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The importance of mean platelet volume lymphocyte ratio and mean platelet volume platelet ratio in COVID-19 patients

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ABSTRACT

Objective: The mean platelet volume lymphocyte ratio (MPVLR) and mean platelet volume platelet ratio (MPVPR) reflect inflammation more effectively and strongly than MPV, lymphocyte, platelet, and neutrophil counts separately, we aimed to evaluate the importance of MPVLR and MPVPR in COVID-19 patients.

Material and Methods: Patients with COVID-19 were divided into two groups based on whether their RT-PCR test resulted in a positive or negative result. MPVLR, MPVPR, neutrophil, lymphocyte, platelet, MPV and RDW levels were compared between these two groups. In addition, the changes in MPVLR, MPVPR, neutrophil, lymphocyte, platelet, MPV, and RDW levels before and after treatment were compared in the whole patient population.

Results: There were 113 patients diagnosed with COVID-19 with a positive PCR test and 79 patients with a negative PCR test. Before treatment, the MPVLR level was 7.2±0.85 in the PCR test positive group and 5.4±0.29 in the PCR test negative group (p=0.04). Post-treatment MPVLR levels were 5.7±0.4 and 4.9±0.26 in the PCR positive and negative groups, respectively (p=0.09). The MPVPR level before treatment was 0.046±0.002 in the PCR test positive group and 0.035±0.001 in the PCR test negative group (p=0.003). After treatment, the MPVPR level was 0.040±0.002 in the PCR-positive group and 0.032±0.001 in the PCR-negative group (p=0.023)

Conclusion: This study is the first to demonstrate high MPVLR and MPVPR in PCR-positive COVID-19 patients. Patients with negative PCR test and high MPVLR and MPVPR should be evaluated with radiological and clinical symptoms.

Keywords: COVID-19, mean platelet volume lymphocyte ratio, mean platelet volume platelet ratio, RT-PCR test.

INTRODUCTION

The new coronavirus (COVID-19), termed severe acute respiratory syndrome coronavirus 2 appeared in Wuhan, China, and extended across the earth (1). The World Health Organization announced d a pandemic (2). Although Reverse Transcriptase-PCR is expensive for diagnosis, time-consuming, inappropriate for screening, and has a 20% false negative rate, it is the gold standard (3). In patients with fever, cough, throat, dyspnea, or covid contact, COVID-19 infection is determined with typical thorax computed tomography (CT) characteristics despite negative RT-PCR results (4).

COVID - 19 has infected millions of people and caused thousands of individual deaths (5). Proinflammatory cytokines and immune inflammation may play a role in the pathophysiology of the high pathogenicity of COVID-19 (6). Neutrophilia and lymphopenia have been reported in various studies. Depending on the severity of inflammation, lymphocyte, neutrophil, and platelet counts and mean platelet volume (MPV) change. An elevated neutrophil-to-lymphocyte ratio has been associated with poor clinical outcomes (7). The mean platelet volume lymphocyte ratio (MPVLR) and mean platelet volume platelet ratio (MPVPR) are parameters that can be used as inflammation markers, similar to the NLR (8, 9). Based on the hypothesis that MPVLR and MPVPR reflect inflammation more effectively and strongly than MPV, lymphocyte, platelet, and neutrophil counts separately, we aimed to evaluate the importance of MPVLR and MPVPR in COVID-19 patients.

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MATERIAL and METHODs

The study was conducted retrospectively using Bolu Provincial Health Directorate pandemic registration system data. Patients aged 18 or older who were diagnosed with COVID-19 disease were included in the study. Ethics committee approval was obtained (Approval no: 2020/113). Cough, fever, dyspnea, covid contact, thoracic CT findings, clinical status (intubated, intensive care unit, inpatient unit), creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), albumin, C-reactive protein (CRP) and hemogram parameters were recorded. Patients with COVID-19 were divided into two groups based on whether their RT-PCR test resulted in a positive or negative result. MPVLR, MPVPR, neutrophil, lymphocyte, platelet, MPV and RDW levels were compared between these two groups. In addition, the changes in MPVLR, MPVPR, neutrophil, lymphocyte, platelet, MPV, and RDW levels before and after treatment were compared in the whole patient population. MPVLR was obtained by dividing MPV into lymphocytes. MPVPR was obtained by dividing MPV into platelets.

Statistical analysis: Data were analyzed with SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were analyzed using the chi-square test or Fisher's exact test. The distribution of variables was analyzed with the Kolmogorov-Smirnov test. An independent t-test was used to analyze homogeneous variables, which were presented as mean±SD. A paired-sample t-test was used to compare MPVLR, MPVPR, neutrophil, lymphocyte, platelet, and MPV levels before and after treatment. The level of significance was set at p 0.05.

RESULTs

In our study, there were 113 patients diagnosed with COVID-19 with a positive PCR test and 79 patients with a negative PCR test. Of the PCR-positive patients, 63 (55.8%) were female and 50 (44.2%) were male. Of the PCR-negative patients, 29 (36.7%) were female, and 50 (63.3%) were male (p = 0.09).

The number of patients with a positive thoracic CT finding was higher in the group with a positive PCR test compared to the group with a negative PCR test (p < 0.001) (Table 1). The number of patients with dyspnea was lower in the PCR-positive group (p < 0.001) (**Table 1**). The number of COVID-19-contacted patients was significantly higher in the PCR-positive patient group (p<0.001). Fever, cough, and clinical status were similar in the PCR test positive and negative groups (p > 0.05 for all) (**Table 1**). The PCR test positive group had significantly higher albumin levels (p 0.001). AST and CRP levels were significantly lower in the PCR test positive group compared to the PCR test negative group (p=0.02, p<0.001, respectively). When the creatinine, hemoglobin, ALT, GGT, and ALP levels were compared between the groups, no significant difference was found (p>0.05 for all). Before treatment, the MPVLR level was 7.2±0.85 in the PCR test positive group and 5.4±0.29 in the PCR test negative group (p=0.04). Post-treatment MPVLR levels were 5.7±0.4 and 4.9±0.26 in the PCR positive and negative groups, respectively (p=0.09). The MPVPR level before treatment was 0.046±0.002 in the PCR test positive group and 0.035±0.001 in the PCR test negative group (p=0.003). After treatment, the MPVPR level was 0.040±0.002 in the PCR-positive group and 0.032±0.001 in the PCR-negative group (p=0.023) (**Figure 1**).

Table 1: Characteristics of the PCR test positive and negative patient groups

		PCR positive group n (%)	PCR negative group n (%)	p
Gender (n)	Female	63 (55.8%)	29 (36.7%)	0.09
	Male	50 (44.2%)	50 (63.3%)	
Thorax computed tomography (n)	Positive	77 (68.1%)	20 (25.4%)	**<0.001**
	Negative	36 (31.9%)	59 (74.6%)	
Clinical status(n)	Intubated	3 (2.7%)	4 (5.1%)	0.1
	intensive care unit	3 (2.7%)	7 (8.9%)	
	inpatient unit	107 (94.6%)	68 (86%)	
Fever (n)	Yes	36 (31.9%)	44 (55.7%)	0.01
	No	77 (68.1%)	35 (44.3%)	
Cough (n)	Yes	42 (37.2%)	49 (62%)	0.01
	No	71 (62.8%)	30 (38%)	
Dyspnea (n)	Yes	20 (17.7%)	35 (44.3%)	**<0.001**
	No	93 (82.3%)	44 (55.7%)	
Covid Contact (n)	Yes	78 (69%)	12 (15.2%)	**<0.001**
	No	35 (31%)	67 (84.8%)	
		PCR positive group Mean±SD	**PCR negative group Mean±SD**	p
Hemoglobin (gr/dl)		12.8±0.4	13.4±0.2	0.12
Creatinine (mg/dl)		0.8±0.02	0.9±0.01	0.34
Alanine aminotransferase (U/L)		25.5±1.6	31.6±3.8	0.14
Aspartate aminotransferase (U/L)		28.08±1.37	35.4±2.8	**0.02**
Gamma glutamyl transferase (U/L)		43.42±2.88	45.6±7.4	0.75
Alkaline phosphatase (U/L)		78.2±2.6	95.9±7.1	0.02
Albumin (gr/dl)		4.2±0.05	3.7±0.05	**<0.001**
C-reactive protein (mg/L)		20.2±3.5	66.9±8.7	**<0.001**

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There was no difference between the PCR positive and negative levels of neutrophil, lymphocyte, platelet, MPV, and RDW before the treatment (p>0.05 for all) (Table 2). Similarly, neutrophil, lymphocyte, platelet, MPV, and RDW levels after treatment were not different between the groups (p>0.05 for all) (**Table 2**).

MPVLR (mean difference = 1.14, p = 0.004), MPVPR (mean difference = 0.004, p = 0.006), and neutrophil (mean difference = 1.09, p<0.001) levels were significantly lower in the entire study population before and after treatment. Lymphocyte (mean difference = -0.24, p<0.001) and platelet (mean difference= -25.1, p<0.001) levels increased significantly. There was no significant difference in MPV (mean difference = 0.05, p=0.45).

Table 2. Comparison of inflammatory parameters before and after treatment in PCR positive and PCR negative groups

	Before the treatment of COVID			After the treatment of COVID		
	COVID PCR positive group	COVID PCR negative group		COVID PCR positive group	COVID PCR negative group	
	Mean±SD		p	Mean±SD		p
MPV to lymphocyte ratio	7.2±0.85	5.4±0.29	**0.04**	5.7±0.4	4.9±0.26	0.09
MPV to platelet ratio	0.046±0.002	0.035±0.001	**0.003**	0.040±0.002	0.032±0.001	**0.023**
Neutrophil (10^9/L)	6.5±0.51	5.9±0.5	0.07	4.6±0.2	3.9±0.15	0.09
Lymphocyte (10^9/L)	1.66±0.07	1.53±0.09	0.25	1.89±0.06	1.8±0.09	0.44
Platelet (10^9/L)	216.6±5.7	236.5±9	0.06	243.3±7.7	259.1±10.2	0.2
MPV (fL)	8.19±0.09	8.13±0.1	0.69	8.07±0.12	8.16±0.11	0.63
RDW (%)	15.2±0.19	15.44±0.2	0.45	15.23±0.19	15.2±0.23	0.95

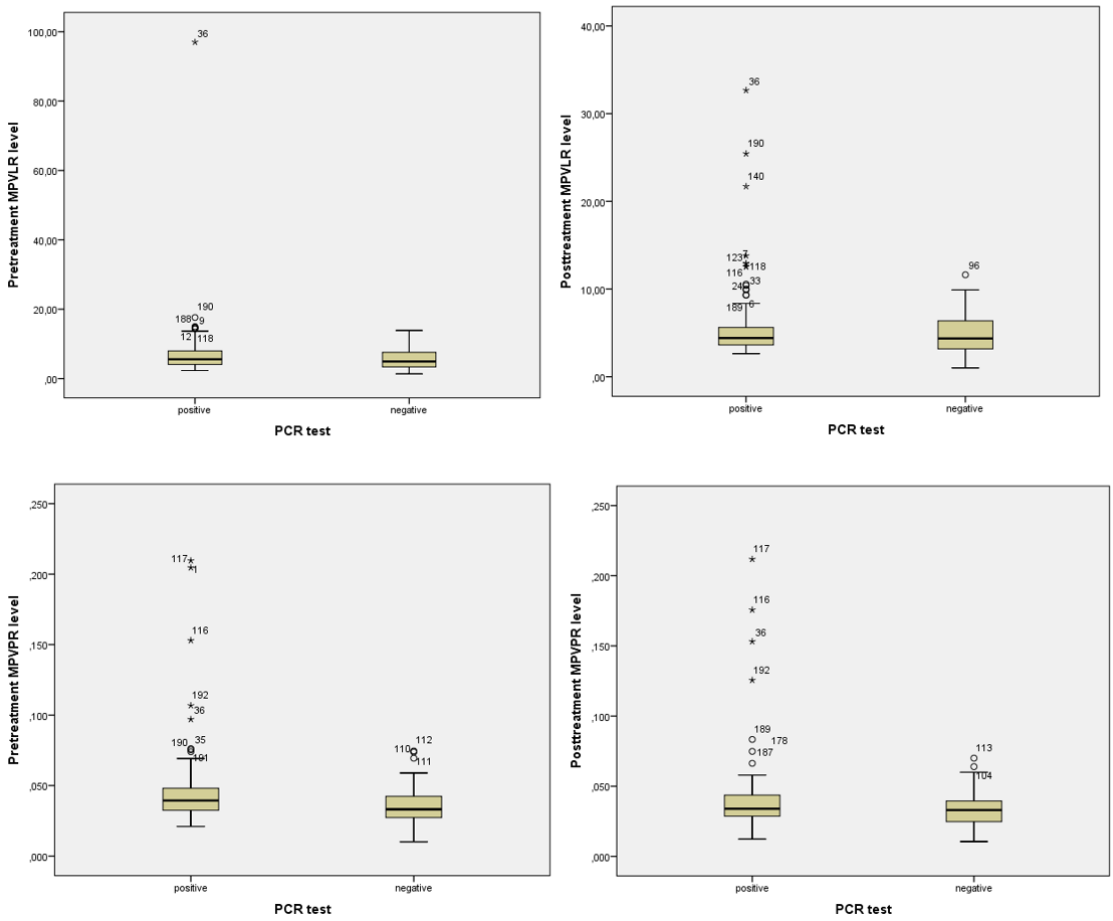

Figure 1: MPVLR and MPVPR levels according to PCR test before and after COVID-19 treatment

DISCUSSION

In this presented study, inflammatory markers MPVLR and MPVPR levels were found to be significantly higher in PCR test-positive patients at the time of diagnosis of COVID-19. In addition, MPVPR was significantly higher in patients with positive PCR tests after COVID-19 treatment. There was a significant decrease in MPVLR, MPVPR, and neutrophil levels and a significant increase in lymphocyte and platelet ratios in the entire patient population after COVID treatment. There was no change in the MPV level. According to these results, it was shown that inflammatory markers in patients with a positive PCR test for COVID-19 differed significantly compared to patients with a negative PCR test for CPVID. In contrast, markers showing subclinical inflammation, such as MPV did not change.

Inflammatory markers obtained from hemogram parameters have been suggested to be associated with various diseases such as solid cancers (10), type 2 diabetes mellitus (9, 11), chronic obstructive pulmonary disease (12, 13), and coronary artery disease (14). Recent studies have focused on new inflammatory markers derived from routine hemogram tests. MPVLR and MPVPR are two of these markers that have been related to a variety of inflammatory conditions, including diabetic nephropathy (8), cancer (15), and type 2 diabetes (16). Our study found higher levels of inflammation in patients with COVID-19 with positive PCR testing than in patients with negative PCR testing. As a result, even if the PCR test is negative, patients with high MPVLR and MPVPR should be evaluated with radiological and clinical symptoms.

COVID-19 is a disease that causes mortality and morbidity. Accurate and rapid identification of COVID-19 is crucial to control outbreaks in the world. PCT testing is the standard in the diagnosis of COVID-19 infection. However, PCR test will never be able to achieve a sensitivity of 100% (16). The sensitivity of the PCR test alters according to the tester and how it performs. PCR test results become positive within 2–8 days (17). Therefore, MPVLR and MPVPR levels should be evaluated in PCR-negative patients, and patients should be followed up with suspected COVID-19 diagnosis.

Our study has some limitations. First, the study was single-center and retrospective. Second, the number of COVID-19 patients is relatively low. However, the patient groups were evenly distributed.

CONCLUSION

This study is the first to demonstrate high MPVLR and MPVPR in PCR-positive COVID-19 patients. Patients with negative PCR test and high MPVLR and MPVPR should be evaluated with radiological and clinical symptoms.

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Author Contributions: Design and initiate**: SO, and EO.** Data collection**: MED and SO.** Analysis, literature review and writing**: SO, MED and EO.** Revision**: EO**

Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study. Written consent was obtained from each patient to use their hospital data. (Local ethic committee Approval No: 2020/113).

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