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Vojislava Milutinović[1,♣], Mirjana Kovač[2,3], Bogdan Crnokrak[1,2], Marija Zdravković[1,2]

Assessment of blood transfusion use during hospital treatment of COVID-19 patients – a single center experience

Примена компонената крви код болесника лечених од инфекције ковида 19 – наша искуства

[1]Bežanijska Kosa University Hospital Medical Center, Belgrade, Serbia;
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[3]Blood Transfusion Institute of Serbia, Belgrade, Serbia

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♣Correspondence to:
Vojislava MILUTINOVIĆ
Bežanijska Kosa University Hospital Medical Center, Dr Žorža Matea bb, 11070 Belgrade, Serbia
E-mail: **vojislavasladic@gmail.com**

Assessment of blood transfusion use during hospital treatment of COVID-19 patients – a single center experience

Примена компонената крви код болесника лечених од инфекције ковида 19 – наша искуства

SUMMARY

Introduction/Objective There is very limited data regarding the need for transfusion and its effect on the overall mortality of patients with coronavirus disease 2019 (COVID-19). The aim of our study is to determine the need for blood component transfusion in patents treated for COVID-19 infection.

Methods This retrospective observational study included 4,426 COVID-19 positive patients, who were treated, in the period between June 23, 2020, and May 2, 2021, at the Bežanijska Kosa University Hospital Medical Center. Of these patients, 826 were treated in the intensive care units of the hospital. Of the total number of patients, 326 (7.4%) received transfusions. The clinical presentation, the structure of the applied transfusion therapy, the laboratory parameters, and the treatment outcome were analyzed in this study.

Results Of the 828 patients treated in the intensive care units, 151 (18.2%) patients required transfusion, while transfusion was necessary in a total of 4.9% of patients treated in the hospital wards. Of the total number of all transfused patients, 86% received erythrocytes, one third of them received fresh frozen plasma, 10% received cryoprecipitate, while platelets were administered in around 6% of the patients. The mortality rate in the tested group was 46%.

Conclusion The frequency of the application of blood components was significantly higher in patients with a severe form of the disease. The presence of comorbidities did not affect the need for transfusion therapy. In the group of patients treated in the intensive care units, 85% received erythrocytes, 39% received fresh frozen plasma, 19% received cryoprecipitate and 7% received platelets.

Key words: transfusion; blood components; COVID-19

САЖЕТАК

Увод/Циљ Постоји веома мало података о потреби за трансфузијом и њеном утицају на укупан морталитет пацијената са инфекцијом ковида 19. Циљ нашег истраживања је да се утврди потреба за трансфузијом крвних компоненти код пацијената лечених од инфекције ковид 19.

Методе У ретроспективну опсервациону студију, која је укључила 4426 болесника позитивних на ковид 19, који су у периоду од 23. јуна 2020. до 2. маја 2021 . године лечени у Клиничко-болничком центру „Бежанијска коса" а 826 у јединицама интензивне неге. Од укупног броја болесника, 326 (7,4%) примало је трансфузију. Анализирана је клиничка слика, структура примењене трансфузиолошке терапије и лабораторијски параметри и исход лечења.

Резултати: Од 828 болесника који су лечени у јединици интензивне неге, 151 (18,2%) је захтевао трансфузију, док је проценат пацијената лечених на одељењима који су захтевали трансфузију 4,9%. Од укупног броја свих трансфундованих болесника, 86% примило је еритроците, трећина је примила замрзнуту свежу плазму, 10% примило је криопреципитат, док су тромбоцити примењени код 6% болесника. Утврђена стопа морталитета у испитиваној групи је 46%.

Закључак: Учесталост примене крвних компоненти је била значајно већа код болесника са тешким обликом болести. Присуство коморбидитета није утицало на потребу за трансфузиолошком терапијом. У групи болесника са тешком клиничком сликом лечених у јединицама интензивне неге, 85% је примило еритроците, 39% примило је замрзнуту свежу плазму, 19% криопреципитат и 7% примило је тромбоците.

Кључне речи: трансфузија; компоненте крви; ковид 19

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly contagious and pathogenic coronavirus which emerged in late 2019, causing the pandemic of the acute respiratory disease – COVID-19 [1]. This disease caused the greatest global health crisis since the influenza pandemic of 1918 and led to the death of more than 6.5 million people worldwide [2].

COVID-19 is a respiratory and vascular which also significantly affects the hematological system and the hemostatic system. It is associated with hypercoagulability, which is directly induced by virally mediated damage or injury to the vascular endothelium, which is caused by cytokines [3].

Clinical presentation varies – from asymptomatic forms of the disease to respiratory insufficiency, which requires mechanical ventilation. Between 17.9% and 33.3% of patients have the asymptomatic form of the disease [4, 5].

In patients with the severe form of COVID-19 acute respiratory distress syndrome (ARDS) may develop, usually a week after the onset of symptoms [6]. Approximately 23% of patients develop the severe form of the disease with a mortality rate of around 6% of COVID-19 patients [7].

There is little data on the need for transfusion and its influence on the overall mortality of patients with COVID-19. Several publications have shown that, in total, between 6.2 % and 13.4% of all patients with the COVID-19 infection require transfusion support [8, 9, 10].

According to the data from the few studies available, the application of blood products is low in mild to moderately severe forms of the disease, and higher in patients with severe clinical presentation [11, 12]. Of the total number of all the components administered, 83% are erythrocytes [12].

The aim of this study is to present the need for transfusion of blood components in our patients treated for COVID-19, the clinical characteristics of these patients, the composition of the transfusion therapy administered, as well as the treatment outcome.

METHODS

The research was carried out as a retrospective observational study, which included 4,426 COVID-19 positive patients, treated at the Bežanijska Kosa University Hospital Medical Center, in the period between June 23, 2020, and May 2, 2021, of whom 826 were treated in the intensive care units of the hospital. In the observational period, the hospital was exclusively designated for treating COVID-19 patients.

Of the total number of patients, 326 (7.4%) received transfusions. The patients who received transfusions were divided into two groups. The first group included 155 patients treated in the hospital intensive care units, while the second group included 147 subjects treated

in the wards of the Bežanijska Kosa University Hospital Medical Center. The main criteria for ICU admission were radiographic or CT scan severity score progression, peripheral oxygen saturation (Sp02) below 93% despite maximal conventional supportive oxygen therapy, laboratory test results, and arterial blood gas test. The study inclusion criteria were as follows: all patients with a verified diagnosis of COVID-19 (confirmed by a PCR test in real time), patients above the age of 18 years, who met the criteria of disease severity for third stage or higher (according to the National COVID-19 Guidelines) [13], and who required blood component transfusion. Criteria for the exclusion of patients from the study were incomplete data and patients transferred to other medical facilities.

In relation to the treatment outcome, data for 326 patients were stratified as deceased and survivors. Survivors were subjects dismissed from hospital. For all patients, data was collected from the electronic medical histories – the *Heliant* information system and the transfusion services operating protocol.

Data related to basic patient demographic characteristics (sex, age, comorbidities, therapy), laboratory parameters (hematological parameters: red blood cell count, white blood cell count, platelet count, hemoglobin levels, hematocrit (HCT), mean corpuscular volume (MCV), hemostatic parameters (prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, D-dimer), biochemical parameters (C- reactive protein (CRP), urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, lactate dehydrogenase (LDH), ferritin), as well as data on oxygen support, were analyzed. All data on administered transfusion therapy are related to the type and number of received blood component units; they were taken from the transfusion services protocol and relate to the application of concentrated erythrocytes and platelets, fresh frozen plasma (FFP), cryoprecipitate, and convalescent plasma.

Statistical analysis

The absolute and relative numbers, in percentages, were used for describing categorical data. Numerical data were described as the arithmetic mean with standard deviation or as the median with range, depending on data distribution. Normality of distribution was tested with mathematical and graphical methods. Two independent groups of subjects (patients with the COVID-19 infection treated in the intensive care units and patients with the COVID-19 infection treated in the hospital wards) were compared in relation to categorical and numerical

variables. The difference in the distribution of categories of nominal data was determined with the chi-square test. For testing the difference in the value of numerical data, Student's t-test or the Mann-Whitney U test were used, depending on the normality of distribution. All statistical methods were considered statistically significant at the significance level of 0.05. Analysis was performed with the IBM SPSS Version 21 software.

The study was approved by the Ethics Committee of Bežanijska Kosa University Hospital Medical Center, Belgrade, Serbia (5425/1/).

RESULTS

The clinical characteristics of all patients who received transfusion therapy during hospitalization, the needs for transfusion therapy, and the treatment outcomes are presented in Table 1. Of the total number of all transfused patients, 86% received erythrocytes, one third of them received fresh frozen plasma, 10% received cryoprecipitate, while platelets were administered in around 6% of the patients. The mortality rate in the tested group was 46%.

The clinical characteristics of the patients who received blood transfusion during their treatment in the intensive care units, i.e., the hospital wards, are presented in Table 2. The distribution of the sexes was significantly different in the two examined groups ($p = 0.005$), with the male sex being more present amongst the patients in the intensive care units. The presence of cardiovascular diseases was significantly more common in COVID-19 patients with more severe clinical presentation treated in the intensive care units of the hospital ($p = 0.041$), while malignancies were more common in patients treated in the hospital wards ($p = 0.029$).

Table 3 presents the values of the hematological, hemostatic, and biochemical parameters prior to the application of transfusion therapy. Patients treated in the intensive care units had significantly lower red blood cell counts ($p = 0.024$) and platelet counts ($p = 0.002$), and significantly higher white blood cell counts ($p = 0.013$). Values of international normalized ratio (INR) ($p < 0.001$), aPTT ($p < 0.001$), and D-dimer ($p < 0.001$) were significantly higher in COVID-19 patients treated in the intensive care units, while the level of fibrinogen ($p = 0.025$) was higher in COVID-19 patients with a milder clinical presentation. All the tested biochemical parameters of liver function (direct bilirubin, $p = 0.001$; total bilirubin, $p = 0.009$; AST, $p < 0.001$; ALT, $p = 0.001$; LDH, $p < 0.001$; ferritin, $p < 0.001$), as well as the level of CRP ($p < 0.001$), were significantly elevated in COVID-19 patients treated in the intensive care

department. Also, all evaluated parameters of kidney function (urea, p = 0.001; creatinine, p = 0.043) were significantly higher in the group of COVID-19 patients treated in the intensive care units, as compared to the patients treated in the hospital wards.

Table 4 presents the composition of the applied transfusion therapy. In the group of patients who received blood transfusion during their treatment in the intensive care units, 85% received erythrocytes, 39% received fresh frozen plasma, 19% received cryoprecipitate and 7% received platelets. A significantly higher number of red blood cell units was given to COVID-19 patients treated in the intensive care units. Also, a significantly greater number of COVID-19 patients treated in the intensive care units received FFP, as compared to patients treated in the hospital wards (39% *vs.* 18%, p < 0.001). The administration of cryoprecipitate was recorded only in patients treated in the intensive care units.

Treatment duration in relation to transfusion therapy is presented in Table 5. The treatment of patients who required red blood cell transfusion during their treatment for COVID-19 lasted significantly longer.

DISCUSSION

This study shows that 7.4% of all patients who were treated in hospital for COVID-19 required the administration of transfusion therapy. Our results are similar to the results published in previous studies, which have shown that transfusion application in COVID-19 patients is not very high, and ranges between 6.2% and 13.4%. [1, 8, 9]. The most commonly applied blood component were erythrocytes, which were indicated in 86% of the total number of all transfused patients. Our results are similar to the results from a previously published study by De Simone et al., where red blood cells made up for 83% of the total number of all administered blood components during hospitalization [12]. Our study showed that significantly greater number of red blood cell units was administered to patients treated in the intensive care units than to patients with a milder clinical presentation, who were treated in the hospital wards. A significantly greater number of patients in intensive care received FFP, as compared to patients treated in hospital wards (39% *vs.* 18%). Similar data can be found in studies by several authors, which have shown that the need for transfusion is significantly greater in patients treated in intensive care [1, 8, 10, 12].

Data analysis shows that the application of cryoprecipitate is indicated in 10% , while the application of concentrated platelets is indicated in 6% of all COVID-19 patients who received

transfusion therapy during hospitalization. Anti-COVID plasma was given to three patients - two patients treated in the intensive care units and one patient treated in one of the hospital wards. The application of transfusions of platelets, FFP, and cryoprecipitate is low in COVID-19 patients who did not have major hemorrhage episodes, which was also confirmed in a study by Doyle et al. [14]. In our study, the percentage of transfused patients treated in the intensive care units was 18.2%, while the percentage of patients treated in the hospital wards who required transfusions was 4.9%. In a study by Grandone et al., the percentage of transfused patients in intensive care was 41.9%, while the percentage of transfused patients treated in the hospital wards was 10.3% [6], which is, in fact, significantly higher than in our study.

The mortality rate registered in our study, in the examined group, was 46%. These data are similar to the data from previous studies showing that mortality among COVID-19 patients who needed transfusions was between 34.8% and 45% [8]. According to the results of previously published studies, a great variation of mortality prevalence amongst COVID-19 patients admitted to hospital, which ranged from 5.8% to 30.7%, was registered [15, 16, 17].

Almost all of our subjects had at least one comorbidity. Amongst these comorbidities, the most frequent ones were cardiovascular diseases and diabetes mellitus, which is in keeping with the data from previous studies [15, 18–22]. The presence of cardiovascular diseases was significantly more frequent in COVID-19 patients with a more severe clinical presentation who were treated in the intensive care units, while malignancies were more present in patients with a milder clinical presentation who were treated in the hospital wards. The male sex was more present in intensive care patients than in patients with a milder clinical presentation treated in the hospital wards. The presence of comorbidities did not affect the need for transfusion support in patients with the COVID-19 infection.

Earlier studies have shown that both sexes have the same susceptibility to the disease, but that men have the tendency to develop a more severe form of COVID-19 and are more likely to have a lethal outcome [23, 24, 25].

Our study showed that patients with a more severe clinical presentation treated in the hospital intensive care units had significantly lower red blood cell counts and platelet counts, and significantly higher white blood cell counts, as compared to COVID-19 patients with a milder clinical presentation treated in the hospital wards, which is in keeping with earlier studies [26, 27, 28]. The platelet count is significantly lower in patients with the more severe form of COVID-19. In COVID-19 patients, a low platelet count is connected with a higher risk of the severe form of disease and of mortality [26].

Controlling the parameters of hemostasis may help in determining the predictors of an unfavorable prognosis in patients with the COVID-19 infection. Tang et al. reported that patients who had died of COVID-19 had significantly higher levels of D-dimer, longer prothrombin time (PT) and longer activated partial thromboplastin time, as compared to the surviving patients [29]. The concentration levels of D-dimer in the serum, in patients with severe forms of COVID-19, were significantly higher than in patients with the milder form of the disease [26, 29].

Similarly to the data published in previous studies [26, 28], our study shows that patients with a more severe clinical presentation of COVID-19 had significantly higher levels of CRP, ferritin, LDH, AST, ALT, bilirubin, urea, and creatinine, as compared to patients with a milder form of the disease treated in the hospital wards.

The administration of FFP was in correlation with the values of INR, aPTT, bilirubin, urea, and ferritin. Patients who received cryoprecipitate had significantly higher values of INR, aPTT, D-dimer, AST, ALT, LDH, and ferritin, and significantly lower levels of fibrinogen, as compared to patients who did not receive cryoprecipitate. In a study by DeSimone et al., high values of PT and aPTT were significantly linked with the need for transfusion, which was not the case with a low level of fibrinogen [12].

The average length of hospital treatment was 18 days, the shortest hospital stay was two days, while the longest was 102 days. In previous studies, the average length of hospital stay was between five and twenty-nine days [30]. Our study showed that the treatment of patients who required red blood cell transfusion during their treatment for COVID-19 lasted significantly longer. However, it should be pointed out that these were patients with a more severe clinical presentation of the disease, whose recovery lasted longer.

As to the study limitations, it should be pointed out that this is a retrospective study and that certain parameters were not available for all the subjects. However, bearing in mind that the study comprehensively analyzes the administration of blood to COVID-19 patients, the results of this study may be a good indicator of the need for transfusion in this category of patients, which is important for planning and carrying out the collection and distribution of blood and blood components, especially during an epidemiological state of emergency.

CONCLUSION

Of the total number of COVID-19 patients hospitalized in the observed period, 7.4% received transfusion support therapy. The frequency of application of blood components was significantly higher in patients with the severe form of the disease. The presence of comorbidity did not affect the need for transfusion therapy. The registered mortality rate in the examined group was 46%, however, we cannot say, with certainty, whether and to what degree transfusion contributed to the registered mortality rate. To provide definite information about the cause-effect relationship, prospective studies are necessary.

Conflict of interest: None declared.

REFERENCES

1. Hu B, Guo H, Zhou P, et Li Shi Z. Characteristics of SARS-CoV-2 and COVID-19. Nature Reviews Microbiology. 2021; 141-154.[DOI:10.1038/s41579-020-00459-7] [PMID: 33024307].
2. World Health Organization, COVID-19 Weekly Epidemiological Update, Edition 114 published 19 October 2022, Global overview, Data as of 16 October 2022
3. Cascella M, Rajnik M, Aleem A, Dulebohn SC et Di Napoli R. Features, Evaluation, and Treatment of Coronavirus (COVID-19)[Updated 2022 Feb 5]. In: StatPearls [Internet]. Treasure Island (FL):StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/[PMID: 32150360]
4. Mizumoto K, Kagaya K, Zarebski A, et Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 2020; 25(10) 2000180. [DOI: 10.2807/1560-7917.ES.2020.25.10.2000180][PMID: 32183930]
5. Nishiura H, Kobayashi T, Miyama T, Suzuki A, Jung S, Hayashi K et al. Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). Int J Infect Dis. 2020; 94:154-155.[DOI: 10.1016/j.ijid.2020.03.020][PMID: 32179137]
6. Grandone E, Pesavento R, Tiscia G, De Laurenzo A, Ceccato D, Sartori MT et al. Mortality and Transfusion Requirements in COVID-19 Hospitalized Italian Patients According to Severity of the Disease. J. Clin. Med. 2021;10(2):242.[DOI:10.3390/jcm10020242]
7. Li J, Huang DQ, Zou B, Yang H, Zi Hui W, Rui F et al. Epidemiology of COVID-19: A systematic review and meta-analysis of clinical characteristics, risk factors, and outcomes. J Med Virol. 2021; 93(3):1449-1458.[DOI: 10.1002/jmv.26424][PMID: 32790106]
8. Dalmazzo L, de Almendra Freitas, A.F. Alves BE, Cardoso DK, de Carvalho EF, Akil F et al. Transfusion profile, clinical characteristics, comorbidities and outcomes of 3014 hospitalized patients diagnosed with COVID-19 in Brazil. Vox Sanguinis. 2021;116(9):983-989.[DOI: 10.1111/vox.13087][PMID: 33634890]
9. Barriteau CM, Bochey P, Lindholm PF, Hartman K, Sumugod R et Ramsey G. Blood transfusion utilization in hospitalized COVID-19 patients. Transfusion. 2020;60(9):1919-1923. [DOI: 10.1111/trf.15947][PMID: 32583506]
10. Delabranche X, Kientz D, Tacquard C, Bertrand F, Roche AC, Tran Ba Loc P, et al. Impact of COVID-19 and lockdown regarding blood transfusion. Transfusion.2021; 61(8):2327-2335. [DOI: 10.1111/trf.16422][PMID: 34255374]
11. Fan BE, Ong KH, Chan SSW, Young BE, Chong VCL, Chen SPC, et al. Blood and blood product use during COVID-19 infection. Am J Hematol. 2020; 95(7):E158-E160.[DOI: 10.1002/ajh.25823][PMID: 32279352]
12. DeSimone RA, Costa VA, Kane K, Sepulveda JL, Ellsworth GB, Gulick RM, et al. Blood component utilization in COVID-19 patients in New York City: Transfusions do not follow the curve. Transfusion. 2021;61(3):692-698.[DOI: 10-1111/trf.16202] [PMID: 33215718]
13. Pelemiš M., Stevanović G., Turkulov V., Matijašević J., Milošević B., Milošević I. et al. National Protocol of the Republic of Serbia to Treat COVID-19 Infection . 10th 2020
14. Doyle AJ, Danaee A, Furtado CI, Miller S, Maggs T, Robinson SE, et al. Blood component use in critical care in patients with COVID-19 infection: a single-centre experience. British Journal of Haematology. 2020;191:382–385.[DOI: 10.1111/bjh.17007][PMID: 32640484]
15. Castro MC, Gurzenda S, Macario EM, et Franca GVA. Characteristics, outcomes and risk factors for mortality of 522 167 patients hospitalised with COVID-19 in Brazil: a retrospective cohort study. BMJ Open. 2021;11:e049089.[DOI: 10.1136/bmjopen-2021-049089] [PMID: 33947740]
16. Bertsimas D, Lukin G, Mingardi L, Nohadani O, Orfanoudaki A, Stellato B, et al. COVID-19 mortality risk assessment: An international multi-center study. 2020; PLOS ONE 15(12): e0243262. [DOI: 10.1371/journal.pone.0243262][PMID: 33296405]
17. Mehra MR, Desai SS, Kuy SR, Henry TD, et Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. N Engl J Med. 2020; 382:e102. [DOI: 10.1056/NEJMoa2007621]
18. Kaswa R, Yogeswaran P et Cawe B. Clinical outcomes of hospitalised COVID-19 patients at Mthatha Regional Hospital, Eastern Cape, South Africa: a retrospective study. South African Family Practice. 2021; 63(1): 5253. [DOI: 10.4102/safp.v63i1.5253][PMID: 34212748]
19. Zhang, Jj., Dong, X., Liu, Gh. et Gao Yd. Risk and Protective Factors for COVID-19 Morbidity, Severity, and Mortality. Clinic Rev Allerg Immunol. 2023; 64: 90–107 . [DOI: 10.1007/s12016-022-08921-5]
20. Jiménez E, FontánVela M, Valencia J, Fernandez-Jimenez I, Alvaro-Alonso EA, Izquierdo-Garcia E, et al. Characteristics, complications and outcomes among 1549 patients hospitalised with COVID-19 in a secondary hospital in Madrid, Spain: a retrospective case series study. BMJ open. 2020; 10:e042398. [DOI:10.1136/bmjopen-2020-042398][PMID: 33172949]
21. Isath A, Malik AH, Goel A, Gupta R, Shrivastav R et Bandyopadhyay D. Nationwide Analysis of the Outcomes and Mortality of Hospitalized COVID-19 Patients. Curr Probl Cardiol.2023;48(2):101440. [DOI:10.1016/j.cpcardiol.2022.101440][PMID: 36216202]

22. Jain V et Yuan JM. Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: a systematic review and meta-analysis. International journal of public health. 2020;65:533-546. [DOI: 10.1007/s00038-020-01390-7][PMID: 32451563]
23. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender differences in patients with COVID-19: focus on severity and mortality. Front. Public Health. 2020; 8:152. [DOI: 10.3389/fpubh.2020.00152][PMID: 32411652]
24. Guilmoto CZ. COVID-19 death rates by age and sex and the resulting mortality vulnerability of countries and regions in the world. MedRxiv, 2020; [DOI: 10.1101/2020.05.17.20097410]
25. Nguyen NT, Chinn J, De Ferrante M, Kirby KA, Hohmann SF et Amin A. Male gender is a predictor of higher mortality in hospitalized adults with COVID-19. PLoS ONE. 2021; 16(7): e0254066. [DOI: 10.1371/journal.pone.0254066]
26. Shang W, Dong J, Ren Y, Tian M, Li W, Hu J, et al. The value of clinical parameters in predicting the severity of COVID-19, Journal of medical virology. 2020; 92(10):2188-2192.[DOI:10.1002/jmv.26031][PMID: 32436996]
27. Kowsar R., Rahimi A.M., Sroka M., Mansouri A., Sadeghi K., Bonakdar E. et al. Risk of mortality in COVID-19 patients: a meta- and network analysis. Sci Rep. 2023; 13, 2138. [DOI:10.1038/s41598-023-29364-8]
28. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis. 2020;ciaa248. [DOI:10.1093/cid/ciaa248][PMID: 32161940]
29. Tang N, Li D, Wang X, et Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020; 18(4): 844-847.[DOI: 10.1111/jth.14768][PMID: 32073213]
30. Rees EM, Nightingale ES, Jafari Y, Waterlow NR, Clifford S, Pearson CAB. et al. COVID-19 length of hospital stay: a systematic review and data synthesis. BMC Medicine. 18, 270 (2020). [DOI: 10.1186/s12916-020-01726-3][PMID: 32073213]

Table 1. Characteristics of all patients who received a transfusion during their hospitalization due to COVID-19

Characteristic	Description
Age (years), $\bar{x} \pm sd$	69.80 ± 13.85
Sex (male *vs.* female), n (%)	172 (52.8) *vs.* 154 (47.2)
Comorbidity (yes), n (%)	315 (96.6)
Cardiovascular diseases (yes), n (%)	254 (77.9)
Diabetes mellitus (yes), n (%)	108 (33.1)
Pulmonary diseases (yes), n (%)	19 (5.8)
Kidney disease (yes), n (%)	44 (13.5)
Gastrointestinal and/or liver diseases (yes), n (%)	47 (14.4)
Thyroid disease (yes), n (%)	20 (6.1)
Malignancies (yes), n (%)	73 (22.4)
Other comorbidities (yes), n (%)	27 (8.3)
Number of comorbidities, med (min-max)	2 (0 - 5)
Severity of clinical presentation (mild illness *vs.* severe illness), n %	175 (53.7) *vs.* 151 (46.3)
Oxygen support, n (%)	
Without	24 (7.4)
Intubation	148 (45.4)
Noninvasive ventilation	13 (4.0)
Oxygen therapy	141 (43.3)
Transfusion support, n (%)	326 (7.4)
Erythrocytes	279 (85.6)
Platelets	21 (6.4)
Fresh frozen plasma	95 (29.1)
Cryoprecipitate	33 (10.1)
Anti-COVID plasma	3 (0.9)
Length of hospital treatment (days), med (min–max)	18 (2–102)
Treatment outcome (discharged *vs.* lethal outcome), n (%)	175 (53.7) *vs.* 151 (46.3)

Table 2. Comorbidities in COVID-19 patients who received a transfusion treated in the hospital intensive care units and wards

Parameter	Intensive care n = 175	Hospital wards n = 151	p*
Age (years), $\bar{x} \pm sd$	70.15 ± 15.44	69.50 ± 12.34	0.674
Sex (male *vs.* female), n (%)	105 (60) *vs.* 70 (40)	67 (44) *vs.* 84 (56)	**0.005**
Comorbidity (yes), n (%)	172 (98.3)	143 (94.7)	0.074
Cardiovascular diseases (yes), n (%)	144 (82.3)	110 (72.8)	**0.041**
Diabetes mellitus (yes), n (%)	60 (34.3)	48 (31.8)	0.633
Pulmonary diseases (yes), n (%)	9 (5.1)	10 (6.6)	0.570
Kidney disease (yes), n (%)	26 (14.9)	18 (11.9)	0.439
Gastrointestinal and/or liver diseases (yes), n (%)	22 (12.6)	25 (16.6)	0.307
Thyroid disease (yes), n (%)	11 (6.3)	9 (6)	0.903
Malignancies (yes), n (%)	31 (17.7)	42 (27.8)	**0.029**
Other comorbidities (yes), n (%)	14 (8)	13 (8.6)	0.842
Number of comorbidities, med (min–max)	2 (0–5)	2 (0–5)	0.712

*For the significance level of 0.05, according to the χ^2 test or the Mann–Whitney U test

Table 3. Hematological, hemostatic, and biochemical parameters prior to transfusion therapy

Parameters	Intensive care n = 175	Hospital wards n = 151	
Red blood cell count ($\times 10^{12}$/L) med (min–max)	2.6 (1.2–6.6)	2.8 (1.3–5.3)	**0.024**
White blood cell count ($\times 10^{9}$/L) med (min–max)	8.6 (0.05–175)	7.8 (0.2–86)	**0.013**
Platelet count ($\times 10^{9}$/L) med (min–max)	168.0 (1–631)	218.0 (13–843)	**0.002**
Hemoglobin (g/l) $\bar{x} \pm sd$	81.65 ± 22.88	82.70 ± 23.45	0.683
Hematocrit $\bar{x} \pm sd$	0.25 ± 0.07	0.26 ± 0.07	0.398
MCV (fL) $\bar{x} \pm sd$	88.89 ± 6.27	86.66 ± 10.32	**0.021**
INR med (min–max)	1.2 (0.8–10)	1.1 (0–11)	< **0.001**
aPTT (s) med (min–max)	29.8 (17.6–558)	25.4 (0–230)	< **0.001**
Fibrinogen (g/L) med (min–max)	3.7 (0.4 – 9.4)	3.7 (1.1–13.9)	**0.025**
D-dimer (ng/mL) med (min–max)	3,680 (203–35,200)	2,000 (23–26,720)	< **0.001**
Direct bilirubin (μmol/L)	4.3 (1.2–169)	3.3 (1.2–395)	**0.001**
Total bilirubin (μmol/L)	11.9 (2.5–183)	8.7 (2.5–634)	**0.009**
AST (U/L)	43 (9–6,500)	30.0 (7.0–481)	< **0.001**
ALT (U/L)	30 (5–6,484)	23 (5–309)	**0.001**
LDH (U/L)	792 (222–14,397)	520.0 (193–3,943)	< **0.001**
Ferritin (μg/L)	823 (36–4,214)	461 (5–9,125)	< **0.001**
Urea (mmol/L)	10.6 (2.1–39)	7.9 (0–80.9)	**0.001**
Creatinine (μmol/L)	116 (29–600)	99 (43–647)	**0.043**
CRP (mg/L) med (min–max)	167.9 (11.9 – 571.4)	73.7 (1.8–408.1)	< **0.001**

MCV – mean corpuscular volume; INR – international normalized ratio; aPTT – activated partial thromboplastin time; AST – aspartate aminotransferase; ALT – alanine aminotransferase; CRP – C-reactive protein; LDH – lactate dehydrogenase;

*For the significance level of 0.05, according to the Mann–Whitney U test

Table 4. Composition and doses of administered blood transfusions

Parameters	Intensive care n = 175	Hospital wards n = 151	p*
Number of patients who received erythrocytes, n (%)	148 (84.6)	131 (86.8)	0.576
Number of erythrocyte doses administered, med (min–max)	2 (1–21)	2 (1–11)	**0.005**
Number of patients who received platelets, n (%)	13 (7.4)	8 (5.3)	0.435
Number of platelet doses administered, med (min–max)	7 (4–13)	9 (5–32)	0.227
Number of patients who received fresh frozen plasma, n (%)	68 (38.9)	27 (17.9)	**< 0.001**
Number of fresh frozen plasma doses administered, med (min–max)	3 (1–23)	2 (0–10)	0.096
Number of patients who received cryoprecipitate, n (%)	33 (18.9)	0 (0)	**< 0.001**
Number of cryoprecipitate doses administered, med (min–max)	9 (5–47)	/	NA
Number of patients who received anti-COVID plasma, n (%)	2 (1.1)	1 (0.7)	0.650
Number of anti-COVID plasma doses administered, med (min-max)	2 (2–2)	2 (2–2)	1.000

*For the significance level of 0.05, according to the χ^2 test or the Mann–Whitney U test

Table 5. Treatment duration in relation to transfusion therapy in patients hospitalized due to COVID-19

Type of transfusion therapy	Treatment duration (days), med (min–max)		p*
	Yes	No	
Erythrocytes	18 (2–102)	15 (3–40)	**0.009**
Platelets	19 (7–42)	18 (2–102)	0.868
Fresh frozen plasma	18 (2–73)	17 (2–102)	0.656
Cryoprecipitate	20 (4–65)	17 (2–102)	0.264
Anti-COVID plasma	20 (19–30)	18 (2–102)	0.384

*For the significance level of 0.05, according to the Mann–Whitney U test

