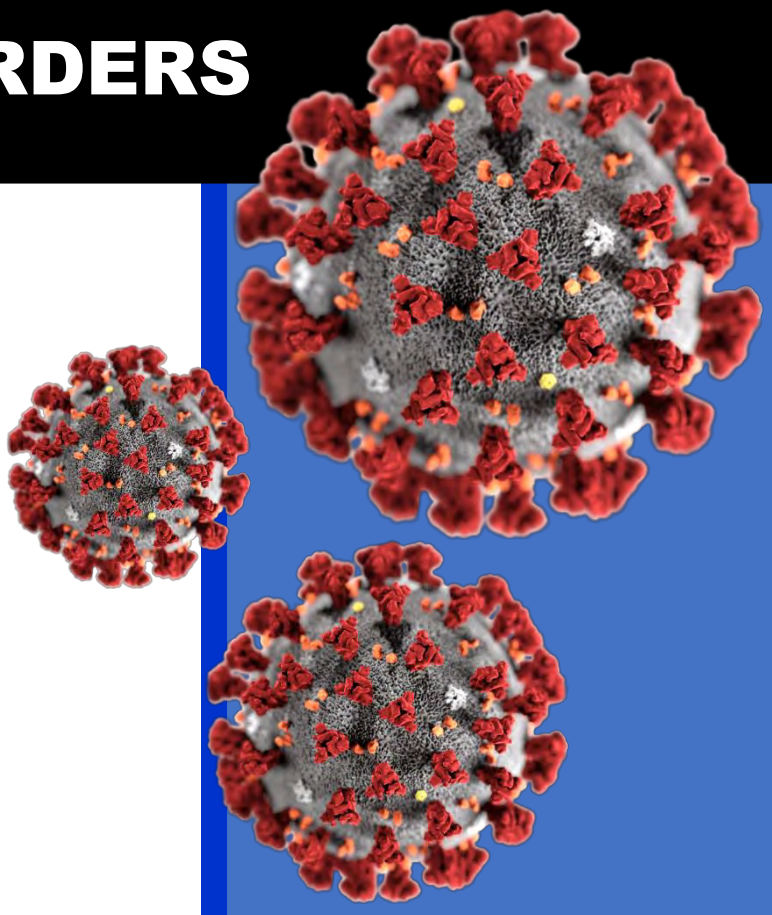
THE COVID–19 PANDEMIC AND HAEMOGLOBIN DISORDERS



A contribution of Thalassaemia International Federation to its global patients' community

Version II (Updated)

THALASSAEMIA INTERNATIONAL FEDERATION

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Introduction

The SARS-CoV-2 infection presents particular challenges and dangers to patients with haemoglobin disorders. The virus affects primarily the respiratory system, from naso-pharyngeal symptoms to full blown pneumonia. The following symptoms may develop in the 14 days after exposure to someone who has COVID-19 infection:

- cough
- difficulty in breathing
- fever

Generally, these infections can cause more severe symptoms in people with weakened immune systems, older people, and those with long-term conditions like diabetes, cancer and chronic lung disease. There is no evidence that children are more affected than other age groups – very few cases have been reported in children. Most people (about 80%) who become infected experience mild illness and recover, but it can be more severe for others. Most deaths are related to respiratory complications requiring intensive care and respiratory support, even though an overexuberant inflammatory response with multi-organ failure may be prevalent in some cases.

So far very little clinical experience of infected patients with haemoglobin disorders has been recorded. Any statement on these subjects may be regarded as speculations; cautionary thoughts are however necessary, in view of the rapid spread of the virus and the possible factors which may render these patients fragile in front of this infection. TIF believes that health services should be alerted to these risks and affected patients warned so that extra precautionary measures can be taken.

Haemoglobin disorders are generally not associated with respiratory conditions. However, complications involving the heart, lungs and the immune system, can be present in these patients and in a SARS-CoV-2 positive patient may trigger very serious complications. In addition, some of these patients might be splenectomised and sickle cell patients may be functionally asplenic.

Sickle cell disease

One group particularly at risk in this respect are sickle cell patients. One serious complications and major cause of death in this hereditary blood disorder is the acute chest syndrome, which is most often triggered by a respiratory infection.

Compared to the general population, patients with SCD are particularly at risk for acute pulmonary complications, including viral infections. For example, administrative records of children with SCD during two influenza seasons (2003-2005) were examined in four states (California, New York, Maryland, and Florida). Overall, children with SCD were hospitalized 56 times more frequently than children without SCD, and rates were twice as high compared to children with cystic fibrosis[1].

The SARS-CoV-2 infection may trigger such a serious complication and require special alertness on behalf of physicians treating infected patients. In addition, any hypoxia, dehydration or acidosis due to respiratory infection may trigger a vaso-occlusive crisis (including acute chest syndrome). Underlying pulmonary hypertension or kidney disease can also increase the risk of these patients becoming unwell if they contract the virus.

Many patients are being treated with hydroxycarbamide (hydroxyurea), a cytotoxic agent, whith possible immune-compromising effects. Even if up to now there is no evidence for an increase in the prevalence and/or severity of known viral infections, we cannot exclude that hydroxycarbamide treatment may be a contributory factor to adverse outcomes in sickle cell patients.

The current advice is to continue treatment and monitoring tests as advised by the treating physicians.

[1] *Bundy DG, Strouse JJ, Casella JF, Miller MR. Burden of Influenza-Related Hospitalizations Among Children With Sickle Cell Disease. Pediatrics. 2010; 125 (2) 234-243; DOI: https://doi.org/10.1542/peds.2009-1465*

Thalassaemia

Thalassaemia patients do not have the same risk of lung infections as patients with sickle cell disease but, especially adults, often have underlying complications including heart disease, liver disease, diabetes and severe iron overload may also be particularly vulnerable to complications of the virus.

One particular endocrine complication, often not recognised, is underactivity of the adrenal glands (adrenal hypofunction), which may not have been diagnosed. In the presence of a serious infection, however, the ability to limit the effects of the infection may be compromised. Dealing with a thalassaemia patient infected by the virus should take this possibility into consideration and the possibility of low-dose glycocorticoid supplementation considered. However it must be taken into account that corticosteroids slow down clearance of viral RNA from respiratory tract in SAR-CoV e MERS-CoV infections and increase complications rate[2].

[2] *Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet. 2020 Feb 15;395(10223):473-475.*

Blood transfusion

At this time there is no evidence that the corona virus may be transmitted through donated blood.

One visible danger is the possibility of under-transfusion during the epidemic due to blood donor reluctance or even infection. Shortage of blood is an issue to be discussed with international, national and local blood authorities and NGOs and further information and guidance is available through their public information sites/services (e.g. Centres for Disease Control and Prevention (CDC), the Advancing Transfusion and Cellular Therapies Worldwide (AABB, formely know as American Association of Blood Banks), the European Centre for Disease Prevention and Control (ECDC), the World Health Organisation (WHO), the International Society of Blood Transfusion (ISBT) and Thalassaemia International Federation (TIF).

The WHO has provided its member countries globally with resolutions/tools and recommendations on how to best address periods of blood shortage during infectious disease outbreaks3. Thalassaemia International Federation (TIF) in continuous and close contact with the WHO and other Official Blood-related Establishments at national and international level to monitor the European and Global situation with regards to the COVID-19 pandemic and its potential impact on blood supplies[4]. (Reference provide some very useful sites for your information)

[3] *WHO, Protecting the Blood Supply During Infectious Disease Outbreaks, Guidance for National Blood Services*
[4] *FDA U.S. Food & Drug Administration https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/updated-information-blood-establishments-regarding-novel-coronavirus-outbreak*
South China Morning Post https://www.scmp.com/news/china/society/article/3075567/people-blood-type-may-be-more-vulnerable-coronavirus-china-study
Joint United Kingdom Blood Transunion and Tissue Transplantation Services Professional Advisory Committee
Canadian Blood Services https://www.transfusionguidelines.org/dsg/wb/guidelines/coronavirus-infection
https://blood.ca/en/covid19
https://www.ecdc.europa.eu/en
https://www.cdc.gov/

TIF advises/suggests to its member patient associations to work very closely with their National Transfusion Services (BTS), Treating Physicians and National Healthcare Authorities (NHA) to:

i. Continue empowering blood donors to give blood provided that safe blood donation environments are ensured for them. BTS and NHA should commit to providing such settings for blood donors.

ii. BTS and NHA should make every effort to strengthen existing and developing new mobile unit services for facilitating blood donors to give blood.

iii. Update and upgrade where necessary the blood donor's Questionnaire to secure the safety of the blood albeit the absence todate of any evidence of transfusion transmittance of this virus.

iv. Continue to spread reliable and updated information to the patients and the community at large regarding the symptoms and risks related to this viral infection and precautions that should be taken in order to facilitate donors for self-deferral.

v. An initiative should begin in creating new and/or strengthening existing pools of donors from family members, friends. It is important to develop tools, questionnaires or other means to ensure knowledge of the history of the blood donors that are encouraged to form these pools. It is important to focus on the diversity of the blood groups in order to support coverage of blood groups of the greatest majority of patients using the different pools of donors and in addition on including also rare groups. Despite the fact that the WHO and TIF have always focused and strongly advocated for voluntary, non-remunerated blood donation practices in extreme circumstances that lead to severe shortages of blood, unfortunately we are left with no other weapons for our patients whose life is depended on lifelong blood transfusion. However, and under no circumstances any paid donation should be encouraged or even considered.

Splenectomy

Thalassaemia patients, particularly of the older age groups were frequently splenectomised and sickle cell patients have often a condition equivalent to splenectomy (functional hyposplenism or asplenia). This renders all patients vulnerable to bacterial infections and trigger serious and life threatening sepsis. If infected by the virus patients may also develop secondary bacterial infections.

Recommendations

1. In patients with symptoms of cough, fever, fatigue or other symptoms suggestive of an acute respiratory illness, test for COVID-19 along with other respiratory viral pathogens

2. If suspicion for COVID-19 is high or test is positive, the treating physician who is fully aware of the individual's care plan, should be contacted immediately.

3. A chest X ray for all sickle cell disease and thalassaemia patients who have respiratory symptoms should be obtained. In addition, a chest X ray should be obtained for sickle cell disease patients who are admitted for a vaso-occlusive crisis.

4. If COVID-19 is present or infiltrates present on Chest X-ray suggestive of ACS (Acute Chest Syndrome) in SCD, patients should be admitted to intensive care and managed according to national and international guidelines for addressing ACS. Likewise, for infected with COVID-19 thalassaemia patients, arrangements for admission to the intensive care, should be made and the treating haematologist/physician should be notified. Close monitoring both by the intensive unit medical staff and the patients' treating physician should be established.

5. Management of ASC in SCD Patients Infected with COVID-19 includes:
   a) Early exchange transfusion
   b) Broad spectrum antibiotics – include MRSA coverage, atypicals, pneumococcus
   c) May be some benefit of plasmapheresis
   d) Consideration of high dose steroids (although not clearly helpful in COVID-19)
   e) Consult Paediatric or Adult Pulmonary as well as Haematology

Important Note!

The effects/consequences and clinical impact of coronavirus particularly in thalassemia (transfusion and non-transfusion depended) patients is not todate well defined or known and meticulous observation and very comprehensive and detailed reporting of the clinical outcome of those patients positive to the coronavirus, whether in intensive care units or other hospital department or quarantine environment, should be ensured.

Such action will contribute to the more prompt management of the various potential medical complications that may arise in infected patients, but also very importantly to the collection and sharing with other treating physicians, of important information and data that will support the better understanding and the consequences of the infection in this special group of patients hence management of the potential medical complications.

Already TIF is collaborating with international medical experts for developing a questionnaire which will focus on the collection of approval and reliable information on clinical outcomes of patients with haemoglobin disorders who had experienced, by confined diagnosis, the COVID-19. The questionnaire will be uploaded on TIF's website and its social media, distributed widely amongst its members - National Thalassaemia Associations and treating physicians and eventually linked to a group of medical experts who handle an international registry.

Please follow TIF's website and social media for further information.

Precautionary measures

Basic information

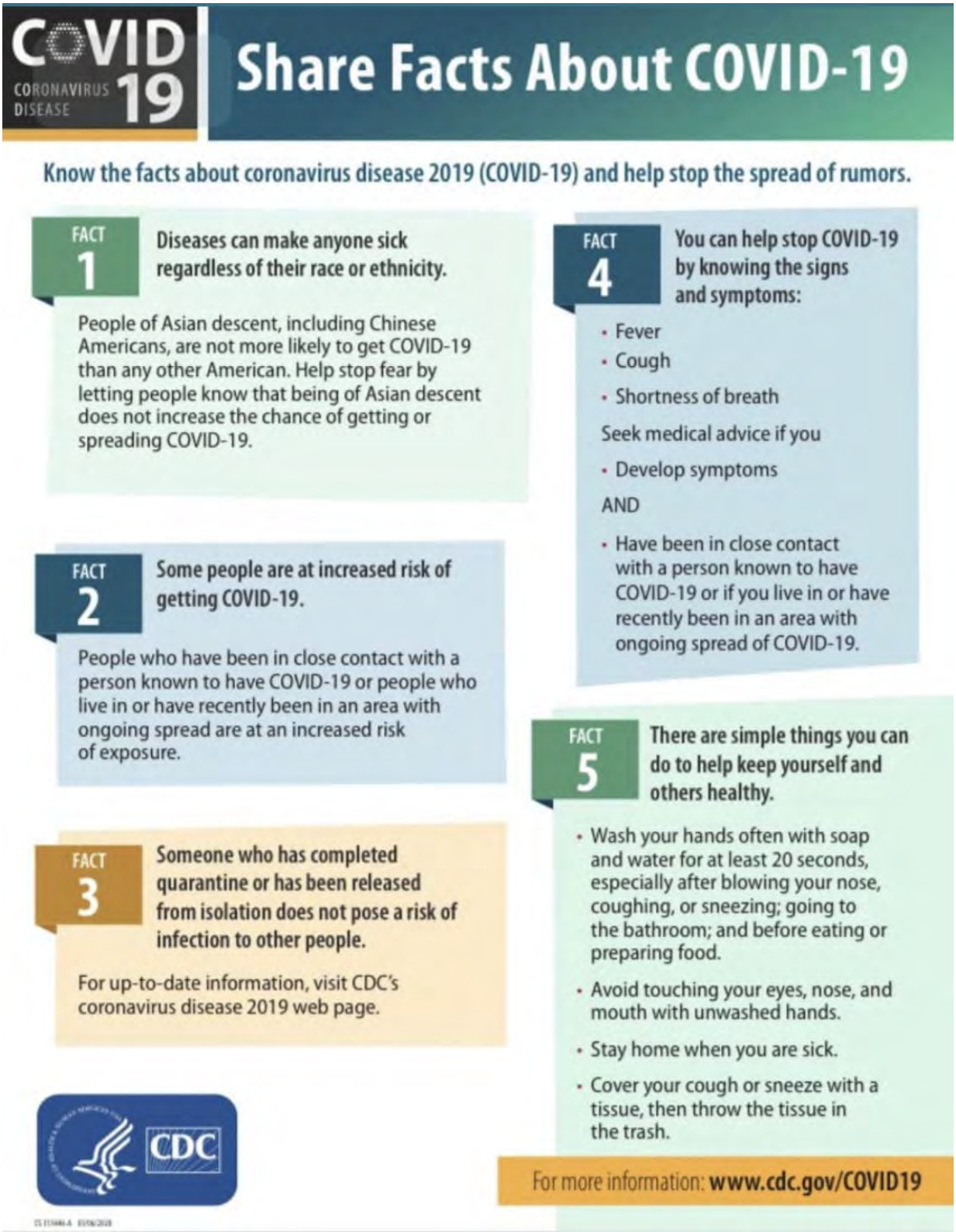
Instructions concerning avoiding SARS-CoV-2 infection, reducing spread of the virus, and what to do if infection is suspected are varying from country to country. Local and national guidance should be faithfully followed.

Adherence to the instructions and recommendations of your National Health Committees is of pivotal importance. Patients should be fully aware of the risk of the exposure and ways of transmission of the virus

General rules to apply to stop the spread of the virus include:

- ✓ washing hands often and properly (well and for over 20 seconds) - with soap and water, or use alcohol sanitiser if handwashing facilities are not available. This is particularly important after taking public transport
- ✓ covering your cough or sneeze with a tissue, then throwing the tissue in a bin. (Catch it, Bin it, Kill it)
- ✓ people who feel unwell should stay at home and should not attend work or any education or childcare setting
- ✓ avoid to meet people if not absolutely necessary
- ✓ limit the interpersonal relationship
- ✓ maintain at least 2 m of distance when talking to other people
- ✓ avoid touching eyes, nose and mouth with hands that have not been washed or disinfected
- ✓ use antibacterial soaps/spray to disinfect all surfaces you touch or use including TV controls, mobiles, telephones.

Information from CDC



It is highly important to alert service providers immediately if patients have scheduled treatments in the hospital (blood transfusions, red cell exchange transfusions, Testosterone injections, Bisphosphonate infusions and others) if they have concerns that they might have come in contact with an infected person of if they have any respiratory symptoms (even mild

The treatment centre should plan for triage and should advice if patients can postpone treatment, self- isolate and when a COVID-19 test is indicated and how this can be arranged. This is to stop infected patients enter the common areas used by all, (especially patients with cancer and on chemotherapy). Efforts should be made to establish a special isolated transfusion room for infected patients, who may not be able to postpone a blood transfusion or other treatments until recovery

Advice and guidance will be reviewed regularly as new information and data become available.

Keep following TIF for updates

TIF Communication Channels

www.thalassaemia.org.cy

Thalassaemia International Federation - TIF

TIF @thalassaemiaTIF

Thalassaemia TIF

tif_thalassaemia

Help Line: thalassaemia@cytanet.com.cy

Please share with us your questions, concerns and experiences.

Your Input is Important to Us!!