

# Hematologic Parameters of Patients with COVID-19 Infection

## COVID-19'lu Hastalarda Görülen Hematolojik Parametreler

Ayca KOCA YOZGAT, H. Nese YARALI

Department of Pediatric Hematology Oncology, Ankara City Hospital of Ankara Health Sciences University, Ankara, Turkey



### 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

### ÖZ

SARS-CoV-2 primer olarak solunum yolu enfeksiyonuna neden olmakla birlikte hematopoietik ve immun sistemlerini de etkileyebilmektedir. Enfekte olan hastalarda, lenfositler, nötrofiller, monositler ve trombositlerde kantitatif ve kalitatif değişiklikler bildirilmektedir. Bu değişiklikler ile hastalığın şiddeti arasında ilişki olduğu da gösterilmiştir. Lenfopeni, SARS-CoV-2 ile enfekte erişkin hastalarda en sık görülen bulgu iken çocuklarda çok daha az görülmektedir. Şiddetli enfeksiyonu olan hastalarda lökositoz saptanabilir, hafif-orta şiddette enfeksiyonu olan hastalarda ise lökositoz daha nadirdir. Klinik ile uyumlu olarak trombositopeni veya trombositoz da görülebilmektedir. Hastaların periferik yaymalarında özellikle nötrofil ve trombositlerde displastik morfolojik değişiklikler saptanabilir.

**Anahtar Kelimeler:** COVID-19, Hematoloji, Lenfosit, Nötrofil, Trombosit

### 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).



KOCA YOZGAT A : 0000-0001-6690-721X  
YARALI HN : 0000-0001-5488-2385

**Conflict of Interest / Çıkar Çatışması:** On behalf of all authors, the corresponding author states that there is no conflict of interest.

**Contribution of the Authors / Yazının Katkısı:** KOCA YOZGAT A: Constructing the hypothesis or idea of research and/or article, Reviewing the article before submission scientifically besides spelling and grammar, Taking responsibility in the writing of the whole or important parts of the study. YARALI HN: Constructing the hypothesis or idea of research and/or article, Reviewing the article before submission scientifically besides spelling and grammar, Taking responsibility in the writing of the whole or important parts of the study.

**How to cite / Atıf Yazım Şekli:** Koca Yozgat A, Yarıalı HN. Hematologic Parameters of Patients with COVID-19 Infection. Turkish J Pediatr Dis 2020;14 (suppl):48-50.

Correspondence Address / Yazışma Adresi:

**H. Neşe YARALI**

Department of Pediatric Hematology Oncology,  
Ankara City Hospital of Ankara Health Sciences University, Ankara, Turkey  
E-posta: neseyarali@yahoo.com

Received / Geliş tarihi : 30.06.2020

Accepted / Kabul tarihi : 20.07.2020

Online published : 27.07.2020

Elektronik yayın tarihi

DOI: 10.12956/tchd.760786

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  $4 \times 10^9/L$ ) and 26 patients (63%) had lymphopenia (lymphocyte count  $< 1 \times 10^9/L$ ). 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  $< 0.6 \times 10^9/L$  increases the risk for intensive care unit admission.

In children, unlike adults, lymphopenia is much less common. In Henry et al. (22) meta-analysis, lymphopenia was seen 3% of 66 pediatric patients in China.

### Leukocytosis and Neutrophilia

The data on neutrophilia are incomplete and suggest that neutrophilia is an expression of the cytokine storm and hyperinflammatory state. In literature, leukocytosis and neutrophilia were generally seen in the case of bacterial infection or superinfection. A meta-analysis of the literature showed that leukocytosis was identified in 11.4% of patients with severe disease compared to 4.8% of patients with mild to moderate disease (23).

In two studies in Wuhan, patients with high troponin-T levels and myocardial injury had higher leukocyte, increased neutrophils and decreased lymphocytes (24,25).

### 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

- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med* 2020; 382: 727-33.
- World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 — 11 March 2020. March 11, 2020. <https://www.who.int/dg/speeches/detail/whodirector-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020> (accessed March 12, 2020)
- Kannan S, Shaik Syed Ali P, Sheeza A, Hemalatha K. COVID-19 (novel coronavirus 2019) — recent trends. *Eur Rev Med Pharmacol Sci* 2020; 24: 2006–11
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. *JAMA*. 2020 [Epub ahead of print]. <https://doi.org/10.1001/jama.2020.2648>
- Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020;21:335–7.
- Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020; 395: 565–74
- Li T, Lu H, Zhang W. Clinical observation and management of COVID-19 patients. *Emerg Microbes Infect* 2020;9:687-90
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020 382:1708-20.
- Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020; 395: 565–74
- Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci* 2020; 12: 8.
- Singh S, Sharma A, Arora SK. High producer haplotype (CAG) of -863C/A, -308G/A and -238G/A polymorphisms in the promoter region of TNF-alpha gene associate with enhanced apoptosis of lymphocytes in HIV-1 subtype C infected individuals from North India. *PLoS One* 2014; 9: e98020.
- Liao YC, Liang WG, Chen FW, Hsu JH, Yang JJ, Chang MS. IL-19 induces production of IL-6 and TNF-alpha and results in cell apoptosis through TNF-alpha. *J Immunol* 2002; 169: 4288-97.
- Aggarwal S, Gollapudi S, Gupta S. Increased TNF-alpha-induced apoptosis in lymphocytes from aged humans: changes in TNF-alpha receptor expression and activation of caspases. *J Immunol* 1999;162:2154-61.
- Chan JF, Zhang AJ, Yuan S, Poon VK, Chan CC, Lee AC, et al. Simulation of the clinical and pathological manifestations of Coronavirus Disease 2019 (COVID-19) in golden Syrian hamster model: implications for disease pathogenesis and transmissibility. *Clin Infect Dis* 2020 Mar 26; ciaa325. doi: 10.1093/cid/ciaa325.
- Fischer K, Hoffmann P, Voelkl S, Meidenbauer N, Ammer J, Edinger M, et al. Inhibitory effect of tumor cell-derived lactic acid on human T cells. *Blood* 2007;109: 3812-9.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395: 497-506.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395: 507-13.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020;323:1061-9.
- Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020 Mar 13: e200994. doi: 10.1001/jamainternmed.2020.0994.
- Deng Y, Liu W, Liu K, Fang YY, Shang J, Zhou L, et al. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study. *Chin Med J (Engl)* 2020;133:1261-7.
- Fan BE, Chong VCL, Chan SSW, Lim KGE, Tan GB, Mucheli SS, et al. Hematologic parameters in patients with COVID-19 infection. *Am J Hematol* 2020; 95:E131-4.
- Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. *Clin Chem Lab Med* 2020;58:1063-9.
- Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID19) and other viral outbreaks. *Clin Chem Lab Med* 2020
- Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. *JAMA Cardiol* 2020 Mar 25: e200950. doi: 10.1001/jamacardio.2020.0950.
- Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol* 2020 Mar 27: e201017. doi: 10.1001/jamacardio.2020.1017.
- Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. *Clin Chim Acta* 2020;506: 145-8.
- Yang X, Yang Q, Wang Y, Wu Y, Xu J, Yu Y, et al. Thrombocytopenia and its association with mortality in patients with COVID-19. *J Thromb Haemost* 2020;18:1469-72.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507-13.