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RESEARCH ARTICLE

Changes in Hemoglobin, Mean Thrombocid Volume and Neutrophil-Lymphocyte Ratio in Covıd-19 Infection

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Abstract
Objective: It is aimed to evaluate the changes in blood and inflammatory markers (Mean Platelet Volume and Neutrophil Lymphocyte Ratio) in COVID-19.
Method: We studied a total of 213 patients. 142 of them consist of patients who have undergone PCR test due to COVID-19 complaints and have a definite diagnosis. The blood values of 71 healthy people of similar age and characteristics without any complaints or symptoms were retrospectively compared.
Results: The mean age of the COVID-19(+) group was 54.62±17.71 years, while the COVID-19(-) group was 50.54±15.74 years. 52.8% (n:75) of the patient group and 54.9% (n:39) of the COVID-19(-) group were women. There was a decrease in the number of platelets especially in the PCR(+) group, but statistically no significant difference was observed between the PCR(+) group and the COVID-19(-) group for hemoglobin and platelet values ($p>0.05$). However, a significant difference ($p<0.01$) was found in Mean Platelet Volume, neutrophil, lymphocyte and Neutrophil Lymphocyte Ratio.
Conclusion: Due to the cytokine storm that develops in COVID-19 infection, a number of changes occur in the blood, especially a decrease in thrombocyte counts. We think that especially the changes in Mean Platelet Volume and Neutrophil Lymphocyte Ratio, which are new inflammatory markers, can be used in the follow-up of this disease and its prognosis.

Keywords: COVID-19, hemoglobin, platelet, neutrophil, lymphocyte

COVID-19'da Hemoglobin, Ortalama Trombosit Hacimleri ve Nötrofil Lenfosit Oranındaki Değişiklikler

Öz
Amaç: Dünya genelinde büyük bir salgın yapan COVID-19 hastalığında, kanda ve inflamatuvar belirteçlerde (Ortalama Trombosit Hacmi ve Nötrofil Lenfosit Oranı) meydana gelen değişimleri değerlendirmek amaçlanmıştır.
Yöntem: Çalışma, toplam 213 kişi ile yapılmıştır. Bunların 142 kişisi COVID-19 şikâyetleri nedeniyle Real Time Polimeraz Zincir Reaksiyonu (PCR) testi yapılmış ve kesin tanısı konmuş hastalardan oluşmaktadır. Benzer yaş ve özellikte hiçbir şikayet ve semptomu olmayan 71 adet sağlıklı insanın kan değerleri ile retrospektif olarak karşılaştırılmıştır.

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Bulgular: COVID-19 pozitif grubun yaş ortalaması 54.62±17.71 yıl iken kontrol grubunun 50.54±15.74 yıl idi. Hasta grubunun %52,8'si (n:75) kontrol grubunun ise %54,9'u (n:39) kadınlardan oluşmaktaydı. Özellikle PCR pozitif grupta platelet sayılarında düşüş saptanmıştır ama istatiksel açıdan PCR pozitif grup ile kontrol grubu arasında hemoglobin ve platelet değerleri için anlamlı bir farklılık gözlenmemiştir ($p>0,05$). Ama Ortalama Trombosit Hacmi, nötrofil, lenfosit ve nötrofil lenfosit oranlarında anlamlı farklılık ($p<0,01$) saptanmıştır.
Sonuç: COVID-19 enfeksiyonunda gelişen sitokin fırtınası nedeniyle kanda trombosit sayılarında azalma başta olmak üzere bir dizi değişiklikler meydana gelmektedir. Özellikle yeni inflamatuvar markerlerdan olan Ortalama Trombosit Hacmi ve Nötrofil Lenfosit Oranında meydana gelen değişiklikler bu hastalığın ve prognozunun takibinde kullanılabileceğini düşünmekteyiz.

Anahtar kelimeler: COVID-19, hemoglobin, trombosit, nötrofil, lenfosit

INTRODUCTION

One of the biggest epidemics throughout the history of the world is undoubtedly the COVID-19 disease caused by the SARS-2 virus (1). Since December 2019, it's influence has been increasing and it's threatening all the people and economies of the world (2). Due to the new mutations, its treatment became more difficult and effectiveness of vaccines are discussed (3). Currently, MPV and Neutrophil/Lymphocyte (NLR) ratios are considered as new inflammatory markers and it has been observed to increase with most diseases (4,5). For example MPV value increases at; coronary heart disease, obesity, vitamin deficiencies, inflammatory diseases and even in cases of malignancy (6-10). It has been shown in some studies that MPV and NLR rates increase in COVID-19 infection (11). In this study, it was aimed to investigate the changes in hemogram and some inflammatory markers in patients diagnosed with COVID-19 by PCR (Real Time Polymerase Chain Reaction) test in Kütahya.

METHOD

This retrospective descriptive study was conducted in a family health center in Kütahya. All COVID-19 patients registered to this family health center between 01 July and 31 August 2021 were included in the study. Medical records and electronic patient tracking system of 142 patients who were suspected due to symptoms that could be seen in COVID-19 and diagnosed by PCR were retrospectively examined and analysed. Individuals with no symptoms or complaints of COVID-19 and PCR(-) were considered COVID-19(-). COVID-19(-) individuals were determined by a simple random method. Those selected for the COVID-19(-) group were selected in terms of age and gender and were similar to the COVID-19(+) group. Seventy-one healthy individuals similar in age and gender without any complaints or symptoms related to COVID-19 were taken as a COVID-19(-) group and their blood values

were analysed and compared. In order not to affect MPV and NLR values, hemoglobin values under normal limits in both groups were excluded from the study. In the COVID-19(-) group, those who had signs of active infection (such as CRP, WBC) and those who used drugs that could affect thrombocytes were also excluded from the study. Hemogram was evaluated with Horiba ABX Pentra DF 120 device. Normal hemogram value is platelet 130 - 400 10^3/uL, hemoglobin 11 - 16 g/dL, lymphocyte 0.9 - 5.2 10^3/uL, neutrophil 0.9 - 6.0 10^3/uL, Mean Platelet Volume 7.2 - 11.8 fL. Our results were categorized as low, normal and high according to these values. RT-PCR (PCR) (Real Time Polymerase Chain Reaction) was evaluated using Bio Rad CFX96 Real Time PCR machine.

The approval of the local ethics committee dated 8.01.2022 and numbered 2022/01-01 and the permission of the provincial health directorate were obtained.

The data were recorded in the SSPS 18.0 package program and statistical analysis was performed. Numerical variables were represented as mean±standard deviation (SD) and categorical variables as number (n) and percentage (%). Pearson's Chi-square test were used to compare categorical variables of the COVID-19(+) and COVID-19(-) groups. The normal distribution was examined with the Kolmogorov-Smirnov test and the kurtosis and skewness values of the data groups. The Independent Sample T-Test was used to compare the numerical data between groups. $p < 0.05$ was considered statistically significant.

RESULTS

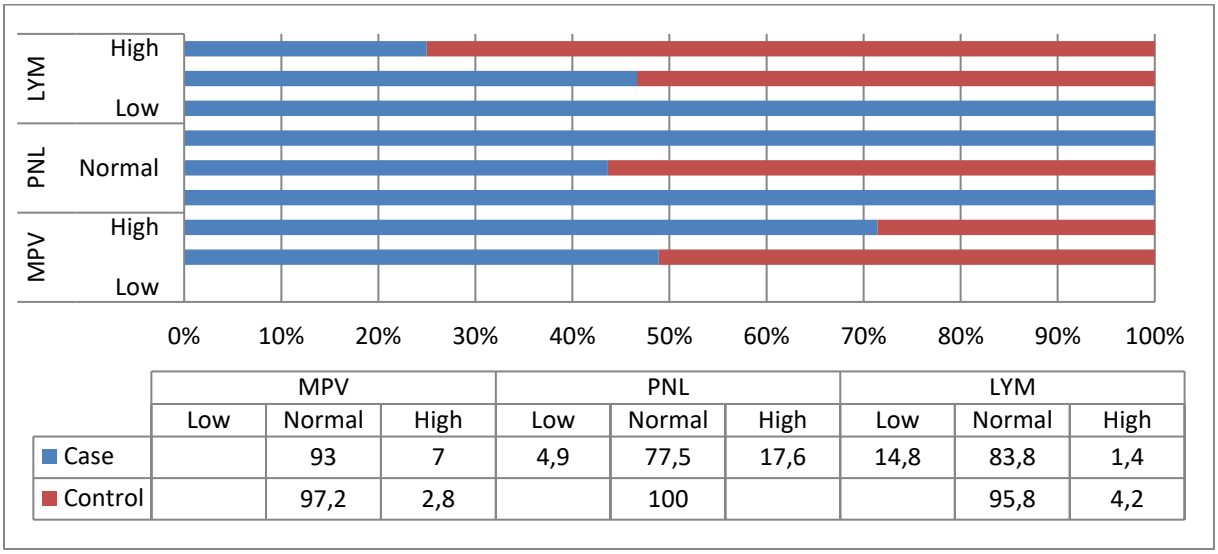
The mean age of the PCR positive COVID-19 patient group was 54.62±17.71 years and 47.2% (n:67) were female and 52.8% (n:75) were male. The mean age of the COVID-19(-) group was 50.54±15.74 years and 54.9% (n:39) were female and 45.1% (n:32) were male. COVID-19(+) and COVID-19(-) groups are similar in terms of age and gender ($p>0.05$). The distributions by sex and age groups are shown in the table (Table 1).

The mean blood values of PCR positive patients, respectively; mean hemoglobin (Hgb) was 13.49±17.71, platelet (Plt) 231.23±2.0, MPV 9.62±0.96, neutrophil 5.09±3.21, lymphocyte 1.65±1.12.; mean blood values of the COVID-19(-) group were Hgb 13.71±1.53, Plt 245.88±58.68, MPV 8.92±0.87, neutrophil (PNL) 3.77±1.12, lymphocyte 2.44±0.72. When the NLR rates were examined, it was found that the average in the group with PCR positive COVİD 19 patients was 4.63±7.67, and the COVID-19(-) group was 1.66±0.64 (Figure 1). In our study, it was observed that there was no statistically significant

difference in hemoglobin and plt values between the COVID-19(+) and COVID-19(-) groups (p> 0.05). When neutrophil, lymphocyte, MPV and NLR values were compared, a statistically significant difference was found between the COVID-19(+) and COVID-19(-) groups (p<0.001) (Table 2).

Table 1: Sex and age distributions of the COVID-19(+) group and the COVID-19(-) group

	COVID-19(+) n (%)	COVID-19(-) n (%)	Total n (%)	Values x^2	p
Sex					
Male	67(47.2)	32(45.1)	99(46.5)	0.084	0.770
Female	75(52.8)	39(54.9)	114(53.5)		
Age distribution					
18-44	46(32.4)	28(39.4)	74(34.7)		
45-64	48(33.8)	26(36.6)	74(34.7)	2.291	0.318
65 and over	48(33.8)	17(23.9)	65(30.5)		
Total	142(100)	71(100)			



	MPV			PNL			LYM		
	Low	Normal	High	Low	Normal	High	Low	Normal	High
Case		93	7	4,9	77,5	17,6	14,8	83,8	1,4
Control		97,2	2,8		100			95,8	4,2

Figure 1: COVID-19(+) and COVID-19(-) group MPV, PNL and LYM comparison

Table 2: Comparison of hgb, plt, mpv, neutrophil, lymphocyte and NLR values of the COVID-19(+) and COVID-19(-) groups

	COVID-19(+) (n=142)	COVID-19(-) (n=71)	t; p
	Mean	Mean	
Hgb	13.49±2.00	13.71±1.53	-0.862;0.390
Plt	231.24±80.11	245.88±58.68	-1.513;0.132
MPV	9.62±0.96	8.92±0.87	5.184;<0.001
Neutrophil	5.09±3.21	3.77±1.12	4.385;<0.001
Lymphocyte	1.65±1.12	2.44±0.72	4.586;<0.001
NLR	4.63±7.67	1.66±0.64	4.586;<0.001

Hgb: hemoglobin, Plt: platelet, MPV: mean platalet volüm, NLR: neutrophil lymphocyte ratio

DISCUSSION

Studies show that hemogram tests are useful in the diagnosis and follow-up of COVID-19 disease (12). The fact that it is easily accessible and inexpensive increases the importance of this test. However, the tests must be reliable. Some values in the hemogram are increasing in importance day by day. For instance, it has recently been reported that MPV values help diagnosis in neoplastic events, inflammatory diseases, infectious diseases and even vitamin deficiency (6-10). It was observed that MPV values also increased in patients with COVID-19 (11,13). Some studies report that the MPV value is still not fully understood and some conditions should be considered during its evaluation. For example, he reports that many factors may affect MPV values, from the sample tube until the time between blood is drawn and given to the machine (14). In our study, blood and PCR tests were performed simultaneously. Therefore, these tests are thought to be reliable and no affected by these adverse conditions at a very low rate. In this study, we examined the hemogram test and MPV and NLR values that are accepted as new inflammatory markers in COVID-19 patients. It was found that there was no significant relationship in hemoglobin and platelet counts in cases with COVID-19 infection compared to the COVID-19(-) group. However, the lymphocyte, neutrophil, MPV values and NLR ratios of patients with COVID-19 were found to differ significantly compared to the COVID-19(-) group. According to the results of our study, neutrophil, lymphocyte, MPV and NLR values were found to be higher in the COVID-19(-) group than in the COVID-19(+) group. It is known that there is an increase in neutrophil and lymphocyte ratios in our body in the event of infection. However, this finding in MPV and NLR values can be considered as a parameter that can be used in the diagnosis of COVID-19. The literature supports this finding (12). In a study by Gümüş et al., it was determined that lymphocyte values

were low and mpv values were high, especially in children with asymptomatic COVID-19 patients. He even later claimed that these values could be used to prevent delays and carriers in the treatment of COVID-19 (8). We found similar findings in our study. However, in order to prevent carriers and delays in treatment, there is a need for new studies with larger case numbers and longer period of time to be used in addition to other markers in the diagnosis of COVID-19 and other infectious and inflammatory diseases (11). In a meta-analysis by Henry et al. in which they compared 21 studies examining 3377 patients and 33 laboratory parameters, several biomarkers were identified that could potentially aid risk stratification models to predict severe and fatal COVID-19. Among these parameters, there are leukocyte, lymphocyte and thrombocyte counts. He stated that these values should be followed closely in terms of diagnosis, treatment and prognosis of the disease. In our study, no evaluation was made in terms of prognosis. However, leukocyte and neutrophil values were affected in most of the patients at the time of diagnosis. In addition, MPV and NLR values were not among the 33 parameters used by Henry et al. In our study, we found similar findings with leukocyte and neutrophil values. In addition, MPV and NLR values were evaluated. At the time of diagnosis, MPV and NLR values were found to be high (15). In another study by Güçlü et al., they investigated the relationship between mortality and platelet count, Mean Platelet Volume (MPV), and platelet distribution width in COVID-19. They found that there was an increase in COVID-19 infection in MPV values, even a 1 unit increase in MPV increased mortality 1.76 times. It's also observed that they had thrombocytopenia. In our study, we found an increase in MPV values and during other diagnosis. When the two studies are evaluated together, besides the effect of the increase in MPV on mortality, the high MPV values at the time of diagnosis may also be important in terms of diagnosis (13,16). In the study of Ozcelik et al., influenza was compared with COVID-19 infection and it was determined that the platelet count and platelet indices were important parameters in terms of differential diagnosis in the diagnosis of COVID-19. It was also stated that they can help differentiate COVID-19 from influenza. We found changes in MPV values in our study and we thought that it may be useful at the time of diagnosis of COVID-19 disease. (17). Özçelik et al. also found that the decrease in platelet counts is important in the follow-up of prognosis, but prognosis was not followed up in our study. Güner et al. found that MPV values increased more in children who needed hospitalization due to COVID-19 compared

to those who did not require hospitalization, but could not give clear information about the prognosis because mortality was not observed in children. In addition, decreases in thrombocyte, lymphocyte and neutrophil values were also detected in PCR positive patients. In our study, it coincided with the work of Güner et al. (18).

Bg et al. report that a decrease in CD4(+) T lymphocytes and an increase in CD8(+) T lymphocytes in systemic infections lead to an increase in NLRs, and that COVID-19 should increase in NLR rates because it causes a systemic infection. In their study, they found that NLR rates increased. However, they found that its use as a prognostic factor was not clear. But he reports that such hematological rates used can help us understand the severity and progression of the disease in COVID-19. In our study, we found similar findings with the work of Bg et al. (19). The finding of high NLR during diagnosis suggests that NLR can be used in diagnosis.

Since the study was conducted only with people registered in a family health center in Kütahya, the results cannot be generalized to the whole of Kütahya and Turkey. The results of the study; It is limited to the date it was made and the records used in accordance with the purpose. As the relevant data could not be obtained in the study, it was not possible to reach conclusions regarding the prognosis of the patients.

CONCLUSION AND RECOMMENDATIONS

As a result, hemogram can help us in the diagnosis and follow-up of the disease in COVID-19 patients. Especially proportional values such as MPV and NLR can help us about the diagnosis of the disease. But more studies are needed on this subject. Controlled studies and observational studies with larger samples may yield more accurate results.

Ethical Approval: This study was approved by Kütahya Health Sciences University Non-interventional Ethics Committee with Date: 18/01/2022 and Decision no: 2022/01-01. This study was carried out in accordance with the Declaration of Helsinki.

Authors Contributions: AD and MY participated in conceiving, designing, drafting, and writing the manuscript. AD participated in collecting data. MY participated in analysis and interpretation. All authors have read and approved the final manuscript.

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