Received: 9 April 2021 | Accepted: 3 May 2021

DOI: 10.1002/ccr3.4331

CASE REPORT

Clinical Case Reports Open Access WILEY

COVID-19 in a pregnant patient with beta-thalassemia major: A case report

Yousef Mohammed Ali Hailan[1] | **Gamal Sayed**[2,3] | **Mohamed A. Yassin**[4]

[1]Internal Medicine Department, Hamad Medical Corporation, Doha, Qatar

[2]Women Wellness and Research Center Medical, Obstetrics/Gynecology, Hamad Medical Corporation (HMC), Doha, Qatar

[3]Clinical Department, College of Medicine, QU Health, Qatar University, Doha, Qatar

[4]National Center for Cancer Care and Research, Hamad Medical Corporation, Doha, Qatar

Correspondence
Yousef Mohammed Hailan, Internal Medicine Department, Hamad General Hospital, Hamad Medical Corporation, Al Rayyan Street, Doha, 00974, Qatar.
Email: yhailan@hamad.qa; yousefhailan@live.com

Funding information
Qatar National Library

Abstract

Further studies are needed on this unique population to better manage them and increase their chances of normal pregnancy and fewer complications and more favorable outcomes.

KEYWORDS

beta-thalassemia major, COVID-19, pregnancy, stillbirth, thalassemia, transfusion-dependent

1 | INTRODUCTION

Beta-thalassemia major, a prevalent disease, is caused by severely reduced or absent beta-globin production. Chances of pregnancy have increased significantly since the introduction of hypertransfusion and iron chelation therapies. We report a case of a 35-year-old Lebanese pregnant lady with a background of beta-thalassemia major who was diagnosed with COVID-19 infection (cycle threshold value 18) during her 23rd gestational week. Unfortunately, the pregnancy outcome was unfavorable as it was complicated by intrauterine fetal death. To our knowledge, this is the first report of such a case.

The coronavirus disease (COVID-19) is caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has a wide range of presentations, and its severity varies from asymptomatic disease to life-threatening sepsis.[1] Since it surfaced in Wuhan, China, in December 2019 and was announced as a pandemic by the World Health Organization (WHO) in March 2020, it has resulted in over 126 million confirmed cases and more than 2.7 million deaths globally unto 30 March 2021.[2,3] Previous studies revealed that droplets, contact, aerosol, and fecal-oral transmissions are the main transmission routes in COVID-19 infection.[4] Vertical transmission is believed to be less of a concern.[5] Although many publications have discussed the association between many comorbidities and the severity of COVID-19 infection, data on the COVID-19 and hemoglobinopathies are still limited.[6-8]

Variants of thalassemia produce a wide range of clinical manifestations. Homozygotes for β-thalassemia may develop either thalassemia major or thalassemia intermedia. β-thalassemia is caused by partial or total reduction in the

β-globin chains in the HbA molecule. Among Arab populations, the carrier rates range from 1% to 11%, and the most frequent mutation is IVS-1-110 (G > A).[9] Furthermore, Khan et al have identified six unique β-thal mutations in six Arab countries.[10]

Beta-thalassemia major manifests in infancy with a constellation of symptoms including pallor, jaundice, and failure to thrive; physical examination findings of hepatosplenomegaly, frontal bossing, and thalassemic facies; and laboratory investigations consistent with a microcytic anemia with hemoglobin <7 g/dL; and hemolysis.[11]

The primary treatment of this type of anemia is with a regular transfusion schedule targeting a pretransfusion hemoglobin level between 9 and 10 g/dL, preferably transfusions of washed, leukocyte-depleted red blood cells to reduce the incidence of reactions, along with addressing the complications as appropriate, namely endocrinopathies such as hyperadrenalism and abnormalities in glycemic control and insulin-like growth factor-1(IGF-1).[11-16]

Unlike patients with alpha-thalassemia, pregnancy in women with beta-thalassemia major was associated with unfavorable outcomes until after the introduction of hypertransfusion and iron chelation therapies in the late 1970s.[17]

We describe a case of a woman with a beta-thalassemia major who acquired a COVID-19 infection during her pregnancy and the outcome of the pregnancy.

2 | CASE REPORT/CASE PRESENTATION

A 35-year-old Lebanese female patient gravida 4 para 1 presented to the hospital with fever and dry cough for 3 days. She is known to have beta-thalassemia major on regular transfusions every 3 weeks, and the last transfusion was 5 days before this presentation. She also has a history of cholecystectomy and splenectomy. She is not known to have any allergies. She was taking aspirin and deferasirox at home. She is a teacher, and both of her parents are carriers of beta-thalassemia trait. Otherwise, family and social history are noncontributory.

Physical examination was nonsuggestive, and admission laboratory investigations (shown in Table 1) showed mild leukocytosis, hemoglobin (Hb) at target, normal renal function, slightly elevated liver enzymes, and markedly elevated ferritin. Chest XR was reported normal.

The evaluation revealed that she has a mild COVID-19 infection with a cycle threshold value of 18. She was pregnant in week 27, as calculated from the last menstrual period (27 September 2020). It was confirmed later by ultrasound (US) to be a single viable fetus aged 23 weeks and 2 days. Upon admission, she was seen by multiple specialties, primarily infectious disease, internal medicine, hematology, and

TABLE 1 Admission laboratory investigations

Detail	Value w/Units	Normal range
WBC	13.84 × 10^3/uL	4.00-10.00
RBC	4.1 × 10^6/uL	3.8-4.8
Hgb	11.6 gm/dL	12.0-15.0
Hct	34.4%	36.0-46.0
MCV	84.4 fL	83.0-101.0
MCH	28.3 pg	27.0-32.0
MCHC	33.6 gm/dL	31.5-34.5
RDW-CV	14.3%	11.6-14.5
Platelet	322 × 10^3/uL	150-400
MPV	10.5 fL	7.4-10.4
Absolute Neutrophil Count Auto# (ANC)	12.4 × 10^3/uL	2.0-7.0
Lymphocyte Auto #	0.6 × 10^3/uL	1.0-3.0
Monocyte Auto #	0.6 × 10^3/uL	0.2-1.0
Eosinophil Auto #	0.1 × 10^3/uL	0.0-0.5
Basophil Auto #	0.09 × 10^3/uL	0.02-0.10
Neutrophil Auto %	89.4%	
Lymphocyte Auto %	4.5%	
Monocyte Auto %	4.7%	
Eosinophil Auto %	0.4%	
Basophil Auto %	0.6%	
Prothrombin Time	10.1 s	9.7-11.8
INR	1.0	
D-Dimer	>4.40 mg/L FEU	0.00-0.44
Fibrinogen	4.78 gm/L	1.70-4.20
APTT	39.6 s	24.6-31.2
Urea	2.60 mmol/L	2.50-7.80
Creatinine	27 umol/L	53-97
Sodium	141 mmol/L	133-146
Potassium	4.1 mmol/L	3.5-5.3
Chloride	98.7 mmol/L	95.0-108.0
Bicarbonate	28.4 mmol/L	22.0-29.0
Bilirubin T	20.6 umol/L	0.0-21.0
Total Protein	72 gm/L	60-80
Albumin Lvl	40.2 gm/L	35.0-50.0
Alk Phos	128.0 U/L	35.0-104.0
ALT	52.0 U/L	0.0-30.0
AST	55 U/L	0-31
Glu Fasting	4.3 mmol/L	3.3-5.5
NT pro-BNP	52.8 pg/mL	0.0-130.0
Troponin-T HS	4.1 ng/L	0.0-14.0
LDH	188 U/L	135-214
CK	23 U/L	2-160

(Continues)

TABLE 1 (Continued)

Detail	Value w/Units	Normal range
G6PD Screen	Normal	
CRP	35 mg/L	0-5
Procalcitonin	0.20 ng/mL	
Ferritin	2,942 mcg/L	8-252
COVID-19 PCR	Positive	
COVID-19 Average CT	18.08	

obstetrics. As per the local Communicable Disease Center (CDC) COVID-19 management protocol, she is for symptomatic treatment.

On day 4 of admission, she reported reduced fetal movement and the urgent obstetric US reported fetal death. The next day, she underwent misoprostol induction protocol for intrauterine fetal death which was uncomplicated. On day 7, she was discharged from the hospital as COVID-19 PCR became negative and her symptoms settled.

3 | DISCUSSION/CONCLUSION

De Sanctis et al published a thorough article in 2019 addressing marital status and paternity in patients with transfusion-dependent thalassemia (TDT) and non-transfusion-dependent thalassemia (NTDT).[18] The notable observations in patients with TDT include the following: The majority of the patients have natural conception (78.5%), the most common cause of infertility is dysspermia (13.3%), and the average level of serum ferritin in the year of paternity is 2211.8 ± 181.8 ng/mL.

The introduction of hypertransfusion and iron chelation therapy has increased the chances for these women for pregnancy and better pregnancy outcomes. The likely mechanism by which pregnancy was highly unlikely in this population is primarily due to anovulation secondary to hypogonadotropic hypogonadism due to iron overload in the hypothalamus and pituitary gland.[17,19,20] The most recent American College of Obstetricians and Gynecologists recommendations advise pregnancy in women with TDT only to those with normal cardiac function, prolonged hypertransfusion therapy to maintain Hb levels at 10 g/dL, and iron chelation therapy with desferrioxamine.

Iron chelating agents aim to excrete the accumulating iron through feces and/or urine. The currently approved chelators are desferrioxamine (DFO), deferasirox (DFX), and deferiprone (DFP).[21,22] However, the safety profile for these agents is not well studied in pregnancy, and the usual recommendation is to hold them during pregnancy. Since holding chelating therapy for the duration of pregnancy may have important consequences on women, some researchers prefer to use DFO in the second and third trimesters as it is a large molecule and less likely to cross the placenta.

A recent systematic review on pregnancy and COVID-19 that included a total of 8 studies involving 95 pregnant women and 51 neonates addressing the maternal, obstetric, and neonatal outcomes concluded that contrary to severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS), SARS-CoV-2 does not appear to increase the risk of pregnancy complications.[23] Another publication suggested that a high rate of maternal and fetal complications is seen in infected individuals.[24] The most common pregnancy complications in women with COVID-19 were fetal distress, premature rupture of membranes, preterm labor, and postpartum fever.[5,23]

No data in the literature address the topic of pregnancy in patients with β-thalassemia major in particular or β-thalassemia in general in COVID-19 patients. Some of the publications discussing pregnancy in a patient with COVID-19 infection mentioned thalassemia, thalassemia trait, and thalassemia minor in the list of comorbidities in the description of their included patients characteristics.[5,25-27] However, no details were provided as to the outcomes and course of the pregnancy in this subset of patients.

Our patient is known to have transfusion-dependent thalassemia and was infected with COVID-19. She was managed from a COVID-19 infection point of view as per version 12 of the local CDC recommendations. The recommendation for pregnant females who have positive COVID-19 PCR with uncomplicated upper respiratory tract infection is isolation, either at home or in an isolation facility, and supportive treatment as needed. From the hematology aspect, when she became pregnant, her transfusion schedule changed to receive packed red blood cell transfusions every 2 weeks instead of every 3 weeks.

Despite being managed by a multidisciplinary team, the outcome of the pregnancy was unfavorable. It can be attributed to COVID-19 infection, β-thalassemia major, and iron excess. The placental sample sent for pathological analysis showed early ischemic changes and other features in favor of mild acute chorioamnionitis. Thrombosis is a major complication of COVID-19 infection, and the placenta is not immune.[28] Whether the early ischemic changes in the report are linked to COVID-19 infection is uncertain and is debatable.

To our knowledge, this is the first case report that highlights COVID-19 infection in a pregnant patient with beta-thalassemia major.

ACKNOWLEDGMENT

We wish to show our gratitude to the Internal Medicine residency program and to Dr Dabia Hamad Almohanadi for their scientific support.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Yousef Mohammed Ali Hailan and Mohamed A Yassin: performed writing, editing, and final approval of the concept. Gamal Sayed: performed editing and approval of the final version.

ETHICS STATEMENT

The case was approved by Hamad Medical Corporation Research Center with reference number MRC-04-21-352. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

DATA AVAILABILITY STATEMENT

Data are available on reasonable request.

ORCID

Yousef Mohammed Ali Hailan https://orcid.org/0000-0002-0760-9906

REFERENCES

1. Wiersinga WJ, Rhodes A, Cheng AC, et al. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A Review. *JAMA*. 2020;324:782-793.
2. Listings of WHO's response to COVID-19, https://www.who.int/news/item/29-06-2020-covidtimeline (accessed April 2 2021)
3. Coronavirus Disease (COVID-19) Situation Reports, https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports (accessed July 4 2020)
4. Zhang W, Du R-H, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect*. 2020;9:386-389.
5. Ashraf MA, Keshavarz P, Hosseinpour P, et al. Coronavirus Disease 2019 (COVID-19): a systematic review of pregnancy and the possibility of vertical transmission. *J Reprod Infertil*. 2020;21:157-168.
6. Soliman A, Nair AP, Masalamani MSA, et al. Prevalence, clinical manifestations, and biochemical data of type 2 diabetes mellitus versus nondiabetic symptomatic patients with COVID-19: A comparative study. *Acta Biomed*. 2020;11:91. https://doi.org/10.23750/abm.v91i3.10214
7. Prevalence, Clinical Manifestations, and Biochemical Data of Hypertensive versus Normotensive Symptomatic Patients with COVID-19: A Comparative Study. - Abstract - Europe PMC. https://europepmc.org/article/pmc/pmc7927505 (accessed 4 April 2021)
8. de Sanctis V, Canatan D, Corrons JLV, et al. Preliminary Data on COVID-19 in Patients with Hemoglobinopathies: A Multicentre ICET-A Study. *Mediterr J Hematol Infect Dis*. 2020;1:12. https://doi.org/10.4084/MJHID.2020.046
9. De Sanctis V, Kattamis C, Canatan D, et al. β-Thalassemia distribution in the old world: an ancient disease seen from a historical standpoint. *Mediterr J Hematol Infect Dis*. 2017;20:9. https://doi.org/10.4084/MJHID.2017.018
10. Khan AM, Al-Sulaiti AM, Younes S, et al. The spectrum of beta-thalassemia mutations in the 22 Arab countries: a systematic review. *Expert Rev Hematol*. 2021;14:109-122.
11. Rachmilewitz EA, Giardina PJ. How I treat thalassemia. *Blood*. 2011;118:3479-3488. https://doi.org/10.1182/blood-2010-08-300335
12. Kanbour I, Chandra P, Soliman A, et al. Severe Liver Iron Concentrations (LIC) in 24 Patients with β-Thalassemia Major: Correlations with Serum Ferritin, Liver Enzymes and Endocrine Complications. *Mediterr J Hematol Infect Dis*. 2018;1:10. https://doi.org/10.4084/MJHID.2018.062
13. Soliman AT, Yassin M, Majuid NMSA, et al. Cortisol response to low dose versus standard dose (back-to-back) adrenocorticotrophic stimulation tests in children and young adults with thalassemia major. *Indian J Endocrinol Metab*. 2013;17:1046.
14. Soliman AT, Yasin M, El-Awwa A, et al. Detection of glycemic abnormalities in adolescents with beta thalassemia using continuous glucose monitoring and oral glucose tolerance in adolescents and young adults with β-thalassemia major: Pilot study. *Indian J Endocrinol Metab*. 2013;17:490-495.
15. De Sanctis V, Soliman AT, Candini G, et al. Insulin-like growth factor-1 (igf-1): demographic, clinical and laboratory data in 120 consecutive adult patients with thalassaemia major. *Mediterr J Hematol Infect Dis*. 2014;6(1): https://doi.org/10.4084/mjhid.2014.074
16. Cappellini M-D, Cohen A, Eleftheriou A, et al. Blood Transfusion Therapy in β-Thalassaemia Major. Thalassaemia International Federation, https://www.ncbi.nlm.nih.gov/books/NBK173967/ (2008, accessed March 29 2021)
17. *Hemoglobinopathies in Pregnancy*. 2021. (accessed March 29 https://www.acog.org/en/clinical/clinical-guidance/practice-bulletin/articles/2007/01/hemoglobinopathies-in-pregnancy).
18. De Sanctis V, Soliman AT, El-Hakim I, et al. Marital status and paternity in patients with Transfusion-Dependent Thalassemia (TDT) and Non Transfusion-Dependent Thalassemia (NTDT): an ICET - A survey in different countries. *Acta Bio Medica Atenei Parm*. 2019;90:225-237.
19. Jensen CE, Tuck SM, Wonke B. Fertility in β thalassaemia major: a report of 16 pregnancies, preconceptual evaluation and a review of the literature. *BJOG Int J Obstet Gynaecol*. 1995;102:625-629.
20. Carlberg KT, Singer ST, Vichinsky EP. Fertility and pregnancy in women with transfusion-dependent thalassemia. *Hematol Oncol Clin North Am*. 2018;32:297-315.
21. Porter J, Viprakasit V, Kattamis A. IRON OVERLOAD AND CHELATION. Thalassaemia International Federation. https://www.ncbi.nlm.nih.gov/books/NBK269373/ (2014, accessed 29 March 2021)
22. Yassin MA, Soliman AT, De Sanctis V, et al. Jadenu® Substituting Exjade® in Iron Overloaded β-Thalassemia Major (BTM) Patients: a preliminary report of the effects on the tolerability, serum ferritin level, liver iron concentration and biochemical profiles. *Mediterr J Hematol Infect Dis*. 2018;10:e2018064.
23. Trocado V, Silvestre-Machado J, Azevedo L, et al. Pregnancy and COVID-19: a systematic review of maternal, obstetric and neonatal outcomes. *J Matern Fetal Neonatal Med*. 2020;9:1-13.
24. Capobianco G, Saderi L, Aliberti S, et al. COVID-19 in pregnant women: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2020;252:543-558.
25. Trippella G, Ciarcià M, Ferrari M, et al. COVID-19 in pregnant women and neonates: a systematic review of the literature with quality assessment of the studies. *Pathogens*. 2020;9:485.
26. Kasraeian M, Zare M, Vafaei H, et al. COVID-19 pneumonia and pregnancy; a systematic review and meta-analysis. *J Matern Fetal Neonatal Med*. 2020;1-8.

27. Zeng Y, Lin L, Yan Q, et al. Update on clinical outcomes of women with COVID-19 during pregnancy. *Int J Gynecol Obstet*. 2020;150:264-266.
28. Mohamed MFH, Al-Shokri SD, Shunnar KM, et al. Prevalence of venous thromboembolism in critically Ill COVID-19 patients: systematic review and meta-analysis. *Front Cardiovasc Med*. 2021;7: https://doi.org/10.3389/fcvm.2020.598846

How to cite this article: Hailan YMA, Sayed G, Yassin MA. COVID-19 in a pregnant patient with beta-thalassemia major: A case report. *Clin Case Rep*. 2021;9:e04331. https://doi.org/10.1002/ccr3.4331