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Differences in some hematological parameters in adult male and female COVID-19 patients: A retrospective study

 Mehmet Ediz Sarihan*Turgut Özal Medical Center; Department of Emergency Medicine, Malatya, Türkiye*

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Abstract

COVID-19 is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2). Depending on the severity of the disease, fever, cough, shortness of breath, more severe pneumonia and death may occur. The aim of this study is to compare some blood parameters between adult male and female patients with COVID-19 to understand the effect of gender on disease pathogenesis. For this purpose, the levels of blood serum the D-dimer, white blood cells, monocyte, lymphocyte, platelet, glucose, hemoglobin and Prothrombin Time/INR were measured in a total of 3101 COVID-19 patients whose 1649 were males and 1452 were females. Statistically significant differences were observed in platelet, white blood cells, Prothrombin Time/INR, hemoglobin and monocyte levels while no differences were detected in lymphocyte, D-dimer, and blood glucose levels between male and female patients. The results indicate that platelet, white blood cells, Prothrombin Time/INR, hemoglobin and monocyte levels were significantly higher in males as compared to female patients with COVID-19.

Keywords: COVID-19, hematological parameters, coronavirus, gender, pandemic

Introduction

On December 31, 2019, the Chinese government notified WHO that unusual cases of pneumonia were seen in Wuhan city of Hubei province. Since the notification that most of the patients were workers of the Huanan Seafood Market, accepting as the focus of the disease, the market was closed on January 1, 2020. The first death due to COVID-19 in China was reported on January 10, 2020. COVID-19 outbreak was declared a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020 by The World Health Organization [1-3]. The first confirmed COVID-19 case in Türkiye was detected on March 11, 2020, which was also the day the disease was declared a pandemic worldwide [4].

COVID-19 is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2), a member of the beta-coronavirus family. The disease is significant with a range of respiratory symptoms, which may differ from fever, coughing, shortness of breath to more severe pneumonia and death depending on the severity of the disease [5]. The virus can

affect all age groups though deaths are most significant in adults and elderly [6]. Increased coagulopathy and thromboembolism were frequently reported in severe cases and are among the main causes of severe and even fatal outcomes in COVID-19 patients [7]. Therefore, venous thrombosis seen in COVID-19 patients is suggested to play an important role in the disease pathogenesis.

In COVID-19, some patients may only have a mild disease course with a good prognosis, while in others it may progress to a severe disease [8]. The course of the disease in COVID-19 patients needs to be strictly followed and for this purpose several tests and imaging methods can be used. Secondary bacterial infection and development of thrombosis are especially important since they may be indicator for the worsened condition and the poor course. Complete blood count (CBC), C-Reactive protein (CRP), and D-dimer level can therefore be used for screening of the disease course [9]. CBC itself is the simplest, most appropriate and effective test in monitoring the patients in general [10]. A simple blood test can be especially useful in providing information about the progression of inflammation.

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Corresponding Author: Mehmet Ediz Sarihan, Turgut Özal Medical Center, Department of Emergency Medicine, Malatya, Türkiye
Email: edizsarihan@hotmail.com

Changes in blood biochemical markers can give the physician an understanding about the course of the disease. Leukopenia, lymphocytopenia, high level of CRP, high D-dimer, prolonged PT, and high levels of fibrinogen were suggested to be good indicators for worsened disease course in the early phases of COVID-19 infection [11, 12]. Although importance of these parameters in COVID-19 patients as the surveillance criteria was indicated in previous studies, differences between male and female COVID-19 patients need to be investigated. Hence, the aim of this study is to compare the blood serum the D-dimer, white blood cells (WBCs), lymphocytes, platelet, blood glucose, Prothrombin Time/INR (PT/INR), hemoglobin (Hgb) and monocytes (MO) levels between male and female patients infected with COVID-19.

Material and Methods

Subject

This retrospective study was conducted with the use of blood parameters of 3101 patients (1649 males and 1452 females) diagnosed with COVID-19 at Inonu University Turgut Özal Medical Center, Department of Emergency Medicine between 1 January 2020 and 31 December 2022. Diagnosis of cases was made by the standard reverse transcription polymerase chain reaction (RT-PCR) test which is based on the presence of SARS-CoV-2 nucleic acid in a combined nasal/oral pharyngeal swab sample. Patients average age was 51.1±18.9 years for men and 48.6±19.4 years for women. Patients diagnosed with COVID-19 for the first time formed the study group. The study protocol was approved by The Inonu University Faculty of Medicine Ethics Committee and complies with the Helsinki Declaration.

Data collection and laboratory tests

About 3 ml of venous blood was collected using the EDTA vacutainer tube from the patients diagnosed COVID-19. The blood samples collected from each individual were analyzed for CBC examination using Automatic Hematology. The blood routine indicators included lymphocyte (Lymph), platelet count (PLT), WBC, D-dimer, blood glucose (BG), PT/INR, Hgb and MO.

Statistical analysis

Variables were summarized by median (95% confidence interval for median). Compliance with normal distribution was checked by the Kolmogorov-Smirnov test. Since the data were not normally distributed, Mann Whitney U test was used for pairwise comparisons. The relationships between the data were analyzed by Sperman correlation analysis and the relationships between the variables were presented in matrix form with scatter plots. p<0.05 was considered statically significant for a given parameter between male and female patients. IBM SPSS 26.0 was used in the analyses.

Results

The results of the blood parameters and their statistical comparison between male and female patients are given in

Table 1. Statistically significant differences were found in PLT, WBC, PT/INR, Hgb, and MO between the males and females. However, lymphocyte, D-Dimer and BG variables did not differ between the groups. The relationships between the variables were analyzed by correlation analysis and the relationships are shown in Figure 1. When the variables with significant correlation values were analyzed, it was found that the correlations between the variables were at a very low level. The highest correlation value was obtained as 0.566 between WBC and LY values. This value shows a medium-level relationship. The correlation coefficients obtained between the other variables are small enough to be ignored and it cannot be said that the variables show a dual relationship with each other, and the relationships found are at low level.

Table 1. Comparison of some blood parameters between male and female COVID-19 patients

Parameters	Gender		p*
	Male	Female	
	Median (95% confidence interval for median)		
PLTs (10 ³ /μl)	228 (224-234)	255.5 (248-262)	<0.001
WBC (10 ³ /μl)	8.38 (8.26-8.51)	7.885 (7.72-8.07)	<0.001
Lymphocyte (%)	1.88 (1.81-2)	1.91 (1.84-2.01)	0.446
D-Dimer (mg/l)	0.63 (0.57-0.71)	0.69 (0.63-0.76)	0.110
BG (mg/dl)	99 (99-104)	98 (98-99)	0.078
PT/ INR	1.1 (1.1-1.12)	1.05 (1.05-1.06)	<0.001
Hgb (g/dl)	14.9 (14.8-15.1)	12.9 (12.8-13)	<0.001
MO (%)	0.79 (0.77-0.81)	0.64 (0.63-0.66)	<0.001

*: Mann Whitney U test

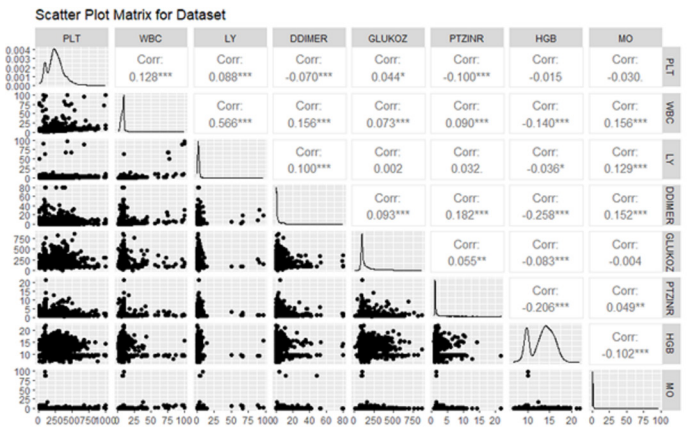


Figure 1. Correlation graph of blood parameters. **: Correlation is significant at the 0.01 level (2-tailed). ***: Correlation is significant at the 0.05 level (2-tailed)

Discussion

Blood parameters routinely tested for diagnosis and prognosis estimation purposes are of great importance. Changes in some blood parameters may be suggestive of certain diseases, however most common parameters can be affected by various diseases or conditions. They may most effectively give information about

the severity and the course of a certain condition. Various inflammatory and hematological parameters were also shown to change in patients with COVID-19 infection. In this study, some blood parameters were monitored and differences between male and female COVID-19 patients were investigated.

Hemoglobin levels of COVID-19 patients were reported to be in normal range in majority of the cases while decreased hemoglobin levels were seen in 29.1% and increased levels were only in 0.6% of the patients [13]. Low levels of hemoglobin were suggested to pose a high risk of viral infections and hence might be significant in some COVID-19 patients. On the contrary to the previous study, increased hemoglobin levels were also reported in COVID-19 patients by others [14]. In comparison of male and female COVID-19 patients in terms of hemoglobin levels, male patients were reported to have higher hemoglobin levels compared to the females [14]. In our investigation, similar to the previous report higher hemoglobin levels were detected in male patients. A positive correlation between the disease and the increased WBC level and decreased lymphocyte level was reported though in majority of the cases these two parameters were detected within the normal ranges in the reported study [13].

Coagulopathy is one of the most important changes affecting the course of the patients with COVID-19 infection. However, the characteristics of COVID-19-associated coagulopathy are unique and not fully understood [15]. D-dimer is an important test to assess the presence of coagulopathy in a patient. In a case-control study, D-dimer levels were compared between 44 COVID-19 patients and 22 controls and the results indicated increased D-dimer levels in COVID-19 patients [16]. In the early times of the pandemic hypercoagulability in the blood was also recorded in hospitalized patients and D-dimer levels were shown to be elevated in correlation with the worsening of the disease [17]. In the current investigation increased D-dimer levels were observed in COVID-19 patients. However, no differences were detected between the male and female patients.

In their study, Usul et al. (2020) reported that the rate of contracting COVID-19 was higher among men compared to that of women [14]. In the present retrospective study, the number of COVID-19 infected men was also seen to be higher than women in the studied medical center. The previous group also reported lower platelet, leukocyte and neutrophil counts and higher hemoglobin levels in COVID-19 patients compared to the controls. Hemoglobin levels were also detected to be higher in men compared to the women [14]. Similarly, statistically significant difference in hemoglobin level between male and female patients were observed in our study, men with COVID-19 infection having higher hemoglobin levels than women.

COVID-19 is a well-known disease with respiratory problems, yet it can manifest several extrapulmonary conditions including thrombotic complications, myocardial dysfunction, arrhythmia and acute coronary syndromes [18]. Blood tests besides others

are therefore of important to assess possible conditions since they have common standards, which makes it easy to compare the values. In a critical review, decreased erythrocytes, lymphocytes and platelet counts and increased D-dimer and fibrinogen levels were indicated to be related with the severity of COVID-19 infection [19]. In addition, in severe and critical conditions, increased levels of PT, APTT and neutrophils were detected while monocytes, eosinophils, and basophils are reported to be reduced moderately. In our study, monocyte levels in COVID-19 patients increased and there was statistically significant difference between male and female patients where it was higher in males. PT/INR level in our study also showed significant difference between male and female patients in that it was higher in males.

In a comprehensive meta-analysis, it was reported that hemoglobin level can be associated with the severity of COVID-19 infection and ferritin, which increased in older male patients, can be a good indicator [20]. Since the hemoglobin cut-off levels may vary by sex there is a need to analyze the outcomes on the basis of gender in anemia. PT and activated partial thromboplastin time (aPTT) prolongation were noted as higher in the COVID-19 patients leading to the life-threatening intravascular coagulation due to thrombocytopenia [21].

In the current investigation, lymphocyte levels for both males and females were seen to be within the normal range and no significant difference between male and female patients was detected. However, others reported lymphopenia prevalently in COVID-19 infection [22]. Reduced platelet (PLT) count was indicated to be associated with the severity of the disease and mortality whereas it was reported that there was no prominent difference of PLT levels in patients with moderate condition [23]. The use of platelet to lymphocyte ratio (PLR) to predict the prognosis and hospitalization care was tested, however it was indicated that low PLT level was not a distinct marker in COVID-19 infection [24]. Although PLT levels increased in COVID-19 patients no significant changes were detected in lymphocytes in the current investigation. However, PLT levels were significantly higher in females than males.

Quantitative changes in leukocytes were indicated to be not significant in the noncritical patients and white blood cell counts were within the normal range or decreased in the early phase of the infection [8]. The percentage of WBCs in the whole blood cell population is mostly unchanged in COVID-19 patients, yet a slightly decreased WBC ratio was observed in the current investigation. Several studies presented that monocyte counts did not change significantly in the infection, however abnormalities in MO ratio may contribute to chronic sequela [25]. Despite the unchanged MO count, monocyte distribution width (MDW) was shown to increase in the patients and suggested to be a diagnostic tool in COVID-19 [26]. Leucopenia was also shown to develop in some COVID-19 patients and suggested that WBC count may provide some information about the severity of the cases [27]. Absence of comparison between healthy and COVID-19 infected patients is the limitations of the study.

Conclusion

There is not enough study investigating the differences between adult male and female patients with COVID-19 infection in terms of blood parameters. The results of this investigation showed that there are significant differences in the PLT, WBC, PT/INR, Hgb, MO levels between male and females COVID-19 patients. PLT values of women infected with COVID-19 were significantly higher than that of men. WBC, PT/INR, Hgb, and MO levels of women were significantly lower than those of men. No significant differences were seen in lymphocyte, D-Dimer and BG between male and female patients. When variables with significant correlation values were analyzed, the correlations between the variables were detected to be quite low. The highest correlation was found between WBC and lymphocyte values with a moderate level of relationship.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical Approval

The study protocol was approved by The Inonu University Faculty of Medicine Ethics Committee (2023/5011) and complies with the Helsinki Declaration.

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