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MATERNAL AND FOETAL OUTCOME IN β THALASSEMIA TRAIT: A PROSPECTIVE HOSPITAL BASED COHORT STUDY

Obstetrics & Gynaecology

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ABSTRACT

Background And Objective: Thalassemia is an inherited haemoglobinopathy, characterized by abnormal haemoglobin production (β chain of globin). β Thalassemia is one of most common single gene disorder worldwide Patients in this study were evaluated and compared on the basis of maternal and foetal outcomes in both thalassemic and non thalassemic group.

Methods: A hospital based prospective cohort study was conducted in MGMC&H, Jaipur involving 36 β thalassemia trait patients and 100 non β thalassemia trait patients from January 2019 to June 2020.

Results: 50% patients had anaemia with Hb between 7.0- 9.9gm/dL. Incidences of other factors were: Hypertensive disorders (8.33%), Gestational diabetes (2.77%), Polyhydromnios (2.77%), Oligohydromnios (13.88%) and IUGR (8.33%). Labour outcomes were as follows: Eclampsia (2.77%), Abruption (2.77%), Pre-term Labour (8.33%), PROM (8.33%), PPH (11.11%), MSL (2.77%), Foetal Distress (2.77%), NPOL (2.77%) and maternal ICU admissions (5.55%). LSCS (38.89%) was significantly more common in patients with the trait .All these factors were not significantly associated with the trait per se. 94.44% of deliveries resulted in live birth and 91.66% delivered baby of foetal weight between 2-4kg. There was no significant neonatal outcome.

Interpretation: Trait was not associated with any adverse maternal and foetal complication. This was mainly due to the fact β-thalassemia was associated with only mild to moderate anaemia

KEYWORDS

β thalassemia trait, Haemoglobin electrophoresis, Foetal outcomes, Maternal outcomes

INTRODUCTION-

The term "thalassemia" refers to haemoglobinopathies characterized by partly or completely suppressed synthesis of one of the two types of polypeptide chains (α or β) as a result of mis-sense/nonsense mutations (single-base substitutions) or frameshift mutations of the genes controlling the structure of the haemoglobin-protein chains in one or both "allelic" globin genes.

Haemoglobinopathies are the commonest hereditary disorders in India and it poses a major health problem. Beta thalassemia being the most common single gene disorder in our country has a very high incidence of over 30 million people carrying the defective gene.[1] The average incidence of beta thalassemia trait in India is 3.3% with 1-2 per 1,000 couple being at risk of having an affected offspring each year and carrier frequency varies from 3 to 17 % in different populations[2][3].The average prevalence of carriers in pregnant females was 2.78 %. [4]It has been estimated that there are 45 million carriers of β thalassemia in India and about 15,000 infants with homozygous β thalassemia are born every year which constitutes about 10 % of the total thalassemics born in the world. [5]

It also has been estimated in a study that the prevalence of pathological haemoglobinopathies in India is 1.2/1,000 live births, and with approximately 27 million births per year [6][7]. This would suggest the annual birth of 32,400 babies with a serious haemoglobin disorder. Within this overall disease classification a 1989 WHO Working Group on guidelines for the control of haemoglobin disorders estimated a 3.9% carrier frequency for β-thalassemia in India, encompassing all types of β -thalassemia trait [8].

This health burden emphasizes the need for prenatal diagnosis, carrier status detection to contain the disease, genetic counselling and selective termination of affected foetuses. India being located in the thalassemia belt of the world hence has a greater need for prenatal diagnosis.

During pregnancy, women with trait often show more significant anaemia, which is often most prominent during the latter half of the second trimester and early third trimester. The added stress of pregnancy on the hematopoietic system can also cause deterioration of maternal status, even for the patients who were asymptomatic before pregnancy. Due to which both maternal and foetal outcomes worsen. Hence making diagnosis of the trait is even more important. All females with the trait then must be monitored closely for worsening of anaemia and the development of pregnancy-associated complications. There is limited amount of studies available on β thalassemia in pregnancy and even less is the availability of its effect on pregnancy and foetal outcomes. As thalassemia has been not explored much especially in the state of Rajasthan making the study even more crucial in today's age when there are both means and methods to detect, diagnose and treat with minimal complications.

The main objective of the study was to evaluate and compare the maternal and foetal outcomes in pregnant females with β-thalassemia trait with the non-thalassemic pregnant females.

With this background, a hospital-based study was done in MGMC&H, Jaipur, Rajasthan, to study thematernal and foetal outcomes of thalassemia trait in pregnant females.

MATERIALS AND METHOD-

A hospital based prospective cohort study was conducted in MGMC, Jaipur involving 36 β thalassemia trait and 100 non β thalassemia trait pregnant patients from January 2019 to June 2020.

Study Design:

Considering prevalence of 2.78% and taking absolute error as 5%, sample size came out to be 43. Taking attrition and loss to follow up to be 10%, a total of 50 patients with β thalassemia trait were involved in the study during the allotted study period. During the time period a total of 36 patients with the trait were studied. So, a ratio of 1:3 was considered while selecting the cohort meaning that 36 β thalassemia trait patients were compared with 100 normal patients.

Singleton pregnancies with diagnosed β thalassemia trait were included in the study while patients with Hb <6gm/dl, chronic illness, multifetal pregnancies, anaemia due to any other cause were excluded.

Each Patient was subjected to CBC including Red Cell Indices, PBF and haemoglobin electrophoresis. Elevation of Hb A2 (equal or more than 3.5%) demonstrated by electrophoresis and column chromatography confirms the diagnosis of β thalassemia trait. If woman is found to have thalassemia trait, husband's blood sample was taken for haemoglobin electrophoresis. If both parents had the trait then they were subjected to genetic counselling after informed consent. Females with the trait were then followed up to assess the

various outcomes of pregnancy. The outcomes were compared with that of females without the trait. Pregnancy outcomes or complications include hypertensive disorders, gestational diabetes mellitus, heart failure, PROM and preterm labour, Polyhydramnios, oligohydramnios and IUGR in term of birth weight. Labour and perinatal outcome includes-placental abruption, caesarean delivery, meconium-stained amniotic fluid, Apgar score at 1 and 5 minutes less than 7, perinatal mortality, postpartum haemorrhage, maternal packed-cell transfusions, SGA and neonatal ICU admission. The patients were subjected to the study only after due clearance from the ethical committee and proper written and verbal consent from the patients.

Pre designed and pretested Performa were used. Collected data was statistically evaluated using appropriate tests and p value <0.05 was considered significant.

RESULTS AND OBSERVATION-

Majority of the patients in cases (83.33%) belonged to the age group of 19-35 years and had rural background (58.33%). 91.66% were Hindu and belonged to lower SES (52.77%). Most of the patients (77.77%) had a BMI between 18.5-24.9 kg/m^2. Gestational age at the time of deliver was 36-39^{+6} weeks in 72.22% in most of the patients while parity was 47.22% in both para1 and para2-para4 groups. Patient with the trait mostly had moderate anaemia (Hb 7.0-9.9 gm/dl) ie 50% while 44.45% had mild anaemia (Hb 10.0-10.9gm/dl).

Table I - Distribution Of Patients According To Obstetric Risk Factors

		No.	Percentage	No.	Percentage	
1.	HYPERTENSIVE DISORDERS (Gestational Hypertension/ Pre-eclampsia)	3	8.33%	11	11.00%	0.651 (NS)
1.	GESTATIONAL DIABETES	1	2.77%	2	2.00%	0.785 (NS)
1.	POLYHYDROMNIOS	1	2.77%	2	2.00%	0.785 (NS)
1.	OLIGOHYDROMNIOS	5	13.88%	13	13.00%	0.892 (NS)
1.	IUGR (intrauterine growth retardation)	3	8.33%	7	7.00%	0.792 (NS)
2.	PLACENTA PREVIA	0	0	1	1.00%	-
3.	OBSTETRIC CHOLESTASIS	0	0	1	1.00%	-
Total-		36	100.00	100	100.00	

Table II- Distribution Of Patients According To Maternal Outcomes In Labour

		CASES (n=36)		CONTROL (N =100)		P-Value
1.		No.	Percentage	No.	Percentage	
2.	ECLAMPSIA	1	2.77%	2	2.00%	0.785 (NS)
1.	ABRUPTIO	1	2.77%	3	3.00%	0.946 (NS)
1.	PRE-TERM LABOUR	3	8.33%	7	7.00%	0.792 (NS)
1.	PROM (premature rupture of membrane)	3	8.33%	8	8.00%	0.949 (NS)
1.	PPH (post-partum hemorrhage)	4	11.11%	10	10.00%	0.850 (NS)
2.	MECONIUM STAINED LIQUOR (MSL)	1	2.77%	5	5.00%	0.577 (NS)
3.	FETAL DISTRESS	1	2.77%	7	7.00%	0.355 (NS)
4.	NPOL	1	2.77%	2	2.00%	0.785 (NS)
1.	MATERNAL ICU ADMISSIONS	2	5.55%	3	3.00%	0.484 (NS)
1.	CARDIAC FAILURE	0	0%	0	0%	-
2.	MATERNAL DEATH	0	0%	0	0%	-
Total-		36	100.00	100	100.00	

61.11% patients with the trait had vaginal delivery compared to 66% in patients without the trait. 27.77% patient with the trait had elective LSCS and 11.12% landed up in emergency LSCS. This was 7% and 27% respectively in our control group.

Few patients had multiple indications for LSCS but the study only includes the major indication for which it was done. Most common cause for elective LSCS was IUGR in 30% of the patients while bad obstetric history/ precious pregnancies (20%), β thalassemia trait itself (20%) and oligohydromnios (10%) were other prominent cause of elective LSCS. Elective LSCS (Lower segment caesarean section) was also done in cases with associated obstetric risk factor like breech, previous LSCS with short birth interval and in cases where vaginal delivery were contraindicated like CPD. This constituted 20% of the cases. Emergency LSCS was done in 4 patients for meconium stained liquor/ foetal distress, abruption, non progression of labour and eclampsia each. Taking all factors in consideration β thalassemia trait per se was not an independent risk factor. It was the association with other high risk factors that led to LSCS.

Table III- Distribution Of Patients According To Foetal Complications

		CASES (n= 36)		CONTROL (N =100)		P-Value
1.		No.	Percentage	No.	Percentage	
2.	APGAR <7 AT 1 MIN	3	8.33%	12	12.00%	0.547 (NS)
3.	APGAR <7 AT 5 MIN	2	5.55%	5	5.00%	0.892 (NS)
4.	CONGENITAL MALFORMATIONS	1	2.77%	2	2.00%	0.785 (NS)
5.	SGA (small for gestational age)	2	5.55%	4	4.00%	0.696 (NS)
6.	FOETAL BLOOD TRANSFUSION	0	0	0	0	-
7.	NEONATAL MORTALITY	0	0	0	0	-
Total-		36	100.00	100	100.00	

Majority (38.8%) of cases required blood transfusion in their post-partum period to correct anaemia. While, 8.33% needed transfusion in intra-partum period and 5.55% required transfusion in ante-partum period. 94.44% pregnancy resulted in live births. 91.66% delivered a baby with birth weight between 2000-4000gm, while 5.55% were <2000gm and 2.77% had weight >4000gm. 13.88% needed NICU admissions post delivery.

DISCUSSION-

β thalassemia trait in pregnancy may have varied presentation and have unique challenges during its management therefore such patients require close surveillance. Antenatal diagnosis and case has improved many folds and maternal and foetal outcomes are favourable and this forms the basis of our study. Therefore, the following study was carried out to better understand and evaluate the maternal and foetal outcomes in females with β-thalassemia trait.

Eyal sheiner et al in 2004 had similar results in gestational age with max (48.7%) belonging between 36-39 weeks. Similarly in their study 52.1% patient's parity belonged between 2 and 4 and had hemoglobin <10gm/dL. [9] Tharangrut Hanprasertpong et al and Charoenboon et al reported maximum of their cases being nulliparous (60.2% and 57.5% respectively). [10], [11] Sedigheh Amooee et al in their study reported maximum patients of age between 19 and 35 years. [12] They also stated almost equal incidences of pre-eclampsia (4.8%), GDM (3.5%), polyhydromnios (1.4%), Oligohydromnios (10.8%) and PROM (3.9%) but rather higher incidences of IUGR and preterm but both of them were not statistically significant. [12] They attributed chronic maternal anaemia as the main culpable factor. Similar findings were seen in placental abruption (2.3%), meconium stained liquor (5.80%) and ICU admissions (6.6%).[12] Eyal sheiner et al and H. Vafaei et al had higher rates of LSCS in their studies corroborating to the findings in

our study. [9], [13] Anahita Chauhan et al study transfusion rates were 8 patients required blood transfusion antenatally and 11 needed transfusions in peripartum period. [14] Evar Mohammed Saeed Ismael et al reported 98% live birth out of which 14.3% needed NICU admissions. [15] Eyal Sheiner et al findings corroborated with our findings as most of his patients delivered a baby between 2500-4000gm (81.6%) followed by <2,500gm (13.8%) and >4000gm (4.6%). [9]

CONCLUSION-

β thalassemia trait is the most common hemoglobinopathy affecting pregnancy. It may cause variety of effects on mother as well as the foetus. It may range from absence of any clinical disease to severe morbidity and mortality. High degree of suspicion can be made by the obstetrician with a thorough clinical history and examination. Since, it is an inheritable disorder therefore; screening, counselling and prenatal diagnosis becomes an integral part of the antenatal check-up. Pregnancy care should be done with multidisciplinary approach with a strict follow up with haematologist, genetic counsellor along with obstetrician to improve outcomes. The pregnancy outcomes both maternal and foetal do not differ from normal group in general. Females with the trait generally do not require any specific therapy during antenatal period apart from folic acid supplementation. Blood transfusion is only needed when anaemia is severe.

Women who are carrier for β thalassemia trait generally appear healthy, other than a mild anemia and therefore, clinicians often mistake the small RBC of the women with the trait as a sign of iron-deficiency anemia and often incorrectly prescribe iron supplements that have no affect on the anemia. Therefore, not only gets misdiagnosed but also get mistreated.

β thalassemia poses a major health issue and burden on health care and also there is no National Health Program presently to address the issue. Lack of knowledge regarding the disease, screening and prevention of the trait from passing on has lead to an alarming rise in children with the disorder. Until gene therapy becomes easily available and cost effective the only feasible method to treat thalassemia is preventing its inheritance.

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