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Original Article

Study of Pregnancy Outcome in E-Beta Thalassaemia Mothers

Authors
Maitryaee Bhattacharyaya,
Associate Professor, Dept. of Haematology, NRS Medical College, Kolkata,
Joydeb Roychowdhury,
Associate Professor, Dept. of G&O, NRS Medical college, Kolkata

Address For Correspondence
Joydeb Roychowdhury
Associate Professor,
Dept. Of Gynaecology & Obstetrics,
NRS Medical College,
138, AJC Bose Road,
Kolkata-70014, West Bengal
E-mail: rcjoydeb@gmail.com

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Abstract:
Forty eight E-Beta thalassaemia patients were studied in NRS Medical College, Kolkata, West Bengal during the period from 2000-2006. In all patients Hb% ranged from 5.2g% - 9.6g%. It was more than 8g% in 17 (35.4%), 6-8g % in 22 (45.8%) and less than 6g% in 9(18.7%) patients. 72.9% patients required regular blood transfusion while the rest (27.1%) received blood transfusion occasionally.81.25% pregnancy were carried up to term whereas 18.75% pregnancy ended in preterm delivery. Vaginal delivery was possible in 85.5% patients.14.5% patients had caesarean delivery due to underlying obstetric problem. Amongst the babies born, 22 (45.8%) were intrauterine growth retarded (IUGR) babies,8.3% pregnancies ended in stillbirth. There were 4 (8.3%) maternal deaths in this study.
Key Words: E-Beta thalassaemia, High performance liquid chromatography (HPLC), Intrauterine growth restriction (IUGR)

Introduction:

Thalassaemia, a quantitative defect of globin chain synthesis is the commonest single gene disorder worldwide. Hemoglobin E-β thalassaemia is a double heterozygous state of HbE & β thalassaemia. It is the most common type of thalassaemia in eastern India. Though there are few studies on pregnancy outcome in homozygous Beta thalassaemia, the world wide report on HbE-β thalassaemia patients is very rare.

This study was done to assess the maternal and perinatal outcome of pregnant HbE- β thalassaemia patients.

Materials and Methods:

The study was conducted jointly by the haematology and the obstetrics & gynaecology department of NRS Medical college, Kolkata from January 2000 to December 2006. During this period 48 E-Beta thalasaemia patients with pregnancy were studied.

Inclusion criteria: The patients were diagnosed as E-Beta thalassaemia on the basis of clinical findings, hemoglobin analysis for thalassaemia by High Performance Liquid Chromography (HPLC) and parental studies

Exclusion criteria: The pregnant patients with other haemoglobinopathy like haemoglobin E trait, β-trait, β-thalassaemia major were excluded from the study.

A detailed history about the age at diagnosis, frequency of blood transfusion, chelation therapy, parity, current pregnancy status, past obstetric history were taken. A thorough physical examination was done to assess the severity of pallor, oedema, degree of splenomegaly, underlying cardiac dysfunction. The serial obstetric examination included weight record, blood pressure measurement, symphisio-fundal height for fetal growth assessment, and fetal heart activity. The patients had planned admission and decision for delivery was taken according to the individual merit of the cases.

Investigations: A complete haemogram was done at the time of initial presentation, every month in the first and second trimester and every fortnight in the third trimester of pregnancy. Hemoglobin (Hb) electrophoresis in cellulose acetate membrane, hemoglobin anlysis for thalassaemia by HPLC (Bio-rad β thal short programme), liver function test, serum ferritin (by ELISA), chest X-ray, ECG, echocardiography, ultrasonography for fetal growth & maturity was done in all cases. The patients were followed up in the obstetric as well as hematology department through out pregnancy & perinatal period.

Results:

The HbE-Beta thalassaemia comprised of 0.07% of total number of pregnant mothers attending antenatal clinic during the study period. Age range varies from 20 - 32 years. Thirty three (68.7%) patients were primigravida, 10 (20.8 %) were second, and 5 (10.4%) were 3rd gravid onwards. Eight patients (16.6%) had history of previous fetal loss, five had (10.4%) one and three (6.25%) had more than one fetal loss.

Thirty five (72.9%) patients required regular blood transfusion while the rest thirteen (27.1%) received blood transfusion occasionally in advanced pregnancy, during labour or immediate after delivery. The baseline Hb% ranged from 5.2g% - 9.6g%. Hb% was more than 8g% in 17 (35.4%), 6-8g% in 22 (45.8%) and less than 6g% in 9(18.7%) patients. (Table 1)

Table 1: Comparative analysis of pregnancy outcome in HbE-ß thalassaemia and pregnancy without HbE-ß thalassaemia

Pregnancy outcome	Pregnancy with HbE-ß thalassaemia (n=48)	Pregnancy without HbE-ß thalassaemia n=68040	P value
IUGR	45.8%	14.6%	**<0.001**
IUD	8.3%	3.86%	0.114
Preterm	22.9%	6.3%	**<0.001**
PPH	6.2%	0.78%	**0.006**
CS	14.5%	24%	0.174
Maternal death	8.3%	0.21%	**<0.001**
* p-values calculated by the Fisher Exact Test.			

The serum ferritin was estimated in all patients. In 20 (40.7%) patients the value was less than1000µg/dl. It was 1000-2000µg/dl in 18 (37.4%) and more than 2000µg/dl in 10 (20.9%) patients. Chelation therapy was withheld during pregnancy.

Chest X- ray, ECG and echocardiography was done in all patients to evaluate cardiac status. Left ventricular hypertrophy was detected in 11(22.9%), 7(14.5%) patients had biventricular hypertrophy and 6 (12.5%) had developed overt cardiac failure.

Pregnancy outcome were analysed in all the cases. Thirty nine (81.25%) pregnancy were carried up to term whereas 9(18.75%) pregnancy resulted in preterm delivery. Vaginal delivery was possible in 41(85.5%) patients, 7 (14.5%) patients had caesarean delivery due to underlying obstetric problem. Amongst the babies born, 22(45.8%) were intrauterine growth retarded (IUGR) babies out of which 11(22.9%) were mild, 8(16.6%) were moderate, 3(6.25%) were severe IUGR babies. Four (8.3%) pregnancies ended in stillbirth. Three (6.2%) patients experienced atonic postpartum haemorrhage. All of them could be managed conservatively. There were 4(8.3%) maternal deaths. Three patients died due cardiac failure. One had a sudden death probably due to pulmonary embolism in the postpartum period.

Table 2: Pregnancy outcome and Hemoglobin%

Pregnancy outcome	Hb <6g% n=9	Hb 6-8g% n=22	Hb>8g% n=17	p value
IUGR	4 (44.4%)	14 (63.6%)	4 (23.5%)	0.103
IUD	2 (22.2)	2 (9.09)	0	0.055
Preterm	3 (33.3%)	4 (18.1%)	2 (11.7%)	0.209
PPH	1 (11.1%)	1 (4.55)	1 (5.88%)	0.709
CS	1 (11.1%)	3 (13.6%)	3 (17.6%)	0.632
Maternal death	3 (33.3%)	1 (4.5%)	0	0.011
* p-values calculated by the Concordance Test for Ordinal Categorical Data				

On analysis of pregnancy outcome according to haemoglobin %, it has been observed that out of 9 pregnancy with baseline haemoglobin less than 6gm%, 4 (44.4%) had IUGR babies. Amongst 22 mothers with baseline haemoglobin of 6-8gm%, 14(63.6%) had IUGR babies, in 17 mothers with Hb level >8g%, only 3(17.6%) had IUGR babies. Preterm delivery was 33.3%, 18.1% and 11.7% in mothers with severe, moderate and mild anemia. 22.2% pregnancy amongst the severe anaemia patients had stillborn babies and 9.09% pregnancy had stillbirths amongst the moderate anaemia group. There were no stillbirths in the patients who had haemoglobin >8gm%. Of the 7 caesarean deliveries, one mother had haemoglobin <6g% and 3 each had moderate and mild pallor. Three of the four mothers who expired were severely anaemic.

Pregnancy outcome in E-β thalassaemia were compared with total patients attended antenatal clinic and delivered during this period. The total deliveries were 68040 from January 2000 to December 2006. Incidence of IUGR was 45.8% amongst the study patients, while the overall incidence of IUGR was 14.6% during these years. Percentage of babies delivered pre-term was 22.9% in HbE -b thalassaemia and 6.3% as a whole. Maternal mortality was 8.3% in the study group whereas it is only 0.21% in the control group.

Discussion:

Pregnancy was a rare event in homozygous thalassaemia patients even a few decades back. The women who survived beyond childhood remained mostly infertile because of hypogonadism as a result of iron deposition in the endocrine glands. With adequate blood transfusion and chelation therapy a significant portion of thalassaemia patients attain reproductive maturity and conceive normally. As such, a number of centres have reported encouraging pregnancy outcome but most of them were β thalassaemia major patients.

Fetal loss was a common event, 16.6% had history of fetal loss in the study group. Patients of HbE-b 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. Chronic maternal anemia during gestation might lead to fetal hypoxia, predisposing the fetus to IUGR.[1] Thus it was suggested that Hb% should be maintained above 10g% during pregnancy. Baseline Hb% was > 8g % in 17 (35.4%) patients only. However no significant association was found between Hb level and IUGR in the present study. All studies investigating pregnancy outcome of patients with b thalassaemia have found a higher rates of cesarean delivery.[2,3] But in the present study the incidence of cesarean delivery was found lower compared to patients without thalassaemia. Cephalopelvic disproportion caused by spleen enlargement was suggested as a possible cause for cesarean delivery.[4] Interestingly, though huge splenomegaly was observed in 15(31.2%) patients, vaginal delivery was successfully performed in all of them. We did not find any relation between spleen size and cesarean section. The 7 Caesarean section was indicated for IUGR, fetal distress and antepartum haemorhage.

Conclusions:

The most significant condition in this group of thalassemic syndromes is the Hb E/β thalassemia, which may vary in its clinical severity from as mild as thalassemia intermedia to as severe as β thalassemia major. The interaction between Hb E (a ß- chain variant) and ß- thalassemia (both very common among Southeast Asians) has created the Hb E/ß thalassemia entity, which is now believed to be the most common thalassemia disorder in many regions of the world. Pregnancy complications like adverse effect of anaemia, IUGR, stillborn are also seen frequently and those who can maintain Hb above 8gm/dl till term enjoy best possible pregnancy outcome

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