Original Article

Outcome of Pregnancy in Thalassemia Patients in Ad-din Women`s Medical College Hospital

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ABSTRACT

Objective: Recent advances in the management of thalassemia have significantly improved life expectancy and quality of life of patients with this hemoglobinopathy, with a consequent increase in their reproductive potential and desire to have children.To observe the outcomes of pregnant women with different types of thalassemia.

Materials & Methods: Prospective observational study. Fifty patients were selected by purposive sampling. Among thepatients attending ANC and Obstetrics & Gynecology ward of AWMC in the set duration of 6 months period; the pregnant patients with thalassemia were enrolled.Data were collected by the active participation of the patients' &interviewed by the preformed data collection sheet.

Results: The data analysis of 50 patients yielded the following results.The mean age of 50 mothers were 25.9 (±5.16) years. The maximum 36 (72%) patients were from 20-30 years age group. Among the 50 thalassemia mothers 8(16%) suffered from beta thalassemia major and 42 (84%) suffered from beta thalassemia minor.Pregnancy was safe in the mothers with thalassemia major as they were under regular ANC and under regular supervision of hematologists so that they could avoid all the pregnancy induced thalassemia related complications.But most thalassemia minor cases were undiagnosed or less emphasized before conceive. So the neglected cases faced most complications. Total 48(96%) mothers gave birth successfully. Every mother conceived a singleton pregnancy. No secondary complications of iron overload developed or worsened during pregnancy. Only 7(14%) were born with low birth weight. Among them 2(28.57%) found as IUD. APGAR score of neonates at 1 min <7 were found in case of 8(16%) and at 5 min were 3(6%). 12 (24%) babies required ICU admission.

Conclusion: Provided that a multidisciplinary team is available, pregnancy is possible, safe and usually has a favorable outcome in patients with thalassemia.

Keyword: Thalassemia,Outcome, Pregnancy.

Introduction

The various types of thalassemia have specific names related to the severity of the disorder. Clinical classification is by phenotype: 1. Thalassemia major 2. Thalassemia minor. Thalassemia may be characterized by reduced or absent production of one or more globin chains, thus disrupting the ratio of α- and β-globin chains in adult hemoglobin A. At the level of α- or β-thalassemia minor, most patients are asymptomatic, and may only be diagnosed after investigation for incidentally detected mild anemia with microcytic, hypochromic red cells. At the other end of the spectrum, β-thalassemia (β-Thai) major is associated with absence or severe deficiency of β-globin chain synthesis leading to a profound and symptomatic anemia that requires regular and life-long transfusion support.According to World health Organization (WHO), there are about 3% beta-thalassemia carriers in Bangladesh.[1]More than 70,000 babies are born with thalassemia worldwide each year and there are 100 million individuals who are asymptomatic Thalassemiacarriers.[5] Thalassemia minor is the commonest hemoglobinopathies in Bangladesh. There are more than 60,000 thalassemia patients in this

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country. Many of these patients are getting married due to a sheer lack of awareness[1]. Thalassemia is a group of genetic, inherited disorders of the blood. More specifically, it is a disorder of the hemoglobin molecule inside RBCs. The basic defect in the thalassemia syndromes is reduced globin chain synthesis withthe resultant red cells having inadequate hemoglobin content. The pathophysiology of thalassemiasyndromes is characterized by extravascular hemolysis due to the release into the peripheral circulation ofdamaged red blood cells and elytroid precursors because of a high degree of ineffective erythropoiesis[1]. Thalassemia major (homozygous thalassemia) results from the inheritance of a defective β-globin genefrom each parent. This results in a severe transfusion-dependent anemia. The heterozygous state, β-thalassemia trait (thalassemia minor) causes mild to moderate microcytic anemia with no significantdetrimental effect on overall health. Modern advances in medical care have enabled patients with Thalassemia Major (TM) to survive successfully into adulthood. The prolonged life expectancy and improvement in quality of life of thalassemia patients has redefined the challenges that couples face as they now have a realistic chance of creating a family.In recent years, TM survival rates have improved with patients suffering fewer complications due to the advances in transfusion treatment and the use of chelation therapy.[2] As a consequence, pregnancy is feasible in these patients. The main cause of infertility in TM is due to pituitary gland haemosiderosis leading to hypogonadotropic hypogonadism[3]. Patients with TM are characterized by severe hemolyticanemia and are dependent on frequent blood transfusions, which consequently results in tissue haemosiderosis. Patients with thalassemia minor, a clinically milder disorder, present with absence of symptoms to mild and moderate anemia. In thalassemia major cases iron deposition affects the cardiac, hepatic and endocrine systems[4]. The usual advanced treatment during pregnancy as follows- Women with thalassemia who have undergone splenectomy or have a platelet count greater than 600 x 109/l are usually offered low-molecular-weight heparin thromboprophylaxis as well as low-dose aspirin (75 mg/day)[5]. Women with thalassemia major or minor have a prothrombotic tendency due to the presence of abnormal red cell fragments. Besides, there are huge pregnancy related complications of both mothers and fetus like preterm delivery, frequency of miscarriage, infective episodes during pregnancy and postpartum period, improper development of fetus as well as still birth[6]. The purpose of this study was to observe the clinical outcomes of pregnant women with thalassemia admitted into obstetric ward in order to document the effectiveness of modern therapeutic advances.

Materials & Methods

The Prospective observational study was conducted in department of Obstetrics & Gynecology of Ad-din Women Medical College Hospital, 2 Bara Moghbazar, Dhaka from October 2015 to June 2016. Fifty patients with diagnosis of β-thalassemia admitted during this period were selected on the basis of purposive sampling. The patients with sickle cell disease and other haemoglobinopathies like HbE trait, disease and E β-thalassemia were excluded from the study.The patients were vividly informed about the study.The hematological profiles of term pregnancy clients were done. The outcome of pregnancy in thalassemia mothers were observed and recorded by a pre structured, peer reviewed and tested case record form. At first, the thalassemia patient was diagnosed through adequate history, proper clinical examination and relevant investigations. From history known case of thalassemia major and minor**,** history of splenectomy, thalassemia faces**,** growth retardation, history of chronic anemia or blood transfusion and history of thalassemia related other complications helped to diagnose thalassemia clinically. Examination usually upholded some positive characteristics in favour of thalassemia likeslanting eyes, flat nasal bridge, Mongolian face**,** bosselated forehead, growth retardation**,** endocrine and cardiac complications CBC (Hb%, ESR, MCV, Platelet count), PBF, RBS, USG of whole abdomen, ECG, Hb electrophoresis were the hematological and imaging profiles that were done to get a confirmatory diagnosis.Antepartum Management was done like- Folic acid, iron supplementation and blood transfusion as required. Review was done through multidisciplinary approach with the members of obstetrician, hematologist, cardiologist and endocrinologist-upto 28 weeks monthly and thereafter fortnightly. And each review was performed by doing thyroid function, cardiac function, blood sugar and as per complications. Blood transfusion was given to theβ-thalassemia major and minor patients as per required. Besides, Thromboprophylaxis has given to splenectomized patient. Low dose aspirin 75mg/day was prescribed in the patient whose platelet count was less than 6 lac/cmm.Intra-partum Management was done as intravenousdeferoxamine 2gm over 24h forβ

thalassemia majoronly during labour. Continuous fetal monitoring was done. Active management of third stage of labour was done to minimize blood loss. Blood transfusion during labour was given only when patients Hb concentration was less than 10gm%. Ethical clearance was taken from the Ethical Review Committee of AWMC before starting the research.

Data analysis and interpretation

All data were checked and edited after collection.Chart by spreadsheet of Windows 7 were done. Frequency distribution and normal distribution of all continuous and categorical variables were calculated.Cross tabulation was prepared and comparisons were made between the respondents from different age, sex, co morbidities, wound type, underlying pathology. Chi-square analysis was done to analyze data in SPSS version 22. 'P' values <0.05 was considered as statistically significant.

Results

There were only 50 respondents finally enrolled in this study after scrutinization by eligibility criteria. Maximum 36 (72%) respondents were from age group 20-30 years followed by 13 (26%) from 31-40 years age group. Only 1 (2%) mother was over 40 years of age. The mean age of the subjects was 25.9±5.16 years (The age range was 20-41 years Figure-I. Among the 50 mothers the maximum 38(76%) mothers reached the term pregnancy whereas 10 (20%) demonstrated premature pregnancy. Only 2 (4%) patients postdated pregnancy Figure-2. Out of 50 mothers 30 (60%) mother proclaimed parity 1 whereas 19 (38%) mother proclaimed 2-4 parity. Only 1 (2%) mother proclaimed parity >4 Figure-3. Among 50 mothers 34 (68%) underwent irregular antenatal checkup whereasmothers underwent regular checkup were 10 (20%) in number. Only 6(12%) mothers did not face any antenatal checkup Figure-4. Among the 50 thalassemia mothers 8(16%) suffered from beta thalassemia major and 42 (84%) suffered from beta thalassemia minor Figure-5. Among the 50 cases the history of patients regarding thalassemia has been featured in Table-I. Among the 50 mothers38 (76%) took no chelation therapy whereas 10 (20%) used to take deferoxamine and 2(4%) used to take Deferasirox 0(0%) took Deferiprone Figure-6. Among the 50 patients distribution of blood transfusion during Thalassemia major 50% & Thalassemia minor 30% Table-II. Among the 50 patients the obstetric risk factors which were accompanied with thalassemia were displayed in Table-III. The pregnancy outcome amongThalassemia mothers were depicted in Table-IV. Distribution of neonatal birth weight showed that 42% neonate born with normal birth weight, 14% were born with low birth weight and 2% baby was overweight Table-V. Among the 50 neonates of 50 mothers 2 (4%) died before birth. Other 48 neonates featured the different outcome portrayed in Table-VI.

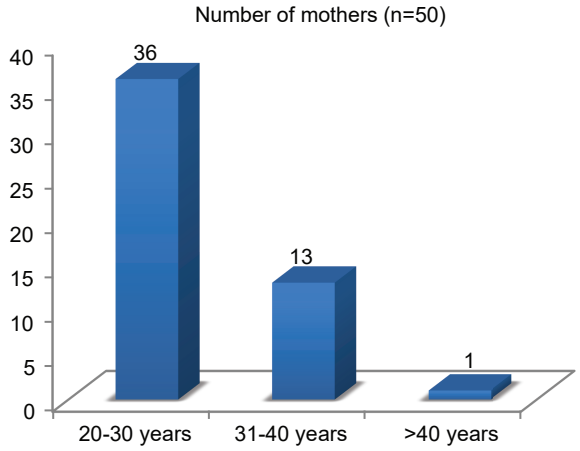

Fig.-1: Age distribution (n=50)

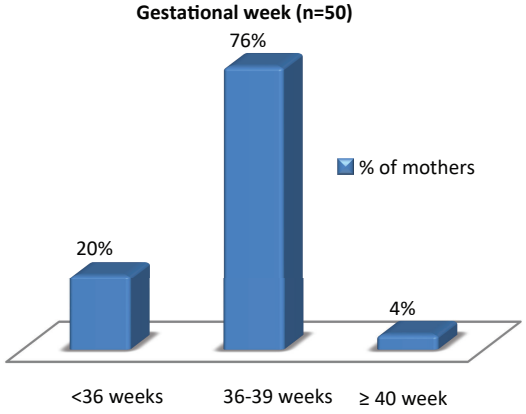

Fig.-2: Gestational age(n=50)

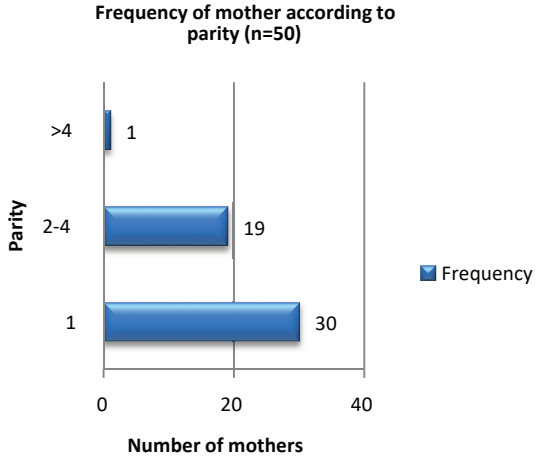

Fig.-3: Parity of respondents (n=50)

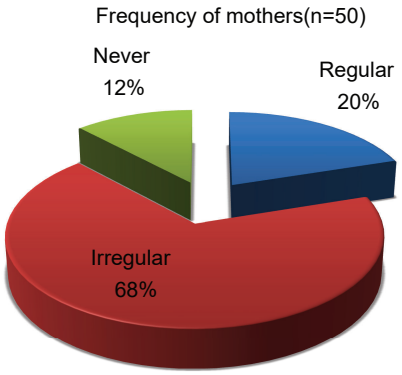

Fig.-4: Antenatal checkup(n=50)

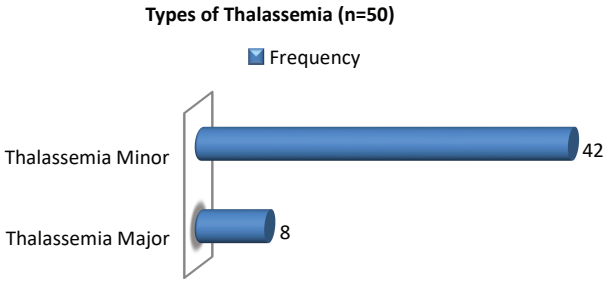

Fig.-5: Different types of thalassemia among respondents(n=50)

Table-I: Patient's history regarding splenectomy (n=50)

Variables	Total No (%)
Age (years), mean(±SD)	25.9 (±5.16)
Age at diagnosis (years)	8.2±9.9
Age at first transfusion (years)	12.4±10.3
Splenectomy done	3 (6%)
Age at splenectomy (years)	14.7±9.6
Transfusion requirement (irrespective of pregnancy)	
Frequently (≥ 8 times per year)	12 (24%)
Occasionally	15 (30%)
Never	11 (22%)
Received chelation	12 (24%)

Data presented as n (%) or mean ± standard deviation. Frequently transfused = those requiring at least four transfusions/year. Occasionally transfused = those transfused in a lifetime under certain conditions such as surgery of pregnancy.

Table-II: Distribution of blood transfusion during pregnancy (n=50)

Type of thalassemia	Total patients patient (n=50)	No. of received blood transfusion	%
Thalassemia major	8	4	50%
Thalassemia minor	42	13	30%

Table-III: Obstetric risk factors of subjects with β-thalassemia(n = 50)

Maternal outcome	Frequency No (%)
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 (Hb <10 mg/dL)	22(44%)
& required blood transfusion (all were newly diagnosed thalassemia minor)	
SF levels at the end of pregnancy (ng/mL)	1,357.5 (336–3,054)

*Number of patients

Table-IV: Pregnancy outcome(n=50)

Pregnancies	Total (n=50) No (%)
Live births	48 (96%)
Intrauterine fetal deatha	2 (4%)
Pre-term deliveryab	10 (20%)
Cesarean deliverya	35(70%)
Intrauterine growth restrictionac	4 (8%)
Thrombotic events	0(0%)
DVT antepartum	0 (0%)
DVT in pregnancy and postpartum	1 (2%)
Placental thrombosis	0 (0%)

Data presented as n (%). [a]After excluding abortions; DVT= deep vein thrombosis [b]defined as delivery at <37 weeks of gestation. [c]defined as <10th percentile for gestational age.

Table-V: Distribution of birth weight of neonates (n=50)

Birth weight*	Frequency(n = 50) No (%)
<2500 grams	7 (14%)
2500-4000 grams	42 (84%)
≥ 4000 grams	1 (2%)

* All mother had the singleton pregnancy.

Table-VI: Neonatal outcome in β-thalassemia mother (n=50)

Neonatal Outcome	Thalassemia major	Thalassemia minor
Meconium-stained amniotic fluid	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%

*Number of neonates.

Discussion

Thalassemia is a very common hematological entity which is not very much uncommon in our country. This study was performed on patients with β-thalassemia to determine the maternal andfetal outcomes and describe most risk factors associated with β-thalassemia during pregnancy. This study consisting 50 β-thalassemia subjects among whom 8(16%) mothers belong to β-thalassemia major and rest of 42(84%) was bearing β-thalassemia minor. Perinatal mortality 2(4%) and Apgar score at 1min <7 were 8 (16%) and at 5 min 3(6%) after delivery which were very similar in to the previous studies results.[7] Thalassemia has been associated with an increased incidence of obstetrical complications.Adverse pregnancy outcome are detected, especially low birth weight (Wt.< 2500gr, 14%), IUGR (8%) and preterm delivery (20%). All the IUGR babies were found in thalassemia minor patients. Chronic maternal anemia during gestation might lead to fetal hypoxia which was found in 22(44%) mothers, and predisposing the fetus to IUGR. Interestingly no IUGR babies were born in chronic anemic mother[8]. In our study, no significant association was found between hemoglobin levels and IUGR among thalassemic women like another study by EyalSheiner and colleagues' study and suggested that a different mechanism is responsible for IUGR in thalassemia minor patients.[9] It is essential to maintain that hemoglobin concentration above 10 g/dL during pregnancies.[10] At least one study showed acute splenic infarct in β-thalassemia minor.[11] This mechanism may cause placental infarction but this theory needs further study to be approved which could not be possible to prove in our study. In our study oligohydramnios was found in 5(10%) of case which was associated with IUGR and might be part of the relative hypoxemic state.[9] In our study, 35(70%) mothers underwent caesarean delivery which is a quite large figure out of 50 (100%) mothers. All studies investigating pregnancy outcome of patients with β-thalassemiafound higher rates of cesarean delivery.[7,9,10] So, the statistics were consistent with the previous studies.

As reported in other studies, the increase in blood transfusions, due to the physiological changes and increased demands of pregnancy as well as the cessation of chelation therapy, resulted in an increased iron overload and aggravates haemosiderosis; this caused further iron deposits in major organs such as the heart, leading to cardiac dysfunction and complications.[11-13] In our study, 4(8%) patients of Thalassemia major and 13(26%) patients of Thalassemia Minor experienced blood transfusion according to the requirements. Among them, 4(8%) patients with thalassemia major received 2 units of blood each whereas according to the record the minor patients received one unit of blood transfusion each. In our study only 8(16%) mothers were thalassemia major group who were under constant supervision and treatment of hematologists since their first diagnosis.Moreover, 3(6%) of them underwent splenectomy in their pre-pregnancy state due to splenomegaly and obviously hypersplenism.But interestingly, here the all chronically anemic mothers were due to thalassemia minor who remained undiagnosed before their current pregnancy and this pregnancy was the 1st pregnancy for 30(60%) mothers out of 50 (100%).We found no handsome statistics in the pregnancy outcome, preterm delivery,birth weight, growth restriction, pregnancy induced hypertension and gestationaldiabetes thalassemia mothers. Due to lack of control we could not prove the statistical significance.[14]

Conclusion

Thalassemia syndrome, including β-thalassemia minor during pregnancy can present unique management challenges and requires close maternal and fetal surveillance. The pregnancy outcome in patients with

beta-thalassemia minor, like prenatal outcomes, is not different from normal group. In spite of an attempt to keep hemoglobin levels above 7.0 g/dl, the incidence of fetal growth restriction and preterm birth has been relatively high, though maternal complications are rather not different from general. Care for such pregnancies should be multidisciplinary, incorporating a maternal–fetal medicine specialist, a genetic counselor, and a hematologist. However, since fetal growth restriction complicates more pregnancies with thalassemia syndrome, the need for close antenatal follow-up and frequent sonographic assessment of fetal growth can be overemphasized. Further prospective studies among high-risk populations for β-thalassemia with larger sampling should investigate the efficacy of such study.

Acknowledgement

We are extremely grateful to expert supervision supports and suggestions and sustained encouragement throughout the course of this research work and article writing. This study was supported by the Ad-din Women`s Medical College Hospital. We would also like to thank all the patients who participated in this study.

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