Importance of haemogram parameters for prediction of the time of birth in women diagnosed with threatened preterm labour

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Abstract

Objective: This study aimed to estimate the importance of complete blood count parameters for predicting the timing of birth in threatened preterm labour cases.

Methods: We performed a retrospective study of 92 patients who were diagnosed with threatened preterm labour (24–34 gestational weeks). The patients were divided into two groups according to the time of birth (group 1: delivered within the first week after diagnosis; group 2: delivered later than 1 week). We compared characteristics and complete blood count parameters between these two groups.

Results: There were no significant differences in maternal age, body mass index, gravida, parity, haemoglobin levels, and gestational weeks between the two groups. The mean cervical length was 24.24 ± 3.60 mm in group 1 and 30.70 ± 5.32 mm in group 2. There were significant differences in the neutrophil to lymphocyte ratio, white blood cell count, red cell distribution width (RDW), absolute lymphocyte cell count, and absolute neutrophil cell count between the two groups.

Conclusion: Maternal serum RDW, the neutrophil to lymphocyte ratio, white blood cell count, absolute lymphocyte cell count, and the absolute neutrophil cell count profile could guide clinicians in predicting the time of birth in threatened preterm labour cases.

Keywords
Red cell distribution width (RDW), neutrophil to lymphocyte ratio (NLR), mean platelet volume (MPV), preterm birth, delivery, cervical length, white blood cells

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Introduction

Preterm birth is the leading cause of perinatal morbidity and mortality worldwide. Determining the risk of preterm birth in pregnant women can be difficult because of its multifactorial aetiology. Prediction of preterm birth is important for saving time for health workers and pregnant women to perform the necessary interventions. Many markers have been used to predict preterm labour. These include the patient’s history, evaluation of maternal signs and symptoms, a clinical examination, biochemical markers, and cervical length. Cervical evaluation by transvaginal sonography, and foetal fibronectin and interleukin-6 levels appear to be the best method for predicting preterm birth.\(^1\)\(^,\)\(^2\) Although preterm labour is the most common cause of perinatal morbidity and mortality, its aetiology is still unclear. Although tocolytic drugs are used for preterm labour, there has been no significant decrease in the frequency of preterm birth in the world. Markers for preterm birth may contain any factor that can be used to predict subsequent spontaneous preterm labour, such as the medical history, demographic factors, personal behaviour, physical characteristics, physical examination findings, evaluation of cervical length by ultrasonography, and measurement of a specific substance in a biological fluid.\(^3\)

A complete blood count (CBC) is simple and inexpensive, and it contains important parameters for many diseases. The red cell distribution width (RDW) is a measure of the distribution of erythrocytes depending on the diameter or volume within the CBC parameters. A positive correlation between RDW levels and inflammatory processes, especially C-reactive protein levels and sedimentation, has been found in recent cohort studies.\(^4\) RDW is a marker of anisocytosis and is related to various inflammatory conditions, such as thyroiditis,\(^5\) ulcerative colitis,\(^6\) rheumatoid arthritis,\(^7\) chronic obstructive pulmonary disease,\(^8\) irritable bowel syndrome,\(^9\) and chronic renal failure.\(^10\) The neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are inexpensive to measure and are easily calculated indices that correlate with the prognosis of systemic inflammatory diseases. They are particularly useful in inflammatory, cardiovascular, and oncological diseases.\(^11\)\(^–\)\(^14\) Mean platelet volume (MPV) is a parameter that is indicative of platelet function and activity.\(^15\) MPV plays an important role in immunological and inflammatory events.\(^16\) The PLR is associated with various conditions, including diabetes mellitus.\(^17\) The NLR is associated with diabetes mellitus,\(^18\) thyroiditis,\(^19\) and thyroid nodules.\(^20\) Similarly, MPV is associated with diabetes mellitus,\(^21\) inflammatory conditions,\(^22\) cardiac conditions,\(^23\) and thyroid conditions.\(^24\) Use of CBC parameters in the field of obstetrics and perinatology has recently been investigated. Orgul et al.\(^25\) found that increased first trimester WBC and neutrophil counts may be predictive for early-onset preeclampsia.

In this study, we aimed to investigate whether CBC parameters can be used for predicting the timing of preterm birth.

Materials and methods

The medical records of Van Training and Research Hospital were reviewed from January 2017 to March 2018. Ninety-two patients who were diagnosed with threatened preterm labour (TPL) were enrolled in the study. This study was designed as a retrospective assessment of data, and therefore, ethics committee approval and informed consent were not required.

In this study, pregnant women at 24 to 34 gestational weeks who were diagnosed with TPL were enrolled. TPL was defined as regular uterine contractions with or without other symptoms, such as pelvic
pressure, backache, increased vaginal discharge, menstrual-like cramps, bleeding, and cervical changes. Pregnant women with preeclampsia, idiopathic thrombocytopenia, urinary tract infection, diabetes, and rheumatic disease were excluded from the study. All patients were hospitalized after the diagnosis of TPL was made and followed up at the hospital. After a foetal ultrasound examination and routine tests, hydration treatment was applied. Additionally, tocolytic treatment was provided with a calcium channel blocker (nifedipine). Prophylactic corticosteroid treatment was performed in all pregnant women.

Haemogram parameters were evaluated using blood samples that were taken before steroid treatment. These parameters included haemoglobin levels, the NLR, white blood cell (WBC) count, RDW, and MPV.

Patients who delivered within the first week after diagnosis of TPL were included in group 1 and those who delivered later than 1 week were included in group 2.

Statistical analyses

The Statistical Package for the Social Sciences (SPSS) version 21.0 for Windows (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. The Shapiro–Wilk test was used to test for the distribution of normality. According to the results of data distribution, non-parametric tests were preferred. We used the Mann–Whitney U test to compare continuous variables. A p value < 0.05 was considered statistically significant.

Results

There were 46 patients in group 1 and 46 patients in group 2. Age, haemoglobin levels, gravidity, parity, body mass index, and gestational weeks were similar between the groups. The mean cervical length of patients in group 1 was significantly lower than that of patients in group 2 (p < 0.001, Table 1).

Table 2 summarizes the haemogram parameters of the two groups. There were no significant differences between the platelet count and MPV between the two groups. However, the NLR, WBC, RDW, and absolute neutrophil cell count were significantly higher in group 1 than in group 2 (all p < 0.05). Additionally, the absolute lymphocyte cell count was significantly lower in group 1 than in group 2 (p = 0.027, Table 2).

Discussion

In this study, we investigated the possible association of the time of birth and

| Table 1. Demographic variables of the groups. |
|---------------------------------------------|
|                                             |
| Group 1 | Group 2 | p value  |
|---------|---------|----------|
| Age (years) | 29.74 ± 3.52 | 29.52 ± 4.59 | 0.518 |
| Parity | 1.54 ± 0.84 | 1.57 ± 0.98 | 0.947 |
| Gestational weeks | 31.28 ± 2.02 | 31.20 ± 1.50 | 0.161 |
| Gravida | 2.78 ± 1.03 | 2.74 ± 1.31 | 0.491 |
| Body mass index (kg/m²) | 24.30 ± 3.89 | 24.42 ± 2.42 | 0.753 |
| Haemoglobin (mg/dL) | 10.88 ± 0.98 | 10.84 ± 1.10 | 0.739 |
| Cervical length (mm) | 24.24 ± 3.60 | 30.70 ± 5.32 | <0.001 |

Values are mean ± standard deviation. Group 1: birth occurred within 1 week after hospitalization with diagnosis of threatened preterm labour; group 2: birth occurred later than 1 week after hospitalization with diagnosis of threatened preterm labour.
maternal CBC variables in patients with TPL. The main findings in our study were as follows. We found that the NLR, WBC count, RDW, and absolute neutrophil cell count were higher in group 1 (those who delivered 1 week after hospitalization with the diagnosis of TPL) than in group 2 (those who did not deliver within 1 week after the hospitalization). We also found that the absolute lymphocyte cell count was lower in group 1 than in group 2. Platelet number and MPV were not different between these two groups. Additionally, cervical length was significantly lower in group 1 than in group 2.

A short cervical length can be predictive for preterm birth, and when coupled with appropriate preterm birth prevention strategies, it is associated with a reduction in spontaneous preterm birth in asymptomatic women with a singleton gestation. Our finding of a short cervical length in group 1 is consistent with previous published studies.27

CBC parameters significantly vary in number and quality in inflammatory events; in particular, neutrophil and platelet counts increase, and lymphocyte counts decrease.28,29 Neutrophils are precursor cells of the immune system and are synthesized in the bone marrow. Many cytokines, chemokines, and growth factors are responsible for synthesis of neutrophils, apart from antimicrobial agents produced in defence.30 Platelets increase secretion of cytokines (similar to neutrophils) at the onset of inflammation, and increased cytokine levels contribute to increased inflammation by increasing new neutrophil and platelet synthesis. Accumulation of neutrophils and platelets leads to sterile inflammation in tissues and increases tissue damage by synthesizing protease and growth factors in immunological conditions.31,32 Use of an index is more practical than evaluating individual parameters and can provide reliable information on disease severity by estimating predictive values based on their relationship with the disease. Indices, such as the NLR and PLR, are useful in the prognostic follow-up of diseases, such as acute coronary syndrome, ulcerative colitis, diabetes, obstructive sleep apnoea, Sjögren syndrome, and systemic lupus erythematosus with predominant inflammatory activity.33–35 The PLR has a significant relationship with cancer and inflammatory diseases, similar to the NLR.36,37

Preterm birth is among the most important causes of perinatal morbidity and mortality. There have been many studies on the aetiology of preterm labour and prevention of preterm labour.38 The exact aetiology of preterm birth is unknown. However, in

|                        | Group 1 | Group 2 | p value |
|------------------------|---------|---------|---------|
| Platelet number (×10³/mm³) | 268.93 ± 40.83 | 271.35 ± 33.56 | 0.549 |
| Mean platelet volume (fL) | 8.38 ± 0.72   | 8.36 ± 0.81   | 0.223 |
| Absolute neutrophil count (cell/mm³) | 4794.65 ± 121.27 | 4091.39 ± 105.72 | <0.05 |
| Absolute lymphocyte count (cell/mm³) | 2167.24 ± 203.73 | 2170.48 ± 172.11 | 0.027 |
| RDW (%) | 14.84 ± 0.77   | 13.90 ± 1.09   | <0.05 |
| NLR (%) | 2.85 ± 0.40    | 2.16 ± 0.28    | <0.05 |
| WBC count (/μL) | 8.0 ± 0.99   | 6.85 ± 0.76   | <0.05 |

Values are mean ± standard deviation. Group 1: birth occurred within 1 week after hospitalization with diagnosis of threatened preterm labour; group 2: birth occurred later than 1 week after hospitalization with diagnosis of threatened preterm labour. RDW: red cell distribution width; NLR: neutrophil to lymphocyte ratio; WBC: white blood cell.
more than half of preterm cases, the aetiological factor is subclinical intrauterine infection and inflammation, which can be detected by increased concentrations of cytokines and prostaglandins in amniotic fluid and maternal blood.39–41

Maternal inflammation and organization of the vascular bed, which are indicated by the NLR, are associated with foetal development and preterm delivery. Consistent with our findings, previous studies have also shown that an increased maternal inflammatory response is accompanied by preterm delivery.42–44

Few studies have investigated CBC parameters in the field of obstetrics and perinatology. The NLR can be used in combination with existing markers to improve detection rates of preterm birth, as shown by Gezer et al.45 In another study conducted by Özel et al.,46 the accuracy of the NLR was detected in pregnancies with preterm premature rupture of the membranes. Several studies have shown that maternal and maternal–foetal inflammation may trigger premature labour.47,48 Previous studies have also shown that maternal inflammation affects birth weight either directly or via preterm labour.49–51 In light of these findings, an increased NLR and PLR can be a result of preterm labour or insufficiency of the maternal–placental–foetal unit. A study that investigated the NLR and PLR in preeclamptic patients found a correlation between the PLR, but not the NLR, and the severity of preeclampsia.52 These authors concluded that the PLR could indicate maternal immune activation in preeclampsia. Monitoring the symptoms observed in pregnant women who have preterm labour and being able to predict preterm birth, and managing complications and neonatal outcomes are important.

To the best of our knowledge, this retrospective study is the first to investigate the associations of the NLR, RDW, absolute neutrophil cell count, and absolute lymphocyte cell count in patients who deliver within 1 week of diagnosis of TPL. Our study suggests that the maternal NLR, RDW, WBC, and absolute neutrophil cell count are positively associated with birth within 1 week of diagnosis of TPL. Additionally, absolute lymphocyte cell count levels are higher in pregnant women who do not deliver in 1 week after diagnosis of TPL.

There is no proven method for prediction of preterm birth. Evaluation of cervical length is relatively successful for predicting preterm birth. A haemogram test is an inexpensive and effective method, but a larger dataset is required to clarify the issue of predicting preterm birth. The combined use of markers may be more useful in predicting preterm delivery.

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