Original Article

# The Pregnancy Outcome in Patients with Minor β-Thalassemia

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## Abstract

**Background:** Physiologic alterations during pregnancy worsen the anemia severity, and they are associated with an increased risk of fetal growth restriction, low birth weight, and preterm birth. **Objective:** The aim of the present study was to determine pregnancy outcomes in women with minor β-thalassemia. **Materials and Methods:** A total of fifty women who attended the consultation clinic of Azadi Teaching Hospital for antenatal care visit were screened consecutively and included in the present cross-sectional study in Duhok, Iraqi Kurdistan. The patients were followed up until delivery for pregnancy outcomes from May 20, 2018 to February 10, 2019. **Results:** About 14.0% of the patients had a history of baby death. The most prevalent clinical features were anemia (18.0%) and a history of preeclampsia (16.0%). Most of the patients had undergone a trial of normal vaginal delivery (80.0%), and 14.3% of their newborns were admitted to the neonatal intensive care unit (NICU). Only one of newborns died at 5 min following delivery due to a low Apgar score. The study showed that neonates who were admitted to the NICU had lower Apgar scores after 1 and 5 min compared to nonadmitted group (5.71 and 6.71 vs. 7.24 and 9.29, respectively). The mothers of the neonates who were admitted to the NICU had a higher prevalence of previous dead baby (42.9%; $P = 0.031$), previous history of preeclampsia (57.1%; $P = 0.005$), and more likely to undergone cesarean section (C/S) (71.4%; $P = 0.001$). **Conclusions:** The present investigation suggests that the β-thalassemia newborn admitted to the NICU had a higher prevalence of clinical issues compared to those not admitted to the NICU.

**Keywords:** Followed up study, minor β-thalassemia, pregnancy outcome

## Introduction

Thalassemia is a heterogeneous group of autosomal recessive genetic disorders. They are presented by the decreased or absent synthesis of globin chains, resulting in anemia and microcytosis. There are two main forms of thalassemia: α-thalassemia and β-thalassemia.[1] They are hemoglobinopathies that are characterized through impairment in the production of the normal globin peptide chains. The prevalence and severity of thalassemia depend on the population. Thalassemia minor leads to a different degree of the disease based on the rate of β-chain production. Usually, it is presented as asymptomatic anemia of mild degree (hemoglobin [Hb] is 1–2 g/dL lower than normal in both sexes).[2] α-thalassemia is considered the most inherited disorder of Hb. It is characterized by the decreased or suppressed production of α-globin chains.[3]

Thalassemia minor has no specific therapy during pregnancy apart from folic acid. Blood transfusion is necessary in the case of severe anemia occurrence during pregnancy. Thalassemia as a heterozygote is diagnosed with mild anemia (HbA level 1 or 2 g below normal range), low mean cell volume, low mean corpuscular Hb, elevated HbA2, and normal or elevated HbF. Pregnant women with thalassemia minor have more significant anemia. It is more common in the latter half of the second trimester and early third trimester.[4,5]

Physiologic alterations during pregnancy worsen the anemia severity. In addition, it has been shown to associate with an increased risk of fetal growth restriction, low birth weight, and preterm birth.[6-8] There are few studies that reported pregnancy outcomes in women with β-thalassemia minor.[9] Since thalassemia syndromes could deteriorate the maternal and neonatal status, especial attention must be paid to these kinds of women.

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Maruotti *et al*. found that the preeclampsia rate in pregnant women affected by β-thalassemia and underwent chorionic villus sampling (CVS) was significantly higher compared to their compartments who were undergone by CVS. Accordingly, they made a hypothesis that a lower maternal level of Hb is a protective mechanism for preeclampsia.[10] However, further research is required to examine the preeclampsia outcome in pregnant women affected by thalassemia diseases. Therefore, it is important to screen these patients for the possible mentioned complications.

The aim of the present study was to determine pregnancy outcomes in women with minor β-thalassemia.

## Materials and Methods

### Study design and sampling methods

Women who attended the outpatient clinic of a tertiary hospital for pregnancy purposes were screened consecutively for the inclusion and exclusion criteria. The patients who were included in the study following taking ethical approval from the local department were followed up until delivery. The patients were selected from Azadi Teaching Hospital which is a specialized tertiary center for general medical conditions of adult populations in this region. The patients were included and followed up every month for medical conditions.

During each antenatal visit, the medical examinations were done including Hb, vital signs, and general condition. In the past 3 months, the patients were seen every 2 weeks. Serum folate was not available until time of delivery; then, all patients were left for spontaneous delivery unless there was an indication for C/S. The data collection was collected between May 20, 2018 and February 10, 2019.

### Inclusion and exclusion criteria

The patients aged 18 years and older who were diagnosed with β-thalassemia minor before delivery and term pregnant irrespective of their general and social information were included in the study. The patients with β-thalassemia major or preterm pregnancy, recurrent pregnancies before 24 weeks of gestation, fetal structural or chromosomal abnormalities during pregnancy (e.g., a history of neural tube defect), history of infertility, and other related hematological issues, such as β-thalassemia major, sickle cell anemia, and a history of thalassemia in family, were excluded from the study.[11]

### Diagnosis and measures

The information collected from the patients were age, number of previous pregnancies, blood transfusion, antepartum hemorrhage (APH), postpartum hemorrhage (PPH), blood groups of mother and father, and Apgar scores at 1 and 5 min.

Anemia was determined where Hb was <10 mg/dl. The diagnosis of thalassemia was performed based on the complete blood count (CBC) and standard Hb electrophoresis criteria in the first trimester. The elevation of HbA2 (≥3.5%) determined through electrophoresis and column chromatography was level that used to diagnosis β-thalassemia.

The patients whose Hb dropped substantially (<7 mg/dl) were given a blood transfusion. In addition, at least oral folate supplement was given to patients 5 mg daily in line with the criteria of the American College of Obstetricians and Gynecologists.[12] The pregnancy outcomes were considered in this study including neonatal intensive care unit (NICU) admission, newborn death, and Apgar scores in the 1$^{st}$ and 5$^{th}$ min.

The patients underwent a CBC, hepatitis B, and urinary analysis at the enrollment. Moreover, ultrasonography was conducted to detect maternal or fetal indications as the required steps of the hospital-based guidelines. The investigators reviewed maternal records and neonatal outcomes. In the present study, the preterm birth was defined as a live birth before 37 gestation weeks. Fetal intrauterine growth restriction (IUGR) was defined as a birth weight <10% of the normal growth curve and macrosomia as birth weight >90% of the normal growth curve. Stillbirth was defined as mortality in utero after 24 weeks of gestation.[11]

### Statistical analysis

The descriptive purposes of the study were presented in frequency distribution either mean and standard deviation or frequency and percentage. The prevalence of current medical conditions, neonate outcome, and NICU admission was presented in frequency and percentage. The association of mothers' complications with admission to the NICU was examined in independent *t*-test or Fisher's exact test. The significant level of difference was determined in $P < 0.05$. The statistical calculations were performed using Statistical Package for the Social Sciences version 24:00 (SPSS 24; IBM Corp; IBM).

### Ethical considerations

The ethical approval of the present protocol was obtained from the Kurdistan Board for Medical Specialties. The confidentiality of the personal information of the patients was protected throughout the study steps. In addition, no invasive method was applied to the patients for the study purposes.

## Results

The mean age of the fifty pregnant patients diagnosed with β-thalassemia minor included in the present study was 31.14 ± 8.02, with their age between 18 and 46 years. The mean values of gravida, para, and abortion were 3.54 ± 2.07, 1.98 ± 1.81, and 0.44 ± 0.73, respectively, and 14.0 of them had a history of baby death. Regarding blood group, the majority of the patients and their husbands had $O^+$ blood group (56.0% and 66.0%, respectively) [Table 1]. The patients participated in the present investigation were nonsmokers. In addition, no preterm, stillbirth, and maternal mortality was not observed by the end of delivery.

The clinical profile of the patients is presented in Table 2. The table revealed that anemia was the most prevalent clinical problem (18.0%) in patients, followed by a history of

preeclampsia (16.0%) and blood transfusion (6.0%). A small percentage of the patients had APH (2.0%) and PPH (4.0%).

Most of the patients had undergone normal vaginal delivery (80.0%) compared to 20.0% for C/S. Only one neonate died following 5 min of delivery (2.0%) due to low Apgar score, and 14.3% were admitted to the NICU. The Apgar scores after 1 and 5 min were 6.88 ± 1.21 and 8.92 ± 1.06, respectively [Table 3].

The association of patients' features with NICU admission showed that the newborns were admitted to the NICU had a lower level of Apgar score after 1 and 5 min (5.71 and 6.71, respectively) versus those not admitted to the NICU (7.24 and 9.29, respectively). In addition, the patients with a previous dead baby had a higher prevalence of NICU admission (42.9%) compared to the nonadmitted NICU group (7.1%; $P = 0.031$). The patients with a history of preeclampsia had a higher prevalence of NICU (57.1%) compared to the nonadmitted NICU group (39.0%), $P = 0.005$. Furthermore, the patients who had undergone C/S were more likely to be admitted to the NICU (71.4%; $P = 0.0001$) [Table 4].

## Discussion

The present study showed that the prevalence rate of NICU admission was 14.3%, and the mortality rate of newborns was 2.0%. In comparison with this study, Amooee *et al*.[2] included 510 β-thalassemia minor patients and 512 healthy controls in a retrospective case–control study in Iran. The patients in both groups were matched in age, gestational age, and a number of previous pregnancies. The authors found that those patients with β-thalassemia minor have a substantially higher prevalence of oligohydramnios and C/S. However, they did not find a significant difference in Apgar score in the 1st and 5th min, IUGR, gestational diabetes mellitus, and preeclampsia between two study groups.

The present study found that only one newborn (2.0%) died 10 min following delivery. Amooee *et al*.[2] reported 7 (1.4%) stillbirths among the case group and 5 (1%) in the control group. They reported other complications among their study groups. Perinatal complications such as IUGR were observed in 3.1% of cases and 1.5% in controls. In similarity with our study, the cases were more likely to deliver their newborns by C/S (38.3%) compared to controls (26.5%; $P = 0.001$). We found that the patients whose newborns were admitted to the NICU were more likely to deliver by C/S. However, they did not find the significant difference in NICU between two study groups.

Amooee *et al*.[2] did not find a significant difference in Apgar score in the 1st and 5th min, while we found that those patients whose newborns were admitted to the NICU had a lower degree of Apgar scores in the 1st and 5th min.

Hanprasertpong *et al*.[11] compared the pregnancy outcomes between the women affected and not affected by thalassemia trait in a retrospective case–control study on singleton women. They included 739 patients with thalassemia and 799 patients with normal pregnancy in the study in Thailand. They did not find a

**Table 1: General information of the parents**

| Patients' characteristics ($n=50$) | Frequency distribution |
|---|---|
| Age (year), mean±SD | 31.14±8.02 |
| Range (years) | 18-46 |
| GPA (range) | |
| G; (1-9) | 3.54±2.07 |
| P; (0-6) | 1.98±1.81 |
| A; (0-3) | 0.44±0.73 |
| History of baby death, frequency (%) | |
| Yes | 7 (14.0) |
| No | 43 (86.0) |
| Mother blood group, frequency (%) | |
| A+ | 9 (18.0) |
| A− | 2 (4.0) |
| B+ | 1 (2.0) |
| AB+ | 5 (10.0) |
| O+ | 28 (56.0) |
| O− | 5 (10.0) |
| Father blood group, frequency (%) | |
| A+ | 7 (14.0) |
| A− | 2 (4.0) |
| AB+ | 2 (4.0) |
| O+ | 33 (66.0) |
| O− | 6 (12.0) |

SD: Standard deviation, GPA: Gravida para abortion

**Table 2: Clinical profile of the mothers**

| Patients' characteristics ($n=50$) | Frequency distribution, frequency (%) |
|---|---|
| Gestational diabetes | 2 (4.0) |
| History of preeclampsia | 8 (16.0) |
| Blood transfusion | 3 (6.0) |
| APH | 1 (2.0) |
| PPH | 2 (4.0) |
| Anemia | 9 (18.0) |

APH: Antepartum hemorrhage, PPH: Postpartum hemorrhage

**Table 3: Delivery mode and neonates' outcomes**

| Patients' characteristics ($n=50$) | Frequency destruction |
|---|---|
| Delivery mode, frequency (%) | |
| C/S | 10 (20.0) |
| NVD | 40 (80.0) |
| Neonate outcome, frequency (%) | |
| Death | 1 (2.0) |
| Live | 49 (98.0) |
| NICU admission, frequency (%) | |
| Yes | 7 (14.3) |
| No | 42 (85.7) |
| Apgar scores, mean±SD | |
| After 1 min (range: 0-8) | 6.88±1.21 |
| After 5 min (range: 8-10) | 8.92±1.06 |

NICU: Neonatal intensive care unit, SD: Standard deviation, NVD: Normal vaginal delivery, C/S: Cesarean section

**Table 4: Association of mothers' complications with admission of neonates to neonate intensive care unit**

| Patients' characteristics | NICU admitted (*n*=7), *n* (%) | Nonadmitted NICU (*n*=42), *n* (%) | *P* (two-sided) |
|---|---|---|---|
| Age | 32.14 (11.02) | 30.98 (7.67) | 0.795* |
| G | 4.57 (3.21) | 3.40 (1.84) | 0.381* |
| P | 2.86 (2.61) | 1.86 (1.66) | 0.360* |
| Apgar 1 min | 5.71 (0.49) | 7.24 (0.43) | **<0.0001*** |
| Apgar 5 min | 6.71 (0.95) | 9.29 (0.46) | **<0.0001*** |
| Previous dead baby | | | |
| Yes | 3 (42.9) | 3 (7.1) | **0.031**** |
| No | 4 (57.1) | 39 (92.9) | |
| GDM | | | |
| Yes | 1 (14.3) | 1 (41.0) | 0.268** |
| No | 6 (85.7) | 2.4 (97.6) | |
| History of PET | | | |
| Yes | 4 (57.1) | 3 (39.0) | **0.005**** |
| No | 3 (42.9) | 7.1 (92.9) | |
| Blood transfusion | | | |
| Yes | 1 (14.3) | 1 (2.4) | 0.268** |
| No | 6 (85.7) | 41 (97.6) | |
| PPH | | | |
| Yes | 0 (0.0) | 2 (40.0) | 1.00** |
| No | 7 (100) | 4.8 (95.2) | |
| Anemia | | | |
| Yes | 2 (28.6) | 7 (16.7) | 0.598** |
| No | 5 (71.4) | 35 (83.3) | |
| Delivery mode | | | |
| C/S | 5 (71.4) | 4 (9.5) | **0.001**** |
| NVD | 2 (28.6) | 38 (90.5) | |

*Independent *t*-test and **Fisher's exact test were performed for statistical analyses. The bold numbers show significant differences. NVD: Normal vaginal delivery, C/S: Cesarean section, NICU: Neonatal intensive care unit, PPH: Postpartum hemorrhage, PET: Positron emission tomography, GDM: Gestational diabetes mellitus

significant difference in maternal complication rates, including gestational diabetes, preterm birth, antepartum and postpartum bleeding, and the rates of neonatal complications, including macrosomia, IUGR, stillbirth, NICU admission, and Apgar scores in the 1st and 5th min. However, the rate of preeclampsia was significantly higher in cases compared to controls, with a risk rate of 1.73. In agreement with the present findings, we found that those patients with the previous history of preeclampsia were more likely that their newborns should be admitted to the NICU compared to those without a previous history of preeclampsia.

It is necessary to mention that pregnancy may not be the only factor of the neonate admission to the NICU, but there are risk factors, such as respiratory complications, hypoglycemia, and jaundice.[13]

## Conclusions

The present investigation suggests that the mothers of the neonates with β-thalassemia minor who were admitted to the NICU had a higher prevalence of clinical issues compared to those not admitted to the NICU.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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