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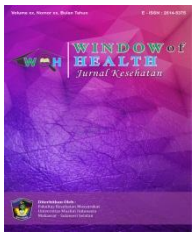

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Comparative Analysis of Maternal Neutrophils, Age, and Parity in PROM and Prolonged Labor

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ABSTRACT

Premature Rupture of Membranes (PROM) and prolonged labor are major obstetric complications associated with maternal inflammatory responses. Maternal neutrophils play an important role in innate immunity and may reflect inflammatory processes associated with membrane rupture and labor progression. This study aimed to compare maternal neutrophil levels between women with PROM and prolonged labor while evaluating the distribution of maternal age and parity. A comparative cross-sectional study was conducted among 50 postpartum women at RSIA Sitti Khadijah 1, Makassar. Maternal neutrophil levels were measured using an automated hematology analyzer, and data were analyzed using the Mann–Whitney U test. Maternal neutrophil levels were significantly higher in the prolonged labor group (82.44 ± 7.01%) than in the PROM group (75.10 ± 9.53%) (p = 0.004). Abnormal neutrophil levels were more frequent in prolonged labor across age categories and parity, particularly among primiparous women, whereas normal neutrophil levels were more common in multiparous women with PROM. Maternal neutrophil levels differed significantly between women with PROM and prolonged labor, suggesting differences in maternal inflammatory responses. Maternal neutrophil levels may represent a potential inflammatory biomarker; however, further validation in larger prospective studies is required.

Keywords : Inflammation; Maternal factors; Neutrophil levels; Prolonged labor; PROM

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INTRODUCTION

Premature Rupture of Membranes (PROM) and prolonged labor are major obstetric complications that contribute substantially to adverse maternal and neonatal outcomes. Although both conditions involve inflammatory activation, they arise through distinct pathophysiological mechanisms [1,2]. PROM is primarily associated with premature weakening of the fetal membranes resulting from extracellular matrix degradation, oxidative stress, and ascending infection, whereas prolonged labor is characterized by sustained uterine contractions, tissue ischemia, mechanical stress, and prolonged inflammatory stimulation [3,4]. These biological differences suggest that maternal inflammatory responses may differ between the two conditions and that inflammatory biomarkers could provide clinically relevant information for distinguishing their underlying pathological processes [5,6].

Among inflammatory biomarkers, maternal neutrophils are among the earliest responders of the innate immune system during pregnancy and labor. Activated neutrophils participate in cytokine release, extracellular matrix remodeling, and membrane degradation through the production of inflammatory mediators and matrix metalloproteinases[7]. Increased maternal neutrophil levels have been reported in both PROM and prolonged labor, suggesting that neutrophils may reflect the magnitude of maternal inflammatory activation. However, whether maternal neutrophil responses differ systematically between these obstetric conditions remains insufficiently understood[8]. Although reported prevalence varies across countries because of differences in diagnostic criteria and study populations, hospital-based studies in Indonesia consistently identify PROM as one of the leading obstetric complications requiring emergency obstetric care, whereas prolonged labor remains an important contributor to maternal and neonatal morbidity[9].

Although both PROM and prolonged labor involve inflammatory activation, the biological mechanisms underlying these conditions are substantially different. In PROM, inflammatory activation is initiated primarily by premature weakening of the fetal membranes, which may result from ascending bacterial infection, oxidative stress, extracellular matrix degradation, and collagen remodeling mediated by matrix metalloproteinases (MMPs)[9]. These processes progressively reduce membrane tensile strength, leading to spontaneous membrane rupture before the onset of labor. In contrast, prolonged labor is predominantly characterized by persistent uterine contractions, repetitive mechanical stress, tissue stretching, and ischemia–reperfusion injury[15]. These mechanical insults stimulate prolonged production of inflammatory cytokines, promote leukocyte recruitment, and sustain neutrophil activation within reproductive

tissues. Consequently, although neutrophils participate in both conditions, their activation in PROM mainly reflects membrane-associated inflammatory remodeling, whereas in prolonged labor it primarily reflects inflammation secondary to prolonged tissue stress and impaired labor progression[16,17]. These mechanistic differences provide the biological rationale for directly comparing maternal neutrophil levels between the two obstetric conditions.

Maternal neutrophils constitute one of the earliest innate immune responders activated during obstetric inflammation. Following inflammatory stimulation, neutrophils migrate to the chorio-decidual interface and release pro-inflammatory cytokines, reactive oxygen species, and matrix metalloproteinases that facilitate extracellular matrix degradation and tissue remodeling[18]. Because neutrophil activation reflects the magnitude of inflammatory responses rather than a single disease process, differences in maternal neutrophil levels may provide clinically useful information for distinguishing the inflammatory profiles associated with PROM and prolonged labor[19].

Maternal neutrophils represent the first line of the innate immune response and play a crucial role in inflammatory processes during pregnancy and labor. Neutrophil activation contributes to cytokine production, extracellular matrix degradation, and tissue remodeling, all of which are involved in membrane rupture and labor progression. Elevated maternal neutrophil levels have been reported in women with PROM and prolonged labor, suggesting that neutrophils may serve as a practical inflammatory marker for differentiating these obstetric conditions [20,21].

Besides inflammatory biomarkers, maternal characteristics such as age and parity may also influence inflammatory responses during pregnancy. Women at extreme reproductive ages (<20 years or ≥35 years) often experience altered physiological adaptation and increased susceptibility to obstetric complications, whereas parity has been associated with differences in cervical remodeling, uterine contractility, and maternal immune adaptation. Consequently, evaluating maternal neutrophil levels together with age and parity may provide a more comprehensive understanding of inflammatory profiles in PROM and prolonged labor[22].

Although previous studies have reported the involvement of inflammatory biomarkers in PROM and prolonged labor, these conditions have generally been investigated independently, with limited emphasis on directly comparing maternal inflammatory responses between them. Furthermore, most studies have focused on single inflammatory biomarkers without simultaneously considering maternal age and parity as factors that may influence inflammatory activation. Consequently, it remains unclear whether differences in maternal neutrophil levels

between PROM and prolonged labor are independent of maternal characteristics or reflect distinct inflammatory profiles associated with each obstetric condition. Addressing this unanswered question is clinically important because distinguishing these inflammatory patterns may improve early risk stratification, facilitate more individualized obstetric management, and support timely clinical decision-making. To our knowledge, no previous study has simultaneously compared maternal neutrophil profiles across PROM and prolonged labor while considering maternal demographic characteristics in an Indonesian obstetric population. This study aimed to determine whether maternal neutrophil levels differ significantly between PROM and prolonged labor and to evaluate whether maternal age and parity contribute to variations in inflammatory responses.

This study aimed to determine whether maternal neutrophil levels differ significantly between PROM and prolonged labor and to evaluate whether maternal age and parity contribute to variations in inflammatory responses.

METHOD

The study design was a comparative analysis using a cross-sectional approach to determine the comparison of neutrophil levels in mothers with PPROM and mothers with prolonged labor. This study was conducted at RSIA Sitti Khadijah 1, Makassar, with a sample size of 50 people, with inclusion criteria including pregnant women over 37 weeks, pregnant women with premature membrane rupture, and mothers with prolonged labor in the first and second stages. The research tools used included structured interview sheets, blood sampling, and written consent.

This study employed a comparative analytic study with a cross-sectional approach to compare maternal neutrophil levels between women with Premature Rupture of Membranes (PROM) and those with prolonged labor. A cross-sectional design was selected because the objective of the study was to evaluate differences in maternal neutrophil levels between two obstetric conditions at the time of clinical presentation rather than to assess temporal changes or causal relationships. This design enabled comparison of inflammatory profiles under similar clinical circumstances without requiring prospective follow-up.

The study was conducted at RSIA Sitti Khadijah 1 Makassar for 4 months. A total of 50 postpartum women were recruited using consecutive sampling, consisting of women diagnosed with term PROM and women diagnosed with prolonged labor based on the clinical diagnosis established by the attending obstetrician. The inclusion criteria were women with singleton pregnancies, gestational age ≥37 weeks, diagnosed with PROM before the onset of

labor or prolonged labor during the first or second stage of labor, and willing to participate by providing written informed consent.

The exclusion criteria included women with clinical or laboratory evidence of systemic infection before delivery, autoimmune disorders, hematological diseases, corticosteroid therapy during pregnancy, antibiotic administration prior to blood sampling, multiple pregnancy, gestational diabetes mellitus, preeclampsia, chronic inflammatory diseases, malignancy, and incomplete medical records, as these conditions may influence maternal neutrophil levels.

Maternal demographic data, including age and parity, were obtained through structured interview questionnaires and confirmed using medical records. Venous blood samples were collected before delivery and analyzed using an automated hematology analyzer according to the hospital's standard laboratory procedures to determine maternal neutrophil percentages, with etics code 002/11/UNF-KEP/21.PN/11/VII/2026.

Data normality was evaluated using the Shapiro–Wilk test. Differences in maternal neutrophil levels between the PROM and prolonged labor groups were analyzed using the Mann–Whitney U test, with a significance level of $p < 0.05$. Statistical analyses were performed using IBM SPSS Statistics version 26.

RESULTS

1. Respondent Characteristics

The analysis was conducted to describe the characteristics of the sample and research variables. Table 1 presents the distribution of respondent characteristics according to maternal age and parity, along with neutrophil levels among mothers with Premature Rupture of Membranes (PROM) and Prolonged Labor (PL). Table 1 shows that most mothers with PROM and prolonged labor were aged **20–35 years**. Among PROM cases, normal neutrophil levels were more common than abnormal levels in both age groups and among multiparous mothers, whereas primiparous mothers had an equal proportion of normal and abnormal neutrophil levels (50.0% each). In contrast, mothers with prolonged labor predominantly exhibited abnormal neutrophil levels across all age and parity categories. All mothers aged **<20 or >35 years** and all primiparous mothers with prolonged labor had abnormal neutrophil levels (100%). These findings suggest that abnormal neutrophil levels are more frequently associated with prolonged labor than with premature rupture of membranes.

a. Age Characteristics and Neutrophil Levels in Mothers with Preterm Labor

In the group of mothers with preterm labor, it was observed that normal neutrophil levels were more commonly found in mothers aged <20 or >35 years. From this age group, there were

4 respondents with normal neutrophil levels (66.7%) and only 2 respondents (33.3%) who had abnormal neutrophil levels. This shows that in PPROM, mothers in the risk age group (<20 or >35 years) were relatively more likely to have neutrophil levels that were still within the normal range.

Table 1. Frequency Distribution based on Respondent Characteristics and Neutrophil Levels in Mothers with Premature Rupture of Membranes (PROM) and Prolonged Labor (PL).

Variable	Neutrophils			
	Normal	Abnormal	Normal	Abnormal
	n	%	n	%
PROM Age				
<20 >35	4	66.7	2	33.3
20-35	11	57.9	8	42.1
PROM Paritas				
Primipara	4	50.0	4	50.0
Multipara	11	65.0	6	35.0
PL Age				
<20 >35	0	0.00	5	100
20-35	2	10.00	18	90.0
PL Paritas				
Primipara	0	0.0	12	100
Multipara	2	15.4	11	84.6

Source: Primary Data

Meanwhile, in the 20–35 age group, the percentage of normal neutrophil levels was also dominant, with 11 respondents (57.9%). However, the number of abnormal neutrophil levels was also quite high, with 8 respondents (42.1%). This figure shows that in the reproductive age range, although most have normal neutrophil levels, the tendency for neutrophils to increase or deviate in cases of PROM is also quite significant. In general, in the PROM group, normal neutrophil levels were found to be higher in both age groups, although neutrophil irregularities appeared more frequently in mothers of productive age (20–35 years) with a smaller percentage difference.

b. Characteristics of Parity and Neutrophil Levels in Mothers with PROM

Maternal age and parity were treated as categorical variables and were included to describe the distribution of maternal characteristics in each study group. These variables were not entered as covariates or potential confounding factors because the primary objective of the study was to compare maternal neutrophil levels between PROM and prolonged labor. Therefore, age and parity are presented descriptively without inferential statistical comparison.

Among women with PROM, the distribution of neutrophil levels varied according to parity. In the primiparous group, normal and abnormal neutrophil levels were observed in equal proportions, with four respondents (50.0%) in each category. In contrast, among multiparous women, normal neutrophil levels were observed more frequently than abnormal neutrophil levels, accounting for 11 respondents (64.7%) and 6 respondents (35.3%), respectively (Table 1).

Because parity was analyzed as a categorical descriptive variable, no statistical test was performed to determine its independent association with maternal neutrophil levels. The observed distributions are presented solely to describe the characteristics of the study population.

c. Age Characteristics and Neutrophil Levels in Mothers with Prolonged Labor (PL)

In the group of mothers with prolonged labor, the distribution of neutrophil levels appeared to be different. In the age groups <20 or >35 years, no one was found to have normal neutrophil levels (0%). All respondents 5 people (100%) were in the abnormal neutrophil count category. These findings indicate a strong tendency for mothers in the risk age range who experience prolonged labor to be more often in a state of inflammation or immune activation, as indicated by abnormal neutrophil counts.

For the 20–35 age group, although there were 2 respondents (10%) with normal neutrophil levels, abnormal neutrophil levels were very dominant, with 18 respondents (90%). This means that in both the risk age and reproductive age groups, prolonged labor tends to be accompanied by an increase or deviation in neutrophil levels. Overall, the high percentage of abnormal neutrophils in prolonged labor may indicate the presence of active inflammation, prolonged labor stress, or the possibility of intrapartum infection.

In the prolonged labor group, abnormal neutrophil levels predominated in both age categories. Among women aged <20 years or >35 years, all respondents (5/5; 100%) had abnormal neutrophil levels. In the 20–35-year age group, abnormal neutrophil levels were

observed in 18 respondents (90.0%), whereas only two respondents (10.0%) had normal neutrophil levels (Table 1).

Similarly, maternal age was categorized into reproductive-risk groups (<20 or >35 years and 20–35 years) for descriptive purposes only. No inferential analysis was conducted to evaluate age as an independent predictor or confounding factor.

d. Parity Characteristics and Neutrophil Levels in Mothers with Prolonged Labor

From the parity aspect, the results showed that in the primipara group with prolonged labor, all respondents (12 people or 100%) had abnormal neutrophil levels. None of the primiparas fell into the normal neutrophil category. This may indicate that primiparas are more prone to high inflammatory responses during prolonged labor, which may be related to their first physiological adaptation to the labor process. In the multiparous group, normal neutrophil levels were found in only 2 respondents (15.4%), while abnormal neutrophils were found in 11 respondents (84.6%). Although abnormal neutrophil levels were also dominant in multiparous women, this pattern still shows that primiparous women in prolonged labor are more likely to experience higher neutrophil activation than multiparous women.

Based on parity, all primiparous women with prolonged labor (12/12; 100%) had abnormal neutrophil levels. Among multiparous women, abnormal neutrophil levels were also predominant, occurring in 11 respondents (84.6%), whereas normal neutrophil levels were found in two respondents (15.4%) (Table 1). Therefore, the parity findings should be interpreted as descriptive distributions rather than evidence of an independent effect on maternal inflammatory responses.

2. Normality Test

A parametric prerequisite test was conducted to measure whether the data were normally distributed or not before performing parametric and non-parametric data analysis. The type of normality test used in this study was Shapiro-Wilk.

Table 2. Shapiro-Wilk Normality Test

Variable	PROM	Prolonged Labor
	Normal	Abnormal
	(n= 25)	(n= 25)
Neutrophils	0.48	0.0001

Source: Primary Data

Based on the results in Table 2, the neutrophil count in the group of mothers with premature rupture of membranes (PROM) showed a p-value of 0.248. This value is above the significance threshold of 0.05, so it can be concluded that the neutrophil count data in the

PROM group is normally distributed. This indicates that the variation in neutrophil values in mothers with PROM is relatively homogeneous and follows a general distribution pattern.

In contrast, neutrophil levels in the group of mothers with prolonged labor showed a p-value of 0.0001, which is well below the threshold of 0.05. Thus, it can be concluded that the neutrophil level data in the prolonged labor group are not normally distributed. This finding shows that the distribution pattern of neutrophil data in the prolonged labor group is more varied, does not follow a normal distribution pattern, and may reflect a more dynamic and heterogeneous inflammatory condition.

3. Comparison of Mean Neutrophil Levels in Mothers with Premature Rupture of Membranes (PROM) and Prolonged Labor (PL)

The comparison of maternal neutrophil levels between women with PROM and prolonged labor is presented in Table 3, while the distribution of neutrophil values in both groups is illustrated in Figure 1. Figure 1 presents the distribution of maternal neutrophil levels using boxplots, allowing visualization of data dispersion, median values, interquartile ranges, and potential outliers in each study group. This graphical presentation complements the statistical comparison by illustrating the variability of neutrophil levels between women with PROM and prolonged labor.

Based on the results of the data normality test, the Mann-Whitney test was used to determine the comparison of neutrophil levels in mothers with PROM and mothers with PL. The results of the analysis are presented in the following table:

Table 3. Comparison of Neutrophil Levels in Mothers with PPROM and Mothers with PTL

Variable	PROM	Prolonged Labor	
	Mean ± SD (f= 25) (mg/l)	Mean ± SD (f= 25) (mg/l)	*P-Value*
Netrofil	75.10 ± 9.525	82.44 ± 7.008	0.004*

*Mann Whitney U

The results of the analysis in Table 3 show a clear difference in the mean neutrophil count between the KPD group and the prolonged labor group. In the PROM group, the mean neutrophil count was 75.10 ± 9.525 mg/L. Meanwhile, in the group of mothers with prolonged labor, the average neutrophil count was higher, at 82.44 ± 7.008 mg/l. This difference in averages indicates that mothers who experience prolonged labor tend to have higher neutrophil counts than mothers with PROM. Based on the laboratory reference range used in this study (normal neutrophil percentage: 40–80%), the mean neutrophil level in the PROM group remained within the normal reference interval, whereas the mean value observed in the prolonged labor group slightly exceeded the upper reference limit. This finding suggests a

greater degree of maternal inflammatory activation among women with prolonged labor and supports the clinical relevance of the observed statistical difference.

The mean maternal neutrophil level was 75.10 ± 9.53% in the PROM group and 82.44 ± 7.01% in the prolonged labor group. The Mann–Whitney U test demonstrated a statistically significant difference between the two groups ($p = 0.004$), indicating that maternal neutrophil levels were significantly higher among women with prolonged labor. Nevertheless, the overlap observed in the boxplots indicates that individual neutrophil values varied within each group. Therefore, maternal neutrophil levels should be interpreted as an inflammatory indicator that complements clinical assessment rather than as a stand-alone diagnostic marker.

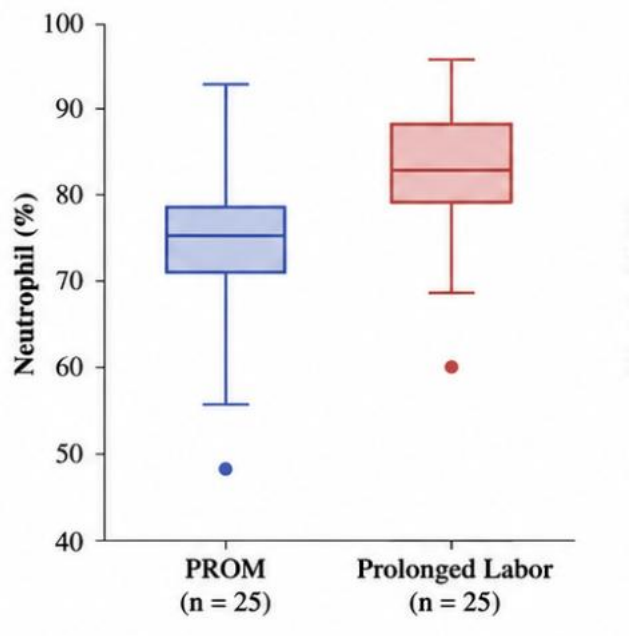

Figure 1. Distribution of Maternal Neutrophil Level Between Women with PROM and Prolonged Labor

The boxplot (Figure 1) demonstrates a higher distribution of neutrophil levels in the prolonged labor group than in the PROM group, although partial overlap between groups was observed.

DISCUSSION

Inflammatory Mechanisms & the Role of Neutrophils in Labor and PROM

The present findings extend these biological concepts by demonstrating that maternal neutrophil levels were significantly higher in women with prolonged labor than in those with PROM. Rather than merely indicating the presence of inflammation, this difference suggests that prolonged labor may induce a more sustained systemic inflammatory response through continuous mechanical stress and repeated uterine contractions. In contrast, inflammatory activation in PROM may occur earlier during membrane weakening and may vary depending

on whether membrane rupture is driven predominantly by infection-related or sterile inflammatory pathways. Therefore, the observed difference in neutrophil levels likely reflects differences in the intensity and duration of inflammatory activation rather than the presence or absence of inflammation alone.

Recent evidence also indicates that activated neutrophils contribute to inflammatory amplification through multiple complementary mechanisms. Besides releasing pro-inflammatory cytokines such as TNF-α and IL-8, activated neutrophils secrete matrix metalloproteinases (particularly MMP-8 and MMP-9), generate reactive oxygen species, and promote extracellular matrix degradation within the fetal membranes. Collectively, these mechanisms weaken membrane integrity, facilitate cervical remodeling, and enhance labor progression, thereby providing a biological explanation for the higher maternal neutrophil levels observed in prolonged labor.

Although the present findings are consistent with previous evidence supporting the role of neutrophils in obstetric inflammation, the biological pathways underlying PROM and prolonged labor should not be considered identical. PROM frequently develops following extracellular matrix degradation and membrane weakening that may be initiated by either microbial invasion or sterile inflammatory activation. Conversely, prolonged labor is characterized predominantly by prolonged mechanical stimulation, ischemia–reperfusion injury, and sustained cytokine production, resulting in prolonged recruitment and activation of neutrophils. These differences may explain why maternal neutrophil levels were significantly higher in the prolonged labor group in the present study.

The significantly higher maternal neutrophil levels observed in women with prolonged labor may reflect a more sustained inflammatory response than that observed in PROM. During prolonged labor, repetitive uterine contractions, tissue stretching, and localized hypoxia can stimulate neutrophil recruitment to the feto-maternal interface. Activated neutrophils subsequently release pro-inflammatory cytokines and proteolytic enzymes that contribute to tissue remodeling and amplification of the inflammatory cascade. In contrast, inflammatory activation in PROM may arise through different biological pathways, including both infection-related and sterile inflammatory mechanisms, resulting in greater variability in maternal neutrophil responses[3,23–25]. This interpretation is supported by the observation that inflammatory responses associated with prolonged labor are maintained throughout the duration of ineffective uterine contractions, whereas inflammatory activation in PROM may stabilize once membrane rupture has occurred. Consequently, prolonged labor may expose

maternal immune cells to inflammatory stimuli for a longer period, resulting in greater neutrophil activation and higher circulating neutrophil levels.

Neutrophils play a central role in the innate immune response during pregnancy by migrating to the chorio-decidual interface following inflammatory stimulation. Once activated, neutrophils release cytokines such as TNF-α and IL-8 together with matrix metalloproteinases (MMPs), particularly MMP-8 and MMP-9, which degrade extracellular matrix components of the fetal membranes. Excessive activation of these pathways weakens membrane integrity and contributes to membrane rupture and labor progression [27]. These mechanisms provide biological support for the higher neutrophil levels observed in women with prolonged labor in the present study [28,29].

These biological mechanisms are consistent with the present findings and reinforce the plausibility that maternal neutrophil levels reflect the magnitude of inflammatory activation rather than merely indicating infection. Therefore, maternal neutrophil measurement may contribute to understanding the inflammatory status associated with different obstetric complications, although it should always be interpreted together with clinical findings and other laboratory parameters.

Although ascending bacterial infection is a well-recognized contributor to PROM, increasing evidence suggests that PROM may also develop through sterile inflammatory pathways. Oxidative stress, mechanical stretching, cytokine-mediated extracellular matrix remodeling, and activation of innate immune pathways may promote fetal membrane weakening even in the absence of overt infection. Therefore, elevated maternal neutrophil levels should not be interpreted exclusively as evidence of infection but rather as part of a broader inflammatory response associated with obstetric complications[28–31]

Additionally, the neutrophil-to-lymphocyte ratio (NLR) in maternal blood as a proxy for the immune system's tilt toward inflammation has been empirically shown to correlate with the occurrence of histological chorioamnionitis [20] . Thus, the approach of using hematological parameters such as absolute neutrophil count, neutrophil percentage, or NLR as potential markers of maternal inflammation and predictors of complicated delivery is biologically justified.

Interpretation of Results: Neutrophils, Age, Parity, and Clinical Implications

The interpretation of these findings, within the framework of inflammation and immune adaptation during pregnancy, is that prolonged labor causes prolonged physiological stress (prolonged uterine contractions, possible tissue hypoxia, mechanical stress, tissue stretching),

all of which can trigger the activation and migration of neutrophils to the uterus and membranes. The accumulation of neutrophils, particularly “aged” neutrophils or low-density granulocytes (LDGs) that have been circulating for a long time, can alter their functional profile: decreased chemotaxis, altered receptor expression, and abnormal phagocytosis or NETosis; contributing to the maintenance of chronic inflammation and worsening of dystocia during labor [32]. Similarly, prolonged labor is increasingly recognized as an inflammatory condition characterized not only by prolonged mechanical stress but also by increased leukocyte infiltration and cytokine production within reproductive tissues. Persistent uterine contractions may enhance neutrophil activation through sustained release of inflammatory mediators, thereby contributing to the higher maternal neutrophil levels observed in this study.

Maternal age may also influence inflammatory responses during pregnancy. Women at advanced reproductive age frequently exhibit alterations in immune regulation and inflammatory homeostasis, whereas younger mothers may demonstrate incomplete physiological adaptation to pregnancy. These age-related changes could contribute to variation in maternal neutrophil responses. However, because age was evaluated descriptively in this study and no multivariable adjustment was performed, the observed differences should be interpreted cautiously [33].

Although ascending infection is a well-recognized contributor to PROM, sterile inflammatory mechanisms involving oxidative stress and cytokine-mediated extracellular matrix remodeling may also increase maternal neutrophil activation.

In addition to prolonged mechanical stimulation, recent evidence suggests that prolonged labor is accompanied by enhanced activation of maternal leukocytes and sustained release of pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-α). These inflammatory mediators promote continuous neutrophil recruitment and activation, amplifying the inflammatory cascade and contributing to prolonged tissue remodeling during labor. Therefore, the higher maternal neutrophil levels observed in the present study likely reflect not only mechanical stress but also cytokine-mediated inflammatory activation [34].

Advanced maternal age has been associated with immunosenescence, a gradual decline in immune regulation characterized by impaired neutrophil chemotaxis, altered cytokine production, reduced phagocytic capacity, and persistent low-grade systemic inflammation. These age-related immune alterations may modify maternal inflammatory responses during

obstetric complications and partly explain the variability in neutrophil activation observed among different maternal age groups[35].

Integration with Current Literature & Validity of Findings

Several recent studies support the role of neutrophils and the NLR ratio (or even other immune cell parameters) as markers of maternal inflammation in the context of childbirth and pregnancy complications: Recent research shows that during labor, there is an increase in IL-8 and neutrophils in the lower uterine segment, as well as increased expression of MMP-8 and MMP-9 enzymes that facilitate tissue remodeling and can weaken the amniotic membrane [26]. [32] concludes that the accumulation of "overaged" neutrophils and LDGs in prolonged labor may indicate a chronic inflammatory state, contributing to obstetric dystocia.

Several previous studies have demonstrated that maternal neutrophils and the neutrophil-to-lymphocyte ratio (NLR) are closely associated with inflammatory responses during pregnancy and labor. Increased neutrophil infiltration, accompanied by elevated expression of inflammatory cytokines such as IL-8 and proteolytic enzymes including MMP-8 and MMP-9, has been reported to contribute to extracellular matrix remodeling and weakening of the fetal membranes during obstetric complications. These biological mechanisms are consistent with the present findings, in which women with prolonged labor exhibited significantly higher maternal neutrophil levels than those with PROM, suggesting a more pronounced inflammatory response during prolonged labor [31,33] .

Overall, the present findings agree with previous reports demonstrating increased neutrophil activation during obstetric inflammation. However, unlike studies that evaluated PROM or prolonged labor separately, the present study directly compared both conditions within the same clinical setting. This comparative approach provides additional evidence that differences in maternal neutrophil levels may reflect distinct inflammatory mechanisms rather than simply differences in disease occurrence. Nevertheless, because maternal age, parity, and other inflammatory biomarkers were not adjusted simultaneously, further multicenter studies employing multivariable analyses are required to confirm these observations.

STUDY LIMITATIONS

This study has several limitations. First, it was conducted at a single referral hospital with a relatively small sample size, which may limit the generalizability of the findings. Second, the cross-sectional design allows identification of associations but cannot establish causal relationships between maternal neutrophil levels and obstetric conditions. Third, multivariable analyses were not performed; therefore, potential confounding factors could not be controlled.

Finally, diagnostic performance analyses such as receiver operating characteristic (ROC) analysis were not conducted, limiting conclusions regarding the clinical utility of maternal neutrophil levels as a diagnostic marker.

CONCLUSIONS AND RECOMMENDATIONS

Maternal neutrophil levels were significantly higher in women with prolonged labor than in women with PROM, suggesting differences in inflammatory responses between these obstetric conditions. Maternal age and parity also showed variations in neutrophil distribution, although these findings should be interpreted descriptively because no multivariable adjustment was performed. Maternal neutrophil levels may represent a potential inflammatory marker associated with PROM and prolonged labor. However, further multicenter prospective studies with larger sample sizes and comprehensive diagnostic accuracy analyses are required before maternal neutrophils can be recommended for routine clinical application.

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