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Anti-SARS-CoV-2 antibody responses in convalescent plasma donors with varying clinical manifestation severity of COVID-19

Anti-SARS-CoV-2 antitela kod rekonvalescentnih davalaca plazme sa različitom težinom kliničke slike COVID-19

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Abstract

Background/Aim. Plasma containing a high titer of anti-SARS-CoV-2 antibodies, donated from individuals who recovered from COVID-19, has the potential to be used as initial therapy for patients who have been infected (passive immunization). It is a challenge to find suitable donors. The aim of the study was to successively monitor antibody titer in donations and to investigate the correlation between antibody titer and the severity of the clinical manifestations. **Methods.** The retrospective study was conducted from May 1 to October 31, 2020, at the Blood Transfusion Institute of Vojvodina. Donors had to meet certain criteria for inclusion in the study: proven SARS-CoV-2 infection, detected SARS-CoV-2 antibodies in the serum/plasma, fulfillment of general criteria for performing plasmapheresis, and adequate laboratory findings. **Results.** During the study, 651 apheresis plasma units were collected and divided into two equal doses. Plasma was donated by 311 COVID-19 convalescents, including 208 (66.9%) men and 103 (33.1%) women. There were 15 (4.8%) plasma donors with asymptomatic infection, 235 (75. 6%) with a mild form of illness, 45 (14.5%) with a moderate form of illness, 16 (5.1%) with a severe form of illness, and none with a critical form of illness. Anti-SARS-CoV-2 IgG antibodies were present in the plasma of donors for more than 6 months after the disease. Plasma donors with a more severe clinical manifestation of COVID-19 had stable antibody levels for a longer period. However, the Pearson correlation of clinical severity and antibody titer did not confirm a statistically significant correlation between the variables. **Conclusion.** Anti-SARS-CoV-2 antibodies were present in the sample of recovered patients, plasma donors, for more than 6 months after the disease. Even though no statistically significant correlation was found between the anti-SARS-CoV-2 antibody titer and the clinical severity of COVID-19, in patients with a more severe clinical manifestations of the disease, stable antibody levels were maintained for a longer period.

Key words:
antibody formation; blood donors; COVID-19 serotherapy; immunization, passive; plasma.

Apstrakt

Uvod/Cilj. Plazma koja sadrži visok titar antitela na SARS-CoV-2, donirana od osoba koje su se oporavile od COVID-19, ima potencijal da se koristi kao inicijalna terapija kod obolelih u vidu pasivne imunizacije. Poseban izazov predstavlja izbor odgovarajućih davalaca plazme. Cilj rada bio je sukcesivno praćenje titra antitela u donacijama plazme i ispitivanje korelacije između titra antitela i težine kliničke slike koju su davaoci imali tokom bolesti. **Metode.** Retrospektivna studija sprovedena je od 1. maja do 31. oktobra 2020. godine na Institutu za transfuziju krvi Vojvodine. Davaoci su morali da ispune određene kriterijume za uključivanje u studiju: dokazana infekcija SARS-CoV-2, prisutna antitela na SARS-CoV-2 u serumu/plazmi, ispunjavanje opštih kriterijuma za izvođenje plazmafereze i referentne vrednosti laboratorijskih nalaza. **Rezultati.** Tokom studije prikupljeno je 651 jedinica aferezne plazme podeljenih u dve jednake doze. Plazmu je doniralo 311 COVID-19 rekonvalescenata, uključujući 208 (66,9%) muškaraca i 103 (33,1%) žena. Davalaca plazme sa asimptomatskom infekcijom bilo je 15 (4,8%), sa blagim oblikom bolesti 235 (75,6%), sa umereno teškim oblikom bolesti 45 (14,5%), sa teškim oblikom bolesti 16 (5,1%).

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Osobe sa kritičnim oblikom bolesti nisu donirale plazmu. Antitela klase IgG na SARS-CoV-2 bila su prisutna kod davalaca plazme više od šest meseci nakon bolesti, pri čemu su davaoci plazme koji su imali težu kliničku sliku COVID-19 imali stabilne vrednosti antitela tokom dužeg vremenskog perioda. Pearson-ova korelacija težine kliničke slike i titra antitela nije potvrdila njihovu statistički značajnu povezanost. **Zaključak.** Antitela klase IgG na SARS-CoV-2 bila su prisutna kod davalaca plazme više od šest meseci nakon bolesti. Iako nije nađena statistički značajna korelacija između titra antitela klase IgG na SARS-CoV-2 i težine kliničke slike COVID-19, utvrđeno je da se kod bolesnika koji su imali težu kliničku sliku bolesti, stabilan titar antitela održavao tokom dužeg vremenskog perioda.

Ključne reči:
antitela, stvaranje; krv, davaoci; COVID-19 seroterapija; imunizacija, pasivna; plazma.

Introduction

The most recently discovered severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) that causes coronavirus disease (COVID-19) appeared in Wuhan, China, in late 2019 [1]. The outbreak of the disease very quickly grew into a pandemic that was officially declared by the World Health Organization (WHO) on March 11, 2020 [2]. The virus, which belongs to the Coronavirus family with single-stranded ribonucleic acid (RNA), penetrates cells through the angiotensin-converting enzyme 2 (ACE2) receptor, which can be found on the cell surface of the heart, lungs, kidneys, gastrointestinal tract, and, as proven most important, on alveolar epithelial cells. It spreads from person to person by droplets, and most patients have a clinical presentation with mild symptoms. However, there may be a sudden deterioration of the patient's health, ranging from mild clinical picture to severe pneumonia with accompanying complications such as acute respiratory syndrome, sepsis, massive thromboembolism, hypercoagulability, and renal failure. Studies show that about 14% of patients with pneumonia develop a severe clinical presentation with a possible fatal outcome [3].

According to the WHO, up to and including January 15, 2021, over 223 countries were affected by the pandemic, and the virus infected 91,816,091 people, of whom 1,986,871 were fatalities (2.16% mortality rate) [4]. Apart from the fact that there is no specific therapy for COVID-19, the vaccine, the administration of which began in late 2020, is not expected to be available in sufficient quantities and in a short period of time in all world countries. The WHO and The Food and Drug Administration (FDA) issued a recommendation for the clinical trial of using convalescent plasma in patients who recovered from COVID-19 in 2020 [5, 6]. That is not the first recommendation for using convalescent whole blood or plasma in patients who have been infected. So far, the WHO has recommended a clinical trial in several cases: human influenza A (H1N1) in 2009, the Ebola epidemic in West Africa in 2014, Middle East respiratory syndrome (MERS) in 2015, and avian influenza A (H5N1) in 2019 [7].

Passive immunization with plasma containing a high titer of anti-SARS-CoV-2 antibodies has the potential to be used as an initial therapy. In addition, previous research shows that its application is most effective in the first three days after diagnosis or hospitalization of the patient [8].

Regardless of examining clinical parameters relevant to the timely administration of plasma, finding convalescent plasma donors with therapeutic potential poses a particular challenge. Studies show that the amount of antibodies that neutralize viral activity in the serum varies drastically among patients. A Chinese study described that 6% of patients did not produce detectable antibodies and that 30% had a very low titer [9].

The first apheresis procedure for the collection of convalescent COVID-19 plasma (CCP) for therapeutic purposes in the territory of Vojvodina was performed on May 1, 2020, as a part of the National Program for the CCP collection in Serbia. The study gives the qualifications which need to be fulfilled by donors in order to be included in the National Program, along with donor demographic characteristics. The main goal of the study was to successively monitor antibody values in donated plasma samples and investigate the correlation between antibody index and the severity of the clinical manifestations of COVID-19.

Methods

Study design

The retrospective study was conducted from May 1 to October 31, 2020, at the Blood Transfusion Institute of Vojvodina (BTIV), Novi Sad, Serbia. Data collected during the preparation of potential donors and during apheresis procedures were recorded in specially formed Registers of anti-COVID-19 plasma donors and the BTIV information system from where they were used for analysis.

The study was approved by the Ethic Committee of the BTIV with approval number 01–809/20 on November 16, 2020.

Donor inclusion criteria

Criteria for inclusion of patients who recovered from COVID-19 (potential donors) in the plasmapheresis procedure were as follows: proven SARS-CoV-2 infection either by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) from a nasopharyngeal swab specimen or serologically detected SARS-CoV-2 IgG antibodies (chemiluminescent immunoassay or enzyme-linked immunosorbent assay) in the serum/plasma of a potential donor – findings from any accredited laboratory were taken into consideration; more than 14 days have passed since the withdrawal of symptoms; there are no signs of acute infection; fulfillment of general criteria for performing plasmapheresis checked through questions in the questionnaire for donors and physician ex-

amination, and, thus, plasma donors can be persons between 18–60 years of age, weighing more than 60 kg, without comorbidities which are permanent contraindications for blood donation; appropriate vascular access for plasmapheresis procedure.

Laboratory testing

On the first arrival and after three months from the start of plasma administration, the following tests were performed: a rapid chromatographic test for antibodies [Innovita 2019-nCoV IgM/IgG Ab Test (Colloidal Gold), Innovita (Tangshan) Biological Technology CO., LTD, Hebei, China]; complete blood count with white blood cell count; biochemical analyses including total proteins, albumin, immunoglobulins (IgG, IgM, IgA), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), total and direct bilirubin, urea, creatinine, C-reactive protein (CRP) test; coagulation status [prothrombin time (PT) and international normalized ratio (INR), activated partial thromboplastin time (aPTT)]; donors with deviations from the normal values of these analyses were temporarily excluded from the procedure until their findings normalized; screening for anti-HLA (human leukocyte antigen) class I and II antibodies was performed for the donors with a prior history of pregnancy or transfusion; positive-test individuals (anti-HLA I and/or II) were excluded from the apheresis procedure (a total of 11 people) due to the prevention of transfusion-related acute lung injury – TRALI.

At each plasma donation, the following tests were performed: a) ABO/RhD blood group; b) red blood cell antibody screening; c) serological and molecular tests for markers of four transfusion-transmitted pathogens (human immunodeficiency virus, hepatitis B virus, hepatitis C virus, Treponema pallidum).

Donors with positive red blood cell antibody screening and/or serological/molecular tests for markers of transfusion-transmitted infections were permanently excluded from the procedure.

Before each plasma donation, in accordance with National Program for the CCP collection in Serbia, the value of the SARS-CoV-2 IgG antibody index was determined for all plasma donors' samples (Virclia COVID-19 ELISA IgG, Vircell S.L, Granada, Spain). Captured anti-SARS-CoV-2 antibodies were total antibodies to spike (S) glycoprotein and nucleocapsid (N) protein. Only donors with an antibody index > 6 were included in the procedure. Interpretation of the value over 6 was considered positive according to manufacturer protocol and used as appropriate for covid plasma donation.

During the first month of the observed period, plasma donors' antibodies were subsequently determined from archived specimens when serological tests became available. Donors with SARS-CoV-2 IgG antibody values below the cut-off were excluded from the program and are not the subject of research. Plasma with minimum antibody values over 12 was used for therapeutic purposes in the BTIV.

Plasma collection procedure

Plasma was collected by apheresis procedure on automated Haemonetics MCS + separators. The procedure lasted from 30 to 40 minutes, while the amount of plasma taken in the standard procedure was from 500 to 600 mL. Each unit taken was divided into two equal doses. Plasma was frozen within 6–8 hrs of collection and labeled "apheresis anti-COVID-19 fresh frozen plasma – clinical trial" with ABO blood group and laboratory testing for the transfusion-transmitted disease.

Assessment of disease severity

A potential donor with SARS-CoV-2 infection was grouped into the following severity of illness categories: Asymptomatic infection (AI): individuals with no symptoms that are consistent with COVID-19; Mild illness (MI): individuals with any of the following various signs and symptoms of COVID-19 – fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell; Moderate illness (MoI): individuals with shortness of breath, dyspnea, or abnormal chest imaging (showed evidence of lower respiratory tract disease during clinical assessment or imaging, oxygen saturation (SpO2) ≥ 94%); Severe illness (SI): individuals with SpO2 < 94%, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) < 300 mmHg, respiratory frequency > 30 breaths/min, or lung infiltrates > 50%; Critical illness (CI): individuals with respiratory failure, septic shock, and/or multiple organ dysfunction.

Statistical analysis

Data collected were analyzed using the statistical program Minitab 16, Wessa.net Pearson Correlation – Free Statistics Software (Calculator), and Microsoft Excel. Descriptive statistics were conducted for all variables. Data are presented in tables and graphs. Statistical significance was set at $p < 0.05$.

Results

During the study, 651 apheresis plasma units were collected and divided into two equal doses. Over the study period, plasma was donated by 311 COVID-19 convalescents, including 208 (66.88%) men and 103 (33.12%) women. The youngest donor was 18 years old, and the oldest was 60 (mean 38.40). Among donors, the most represented age group was 35–39 (Figure 1).

Donors distribution was as follows: a) by the place of residence: 3 donors from rural areas, 91 from urban settlements, and 217 from the city; b) by the time of falling ill: March 31, April 17, May 14, June 15, July 18, August 15, September 29, October 12; c) by the region of residence: South Bačka 200, West Bačka 9, North Bačka 13, North Banat 5, Central Banat 6, South Banat 28, Srem 44, Belgrade 4, Valjevo 2.

The number of donations during the study period was as follows: May 43, June 79, July 115, August 123, September 150, and October 141. Of the 311 convalescents, 52.7% donated plasma once (n = 164), 18.7% twice (n = 58), 10.9% three times (n = 34), 8.4% four times (n = 26), 4.8% five times (n = 15), 2.6% six times (n = 8) and 1.9% seven times (n = 6). Among donors residing outside the South Bačka district, 60.4% (n = 67) donated plasma only once.

In donors who donated plasma more than three times, it was noticeable that antibody titer values were maintained even after 6 months.

The index values of the serological test for SARS-CoV-2 IgG antibodies in donors ranged from 1.02 to 117.03 (average value 29.54). The distribution of donors with different SARS-CoV-2 IgG antibody index values is shown in Figure 2.

The rapid antibody detection test was positive in 187 (60.13%) and negative in 124 (39.87%) donors. The lowest value of SARS-CoV-2 IgG at which the rapid test was positive was 19.75. The rapid test was positive in all donors with a SARS-CoV-2 IgG index greater than 30.

During the six months of the observed period, donors from all groups with different illness severity criteria donated plasma at different time intervals (from 14 days and up) and a different number of times (from 1 to 7). On the first donation: the value of the index in the donors with MI and AI ranged from 1.03 to 117.03 (lower and upper extremes of a set of data), while in the donors with MoI and SI the values ranged from 3.97 to 102.82; the median was 60 in the donors with MI and AI and 54 in the donors with MoI and SI; the upper quartile (the median of the upper region) and the lower quartile (the median of the lower region) was 88 and 30 in

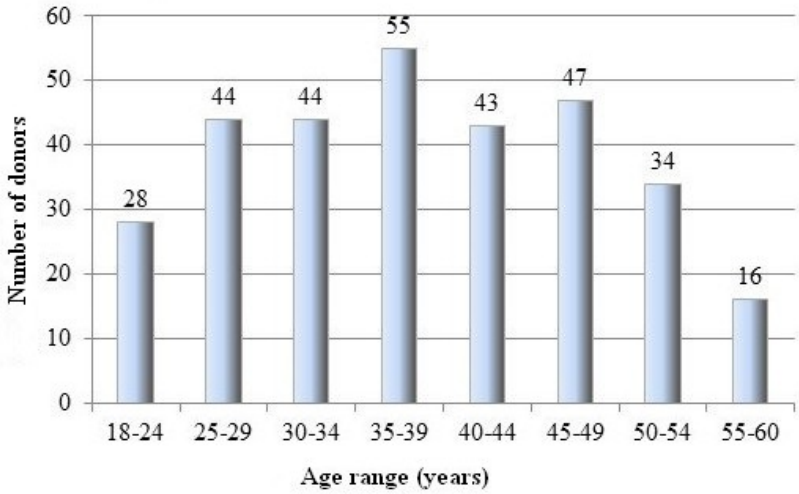


Fig. 1 – Age distribution of convalescent plasma donors.

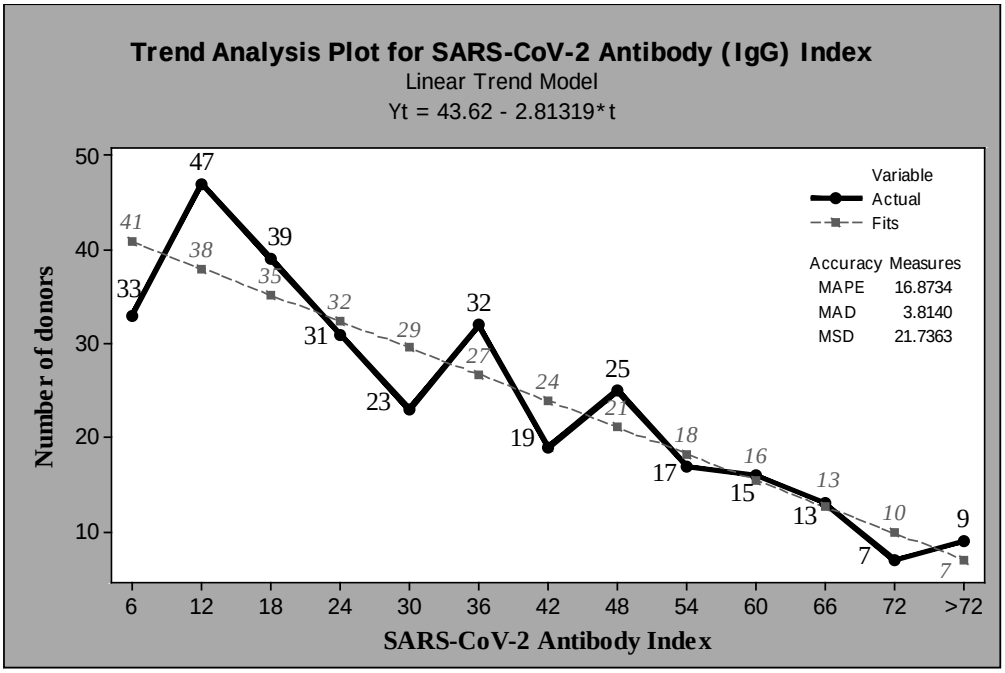


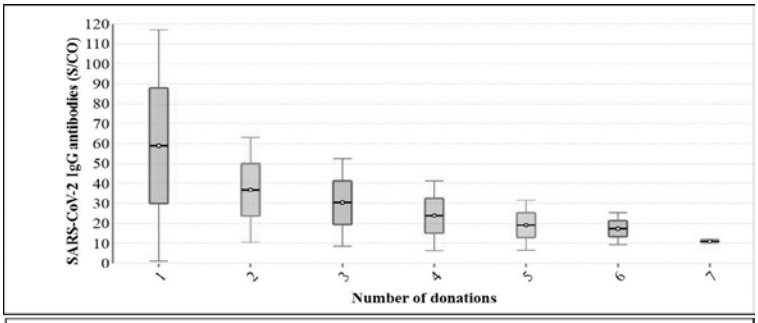
Fig. 2 – Distribution of covalescent plasma donors with different SARS-CoV-2 IgG antibody index.

the respective order in the donors with MI and AI and 29 and 78 in donors with MoI and SI (Figures 3 and 4).

Similar results of the index value were obtained during subsequent plasma donations among donors with MI and AI and donors with MoI and SI, suggesting that there is no statistical significance between the value of the antibody index and the clinical severity of the disease.

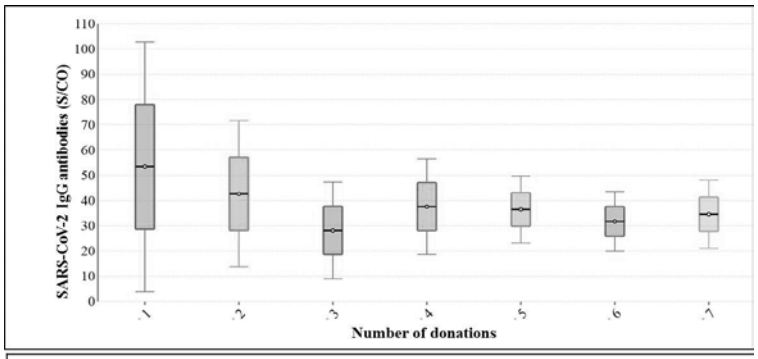
Among the 311 donors, there were 15 (4.8%) with AI, 235 (75. 6%) with MI, 45 (14.5%) with MoI, 16 (5.1%) with SI, and 0 with CI (Table 1).

The correlation of clinical severity and antibody titer analyzed by the Pearson correlation test showed a value of 0.2575, which does not confirm a statistically significant correlation of the variables.



SARS-CoV-2 IgG antibodies (S/CO) in donated plasma, obtained from people who have recovered from asymptomatic or mild COVID-19							
№ of donations	1	2	3	4	5	6	7
№ of donors	131	46	27	21	11	5	3
Min S/CO	1.02	10.61	8.61	6.46	6.71	9.33	9,84
Max S/CO	117.03	63.21	52.39	41.45	31.59	25.42	12.32

Fig. 3 – A range of anti-SARS-CoV-2 antibody (IgG) index among plasma donors who recovered from asymptomatic/mild illness.



SARS-CoV-2 IgG antibodies (S/CO) in donated plasma, obtained from people who have recovered from moderate or severe COVID-19							
№ of donations	1	2	3	4	5	6	7
№ of donors	33	12	7	5	4	3	3
Min S/CO	3.97	13.68	9.05	18.62	23.15	19.89	21.12
Max S/CO	102.82	71.63	47.29	56.58	49.76	43.56	48.04

Fig. 4 – A range of SARS-CoV-2 antibody (IgG) index among plasma donors who recovered from moderate/severe illness.

Table 1

Distribution of convalescent plasma donors according to clinical severity of COVID-19 and antibody index value

Antibody index	Clinical severity				Total n (%)
	Asymptomatic infection	Mild illness	Moderate illness	Severe illness	
1–6	6	29	3	0	38 (12.22)
7–26	6	100	10	5	121 (38.90)
27–46	2	63	15	5	85 (27.33)
47–66	1	35	11	4	51 (16.40)
67–86	0	5	3	2	10 (3.22)
87–106	0	2	3	0	5 (1.61)
≥ 107	0	1	0	0	1 (0.32)
Total n (%)	15 (4.82)	235 (75.56)	45 (14.47)	16 (5.15)	311 (100)

In all donors, the values of the antibody index decreased from the second to the last donation, but plasma donors with a more severe clinical manifestation of COVID-19 had stable antibody levels for a longer period of time.

Discussion

The study investigated the presence of SARS-CoV-2 IgG in 311 plasma donors. The study is based on the fact that a high titer of total IgG antibodies (anti-S and anti-N) implies an equally high titer of neutralizing antibodies that have a significant protective role in the immune response to viral infection and that IgG titer could also affect the clinical severity. The correlation between the number of antibodies detected after recovery and the clinical severity of the disease, as well as studies related to the duration of the high level of antibodies after the infection, are still the topic of scientific debates [10–13].

When taking note of anamnesis from plasma donors, special attention was paid to the symptoms they had during the disease. The highest percentage of our donors (75.6%) was found to have mild symptoms such as fever, cough, sore throat, headache, myalgia, and loss of sense of taste and smell, while only 4.8% of donors were asymptomatic. This representation of mild or asymptomatic donors is similar to the representation of donors in the convalescent plasma collection programs of other countries [14, 15]. In the donors of this group, the symptoms quickly withdrew, after which they reported no further complaints, while the laboratory findings were within normal limits. Donors with MoI (14.5%), of whom seven (2.25%) were hospitalized, had signs of pneumonia as well as accompanying symptoms on X-ray or CT scans. Donors from the SI group (5.1%) were the least represented in the convalescent plasma collection program, primarily because the severity of their illness required hospitalization with oxygen support and longer recovery time after discharge. No critically ill donor with applied invasive mechanical ventilation was present. A higher prevalence of donors under the age of 50 (83.9%) may also be associated with faster recovery from illness consequences and better psychophysical readiness to be included in plasma collection procedures.

The frequency of plasma donation during the study period depended on several factors, with the most significant value certainly being the SARS-CoV-2 IgG antibody index. However, the place of residence also significantly impacted the frequency of donations. The collection of convalescent plasma during the study was performed exclusively at the Institute for Blood Transfusion of Vojvodina as it was not possible to form an adequately equipped mobile unit that would collect plasma throughout the territory of Vojvodina. Transportation was organized for donors outside this district, but this fact was still a limiting factor for more frequent plasma donations. For this reason, the largest number of plasma donors came from the territory of the South Bačka district, where the Institute is located. In addition, 60.4% of donors residing outside the South Bačka district donated plasma only once.

Upon the first arrival, apart from other laboratory analyses, each donor underwent a rapid chromatographic test for antibodies, which, like most others, is based on lateral flow detection. The rapid test was positive in 60.1% of donors who donated plasma. Compared with the SARS-CoV-2 IgG antibody index, the limit of detection of the rapid test was 19.75, although in two donors with index values of 23.25 and 23.87, the rapid test was negative. Research shows that one-step delivery of the target analyte and detection reagents limit their accuracy [16]. In other infectious diseases detection, multi-step paper-based platforms, in which delivery of the target analyte was time- and volume-controlled, were used [17, 18]. That is considered to be the possible reason for the lower specificity and sensitivity of rapid anti-SARS-CoV-2 antibodies detection tests, which, according to previous research, detect only a high antibody titer [16].

To demonstrate the presence of SARS-CoV-2 IgG antibodies in plasma donors, a qualitative ELISA assay using SARS-CoV-2 recombinant antigens of solid-phase structural proteins (S and N) was used. Although the ELISA index value (ratio between sample and cut-off, S/CO) is expressed by a number, it does not show the level of antibodies, so the result is expressed as positive, negative, or indeterminate (± 10% of index value). In contrast, semi-quantitative and quantitative tests show the level of antibodies in the blood [titers, arbitrary units per milliliter (AU/mL), unit per milliliter (U/mL)]. However, it is important to note that the results of qualitative and quantitative assays are comparable as, in both cases, they depend on the analytical sensitivity of the test [19, 20].

Virus neutralization remains the gold standard for the determination of antibody efficacy. Szabó et al. [20] compared virus neutralization activity and results of anti-SARS-CoV-2 serological tests in plasma donors. Among the tests which showed the best sensitivity to neutralization was the test used in our study. They suggested the ELISA test as the first-pass test to rule out potential plasma donors with insufficient levels of neutralizing antibodies.

Dulipsingh et al. [21] used a quantitative assay to detect antibody titer and stated that > 6.5 AU/mL corresponds with an IgG antibody titer of about 1 : 320. In our study, selecting plasma donors based on antibody level was done for several reasons. First, during the early days of the pandemic (April-May 2020) in Serbia, the first and the only available test for screening plasma donors was the rapid test, and a little bit later, the test for detecting the presence of total antibodies against SARS-CoV-2. Early reports suggested that the total antibody test indicated a humoral response to COVID-19 infection. At that time, FDA guidelines did not require antibody testing, considering that the plasma collected from donors who recovered from the COVID-19 infection had quite enough neutralizing antibodies. Second, different studies observed that antibodies to both nucleocapsid and spike are correlated in the same patients [22, 23]. At the same time, no specific protocol for antibody testing was provided by FDA, and the minimum recommended titer was 1 : 80. In following recommendations, FDA determined 1 : 320 titer as the minimum level

required to achieve the therapeutic effect of plasma. Later, the requirement was reduced to 1 : 160 [5]. Our National protocol recommended the collection of COVID-19 convalescent plasma for therapeutic purposes if the least antibody index level was 6, according to manufacturer instructions. Although the BTIV collected plasma with such antibody levels, this plasma was not used in the treatment of patients. It should be emphasized that the testing was carried out at the very beginning of the epidemic when only qualitative tests were available. At that time, manufacturers were still developing other types of tests.

The humoral immune response is most important in eliminating cytopathogenic viruses and plays a major role in the prevention of viral reinfection [24]. Neutralizing IgG antibodies produced by B lymphocytes can be an indicator of protective immunity. Studies of the titer of neutralizing antibodies in infections with other coronaviruses show that over time the titer level slowly decreases: in the course of one year in influenza virus, three years in SARS-CoV, and two years after MERS-CoV [25]. Duration of antibodies after SARS-CoV-2 infection is still the subject of many studies, some of which show a decline in neutralizing antibodies within 2–3 months [26] and in IgG antibodies against the receptor-binding domain of spike protein within 75 days [27]. On the other hand, some studies question short-term immunity after infection and speculate that people with a more severe clinical manifestation had longer-lasting immunity than people with mild or asymptomatic clinical features [28]. Several Serbian authors describe a case report of a progressive decrease in IgG values for 6 months after COVID-19 infection [29]. In our study, no correlation was found between the clinical severity and the antibody titer in plasma donors. The analysis determined no statistically significant correlation between these two observed parameters. During the initial testing, the largest number of donors, 205/311 (65.9%), had a titer less than half the value of the highest titer (36.15), while the median was 26.07. The highest antibody index in our study was found in donors with a mild form of the disease, while 38.90% of donors with severe illness had lower values of antibody index. Studies show that the titer of neutralizing antibodies is not different between mild/moderate and severe cases [30–33] and that this is a significant deviation from SARS-CoV infections where antibody titer and clinical severity correlate [34–37].

A possible limitation of our study could be the sample size that was analyzed. A significant finding of the study is that during the observed time interval in all donors with severe and moderate clinical manifestation who repeatedly donated plasma, the antibody titer had slight oscillations. In mild or asymptomatic cases of donors, antibodies progressively decreased during the observed period. These results are consistent with data from the available literature [26, 33, 35]. Recovered individuals with a severe clinical manifestation developed a strong immune response by producing competent neutralizing antibodies [36]. Although there is no definite explanation, one of the possible reasons is that the specific anti-SARS-CoV-2 antibodies require enhanced and prolonged stimulation of B cell receptors, which occurs in patients with severe disease symptoms, and, thus, antibody titer values remain present for a longer period of time [38].

Conclusion

The study found that anti-SARS-CoV-2 antibodies were present in the sample of recovered patients, plasma donors, for more than 6 months after the disease. Even though no statistically significant correlation was found between the anti-SARS-CoV-2 antibody index value and the clinical severity of COVID-19, it has been proven that in patients with a more severe clinical manifestation, antibody values are maintained for a minimum of six months, which was the observed period. The data obtained are encouraging both for convalescent plasma collection programs and in terms of contribution to collective immunity. Characteristics of immunity developed following SARS-CoV-2 infection remain a topic for further research.

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No specific funding was received for this study.

Conflict of interest

The authors declare no conflict of interest.

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