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"Thalassaemia trait mothers are in risk of development of anemia during pregnancy"-results from a hospital based study in Eastern India

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Abstract

Background: *The thalassaemia syndromes are a heterogeneous group of inherited disorders of hemoglobin synthesis. Most common causes of microcytic and hypochromic anaemia are iron deficiency anaemia and thalassaemia traits.*

Methods: *A longitudinal study was conducted in a tertiary care setup. Every 3rd alternate positive thalassaemia trait mother was selected & age, residence, socio economic status (SES) matched antenatal mothers was taken as control for this study. High performance liquid chromatography (HPLC) was used for screening of various types of hemoglobin variants (HbA0, HbF, HbA2) among the thalassaemia mothers.*

Result: *It has been noted that, differences of mean Hb% are statistically significant in both the groups throughout the pregnancy and the differences have increased as pregnancy advances. 25% of thalassaemic trait mother had microcytic hypochromic anaemia while 15% of normal mother developed the same and the difference is not statistically significant.*

Discussion: *Study did not observe any significant difference in estimated fetal weights in second trimester and third trimester. There was no significant difference observed among the two groups in regards of Apgar scoring, estimated liquor volume, birth weight and mean hemoglobin among new borns. Among thalassaemia traits during stress, like pregnancy refractory microcytic hypochromic anaemia results. During pregnancy, maternal hemoglobin levels may fall to some extent but severe anaemia does not result.*

Conclusion: *Differences of mean Hb% are statistically significant in both the groups throughout the pregnancy and the differences have increased as pregnancy advances Thalassaemia trait does not have any significant influence over estimated fetal weight or liquor volume or perinatal outcome in respect to hemoglobin of baby, birth weight, one minute Apgar score.*

Keywards: *Anemia, Antenatal mother, thalassaemia, perinatal outcome, Hb%*

I. Introduction

The thalassaemia syndromes are a heterogeneous group of inherited disorders of haemoglobin synthesis. It is due to result of the deletion or mutation of one or more of the genes that code for the alpha-globin chains or the beta-globin chains, which causes an imbalance in the rates of globin-chain production. [1] Thalassaemia syndromes were initially believed to be restricted to the populations around the Mediterranean Sea.[1] Now recognized as a global health concern, the thalassaemia syndromes are endemic to the Mediterranean region, the Middle East, India, Southeast Asia, Oceania, and sub-Saharan Africa. Most common causes of microcytic and hypochromic anaemia are iron deficiency anaemia and thalassaemia traits. [2] The thalassaemia syndromes are the most common genetic disorder of humans. Estimates of the number of carriers of hemoglobinopathy may be as many as 270 million people worldwide.[3] In India the frequency of beta thalassaemia trait is reported from <1% to 17% and average of 3.3%[4] . A high frequency of HbD found from North and Punjabi population, HbE in Eastern India and HbS from populations of tribal origin from different parts of country.[5] By virtue of screening programme and antenatal diagnosis, birth rates of homozygous beta thalassaemia in different parts of the world have reduced considerably. Thalassaemia trait is the most common maternal genetic abnormality associated with pregnancy, there is still uncertainty regarding clinical course, complications and management.[6] Both traits are asymptomatic and suspected in a patient with refractory microcytic hypochromic anemia, not responding to iron therapy. Anaemia usually worsens at times of clinical stress, notably infection and commonly pregnancy. Female patient may be diagnosed for the first time during

pregnancy. [7] As assessed by serum estradiol concentration, there is no abnormality of placental function or fetal development, no increase in maternal or fetal morbidity in pregnancy.[7] The objective of the present study is to assess the effect of thalassaemia traits in pregnancy as well as its effect in newborn outcome.

II. Methodology

The study was conducted through one year (May, 2012 to April, 2013) in a tertiary care hospital Kolkata, West Bengal. Out of 1839 new antenatal mothers examined in Gynae OPD during the year, 142 (7.72%) were screened positive for thalassaemia trait. From positive thalassaemia trait, 40 antenatal mothers (every 3rd alternate) who gave consent, were taken as cases and another 40 age, residence , socio economic status (SES) matched antenatal mothers were taken as control for this study. Subjects already having diagnosed anaemia, multiple pregnancies were excluded from the study. High performance liquid chromatography (HPLC) was used for screening of various types of hemoglobin variants (HbA0, HbF, HbA2) among the Thalassaemia mothers. Hemoglobin levels among both the groups were checked at 12week, 20week, 28week, 38week by "sysmax kx 21 machine" and red blood cell (RBC) morphology was checked by expert after doing peripheral smear examination in Clinical Pathology Department of the same institute. Estimated fetal weight and liquor amount of such pregnancies were checked by ultra sonography in Department of Gynae and Obstetrics. Newborn outcomes were measured by taking Apgar score at one minute by attending doctor, birth weight were measured by new born weight measuring scale nearest up to 0.01kg and Hb% of new born babies were estimated by "sysmax kx 21 machine". All the study variables were tabulated in Microsoft Excel 2007 and analysed by SPSS version 16.0

III. Results

The mean age of thalassaemia trait mothers was 27.18 years and that of normal mothers 28.52 years. Table1. Showed parity wise distribution of subjects among thalassaemia traits and non-thalassaemic groups. Table 2. showed distribution of maternal hemoglobin levels at 12 weeks, 20 weeks, 28 weeks and 38 weeks among the two groups. It has been noted that, differences of mean Hb% are statistically significant in both the groups through out the pregnancy and the differences have increased as pregnancy advances. Table 3. showed comparison of RBC morphology in peripheral blood smear between thalassaemia traits and non-thalassaemic groups. 25% of thalassaemic trait mother had microcytic hypochromic anaemia while 15% of normal mother developed the same and the difference is not statistically significant. Table 4. showed comparison between estimated fetal weight (gm) of thalassaemia trait mothers and non-thalassaemic mothers in second (20wk) and third trimester (35wk). Unpaired't' test showed no significant difference in estimated fetal weights in second trimester and third trimester (p=0.861 and 0.353 respectively). Table 5. compares liquor volumes among two groups in first, second and third trimesters. Mann-Whitney U test did not find any statistical significant differences among the two groups. Table 6. compares the birth weights of babies among thalassaemia trait mothers and non-thalassaemic mothers. Mann-Whitney U test shows no significant (p=0.832) influence of thalassaemia traits on birth weight of babies. Mean and standard deviation of Apgar score at 1 minute after delivery among the babies of thalassaemia trait mothers was 8.45(±1.648) and that of non-thalassaemic mothers was 8.75 (±1.581). There is no significant difference observed among the two groups (p=0.409). Mean and standard deviation of Hb% among neonates in thalassaemic and non thalassaemic groups are 15.72 (±1.195) and 15.89 (±1.127) respectively and the difference is not statistically significant (p = 0.533).There were 3 IUGR babies in thalassaemia trait group and no occurrence of IUGR baby in normal group and the difference was statistically non significant (p value 0.241)

IV. Discussion

HbE trait was more frequent according to present study, which supports the result of the study by Nishi Madan et al. The study by Nishi Madan et al found a high frequency of HbD from North and Punjabi population, HbE in eastern India and HbS from populations of tribal origin from different parts of country. [5] There was significant difference in hemoglobin levels between thalassaemia trait mothers in comparison to normal group and pregnant women with thalassaemia trait become more anaemic with advancement of pregnancy. A study by JM White, R Richards, M Byrne, T Buchanan, YS White, G Jelenski[8] in 1985, showed patients with thalassaemia become significantly more anaemic during pregnancy, ($\beta > \alpha$) . RBC morphology studied in peripheral blood smear between thalassaemia traits and non-thalassaemic groups. Fisher exact test failed to find out any effect of thalassaemia trait over RBC morphology on peripheral blood smear (p= 0.402). Melissa Santiago [2] in 2009 mentioned that β thalassaemia trait presented with microcytosis, mild to moderate hypochromia, decreased MCH and MCV and increased RBC count. Both traits were asymptomatic and presented with refractory microcytic hypochromic anaemia, not responding to iron therapy. According to Yeo GS, Tan KH, Liu TC of Maternal Fetal Medicine Department, Kandang Kerbau Hospital, Singapore [9] both β thalassaemia trait and HbE trait were microcytic red cell disorders. However, pregnancy induced macrocytosis

to some extent, MCV rose only 2%. There may be co-existence of iron deficiency anaemia which was very common during pregnancy due to increased demand of growing fetus which may interfere with results. Comparison between estimated fetal weight (gm) of thalassaemia trait mothers and non-thalassaemic mothers in second (20wk) and third trimester (35wk) done by Student's unpaired t test. There was no significant difference in estimated fetal weights in second trimester (p value 0.861) and in third trimester (p value 0.353). In a study by JM White, R Richards, M Byrne, T Buchanan, YS White, G Jelenski[8] , no abnormality of placental function or fetal development was detected with maternal thalassaemia as assessed by serum oestriol concentration and also there seemed to be no increase in fetal morbidity in pregnancy. In a study by Sedigheh Amooee M.D [10] in Iran regarding pregnancy outcome of β thalassaemia minor patients, found no statistical significant difference in the pregnancy outcome, preterm delivery, growth restriction, pregnancy induced hypertension and gestational diabetes between thalassaemic and non thalassaemic patients. Liquor volumes in two groups in first, second and third trimesters were compared by Mann-Whitney U test which showed, thalassaemia trait have no significant influence on liquor volume in any trimester. A study by Sedigheh Amooee1 M.D., Alamtaj Samsami M.D., Jamileh Jahanbakhsh M.D., Mehran Karimi M.D. in Iran, in 2010 [10] showed cases with β-thalassaemia minor had significantly higher prevalence of oligohydramnios ($p<0.001$). This may be due to exaggerated condition of thalassaemia minor than thalassaemia traits.Comparison of Apgar score at 1 minute and hemoglobin levels of babies of thalassaemia trait mothers and non-thalassaemic mothers showed no significant difference in perinatal outcome in regards to Apgar score at 1 minute (p value 0.409) and hemoglobin levels of neonates (p value 0.533). Study by JM White, R Richards, M Byrne, T Buchanan, YS White, G Jelenski[8] in 1985, indirectly proved that there seemed to be no increase in fetal morbidity in pregnancy and as a result perinatal outcome do not vary in thalassaemia trait group compare to normal pregnancies. Almost the same findings were depicted in a recent study by Sedigheh Amooee M.D., Alamtaj Samsami M.D., Jamileh Jahanbakhsh M.D., Mehran Karimi M.D. in Iran [10]. According to that, there was no significant difference ($p=0.65$) in one minute Apgar score in spite of exaggerated condition of thalassaemia minor than thalassaemia trait. Comparison between birth weights of babies of thalassaemia trait mothers against that of non-thalassaemic mothers found no significant difference. Incidence of IUGR was compared between 2 groups by Fisher's exact test. There were 3 IUGR babies in thalassaemia trait group and no occurrence of IUGR baby in control group which was statistically non significant ($p= 0.241$). Anwar H. Nassar et al[11] in Lebanon, found mean birth weight was 2282±589 gm with IUGR complicating 57.1% of cases. This may be due to exaggerated condition of thalassaemia intermedia in that study.

V. Conclusion

Among thalassaemia traits during stress, like pregnancy refractory microcytic hypochromic anaemia occurs. Differences of mean Hb% are statistically significant in both the groups through out the pregnancy and the differences have increased as pregnancy advances.During pregnancy, maternal hemoglobin levels may fall to some extent but severe anaemia does not result. Thalassaemia trait does not have any significant influence over estimated fetal weight or liquor volume or perinatal outcome in respect to hemoglobin of baby, birth weight, one minute Apgar score.

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Tables and Charts

Table 1: Parity wise distribution among thalassaemia trait and normal group (n=80)

Parity	P1+0 N (%)	P2+1 N (%)	P1+1 N (%)	P2+0 N (%)	P3+0 N (%)	P1+2 N (%)	P2+2 N (%)	P1+3 N (%)	Total
Thalasaemia trait	16(40)	5(12.5)	5(12.5)	10(25)	2(50)	2(5)	0(0)	0(0)	40
Normal	22(55)	1(2.5)	2(5)	7(17.5)	3(7.5)	2(5)	2(5)	1(2.5)	40
Total	38	6	7	17	5	4	2	1	80

Table 2: Distribution of maternal hemoglobin (gm/dl) levels among the two groups in different gestational ages (n=80)

Gestational age	Pregnancy with Thalassaemia Hb% (SD)	Normal pregnancy Hb% (SD)	p value
12 weeks	11.75 (±1.348)	10.66 (±1.021)	<0.001
20 weeks	11.38 (±1.232)	10.56 (±1.086)	<0.002
28 weeks	11.52 (±0.984)	10.37 (±0.993)	<0.001
38 weeks	11.31 (±0.808)	10.08 (±0.915)	<0.001

Table 3: Comparison of RBC morphology in peripheral blood smear in both groups (n=80)

Blood smear	Normocytic normochromic	Microcytic hypochromic	Total

	N (%)	N (%)	
Thalassaemia trait	30(75)	10(25)	40
Normal group	34(85)	6(15)	40
Total	64	16	80

Table 4: Estimated fetal weight (gm) in second trimester (20 week) and third trimester (35 week) in both groups (n=80)

Pregnancy trimester	Thalassaemia traits with pregnancy EFW (SD)	Non-thalassaemic mothers EFW (SD)	p value
Second trimester	349.33 (±17.181)	349.93 (±12.998)	0.861
Third trimester	2576.28 (±157.005)	2545.52 (±136.616)	0.353

Table 5: Comparison of liquor volumes in first, second and third trimesters between both groups (n=80)

Pregnancy Trimester	Liquor volume of thalassaemia trait mothers, Mean (±SD)	Liquor volume of Normal mothers, Mean (±SD)	p value
First trimester	101.03(±0.158)	101(±0.00)	0.847
Second trimester	101.08(±0.267)	101.08(±0.267)	1.000
Third trimester	101.13(±0.335)	101.10(±0.304)	0.847

Table 6: Comparison between birth weights of babies of thalassaemia trait mothers against that of non-thalassaemic mothers (n=80)

Birth weight of baby	Mean (SD)	Lower quartile	Upper quartile
B/O thalassaemia trait mother	2693.78 (166.067)	2590	2770
B/O normal mother	2689.40 (167.037)	2560	2759

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