

## Pregnancy outcomes in women with thalassemia major and minor: an observational cross-sectional study

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Received: 12 November 2025

Revised: 16 December 2025

Accepted: 17 December 2025

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### ABSTRACT

**Background:** Recent advances in the management of thalassemia have significantly improved life. Expectancy and quality of life in patients with this hemoglobinopathy result in a consequent increase in their reproductive potential and desire to have children. This study aimed to assess the pregnancy outcome in thalassemia patients.

**Methods:** This observational cross-sectional study was conducted at the Department of Obstetrics and Gynaecology of Bangabandhu Sheikh Mujib Medical University and Dhaka Medical College, Dhaka, Bangladesh, from October 2014 to March 2015. A total of 50 admitted patients in the Obstetrics and Gynaecology wards of BSMMU in the set duration of 6 months; the pregnant patients with thalassemia were enrolled in this study purposively. Data were analyzed using Microsoft Office tools.

**Results:** The data analysis of 50 patients yielded the following results. The mean age of 50 mothers was 27.67 ( $\pm 7.59$ ) years. The maximum 36 (72%) patients were from the 21-30 years' age group. Among the 50 mothers with thalassemia, 8 (16%) were diagnosed with thalassemia major, and the remaining 42 (84%) were diagnosed with thalassemia minor. Pregnancy was relatively less complicated in the mothers with thalassemia major, as they were under regular ANC and regular supervision of hematologists, so that they could avoid pregnancy-induced thalassemia-related complications. But most thalassemia minor cases were undiagnosed or less emphasized before they became pregnant. So, they faced more complications. A total of 48 (96%) mothers gave birth successfully. Every mother bore a singleton pregnancy. 7 (14%) were born with low birth weight. Among them, 2 (28.57%) were found as intra uterine devices (IUDs). APGAR scores of neonates at 1 min <7 were found in case of 8 cases (16%), and at 5 min were 3 (6%). 12 (24%) babies required ICU admission.

**Conclusion:** Pregnancy is possible, safe, and usually has a favourable outcome in patients with thalassemia, in the presence of a multidisciplinary team.

**Keywords:** Intrauterine fetal death, Live births, Outcome, Pregnancy, Pre-term delivery, Thalassemia

### INTRODUCTION

Thalassemia is a broad hematologic term encompassing a variety of disorders characterized by defective hemoglobin production due to deficient synthesis of one or more polypeptide chains of globin. The underlying cause is

genetic, and the disorder is typically inherited either in a carrier state or in an affected form. The various types of thalassemia are named based on the severity of the disease. Clinically, thalassemia is classified by phenotype into two main types: thalassemia major and thalassemia minor.<sup>1</sup> Thalassemia is marked by reduced or absent production of one or more globin chains, disrupting the balance between

$\alpha$ - and  $\beta$ -globin chains in adult hemoglobin A. In  $\alpha$ - or  $\beta$ -thalassemia minor, most individuals are asymptomatic, often diagnosed incidentally during evaluation of mild anemia, typically, with microcytic, hypochromic red cells. At the other end of the spectrum,  $\beta$ -thalassemia ( $\beta$ -Thal) major involves an absence or severe deficiency of  $\beta$ -globin chain synthesis, resulting in profound symptomatic anemia requiring regular and lifelong blood transfusions. According to the World Health Organization (WHO), approximately 3% of the population in Bangladesh are  $\beta$ -thalassemia carriers.<sup>1,2</sup> Globally, over 70,000 babies are born with thalassemia each year, and more than 100 million individuals are asymptomatic carriers. In Bangladesh, thalassemia minor is the most common hemoglobinopathy, with over 60,000 affected patients.<sup>1,3</sup> Many carriers remain unaware of their status and marry without knowledge of the risks, primarily due to a lack of awareness. Thalassemia refers to a group of inherited blood disorders affecting the hemoglobin molecule within red blood cells. The core defect in thalassemia syndromes is reduced globin chain synthesis, leading to red blood cells with inadequate hemoglobin content. The pathophysiology is characterized by extravascular hemolysis, resulting from the release of damaged red blood cells and erythroid precursors into the peripheral circulation due to markedly ineffective erythropoiesis.<sup>4</sup> Thalassemia major (homozygous thalassemia) results from inheriting defective  $\beta$ -globin genes from both parents, causing severe transfusion-dependent anemia. In contrast, the heterozygous state, known as  $\beta$ -thalassemia trait (thalassemia minor), causes mild to moderate microcytic anemia with minimal impact on overall health. With modern medical advancements, patients with thalassemia major (TM) are now surviving well into adulthood. Improved life expectancy and quality of life have made parenthood a realistic possibility for these individuals. In recent years, survival rates have significantly improved due to advances in transfusion practices and the introduction of effective iron chelation therapy.<sup>5</sup> Consequently, pregnancy has become feasible in many TM patients. The main cause of infertility in TM is pituitary gland hemosiderosis, which leads to hypogonadotropic hypogonadism.<sup>6</sup>

Patients with TM often experience severe hemolytic anemia and require frequent transfusions, which in turn result in tissue hemosiderosis. In thalassemia major, iron deposition may adversely affect the cardiac, hepatic, and endocrine systems.<sup>7</sup> During pregnancy, women with thalassemia who have undergone splenectomy or have a platelet count greater than  $600 \times 10^9/l$  are typically offered low-molecular-weight heparin for thromboprophylaxis, in addition to low-dose aspirin (75 mg/day).<sup>8</sup> Both thalassemia major and thalassemia minor are associated with a prothrombotic state due to abnormal red cell fragments. Moreover, pregnancy-related complications are common and may include preterm delivery, recurrent miscarriage, increased susceptibility to infections during pregnancy and the postpartum period, fetal growth restriction, and stillbirth.<sup>9</sup> This study aimed to evaluate the

clinical outcomes of pregnant women with thalassemia admitted to the obstetric ward, to document the impact and effectiveness of modern therapeutic interventions.

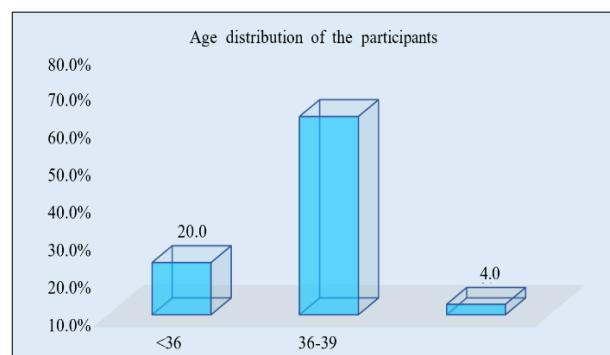
## METHODS

This observational cross-sectional study was conducted in the Department of Obstetrics and Gynaecology at Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College, Dhaka, Bangladesh, from October 2014 to March 2015. A total of 50 pregnant patients with thalassemia admitted to the Obstetrics and Gynaecology wards of BSMMU and Dhaka Medical College, Dhaka, Bangladesh, during these six months were enrolled using a purposive sampling technique. Diagnosis of thalassemia was based on detailed history-taking, thorough clinical examination, and relevant investigations. Ethical approval for the study was obtained from the institutional ethical committee, and informed written consent was collected from all participants prior to data collection. As per the inclusion criteria, all pregnant thalassemia patients admitted during the study period were included. Patients who declined participation or were diagnosed with sickle cell disease or other hemoglobinopathies, such as HbE trait, HbE disease, or E-thalassemia, were excluded according to the exclusion criteria. Data were analyzed using Microsoft Office tools.

## RESULTS

In this study of 50 pregnant women with thalassemia, 38 (76%) reached term pregnancy, 10 (20%) had preterm deliveries, and 2 (4%) experienced post-dated pregnancies (Figure 1). Among them, 8 (16%) had  $\beta$ -thalassemia major, and 42 (84%) had  $\beta$ -thalassemia minor (Figure 2). Regarding chelation therapy, 38 (76%) did not receive any, while 10 (20%) used Deferoxamine and 2 (4%) used Deferasirox (Figure 3).

Live births occurred in 48 cases (96%), with 2 cases (4%) of intrauterine fetal death (IUD), excluding abortions. Preterm delivery (<37 weeks) was observed in 10 patients (20%), and caesarean section was the mode of delivery in 35 cases (70%) (Table 2).



**Figure 1: Column chart showing distribution of participants as per gestational age (n=50).**

**Table 1: Obstetric risk factors of subjects in the study population.**

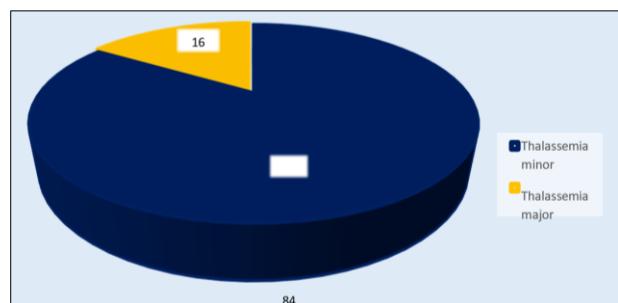
Maternal outcome	N (%)
Preeclampsia	2 (4)
Gestational diabetes	1 (2)
Hydramnios	1 (2)
Oligohydramnios	5 (10)
Intrauterine growth restriction	4 (8)
Premature rupture of membranes	4 (8)
Preterm labor	10 (20)
Maternal anemia and blood transfusion	22 (44)
SF levels at the end of pregnancy (ng/ml)	1,357.5 (336-3,054)

**Table 2: Pregnancy outcome.**

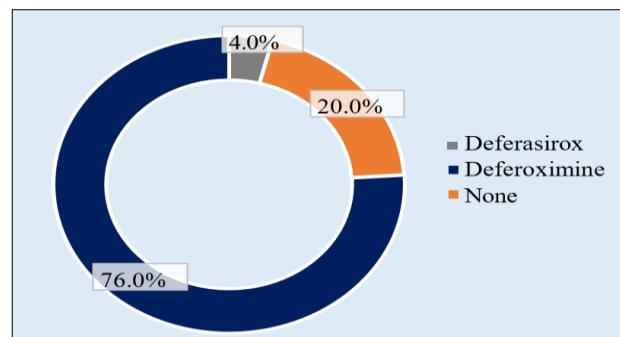
Pregnancies type	N	%
Live births	48	96.0
Intrauterine fetal death	2	4.0
Pre-term delivery	10	20.0
Cesarean delivery	35	70.0
Intrauterine growth restriction	4	8.0
DVT in pregnancy and postpartum	1	2.0

Intrauterine growth restriction (IUGR), defined as fetal weight below the 10th percentile for gestational age, was seen in 4 cases (8%). One patient (2%) developed deep vein thrombosis (DVT) during pregnancy or the postpartum period. Of the 50 newborns, including 2 IUDs, 42 (84%) had birth weights between 2500–4000 grams, 7 (14%) weighed <2500 grams, and 1 (2%) weighed >4000 grams (Table 3).

Neonatal outcomes differed between the  $\beta$ -thalassemia types. MSAF and IUD occurred only in the  $\beta$ -thalassemia major group (4% each). IUGR was observed exclusively in neonates of mothers with  $\beta$ -thalassemia minor (8%). ICU admission was required in 6 neonates (12%) from each group. An Apgar score <7 at 1 minute was more frequent in the major group (12%) compared to the minor group (4%), while at 5 minutes, low scores were noted in 3 cases (6%) in the major group and none in the minor group (Table 4).



**Figure 2: The distribution of types of thalassemia (n=50).**



**Figure 3: Ring chart showed the distribution of mothers as per receiving chelation therapy (n=50).**

In this study, the most prevalent obstetric risk factor was maternal anemia requiring blood transfusion (44%), followed by preterm labor (20%). Other notable factors included oligohydramnios (10%), intrauterine growth restriction (8%), and premature rupture of membranes (8%), while preeclampsia, gestational diabetes, and hydramnios were less common. The median serum ferritin level at the end of pregnancy was 1,357.5 ng/ml (Table 1).

**Table 3: Distribution of birth weight of neonates.**

Birth weight (grams)	N	%
<2500	7	14.0
2500-4000	42	84.0
≥4000	1	2.0

**Table 4: Neonatal outcome in  $\beta$ -thalassemia mother.**

Neonatal outcome	Thalassemia	
	Major (%)	Minor (%)
MSAF	2 (4)	0
IUD	2 (4)	0
IUGR	0	4(8)
ICU admission	6 (12)	6 (12)
Apgar score at 1 min <7	6(12)	2(4%)
Apgar score at 5 min <7	3 (6)	0

## DISCUSSION

In this current study involving 50  $\beta$ -thalassemia patients, 8 (16%) were diagnosed with  $\beta$ -thalassemia major and 42 (84%) with  $\beta$ -thalassemia minor. Perinatal mortality was observed in 2 cases (4%), while Apgar scores below 7 were noted in 8 neonates (16%) at 1 minute and in 3 neonates (6%) at 5 minutes—findings comparable to those reported in previous studies.<sup>10</sup> Thalassemia has been associated with an increased incidence of obstetric complications.<sup>11</sup> Adverse pregnancy outcomes identified in this study included low birth weight (<2500 g, 14%), intrauterine growth restriction (IUGR, 8%), and preterm delivery (20%). Interestingly, all IUGR cases were observed in mothers with thalassemia minor. Chronic maternal anemia during pregnancy, which may lead to fetal hypoxia, was detected in 22 mothers (44%). However, no IUGR was

noted among the chronically anemic mothers in this cohort.<sup>12</sup> Consistent with the findings of Eyal Sheiner et al, our study did not find a significant association between hemoglobin levels and IUGR, suggesting that alternative mechanisms may underlie IUGR in thalassemia minor patients.<sup>13</sup> Maintaining maternal hemoglobin above 10 g/dl is considered essential during pregnancy.<sup>14</sup> While one study reported an acute splenic infarct in β-thalassemia minor, potentially causing placental infarction, this mechanism could not be confirmed in our study.<sup>30</sup> Oligohydramnios was observed in 5 cases (10%), frequently associated with IUGR and possibly linked to a relative hypoxic state.<sup>15</sup> Caesarean section was performed in 35 cases (70%), aligning with previous studies reporting increased caesarean rates in β-thalassemia pregnancies.<sup>16,17</sup> As noted in the literature, increased blood transfusion requirements driven by physiological changes of pregnancy and discontinuation of chelation therapy often result in iron overload, leading to haemosiderosis and possible cardiac complications.<sup>18,19</sup> The high caesarean delivery rate observed in this study is consistent with contemporary data and is often driven by a heightened vigilance for fetal growth restriction, non-reassuring fetal status, and maternal comorbidities in this high-risk population.<sup>20</sup> The management of iron overload remains a critical challenge in the perinatal period. The physiological anemia of pregnancy, compounded by the underlying hemoglobinopathy, frequently necessitates transfusions, which exacerbates maternal iron stores. Elevated serum ferritin, as noted in our cohort, is increasingly recognized not only as a marker for long-term end-organ damage but also as an independent risk factor for adverse obstetric outcomes, including gestational diabetes and preeclampsia.<sup>21,22</sup>

This underscores the necessity of meticulous preconception and antenatal management of iron burden. A multidisciplinary care model, integrating maternal-fetal medicine, hematology, and cardiology, is now considered the standard of care. This approach is crucial for optimizing maternal health, tailoring the timing and mode of delivery, and ensuring appropriate long-term follow-up to mitigate the risks of iron-induced complications postpartum.<sup>23,24</sup> In our study, the requirement for blood transfusion was more frequent in patients with β-thalassemia minor (21 patients, 42%) than in those with β-thalassemia major (8 patients, 16%). The transfusion volume also differed, with each major patient receiving two units of blood, compared to one unit per minor patient.

All major patients had been under continuous hematologic supervision since diagnosis, and three (6%) had undergone splenectomy before pregnancy due to hypersplenism. In contrast, chronic anemia was exclusively identified in thalassemia minor patients who had remained undiagnosed until their current pregnancy. A notable demographic feature of the cohort was that 30 mothers (60%) were primigravidae.

## Limitations

This study had several limitations. The duration of the study was relatively short, and the sample size was small, which may limit the generalizability of the findings. As the study was conducted in selected institutions using a cross-sectional design, it does not fully represent the nationwide scenario.

## CONCLUSION

In this study, all thalassemia major cases required blood transfusion and caesarean delivery, with no maternal deaths and two IUDs. Several thalassemia minor cases also needed transfusions, but had no maternal or fetal mortality. With timely transfusion, close monitoring, and proper obstetric care, satisfactory pregnancy outcomes are achievable in thalassemic women. Delivery should be conducted in tertiary care centers to ensure comprehensive management and minimize complications.

## Recommendations

Thalassemic pregnancies should be closely monitored with regular antenatal checkups, appropriate transfusion support, and multidisciplinary care. Delivery must be planned in tertiary care hospitals with facilities for emergency obstetric and neonatal management to ensure optimal maternal and fetal outcomes.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Begum UAM, Saha E, Meherunnesa S, Khatun T, Haq AFMA. Pregnancy outcomes in women with thalassemia major and minor: an observational cross-sectional study. *Int J Reprod Contracept Obstet Gynecol* 2026;15:203-7.