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Severe Acute Respiratory Syndrome Coronavirus 2 and Blood Safety: An Updated Review

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Keywords

Severe acute respiratory syndrome coronavirus 2 · Coronavirus disease 2019 · Blood transfusion · Blood safety

Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel human coronavirus first identified in late 2019 and subsequently declared a worldwide pandemic in March 2020. In this review, we provide an overview of the implications of SARS-CoV-2 for blood safety and sufficiency. ***Summary:*** Approximately one-third of SARS-CoV-2 infections are asymptomatic. The reported mean incubation period typically varies from 2 to 11 days, but longer periods up to 22 days have been reported. The blood phase of SARS-CoV-2 appears to be brief and low level, with RNAaemia detectable in only a small proportion of patients, typically associated with more severe disease and not demonstrated to be infectious virus. A small number of presymptomatic and asymptomatic blood phase cases have been reported. Transfusion-transmission (TT) of SARS-CoV-2 has not been reported. Therefore, the TT risk associated with SARS-CoV-2 is currently theoretical. To mitigate any potential TT risk, but more importantly to prevent respiratory transmission in donor centers, blood services can implement donor deferral policies based on travel, disease status, or potential risk of exposure and encourage staff vaccination. ***Key Messages:*** The TT risk of SARS-CoV-2 appears to be low. The biggest risk to blood services in the current COVID-19 pandemic is to maintain the sufficiency of the blood supply while minimizing respiratory transmission of SARS-CoV-2 to donors and staff while donating blood.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel human coronavirus and the etiological agent of COVID-19 [1]. The virus was first identified in China's Hubei Province in December 2019 and has subsequently spread globally, being declared a pandemic by WHO on 11 March 2020 [2]. We have previously reviewed the implications of SARS-CoV-2 for blood safety and sufficiency [3]. As there have been substantial developments since that time, in this updated review we provide (i) a brief summary of those characteristics of SARS-CoV-2 and COVID-19 that are particularly relevant to assessing the potential risk to blood safety and sufficiency, (ii) an overview of the implications of SARS-CoV-2 for blood safety and sufficiency, and (iii) a discussion of some of the challenges posed by the COVID-19 pandemic for blood services, including sufficiency of supply.

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Characteristics of SARS-CoV-2 and COVID-19

Modes of Transmission

The primary mode of SARS-CoV-2 transmission is person-to-person [4–6]. This is indicated by the observation that COVID-19 cases have been reported in clusters typified by people coming into close contact in confined spaces, often with the identification of "superspreaders" [7–9]. The predominant mode of human-to-human SARS-CoV-2 transmission appears to be via close contact and mediated by airborne droplets of varying sizes from larger droplets to aerosols [5, 10, 11]. While there is some evidence that SARS-CoV-2 can be transmitted by aerosol particles under some circumstances, such as crowding in confined spaces with inadequate ventilation and airflow [12, 13], it has not been demonstrated to be a major mode of transmission [5, 14]. As indicated by both natural and experimental laboratory contaminations of inanimate surfaces, fresh fish, and human skin, SARS-CoV-2 RNA can remain detectable on these surfaces for a limited time [12, 15–19]. However, the importance of fomites, food, and human skin in the transmission of SARS-CoV-2 has not been defined, but does not appear to be a major mode of transmission [5, 19, 20].

Intrauterine transmission of SARS-CoV-2 may be possible, but appears to be rare with only a small number of reported probable cases [21–24]. SARS-CoV-2 does not appear to be transmissible intrapartum [21, 23, 25, 26], by human breast milk [21, 23, 27–31] or sexually [32, 33]. Transmission by the ocular conjunctival route [34, 35], fecal-oral, or fecal aerosol [36–38] has not been confirmed.

Disease Characteristics

Estimated overall asymptomatic rates for SARS-CoV-2 infection between approximately 22% and 35% have been reported, based on meta-analyses of studies where there was adequate follow-up of patients to exclude subsequent development of symptoms and estimates of total infections were based on either seroprevalence or follow-up testing of defined populations [39–42]. However, there is some uncertainty and variation with regard to reported asymptomatic rates. For example, in a recent meta-analysis, the authors reported substantial regional variation with an overall rate of 64% in Africa, 40% in America, 28% in Europe, and 18% in Asia [41]. Several meta-analyses of the COVID-19 incubation period from estimated time of exposure show relatively consistent estimates with mean values varying between 5.08 (95% CI: 4.77–5.39) and 6.7 days (95% CI: 6.0–7.4) [43–46]. The estimated ranges of the incubation period were variable, but most were within the range of 2–11 days and almost all infections developed symptoms by day 14. There have been reports of longer incubation periods, including a Chinese study that estimated a median period of 22 days [47].

Studies from several countries have demonstrated that the majority of reported confirmed COVID-19 cases in the general population are mild/moderate [48–50]. Although there is some variation between studies, during the first half of 2020 (prior to mass vaccination programs and widespread reporting of delta variant cases), typically the most common reported symptoms were fever (59–98%), cough (54–81%), myalgia/fatigue (44–70%), and breathing difficulties (31–65%) [48–51]. Acute temporary loss or impaired taste and olfactory function have been recognized as common (40%– >60% in some studies) and specific early symptoms of SARS-CoV-2 infection [52]. Less common symptoms include cardiovascular, gastrointestinal, and neurological complications [53, 54]. A number of studies have modeled the overall infection fatality rate prior to mass vaccination programs and taking underreporting into account. While the mean infection fatality rate varied between studies from approximately 0.03–2.2%, most estimates were between 0.45% and 1.15% [55, 56].

SARS-CoV-2: Implications for Blood Safety and Sufficiency

Broadly, emerging infectious disease (EID) pathogens can be classified into two categories: first, those that are vector-borne, with limited or no human-to-human transmission, and second, those that are spread predominately human-to-human, such as respiratory viruses. Both categories of pathogen may impact blood safety due to the potential transfusion-transmission (TT) risk, albeit that TT of respiratory viruses has not been demonstrated, and the sufficiency of the blood supply due to infected donors/staff being unwell and unable to donate/attend work or the loss of donors due to deferrals or social disruption. Pathogens that are predominately transmitted human-to-human may also impact sufficiency of supply due to donors being reluctant to attend donor centers out of fear of being infected.

The following criteria can be used to assess if an EID pathogen is a potential risk to blood safety: (i) able to establish infection in humans and spread within populations, (ii) infection includes an asymptomatic blood phase, (iii) able to survive during blood processing and storage, (iv) transmissible by the intravenous route, and (v) associated with a clinically apparent disease in at least a proportion of recipients [57].

As summarized in the first part of this review, it is now clear that SARS-CoV-2 can establish infection in humans and cause disease (COVID-19), which may result in severe symptoms and death, and spread efficiently from

human-to-human within populations. The relative viral loads in the different constituents of blood and whether viable SARS-CoV-2 (if present in blood) is able to survive during blood processing and storage (for fresh products) have not been determined.

Blood Phase

SARS-CoV-2 RNA detection in blood (RNAaemia) appears to be primarily associated with symptomatic disease. The proportion of patients with detectable RNAaemia varies substantially between studies, from approximately 1–50% for mild infections [58–61], up to 88% in patients with severe COVID-19 [59, 61–63] and up to 100% in critically ill patients [59, 61]. Detectable RNAaemia is a risk factor for severe disease and mortality, the risk increasing with higher levels of RNAaemia and lower reverse transcriptase polymerase chain reaction cycle threshold values [59, 60, 63–68], and a predictor of post-acute symptoms [69].

The duration of detectable RNAaemia appears to be brief and characterized by low levels of viral RNA. Limited data suggest a median detectable RNAaemic period of approximately 16 days (IQR: 11–20 days) and can extend to >30 days in patients with severe disease [70]. Viral RNA levels decline substantially within 10 days [59]. A case study of a patient with an extended period of RNAaemia (approximately 40 days post-symptom onset) has been reported [71]. However, the RNA levels were low, anti-SARS-CoV-2 IgG was detectable, and the presence of infectious virus was not demonstrated. Extended RNAaemia periods have also been reported in case studies of immunocompromised patients [72]. In 1 case, the patient had intermittently detectable RNAaemia for over 200 days from diagnosis and experienced COVID-19 clinical relapses [73]. Reported serum RNAaemia loads vary between approximately <10–10^6 copies/mL [72, 74]. There have been reports of SARS-CoV-2 detection in peripheral blood mononuclear cells [75] and platelets (PLTs) [76, 77]. However, this appears to be rare, the levels of RNA in these cases were low, and the presence of infectious virus was not demonstrated. A case of presymptomatic SARS-CoV-2 RNAaemia has been reported, a patient with acute myeloid leukemia and relapse after allogeneic hematopoietic stem cell transplantation [78]. However, the patient had a serious underlying disease and therefore would not be presenting to donate and the presence of infectious virus was not demonstrated.

The association between SARS-CoV-2 RNAaemia and infectious virus in blood has not been determined [79, 80]. One study has reported that SARS-CoV-2 RNAaemia in COVID-19 patients was not associated with infectious virus [81]. In addition, a recent study has reported that in 3 patients with detectable RNAaemia, following high-speed centrifugation, most of the recoverable viral RNA was associated with the pellet rather than the supernatant [59]. The pellet was shown to contain SARS-CoV-2 virions by immune-electron microscopy, but the study did not attempt to demonstrate infectiousness.

It is acknowledged that the small number of reported cases of SARS-CoV-2 RNAaemia detection in the blood of presymptomatically or asymptomatically infected individuals may, at least in part, be due to infrequent testing of blood as respiratory swabs are primarily used for laboratory diagnosis, it is likely that a substantial proportion of cases referred for laboratory testing are symptomatic, and the viremic period appears to be brief and low level. However, the detection of RNAaemia in only a small proportion of asymptomatic blood donors (Table 1) [82–88] would suggest that asymptomatic/presymptomatic RNAaemia is relatively rare.

A number of studies have reported SARS-CoV-2 antibody seroconversion times relative to time of symptom onset with mean/median times varying from 5 to 11 days for total antibody, 4–17 days for IgM, and 4–15 days for IgG [89–91]. Neutralizing antibodies become detectable within 7–15 days of symptom onset and correlate with IgG levels [89, 91, 92]. Longitudinal studies have indicated that IgG levels peak between 3 and 7 weeks post-symptom onset; while levels subsequently decline, IgG may remain detectable for the duration of follow-up, which can be up to 10–15 months in some studies [92–96]. Loss of detectable antibodies (seroreversion) in a small proportion of patients after follow-up periods between 3 and 15 months has been reported, primarily in patients with mild or asymptomatic infection [95–99]. The absence of detectable seroconversion in SARS-CoV-2 RNA-positive patients has also been reported [100]. SARS-CoV-2 RNA and antigen levels are inversely correlated with antibody levels and decline as antibody titers rise [67, 93]. Therefore, even if it was assumed that detectable RNAaemia represented infectious virus, it would be expected that blood would no longer be infectious once rising titers of IgG or total antibody become detectable and viral RNA levels declined [90, 101]. This is also indicated by the association between seroconversion and rising blood antibody titers with declining levels of RNA and infectious virus in respiratory samples [102].

Transfusion-Transmissibility

As noted, several studies have reported results of SARS-CoV-2 RNA testing of plasma samples from asymptomatic blood donors and are summarized in Table 1 [82–88]. These studies reported that RNAaemia was either not detected or detected in only a very small proportion of blood donors and viral loads, where reported, were low. In addition, infectious virus was not detected in those studies that tested for infectiousness.

Table 1. Studies reporting SARS-CoV-2 RNA testing of plasma samples from asymptomatic/presymptomatic blood donors

Country	Donors tested, *n*	Donors positive, *n* (%)	Comments	Reference
China (Wuhan)	7,425	4 (0.05)	Testing in MPs of 6–8 samples; RT-PCR results showed low signal strength suggesting low levels of RNA; infectious virus not confirmed; samples collected on January 2020	[83]
China (Hubei)	94,342	0	96.1% of samples tested in MP of 8 and 3.9% tested as ID; samples collected on February–April 2020	[82]
Pakistan	600	2 (0.33)	Not indicated if ID or MP testing; samples collected on March–April 2020	[84]
Brazil	4,103	1 (0.02)	Testing in MPs of 4; low viral load; 27 donors had detectable RNA in saliva samples, 8 with high viral load; samples collected on June–September 2020	[86]
USA	258,000 samples tested in 17,995 MPs	3 (0.001)	Testing in MPs of 6 or 16; low viral loads ($<10^3$–$<4 \times 10^4$ copies/mL); infectious virus not detected; samples collected on March–September 2020	[85]
Italy	1,797	0	Not indicated if ID or MP testing; 10 of 1,797 donors were SARS-CoV-2 antibody positive and tested for RNA; 0 of 10 were positive; samples collected on March–June 2020	[87]
Portugal	543	0	Not indicated if ID or MP testing; 7 donor samples were SARS-CoV-2 IgM positive; samples collected on June-July 2020	[88]

RT-PCR, reverse transcriptase polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; MP, minipool; ID, individual donation.

Similar to other human coronaviruses (including SARS-CoV and Middle East respiratory syndrome CoV), TT of SARS-CoV-2 has not been reported, despite 251 million reported confirmed cases globally as at 11 November 2021 [103, 104]. There have been several reports of transfusion of blood products (PLTs, red blood cell [RBCs], and granulocyte concentrate) from donors who were subsequently diagnosed with SARS-CoV-2 infection (Table 2) [84, 105–113]. In all reported cases, including at least three donors who had detectable RNAaemia at time of donation [84, 105], there was no evidence of TT of SARS-CoV-2 to recipients. One recipient tested SARS-CoV-2 antibody positive, but time of infection was uncertain, other modes of transmission could not be excluded, and given the donor became symptomatic 4 days post-donation, it is very unlikely to be related to the transfusion [110]. There has been a reported case of SARS-CoV-2 transmission to recipient of a lung transplant from an infected donor with transmission confirmed by genomic sequencing [114].

Risk Mitigation Strategies

Although many countries have now implemented SARS-CoV-2 vaccination programs [115], it will take some time before a substantial proportion of the global population has been vaccinated, helping to bring an end to the current pandemic. In addition, the effectiveness of SARS-CoV-2 vaccines against viral variants is still being evaluated [116]. While SARS-CoV-2 transmission by transfusion has not been reported and appears unlikely, as a precautionary approach given the virus was only recently identified, there are a number of strategies blood centers can implement. While these strategies mitigate the theoretical TT risk, more importantly they minimize the likelihood of respiratory transmission while donating blood. This has been important to ensure donors continued to feel safe while donating during the pandemic. Current evidence suggests that specific SARS-CoV-2 TT risk mitigation strategies may not be required.

Donors with symptomatic infection, if presenting to donate, would likely be deferred from donating. In addition, blood donors should be encouraged to notify the blood center if they develop symptoms in the 2 days post-donation. This would partly mitigate any theoretical TT risk associated with donors in the incubation period but, more importantly, allow contact tracing to occur if required [108].

For the few remaining countries or regions that do not have sustained human-to-human transmission or have effectively eliminated the virus, the primary risk is associated with imported cases. For these countries, the potential SARS-CoV-2 TT risk can be reduced by travel-related donor deferrals for donors returning from countries/regions assessed as high risk for SARS-CoV-2 infection or even all donors returning from overseas.

A deferral for donors infected with or potentially exposed to SARS-CoV-2 can be implemented to further reduce any potential TT risk and is recommended by several agencies. The Asia Pacific Blood Network (ABPN) guidelines recommend a deferral period of 28 days for donors after possible exposure and the deferral of recovering confirmed cases of SARS-CoV-2 for at least 28 days after symptom resolution [117]. WHO recommends a 14-day deferral for donors with close contact to a confirmed

Table 2. Studies reporting transfusion of blood components from donors subsequently diagnosed with SARS-CoV-2 infection

Country	Donors, recipients, and components transfused, *n*	Donor details	Recipient details	Reference
Korea	One donor One recipient received apheresis PLT	Donor diagnosed with COVID-19 3 days post-donation and 1 post-transfusion of PLT	Recipient did not develop COVID-19-associated symptoms and was negative for SARS-CoV-2 RNA over 2 weeks of follow-up	[106]
Brazil	Five donors Nine recipients: 6 received PLT One received RBC and 2 received granulocyte concentrates	Two donors diagnosed by PCR, 2 by anti-SARS-CoV-2 serology, and 2 had presumptive diagnosis	Recipients did not develop COVID-19-related symptoms during follow-up; recipients were immunocompromised	[113]
Korea	Six donors Nine recipients: 6 recipients received PLT, and 3 received RBC	Three of 6 donors reported symptom onset 3–10 days post-donation; COVID-19 diagnosed in all donors between 6 and 16 days post-donation. Donation repository samples SARS-CoV-2 RNA negative for all 6 donors	Recipients did not develop symptoms and tested SARS-CoV-2 RNA negative	[107]
Pakistan	Two donors Two recipients, both received RBC	Donors identified by retrospective testing of repository samples at time of donation; FFP from donors was positive for SARS-CoV-2 RNA	Recipients did not develop symptoms and tested SARS-CoV-2 RNA negative	[84]
France	One donor Two recipients: recipient 1 received pathogen-reduced PLT, and recipient 2 received RBC	Donor was SARS-CoV-2 RNA positive at day 4 post-donation (respiratory sample); plasma from donation was SARS-CoV-2 RNA positive but virus not detected by culture	Recipient 1 not tested for SARS-CoV-2, remained asymptomatic; recipient 2 was a COVID-19 patient	[105]
China	One donor One recipient who received PLT	Donor reported symptoms 4 days after donation; donor SARS-CoV-2 RNA positive (respiratory sample)	Recipient did not develop symptoms and was SARS-CoV-2 RNA negative (respiratory swab and plasma) 4 days after transfusion	[111]
Saudi Arabia	One donor One recipient who received apheresis PLT	Donor developed symptoms 5 days post-donation and was SARS-CoV-2 RNA positive 6 days post-donation (respiratory sample); stored PLT segment was SARS-CoV-2 RNA negative	Recipient was SARS-CoV-2 RNA negative (respiratory sample) days 4 and 10 post-transfusion	[109]
Greece	One donor Two recipients: recipient 1 received RBC, and recipient 2 received PLT	Donor tested SARS-CoV-2 RNA positive 8 days post-donation (respiratory sample)	Recipient 1 was SARS-CoV-2 RNA negative (respiratory sample) 7 days post-transfusion; recipient 2 was SARS-CoV-2 RNA negative 4 and 11 days post-transfusion and SARS-CoV-2 antibody negative 21 days post-transfusion. Recipients did not develop symptoms over 4 weeks of follow-up	[112]
Iran	One donor One recipient who received RBC	Donor reported symptoms 16 days before donation, tested SARS-CoV-2 RNA positive (presumed respiratory sample)	Recipient (newborn) did not develop symptoms during 46 days of follow-up, not tested for SARS-CoV-2 RNA	[108]
Brazil	One donor Two recipients: recipient 1 received PLT, and recipient 2 received RBC	Donor reported symptoms and was SARS-CoV-2 RNA positive (respiratory sample) 4 days post-donation	Recipient 1 was SARS-CoV-2 RNA negative (respiratory sample) and SARS-CoV-2 antibody negative, and died 7 days post-transfusion. Recipient 2 was SARS-CoV-2 RNA negative (respiratory sample) at 7 days post-transfusion, SARS-CoV-2 RNA indeterminate and antibody negative (IgG) at 9 days post-transfusion, SARS-CoV-2 RNA negative (respiratory sample) at 12 days post-transfusion. Source of infection in recipient 2 not confirmed as transfusion	[110]

SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; COVID-19, coronavirus disease 2019; RBC, red blood cells; PLTs, platelets.

case, who have had a positive test for SARS-CoV-2 or who have recovered from diagnosed COVID-19 [103]. The ECDC suggests the deferral of potential donors of blood, cells, and tissues for 14 days after contact with confirmed case of COVID-19 [118]. In addition, persons recovering from confirmed COVID-19 should be deferred for at least 14 days after symptom resolution due to the current uncertainty regarding possible viremia and/or viral shed-

ding in body fluids [118]. In the USA, the FDA recommends that individuals diagnosed with COVID-19 or suspected of having COVID-19 refrain from donating blood for at least 14 days after complete resolution of symptoms and individuals who have had a positive diagnostic test for SARS-CoV-2 but never developed symptoms refrain from donating for at least 14 days after the date of the positive test result [119]. Australian Red Cross Lifeblood recommends a 7-day deferral from date of recovery for donors with a current SARS-CoV-2 infection. This balances the respiratory transmission risk, but ensures sufficiency which could be impacted by excessively long deferrals.

Other potential risk mitigation strategies that can be used to reduce the TT risk of EIDs include pathogen reduction technologies (PRTs), donor laboratory screening, and quarantine of blood components with delayed release if there is no subsequent illness reported by the donor. Commercial PRTs are effective for Middle East respiratory syndrome CoV and SARS-CoV, and at least one is effective for SARS-CoV-2 [120–122]. However, for countries that have not already implemented PRTs, it is unlikely to be a cost-effective strategy, particularly as TT of SARS-CoV-2 has not been reported [103, 118, 119, 123]. For each country, the implementation of blood donor screening by NAT for SARS-CoV-2 would require a validated assay approved by that country's regulator and, at present, this is not an option for most countries. In addition, given the low risk, if any, of transmitting SARS-CoV-2 by transfusion, implementing a donor screening assay would not be cost-effective. Quarantining of components would be difficult to implement operationally and, particularly if there is widespread transmission of SARS-CoV-2, could potentially impact the sufficiency of supply. In addition, quarantining PLTs would not be feasible due to the short shelf life and is not recommended given the TT risk is theoretical and asymptomatic infection occurs.

The COVID-19 Pandemic: Challenges for Blood Services

While SARS-CoV-2 does not appear to represent a direct threat to blood safety, approximately 18 months after the COVID-19 pandemic was declared, blood services have reported a number of challenges. Some blood services have reported a decline in donor numbers, particularly during the early stages of the pandemic [124–126] which may, in part, be due to donor fear of infection [124]. However, a number of blood services have reported that the decline in donor numbers has been accompanied by a decline in demand for blood components [124, 126]. Changing donor demographics has also been reported with a number of blood services reporting an increase in new donors, raising concerns about an increase in risk to blood safety as new donors typically have a higher prevalence of blood-borne infections [127]. Attracting and selecting suitable donors is an important challenge, particularly given that convalescent plasma [128], intravenous immunoglobulin, and hyperimmune globulin [129, 130] are being investigated as potential treatment options for COVID-19. However, many countries have now ceased convalescent plasma collection as it does not appear to be effective in hospitalized patients [131].

In response to these challenges, blood services need to ensure adequate infection control measures in donor centers, recommend or at least encourage staff vaccination, develop educational strategies to reassure donors that it is safe to donate, consider changes to donor acceptance criteria, and manage potential blood shortages and changing blood usage patterns [132–134]. With the widespread implementation of vaccination programs globally [115], the management of vaccinated donors represents an additional challenge for blood centers. The US FDA recommends that individuals who received a nonreplicating, inactivated, or mRNA-based COVID-19 vaccine can donate blood without a waiting period, while those who received a live-attenuated vaccine refrain from donating blood for a short waiting period (e.g., 14 days) after receipt of the vaccine [119]. The ECDC recommends that after vaccination with attenuated viruses (e.g., replication-competent virus vector-based vaccines, live-attenuated virus vaccines), donors must be deferred for 4 weeks. Those vaccinated with inactivated/killed viruses or vaccines that do not contain live agents (i.e., mRNA vaccines, nonreplicating/replication-deficient virus vector-based vaccines, and protein subunit vaccines) may be accepted as donors if well [118]. The WHO recommends a 28-day deferral for donors who have received a live-attenuated virus vaccine [103]. However, because of the incidence of vaccine side effects, some countries, including Australia, have implemented a short-term deferral for donor safety reasons [135] which is also recommended by the WHO [103].

Decisions about implementing donor travel deferrals need to balance both the safety and sufficiency of the blood supply. For example, the deferral of donors will result in the loss of product in the short-term and, potentially in the longer term, donors. The deferral of blood donors can have adverse psychological impacts on donors and negatively impact future donation intention [136]. In addition, it is important that both blood services and government health departments carefully manage their response to infectious disease outbreaks, taking care not to create undue concern among donors and the general population as donors may be reluctant to attend donor centers due to a fear of being infected and/or reluctance to travel

due to restrictions [124, 125, 137]. Therefore, it is important for blood services to take proportionate appropriate measures to mitigate the risk of SARS-CoV-2 transmission in donor centers, as this will reassure donors and minimize the risk of transmission to staff.

Conclusions

Given that the SARS-CoV-2 blood phase appears to be brief, low level and primarily associated with symptomatic cases, and the absence of reported TT of coronaviruses, the risk of transmitting SARS-CoV-2 by transfusion appears to be low or may not occur at all, and is certainly substantially lower than the respiratory route. Accordingly, the biggest challenge to blood services in the current COVID-19 pandemic is to maintain the sufficiency of the blood supply, including adequate provision of plasma, while minimizing respiratory transmission of SARS-CoV-2 to donors and staff while donating blood. Therefore, maximum uptake of vaccination by staff and donors is required for long-term minimization of transmission risk and, more importantly, to minimize severity of consequences. For countries that were without a substantial number of reported COVID-19 cases or where most cases were imported, originally the potential respiratory and TT risk associated with SARS-CoV-2 was reduced by the implementation of deferral policies relating to potential geographical exposure, a history of SARS-CoV-2 infection or potential local exposure to SARS-CoV-2 cases. Given recent large outbreaks and no demonstrated blood safety risk, we recommend decreasing the deferral period to ensure sufficiency whilst balancing the risk of respiratory transmission. For countries with widespread and sustained local transmission, in addition to the deferral of confirmed cases and those potentially exposed, PRT may be an option to reduce the potential TT risk, but is unlikely to be cost-effective given that transmission of SARS-CoV-2 has not been demonstrated and appears unlikely.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

P.K. drafted the initial manuscript. All authors contributed to the subsequent reviews, revisions, discussions, and final approval.

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