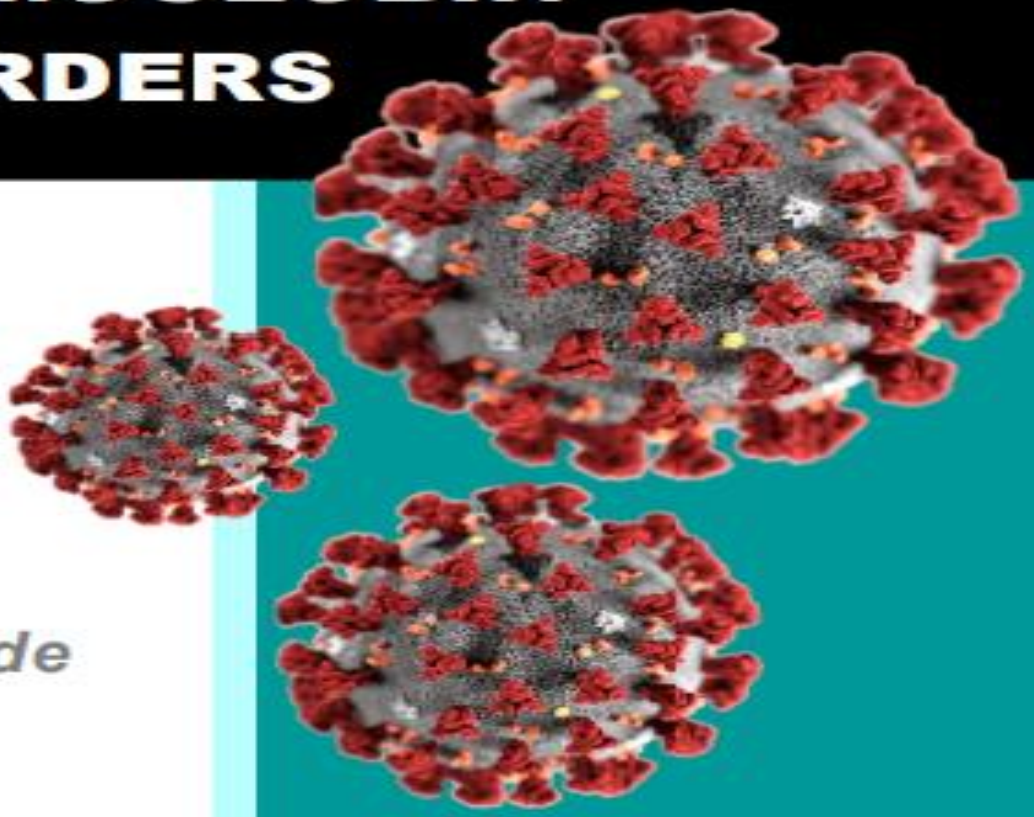
In the name of GOD

Parastoo Molaei Tavana , MD.

Assistant Professor

Shahid Beheshti University of Medical Sciences

THE COVID–19 PANDEMIC AND HAEMOGLOBIN DISORDERS



BLOOD & COVID-19

An Informational Guide from the Thalassaemia International Federation (TIF)

THALASSAEMIA INTERNATIONAL FEDERATION

Thalassemia International Federation

The information in this document is only a compilation of recommendations or guidance with regards to COVID-19 and Hemoglobin Disorders retrieved from published information found in either peer reviewed papers or at official government sites of some Western countries mainly including the UK, Germany, Italy, France, Cyprus and the USA

Introduction

- From data reaching the TIF office, either through published literature or by contact with member associations or experts(120 infections in thalassemia patients, and over 700 in sickle cell patients)

- Infection rates seem to be lower in thalassemia but for both groups mortality rate is about 6% and is higher than the general population

- This is probably related to frequent co-morbidities that are encountered in both sickle cell and thalassemia syndromes

Introduction

- **Fifteen confirmed cases (12 TDT and 3 NTDT) and eight symptomatic suspected β18 thalassemia patients (6 TDT and 2 NTDT)**
- **Seventeen patients (73.9%) had mild to moderate symptoms and recovered, while 6 patients died (26.1%, 2 TDT and 4 NTDT).**
- **More than 60% of all patients had at least one comorbidity**

Prevalence and Mortality due to Outbreak of Novel Coronavirus Disease 9 (COVID-19) in β-Thalassemias : The Nationwide Iranian Experience

Br J Haematol. 2020 Jun 2 : 10.1111/bjh.16911

Susceptibility of β-Thalassemia Heterozygotes to COVID-19

- **255 positive COVID-19 unvaccinated patients**
- **Severe-critical COVID-19 was strongly associated with male sex ($p = 0.023$), increased age ($p < 0.001$), and β-thalassemia heterozygosity ($p = 0.002$, OR = 2.89)**
- **Mortality was linked to male sex ($p = 0.036$, OR = 2.09), increased age ($p < 0.001$) and β-thalassemia heterozygosity ($p = 0.010$, OR = 2.79) in multivariate analysis**

Susceptibility of β-Thalassemia Heterozygotes to COVID-19
J. Clin. Med. **2021, *10*(16), 3645; https://doi.org/10.3390/jcm10163645**

Thalassemia International Federation

- **Disease related complications may affect multiple organs include the heart, liver, endocrine glands, lungs, the immune system diabetes and severe iron overload**
- **CARRIERS of any hemoglobin disorders are NOT CONSIDERED as 'VULNERABLE' or individuals 'AT RISK' . They are healthy individuals and will only be considered 'vulnerable' or 'at risk' if they have an underlying condition**

Risk groups

- **Group A, patients at“moderate risk”**
- **Group B, patients at “high risk”**
- **Group C, patients at “highest risk”**
- **It should be stressed that the proposed risk classification is mainly based on the level of adherence to disease-specific care, since quality of care is the crucial determinant of morbidity in these patients**

Group A:Moderate risk

- **Thalassemia patient with all of the following:**

1. **Optimal transfusions with pre-transfusion Hb 9.5-10.0 g/dl (for ≥3-4 previous years)**
2. **Optimal iron chelation with cardiac T2* >20ms, LIC <7mg/g DW or serum ferritin <2000mg/L (for ≥3-4 previous years)**
3. **No underlying comorbidities**
4. **No splenectomy**

Group A:Moderate risk

- **Guidance:**

Assume work/schooling/education without any additional measures besides national guidelines for general population (distancing, hand washing, wearing mask)

Group B: High risk

- **Thalassemia patient with 2 or more of the following:**

1. **Sub-optimal transfusions with pre-transfusion Hb 8.0-9.0g/dl (currently and in ≥2-3previous years)**
2. **Moderate iron load with cardiac MRI T2* 10-20 ms , LIC 7-10 mg/g DW or serum ferritin2000-4000 mg/L (currently and in ≥2-3 previous years)**
3. **One underlying comorbidity including diabetes, cardiac, endocrine, hepatic or respiratory disease**
4. **Splenectomy**

Group B: High risk

❑ **Guidance :**

Assume work/schooling/education keeping national guidelines for general population(distancing, hand washing, wearing mask) unless job involves treating/caring patients or other vulnerable groups (healthcare professionals) or frequent contact with people(receptionists, shop assistants)

Group C:Highest risk

- **Sickle cell disease patient**
- **Thalassemia patient with 2 or more of the following:**

1. **Age >50 years**
2. **Sub-optimal transfusions with pre-transfusion Hb <7 g/dl (currently and in ≥2-3 previous years)**
3. **Severe iron load with cardiac MRI T2* <10 ms, LIC >10 mg/g DW or serum ferritin >4000 mg/L (currently and in ≥2-3 previous years)**
4. **One or more underlying comorbidity including diabetes, cardiac, endocrine, hepatic or respiratory disease**
5. **Splenectomy with one or more of comorbidities**

Group C:Highest risk

- **Guidance:**

Refrain from any type of work/schooling/education activities and remain at home, avoiding any gatherings or contact with potential COVID-19 (relative symptoms) until the pandemic is declared well over at country level . Keep national guidelines of distancing, hand washing and wearing mask at least 6 months after the pandemic is declared over at country level

Monitoring tests and medications

- **The routine tests : full blood count, pre-transfusion hemoglobin levels and serum ferritin should continue**
- **Annual routine monitoring tests: MRI, Ferri scan , dual-energy X-ray absorptiometry (DEXA), ophthalmology & audiology tests should better be postponed until after the end of the pandemic in clinically stable patients with low iron load and no new indications for these tests**

Safety of blood transfusions

- **Coronavirus RNA can be amplified from patients' blood**
- **All respiratory viruses (except for adenoviruses) normally attach to receptors in the airways and their blood-borne transmission is unknown**
- **Viremia in the incubation period, asymptomatic course of infection and after symptoms' resolution has not been documented**
- **Transmission of other 'similar' viruses, SARS-CoV, MERS-CoV and … through transfusion or transplantation has not been reported to date**

COVID-19 Is Not Transmitted Through Blood Transfusion

Some people with thalassemia worry that COVID-19 may be transmitted through the blood supply. There has been no evidence that COVID-19 can typically be transmitted through blood transfusions, nor have any previous coronaviruses (the family of viruses to which COVID-19 belongs) shown this ability.

Safety of blood transfusions

- **The WHO, the AABB, the FDA and the US CDC mention that:**

  there is no data suggesting a risk of transmission of SARS-CoV2 through transfusion

- **Screening of the blood and blood product supplies for SARS-CoV-2 is not currently recommended in the absence of documented transfusion transmission**

Patients with Cardiac T2*< 10 ms and proven or suspected Covid-19 infection:

- **Intravenous iron chelation therapy through a central venous access device or on oral iron chelation (monotherapy or combination therapy):**
- **Daily contact with patients by specialist team either via email or telephone**
- **If symptoms mild and patient not febrile advice to continue chelation and liaise with team on a daily basis**

Stopping chelation

Desferrioxamine should be immediately discontinued if signs of bacterial superinfection exist and deferiprone should be discontinued because leukopenia is often observed during infections. However, there seems to be no need to discontinue deferasirox

Patients with Cardiac T2*< 10 ms and proven or suspected Covid-19 infection:

- **If patient has fever > 37.80 C then they should be admitted:**
- **Cardiac status must be assessed - Focused echo for LV function & TRjet Vmax (if any TR)**
- **BNP if symptoms of breathlessness (a negative BNP rules out cardiac failure)**
- **Baseline ECG**
- **Other causes of fever should be ruled out(infected lines, Gram negative bacteremia or Yersinia infection)**
- **Patients where other causes are excluded and are COVID-19 POSITIVE : continue on intravenous iron chelation with desferrioxamine and stop the oral iron chelation medication until the infection resolves**
- **Careful monitoring**

Cardiac T2* > 10 ms and proven or suspect Covid-19 infection

- **If symptoms are mild and no fever then advise to continue iron chelation and daily contact with the team**
- **If febrile they should present for face to face assessment at the hospital and possibly a COVID swab**
- **If no cardiac symptoms and cardiovascularly stable, then patients should aim to continue chelation therapy after acute bacterial infection has been reasonably excluded**
- **If patient develops palpitations, ankle swelling and worsening shortness of breath then to contact their team and attend hospital as a matter of urgency, be admitted and managed as per those patients with T2***

Transplanted patients

- **Patients who have had Hematopoietic Stem Cell Transplantation (HSCT) or Gene Therapy/Editing or organ transplant, particularly within the last two years**
- **‘Highest risk’ scoring**
- **Not returning to any type of work except electronic one, self-isolation and every effort should be made to be provided with home transfusion or in very ‘isolated’ spaces dedicated for the transfusion of the patients**

Treatment of covid-19 in thalassemia

- **No specific recommendations for patients with Thalassemia major / intermedia for the therapy of COVID-19**
- **For patients with thalassemia intermedia :Potential option of therapy with hydroxychloroquine (Drug-induced hemolytic crises may occur in G6PD deficient patients)**
- **This enzyme deficiency may also have been co- inherited with thalassemia**

Treatment of covid-19 in thalassemia

- **Adrenal hypofunction :**

- **One particular endocrine complication which may not have been diagnosed**

- **In dealing with a thalassemia patient infected by the virus this possibility should be taken into consideration and although the possibility of provision of low-dose glycocorticoid supplementation may be considered**

Splenectomised patients

- **Based on knowledge of the immunological functions of the spleen, there is no evidence that the lack of a spleen or part of a spleen or a non -functioning spleen on its own renders patients at higher risk of Covid-19**
- **Recommendations for shielding will therefore depend in the underlying cause for splenectomy or asplenia and any associated comorbidities and treatments**

New fever in splenectomised patients

- **All patients should be instructed to seek urgently medical advice**
- **Consideration should be given to the presence of bacterial infection, particularly with capsulated pathogens**

Thromboembolic events

- **Higher risk for thrombosis or cerebrovascular disease: patients with thalassemia major particularly non transfusion dependent thalassemia**
- **Splenectomised patients and in addition with pulmonary hypertension; LIC≥5mg/g DW, or Ferritin ≥800mg/L**
- **In such an event: Prophylactic intervention with anticoagulant or anti aggregants(aspirin and LMWH) are recommended for adult patients with COVID-19 and inpatient treated adolescent patients with COVID19**

German Society of Thrombosis and Haemostasis Research (GTH)

Lifestyle and nutritional considerations

1. **Sufficient hydration :** 2-3 liters of water consumed throughout the day
2. **Adequate rest :** 7-8 hours of sleep daily
3. **Regular but not exhaustive exercise :** half-hour walk, 3 days a week
4. **Normal body weight maintenance :** well-balanced diet , frequent small and light meals, mainly consisting of fruits and vegetables

Lifestyle and nutritional considerations

5. Effective stress management through calm mindfulness
6. Continuous management of chronic comorbidities: cardiac and pulmonary conditions, and diabetes mellitus.
7. Self-disciplined smoking cessation as even otherwise healthy smokers are considered of high risk for suffering severe complications from Covid-19
8. Controlled brief exposures to direct sunlight for mood boosting, sleep regulation, as well as for essential vitamin D

Lifestyle and nutritional considerations

- **Natural sources containing vitamin C (citrus fruits), vitamin D (sardine, mackerel, dairy products), zinc (legumes, seeds and nuts) and omega-3 fatty acids (sardine, mackerel) : boost the immune response**
- **There are no clinical data available there is a belief that probiotics (especially preparations with *lactobacilli* and *bifidobacteria* species) could help against most viral infections, Covid-19 included**
- **Potentially beneficial phytochemicals against the coronavirus infection(found within a flavonoid rich plan), with strong preclinical evidence include procyanidins lectins , luteolin , hesperetin , catechins and ,sulforaphanes**

References

1. World Health Organization (WHO). WHO COVID-19 Dashboard .https://who.sprinklr.com.Last accessed on May 12, 2020
2. Thalassemia International Federation. Guidelines for the Management of Transfusion Dependent Thalassemia-The COVID-19 Pandemic & Haemoglobin Disorders (2020)
3. AABB (formerly known as the American Association of Blood Banks) - AABB's Resources for: FDA's Updated Information for Blood Establishments Regarding the Novel Coronavirus (COVID-19) Outbreak March 2020
4. Centers for Disease Control and Prevention. Coronavirus (COVID-19). https://www.cdc.gov/coronavirus/2019-ncov/index.html. Last accessed on April 14, 2020
5. Farmakis D, Giakoumis A, Angastiniotis M, Eleftheriou A. The changing epidemiology of the ageing thalassaemia populations: A position statement of the Thalassemia International Federation. Eur J Hematol. 2020 Mar 21. doi: 10.1111/ejh
6. Motta I, Migone De Amicis M, Pinto VM, Balocco M, Longo F, Bonetti F, Gianesin B, Graziadei G, Cappellini MD, De Franceschi L, Piga A, Forni GL. SARS-CoV-2 infection in beta thalassemia: Preliminary data from the Italian experience. Am J Hematol. 2020 Apr 20. doi:10.1002/ajh.25840.

THE COVID–19 PANDEMIC AND HAEMOGLOBIN DISORDERS

Thalassaemia & Sickle Cell Disease: Classification of Risk Groups & Other Considerations

Guidance for Patients, Parents & Healthcare Professionals

Prepared by:
Dr Androulla Eleftheriou
TIF Executive Director
Dr Michal Angastiniotis
TIF Medical Advisor

UPDATED NOVEMBER 2020

THALASSAEMIA INTERNATIONAL FEDERATION

Question

Should any changes in transfusion schedules or thresholds be made in the context of the COVID-19 pandemic?

- **It is advisable to maintain the individual's chronic transfusion regimen**

1. **Roy NBA, et al. Protecting vulnerable patients with inherited anaemias from unnecessary death during the COVID-19 pandemic. Br J Haematol. 2020 May;189(4):635-639**
2. **Motta et al, Am J Hematol, 2020 SARS-CoV-2 infection in beta thalassemia: preliminary data from the Italian experience. https://doi.org/10.1002/ajh.25840**