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Evaluation of the use of first and third-trimester hemogram parameters in prediction of preterm labor

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Abstract

Objective: Various combinations of hemogram parameters such as white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM), platelet (PLT), neutrophil-lymphocyte ratio (NLR), mean platelet volume (MPV), and platelet-lymphocyte ratio (PLR) are used as inflammatory markers. In this study, we aimed to determine the potential role of hemogram count parameters in predicting preterm birth.

Methods: The study included 212 singleton pregnant women aged 17-40 years who were diagnosed with preterm labor and had preterm delivery and whose gestational weeks were between 24 weeks and 36 weeks and 6 days. The control group included 120 pregnant women between the ages of 17 and 40 who were delivered at 37 weeks or later and had no obstetric complications were included. The preterm labor group was divided into 2 subgroups: early preterm (n:108) and late preterm (n:104). Inflammatory markers were compared separately for the 1st and 3rd trimesters among the study groups. Changes between the 1st and 3rd trimester values were also assessed.

Results: When the 1st trimester and 3rd trimester hemogram parameters were analyzed, in the preterm group, WBC, NEU and NLR values were found to be increased and MPV value decreased. A statistically significant difference was found between WBC, NEU, MPV and NLR values ($p<0.05$). In the term group only the increase in MPV was statistically significant. Markers for prediction of preterm birth cut-off levels as in 1st trimester WBC >9450/mm3, NEU >6650/mm3, NLR >3.86, MPV <9050/mm3 and in thirt trimester WBC >11300/mm3, NEU >8350/mm3, NLR >4.69, MPV <9250/mm3.

Conclusion: In our study we have found that 1st and 3rd trimester hemogram parametes as WBC, NEU, MPV and NLR varies among term and preterm birth and could be useful as proinflammatory markers. More comprehensive studies in different populations are needed to apply the results of our study to clinical practice.

Keywords: Preterm Labor, neutrophil, lymphocyte, neutrophil-lymphocyte ratio

Introduction

Preterm labor is defined as labor occurring before the 37th gestational week. Early preterm birth occurs before 34 weeks of gestation, and late preterm birth occurs between 34 and 37 weeks of gestation. [1] Preterm birth is the most common cause of mortality and morbidity in infants and children under 5 years of age worldwide.[2] Preterm infants are also at risk for acute and chronic respiratory, infectious, metabolic and neurological problems. Mortality and morbidity have been observed to be higher in babies born in the early preterm period compared to babies born in the late preterm period.[3] Therefore, the prediction of preterm labor and prevention of preterm delivery is important in terms of reducing fetal mortality and morbidity.

Preterm labor's pathogenesis is not well understood. Intrauterine infection, uterine ischemia, abnormal uterine contraction, abnormal immunogenic sensitization, cervical pathologies, and endocrine disorders are among the etiological causes. [4] The resulting tissue damage, infection, immunologic reactions, and inflammatory process cause a systematic response in pregnant women, which can be acute or chronic.[5] The association of inflammation and infection is the most thought pathologic

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process whose molecular pathophysiology has been defined among the causes of preterm labor.[6] Of the preterm deliveries, 80% of them are caused by spontaneous preterm labor and preterm premature rupture of membranes.[7] The remaining 20% are maternal and fetal pathologies.[8]

Maternal intraamniotic infection with a subclinical course is common in 25% of babies delivered as a result of preterm labor.[9] Predicting and preventing preterm labor is critical for both fetal and maternal health. In this study, we attempted to determine the role of inflammatory markers obtained from 1st and 3rd trimester hemogram examination in the prediction of preterm labor and to identify potential risk factors.

Methods

Patients who applied to Tepecik Education and Research Hospital, Gynecology and Obstetrics Clinic between 2017 and 2023 were evaluated retrospectively. The study included 212 pregnant women aged 17 to 40 years old who had been diagnosed with preterm labor and preterm delivery and whose gestational weeks ranged from 24 to 36 weeks and 6 days according to the last menstrual period (LMP). The control group included 120 pregnant women in the same age group with no obstetric pathology and a gestational age of 37 weeks or more according to LMP. The preterm labor group was divided into two subgroups: early preterm (n:108) and late preterm (n:104). Pregnant women with gestational hypertension, gestational diabetes, thyroid disorders, hematologic disorders, hyperemesis gravidarum, active infection, a history of preterm labor, or multiple pregnancies were excluded. The data of 332 pregnant women were accessed via the analysis of the hospital database.

Age, gravida, gestational week, race, mode of delivery, 1st and 3rd trimester white blood cell (WBC), lymphocyte (LYM), platelet (PLT), neutrophil (NEU), mean platelet volume (MPV) values, postnatal 1st minute and 5th minute APGAR scores, infant height, weight and sex were recorded. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated from hemogram parameters in the 1st and 3rd trimesters.

The data were analyzed using IBM Statistics version 21.0. The t-test was used for categorical variables. Shapiro-Wilk test was performed to determine the distribution of quantitative data. The variables meeting the normality criteria were evaluated using ANOVA, and the variables that deviated from the normal distribution were evaluated using the Kruskal-Wallis test. Evaluations with $p>0.05$ were considered statistically significant.

Results

Our study included 332 pregnant women who had given birth. The mean age was 27.7±6.49 years, while the average parity was 2.32±1.165. It was found that the deliveries occurred as follows: 108 (32.5%) as preterm deliveries, 104 (31.3%) as late preterm deliveries, and 120 (36.1%) as term deliveries. Cesarean sections were performed in 78 (72.2%) preterm deliveries, 72 (69.2%) late preterm deliveries, and 82 (68%) term deliveries. When demographic data were analyzed, it was discovered that the preterm group had a higher age, gravida, and parity, but there was no statistically significant difference between the two groups (Table 1).

Table 1. Demographic data of pregnant women who had term and preterm deliveries

	Term birth Within the last 1 week (n:120 mean±SD)	Preterm birth <37 weeks (n:212 mean±SD)	p value
Gestational Age (week)	38.8±1.07	33±3.52	<0.001
Age (years)	27.85±5.71	27.93±6.92	0.825
Gravida(n)	2.3±1.2	2.4±1.4	0.342
Parity (n)	2.2±1.0	2.3±1.1	0.342

p<0.05: Statistically significant

When the 1st trimester hemogram parameters were analyzed, in the preterm group, WBC, NEU and NLR values were found to be increased and MPV value decreased. A statistically significant difference was found between WBC, NEU, MPV and NLR values (p<0.05). In the term group only the increase in MPV was statistically significant. Table 2 shows the 1st-trimester hemogram parameters of the pregnant women who participated in the study.

Table 2. 1st-trimester hemogram parameters

	Term birth within the last 1 week (n:120 mean±SD)	Preterm birth <37 weeks (n:212 mean±SD)	p value
WBC (103/µL)	9051.67±2582	106433±2767	**<0.001**
NEU (103/µL)	6373±2319	8035±2921	**<0.001**
LYM (103/µL)	1891±558	1806±541	**0.395**
PLT (103/µL)	245095±76715	238156±75038	0.271
MPV (f/L)	9.3±1.37	9.03±0.97	**<0.001**
N/L ratio (NLR)	3.5±1.16	4.93±2.36	**<0.001**
P/L ratio (PLR)	136±50.41	138.17±51.36	0.780

p<0.05: Statistically significant

When the 3rd trimester hemogram parameters of term and preterm pregnant women were compared, WBC, NEU, and NLR values were found to be higher in the preterm group. The increased WBC, NEU, and NLR levels were statistically significant (p<0.05). In the term group only MPV elevation was statistically significant. The 3rd trimester hemogram parameters of the pregnant women who participated in the study are summarized in Table 3.

Table 3. 3rd-trimester hemogram parameters

	Term birth within the last 1 week (n:120 mean±SD)	Preterm birth <37 weeks (n:212 mean±SD)	p value
WBC (103/☹<L)	10703.33±3302	14491.51±4941	**<0.001**
NEU (103/☹<L)	8903.33±7354	11332.83±5401	**<0.001**
LYM (103/☹<L)	1748.33±585	1730.19±752	0.184
PLT (103/☹<L)	238740±86517	238847±70197	0.667
MPV (f/L)	9.4±1.25	9.2±1.24	**<0.001**
N/L ratio (NLR)	6.81±8.87	8.19±6.69	**0.01**
P/L ratio (PLR)	189.31±250	155.14±61.70	0.09

p<0.05: Statistically significant

In the comparison of statistically significant parameters, WBC and NLR values decreased significantly in the term group in terms of 1st trimester comparisons. MPV values were found to be significantly increased compared to the other groups. In the preterm group, no statistically significant difference was observed between the early and late preterm groups. 1st-trimester hemogram parameters of the sub-groups of preterm pregnant women who participated in the study are shown in Table 4.

Table 4. Comparison of 1st-trimester hemogram parameters of pregnant women with early preterm and late preterm labor

	Preterm		
	34-37 weeks (n:104) (mean±SD)	<34 weeks (n:108) (mean±SD)	p value
WBC (103/㎕)	10500±2820	10788±2735	0.712
N/L ratio (NLR)	4.91±2.09	4.94±2.61	0.494
P/L ratio (PLR)	133.65±41.23	142.53±59.59	0.707
MPV (f/L)	9.02±1.4	9.01±1.33	0.633

p<0.05: Statistically significant

WBC and NLR values were found to be significantly lower in the term group in the third trimester in terms of the comparison of the statistically significant parameters. In the preterm group, MPV values were found to be significantly increased compared to the term group. In the preterm group, no statistically significant difference was observed between the early and late preterm groups (Table 5). When the groups were compared, the term group had significantly higher neonatal weight and 1st and 5th minute APGAR scores than the late-preterm and early-preterm groups (Table 6).

Table 5. Comparison of 3rd-trimester hemogram parameters of pregnant women with early preterm and late preterm labor

	Preterm		
	34-37 weeks (n:104 mean±SD)	<34 weeks (n:108 mean±SD)	p value
WBC (103/㎕)	12080±5344	13916±4495	0.266
N/L ratio (NLR)	8.87 ± 7.45	7.54 ± 5.86	0.602
P/L ratio (PLR)	156.91 ± 58	153.44 ± 65.56	0.620
MPV (f/L)	9.82 ± 1.241	9.14 ± 1.26	0.852

p<0.05: Statistically significant

When the perinatal outcomes were analyzed based on the gestational week, neonatal weight, and 1st and 5th minute APGAR scores were found to be statistically significantly higher in the term group. When the groups were compared among themselves, neonatal weight, and 1st and 5th-minute APGAR scores were found to be statistically significantly higher in the term group compared to the late preterm and early preterm groups (Table 6).

Table 6. Perinatal results according to weeks of birth

	Term birth within the last 1 week (n:120)	Preterm birth <37 weeks (n:212)	p value
Gestational age (week)	38.8 ±1.07	33.08±3.52	<0.001
Neonatal birth weight (gr)	3249.77±518	2138.73± 918	<0.001
1st minute APGAR score (n)	7.74±0.678	4.88±2.61	<0.001
5th minute APGAR score (n)	8.67±0.673	5.75±2.94	<0.001
Frequency of cesarean section (%)	41.9%	74.1%	0.438
Live birth (%)	100%	%96.5	0.061

p<0.05: Statistically significant

We've found that in our study, markers for prediction of preterm birth cut-off levels as in 1st trimester WBC >9450/mm3, NEU >6650/mm3, NLR >3.86, MPV <9050/mm3 and in 3rd trimester WBC >11300/mm3, NEU >8350/mm3, NLR >4.69, MPV <9250/mm3.

Discussion

Hemogram parameters are a simple, low-cost test that can be easily performed in many healthcare centers nowadays. During pregnancy, hemogram evaluation is important in determining the inflammatory process for many pathologic conditions. We compared the 1st and 3rd trimester hemogram parameters of term and women who had given preterm birth in this study. An increase in WBC, NEU, and NLR parameters, as well as a decrease in MPV, were found to be associated with preterm labor when 1st and 3rd trimester hemogram parameters were evaluated.

Elevated WBC is a common finding of acute infection and inflammation.[10] Physiologic leukocyto-

sis during pregnancy, as well as appendicitis, cholecystitis, cystitis, and other inflammatory processes, are more common in inflammatory processes.[11] WBC elevation was reported to be a marker that could be used to predict preterm delivery in a study conducted by Liyin et al. with 400 pregnant women. [12] The findings in this study were linked to histologic chorioamnionitis. Karen et al. reported that in a study of 218 pregnant women, WBC elevation could be used to predict preterm delivery in symptomatic women (p:0.001).[13] Births before 28 weeks of gestation were associated with subclinical infections, while births after 28 weeks were associated with maternal and/or fetal hypothalamic pituitary adrenal axis. In our study, the increase in WBC in the 1st and 3rd trimesters was found to be statistically significant in pregnant women with preterm delivery (p:0.001).

It has been shown that platelet activation and inflammation-related processes may also play a role in decreased MPV levels during preterm labor. During pregnancy, many subjects, such as ectopic pregnancy, preeclampsia, and cholestasis have been studied. [14, 15] Yurtçu et al. found no statistically significant difference between 1st and 3rd trimester MPV values in a similar study with 1049 pregnant women.[16] This study does not coincide with the results of our study. MPV was found to be a reliable predictor of preterm delivery in a study by Ma et al.[17] The MPV cut-off value was determined to be 10 f/L. The difference between this study and ours is that the mean of all groups was 10 f/L. A statistically significant decrease in MPV levels was found in pregnant women with preterm delivery in the study of Aktün et al. with 270 pregnant women.[18] In our study, the decrease in MPV in the 1st and 3rd trimesters was statistically significant in pregnant women with preterm delivery, which is similar to the study by Aktün et al. (p<0.001).

Elevated NEU is used as a marker of acute infection and inflammation together with WBC.[19] NEU assessment was also performed in studies related to inflammation in which other hemogram parameters were evaluated in pregnancy.[14,15] In a study conducted by Tolunay et al. with 92 pregnant women, pregnant women between 24-34 weeks who were at risk in terms of preterm labor were evaluated. The results of this study revealed that the increase in NEU in pregnant women who gave birth within one week was found to be increased compared to pregnant women who gave birth after one week.[20] In a study conducted by Zhang et al. on 175 pregnant women, hemogram parameters of pregnant women who had preterm birth and healthy pregnant women were compared.[21] No statistically significant difference was found between the groups in terms of the NEU. In our study, the increase in NEU in the 1st and 3rd trimesters was found to be statistically significant in pregnant women with preterm delivery (p:0.001).

Existing studies have shown that the NLR is an inflammatory biochemical marker and that an increase in it is associated with poor obstetric outcomes.[22-24] Although an inverse correlation between increased NLR and preterm birth and low birth weight was detected in the study by Akgün et al., no statistically significant difference was found.[25] In a study conducted with 78 pregnant women, Yüce et al. divided the pregnant women at risk of preterm delivery into two groups those who gave birth within one week and those who did not. It was observed that NLR increased statistically significantly in the group of pregnant women who delivered within one week.[26] In our study, in terms of NLR results, 1st and 3rd trimester NLR increase was statistically significant in pregnant women with preterm labor (1st trimester p:0.001, 3rd trimester p:0.01).

Limitations

The retrospective design of our study is a limitation. CBC test which is a non-invasive test are strength for our study.

Conclusion

In our study we have found that 1st and 3rd trimester hemogram parametes as WBC, NEU, MPV and NLR varies among term and preterm birth and could be useful as pro-inflammatory markers. More

comprehensive studies in different populations are needed to apply the results of our study to clinical practice.

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