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COVID-19 infection In Beta Thalassemia Major: Case series

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ABSTRACT

COVID-19 infection was first described in Wuhan, China after an increasing spread of atypical pneumonia of unknown pathogen. Unfortunately, this novel virus continues spreading causing a pandemic. Thalassemia considered one of the most common hemoglobinopathies. Beta thalassemia is the commonest type with a variety in clinical picture due to the deference in homozygous. A lot of vulnerable categories were at high risk of getting infected with the coronavirus and more even its complication. Despite the conflicting data and ongoing research on this topic, thalassemia patients were categorized among the high-risk population.

Here we present a case series describing the clinical progression of two splenectomised patients who has transfusion dependent beta thalassemia major.

Keywords: COVID-19; Beta Thalassemia Major; Haemoglobinopathies; Splenectomy; blood transfusion

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Introduction

Starting from Wuhan in China the novel Coronavirus was first discovered in December 2019 after the spread of atypical pneumonia without known pathology. On 11 February 2020, WHO named it as COVID-19 (coronavirus disease 2019) that spread rapidly causing a global pandemic. COVID-19 virus belongs to a group of severe acute respiratory coronaviruses (SARS-CoV), thus it was named as SARS-CoV-2.

Similar to the SARS-CoV and Middle East respiratory syndrome coronavirus MERS-CoV, COVID-19 main presentation was lower respiratory tract syndrome that can even lead to SARS [1].

The clinical course of COVID-19 infection is variable amongst those who are infected. Asymptomatic infection was described as well as the progression to SARS. However, the presenting symptoms was categorized into typical symptoms such as fever, dry cough, myalgia, dyspnea and anorexia or atypical presentations like gastrointestinal symptoms or hyponatremia [2,3].

Haemoglobinopathies consider the most common recessive monogenic globally. Consisting of two large groups: The thalassemia syndromes and the hemoglobin defects. Thalassemia has many types, α, β, and δβ thalassemia are significantly important clinically. Depending on the homozygotes Beta thalassemia may present as major or intermediate thalassemia. This wide variant result in a range of clinical pictures. Beta thalassemia major (BTM) patients are most likely to be diagnosed earlier and become blood transfusion dependent for their whole life whereas beta thalassemia intermedia (BTI) patients have milder disease course, thus diagnosed later life. Depending on this clinical course Thalassemia was categorized into transfusion dependent thalassemia (TDT) and non-transfusion dependent thalassemia (NTDT) [4,5]

COVID-19 pandemic was considered to cause a real challenge for haemoglobinopathies patients, their surroundings including families and medical staff as per the statement from Thalassemia international Federation (TIF) which published on the 13th of July 2020 considering patients with hemoglobinopathies at greater risk to get the infection. However, they also emphasized the lack of evidence regarding the clinical course of COVID-19 infections in this category of patients [6]. Here we present a description of two BTM cases infected with COVID-19 in Qatar.

Case presentation

During the pandemic of COVID-19 infection in Qatar, two cases of male and female with TD-BTM presented to our hospital, after initial investigations they appeared to be COVID-19 positive. In fact, they had somehow smooth clinical course of infection. A detailed description of the cases is described in the following table:

Table 1.

	Case 1	Case 2
Age (years)	31	30
Gender	Female	Male
Nationality	Pakistani	Qatari
Blood type	B negative	B positive
Co-morbidities	TD - BTM Diabetes Mellitus type II	TD – BTM
Iron overload	Severe liver overload. Mild myocardial overload.	Moderate liver overload. No myocardial overload.
Splenectomy	Yes	Yes
Source of infection	Sick contact	Not defined
Nasopharyngeal swab result	Positive	Positive
Presenting symptoms	Fever, Sore throat, dyspnea, fatigue, and Cough	Asymptomatic
Duration of symptoms	4 days	NA

Hospital admission	Yes	Yes
Investigations		
Chest Xray:	There are multiple subtle opacities in bilateral mid and lower zones suggestive of infective changes	Not done
ECG	QTc No signs of ischemia	QTc No signs of ischemia
Blood tests:		
Hemoglobin (13-17 gm/dL)	9.1	7.8
RBCs (4.5-5.5 x 10^6)	4.2	2.8
WBCs (4-10 X 10^3 /UL)	15.93	7.1
PLT (150-400×10^3/UL)	535	845
Lymphocytes count (1-3 x 10^3/UL)	27.9	47.8
Ferritin (8-252 mcg/L)	11,574	431
CRP (0-5 Umg/L)	13	4.2
D-dimer (0.00 -0.4 mcg/L)	0.60	NA
LDH (135-214 U/L)	451	41
Renal function tests (Urea / Cr) (2.1- 8.8mmol/L) (44- 80Umoll/L)	4.40 / 15	5.9 /79
ALT / AST (0-33 U/L) (0-32 U/L)	180 /247	33 / 41
Albumin (35-50 gm/L)	33.5	45
G6PD	Normal	Normal
Length of hospital stay (days)	12	1
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. Dexamatasone 6 mg daily for 7 days. Enoxaparin 40 mg Sc daily.	No
Blood transfusion	Yes	Yes
Iron chelation therapy	Yes Deferasirox 1080 mg daily.	Yes Deferasirox 720 mg daily.
Outcome: recovery	improved	asymptomatic course
Isolation	Yes	Yes
COVID-19 repeated result.	Negative Interval between the positive and negative results was 3 weeks.	As per our guidelines if the patient is asymptomatic then isolation without repeating the swab.

Discussion

The initial source of SARS-CoV-2 is still unknown despite all previously suggested primary sources like sea food or even the bat. Multiple mechanism of transmission was prescribed, most importantly via droplet, close contact as well aerosol if continuous exposure and close environment are present and rarely it was suggested that due to the gastrointestinal symptoms as vomiting and diarrhea, this may be another route of getting infected. The clinical presentation of COVID-19 infection is variant ranging from asymptomatic cases to critically ill with severe acute respiratory syndrome (SARS). Symptoms were categorized as typical and atypical. Typical symptoms include fever, dry cough, myalgia, dyspnea and less commonly sore throat, runny nose, and headache, whereas atypical symptoms are gastrointestinal in nature like vomiting, diarrhea, and nausea. Hyponatremia, loss of smell or test are also reported. [3,7,8]

Thalassemia and sickle cell disease are the most common monogenic disorders in human among inherited hemoglobin disorder and haemoglobinopathies. Beta thalassemia is a common type of thalassemia syndrome occurs due to inherited defect in hemoglobin synthesis that leads to persistent hemolysis and earlier death of Red blood cells (RBCs) in their cycle of life, thus compensatory expansion in the boon marrow as well chronic anemic status [9-11].

The classification of thalassemia depends on its genetic background and clinical picture, Beta thalassemia major (BTM), beta thalassemia intermedia (BTI) and Beta thalassemia minor (BTM) are the main categories. From clinical aspect Beta thalassemia can be classified into transfusion dependent thalassemia (TDT) and non-transfusion dependent thalassemia (NTDT). Usually BTM is diagnosed earlier in life than BTM due to the severe anemia and the need for blood transfusion to survive. Thalassemia patients need a well-defined plan and close follow up due to the multisystemic involvement and the lifelong therapy. The most noticeable side effects from recurrent blood transfusion are infection transmission, antibody formation and most importantly iron overload with cardiovascular and liver diseases being the leading cause of morbidity and mortality [11-15].

Thalassemia can lead also to osteoporosis, hypogonadotropic hypogonadism, affect growth, spermatogenesis and adrenocortical function [16-19].

Thus, Iron chelation therapy (ICT) consider a cornerstone in the management plan as it alleviates the morbidities associated this complication [20,21].

Despite the paucity in literature regarding COVID-19 infection in hemoglobinopathies patients, this virus is still causing a real challenge in haemoglobinopathies patients and their surrounding including family and medical staff due to the multiple hospital visits. They are as well at risk of developing complication if there are any co-morbidities like viral illness. Mostly because of the multiple organ involvement which occurs in thalassemia patients due to iron overload and chronic anemia status that affect the heart, lungs, liver, and endocrine glands. Thus, those patients were added to other vulnerable population at risk of COVID-19 infection and complications [6,21].

Also, Previous studies demonstrated that beta thalassemia patients tend to have may changes in their immune system like higher levels of IL-1α, TNF-α and IL-1β, IL-6, IL-8, C-reactive protein, neopterin, reduced C3 level and complement activity. Therefore, those patients are more prone to respiratory compromise than normal population. Contrary, the available data hypothesized that beta-chain changes in thalassemia patients might have a protective role against covid-19 infection [22-24].

While splenectomy, a common intervention in thalassemia patients, was thought to play a role in pulmonary hypertension, its role in the progression of COVID-19 infections in Thalassemia patients still vague. However, upon the current literature it seems that splenectomy does not increase the risk of COVID-19 infection or even worsen it is course. A will recognized reasons that increase the risk of infections are iron overload, reduced immunity, multiple blood

transfusions and in older patients splenectomy and adrenal hypofunction might have a role [21,25].

Here we present a brief conclusion from the literature regarding the prognosis of COVID-19 infection in thalassemia major patients. [24,26-29]

Table 2.

Study name	Type of study	Patient number	Mean age	Splenectomy	Conclusion regarding the outcome
Prevalence and mortality in b-thalassemia due to outbreak of novel coronavirus disease (COVID-19): the nationwide Iranian experience	Multicentric, retrospective, cross sectional study	15	36 ±12 years	12 patients out of 15	11 recovered 4 died
SARS-CoV-2 infection in beta thalassemia: Preliminary data from the Italian experience10	Single center cohort study	11	44 ± 11 years	8 patients out of 11	10 recovered 1 died
Impact of SARS CoV-2 in Hemoglobinopathies with Immune Disfunction and Epidemiology. A Protective Mechanism from Beta Chain Hemoglobin Defects?	Cross sectional	105 TDT screened 1 female positive	59 years	yes	one old female tested positive and she was asymptomatic, repeated test was negative after 14 days
. COVID-19 in a Patient with β-Thalassemia Major and Severe Pulmonary Arterial Hypertension	Case report	1	57 years old	yes	Patient had severe pulmonary artery hypertension was admitted for 10 days, then recovered
Preliminary Data on COVID-19 in Patients with Hemoglobinopathies: A Multicenter ICET-A Study	Multicenter ICET-A Study	4962 TDT 7 of them tested positive	35.7 ± 11 .3 years	4	5 patients were females 3 patients had DM 6 patients had mild to moderate symptoms and recovered One patient had severe COVID pneumonia and died

Conclusion

Due to the recent global pandemic caused by Coronavirus and the impact in the society, haemoglobinopathies patients are at risk to be infected as their disease may push them into visiting the hospital more than other patients. As well the lack of data that describe the clinical progression of COVID-19 infections among those patients makes it hard to predict the outcome for them till now. Multiple studies are conducting to reach a clear conclusion. Till then, preventive measurement and close monitoring for hemoglobinopathies patients is the cornerstone to prevent them from being infected at the first place.

A good outcome is describer before yet due to the lack in reporting cases of COVID-19 in haemoglobinopathies patients we believe it is worthy to present this case series of two beta thalassemia patients who recovered successfully from COVID-19 infections without any complications even though both were splenectomized and one patient has diabetes as a co-morbidity.

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Statement of Ethics

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

Declaration of interest

The authors report no conflicts of interest.

Authors contribution:

All authors contributed equally in writing the manuscript.

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