*Case Report*

# *COVID-19 in a Pregnant Patient with Beta-Thalassemia Major: A Case Report*

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## Abstract

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-years-old Lebanese pregnant lady with a background of beta-thalassemia major who was diagnosed with COVID-19 infection (Cycle threshold value 18) during her 23$^{rd}$ 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.

## Introduction

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 March 30, 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 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 is 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 6 unique β-thal mutations in six Arab countries [10].

Beta thalassemia 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 usually < 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 9-10 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 hyper-transfusion 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.

## Case Report/Case Presentation

A 35-years-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, 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 non-suggestive 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 (September 27, 2020). 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 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 intra-uterine fetal death which was uncomplicated. On day 7, she was discharged from the hospital as COVID-19 PCR became negative and her symptoms have settled.

## 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, majority of the patients have natural conception (78.5%), the most common cause of infertility is dysspermia (13.3%), and that 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 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 are 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 addresses 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 has 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.

## Key Clinical Message

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

## Statements


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### Statement of Ethics

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.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.


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## 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.

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**Table 1** showing admission laboratory investigations

| Detail | Value w/Units | Normal Range |
|---|---|---|
| WBC | 13.84 x10^3/uL | 4.00-10.00 |
| RBC | 4.1 x10^6/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 x10^3/uL | 150-400 |
| MPV | 10.5 fL | 7.4-10.4 |
| Absolute Neutrophil count Auto# (ANC) | 12.4 x10^3/uL | 2.0-7.0 |
| Lymphocyte Auto # | 0.6 x10^3/uL | 1.0-3.0 |
| Monocyte Auto # | 0.6 x10^3/uL | 0.2-1.0 |
| Eosinophil Auto # | 0.1 x10^3/uL | 0.0-0.5 |
| Basophil Auto # | 0.09 x10^3/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 seconds | 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 seconds | 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 |
| 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 | |