Hematologic Parameters of Patients with COVID-19 Infection
COVID-19’lu Hastalarda Görülen Hematolojik Parametreler

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ABSTRACT
SARS-CoV-2 causes primarily respiratory tract infection, but can also affect hematopoietic and immune systems. Quantitative and qualitative changes in lymphocytes, neutrophils, monocytes and platelets, are reported in infected patients. These changes are related to the severity of the disease. Lymphopenia is the most common finding in adult patients infected with SARS-CoV-2, while it is much less common in children. Leukocytosis can be detected in patients with severe infection, but rare in patients with mild to moderate infection. Thrombocytopenia or thrombocytosis can also be seen in accordance with the clinic. Dysplastic morphological changes in neutrophils and platelets can be detected in peripheral smear of patients.

Key Words: COVID-19, Hematology, lymphocyte, Neutrophil, Thrombocyte

INTRODUCTION
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19) has rapidly evolved from an epidemic outbreak in Wuhan, China (1). World Health Organization (WHO) describes SARS-CoV-2 as a pandemic on March 11, 2020 that infecting more than one million individuals all over the world (2). The SARS-CoV-2 viruses are positive single-stranded RNA viruses and primarily manifested as a respiratory tract infection. It may be cause systemic disease including cardiovascular, respiratory, gastrointestinal, neurological, hematopoietic and immune system (3). Clinical studies showed that the most threatened population are the elderly people. Cases of COVID-19 in those aged <20 years comprise around 2% of those infected and if infected, deaths in this age group appear very rare (4).

Given the immunosuppressive nature of cancer therapies, patients with cancer have a statistically higher incidence of severe events such as intensive care unit admission, ventilation and death after contracting COVID-19 in China (5).
We aimed to examine the hematological parameters especially in hemogram observed in the diagnosis and treatment process of patients diagnosed with COVID-19 in the light of current literature.

**Lymphopenia**

In laboratory examinations, lymphopenia is a common finding in COVID-19 patients (6). During the early phase of the disease, especially incubation period (ranging from 1 to 14 days) leukocyte and lymphocyte counts are normal or slightly reduced. About 7 to 14 days after the onset of the initial symptoms, approximately 7 to 14 days from the onset of the initial symptoms, “cytokine storm” appears with a pronounced systemic increase of inflammatory mediators and cytokines. In this instance, significant lymphopenia becomes evident (7). In a recent study of 1099 patients in China, lymphocytopenia was present in 914 (83.2%) of the patients on admission (8). Moreover, Lu et al. (9) showed that patients with lymphocytopenia have an increased risk of cytokine storm and disease severity. In many studies the mechanism of this has been shown that lymphocytes express the ACE2 (angiotensin converting enzyme) receptor on their surface; thus COVID-19 may directly infect those cells and lead to their lysis. Furthermore, as a result of cytokine storm, interleukins such as IL-2, IL-6 and TNF-alpha levels increase, which may induces lymphocyte apoptosis (10-13). In addition, cytokine activation may be also associated with atrophy of lymphoid organs, including the spleen, and can also disrupt lymphocyte turnover (14). Development of lactic acidosis in patients with severe disease and cancer who are at increased risk for complications may also inhibit lymphocyte proliferation (15). In addition to these mechanism, medications used for the treatment of COVID-19 like steroids can also cause lymphopenia.

Huang et al. (16) showed that, in their study of 41 adults with COVID-19 infection, on admission 10 patients (25%) had leukopenia (white blood cell count less than 4 x 10⁹/L) and 26 patients (63%) had lymphopenia (lymphocyte count < 1 x 10⁹/L). Similarly, these results were consistent in other descriptive studies in China (17). Also in these studies, Huang et al. (16) and Wang et al. (18) emphasized a relationship between need for intensive care and lymphopenia. In addition, Wu et al. (19) showed an association between lymphopenia and acute respiratory distress syndrome (ARDS) development and increased risk of ARDS was significantly associated with increased neutrophils, which was associated with increased risk of death.

In another study, Deng et al. (20) has also been reported that patients with severe disease and fatal outcomes present with a decreased lymphocyte/white blood cell ratio both in admission. Similarly, Fan et al. (21) identified that lymphocyte count of < 0.6 x 10⁹/L increases the risk for intensive care unit admission.

**Thrombocytopenia**

Thrombocytopenia is an important indicator of COVID-19 patients and can be seen in the severe form of infection. In a study of Guan et al. (8), thrombocytopenia was observed in 36% of 1099 patients with COVID-19 infection and this finding was more prominent among severe versus non-severe cases. To support this study, a meta-analysis of nine studies has suggested that thrombocytopenia is significantly associated with the severity of the COVID-19 disease and a decrease in platelet count was more evident especially in nonsurvivors (26). In another study, thrombocytopenia was identified in up to 57.7% of patients with severe infection and 31.6% of patients with less significant symptoms (23). In the literature the studies suggest that the cause of thrombocytopenia may be due to sepsis, multiorgan failure, inhibition of megakaryocytes in the bone marrow and blocks the release of platelet, or platelet being consumed because of pulmonary thrombus formations (27).

Chen et al. reported that thrombocytopenia was seen in 12% of 99 patients and interestingly they also identified thrombocytosis in 4% patients (28).

**CONCLUSION**

In conclusion, COVID-19 infection has significant manifestations in the hematopoietic system. It would be better to include as many patients as possible to get a more comprehensive understanding of COVID-19 infection. Careful evaluation of laboratory indices at baseline and during the disease course can assist clinicians in formulating an appropriate treatment approach and provide intensive care to those who are in greater need.

We expect that in the months to come, more detailed studies will be forthcoming on the impact of COVID-19 infection, including the risk of infection and treatment strategies.
REFERENCES


