Pregnancy Outcome in Patients with Well Treated Beta-Thalassemia Major

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Abstract

Aim of the Study: To assess maternal and fetal outcome in pregnant patients with Beta-thalassemia major.

Material and Methods: A prospective study of pregnancy outcome of women with beta-thalassemia major admitted to the High Risk Pregnancy Unit, Department of Obstetrics and Gynecology, Kasr Al Aini hospital over the period of March 2010 to October 2013.

Results: A total of 22 pregnant patients with beta-thalassemia major were included in the study. The percentage of cesarean delivery was (81.8%) and VD was (13.6%) and one abortion (4.5%). The percentage of oligohydramnios and intrauterine growth restriction (IUGR) was (31.8%), IUFD (9.1%), preterm delivery (13.6%). There was one case of maternal mortality, postpartum (4.5%) and one neonatal death in the incubator.

Conclusion: Patients with Beta-thalassemia major must have close follow-up during pregnancy to improve maternal and neonatal outcome.

Key Words: Pregnancy outcome – Beta-thalassemia patients.

Introduction

In Egypt, beta (β) thalassemia major represents a major public health problem. The carrier rate varies between 5.5 and 9%; i was estimated that 1000/1.5 million per year live births have β-thalassemia [1]. Modern advances in medical care offered to Thalassaemia Major (TM) patients including therapeutic advances, the availability of oral iron chelators and new non-invasive methods for detection and treatment of iron overload, have improved life quality and prolonged the life expectancy of these patients enabling them to survive into child bearing age [2]. Therefore the reproductive potential and desire to have children by TM patients have gained increased attention [3].

Patients with TM are characterized by severe hemolytic anemia and are dependent on multiple blood transfusions leading to tissue haemosiderosis due to increased iron absorption from the gastrointestinal tract. Iron deposition affects the cardiac, hepatic and endocrine systems. These patients can also have splenomegaly and skeletal deformities due to bone marrow expansion [4].

Despite the progress of iron chelation therapy in patients with thalassemia major, hypogonadotropic hypogonadism remains a common condition. Patients with thalassaemia major who are regularly transfused and well chelated usually have a preserved hypothalamic-pituitary-gonadal axis with normal menstrual cycles and can become pregnant spontaneously. Also patients with primary or secondary amenorrhea and chronic anovulation are able to conceive after gonadotrophin stimulation [5-7].

There is increase in ferritin levels during pregnancy as iron chelation therapy due to its possible teratogenic effects, is stopped once pregnancy happens or being planned and also because of the increased amount of blood transfusions. The prevalence of fetal and maternal complications is reported to be higher in pregnancies complicated by TM. Chronic maternal anemia in these patients may result in fetal hypoxia that can predispose to abortions, intrauterine growth retardation (IUGR) and premature labour, or even may result in intrauterine fetal death [8-10].

All pregnant patients with TM must have a close follow-up during pregnancy by an obstetric and hematology team. The aim of this study is to assess the pregnancy outcome in women with well-treated beta-thalassaemia major patients.
Material and Methods

Our study was a prospective study that included 22 pregnant patients with Beta-Thalassaemia major admitted to the High Risk Pregnancy Unit, Department of Obstetrics and Gynecology, Kasr Al Aini hospital over the period from March 2010 to October 2013.

All patients were diagnosed before pregnancy as TM; they received regular prolonged treatment with blood transfusion and iron chelation therapy since infancy. All pregnancies were managed by both obstetric and hematology team with maternal and fetal outcome being studied. The patients were either admitted to the High Risk Unit or the Hematology department at the initial presentation during pregnancy. All patients were followed through the antenatal period and all the data were recorded. Decision of delivery was taken individually to every patient after obstetric and hematology consultation. Also the co-ordination of a cardiology and neonatology team was needed. Hematologic, cardiac, endocrinologic, and hepatic parameters were initially assessed once the patient was admitted and monitored throughout pregnancy and after delivery. Patients were delivered at High Risk Department. Elective cesarean section was done due obstetric indication as previous cesarean or preterm labour or others.

Inclusion criteria:
- Pregnant patients previously diagnosed as Beta thalassaemia by hemoglobin analysis for thalassaemia by high performance liquid chromatography (HPLC).
- Any gestational age of pregnancy.
- All patients were regularly transfused and well chelated before pregnancy.

Exclusion criteria:
Pregnant patients with other haemoglobinopathies as (sickle cell diseases, beta-thalassaemia minor, haemoglobin E trait, β-trait) were excluded from the study.

During the study period a protocol was designed for follow-up of pregnant thalassaemic women. The patients were followed-up in the obstetric as well as hematology department throughout pregnancy. All maternal demographic and medical data were recorded, including full medical and obstetric history, frequency of blood transfusion, and investigations done. Also a serial clinical examination was done to all patients to assess the severity of pallor, presence of edema, degree of splenomegaly, and if any underlying cardiac dysfunction.

Investigations:

At admission: Complete blood picture, Hemoglobin (Hb) electrophoresis, hemoglobin analysis for thalassaemia by HPLC if needed, liver and kidney functions, with screening for hepatitis B and C virus, fasting and postprandial blood sugar tests, serum ferritin, chest X-ray, ECG and echocardiographically were done to all patients to ensure normal resting left ventricular function. The Hb levels were assessed weekly by complete blood picture, while serum ferritin was repeated every four weeks to avoid iron overload.

Obstetric evaluation:

Serial obstetric examination included weight, blood pressure measurement and ultrasonography for fetal growth, detection of IUGR (growth less than 10th percentile) and maturity assessment were done in all cases. Ultrasound examination was done every 4 weeks in the first trimester, every 2 weeks till 36 weeks. From 36 weeks ultrasound, Doppler and CTG were done weekly till the end of pregnancy (or every 48hrs in cases of IUGR and diminished amniotic fluid till delivery). Close follow-up of the patients was done as most of our patients had bad obstetric history of recurrent abortions or IUFD.

According to the Hematology Department, the regimen for transfusions administration for pregnant patients include either Hb less than 10g/dL or for symptomatic patients. Careful monitoring of vital signs during the transfusion should be done. Also regular evaluation of cardiac function should be done in all pregnant thalassaemic women to prevent fluid overload.

Statistical analysis:

Data are statistically described in terms of range, mean, standard deviation, frequencies and percentages.

Results

A total of 22 pregnant patients with B-thalassaemia major were included in the study and their pregnancy outcome was studied. There was 13 (59.1%) spontaneous pregnancy (patients had normal menstrual cycles and conceived spontaneously) and 7 (31.8%) patients with history of ovarian stimulation by gonadotropins induction (history of secondary amenorrhea or unovulatory cycles), and 2 (9.1%) patients pregnant with ICSI as shown in Table (1).
In this study apart from one patient, the patients did not suffer any major complications in the antenatal period, delivery or postpartum, only 3 of the patients developed mild atonic postpartum hemorrhage. However one patient developed significant cardiac complications in the form of heart failure and was delivered preterm at 32 weeks according to cardiology recommendations.

The age of the patients range from 19-33 years. The mean age of the patients was 25.59±3.29 years. From the 22 patients 4 (18.2%) were primigravidas, 8 (36.3%) were second, and 10 (45.5%) were 3rd gravida onwards.

There were 14 (63.6%) patients with previous history of fetal loss in the form of abortions or intrauterine fetal death in this study. Nine patients (41%) had history of abortions, 2 (9.1%) with IUFD and 3 (13.6%) patients with history of both abortions and IUFD. The range of abortions of the patients in the study was between (1-9) abortions. The number of IUFD of patients was from (1-3) cases. There were 4 patients (18.2%) with history of one fetal loss, and 10 patients (45.5%) had more than one fetal loss as shown in Table (1). There were 2 (9.1%) patients with history of splenectomy before pregnancy.

During the antenatal period 7 (31.8%) patients developed gestational diabetes, 2 of them had history of impaired glucose tolerance before pregnancy, none of the patients developed pre-eclampsia or placental abruption or thromboembolic complication during pregnancy.

Throughout pregnancy Hb levels were measured weekly and regular blood transfusion was received by all patients to maintain Hb level around 10g/dl. The number of transfusions increased as compared to pre-pregnancy time, almost weekly. Hb levels were also measured immediately after delivery. The range of baseline Hb at delivery was from 8.7/dl% to 9.5g/dl%. The mean Hb level at delivery was 9.1±0.29%.

In order to evaluate cardiac function, chest X-ray, ECG and echocardiography was done to all patients included in the study to evaluate cardiac status. Left ventricular hypertrophy was detected in 3 (13.6%), patients and one patient (4.5%) developed heart failure from increased cardiac overload and died in ICU as shown in Table (2).

All patients in the study were delivered at High Risk Department, 18 (81.8%) patients had elective caesarean delivery while 3 (13.6%) hadVD and one SE (4.5%). There was 16 (72.7%) patients who had full term pregnancy (delivered after 37 weeks), whereas 3 patients (13.6%) had preterm delivery. Two (9.1%) patients had sudden IUFD at 29 and 31 weeks despite the close follow-up of patients, there was no IUGR or oligohydraminos in these patients and one patient had missed abortion at 12 weeks with SE done.

There was 19 neonates born as (2 patients had IUFD, delivered stillbirth and one abortion). There were 7 pregnancies with IUGR and decreased amniotic fluid (31.8%) neonates were intrauterine growth retarded (IUGR) as shown in Table (2). They were followed very closely by Doppler and CTG. There were 4 (18.2%) admissions to neonatal ICU. There was one case of neonatal death (4.5%) at the incubator, the baby was born at 34 weeks and the mother had a bad obstetric history of previous nine abortions, but postmortem examination was not done.

After delivery 3 (13.6%) patients had mild aatomic postpartum hemorrhage but they were managed conservatively. There was one case of maternal mortality due cardiac overload and failure, the patient was delivered preterm at 32 weeks, died at ICU 10 days after delivery.

<table>
<thead>
<tr>
<th>Table (2): Complications of pregnancy in β-thalassaemia patients.</th>
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<td>Complication</td>
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<td>IUGR</td>
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<td>Abortion</td>
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<td>Atonic postpartum Hg</td>
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Also regular hepatic screening was done, there was 15 (68.2%) of the 22 patients were hepatitis C positive and all patients were hepatitis B negative as shown in Table (2).
Discussion

This study was designed to evaluate the pregnancy outcome of 22 pregnant patients with β-thalassemia major. All patients included in the study were regularly transfused and well-chelated women. The first successful pregnancy in a woman with thalassemia major was described by Walker in 1969 then followed by many studies reporting other several successful pregnancies [11-13]. Patients with beta thalassaemia often have cardiac, hepatic and endocrine dysfunction because of hypoxia and iron deposition. Hemodynamic changes related to gestation may aggravate the underlying multi-organ damage of the pregnant mother and lead to high fetal wastage [2].

Pregnant thalassaemia patients need additional medical care and close follow-up in addition to the routine antenatal care. Regular blood transfusion is needed to maintain the Haemoglobin levels at 10g/dL, to ensure the best maternal and fetal outcome. Although desferrioxamine therapy is not proved to have any harmful effect on the fetus, the current recommendation is its discontinuation, both once pregnancy is identified and during the induction period [11-13]. Some studies assumed that pregnancy is an efficient chelator of iron due to its haemodilution effect and the fetal consumption of free iron however several studies stated that serum ferritin levels rise by about 10% or less during pregnancy when compared to the pre-pregnancy level [6,7].

There are higher rates of cesarean delivery in all studies investigating pregnancy outcome of patients with β-thalassemia [2,7,14-16]. In this study 81.8% of patients were delivered by elective cesarean section. The obstetric indications include cephalo-pelvic disproportion, oligohydramnios, IUGR, and previous cesarean delivery. Other studies reported that significant spleen enlargement in thalassemic patients may cause cephalo-pelvic disproportion leading to dystocia during labor and cesarean delivery [2,7,8].

In this study the incidence of complications as premature labour was 13.6%, and intrauterine growth retardation (IUGR) was 31.8%. The rates of IUGR and oligohydramnios are found to be higher in the thalassemic patients than in the rest of our population. Chronic maternal anemia during gestation might lead to fetal hypoxia, predisposing the fetus to IUGR. Thus, it was suggested that hemoglobin concentration should be maintained above 10g/dL during pregnancy [7,9,14]. Also we had 2 (9.1%) cases of unexplained IUFD despite the close monitoring of patients.

Cardiac function was not impaired during pregnancy. This can be partly explained by the normal cardiac status before pregnancy. Left ventricular hypertrophy was detected in 3 (13.6%), patients and one patient (4.5%) developed heart failure from increased cardiac overload and died in ICU after delivery. There is always the risk of deterioration cardiac function in pregnant woman with thalassaemia as a result of myocardial haemosidrosis and changes in the hemodynamic state. Accelerated erythropoiesis and expansion of the total red cell volume occur, which consequently increase the cardiac output. This may lead to cardiac failure. In a previous study, there were no clinical or electrocardiographic changes during cardiac examination. It is important for women to start pregnancy with low ferritin levels in order not to have a decrease in their systolic function indices [17].

The management of the pregnant thalassaemia patients during the period of the study was according to a protocol between the hematology department and the high risk unit which included:

- Iron chelation therapy must discontinue once pregnancy is known.
- Maintenance of haemoglobin level at 10g/dL and not below 7g/dL.
- Frequent low volume blood transfusions.
- Regular cardiac monitoring every 3 months.
- Assessment of hematologic, cardiac, hepatic and endocrine function.
- Management of patients by a team of obstetric, hematology, cardiac, neonatologist and endocrinologist if needed.
- Genetic counseling for future pregnancies, partner’s carrier status and fertility.

Conclusion:

Pregnancy in women with thalassaemia major needs close follow-up by a team of obstetric, hematology, cardiology, endocrinology and finally neonatology. The results of our study can be further improved in the future. The course of pregnancy of patients with β-thalassaemia major, including perinatal outcomes can be more favorable, although this conclusion requires confirmation by another study with large number of patients.

References


