J Surg Med. 2021;5(5):508-511.
DOI: 10.28982/josam.918863



Journal of Surgery and Medicine
e-ISSN=2602-2079

# Evaluation of third-trimester neutrophil-lymphocyte and platelet-lymphocyte ratios and their correlation with birth weight

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**Ethics Committee Approval**
Permission for this study was granted by the Ethics Committee of Marmara University Faculty of Medicine (Decision number: 09.2021.99). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

**Conflict of Interest**
No conflict of interest was declared by the authors.

**Financial Disclosure**
The authors declared that this study has received no financial support.

**Published**
2021 May 15



## Abstract

**Background/Aim:** Fetal development is affected by the maternal environment and one of the environment determinants is inflammation. Neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) have been used as markers of inflammation in many disciplines. The aim of this study is to evaluate the relationship between the value of these easily accessible markers in the 3rd trimester and birth weight, which is the result of fetal development.

**Methods:** This retrospective cohort study comprised 442 pregnant women who delivered within the last 2 years and met the inclusion criteria. As a result of a percentile adjustment made according to the Alexander growth curves, pregnant women were grouped according to the birth weight of their neonates, as normal birth weight (AGA) and large birth weight (LGA). Statistical analyses were conducted using the birth weights and hemogram parameters between the groups.

**Results:** There was no significant difference in hemoglobin, neutrophil, platelet, NLR and PLR levels ($P>0.05$ for each) between the groups; however, a negative correlation was observed between lymphocyte and gestational weight ($P=0.014$). When comparing hemogram parameters between the groups, hemoglobin, neutrophil, platelet, NLR, and PLR counts were similar ($P>0.05$ for each). We observed that the lymphocyte counts were lower in the LGA group ($P=0.019$). There was no significant relationship between birth weight, and NLR and PLR counts during the third trimester ($P=0.100$, $P=0.997$, respectively).

**Conclusion:** NLR and PLR counts are used in many disciplines as indicators of inflammation and have been used to predict many perinatal complications during pregnancy. In the present study, no relationship was found between fetal weight and third trimester NLR and PLR counts.

**Keywords:** Neutrophil lymphocyte ratio, NLR, Platelet lymphocyte ratio, PLR, Birth weight

**How to cite:** Kırlangıç MM, Sade OS, Yalman MV, Akdemir E. Evaluation of third-trimester neutrophil-lymphocyte and platelet-lymphocyte ratios and their correlation with birth weight. J Surg Med. 2021;5(5):508-511.

## Introduction

The maternal environment during pregnancy affects fetal development. Although there is an increase in systemic inflammation during normal pregnancy, when there is abnormal maternal inflammation, blood flow to the uterus is impaired, and so is fetal development, secondary to the vascular dysfunction in the placenta [1]. The ratio of neutrophils to lymphocytes (NLR) and the ratio of platelets to lymphocytes (PLR) are used as inflammation markers and can be easily calculated using a simple blood test. These parameters, which show the inflammatory response, have been used under many conditions and for many complications.

There are several studies on NLR and PLR that have address gynecological diseases, such as ovarian hyperstimulation syndrome [2], premature ovarian failure [3], endometriosis [4], tubular ovarian abscess [5], adenomyosis and leiomyoma [6], and even gynecological cancers [7]. In addition, perinatal complications, such as hyperemesis gravidarum [8], gestational diabetes [9], intrahepatic cholestasis resulting from pregnancy [10], preeclampsia [11], and preterm labor [12] were also studied. NLR and PLR values are used not only in obstetric and gynecological practice but also in internal and surgical disciplines [13-16]. NLR increases in neutrophil count during acute inflammation and lymphopenia resulting from physiological stress. PLR indicates platelet activation, lymphocyte function, and immune response [17]. Previous studies have shown that using NLR and PLR to predict birth weight can help determine related neonatal morbidities [18]. The aim of the present study was to investigate the effect of inflammation markers, NLR and PLR, on fetal birth weight, which reflects fetal development.

## Materials and methods

This was a retrospective study that comprised 442 pregnant women who delivered at Tuzla Government Hospital, Turkey, between 01/01/2019 and 12/31/2020. Permission for this study was granted by the Ethics Committee of Marmara University Faculty of Medicine (Decision number: 09.2021.99). The study was conducted in accordance with the Declaration of Helsinki.

The inclusion criteria were as follows: 1) Pregnant women between the ages of 18 and 45 years, 2) singleton and noncomplicated term pregnancies, and 3) a hemogram value at routine follow-up during the third trimester before labor began. The exclusion criteria were as follows: 1) Preeclampsia, 2) hemolysis, elevated liver enzymes, low platelet count syndrome, 3) gestational diabetes, 4) cholestasis resulting from pregnancy, 5) chronic systemic disease, 6) hematologic disease, or 7) no hemogram value measured in the third trimester. In addition, immigrants were excluded from the study because of their different races that would have affected the study set and perinatal results. Gravida, parity, abortion, fetal sex, gestational week, delivery type, and birth weights were recorded. The Sysmex XN-1000 (Sysmex Corporation, Kobe, Japan) was used for hemogram analyses. The hemogram parameters were hemoglobin (g/dL), neutrophil (*10³/µL), lymphocyte (*10³/µL), and platelet counts (*10³/µL). The pregnant women were classified according to their birthweights of their neonates using Alexander growth curves, as large for gestational age (LGA) (>90$^{th}$ percentile), and appropriate for gestational age (AGA) (10$^{th}$-89$^{th}$ percentiles) [19].

**Statistical analysis**

Statistical analyses were conducted using SPSS v 22.0 (IBM Corp., Armonk, NY, USA) and Microsoft Excel 2019 (https://www.microsoft.com/en-us/). Categorical variables, such as birth weight, gravida, parity, number of abortions and survivors, gestational week, mode of delivery, and sex, were expressed as numbers and percentages. The Shapiro–Wilk test was used to analyze normally distributed data, including age, fetal weight and neutrophil, lymphocyte, platelet, hemoglobin, NLR, and PLR counts. Descriptive data for these variables are expressed as mean, standard deviation, median, and interquartile range. The nonparametric Kruskal–Wallis test was used to analyze statistical differences among NLR, PLR, hemoglobin, platelet, neutrophil, and lymphocyte counts in terms of birth weight. The Mann–Whitney U test was used to evaluate the statistical differences of NLR, PLR hemoglobin, thrombocyte, neutrophil, and lymphocyte counts between AGA and LGA according to their grouped percentiles. Box-plot graphs were drawn for variables showing statistical significance. *P*-value <0.05 was considered statistically significant.

## Results

The present study evaluated 442 pregnant women with an average age of 29.50 (5.17) years. The average birth week at delivery was 38.67 (0.77), of which 65 (14.7%) were normal vaginal deliveries, and 377 (85.3%) were cesarean deliveries. Of the newborns, 198 (44.8%) were female and 244 (55.2%) were male. The demographic characteristics of the pregnant women are presented in Table 1.

The mean hemoglobin count was 11.40 (1.22) g/dL, mean neutrophil count was 6.58 (1.38) x10$^3$/µL, mean lymphocyte count was 1.95 (0.47) x10$^3$/µL, and the mean platelet count was 237.57 (69.44) x10$^3$/µL. The mean NLR was 3.50 (0.93), and the mean PLR was 126.63 (42.70) (Table 2).

Table 1: Demographic characteristics of the pregnant women

| | | Mean (SD) | Min–Max |
|---|---|---|---|
| Age | | 29.50 (5.17) | 18–43 |
| Gravidity | | 2.69 (1.25) | 1–11 |
| Parity | | 1.38 (0.81) | 0–4 |
| Abortions | | 0.32 (0.85) | 0–7 |
| Live births | | 1.36 (0.78) | 0–4 |
| Birth week | | 38.67 (0.77) | 37–42 |
| Birth weight (g) | | 3407.98 (397.31) | 2550–4650 |
| Sex (n (%)) | Female | 198 (44.8) | |
| | Male | 244 (55.2) | |
| Type of birth (n (%)) | Normal vaginal delivery | 65 (14.7) | |
| | Cesarean section | 377 (85.3) | |
| Percentile (n (%)) | AGA | 381 (86.2) | |
| | LGA | 61 (13.8) | |

SD: Standard Deviation, AGA: appropriate for gestational age, LGA: large for gestational age

Table 2: Hemogram parameters of the pregnant women

| Parameter | Mean (SD) | Min–Max |
|---|---|---|
| Hemoglobin (g/dL) | 11.40 (1.22) | 7.60–14.40 |
| Neutrophils (*10³/µL) | 6.58 (1.38) | 3.10–10.10 |
| Lymphocytes (*10³/µL) | 1.95 (0.47) | 1.00–4.40 |
| Platelets (*10³/µL) | 237.57 (69.44) | 92–608 |
| NLR | 3.50 (0.93) | 1.15–7.27 |
| PLR | 126.63 (42.70) | 36.80–345.71 |

SD: Standard Deviation, NLR: neutrophil/lymphocyte ratio, PLR: platelet lymphocyte ratio

The result of the parameter measurements did not provide a definite conclusion on a correlation between hemoglobin, neutrophil, platelet, NLR, and PLR (*P*=0.524,

*P*=0.970, *P*=0.063, *P*=0.100, *P*=0.997, respectively) and birth weight; however, a negative correlation was observed between lymphocyte count and gestational weight (*P*=0.014) (Table 3).

After adjusting the percentile according to the Alexander growth curves, the babies of 381 (86.2%) pregnant women were grouped as AGA and those of 61 (13.8%), as LGA. The distribution of demographic characteristics and hemogram parameters in the two groups is given in Table 3. When comparing hemogram parameters between the groups, the hemoglobin, neutrophil, platelet, NLR, and PLR values were similar (*P*=0.849, *P*=0.350, *P*=0.053, *P*=0.238; and *P*=0.959 respectively). We also observed that the lymphocyte values were lower in the LGA group (*P*=0.019) (Table 4).

Table 3: Correlation between hemogram parameters and birth weight

| Parameter | Weight | |
|---|---|---|
| | R | *P*-value |
| Hemoglobin (g/dL) | -0.030 | 0.524 |
| Neutrophils (*10³/µL) | 0.002 | 0.970 |
| Lymphocytes (*10³/µL) | -0.117 | 0.014 |
| Platelets (*10³/µL) | -0.088 | 0.063 |
| NLR | 0.078 | 0.100 |
| PLR | 0.000 | 0.997 |

NLR: neutrophil/lymphocyte ratio, PLR: platelet lymphocyte ratio

Table 4: Comparison of groups according to birth weight

| Parameter | AGA | LGA | Z | *P*-value |
|---|---|---|---|---|
| Age | 29.25 (5.19) | 31.07 (4.80) | -2.524 | 0.120 |
| Hemoglobin (g/dL) | 11.40 (1.21) | 11.43 (1.26) | 0.000 | 1.000 |
| Neutrophils (*10³/µL) | 6.60 (1.39) | 6.43 (1.32) | -0.714 | 0.475 |
| Lymphocytes (*10³/µL) | 1.97 (0.48) | 1.82 (0.37) | -2.616 | 0.009 |
| Platelets (*10³/µL) | 240.13 (71.09) | 221.59 (55.91) | -1.740 | 0.082 |
| NLR | 3.48 (0.92) | 3.63 (0.95) | -1.124 | 0.261 |
| PLR | 126.67 (42.85) | 126.36 (42.13) | -0.046 | 0.963 |

AGA: appropriate for gestational age, LGA: large for gestational age, NLR: neutrophil/lymphocyte ratio, PLR: platelet lymphocyte ratio

## Discussion

Fetal growth can be affected by many factors, such as race, the environment, vitamins used during pregnancy, nutrition, maternal age and weight, and inflammation. The purpose of the present study was to investigate the effect of inflammation markers NLR and PLR on fetal weight, which is a result of fetal development.

Several studies have shown that NLR and PLR can be used as markers of inflammation in cardiology [13], surgery [14], gastroenterology [15], and oncology [16]. These inflammation markers are also beginning to be used for obstetrics and gynecological conditions [2, 7-11, 20, 21]. In several previous studies on pregnancy and inflammation, maternal serum C-reactive protein (CRP) was used to characterize fetal exposure to inflammation [1, 22, 23]. In recent studies, NLR and PLR, which are new parameters that can be measured using a simple blood test, have begun to be used as indicators of inflammation. In a study comparing NLR and CRP in pregnancy, İlhan et al. [20] have found that NLR has a better diagnostic value than maternal serum CRP in cases of acute pancreatitis associated with pregnancy. Another study found that high NLR and normal CRP used to show the placental inflammatory response indicate that preterm delivery is approaching [24]. These studies emphasize that NLR can help to diagnose pregnancy difficulties.

No relationship was observed between birth weight and NLR and PLR counts in the third trimester. However, the lymphocyte count was lower in the group with LGA. Christoforaki et al. [25] have compared first trimester NLR and PLR rates with pregnancy outcomes and found no relationship between those parameters and birth weights; however, Akgün et al. [26] have found a negative correlation between PLR and birth weight. They reported that NLR was not related with birth weight. Several studies have investigated the use of NLR and PLR for predicting perinatal complications; however, results have been inconsistent when comparing complications with NLR and PLR. Although Yücel et al. [27] could not find NLR to be a predictor for pregnancy-related hypertension, Serin et al. [11] have shown that NLR increases significantly in patients with preeclampsia. Similarly, contradictory results have been reported from studies testing NLR and PLR in pregnant women with gestational diabetes. Although Sargin et al. [9] have reported that NLR and PLR significantly increase in gestational diabetes, Aktulay et al. [28] have reported no evidence of NLR and PLR being predictors of gestational diabetes in their retrospective study. In a study that included nonpregnant volunteers during their reproductive period, the mean NLR and PLR values were 1.73 (1.55) and 133.7 (85.6), respectively [29]. Kırbas et al. [10] have found in their trimester-based NLR and PLR study that the mean NLR and PLR values were 2.6 (1.0) and 136.3 (44.3) during the first trimester, 4.0 (1.4) and 144.6 (47.1) during the second trimester, and 3.5 (1.2) and 118.1 (42) during the third trimester, respectively.

### Limitations

There were some limitations to the present study. First, not all factors that may affect birth weight, such as vitamins, nutrition, maternal body weight, smoking, alcohol and substance use, and environmental conditions, were evaluated. Second, because the number of normal vaginal deliveries was high among those who were not followed up in the clinic but only applied for birth, the number of births with cesarean sections appeared to be high among the delivery types. Additional larger studies are needed that can assess the correlation between NLR, PLR and birth weight. It would be more appropriate to establish a relationship between hemogram values and birth weight by comparing baseline values at the beginning of the pregnancy with the those obtained at the end of the third trimester.

### Conclusion

In the present study, we investigated the relationship between NLR and PLR, which were used as inflammation markers during the third trimester of pregnancy, and birth weight in uncomplicated pregnant women. We found no relationship between NLR and PLR measured only in the third trimester and birth weight.

We noted from previous studies that NLR and PLR do not stably progress from pre-pregnancy to pregnancy because of the effect that pregnancy has on physiology. These values can predict pregnancy complications in some cases in which reference intervals are constantly changing and not in others. Because pregnancy is a dynamic process, hemogram parameters differ on a trimester basis.

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