



# Hematological Parameters in Measles

## Kızamıkta Hematolojik Parametreler

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### Abstract

**Objective:** This study aimed to investigate the WBC, MCV, MPV, PLT, CRP, Neutrophil-lymphocyte ratio, platelet-lymphocyte, and PLR values of the patients with measles and compare them with the healthy control group to see if these parameters are suitable to determine the inflammatory disease in measles patients.

**Material and Methods:** Eighty patients with measles who had applied to our pediatrics clinic between January 2019 and December 2019 as the case group and 80 healthy children who applied to our clinic for any reason as the control group were included in our study. SPSS version 26.0 was applied. Normal distribution of the data was demonstrated with the Kolmogorov-Smirnov test. Mann-Whitney U test and Independent student t-test were used to evaluate the differences between two groups related to demographical and clinical variables. Spearman correlation test was applied to assess the correlation between NLR and PLR and the outcome. Multivariate logistic regression analysis was performed for the independent variables after the univariate logistic regression.

**Results:** WBC in the case group was significantly lower than that in the control group ( $p=0.035$ ). Besides, the values of neutrophil ( $p<0.001$ ), hemoglobin ( $p<0.001$ ), hematocrit ( $p<0.001$ ), MCV ( $p<0.001$ ), MPV ( $p=0.001$ ), NLR ( $p<0.001$ ) and PLR ( $p=0.011$ ) were significantly lower in the case group than those in the control group while the values of lymphocyte ( $p=0.001$ ), and CRP ( $p<0.001$ ) were higher in the case group. NLR showed a significant correlation with outcome ( $r=0.382$ ,  $p<0.001$ ). Besides, PLR was significantly correlated with outcome ( $r=0.201$ ,  $p=0.011$ ). PLR was associated with the outcome (OR, 0.961; CI, 0.924-1.000;  $p=0.049$ ) whilst NLR was not significantly associated with outcome (OR, 2.241; CI, 0.623-8.058;  $p=0.217$ ).

**Conclusion:** It is concluded that WBC can be used as a suitable parameter for evaluating inflammation, and neutrophil, hemoglobin, hematocrit, MCV, MPV, NLR, and PLR can be used to predict measles. NLR is a poor predictor of measles while PLR is a suitable predictor of patient outcome in measles.

**Keywords:** Measles, neutrophil-lymphocyte ratio, platelet-lymphocyte, C-reactive protein

### Öz

**Giriş:** Bu çalışmanın amacı, kızamıklı hastalarda WBC, MCV, MPV, PLT, CRP, Nötrofil-lenfosit oranı, trombosit-lenfosit, ve PLR değerlerini incelemek ve bu değerleri sağlıklı kontrol grubuyla karşılaştırıp, bu parametrelerin kızamık hastalarında inflamatuvar hastalığı belirlemeye uygun olup olmadığını görmektir.

**Gereç ve Yöntemler:** Pediatri kliniğimize Ocak 2019 ve Aralık 2019 tarihleri arasında başvuran 80 kızamıklı çocuk hasta grubuna ve herhangi bir nedene bağlı olarak kliniğimize başvuran 80 sağlıklı çocuk da kontrol grubuna dahil edildi. SPSS versiyon 26.0 uygulandı. Verilerin normal dağılımı Kolmogorov-Smirnov testi ile gösterildi. Demografik ve klinik değişkenlerle ilgili iki grup arasındaki farklılıkları değerlendirmek için Mann-Whitney U testi ve Bağımsız student t-testi kullanıldı. NLR ve PLR ile sonuç arasındaki korelasyonu değerlendirmek için Spearman korelasyon testi uygulandı. Tek değişkenli lojistik regresyondan sonra bağımsız değişkenler için çok değişkenli lojistik regresyon analizi yapıldı.

**Bulgular:** WBC, hasta grubunda kontrol grubuna göre anlamlı derecede düşük bulundu ( $p=0.035$ ). Ayrıca, hasta grubunda nötrofil ( $p<0.001$ ), hemoglobin ( $p<0.001$ ), hematokrit ( $p<0.001$ ), MCV ( $p<0.001$ ), MPV ( $p=0.001$ ), NLR ( $p<0.001$ ) ve PLR ( $p=0.011$ ) değerleri kontrol grubuna göre anlamlı derecede düşüken, ( $p=0.001$ ) ve CRP ( $p<0.001$ ) yüksekti. NLR ile sonuç arasında anlamlı bir korelasyon bulundu ( $r=0.382$ ,  $p<0.001$ ). Ayrıca, NLR ile sonuç arasında anlamlı bir korelasyon bulundu ( $r=0.201$ ,  $p=0.011$ ). PLR sonuçla ilişkili (OR, 0.961; CI, 0.924-1.000;  $p=0.049$ ) bulunurken, NLR ve sonuç arasındaki ilişki anlamlı değildi (OR, 2.241; CI, 0.623-8.058;  $p=0.217$ ).

**Sonuç:** WBC'nin inflamasyon değerlendirmesinde uygun bir parametre olarak kullanılabileceği ve kızamık hastalığını öngörmek için nötrofil, hemoglobin, hematokrit, MCV, MPV, NLR ve PLR'nin kullanılabileceği sonucuna varılmıştır. NLR kızamık için zayıf bir prediktör parametreyken, PLR kızamıkta hasta akıbetini öngörmede uygun bir prediktör parametredir.

**Anahtar Kelimeler:** Kızamık, nötrofil-lenfosit oranı, trombosit-lenfosit, C-reaktif protein

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## Introduction

Measles is defined as a respiratory tract infection, which mainly damages the surface mucosal lining cells (1). It is a contagious, acute, feverish exanthematous infection that occurs after a 3 to 4-month course of the winter-spring outbreak and which may occur every 2 to 5 years (2).

Using the live attenuated vaccines significantly reduces the epidemiology and incidence of the disease (3). Measles virus infection makes the patients with measles susceptible to secondary infection due to the profound immunosuppression, resulting in high mortality and morbidity. The main causes of such immunosuppression are severe monocytopenia and lymphopenia (4). Measles affects most of the children and is transmitted through small drops from the nose, mouth, or throat of the infected persons while sneezing, coughing, or due to direct contact with the secretions of the infected nose or throat. The virus will be transmitted or becomes active in the air or on the infected surfaces for about two hours. It can be transmitted 4 days before the rash starts to 4 days after the eruption of the rash (5).

Measles is a disease that has high chance for recovery in uncomplicated cases, but it has a high mortality rate in patients with complications. There are mortality rates of 3-5% above in the developing world, and such rates remain high for several reasons in developing countries, such as the frequent occurrence of measles under age of one year in these regions and unfavorable environmental conditions, leading to the secondary bacterial infections (6).

Symptoms of measles virus infection are cough, conjunctivitis, high fever, coryza, and development of skin eruptions (7).

Some studies have shown that a better predictor of inflammation under certain medical conditions is the platelet-to-lymphocyte ratio in cardiovascular diseases, autoimmune diseases, and chronic renal failure (8,9). Serum inflammatory markers based on the NLR, differential WBC count, and PLR can better predict mortality and patient outcome under different medical conditions and also predict cardiovascular risk better than con-

ventional infection markers including the total leucocyte count or C-reactive protein (CRP) (10,11).

Therefore, it is important to evaluate the inflammatory parameters such as WBC, MCV, MPV, PLT, NLR (Neutrophil-lymphocyte ratio), CRP (C-reactive protein), PLR, and platelet-lymphocyte in patients with measles. This study aimed to investigate the WBC, MCV, MPV, PLT, CRP, Neutrophil-lymphocyte ratio, platelet-lymphocyte, and PLR values of the patients with measles and compare them with the healthy control group to see if these parameters are suitable for determining the inflammatory disease in measles patients. To this end, the differences between the two groups related to demographical and clinical variables were evaluated. The correlation between PLR and NLR and outcome was assessed, and the relationship between PLR and NLR and the outcome was analyzed.

## Materials and Methods

For statistical analyses, Statistical Package for Social Sciences (SPSS) version 26.0 was applied (SPSS Inc., Chicago, IL, USA). Normal distribution of the data was demonstrated using the Kolmogorov-Smirnov test. Differences between the two groups related to demographical and clinical variables were evaluated using Mann-Whitney U test and Independent student t-test. Additionally, to assess the correlation between PLR and NLR and the outcome, Spearman correlation test was applied. Multivariate logistic regression analysis was performed for independent variables ( $p < 0.2$ ) following the univariate logistic regression to analyze the relationship between NLR and PLR and the outcome. Normally distributed data are expressed as mean (SD) and non-normally distributed data are expressed as median (interquartile range). Also, categorical variables were expressed as n (%).  $P < 0.05$  was considered statistically significant in this study.

When the sample size was calculated with the GPower 3.1 (<http://www.gpower.hhu.de/>) program, the total mean of the two groups compared based on the t-test measure with the effect size of 22%, power of 80% and 0.05 type 1 error, was found to be at least 157 patients.

**Table 1.** Baseline characteristics of the patients

Variable	Case (n= 80)	Control (n= 80)	p
Age, months	9 (6)	10 (15.8)	0.117*
Weight, kg	8 (3)	8.55 (3.9)	0.079*
Height, cm	70 (8.75)	71.50 (17.88)	0.115*
BMI, kg/m <sup>2</sup>	16.49 (1.77)	16.68 (1.15)	0.413**
Sex, male (%)	50 (62.50)	45 (56.25)	0.421***

Non-parametric data are expressed as median (interquartile range); data with normal distribution are expressed as mean (SD); categorical data are expressed as n (%); BMI indicates body mass index.

\*Mann-Whitney U test

\*\*Independent student t-test.

\*\*\*Chi-square test.

## Results

### Baseline Characteristics

Eighty patients with measles and 80 healthy subjects participated in the study. Sixty-two point fifty percent of the patients with measles was male and 56.25% of the case group was male. The median age of the patients in the case group was 9 (6) months and the median age of the control group was 10 (15.8) months, but the difference between the two groups was not significant ( $p= 0.117$ ). Besides, the differences between the two groups in terms of weight ( $p= 0.079$ ), BMI ( $p= 0.413$ ) and height ( $p= 0.115$ ) were not significant. Table 1 shows the summary of the baseline characteristics of the two groups.

### Laboratory Characteristics

Clinical variables of the two groups are shown in the Table 2. WBC in the case group was significantly lower than that in the control group ( $p= 0.035$ ). Besides, the case group had the significantly lower values of neutrophil ( $p< 0.001$ ), hemoglobin ( $p< 0.001$ ), hematocrit ( $p< 0.001$ ), MCV ( $p< 0.001$ ), MPV ( $p= 0.001$ ), NLR ( $p< 0.001$ ) and PLR ( $p= 0.011$ ) than the control group had while the values of lymphocyte ( $p= 0.001$ ), and CRP ( $p< 0.001$ ) were higher in the case group. Finally, no significant difference was found between two groups in PLT ( $p= 0.104$ ).

### Spearman Correlation Test

According to the results, NLR showed a significant correlation with outcome ( $r= 0.382$ ,  $p< 0.001$ ). Besides, PLR was significantly correlated with outcome ( $r= 0.201$ ,  $p= 0.011$ ). The results of the Spearman correlation test between NLR and PLR with the outcome were summarized in Table 3.

### Logistic Regression Analysis

All independent variables were included in the logistic regression analysis for the prediction of outcome. After univariate analysis, variables with a  $p< 0.2$  were included in the multivariate logistic regression analysis. Univariate analysis demonstrated that NLR (OR, 1.372; CI, 1.133-1.662;  $p= 0.001$ ) and PLR (OR, 1.005; CI, 1.001-1.009;  $p= 0.023$ ) were independently associated with the outcome. Multivariate logistic regression analysis adjusted for weight, age, height, sex, neutrophil, lymphocyte, hemoglobin, hematocrit, MCV, MPV, PLT and CRP demonstrated that PLR is associated with the outcome (OR, 0.961; CI, 0.924-1.000;  $p= 0.049$ ), whilst NLR was not significantly associated with outcome (OR, 2.241; CI, 0.623-8.058;  $p= 0.217$ ).

Data are expressed as median (interquartile range); WBC indicates white blood cells; MPV is mean platelet volume; PLT, platelets; MCV is mean corpuscular volume; NLR, Neutrophil-I-

**Table 2.** Clinical variables of case and control groups

Variable	Case (n= 80)	Control (n= 80)	p
WBC, unit	8.41 (5.05)	9.53 (2.28)	0.035
Neutrophil, unit	3.39 (3.42)	4.81 (3.82)	< 0.001
Lymphocyte, unit	3.45 (3.23)	2.61 (1.74)	0.001
Hemoglobin, unit	11.17 (1.10)	12.85 (1.58)	< 0.001
Hematocrit, unit	34.48 (4.89)	38.80 (5.94)	< 0.001
MCV, unit	74.59 (9)	79.01 (8.72)	< 0.001
MPV, unit	6.34 (1.55)	7.23 (1.96)	0.001
PLT, unit	335.10 (165.3)	306.60 (92.4)	0.104
CRP, unit	0.41 (1.14)	0.03 (0.16)	< 0.001
NLR, unit	0.95 (1.25)	1.66 (3.28)	< 0.001
PLR, unit	92.01 (83.31)	118.79 (85.72)	0.011

Data are expressed as median (interquartile range); WBC indicates white blood cells; MPV is mean platelet volume; PLT, platelets; MCV is mean corpuscular volume; NLR, Neutrophil-lymphocyte ratio; CRP is C-reactive protein; PLR is platelet-lymphocyte.

**Table 3.** Correlation test between NLR and PLR with the outcome

	Outcome
NLR	$r= 0.382^{**}$ $p< 0.001$
PLR	$r= 0.201^{*}$ $p= 0.011$

\*Correlation is significant at the 0.01 level.

\*\*Correlation is significant at the 0.05 level.

lymphocyte ratio; CRP is C-reactive protein; PLR is platelet-lymphocyte.

## Discussion

160 subjects (80 measles patients and 80 healthy subjects) were included into the study. The median age of the case group was 9 (6) months and the median age of the control group was 10 (15.8) months, indicating no significant difference between the two case and control groups. The two groups showed no significant difference in BMI, weight, and height. The results showed that WBC in the case group was significantly lower than that in the control group and the case group had significantly lower neutrophil, hemoglobin, hematocrit, MCV, MPV, NLR and PLR than the control group had while the case group had higher lymphocyte, and CRP. PLT showed no significant difference between the two groups. A significant correlation was found between NLR and the outcome and a significant correlation was between PLR and the outcome. PLR was associated with the outcome while NLR had no significant association with the outcome. In other words, NLR is a poor predictor of measles while PLR is a suitable predictor of outcome in measles.

The mechanisms of lymphopenia in measles have been studied extensively. Apoptosis of the uninfected lymphocytes which causes lymphopenia has been found in measles (4). Neutrophils produced in the bone marrow stimulated by several cytokines are also effective in the protection of the body against bacterial infection (12).

A study by Kim (13) has shown that the measles patients had lower leukocyte, neutrophil, and the lymphocyte counts than the healthy group had while our study found that the case group had significantly lower neutrophil than the control group had and higher lymphocyte was found in the case group.

White blood cells (WBCs), as the inflammation main cells, are effective pathogenesis of several diseases. Increasing neutrophil counts at the time of the acute inflammation as well as reducing the lymphocyte counts due to acute stress will cause change in the immune system. Leukocytosis or increase in white blood cells indicates inflammation or infection (14). The Neutrophil-lymphocyte ratio (NLR) as a cost-effective, simple, and highly accurate parameter has been used recently as a critical prognostic factor of inflammatory diseases generally and particularly in several types of cancer and cardiovascular system diseases (15,16).

A study by Choi (17) has found no statistical differences between the 20-49 mg/L Group or 6-19 mg/L group and negative groups in terms of white blood cell count while the 50 mg/L group showed a higher mean level of WBC count and there was the relationship between CRP level and WBC count while our study showed that the case group had significantly lower WBC than the control group had.

NLR has been recently used as one of the new markers used to measure an inflammatory condition. NLR is used to evaluate the systemic inflammatory response to several diseases such as local and systemic infections, diabetes mellitus, metabolic syndrome, cancer, and cardiovascular diseases (18,19).

Solmaz (20) has found that PLR and NLR values were confirmed to be higher in patients with measles than those in the control group but the difference was not statistically significant while the present study showed significantly lower NLR and PLR in the case group than that in the control group.

According to Güzelsoy (21), the patient group had significantly lower PLR values and higher lymphocyte, suggesting that PLR value can indicate subclinical inflammation among the children with cervical LAP.

Several studies in the literature have shown that mean platelet volume (MPV) is one of the parameters used to evaluate the platelet size and assess both response to treatment and systemic inflammatory activity (22-25). A study found that the platelet count was high and MPV was measured to be low during the inflammation and infection active period, indicating that they were suggested as reliable markers (25).

Solmaz (20) has also found lower MPV values of measles patients than those of the control group, and showed that the two groups had statistically significant difference, which is consistent with our study results which found that MPV was significantly lower in the case group than that in the control group.

Griffin (26) has found the start of the rash in measles patients increases serum C-reactive protein (CRP) levels, of whose elevations become longer in measles and are complicated by pneumonia, showing a secondary elevation of measles which are complicated by encephalitis, which supports our finding that CRP increased in the case group.

## Conclusion

It is concluded that the case group had significantly lower WBC than the control group and shown that WBC can be used as a suitable parameter for evaluating inflammation. The case group had significantly lower neutrophil, hemoglobin, hematocrit, MCV, MPV, NLR and PLR than the control group had, indicating that neutrophil, hemoglobin, hematocrit, MCV, MPV, NLR, and PLR can be used to predict measles. PLR was associated with the outcome while NLR was not significantly associated with the outcome. In other words, NLR is a poor predictor of measles while PLR is a suitable predictor of outcome in measles.

**Ethics Committee Approval:** Ethical approval for this study was obtained from Harran University Ethics Committee (Decision no: HRÜ/19.06.23, Date: 13.06.2019).

**Informed Consent:** Patient consent was obtained.

**Peer-review:** Externally peer-reviewed.

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