup>a</sup>
Parity (number)	0.65±0.05	0.74±0.74	0.68 <sup>a</sup>
Lymphocyte count (/ mm <sup>3</sup> )	1700±413	1795.3	0.178 <sup>b</sup>
Platelet count (×1000/mm <sup>3</sup> )	160.8± 34.3	133.2±40.2	0.0001 <sup>b</sup>
PLR	265.5±55	226.3±52.2	0.0001 <sup>b</sup>

Note. PROM: premature rupture of membranes; PLR: platelet-to-lymphocyte ratio.

<sup>a</sup>Independent sample *t* test; <sup>b</sup>Mann Whitney U test.

**Table 2.** The Association Between Individual Demographic Characteristics in the Group of Pregnant Women With PROM and PLR

Variable		PLR
Age (y)	Pearson correlation	R = 0.063
	P value	0.44
	Type of correlation	No correlation
Gestational age (wk)	Pearson correlation	r = -0.283
	P value	0.0001
	Type of correlation	Negative correlation
Gravidity	Pearson correlation	R = 0.044
	P value	0.591
	Type of correlation	No correlation
Parity	Pearson correlation	r = 0.018
	P value	0.823
	Type of correlation	No correlation
Birth weight (g)	Pearson correlation	r = -0.158
	P value	0.053
	Type of correlation	No correlation

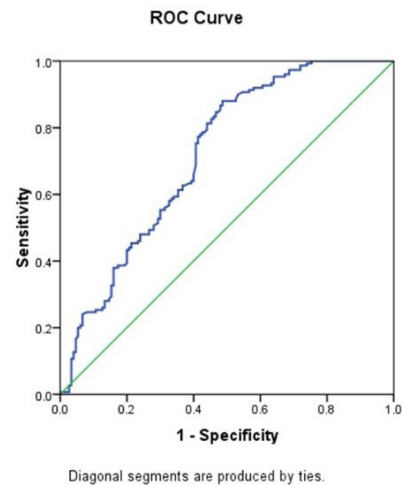
Note. PLR: Platelet to lymphocyte ratio; PROM: Premature rupture of membranes.

**Table 3.** The Association Between Individual Demographic Characteristics in the SPL Group (Pregnant Women Without PROM) and PLR

Variable		PLR
Age (y)	Pearson correlation	R = -0.075
	P value	0.363
	Type of correlation	No correlation
Gestational age (wk)	Pearson correlation	R = -0.017
	P value	0.841
	Type of correlation	No correlation
Gravidity	Pearson correlation	R = 0.017
	P value	0.837
	Type of correlation	No correlation
Parity	Pearson correlation	R = 0.003
	P value	0.975
	Type of correlation	No correlation
Birth weight (g)	Pearson correlation	R = 0.182
	P value	0.026
	Type of correlation	Positive correlation

Note. PLR: Platelet to lymphocyte ratio; PROM: Premature rupture of membranes; SPL: Spontaneous preterm labor.

a negative association was observed between gestational weeks and PLR only in the SPL group. Our findings are in line with those of Toprak et al (13). It is noteworthy that the ongoing inflammatory process results in a higher rate of megakaryocytic series proliferation and thus relative thrombocytosis. In addition, lymphocyte count decreases in sustained inflammation due to the further occurrence of apoptosis phenomena. Up to now, PLR values have not been restricted to detect early PROM. Rather, these values have been investigated with promising results in several other conditions, and evidence indicates the adverse prognostic impact of PLR in malignancies and coronary



**Figure 1.** ROC Appropriate Cut-off Point for PLR Index Regarding Detecting PROM. Note. ROC: Receiver-operator curve; PROM: Premature rupture of membranes.

artery diseases. For example, Bharadwaj et al demonstrated that PLR can be a rapid, simple, and available indicator for the early diagnosis of neonate sepsis and provides the opportunity for clinicians to appropriately manage these cases (14). Similarly, Koh et al found that PLR was an independent marker for the increased mortality risk in breast cancer (15). Likewise, Templeton et al reported a notable association between PLR and gastrointestinal cancer poor outcomes (16). In another study, Yüksel et al suggested that higher PLR values appear to be a high-risk factor for the severity of atherosclerosis (17). Contrarily, Serrano et al found no predictive role of higher PLR values in inflammatory conditions (18). Generally, an inflammatory pathophysiologic base with limited data has been strongly suggested for the PROM process. Further investigations are required considering the importance of the issue for both the health of the mother and the baby and the advantages of this marker.

### Limitations

It was a single-center study with a small sample size. Furthermore, the investigated factors were restricted to those documented in the files due to the nature of a retrospective study. Accordingly, the findings should be generalized with caution, and future studies should consider the above-mentioned issues.

### Conclusion

In general, the findings of this research revealed that the PLR was significantly associated with a higher risk of PROM. Therefore, in clinical practice, more attention should be paid to cases with PLR values higher than 142.2, especially when other PROM risk factors are detected as well. Accordingly, well-planned cohort studies are welcomed regarding finding any prognostic role for this marker.

### Authors' Contribution

GB: Study concept and design; HSH: Critical revision of the manuscript; FF: Study supervision; MA: Manuscript drafting; NHS: Data acquisition; ZA: Statistical analysis for important intellectual content; MRH and YCh: Administrative, technical, and material support; MKH: Data analysis and interpretation.

#### Conflict of Interests

Authors declare that they have no conflict of interests.

#### Ethical Issues

We received ethical exemption status from the Research Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1398.038).

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#### References

- Igbinosa I, Moore FA, 3rd, Johnson C, Block JE. Comparison of rapid immunoassays for rupture of fetal membranes. *BMC Pregnancy Childbirth*. 2017;17(1):128. doi:10.1186/s12884-017-1311-y
- Dars S, Malik S, Samreen I, Kazi RA. Maternal morbidity and perinatal outcome in preterm premature rupture of membranes before 37 weeks gestation. *Pak J Med Sci*. 2014;30(3):626-629. doi:10.12669/pjms.303.4853
- Thuillier C, Hot N. Prolonged premature rupture of membranes in nullipara and the risk of spontaneous premature birth in the subsequent pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2019;234:e18. doi:10.1016/j.ejogrb.2018.08.190
- Bond DM, Middleton P, Levett KM, et al. Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome. *Cochrane Database Syst Rev*. 2017;3(3):CD004735. doi:10.1002/14651858.CD004735.pub4
- Linehan LA, Walsh J, Morris A, et al. Neonatal and maternal outcomes following midtrimester preterm premature rupture of the membranes: a retrospective cohort study. *BMC Pregnancy Childbirth*. 2016;16:25. doi:10.1186/s12884-016-0813-3
- Ocviyanti D, Wahono WT. Risk factors for neonatal sepsis in pregnant women with premature rupture of the membrane. *J Pregnancy*. 2018;2018:4823404. doi:10.1155/2018/4823404
- Assefa NE, Berhe H, Girma F, et al. Risk factors of premature rupture of membranes in public hospitals at Mekele city, Tigray, a case control study. *BMC Pregnancy Childbirth*. 2018;18(1):386. doi:10.1186/s12884-018-2016-6
- Ha S, Liu D, Zhu Y, Sherman S, Mendola P. Acute associations between outdoor temperature and premature rupture of membranes. *Epidemiology*. 2018;29(2):175-182. doi:10.1097/ede.0000000000000779
- Azam A, Husnain HM, Marryum I. Premature rupture of membranes; diagnostic accuracy of  $\beta$ -hCG test in vaginal washings taking amniotic fluid pooling as gold standard of diagnosing pron. *Prof Med J*. 2018;25(2):168-172. doi:10.29309/tpmj/18.4219
- Chaemsaihong P, Romero R, Korzeniewski SJ, et al. A point of care test for interleukin-6 in amniotic fluid in preterm prelabour rupture of membranes: a step toward the early treatment of acute intra-amniotic inflammation/infection. *J Matern Fetal Neonatal Med*. 2016;29(3):360-367. doi:10.3109/14767058.2015.1006621
- Li H, Ma AP. Changes of cytokines and matrix metalloproteinases in patients with premature rupture of chorioamion and its clinical significance. *J Hainan Med Univ*. 2017;23(20):73-76.
- Romero R, Miranda J, Chaemsaihong P, et al. Sterile and microbial-associated intra-amniotic inflammation in preterm prelabour rupture of membranes. *J Matern Fetal Neonatal Med*. 2015;28(12):1394-1409. doi:10.3109/14767058.2014.958463
- Toprak E, Bozkurt M, Dinçgeç Çakmak B, et al. Platelet-to-lymphocyte ratio: a new inflammatory marker for the diagnosis of preterm premature rupture of membranes. *J Turk Ger Gynecol Assoc*. 2017;18(3):122-126. doi:10.4274/jtgga.2017.0028
- Bharadwaj N, Singh HB, Anjum S, Tadury A. Does the platelet to neutrophil ratio and platelet to lymphocyte ratio predict newborn sepsis a case control study. *Paripex Indian J Res*. 2018;7(12):192-193.
- Koh CH, Bhoo-Pathy N, Ng KL, et al. Utility of pre-treatment neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as prognostic factors in breast cancer. *Br J Cancer*. 2015;113(1):150-158. doi:10.1038/bjc.2015.183
- Templeton AJ, Ace O, McNamara MG, et al. Prognostic role of platelet to lymphocyte ratio in solid tumors: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2014;23(7):1204-1212. doi:10.1158/1055-9965.epi-14-0146
- Yüksel M, Yıldız A, Oylumlu M, et al. The association between platelet/lymphocyte ratio and coronary artery disease severity. *Anatol J Cardiol*. 2015;15(8):640-647. doi:10.5152/akd.2014.5565
- Serrano CV Jr, de Mattos FR, Pitta FG, et al. Association between neutrophil-lymphocyte and platelet-lymphocyte ratios and coronary artery calcification score among asymptomatic patients: data from a cross-sectional study. *Mediators Inflamm*. 2019;2019:6513847. doi:10.1155/2019/6513847

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