

The medical concerns of patients with thalassemias at the time of COVID-19 outbreak: The personal experience and the international recommendations

Duran Canatan¹, Vincenzo de Sanctis²

¹Director of Hemoglobinopathy Diagnosis Center of Mediterranean Blood Diseases Foundation Antalya, Turkey; ²Pediatric and Adolescent Outpatient Clinic, Quisisana Hospital, Ferrara, Italy

Dear Sir,

Thalassemias are a global disease that is most highly prevalent in Southeast Asia, Africa, and Mediterranean countries. Patients with β -thalassemia major (BTM) require regular blood transfusions, supported by appropriate iron chelation therapy throughout their life. Patients with BTM are also at risk of transfusion-transmitted infections (TTI), unless appropriate blood screening and safety practices are in place (1).

In India, HIV, HBV, HCV, Syphilis, Malaria, Hepatitis A, Hepatitis G, Epstein Barr Virus, Cytomegalo Virus (CMV), Parvo virus B-19, Human T Lymphocytic virus (HTLV-1 and HTLV-2) and bacterial infection were the most important causes of concern (2).

In a previous study we evaluated the incidence of transfusion-transmission diseases in 246 patients with BMT (63.4%), 86 with non-transfusion-dependent thalassemia (22.1%), 23 with Sickle cell/ β -thalassemia (5.9%), 20 with Sickle Cell Disease (SCD; 5.1%), and 13 with other hemoglobin abnormalities (3.3%). The seroreactivity for hepatitis A virus IgG was 97.5%, 99.5% for HBs Ab, 0.5% for HBs Ag, 18% for HCV Ab, 72.3% for CMV IgG, 2% for CMV IgM, and 0% for HIV-Ab (3).

There are about 6,000 patients with hemoglobinopathy in Turkey, 57 % of them are BTM, each of them receive 2-3 units of filtered red blood cells (RBC) regularly each month, thus they need about a total of

7,000 units RBC per month. Filtered RBCs are provided, free of charge, by the Turkish Red Crescent (4).

Background and patient's concerns

The novel coronavirus disease (COVID-19) is a highly contagious respiratory disease caused by the SARS-CoV-2 virus. It has become a pandemic, and by the end of March 2020, over 465,000 cases had been recorded worldwide, with a high mortality rate. Therefore, the novel coronavirus outbreak represents a public health emergency of international concern.

The CDC is working closely with state and local health partners to develop and disseminate information to the public on general prevention of respiratory illness, including the 2019-nCoV. This includes everyday preventive actions, such as: washing hands, covering the mouth and nose when coughing or sneezing, and staying home.

However, the huge amounts of information in circulation can sometimes seem overwhelming and confusing. Understandably, we have received many enquiries from patients with thalassemias about COVID-19 and the possible impact their health. In particular, on blood safety and supply, susceptibility to SARS-CoV-2 infection in splenectomized patients, and presence of associated co-morbidities. The aim of our letter is to report the major patient's worries and concerns at the time of COVID-19 outbreak:

Safety of blood transfusions and measures to minimise the risk of transmission

The SARS-CoV-2 has a long incubation period (generally, 1-14 days; on average, 5-6 days; longest reported, 24 days) and causes asymptomatic infection in a large number of individuals, which poses huge challenges in the recruitment of blood donors, in blood collection and blood safety.

Available evidence indicates that human transmission of SARS-CoV-2 occurs via close contact with respiratory droplets produced when a person exhales, sneezes, or coughs, or via contact with fomites. The virus has been detected in blood, saliva, tears, and conjunctival secretions (5).

Blood type may contribute to the susceptibility to infection. The individuals with blood group A may be most vulnerable to COVID-19, whereas those with blood group O may have a significantly lower risk for the infection. However, more evidence is still needed before this observation can be confirmed (6).

Blood transfusion is an essential part of thalassemias patient's care. The risk of transmission of SARS-CoV-2 through blood and components has not been determined and respiratory viruses have never been reported to be transmitted by blood transfusion, including coronaviruses like SARS-CoV (the Severe Acute Respiratory Syndrome Coronavirus) and MERS-CoV (which causes Mideast Respiratory Syndrome) (7).

Although there are uncertainties regarding the presence of viraemia in asymptomatic individuals (e.g., during incubation period, asymptomatic infection or after symptom resolution), the potential risk of viral transmission from blood collected from such individuals is theoretical (8).

The WHO guideline document for blood transfusion services in the event of a pandemic influenza outbreak states: "The transmission of a respiratory virus by transfusion is very unlikely to result in an infection in the transfused patient although, in the most extreme cases where the blood donor is viraemic with a particularly high viral load, the possibility of transmission has to be considered; in these circumstances, however, the donor is unlikely to be well enough to donate" (9).

Therefore, any actions taken to mitigate risk are

therefore precautionary. Many emergency measures have been taken in several countries (10-12).

The Asian Association of Transfusion Medicine recommend that "donor selection and screening measures should exclude any individual who is not in good health or with symptoms and signs of fever or respiratory disease – common cold, flu or influenza over the past 14 days" (11).

Proactive measures such as the temporary isolation of blood for 14 days after collection and delaying its release for clinical use have also been taken in areas affected by COVID-19 (13).

The Chinese Society of Blood Transfusion recommend to donors to postpone their donation for 28 days following travel to China and its special administrative regions, Hong Kong and Macau, as well as Iran, Italy and South Korea, or contact with a person who has the virus, or is suspected to have it (10).

Preliminary data indicate that viraemia is present in 15% of patients, although with low RNA concentrations (14). The efficacy of pathogen reduction techniques on the inactivation of SARS-CoV-2 is being evaluated (14) and this could become part of a solution aimed at lowering the risk for transfusion of platelets and plasma (but not for red cells) (15).

Blood donation and collection

With the COVID- 9 outbreak, healthy potential donors are less available to donate blood, due to closure of organizations, transport restrictions, and other social distancing measures. Furthermore, donors are scared to be infected due to the close contact with other donors. Therefore, proportionate actions and evidence-based operating procedures must be taken into consideration: facilitating the donor recruitment, donation and transportation, and following international protocols to ensure the safety of donors and staff.

For mitigating the impact of reduced availability of blood donors, the WHO also recommend: "A proactive communication strategy is needed to address donor anxiety, which often stems from lack of awareness, misinformation or fear of becoming infected during blood donation. Effective public awareness campaigns on the importance of maintaining an adequate

national blood supply, need for blood donors, and safety of the donation process should be disseminated continuously” (16).

Associated co-morbidities

Thalassemia and SCD patients, especially adolescents and adults, may have associated co-morbidities, such as: liver, cardiac and endocrine complications (diabetes and biochemical hypocortisolism) and therefore are potentially exposed to a major risk of infection or complications.

Splenectomy is not known to increase the general risk of viral infection or severe viral disease, but no specific data exists for SARS-CoV-2. Splenectomized patients who develop fever should be evaluated also for possible bacterial infection and treated with antibiotics according to the international guidelines. Interruption of iron chelation and hydroxyurea is advisable and, as vulnerable patient, phone consultation with a COVID-19 Unit should be taken into consideration.

Data on the management of specific comorbidities, in patients with COVID-19, is limited and should be tailored to the patient's chronic disease.

In summary, we acknowledge that the situation is changing rapidly and also that local practice may differ depending on available resources and infrastructure. However, Governments and Scientific Societies are continually updating their advice and information in relation to COVID-19. Reduction of donor numbers before, during and after a COVID-19 outbreak is a major risk for blood services. Effective public awareness campaigns on the importance of maintaining an adequate national blood supply, need for blood donors, and safety of the donation process should be disseminated continuously.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Shah FT, Sayani F, Trompeter S, Drasar E, Piga A. Challenges of blood transfusions in β -thalassemia. *Blood Rev.* 2019;37:100588. doi:10.1016/j.blre.2019.100588.
2. Vidja PJ, Vachhani JH, Sheikh SS, Santwani PM. Blood transfusion transmitted infections in multiple blood transfused patients of Beta thalassaemia. *Indian J Hematol Blood Transfus.* 2011;27:65–69.
3. Canatan D. The Thalassemia center of Antalya State Hospital: 15 years of experience (1994 to 2008). *J Pediatr Hematol Oncol.* 2013;35:24–27.
4. Canatan D. Thalassemias and Hemoglobinopathies in Turkey. *Hemoglobin.* 2014;38:305–307.
5. de Sanctis V, Ruggiero L, Soliman AT, Daar S, Salvatore Di Maio S, Kattamis C. Coronavirus Disease 2019 (COVID-19) in adolescents: An update on current clinical and diagnostic characteristics. Submitted for publication to *Acta Biomedica.* 2020.
6. Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X, Zhang Z, Liu L, Liu T, Liu Y, He Y, Sun B, Wei M, Yang G, Wang X, Zhang L, Zhou X, Xing M, Wang PG. Relationship between the ABO blood group and the COVID-19 susceptibility. [Accessed on: 23/03/2020.] *medRxiv* 2020.03.11.20031096; doi: <https://doi.org/10.1101/2020.03.11.20031096>.
7. <https://www.redcross.org/about-us/news-and-events/press-release/2020/red-cross-media-statement-on-2019-novel-coronavirus.html>.
8. World Health Organization. Maintaining a safe and adequate blood supply during the pandemic outbreak of coronavirus disease (COVID-19): Interim guidance [20 March 2020]. WHO/2019 NCOV/BLOODSUPPLY/2020.1.
9. World Health Organization. Maintaining a safe and adequate blood supply during pandemic influenza: Guidelines for Blood Transfusion Services. Geneva, Switzerland: World Health Organization; 2011.
10. Chinese Society of Blood Transfusion [Internet]. Recommendations for blood establishments regarding the novel coronavirus disease (COVID-19) outbreak. Available at: <http://eng.csbt.org.cn/portal/article/index/id/606/cid/7.html>. Accessed on: 23/03/2020.
11. Asian Association of Transfusion Medicine. Recommendations to prevent COVID-19 infection through the blood supply. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public>.
12. Centro Nazionale Sangue [Internet]. [Coronavirus, precautionary measures updated]. Available at: <https://www.centronazionalesangue.it/node/831>. Accessed on 31/03/2020. [In Italian].
13. Cai X, Ren M, Chen F, Li L, Lei H, Wang X. Blood transfusion during the COVID-19 outbreak. *Blood Transfus.* 2020; 18: 79–82.
14. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, Cleary P, Fu-Meng Khaw FM, Wei Shen Lim WS, Sophia Makki S, Kevin D Rooney K, Nguyen-Van-Tam J S, Beck CR, Convalescent Plasma Study Group. Convalescent Plasma Study Group. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review

- and exploratory meta-analysis. *J Infect Dis* 2015; 211: 80-90.
15. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, , Cleary P, Fu-Meng Khaw FM, Wei Shen Lim WS, Sophia Makki S, Kevin D Rooney K, Nguyen-Van-Tam J S, Beck CR, Convalescent Plasma Study Group. Convalescent Plasma Study Group. The effectiveness of convalescent plasma and hyper-immune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. *J Infect Dis.* 2015; 211: 80-90.
16. World Health Organization. Maintaining a safe and adequate blood supply during the pandemic outbreak of coronavirus disease (COVID-19): Interim guidance [20 March 2020]. WHO/2019 NCOV/BLOODSUPPLY/2020.1.

Received: 12 April 2020

Accepted: 14 April 2020

Correspondence:

Prof. Dr. Duran Canatan

Pediatric Hematologist & Geneticist

President Mediterranean Blood Diseases Foundation

Director of Hemoglobinopathy Diagnosis Center Antalya -Turkey

www.akhav.org.tr

E-mail: durancanatan@gmail.com