

# Detection of SARS-CoV-2 RNA in the Serum Samples of Healthy Blood Donors

## Sağlıklı Kan Donörlerinin Serum Örneklerinde SARS-CoV-2 RNA Tespiti

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<sup>1</sup>Rize Public Health Laboratory, Rize, Turkey

<sup>2</sup>Tokat Gaziosmanpaşa University Faculty of Medicine, Department of Medical Microbiology, Tokat, Turkey

<sup>3</sup>İnönü University Faculty of Medicine, Department of Medical Microbiology, Malatya, Turkey

<sup>4</sup>Tatvan State Hospital, Medical Microbiology Laboratory, Bitlis, Turkey

### Abstract

**Introduction:** The transmission rate of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by blood transfusion is thought to be low; however, it has not yet been proven whether the virus is transmitted by blood transfusion. Published studies have reported that SARS-CoV-2 RNA has been detected in the blood, plasma, or serum of infected individuals. This study aimed to investigate the presence of SARS-CoV-2 RNA in the serum of blood donors and evaluate the risk of transmission of SARS-CoV-2 by transfusion.

**Materials and Methods:** In this study, 200 blood samples were taken from volunteer blood donors. In all serum samples, SARS-CoV-2 RNA was detected by reverse-transcription quantitative polymerase chain reaction assay. Medical records of the donors and recipients were retrospectively reviewed.

**Results:** SARS-CoV-2 RNA was detected in seven (3.5%) of the donor serum samples. None of the positive donors had symptoms of coronavirus disease 2019 (COVID-19), and none had been admitted to the hospital after donation. Seven SARS-CoV-2 RNA-positive donor blood components were given to 12 recipients. No medical records indicated that COVID-19 occurred after the transfusion of blood components for recipients.

**Conclusion:** This study demonstrated the presence of SARS-CoV-2 RNA in the serum of asymptomatic donors. Although our data suggest that the transfusion of blood products from asymptomatic donors to recipients with SARS-CoV-2 RNA in their serum may not result in COVID-19, further studies are needed to prove that SARS-CoV-2 is not transmitted by blood transfusion.

**Keywords:** SARS-CoV-2 RNA, blood donor, transfusion

### Öz

**Giriş:** Şiddetli akut solunum sendromu koronavirüs 2'nin (SARS-CoV-2) kan transfüzyonu ile bulaşma olasılığının düşük olduğu düşünülmektedir ancak virüsün kan transfüzyonu ile bulaşıp bulaşmadığı henüz kanıtlanmamıştır. Yayımlanmış çalışmalarda, SARS-CoV-2 RNA'sının, enfekte kişilerin kanında, plazmasında veya serumunda tespit edildiği bildirilmektedir.

**Gereç ve Yöntem:** Çalışmamızda gönüllü kan donörlerinden 200 kan örneği alındı. Tüm serum numunelerinde revers-transkripsiyon kantitatif polimeraz zincir reaksiyonu testi ile SARS-CoV-2 RNA'sı arandı. Donörlerin ve alıcıların tıbbi kayıtları geriye dönük olarak incelendi.

**Bulgular:** Donör serumlarının yedisinde (%3,5) SARS-CoV-2 RNA'sı tespit edildi. Pozitif donörlerin hiçbirinde koronavirüs hastalığı 2019 (COVID-19) semptomu yoktu ve hiçbiri başıştan sonra hastaneye başvurmamıştı. Şiddetli akut solunum sendromu koronavirüs 2 RNA pozitif yedi donöre ait kan ürünü 12 alıcıya verilmişti. Alıcılar için kan bileşenlerinin transfüzyonundan sonra COVID-19 oluştuğuna dair tıbbi bir kayıt bulunmadı.

**Sonuç:** Verilerimiz, serumunda SARS-CoV-2 RNA'sı bulunan asemptomatik donörlerden alıcılara kan ürünlerinin transfüzyonunun COVID-19 ile sonuçlanmayabileceğini öne sürse de, SARS-CoV-2'nin kan transfüzyonu ile bulaşmadığını kanıtlamak için ileri çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler:** SARS-CoV-2 RNA, kan donörü, transfüzyon

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Address for Correspondence/Yazışma Adresi: Bahise Çağla Taşkın Dalgıç MD, Rize Public Health Laboratory, Rize, Turkey  
Phone: +90 546 618 34 25 E-mail: bahise91@hotmail.com ORCID ID: orcid.org/0000-0002-1271-7522

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## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is primarily transmitted from person to person by droplets. The virus may also spread by direct or indirect close contact with the respiratory secretions of the infected individuals<sup>[1,2]</sup>. Previous studies have reported that the RNA of SARS-CoV-2 is found in the blood, plasma, or serum of infected patients<sup>[3,4]</sup>. Therefore, another route of transmission can be blood transfusions. However, no data have been published about SARS-CoV-2 transmission to individuals via blood transfusion. Therefore, the possibility of transmission of SARS-CoV-2 via blood remains unclear and requires further investigation<sup>[5,6]</sup>.

To prevent the transmission of blood-borne agents to recipients, the World Health Organization (WHO) recommends screening all donated blood for transfusion-transmissible infections, including human immunodeficiency virus, hepatitis B, hepatitis C, and *Treponema pallidum* routinely. However, the WHO does not recommend screening blood products for SARS-CoV-2<sup>[7]</sup>. Thus, this study aimed to investigate the presence of SARS-CoV-2 RNA in the serum of blood donors and evaluate the risk of transmission of SARS-CoV-2 by transfusion.

## Materials and Methods

After coronavirus disease 2019 (COVID-19) was declared a pandemic, some exclusion criteria were applied for blood donor selection, such as having a COVID-19 in the last 28 days, fever, cough, sore throat, and difficulty in breathing in the last 28 days, being in contact with anyone with COVID-19 in the last 28 days, traveling to any foreign country in the last 28 days, or being in contact with anyone who returned from a foreign country in the last 28 days<sup>[8]</sup>. Therefore, blood donors were not tested for SARS-CoV-2 RNA at the time of donation. In this study, we planned to investigate the presence of SARS-CoV-2 RNA in the blood donor serum apart from the routine procedures of the blood center. Accordingly, a total of 200 blood samples were collected from voluntary blood donors who applied to the Tokat Gaziosmanpaşa University Hospital Blood Center between November 2020 and May 2021. All donors were informed about the study. All donors participating in the study signed an informed consent form. Serum samples were separated by centrifugation of the blood samples. All serum samples were stored at -80 °C until tested.

Viral RNA was extracted using a QIAAsymphony DSP Virus/Pathogen Midi kit (Qiagen GmbH, Germany). A one-step reverse-transcription quantitative polymerase chain reaction (RT-qPCR) test was performed with Bio-Speedy® COVID-19 qPCR detection kit (Bioeksan R&D Technologies Limited, Turkey). Positive samples were tested three times. SARS-CoV-2 RNA-

positive samples were screened by Bio-Speedy® SARS-CoV-2 Variant Plus Kit (Bioeksan R&D Technologies Limited) for the detection of B.1.1.7 (UK), B.1.351 (South Africa), P.1 (Brazil), and B.1.526 (New York City) variants.

In this study, RT-qPCR tests were performed after 200 blood samples were collected. Then, the donor medical records of the donors and recipients were reviewed retrospectively. Of the 12 blood recipients, 4 had the results of the upper respiratory tract SARS-CoV-2 RNA PCR test performed on days 0, 1, 2, and 5 after transfusion.

## Statistical Analysis

Obtained data were transferred to Microsoft Office Excel, and the frequency and percentage was calculated using the Statistical Package for the Social Sciences program.

## Results

Of these donors, 188 (94%) were male and 12 (6%) were female. The median ages of the male and female donors were 36.9 (22-54) and 22.7 (22-39) years, respectively. Among 200 serum samples, seven were positive for SARS-CoV-2 RNA according to the RT-qPCR results. Severe acute respiratory syndrome coronavirus 2 was detected in 3.5% (95% confidence interval). The cycle threshold (Ct) values of SARS-CoV-2 RNA-positive donor samples are shown in Table 1. Severe acute respiratory syndrome-Coronavirus-2 B.1.1.7 (UK), B.1.351 (South Africa), P.1 (Brazil), and B.1.526 (New York city) variants were not detected in any of the seven positive samples.

None of the positive donors had COVID-19 symptoms, and according to the medical records, none of them were referred to the hospital after the donation.

Two of the donations were made by thrombocyte apheresis. Other five donations were converted to plasma and red blood cell components and transferred to 10 recipients. Thus, SARS-CoV-2 RNA-positive blood components of the seven donors were given to 12 recipients ranging in age from 35 to 90 years. Of these recipients, nine were male and three were female. Among them, seven recipients had malignancy, two had severe injury,

**Table 1. Cycle threshold values of severe acute respiratory syndrome coronavirus 2 RNA-positive donor samples**

Donor	Cycle threshold value
68	32.27
118	29.78
124	29.66
125	29.68
130	29.41
136	29.06
180	31.84

one had Crimean–Congo hemorrhagic fever, one had ruptured ectopic pregnancy, and one had trochanteric fracture. Of the 12 blood recipients, 4 had the result of the upper respiratory tract SARS-CoV-2 RNA PCR test performed on days 0, 1, 2, and 5 after transfusion. The results were negative. Based on the medical records of the recipients, no COVID-19 occurred after the transfusion of blood components.

## Discussion

The risk of SARS-CoV-2 transmission through blood products is still unclear<sup>[6]</sup>. Early studies have shown that between 15% and 40% of individuals infected with SARS-CoV-2 have detectable RNAemia<sup>[3,4,9]</sup>. In this study, we detected SARS-CoV-2 RNA in the serum of seven of 200 healthy blood donors. Chang et al.<sup>[10]</sup> examined the plasma of approximately 7500 donors and found that 4 of them were positive for SARS-CoV-2 RNA. Moreover, they reported that all positive donors were asymptomatic. In their studies, the Ct values of positive plasmas showed high values ranging from 34.004 to 40.219. Likewise, all SARS-CoV-2 RNA-positive donors in our study were asymptomatic. In this study, the Ct values of the seven positive serums showed values between 29.06 and 32.27. These high Ct values are indicative of low viral load in asymptomatic individuals. Both the PCR positivity in asymptomatic individuals and the prolonged PCR positivity after an asymptomatic infection may explain the SARS-CoV-2 RNA positivity in the serum of healthy blood donors. Corman et al.<sup>[6]</sup> investigated the presence of RNA in the blood of 18 symptomatic and asymptomatic patients with COVID-19, while detecting RNAemia in a patient with severe, advanced infection and acute respiratory distress syndrome, and they could not demonstrate the presence of RNA in the blood of 14 patients diagnosed with mild COVID-19 and three asymptomatic individuals. Similarly, in a study conducted in China, SARS-CoV-2 genome was detected in the blood of 6 of 57 patients, and RNAemia was found to be associated with a more severe clinical picture<sup>[11]</sup>. Accurate information on the prevalence of asymptomatic/presymptomatic infection and whether RNAemia or, more relevantly, viremia occurs in the absence of disease (especially in healthy donors) will enable us to better discuss the risk of transfusion transmission of SARS-CoV-2.

In a few studies investigating SARS-CoV-2 RNA in blood donors, positive blood was quarantined and not transfused<sup>[12]</sup>. Therefore, they lack evidence of recipient tracking or viremia. In this respect, our study is valuable in terms of giving information about recipient status. In our study, the blood components of positive donors have been transfused in 12 recipients. Retrospective screening of medical records of both seven positive donors and 12 recipients showed that neither the donors nor the recipients were diagnosed with COVID-19 following the donation. Moreover, four of the 12 blood recipients also had negative PCR

results after donation. Considering other studies with recipient follow-up, Kwon et al.<sup>[13]</sup> screened recipients of blood products from seven donors diagnosed with COVID-19 following the donation and reported that none of the recipients developed COVID-19 or tested positive for SARS-CoV-2 RNA.

Similarly, Cho et al.<sup>[14]</sup> reported a patient with severe aplastic anemia who received platelet transfusion from a donor diagnosed with COVID-19 after three days of the donation. They documented that the recipient did not develop COVID-19, although his immune system was suppressed.

For a pathogen to cause transmission by transfusion, the following four basic characteristics are needed: (i) The donor must have a pathogen in his/her blood. (ii) The pathogen must survive in the collected components. (iii) It must have an intact organization to ensure infection and proliferation and must find susceptible cells. (iv) The pathogen must cause disease in the blood recipient<sup>[15]</sup>. Therefore, the detection of viral RNA in the blood does not mean transmission by transfusion.

## Study Limitations

The obvious study limitation is that the data are for RNA only. A critical correlation analysis of SARS-CoV-2 RNAemia with infectious virus has not been conducted. Once RNA-positive donors are identified, further studies are needed to isolate the virus from the donated blood and/or demonstrate its infectivity in animal models and/or tissue culture.

## Conclusion

This study showed the presence of RNAemia in asymptomatic donors with available data. Since we did not evaluate infectious viremia, we cannot say whether this poses a risk of transfusion-related transmission; however, the absence of infection in recipients supports the notion that the risk of transmission by transfusion is low. To completely eliminate the risk of transmission of COVID-19 through blood, further strong studies in which asymptomatic donors and recipients are followed and tested more closely and studies on infectious viremia are needed.

## Ethics

**Ethics Committee Approval:** The study was approved by the Tokat Gaziosmanpaşa University of Local Ethics Committee (protocol no: 20-KAEK-167, date: 09.07.2020).

Informed consents were obtained from all participants. therefore not retrospective study.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: B.Ç.T.D., G.Y., Design: B.Ç.T.D., G.Y., Data Collection or Processing: B.Ç.T.D., E.S.T., A.A., Analysis or Interpretation: B.Ç.T.D., E.S.T., B.O., Literature Search: B.Ç.T.D., G.Y., Writing: B.Ç.T.D., G.Y.

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