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Case Report

Pregnancy in women with thalassemia dependent transfusion: A case report on the importance of multidisciplinary surveillance to improve maternal and child safety

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ABSTRACT

A 38-year-old woman is pregnant with her fourth child at 35 weeks of gestation. This woman was diagnosed with Hemoglobin-E (Hb-E) thalassemia-dependent transfusion (Hb electrophoresis showing Hb-E 51.5%, Hemoglobin-F (Hb-F) 41.5%, and Hemoglobin-A (Hb-A) 3.5%). The Patient appeared pale with anemic conjunctiva, white sclera, and abdominal enlargement due to pregnancy. The Patient weighs 42 kg and is 150 cm tall (Body Mass Index (BMI) 18.67). Laboratory results were microcytic hypochromic anemia with hemoglobin 7.4 g/dL, erythrocytes 3.12 million/µL, mean cell volume (MCV) 74.0 fL, mean cell hemoglobin (MCH) 23.7 pg, mean cell hemoglobin (MCHC) 32 g/dL, and platelet count of 133,000/µL. A cesarean method was chosen to terminate the pregnancy. There were no intrapartum or postpartum complications in this Patient. Her baby weighed 1.860 grams and measured 47 cm in length, with no abnormalities found on neonatal examination. Various complications may arise in pregnant women with thalassemia, including a high risk of severe anemia, which can lead to intrauterine growth restriction or even fetal death. Blood transfusion remains the mainstay of management to maintain optimal hemoglobin levels throughout pregnancy. Cesarean delivery is often chosen to ensure the safety of both the mother and the infant. In conclusion, Management of pregnant women with thalassemia requires special attention from preconception, during pregnancy, and toward delivery time. Multidisciplinary care involving hematologists, obstetricians, cardiologists, and endocrinologists is essential to anticipate complications such as severe anemia, iron overload, and fetal growth restriction, ensuring optimal maternal and neonatal outcomes.

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INTRODUCTION

Hemoglobinopathies constitute the most common monogenic disorders in humans. Approximately 7% of the global population is a carrier, and 300,000–500,000 children are born with a severe hemoglobin disorder annually (Ruangvutilert, Phatihattakorn, Yaiyiam, *and* Panchalee, 2023). At least 5.2% of the world's population and around 7% of pregnant women carry abnormalities in Hemoglobin, and more than 1% are at risk of having children with abnormalities in hemoglobin (Wulandari, 2018).

Thalassemia is one of the most common monogenic disorders genetically inherited in an autosomal recessive pattern (Farmakis *et al.,* 2022). It affects hemoglobin production and is highly prevalent in Southeast Asia, the Middle East, and the Mediterranean Basin (Farmakis *et al.,* 2022; Ruangvutilert *et al.,* 2023).

Hemoglobin E (HbE)-beta-thalassemia is frequently found in the Indian subcontinent, Bangladesh, Myanmar, and Southeast Asia. In contrast, severe cases of alpha thalassemia are confined to Southeast Asia (Wulandari, 2018). According to data from the Indonesian Thalassemia Foundation, cases of thalassemia have been increasing steadily. Since 2012, there have been 4,896 cases until June 2021; data for people with thalassemia in Indonesia are 10,973 cases (Layarta, Prijatna, *and* Widyastuti, 2019).

Thalassemia, particularly transfusion-dependent thalassemia, is a demanding clinical condition requiring lifelong care and follow-up (Ruangvutilert *et al.,* 2023). The expectation of having a family is an important aspiration for patients with transfusion-dependent thalassemia. Pregnancies in patients with thalassemia major are high risk for the mother and the baby, including preterm labor, intrauterine growth restriction, and low birth weight (Farmakis *et al.,* 2022; Ruangvutilert *et al.,* 2023)

Blood consumption increases in women with thalassemia major, has been reported in most studies, due to the physiological changes of pregnancy (Origa *and* Comitini, 2019). However, pre-pregnancy counseling can minimize these risks involving various multidisciplinary team members: the hematologist, the reproductive medicine specialist, the cardiologist, and the obstetrician (Ruangvutilert *et al.,* 2023). Comprehensive examinations must be carried out from preconception through pregnancy and toward delivery. This integrative approach not only minimizes maternal morbidity and fetal risk but also aligns with international guidelines emphasizing individualized, team-based care for high-risk pregnancies in thalassemia.

CASE REPORT

A 38-year-old woman who was transfusion-dependent with Hb-E thalassemia came to the Internal Medicine Center at Husada Utama Hospital, Surabaya, with complaints of weakness in her body and a pale face. The Patient was pregnant with 35 weeks of gestation and an estimated fetal weight of 1,800 grams. Her obstetric history showed that the first pregnancy resulted in intrauterine fetal death (IUFD) at 20 weeks of gestation. The second pregnancy ended in a preterm cesarean delivery at 35 weeks, resulting in a live birth with a birth weight of 1.900 grams. The third pregnancy also resulted in a preterm cesarean delivery at 32 weeks, with a live birth weighing 2.100 grams. Notably, all of the patient's children were diagnosed with β-thalassemia.

The patient presented with pale conjunctiva and abdominal distension attributed to pregnancy and splenomegaly, corresponding to Schuffner grade 2. Edema of the lower extremities and acral pallor were also observed, with a

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capillary refill time exceeding 2 seconds. The patient weighed 42 kg with a height of 150 cm (Body Mass Index (BMI) 18.67 kg/m²). Blood pressure was 137/89 mmHg, and the heart rate was 98 beats per minute.

Laboratory evaluation revealed microcytic hypochromic anemia, with a hemoglobin level of 7.4 g/dL, erythrocyte count of 3.12 × 10^6/µL, mean corpuscular volume (MCV) of 74.0 fL, mean corpuscular hemoglobin (MCH) of 23.7 pg, mean corpuscular hemoglobin concentration (MCHC) of 32 g/dL, and a platelet count of 133 × 10^3/µL.

During her fourth pregnancy, her average hemoglobin level was approximately 8 g/dL. The patient had been receiving regular blood transfusions of one unit per month since 2017 and was on iron chelation therapy with Ferriprox® (deferiprone 500 mg), which was discontinued during pregnancy. Hemoglobin electrophoresis revealed Hb-E 51.5%, Hemoglobin-F (Hb-F) 41.5%, and Hemoglobin-A (Hb-A) 3.5%. Based on monthly hemoglobin monitoring, the hematologist decided to increase the transfusion volume per session rather than the frequency. Accordingly, the patient received four units of leukocyte-depleted packed red cells at 12 weeks of gestation and six units at 35 weeks. Subsequently, she was prepared for cesarean section due to continuous uterine contractions and a cervical dilatation of 3 cm.

Preoperative laboratory evaluation showed a hemoglobin level of 8.9 g/dL, erythrocyte count of 3.55 × 10^6/µL, MCV of 77.5 fL, MCH of 25.1 pg, MCHC of 32.4 g/dL, and platelet count of 90 × 10^3/µL. Bleeding time was 1 minute, clotting time was 10 minutes, plasma prothrombin time (PT) was within the normal range at 13.1 seconds (reference: 11.1–14.6 seconds), and activated partial thromboplastin time (aPTT) was slightly prolonged at 38.7 seconds (reference: 28–38 seconds).

A male infant was delivered, weighing 1.860 grams, with a body length of 42 cm, chest circumference of 27 cm, and head circumference of 30 cm. The APGAR score was 7 at one minute and 8 at five minutes. Physical examination of the newborn revealed no abnormalities. The patient experienced no intraoperative or postoperative complications.

DISCUSSION

For many years, pregnancy was impossible due to hypogonadal hypogonadism and considered a high risk for thalassemia patients (Cassinerio *et al.,* 2017). The expectation of having a family is an essential aspiration for patients with transfusion-dependent thalassemia. There is no prohibition for women with thalassemia to get pregnant, but exceptional management is needed for their pregnancy.

The problem for thalassemia patients is fertility. Hypogonadotropic hypogonadism remains a common condition affecting 40%-90% of patients with transfusion-dependent thalassemia. This condition leads to infertility and sexual dysfunctions and develops pubertal failure (Origa *and* Comitini, 2019; Petrakos *et al.,* 2016).

Our Patient does not show signs of infertility or sexual dysfunctions. She has a regular menstrual cycle and duration. The Patient had never done counseling for pregnancy planning; she is pregnant with spontaneous conception. In a study by Origa *et al.* (2010), the women with thalassemia major who became pregnant, conception was spontaneous in 18 (out of 19) women with eumenorrhea, six with oligomenorrhea, and one with secondary amenorrhea (25 pregnancies in total). The results of these studies are consistent with those observed in our patients.

Our Patient, a 38-year-old woman with Hb-E dependent transfusion, has had four

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pregnancies with a history of abortion in her first pregnancy; her second, third, and fourth pregnancies were born prematurely using cesarean section. The Patient's pregnancy occurred spontaneously from the first child's pregnancy to the fourth child's pregnancy.

Origa and Comitini (2019) state that thalassemia women need pre-counseling before their pregnancy. A planned pregnancy is essential in spontaneous conception and assisted reproductive techniques to minimize risks to the mother and baby. A multidisciplinary team, including a cardiologist, an endocrinologist, and a gynecologist, should be involved under the supervision of an expert in beta-thalassemia (Origa *and* Comitini, 2019). The Patient did not do pregnancy planning or pregnancy counseling, but our Patient had her pregnancy checked and received supervision from a hematologist.

The complication encountered in our Patient is anemia. During this pregnancy, the number of blood transfusions increased. Anemia in pregnant women with thalassemia needs special attention. Blood consumption increases in women with thalassemia major, as reported in most studies, due to the physiological changes of pregnancy. Maternal anemia influences the general population's birth weight and preterm delivery (Origa *and* Comitini, 2019).

According to Thilakarathne *et al*. (2025), in women with thalassemia, there was a significant increase in blood transfusions. The hemoglobin level that prompted the decision for blood transfusion ranged from 6.7–7.4 g/dL, with a mean of 7.1±0.23 g/dL in the second trimester, while the mean value was 7.7±0.23 g/dL in the third trimester. Blood transfusion is considered the mainstay of treatment. Our Patient's hemoglobin level during pregnancy averages 8 g/dL. However, the authors did not examine ferritin levels, which we realize is a weakness in this report.

Most centers transfuse pregnant women aiming to maintain hemoglobin at the preconception goal to ensure proper fetal growth. (Origa *and* Comitini, 2019; Petrakos *et al.,* 2016). The preparation of packed red cells is strictly monitored. The transfusional support during pregnancy increases, with the target transfusion threshold at a hemoglobin level of 10 g/dL (Cassinerio *et al.,* 2017). In a study by Voskaridou *et al.* (2014)Women with thalassemia intermedia may require transfusion for the first time during pregnancy to maintain a hemoglobin level >8 g/dL. Regular transfusion suggests cases where women complain about fatigue, weakness, and dizziness with total hemoglobin levels (<8 g/dL).

Guideline from the Royal College of Obstetricians and Gynaecologists for pregnant women with thalassemia (2014), regular transfusions should be started, aiming for maintenance of pretransfusion haemoglobin concentration above 100 g/L. Initially, a 2–3 unit transfusion should be administered with additional top-up transfusion if necessary, the following week until the haemoglobin reaches 120 g/L.

According Voskaridou *et al.* (2014), no particular transfusion regimen emerges, and transfusion requirements depend on the clinical profile of individual cases. Our hematologist maintained the Patient's clinical condition by administering a packed red cell, leukocyte-depleted transfusion, resulting in a hemoglobin value> 8 g/dL. Leukocyte-depleted blood with extended antibody typing is generally used to reduce the risk of alloimmunization (Singh, Sharma, Venkateswaran, *and* Trikha, 2021).

Although it is undeniable that the increase in blood consumption and the interruption of chelation result in serum ferritin increases in

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most pregnancies. Origa *et al.* (2010) reported a statistically significant increase in serum ferritin levels from 1,463±1,306 ng/mL to 2,692±1,629 ng/mL, P<0.001. In Oman, serum ferritin levels in 10 thalassemia women (15 pregnancies) went from 585.6 ng/mL (range 236-1,258) to 1,357.5 ng/mL (range 336-3,054) (Origa *and* Comitini, 2019). With the possibility of increased serum ferritin levels, our hematologist and Obstetricians do not provide iron supplementation. The Patient only received folic acid and calcium supplementation.

Hematologists also stopped giving chelation therapy during pregnancy. Although chelation therapy is essential for reducing iron overload, deferoxamine and deferiprone have been shown to be teratogenic in animals (Origa *et al.,* 2010). The current standard of practice is to discontinue chelation therapy as soon as pregnancy is established and hold throughout pregnancy due to the concern of teratogenicity. Fetal malformations, including skeletal anomalies, were reported in the offspring of rats after deferoxamine exposure (Carlberg, Singer, *and* Vichinsky, 2018). A study by Singh et al. (2021) recommends that, whenever possible, deferiprone and deferasirox should be discontinued at least 3 months before conception. Deferoxamine should be avoided in the first trimester of pregnancy due to a lack of safety data, but it can be used safely after 20 weeks of gestation in low doses. Nevertheless, in patients at high risk (severe heart and liver iron overload), it may be reasonable to consider restarting chelation therapy with deferoxamine toward the end of the second trimester (Carlberg *et al.,* 2018; Origa & Comitini, 2019). According to experts, deferoxamine should be avoided during the first trimester. However, subcutaneous administration may be considered in the second and third trimesters for patients with a strong indication for treatment (Petrakos *et al.,* 2016).

In a study Voskaridou *et al.* (2014)The indication for cesarean delivery in most cases was suboptimal fetal growth (12 cesarean deliveries with fetal weight <3,200 grams) and hemoglobin levels <8.1 g/dL. Cesarean delivery also prevents a prolonged delivery, with all the associated risks to the mother and the newborn (Cassinerio *et al.,* 2017). The delivery method for women with thalassemia can be done by normal or cesarean. Our Patient delivery was performed by cesarean, due to a history of previous deliveries. Our Patient's gestational age was still premature, 35 weeks, with an estimated baby weight of 1,800 grams. In addition, the Patient's hemoglobin value was 8.9 g/dL.

Planned cesarean delivery is advisable for thalassemia patients as it avoids the cardiovascular stress associated with labor and overcomes the high incidence of cephalopelvic disproportion due to the short stature found in thalassemia patients. Factors favoring cesarean delivery include cephalopelvic disproportion, abnormal fetal lie, and severe cardiac disease (Singh *et al.,* 2021). The choice of Cesarean section for delivery remains controversial and is primarily determined by center-specific policies. For example, in Cagliari, Genoa, and Brindisi, thalassemia per se has been considered an indication for Cesarean delivery. Turin's policy has been to support the individual Patient if she chooses to attempt a vaginal delivery without risk factors (Origa *et al.,* 2010).

The baby showed no abnormalities—regular physical examination without anemia. The Patient already had two children, and both of them have thalassemia. The Patient's first child was diagnosed with -Thalassemia (Hb-A value 94.4% and Hb-A2 value 4.7%), while the Patient's second child also suffered from β-Thalassemia (Hb-A value 88.5% and Hb-

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A2 value 4.7%). Presence of a child with thalassemia, the hematologist advised the Patient to have a thalassemia screening test for her baby.

Children with thalassemia appear healthy at birth but develop anemia that worsens due to the partial or total absence of hemoglobin (Wahyuni, Ali, Rosdiana, & Lubis, 2011). Screening for thalassemia carriers was based on Hemoglobin, MCV, MCHC, MCH, and hemoglobin electrophoresis. An MCV value of less than 80 fL, an MCH value of less than 27 pg (for children according to age), and a suggestive finding on peripheral blood smear were used as cut levels to initially identify participants as potential thalassemia carriers. These are the widely recommended red blood cell indices to continue hemoglobin analysis using capillary electrophoresis (Susanah *et al.,* 2022).

Thalassemia harms children's quality of life due to the effects of the disease and its treatment on their social, emotional, and school functioning, reducing their quality of life. Assessing the quality of life in thalassemic children and their family members is essential to determine the actions to improve the quality of life (Wahyuni *et al.,* 2011).

CONCLUSION

We present a case report of the fourth pregnancy in a woman with thalassemia-dependent transfusion. Thalassemia is not an obstacle to patients having a family and children. Management of pregnant women with thalassemia requires special attention from preconception, during pregnancy, and toward delivery time.

Multidisciplinary involvement, such as hematologists and obstetricians, is the primary key to the safety of mothers and children. Hemoglobin levels during pregnancy are routinely monitored to ensure optimal fetal growth. The choice of delivery method can be made by cesarean section or normal delivery, which is adjusted for each individual with thalassemia. Babies born to thalassemia parents should be screened for thalassemia to improve their quality of life.

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