Japan Journal of Research

Original Article

The Effects of Different Treatment Methods on Blood Hematological Parameters İn COVID 19: A Retrospective Look at Patients in Pandemic İntensive Care Unit During The First Wave of the Pandemic

Yesim Cokay ABUT[1,2], Kubra Bolat Gursoy[3], Fusun ADAM[1,2], Didem SARI[1,2], Ece KISA[1,2]

[1]University of Health Sciences, Faculty of Medicine, Istanbul, Turkey
[2]Education and Training Hospital, Anesthesiology and Reanimation Department, Fatih, Istanbul, Turkey
[3]Saray Hospital, Kirklareli, Turkey

Correspondence

Yesim Cokay ABUT, MD Assoc.Prof

Topkapi Mah.Kahalbasi Sok.No:46 DA:3 Fatih Istanbul TURKEY
Tel: 90 537 681 26 40
E-Mail: yesimabut2000@yahoo.com
ORCID id: 0000-0001-8763-605X

- Received Date: 11 Sep 2024
- Accepted Date: 20 Sep 2024
- Publication Date: 21 Sep 2024

Keywords

COVID , favipiravir, methylprednisolone, tocilizumab

Abstract

Introduction: *In this study, we compared the pre- and post-treatment values of basic hematological parameters in severe COVID 19 patients, whose were received favipiravir, tocilizumab, methylprednisolone and convalescent plasma therapy.*

Methods: *Hematological parameters such as eosinophyl, neutrophil, lymphocyte, platelet count and, neutrophil / lymphocyte, platelet/ lymphocyte ratio were investigated pre and post treatment of favipiravir, tocilizumab convalescent plasma and methylprednisolone in severe COVID 19 patients in ICU.*

Results: *Lymphocyt values were increased after convelescent plasma theraphy and i.v. methyl prednisolon group. Eosinophil count improvement was only in the favipiravir group . We found that favipiravir, convalescent plasma andmethyl prednisolon treatment, were statistically significant increased both NLR and PLR.*

Conclusion : *Hematologic parameters and their contribution of the respond of the treatment and clinical improvement should be taken into account.*

Introduction

By the end of 2019, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was first defined in China. Then the disease was named as Coronavirus Disease 2019 (COVID 19) which spread out all over the world and became a pandemic, unfortunately causing huge mortality and collapse of the healthcare and economic systems globally [1,2]. The first COVID 19 case announced to the public in Turkey on March the 11th, 2020.

COVID 19 is a disease that can damage organs and systems. The main methods used in the diagnostics of COVID 19 are polymerase chain reaction (PCR), thoracal computerized tomography (CT), some biochemical parameters like C-reactive protein (CRP), fibrinogen, D-dimer, interleukin (IL) 5, 6, 10, and complete blood count. Complete blood count is commonly used as a routine test in medical laboratories and in clinical practice. It is performed easily, quickly; and provides cost-effective results. Today there are many reports about the hematological parameters and their role for the prognosis of COVID 19.

Most commonly used parameters to determine prognosis and outcome in COVID 19 patients are lymphopenia, neutrophilia, leukocytosis, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and monocyte-to-lymphocyte ratio (MLR). It is well-known that they are correlated with overall disease severity, progression and mortality [3-6]. According to some studies, changes in eosinophile and platelet counts were also important in these patients [7-9].

In this study, we compared the pre- and post-treatment values of basic hematological parameters in severe COVID 19 patients, who had been treated with favipiravir, tocilizumab, methylprednisolone and convalescent plasma.

Material and methods

We conducted an observational, retrospective study of the data of 102 patients admitted with severe COVID 19 pneumonia, in Turkey, at xxxx Pandemic COVID 19 Intensive Care Unit which was established under emergency conditions, between 29th March 2020 and 15th June 2020.

Citation: Abut YC, Gursoy KB, Adam F, Sari D, Kısa E. The Effects of Different Treatment Methods on Blood Hematological Parameters İn COVID 19: A Retrospective Look at Patients in Pandemic İntensive Care Unit During The First Wave of the Pandemic. Japan J Res. 2024;5(8):059

This study was performed with the permissions of Scientific Research Platform of the Republic of Turkey Ministry of Health (Permit No: 2020-06-11T12_14_26) and University of Health Sciences İstanbul Training and Research Hospital Ethics Comiteee (decision no: 2020/2472, date: 10th July 2020).

COVID 19 pneumonia was diagnosed with real time-PCR (RT-PCR), CT scan and patients' contact history.

Severe illness was defined as present or suspected respiratory infection with/without fever, and in addition, respiratory rate >30 breaths/min or severe respiratory distress or oxygen saturation (SpO2) ≤93% on room air. Critical illness was defined as present acute respiratory distress syndrome or sepsis with any acute organ dysfunction [10]. All the patients who had severe or critical illness were followed and treated in the intensive care unit.

The treatments of the patients were planned according to the COVID 19 Adult Patient Treatment Guide which is relevant to the General Directorate of Public Health Department of the Turkish Ministry of Health. With the contribution of infectious diseases and hematology specialists, the current guidelines of WHO and Turkish Republic Ministry of Health were analyzed and performed.

Favipiravir and tocilizumab orders were prescribed according to the recommendations of the Health Ministry by the infectious diseases specialists based on patients' IL-6 and ferritin levels. Plasma treatments were given accordingly to the hematologists' advice.

According to this guide, treatment protocols were as follows:

Tocilizumab treatment

The first dose of tocilizumab was administered as 400 mg, and a dose of 400 mg was repeated within 24 hours. [11]

Convalescent plasma application:

Convalescent plasma was prepared by the Turkish Red Crescent and obtained from volunteers' donors' suitable blood who have recently recovered in two weeks and with neutralizing antibody titer above 1: 640. We transfused patients with a dose of 200 mL of inactivated convalescent plasma in 4 hours according to the World Health Organization (WHO) blood transfusion protocol.

Steroid application:

Patients with procalcitonin level over 1 and above during follow-ups were considered as affected by secondary infection. In patients with procalcitonin level < 1, methylprednisolone was administered (40 mg/day for 3 days and gradually reduced and stopped in 5 days).

Demographic data and laboratory values of 102 patients were obtained from the formal medical records of hospital. Complete blood count parameters (ADVIA 2120 Hematology System -Siemens Healthcare Diagnostics, Erlangen, Germany) were recorded at the admission of intensive care unit before and 24 hours after the end of each treatment.

Pre- and posttreatment values of eosinophils, neutrophils, lymphocytes, platelets count, NLR and PLR were compared in favipiravir, tocilizumab, convalescent plasma and methylprednisolone treatments.

Statistics

Statistical analyzes were performed with the help of SPSS version 25.0 program. The conformity of the variables to the normal distribution was examined by histogram graphics and the Kolmogorov-Smirnov test, and it was observed that they were not normally distributed. Mean, standard deviation, median and quartile values were used when presenting descriptive analyzes. Pre-post changes in measured values were analyzed by Wilcoxon Test because the analyzed differences did not normally distribute. Results where the p value was below 0.05 were considered as statistically significant.

Results

The effects of favipiravir, convalescent plasma, methylprednisolon and tocilizumab treatments on lymphocyte, neutrophil and paletelet counts, NLR and PLR in 102 patients who were hospitalized in the Haseki Pandemic Intensive Care Unit due to severe COVID 19 infection were retrospectively analyzed. Female / male ratio was 42/60 and mean age was 63.46±2.2 years. 14 patients who were admitted to intensive care unit died before completing their first 24-hour-period. 30 patients in total couldn't complete their treatments in the first 7 days. Their data were not included. Comorbidities were asthma (n:4), Alzheimer and Parkinson disease (n:8), cardiovascular events (Previous heart failure, atrial fibrillation) (n:31), renal insufficiency (n:17), malignant diseases (n:17), previous cerebrovascular accident (n:9),COPD (n:5), Diabetes Mellitus (n:19), arterial hipertension (n:29)

APACHE II scores of 78 patients were above 30 and none of the APACHE scores was below 20. Mean score was 26. Prone position was performed on 32 patients for 8-hours-period. 18 patients were followed with HFNO and NIMV. 11 patients were followed with O2 mask on prone position. 3 of them were intubated after 48 hour after their admission of the ICU. The rest of the patients were intubated right away at the admission to hospital.

53 patients received Favipravir, 14 patients received plasma, 17 patients received methylpredisolone, 19 patients tocilizumab and 30 patients received multiple drug treatment. 7 patients receieved all treatments with at least 1 week breaks. 4 patients received favipravir plus tocilizumab and plasma, 4 patients received favipravir and methylprednisolone, 10 patients received favipravir and both tocilizumab, 6 patients received favipravir and methylprednisolone.

6 of the 14 patients receiving plasma were deceased. 9 of the 19 patients receiving tocilizumab died. 9 of the 16 patients receiving methylprednisolone were deceased. Mean intensive care unit stay was 10.73±13.35 days (Table 1)

18 of the patients survived in the 30-day-follow-ups. Major mortality causes were cardiac thromboembolism (n:37) and kidney failure (n:12) and pneumosepsis (n:10).

Eosinophil, NLR and PLR levels after favipiravir treatment were significantly higher than pretreatment levels (Table 2).

No statistically significant differences were found between pre- and posttreatment hematologic measurements of patients receiving tocilizumab treatment.

The differences between eosinophil, neutrophil, PLR values before and after convalescent plasma treatment were not statistically significant neither. Lymphocyte and NLR levels before treatment with immune plasma were significantly higher than posttreatment levels.

There was no significant difference between pre- and posttreatment levels of eosinophil, neutrophil, NLR and PLR with methylprednisolone treatment. However, lymphocyte levels significantly increased after methylprednisolone treatment.

Table 1. *Demographic Characteristic of The Patients*

		n	%
Gender	Female Male	42 60	(41.17) (58.82)
Age(Year)	63.46±2.4*		
APACHE II Skore	25.09±6.59*		
PCR	+ -	55 42	(57.29) (41.17)
Comorbidities	Hypertension Ischemic Heart Disease Diabetes Mellitus Astım COPD Renal insufficiency CVA Alzheimer/Parkinson Pregnancy Cancer	29 31 19 2 5 17 9 8 1 17	(28.43) (30.39) (18.62) (1.96) (4.90) (16.6) (6.84) (8.82) (0.96) (16.66)
Treatments	Favipiravir Tocilizumab M.prednisolone	53 19 16	(51.96) (18.62) (15.68)
Convalescent	Plasma Exitus(<7 days) Exitus (ICU Follow up) Recovery ICU stay(day) Survive (30 day)	14 14 45 43 10.73±13.35* 18	(13.72) (13.72) (44.11) (42.16) (17.64)

*:Mean±SD PCR (Polymerase Chain Reaction), COPD (Chronic obstructive pulmonary disease), CVA (cerebrovascular accident) ICU(Intensive Care Unit)

Table 2. *Hematological variable results before and after Favipiravir, CP and MP treatment*

		Mean	S.D.	Med	Q1	Q3	p
	Pre- T* eosinophyl	0.04	±.08	0.01	0	0.03	<0.001
	Post- T eosinophyl	0.07	±.11	0.03	0	0.1	
Favipiravir	Pre –T- NLR	9.21	±9.34	6.13	3.59	10.88	0.049
	Post- T- NLR	11.23	±9.33	9.22	4.72	14.6	
	Pre- T- PLR	302.98	±593.67	202.52	103.37	350	0.02
	Post -T - PLR	318.54	±243.73	249.38	147.87	454.55	
		0.93	±.43	0.97	0.53	1.28	0.022
Convalescent Plasma	Pre- T Lymphocyte						
	Post- T Lymphocyte	1.39	±1.23	1.06	0.73	1.56	
	Pre –T- NLR	11.46	±9.56	8.83	5.05	15.95	0.013
	Post –T- NLR	7.3	±4.82	5.53	3.56	12.09	
Methylprednisolone		0.73	±.50	0.65	0.48	0.94	0.023
	Pre- T -Lymphocyte						
	Post- T- Lymphocyte	1.24	±1.22	0.92	0.51	1.57	

CP:Convelescent Plasma, MP:Methyl Prednisolone, T*: Treatment, NLR:Neutrophyl Lymphocyt Ratio, PLR:Platelet Lymphocyt Ratio
Wilcoxon Paired Two Sample Test

Discussion

There are many reports today about the hematological parameters and their role for the prognosis of COVID 19. Especially lymphopenia, neutrophilia, thrombocytopenia, eosinopenia and their proportional values were studied. However, the effects of various treatment modalities which were used in COVID 19 on these hematological parameters have not been investigated.

The most frequently reported hematological abnormality/ pathology/dysfunction in COVID 19 is lymphopenia and it can be explained with direct lymphocyte lysis through virus binding to angiotensin converting enzyme 2 (ACE2) receptors, cytokine storm related lymphocyte apoptosis and exhaustion of T lymphocytes [4,12]. Additionally, lymphopenia has been found inversely related to viral load [13] In our study, lymphocyte values were increased after convalescent plasma treatment and intravenous methylprednisolone treatment, as expected.

Khalid et al. reported that neutrophilia occurred commonly in COVID 19 patients who needed hospital admission, and they pointed out that the cause of neutrophilia may be the cytokine storm due to elevated IL levels [14]. Additionally, superimposed bacterial infections and drugs used for treatment in COVID 19 might also cause this presentation [7,15-18]. However, in our study, treatments with various drugs such as favipiravir, tocilizumab, convalescent plasma and methylprednisolone did not create any changes in neutrophil counts.

Palladino et al and Lippi et al reported that the presence of thrombocytopenia is strongly related to the severity of COVID 19 pneumonia. The virus may cause thrombocytopenia by three mechanisms. The first one is the virus' invading the bone marrow and therefore inhibiting platelet production; the second one is the destruction of platelets by the cells of immune system and the last one is the aggregation of platelets in the lungs with the formation of microthrombi [19-22].

On the contrary, when we compared the platelet values before and after various treatments in COVID 19, we did not find any change.

Neutrophil to lymphocyte ratio and PLR are the signs of systemic inflammation, and they are strongly related to immune responses. There are many studies about these parameters and their relationships with other diseases. For example, NLR has been associated with coronary heart disease, inflammatory bowel disease, thyroiditis, malignancies and diabetes mellitus, and PLR is associated with diabetes mellitus or tumors [23-29].

Some studies have also shown that NLR and PLR are prognostic and independent risk factors for COVID 19, and neutrophil count and NLR were significantly higher in non-severe patients [7,30,31]. Sun et al. found higher PRL levels, lower eosinophil and lymphocyte counts in COVID 19 patients compared to the control group, however, Shang et al. claimed that NLR was the best determinant of all [32,33]. Similarly, Kazancioglu et al comparing influenza and COVID 19 found that the lymphocyte count, and NLR and PLR values were seen as more useful parameters than the others [34].

In the light of these data, we investigated the NLR and PLR responses to various treatment methods against COVID 19 and found that in severe COVID 19 patients, favipiravir, convalescent plasma and methylprednisolone treatments caused statistically significant increases in both NLR and PLR.

In our study, we evaluated the lymphocyte, neutrophil, platelet and eosinophil counts and NLR and PLR values derived from the count changes of these parameters as a response to various treatment methods against COVID 19. Lymphocyte values were increased after convalescent plasma treatment and intravenous methylprednisolone group. Recovery in eosinophil count was only seen in the favipiravir group.

Favipiravir, tocilizumab, convalescent plasma and methylprednisolone treatments did not create any changes on neutrophil and platelet counts. We found that favipiravir, convalescent plasma and methylprednisolone treatments caused statistically significant increases in both NLR and PLR.

Eosinophils have many functions including immunoregulation and antiviral activity. It has been reported that eosinopenia may predict an important role for prognosis in COVID 19 and may return to normal values before discharge [35-37]. However, we found statistically significant eosinophil count increase only in the favipiravir group in our study.

Limitations

One of the limitations of our study is that it was conducted in a field hospital under scant emergency pandemic conditions. In addition, the patients with multiple co-morbidities and the ones using multiple medications were included. If we had sufficient number of patients, it could be investigated whether these hematological changes related to treatment agents have any effect in mortality and recovery. In literature, there is a little clinical evidence about the patients' hematological responses to different treatment methods in COVID 19.

Conclusion

We would like to state that the positive aspects of our work are that the tension in the first peak of COVID 19, under the complicated conditions of these days, the follow-ups were in an isolated intensive care unit by a small number of experts in a coordinated manner and that the datas were collected carefully and documented in a healthy manner after the chaos had passed.

In addition, as it is known, diseases who affected more than one organ system , are usually treated with different treatment methods and it is difficult to evaluate the effectiveness of each treatment individually .Especially in this epidemic, we observe that the disease progresses very rapidly, the treatments change rapidly, but the effectivities of the treatments cannot be followed at an equal rate.

There are many new treatment options for the COVID 19 today even if there is no absolute cure yet. We would like to state that these follow-up parameters can be counted among the fast and inexpensive methods that can be used anywhere and anytime, especially in epidemics, not only for prognosis but also for evaluating the effectivities of the treatments of the disease.

Conflict of interest

The authors declare that there is no conflict of interest that may have influenced either the conduct or the presentation of the research between them.

References

1. Ju H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan,China:the mistery and miracle.J Med Virol.2020;92:401-2. Doi: 10.1002/jmv.25678
2. Lu R, Zhao X, Li J, et al.Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. The Lancet 2020;395:565–574. Doi: 10.1016/S0140-6736(20)30251-8

3. Karimi A, Shobeiri P, Kulasinghe A, Rezaei N. Novel Systemic Inflammation Markers to Predict COVID-19 Prognosis. Front Immunol. 2021 Oct 22;12:741061. Doi: 10.3389/fimmu.2021.741061
4. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Hematological findings and complications of COVID -19. Am J Hematol. 2020;95:834–847. Doi: 10.1002/ajh.25829
5. Yang H, Xu Y, Li Z, et al. The clinical implication of dynamic hematological parameters in COVID-19: a retrospective study in Chongqing, China. Int J Gen Med. 2021;14:4073–4080. doi:10.2147/IJGM.S321292
6. Huang W, Berube J, McNamara M, et al. Lymphocyte subset counts in COVID-19 patients: a meta-analysis. Cytom Part A. 2020;97(8):772–776. doi:10.1002/cyto.a.24172
7. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharmacol. 2020;84:106504. doi:10.1016/j.intimp.2020.106504
8. Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J Infect. 2020;81(1)–e12. doi:10.1016/j.jinf.2020.04.002
9. Seyit M, Avci E, Nar R, et al. Neutrophil to lymphocyte ratio, lymphocyte to monocyte ratio and platelet to lymphocyte ratio to predict the severity of COVID-19. Am J Emerg Med. 2021;40:110–114. doi:10.1016/j.ajem.2020.11.058
10. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance. March 13, 2020. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-whennovel-coronavirus-(ncov)-infection-is-suspected
11. Turkish Ministry of Health. COVID-19 adult patient management and treatment guideline, 22 March 2020. Turkish Ministry of Health; 2020.
12. López-Collazo E, Avendaño-Ortiz J, Martín-Quirós A, Aguirre LA. Immune response and COVID-19: a mirror image of sepsis. Int J Biol Sci. 2020;16(15):2479–2489. doi:10.7150/ijbs.48400
13. Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci. 2020;63(3):364–374. doi:10.1007/s11427-020-1643-8
14. Khalid A, Jaffar MA, Khan T, et al. Hematological and biochemical parameters as diagnostic and prognostic markers in SARS-COV-2 infected patients of Pakistan: a retrospective comparative analysis. Hematology. 2021;26(1):529–542. doi:10.1080/16078454.2021.1950898
15. Gong J, Ou J, Qiu X, et al. A tool for early prediction of severe coronavirus disease 2019 (COVID-19): a multicenter study using the risk nomogram in Wuhan and Guangdong, China. Clin Infect Dis. 2020;71(15):833–840. doi:10.1093/cid/ciaa443
16. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020;71(15):762–768. doi:10.1093/cid/ciaa248
17. Metzemaekers M, Cambier S, Blanter M, et al. Kinetics of peripheral blood neutrophils in severe coronavirus disease 2019. Clin Transl Immunol. 2021;10(3) . doi:10.1002/cti2.1271
18. Liu X, Zhang R, He G. Hematological findings in coronavirus disease 2019: indications of progression of disease. Ann Hematol. 2020;99(7):1421–1428. doi:10.1007/s00277-020-04103-5
19. Palladino M. Complete blood count alterations in COVID-19 patients: a narrative review. Biochem Med. 2021;31(3):030501. doi:10.11613/BM.2021.030501
20. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. Clin Chim Acta. 2020;506:145–148. doi:10.1016/j.cca.2020.03.022
21. Zong X, Gu Y, Yu PH, Li Z, Wang Y. Thrombocytopenia is associated with COVID-19 severity and outcome: an updated meta-analysis of 5637 patients with multiple outcomes. Lab Med. 2021;52(1):10–15. doi:10.1093/labmed/lmaa067
22. Thachil J. What does monitoring platelet counts in COVID-19 teach us? J Thromb Haemost. 2020;18(9):2071–2072. doi:10.1111/jth.14879
23. Hideki W, Tomotaka D, Katsumi M, et al. Neutrophil to lymphocyte ratio and long-term cardiovascular outcomes in coronary artery disease patients with low high-sensitivity C-reactive protein levels. Int Heart J. 2020;61(3):447–453. doi:10.1536/ihj.19-543
24. Posul E, Yilmaz B, Aktas G, Kurt M. Does neutrophil-to-lymphocyte ratio predict active ulcerative colitis? Wien Klin Wochenschr. 2015;127(7-8):262–265. doi:10.1007/s00508-014-0683-5
25. Gulali A, Mustafa S, Oguz D, et al. Elevated neutrophil-to-lymphocyte ratio in the diagnosis of Hash-imoto's thyroiditis. Rev Assoc Med Bras. 2017;63(12):1065–1068. doi:10.1590/1806-9282.63.12.1065
26. Sit M, Aktas G, Erkol H, et al. Neutrophil to lymphocyte ratio is useful in differentiation of malign and benign thyroid nodules. P R Health Sci J. 2019;38(1):60–63. PMID: 30924917
27. Duman TT, Aktas G, Atak BM, et al. Neutrophil to lymphocyte ratio as an indicative of diabetic control level in type 2 diabetes mellitus. Afr Health Sci. 2019;19(1):1602–1606. doi:10.4314/ahs.v19i1.35
28. Atak B, Aktas G, Duman TT, et al. Diabetes control could be monitored through platelet-to-lymphocyte ratio in hemograms. Rev Assoc Med Bras. 2019;65(1):38–42. doi:10.1590/1806-9282.65.1.38
29. Dalpiaz O, Krieger D, Ehrlich GC, et al. Validation of the preoperative platelet-to-lymphocyte ratio as a prognostic factor in a European cohort of patients with upper tract urothelial carcinoma. Urol Int. 2017;98(3):320–327. doi:10.1159/000452109
30. Ding X, Yu Y, Lu B, et al. Dynamic profile and clinical implications of hematological parameters in hospitalized patients with coronavirus disease 2019. Clin Chem Lab Med. 2020;58(8):1365–1371. doi:10.1515/cclm-2020-0411
31. Qu R, Ling Y, Zhang YHZ, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19. J Med Virol. 2020;92(9):1533–1541. doi:10.1002/jmv.25767
32. Shang W, Dong J, Ren Y, et al. The value of clinical parameters in predicting the severity of COVID-19. J Med Virol. 2020;92(10):2188–2192. doi:10.1002/jmv.26031
33. Sun S, Cai X, Wang H, et al. Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China. Clin Chim Acta. 2020;507:174–180. doi:10.1016/j.cca.2020.04.024
34. Kazancioglu S, Bastug A, Ozbay BO, et al. The role of haematological parameters in patients with COVID-19 and influenza virus infection. Epidemiol Infect. 2020;148
35. . doi:10.1017/S0950268820002742

36. Lindsley AW, Schwartz JT, Rothenberg ME. Eosinophil responses during COVID-19 infections and coronavirus vaccination. J Allergy Clin Immunol. 2020;146(1):1–7. doi:10.1016/j.jaci.2020.04.021

37. Chen R, Sang L, Jiang M, et al. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19 patients in China. J Allergy Clin Immunol. 2020;146(1):89–100. doi:10.1016/j.jaci.2020.05.003

38. Liu F, Xu A, Zhang Y, et al. Patients of COVID-19 may benefit from sustained lopinavir-combined regimen and the increase of eosinophil may predict the outcome of COVID-19 progression. Int J Infect Dis. 2020;95:183–191. doi:10.1016/j.ijid.2020.03.013