#### CASE REPORT

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# First report of COVID-19 reinfection in a patient with beta thalassemia major

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#### Abstract

To optimize care for patients with hemoglobinopathies, frequent screening for COVID-19 is prudent as viral kinetics in asplenic patients are unknown and differentiating prolonged viral shedding versus reinfection remains a challenge.

#### **KEYWORDS**

corona virus, COVID-19 Reinfection, hemoglobinopathies, thalassemia beta major

## **1** | INTRODUCTION

Patients with hemoglobinopathies might be at risk of COVID-19 reinfection due to multiple factors. According to the TIF, those patients are considered vulnerable; however, a clear prognosis and the possibility of prolonged shedding or reinfection are not described. We report here the first case of thalassemia beta major patient who had asymptomatic COVID-19 reinfection.

Severe acute respiratory syndrome coronavirus 2 (SARS-COV2) was responsible for the latest outbreak, presenting mainly as respiratory symptoms and carrying high mortality rate.<sup>1</sup> All people are at risk of COVID-19 infection if protective measures are not taken, including those with hemoglobinopathies. Multiple factors increase the risk for infections in patients with hemoglobinopathies, yet the occurrence of reinfection and its implications either on them or on the community are not yet clear. Thalassemia is one of the most common hemoglobinopathies and requires life-long management and follow-up. Splenectomy, regular blood transfusion, and iron chelation therapy are essential components in the management

plan. Unfortunately, those long-term measurements might cause some complications that increase the susceptibility of bacterial and viral reinfection.<sup>2</sup> The impact of these factors on COVID-19 infection has not been well established.

Here, we report a case of a 31-year-old splenectomized lady with transfusion-dependent beta thalassemia major who had asymptomatic COVID-19 reinfection.

## 2 | CASE PRESENTATION

A 31-year-old Pakistani lady with past medical history of transfusion-dependent beta thalassemia major, type II diabetes mellitus and hypothyroidism visited the hematology department for follow-up and routine blood transfusion. Due to the ongoing spread of COVID-19 infection in Qatar, polymerase chain reaction (PCR) via nasopharyngeal swab was done following the local screening plan before admitting her for the blood transfusion. PCR result was positive.

The patient was admitted before due to COVID-19 infection; her previous course was smooth without any

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862

WILEY\_Clinical Case Reports

complications as the current one. The period between both PCRs was 55 days. Her current management plan and home medications were as follows: regular blood transfusion and iron chelation therapy for thalassemia, insulin, Sitagliptin/ Metformin, levothyroxine, and Tramadol. A comparison between the two presentations as well as the investigations results is mentioned below. Table 1.

## 3 | DISCUSSION

Coronaviruses are known for their mild presenting symptoms like common cold. However, the world has recently seen a huge outbreak caused by sever acute respiratory syndrome coronavirus (SARS-COV2) which was highly pathogenic and spread rapidly starting from China to all over the world with unfortunate increase in mortality rate.<sup>3</sup> COVID-19 presentation was categorized into typical and atypical symptoms with fatigue, fever, dry cough, and dyspnea being the most common presentations, especially at onset of infection, while headache, sore throat, runny nose, diarrhea, and vomiting were considered as less common manifestations. However, asymptomatic cases were also documented and played an important role in the spread of the infection.<sup>4</sup>

Although COVID-19 reinfection was reported in a previous studies, the mechanism is not clear and it is still unknown if affected patients might present as carriers for the virus.<sup>5</sup>

Hemoglobinopathies are well-known widely spread hematological disorders. Thalassemia is one of the most common forms of these disorders. It is mainly due to either alpha or beta chains hemoglobin reduction leading to defects that cause a wide range of clinical presentations. Thalassemia can also be categorized into transfusion dependent or independent.<sup>6</sup>

Severity of COVID-19 infection has been linked to many factors like the presence of other comorbidities such as diabetes, immunocompromised status, old age, and malignancy.<sup>7</sup> Data regarding patients with hemoglobinopathies vary in results. However, the majority described a smooth course of infection and a favorable outcome.8 The current statement from Thalassemia International Federation (TIF) emphasizes on the challenges during providing care for hemoglobinopathies patients in the pandemic, this concern arises mainly from the lack of clear evidence regarding COVID-19 infection progression and the frequent need for visiting healthcare facility either for follow-up of for blood transfusion.<sup>9</sup>Thus, TIF also suggests that healthcare facilities should take extra caution while dealing with those patients. However, hemoglobin disorders have not been linked directly to respiratory conditions, yet close monitoring is necessary as thalassemia patients could have multi-organ damage including heart, lung, liver, endocrine, and immune system damage due to the iron overload that might increase their COVID-19 complications risk.<sup>10-14</sup>

Thalassemia patients are usually splenectomized as part of the therapeutic interventions provided for them, thus they are more vulnerable for recurrent bacterial infections. Asplenic patients may have profound compromised humoral and cellular immunity thus behaving like other immunocompromised patients. Patterns of viral tropism and shedding may be distinctive in this subset of patients.<sup>15</sup> Till the day of writing this case, there is no evidence that splenectomy is correlated with an increased risk of COVID-19 infection and complications.<sup>16</sup>

Immune response to the pathogens differs among individuals due to genetic variations. Complications related to the impaired immunity in beta thalassemia patients were considered as an important cause of morbidity and mortality. Also, iron overload was labeled as the main reason behind immune deficiency in those patients. However, there is no evidence regarding iron chelation therapy role in COVID-19 patients with beta thalassemia major; in our case, the patient was on iron chelation therapy when she was reinfected.<sup>16</sup>

Immune response in COVID-19 patients is not well known till this time. Initial data suggested that more than 90% of infected adults had positive antibodies against SARS-CoV2 yet the duration and efficacy for this response is not clear.<sup>17</sup> One cohort study published by Zhae et al described the seroconversion rate for the antibodies; total, IgM, and IgG were 93%, 83%, and 65% respectively,<sup>18</sup> while Kissler et al suggested that immunity may last for a year.<sup>19</sup> There is lack of data regarding COVID-19 reinfection in patients with hemoglobinopathies.

In our case, the patient was confirmed to have COVID-19 reinfection with high infectivity depending on the results of COVID-19 PCR and antibody titer.

To the best of our knowledge, there are no reported cases in the literature regarding COVID-19 reinfection among patients with hemoglobinopathies. It is worthwhile to note that even with reinfection in our case which was detected by routine screening, the patient was asymptomatic at presentation and the disease course was uneventful. However, the presence of multiple comorbidities in this case like splenectomy and iron overload might have increased her risk for reinfection yet not the risk for complications.

We suggest that even if thalassemia patients seem to have a smooth clinical course of COVID-19 infection, the possibility of being reinfected should be kept in mind. Screening them for COVID-19 infection should be done at each healthcare visit to provide close monitoring, avoid unexpected deterioration and control the spread of infection. 
 TABLE 1
 Comparison between the first presentation and the recurrence

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	Previous presentation	Current presentation
Blood type	B negative	
Comorbidities	TD - BTM Diabetes Mellitus type II Hypothyroidism	
Iron overload	Severe liver overload. Mild myocardial overload.	
Splenectomy	Yes	
Source of infection	Sick contact	No sick contact
Nasopharyngeal swab result	Positive	Positive
Presenting symptoms	Fever, sore throat, dyspnea, fatigue, and cough	Asymptomatic
Vitals on presentation	Within normal range.	Within normal range.
Duration of symptoms	4 days	NA
Hospital admission	Yes	No
Investigations		
Chest X-ray:	There are multiple subtle opacities in bilateral mid and lower zones suggestive of infective changes	Not done.
ECG	cQT : normal. No signs of ischemia	Not done.
Blood tests:		
Hemoglobin (13-17 gm/dL)	9.1	10.5
RBCs $(4.5-5.5 \times 10^6)$	4.2	3.9
WBCs $(4-10 \times 10^3 / \text{UL})$	15.93	14.6
PLT $(150-400 \times 10^{3}/\text{UL})$	535	838
Lymphocytes count $(1-3 \times 10^3/\text{UL})$	27.9	6.1
Ferritin (8-252 mcg/L)	11,574	-
CRP (0-5 Umg/L)	13	-
D-dimer (0.00 -0.4 mcg/L)	0.60	-
LDH (135-214 U/L)	451	-
Renal function tests (Urea / Cr) (2.1- 8.8 mmol/L) (44- 80 Umoll/L)	4.40 / 15	-
ALT / AST (0-33 U/L) (0-32 U/L)	180 /247	-
Albumin (35-50 gm/L)	33.5	-
G6PD	Normal	-
Length of hospital stay (days)	12	Admission to quarantine facility

	Previous presentation	Current presentation
Clinical course	Stable No oxygen supplementation was needed	Stable No oxygen supplementation was needed
COVID-19 specific treatment	Yes: Azithromycin for 500 mg BID for 7 days. Dexamethasone 6 mg daily for 7 days. Enoxaparin 40 mg Sc daily.	None.
Blood transfusion	Yes	Yes
Iron chelation therapy	Yes Deferasirox 1080 mg daily.	
Outcome: recovery	improved	NA
Isolation	Yes	Yes.
COVID-19 repeated result.	Negative PCR after 19 days.	Negative. PCR after 18 days.

Abbreviations: cQT, Corrected QT; TD-BTM, Transfusion-dependent beta thalassemia major.

# 4 | CONCLUSION

TIF categorized patients with hemoglobinopathies in the vulnerable group for COVID-19 complication and emphasized that those patients need extra precaution during their recurrent visits to the healthcare facilities, mainly due to the lack of current evidence in terms of COVID-19 infection progression. However, published literature showed a favorable outcome among many thalassemia patients who had COVID-19 infection. No data were found regarding the recurrence of this infection. We suggest that all physician should screen those patients for COVID-19 whenever they visited the hospital as they might develop asymptomatic recurrence and even though the clinical course seems to be smooth, screening is essential to control this pandemic and protect this vulnerable population because their outcome is still unpredictable.

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### **CONFLICT OF INTEREST**

None declared.

#### **AUTHOR CONTRIBUTIONS**

All authors contributed equally to writing the manuscript.

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## STATEMENT OF ETHICS

Consent was obtained from the patients. Case approved by HMC Medical Research center.

#### DATA AVAILABILITY STATEMENT

All data related to this article are available upon request.

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