Dear Editor,

The clinical presentation generally includes respiratory infection with symptoms’ severity ranging from mild common- cold like symptoms, which recover without special treatments, to severe viral pneumonia leading to acute respiratory distress syndrome that is potentially fatal.

Although characteristic symptoms include fever, cough and dyspnea, however some patients may be asymptomatic (1). Thalassemia and hemoglobin variants represent, with reference to WHO, more than 7% of the world population. The beta-thalassemia have extremely diverse clinical spectrum, from non-transfusion dependent type to severe, transfusion dependent or beta-thalassemia major (βTM) which require chronic red blood cell transfusion from infancy, monitoring their growth and iron chelation therapy.

Moreover, Glucose-6-phosphate dehydrogenase (G6PD) deficiency among blood donors, alert both physicians and patients regarding the drugs and food safety to prevent hemolysis of the transfused units (2,3). Many βTM patients undergo splenectomy as part of their management plan which makes them vulnerable to infection (4). Individuals with hemoglobin disorders (hemoglobinopathies) are classified as ‘vulnerable’ group of patients in most countries worldwide. Infectious complications, mainly from bacteria, constitute a common cause of mortality and morbidity in βTM. Stress erythropoiesis, iron overload, splenectomy and adrenal insufficiency among others may contribute to increase susceptibility to infection (5).

A recent two pre-print research papers have addressed important issues in Covid-19 infection, the first hypothesized that structural and non-structural glycoproteins attack heme in the hemoglobin, making it inefficient for oxygen-carbon dioxide gas exchange, leading to further hypoxia and exacerbate the inflammatory process (6).

The second, paper hypothesized that beta thalassemia patients, might develop an immunity against SARS-CoV-2 as infectious consequences on hemoglobin, as the beta chain, potential target of the virus, which could be either absent or less prominent in the blood (7). This study only developed the hypothesis based on the validity of the preprint research by Liu &Li, which has to be confirmed by in vitro and later in vivo experiments. Although, patients with pre-existent chronic morbidities are likely to be at higher risk of infection by SARS-Cov2, but no solid data are available regarding βTM. Hereditary Blood Diseases Center (HBDC), AlAhsa district, Eastern province of Saudi Arabia, manage all thalassemia cases. During the study period three βTM cases were diagnosed with COVID-19 out of 150 βTM cases being followed in the center. Up to 25 June 2020, a total of 14,000 COVID-19 cases were reported in ALahsa.

First Case
A 31-year-old female, βTM, splenectomised during early childhood, with severe iron overload (Ferritin 6648 µg/l) because of poor compliance on iron chelation therapy. She is on chronic red blood cells transfusion regimen, presented to the HBDC with high fever 38.9°C and dry cough. The COVID-19 infection was confirmed by positive nasopharyngeal swab for SARS-CoV-2. She was admitted and treated with paracetamol, oxygen supplementation by facemask, Hydroxychloroquine (HCO), enoxaparin and ceftriaxone. After 8 days of initiating the therapy and isolation she had been discharged with oxygen saturation >95% by pulse oximeter.

Second Case
A 6-year-old boy, βTM, on chronic red blood cells transfusion every 3 weeks, suffers from iron overload (S. Ferritin 2524 µg/l) despite being on chronic chelation therapy.
He was in direct contact with symptomatic COVID-19 family member who works as a nurse in pediatric department. The patient was asymptomatic at presentation time, examination was unremarkable, Nasopharyngeal swab was positive for SARS-CoV-2 and admitted for observation. He was admitted in hospital for observation, remained asymptomatic for 4 days, then discharged well.

Third Case
A 27-year-old female βTM who was splenectomised during childhood. She is on chronic red blood cells transfusion every 3 weeks, with iron chelation therapy and S. ferritin of 4090 µg/l. She was diagnosed with COVID-19 while screening the family of the first case. She was asymptomatic, admitted for a couple of days for observation and discharged well. No medications were prescribed for her.

All the patients experienced mild disease, they recovered within 10 days, and only one patient received therapy. Two patients were splenectomised, which did not have negative impact on their clinical course, also the hemoglobin drop per week was not affected by COVID-19 i.e. there was no increase in blood transfusion requirements. Similarly, severe iron overload did not affect the outcome of the patients (Table 1 and 2).

Our data, though small size, on one hand it indicates that βTM are not at higher risk group for COVID-19 infection, on the other hand βMT did not adversely affect the patients’ outcome.

We need to have more patients enabling us to draw conclusions about the disease impact. Another point to be noted that blood components are not screened for G6PD status despite that one third of the donors are G6PD deficient and hemolysis might occur in the βTM who receive their blood while treated for Covid-19 as HCQ is integral part of its therapy.

### Table 1. Clinical features of βTM in patients affected by the SARS-Cov2 infection

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Splenectomy</th>
<th>Respiratory disease</th>
<th>Cardiomyopathy</th>
<th>Renal impairment</th>
<th>Chronic hepatopathy</th>
<th>Diabetes</th>
<th>Hypothyroidism</th>
<th>Osteoporosis</th>
<th>Hypogonadism</th>
<th>Ferritin (µg/l)</th>
<th>Liver T2* (mg/g dry weight.)</th>
<th>Hepatic T2* (m.s)</th>
<th>Iron Chelator</th>
<th>Likely source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>31Ys</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>6648</td>
<td>4.4</td>
<td>33.2</td>
<td>DFX</td>
<td>UNKNOWN</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>6Ys</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2524</td>
<td>-</td>
<td>-</td>
<td>DFX</td>
<td>Close contact with positive COVID-19 relative</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>27Ys</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>4090</td>
<td>4.1</td>
<td>36</td>
<td>DFX</td>
<td>Contact with positive COVID-19 RELATIVE</td>
</tr>
</tbody>
</table>

P: Female; M: Male; βTM: Beta thalassemia major; DFX: Deferasirox; DFP: Deferiprone. Empty cells correspond to the absence of the characteristics

### Table 2. Clinical features of βTM in patients affected by the SARS-Cov2 infection

<table>
<thead>
<tr>
<th>Fever</th>
<th>Cough</th>
<th>Anosmia</th>
<th>Pain</th>
<th>Fatigue</th>
<th>Diarrhea</th>
<th>Others</th>
<th>RX</th>
<th>CT</th>
<th>Hospital admission</th>
<th>O2/CPAP/MV</th>
<th>Specific therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>yes</td>
<td>yes</td>
<td>No</td>
<td>yes</td>
<td>yes</td>
<td>Dry throat</td>
<td>yes</td>
<td>-</td>
<td>yes</td>
<td>O2</td>
<td>HCQ</td>
<td>Recovered</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>yes</td>
<td>-</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>Recovered</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>yes</td>
<td>-</td>
<td>yes</td>
<td>No</td>
<td>No</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

02:Oxygen ; CPAP:Continous Positive Airway Pressure; MV:Mechanical Ventilation; HCQ: Hydroxychloroquine
REFERENCES


