

Original Research Article

Comparison of platelet to lymphocyte ratio and neutrophil to lymphocyte ratio in women with preterm premature rupture of membranes and women with preterm delivery

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ABSTRACT

Background: Considering the adverse effect of PROM on birth outcomes and the condition of mother and fetus, early identification of risk factors of PROM and their control can reduce the occurrence of adverse outcomes for mother and fetus and improve their health. This study was conducted with the aim of comparing PLR and NLR in women with PROM and women with preterm delivery.

Methods: This case-control study was conducted on 155 women with PPROM as case group and 155 women with preterm delivery as control group. Age, gestational age, type of delivery, baby's birth weight, gravida, parity, APGAR score, rate of hospitalization in Neonatal Intensive Care Unit (NICU), occurrence of neonatal sepsis and development of respiratory distress syndrome (RDS) were recorded from women's medical records. Also, the results of blood tests and PLR and NLR values were calculated for each pregnant woman. Collected data were analyzed by statistical methods in SPSS version 24.

Results: The average gestational age and weight of babies at birth time in the case group were significantly lower than those with preterm delivery. The mean of NLR in case group with 4.8 ± 2.5 was significantly higher than control group with 4.2 ± 2.2 . The mean of PLR in case group with 111.5 ± 47.6 was significantly higher than control group with 100.98 ± 43.4 .

Conclusions: The high values of PLR and NLR in the women with PROM compared to women with preterm delivery can be a marker to identify the risk of PPROM in pregnant women.

Keywords: Neutrophil to lymphocyte ratio, Preterm delivery, Preterm premature rupture of membranes

INTRODUCTION

Premature Rupture of Membranes (PROM) is a significant obstetric problem. Evaluation of neutrophil-lymphocyte ratio (NLR) is expected to throw light on the potential scope of early prediction of PPROM.¹

PROM is often leads to adverse maternal outcomes like chorioamnionitis, endometritis and post-partum

hemorrhage and is associated with a wide range of mortality and socioeconomic disability. Low socioeconomic status and sexually transmitted diseases have been attributed in the PPROM. Evaluation of NLR can play a good role in early prediction of PPROM.²

Both spontaneous preterm labour and PPROM are important risk factors for prematurity and infectious conditions such as sepsis that cause morbidity and

mortality in the neonatal period. Early diagnosis and appropriate management is very important for preventing poor outcomes because of these serious problems.³

One of the factors that can increase the death rate of mothers and babies is premature rupture of membranes or PROM, which is called the rupture of the fetal membranes before the onset of labor pains before the 37th week of pregnancy.⁴ A review of various studies shows that the probability of PROM in women with a history of premature rupture of membranes is 4.45 times higher than other women.⁵ Studies from the United States of America, Sweden, India, Thailand, Egypt, Nigeria, and Uganda showed that previous PROM is an important risk factor for the next PROM.⁶ Also, PROM has a significant relationship with the history of previous premature birth.⁷ In addition, age less than 20 years and more than 35 years, number of births more than twice and education less than high school are associated with PROM.⁴ Therefore, providing evidence-based information about the factors related to the frequency of PROM in pregnant women can prevent PROM and damage to the fetus and mother. Also, this information can be useful for health system officials and in order to plan and follow up on this issue, it should be used with the aim of maintaining and improving of women' health during pregnancy and minimizing the complications caused by it. Despite significant advances in prenatal care over the past three decades, the rate of PPROM and its associated preterm births has not decreased. Optimal management of pregnancy complicated by PPROM is the most controversial issue in pregnancy care. Issues such as the use of corticosteroids, the role of fetal lung maturity testing, antenatal strategies and prompt delivery versus expectant management of PPROM remain a matter of debate.⁸ Also, the management of women who develop PPROM varies considerably among obstetric care providers. Therefore, correct and timely diagnosis of PROM is vital to achieve ideal pregnancy results. In addition, early diagnosis of PPROM due to its serious complications is very important for the health of mother and fetus due to its serious complications. So far, several studies have been conducted on other inflammatory markers for the rapid, accurate and early diagnosis of PPROM.⁹⁻¹⁰ Considering the limited information about the relationship between PLR, NLR and the presence of PPROM in existing studies, the present study aims to determine the ratio of platelets to lymphocytes and the ratio of neutrophils. It was performed on lymphocytes in women with premature rupture of membranes and women with preterm delivery.

METHODS

Study design and participants

This case-control study was conducted on pregnant women referring to Alavi hospital in Ardabil city from September 2022 to September 2023. Of all women, 155 pregnant women with PPROM were considered as the

case group and 155 women with preterm delivery who were age-matched with the case group were considered as the control group. Age, gestational age, type of delivery, baby's birth weight, gravida, parity, APGAR score, rate of hospitalization in Neonatal Intensive Care Unit (NICU), presence of neonatal sepsis and development of Respiratory Distress Syndrome (RDS) were extracted from the women's file. Blood tests including complete blood cell count (CBC) were recorded and PLR values were calculated by dividing the number of platelets to the number of lymphocytes and NLR by dividing the number of neutrophils to the number of lymphocytes.

Inclusion criteria

Women with PPROM diagnosed between 24-34 weeks of pregnancy based on PPROM criteria and having consent to participate in the plan and provide information on blood tests and other perinatal clinical findings were included in the study.

Exclusion criteria

Women with multiple pregnancy, hematological disorders, malignancy liver diseases, history of autoimmune diseases, inflammatory diseases of pregnancy such as gestational diabetes and preeclampsia, any acute or chronic infectious or inflammatory diseases, pregnancy with fetal chromosomal disorders, intrauterine growth restriction, any fetal infection and also women who underwent any invasive procedure such as amniocentesis were excluded from the study.

Statistical analysis

The collected data were reported descriptively using frequency tables and diagrams, and T-test and chi-square were used to analyze the relation between data. SPSS version 24 was used for analysis of data and a significant level less than 0.05 was considered as significant.

RESULTS

The average age of women in the group with PROM was 29.68 ± 7.61 years and in the group of women with preterm delivery was 29.70 ± 6.19 years and the difference was not significant. The gestational age of women in the case group with 34.81 ± 3.45 weeks was significantly lower than the women in the control group with 35.65 ± 1.48 . Also, the average weight of babies in case group with 2586.13 ± 573.62 grams was significantly lower than control group with 2768.06 ± 531.90 grams. There was a significant difference in the average number of neutrophils and platelets in the women of the two groups. The mean number of lymphocytes was not significant between two groups. The mean of NLR and PLR was significantly different between women of two groups (Table 1).

In women with PROM, in terms of the frequency of gravid one in number (39.4%), 61 cases had the highest percentage of gravid, and in the group of women with preterm delivery, in terms of the frequency of gravid in

number (5.5) 55 cases had the highest percentage of 35%. There was a statistically significant difference in the number of gravids in the two studied groups (Table 2).

Table 1: Gestational age in the studied groups.

| Variables | Group | | P value |
|-----------------|------------------|------------------|---------|
| | PPROM | Control | |
| Gestational age | 3.45±34.81 | 35.65±1.48 | 0.006 |
| Baby's weight | 2586.13±573.62 | 2768.06±531.90 | 0.004 |
| Neutrophil | 9371.91±6801.04 | 7814.68±2545.22 | 0.008 |
| WBC | 11139.35±2886.25 | 10267.74±2805.60 | 0.007 |
| NLR | 4.78±2.50 | 4.21±2.20 | 0.035 |
| PLR | 111.51±47.56 | 100.98±43.41 | 0.043 |

Table 2: Comparison of sepsis in the studied groups.

| Variables | | Group | | P value |
|------------------|----------|------------|------------|---------|
| | | PPROM (%) | PTL (%) | |
| Sepsis | + | 22 (14.2) | 10 (6.5) | 0.025 |
| | - | 133 (85.8) | 146 (93.5) | |
| Type of delivery | NVD | 64 (41.3) | 25 (16.1) | 0.001 |
| | CS | 91 (58.7) | 130(83.9) | |
| Gravid | 1 | 61 (39.4) | 22 (14.2) | 0.001 |
| | 2 | 32 (20.6) | 55 (35.5) | |
| | 3 | 37(23.9) | 38 (24.5) | |
| | 4 | 18 (11.6) | 22 (14.2) | |
| | 5 and up | 7 (4.5) | 18 (11.6) | |
| Parity | 1 | 61(39.4) | 22 (14.2) | 0.001 |
| | 2 | 32 (20.6) | 55 (35.5) | |
| | 3 | 37 (23.9) | 38 (24.5) | |
| | 4 | 18 (11.6) | 22 (14.2) | |
| | 5 | 6 (3.9) | 11 (7.1) | |

The incidence of sepsis in the case group was significantly higher than the control group. The odds ratio of getting sepsis in the group with PROM was 2.39 and according to the level of the confidence interval given for the odds ratio, the result was significant (OR = 1.09 - 5.25, 2.39). The type of cesarean delivery in the women of the study group was significantly higher than that of the women in the control group. In the women of the case group, parity one had the highest percentage (39.4%) of 61 cases, and in women of the control group, parity two had the highest percentage of parity (35.5%) in 55 cases, and the difference between the two groups was significant.

There was no significant difference between women in the two groups in terms of the incidence of RDS and the need for admission to the NICU. In both groups of women with PPRM and pre-term delivery, the Apgar scores of the first and fifth minutes were 9 and 10, respectively. There was no statistically significant difference in the two groups in terms of Apgar scores of the first and fifth minutes.

DISCUSSION

Alijani et al's study emphasized the existence of an effective relationship between vaginal infections and PROM and introduced it as a factor influencing the occurrence of PROM for several reasons, which was in line with the results of the present study.⁸ Balciuniene and his colleagues in 2021 in Lithuania during a research entitled “Neutrophil-lymphocyte ratio for the prediction of histological chorioamnionitis in cases of preterm premature rupture of membranes: a case-control study” showed that NLR has a good predictive value for HCA and could be used as an additional diagnostic marker for predicting histological chorioamnionitis in cases with preterm premature rupture of membranes before 34 weeks of gestation.¹¹ Lakshmi et al stated in a study that NLR can significantly help in the early prediction of PPRM and minimize adverse maternal and neonatal outcomes, and in this study, we precisely concluded that this marker can be a good predictor for PPRM.¹² Sharami et al stated that there is a significant relationship between PLR and PROM.¹³ Horasanlı et al stated that CRP and WBC

values were higher in the group with PROM than in the group with threat of premature delivery, and in the present study, the WBC value in the PPROM group was significantly higher than the control group.¹⁴ Uçkan et al stated that there is a positive relationship between premature rupture of membranes and platelet count, average platelet volume, neutrophil-to-lymphocyte ratio, and monocyte-to-lymphocyte ratio, and NLR and PCT parameters (platelet crit) were associated with adverse neonatal outcomes.¹⁵ Kurban et al stated that neutrophil to lymphocyte ratio and mean platelet volume may be decisive as a marker of pro-inflammatory process in patients delivering before 37 weeks. Premature delivery and fetuses of pregnant women with a high neutrophil-lymphocyte ratio and low mean platelet volume may be more likely to be referred to the NICU.¹⁶ In the study of Ozel et al, the number of peripheral blood platelets, neutrophils and lymphocytes in women with PPROM and threatened preterm labor (TPL) were compared to pregnancy-matched controls. Laboratory including complete blood count, CRP were recorded from all participants. The ratio of neutrophils to lymphocytes in the PPROM group was significantly higher than the TPL and the healthy control group. In addition, this study stated that NLR can predict the occurrence of neonatal sepsis. In this study, it was stated that high NLR values may be useful for predicting adverse outcomes in PPROM and TPL patients as a cost-effective method.¹⁷ In a study, Esercan et al showed that the NLR in the PPROM group was significantly higher than the control group ($p=0.001$).¹⁸ In the studies of Rehman et al and Carranza et al, NLR, as an early biological marker, was associated with the prediction of sepsis.¹⁹⁻²⁰ It is worth noting that NLR increases rapidly after infection. Since the presence of chorioamnionitis is considered the most important prognostic factor in PPROM, many studies have focused on early and non-invasive diagnosis, including some on white blood cells and CRP.¹⁸ Islamoglu and colleagues stated in a study that NLR and PLR, calculated with the simple, cheap, and easily accessible hemogram test requested for diagnosis and follow-up of COVID-19 disease, were correlated with the total score for radiological findings and duration of hospitalization, and we observed NLR and LMR may predict disease severity.²¹ Therefore, an easy, cheap and routine early diagnostic test for chorioamnionitis is needed. Not consistent with the results of the present study, in the Esercan study, there was no statistically significant difference between the PPROM and control group in terms of PLR, but consistent with the results of the present study, the amount of NLR in preterm labor compared to PLR significantly increased.¹⁸ In a study, Uçkan et al found a positive correlation between PPROM and PCT (platelet crit), MPV (mean platelet volume), NLR and MLR (monocyte/lymphocyte ratio).¹⁵ In a study, Herafteh et al showed that the ratio of neutrophils to lymphocytes in the preeclampsia group was significantly higher than the control group ($p=0.008$), but the ratio of platelet to lymphocyte was not significantly different between the two groups ($p=0.236$).²²

Zhang et al in a study showed that, the amounts of PLR and NLR have a high predictive value for premature rupture of membranes complicated by sepsis. Among them, the predictive value of PLR was greater than NLR.¹ Yuce et al in a study showed that, the amounts of NLR and PLR values predict spontaneous preterm birth with high sensitivity and specificity. By predicting preterm birth, the pregnancy process can be managed sensitively and smoothly.³ One of the limitations of this study is that it is not possible to determine precisely whether the inflammatory markers are elevated due to membrane rupture or vice versa, and it does not seem possible to conduct a study to prospectively predict this.

CONCLUSION

The results of the present study showed that the NLR as well as PLR can be used as a cost-effective and easily accessible marker for the diagnosis of PPROM. However, more supportive studies are needed for its routine use in the clinical study. Also, more studies are needed to determine whether these parameters can predict whether a pregnant woman who is at risk of preterm delivery will have an adverse perinatal outcome. In the management of patients with PPROM, values of PLR, NLR can be used as a more economical method than other blood parameters which require the use of a kit. It is suggested that studies with a larger sample size be conducted in other places in this field. It is also suggested to evaluate NLR and PLR in the first and second trimester of pregnancy in future studies.

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