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PROFILE OF PREGNANCY IN THALASSAEMIC PATIENTS AND ITS EFFECTS ON MATERNAL AND PERINATAL OUTCOME – AN OBSERVATIONAL STUDY.

Obstetrics and Gynaecology

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ABSTRACT

The thalassemia syndrome is the commonest genetic blood disorder, clinically divided into three broad groups: thalassemia major, intermedia and minor. Now-a-days, with adequate transfusion and chelation therapy, survival is prolonged into teens and early 20s and few successful pregnancies are possible. But, only a few studies are available on the effects of thalassemia in pregnancy. This study was conducted in the Department of G&O, NRS Medical College, Kolkata with an objective to determine the frequencies of different types of thalassemia in pregnancy, its effects on pregnancy, find out measures to reduce the complications attributable to it during pregnancy, and to improve maternal and perinatal outcome.

KEYWORDS

Pregnancy, Thalassaemic Patients, maternal outcome and perinatal outcome

INTRODUCTION

The thalassemia syndrome is the commonest genetic blood disorders, constituting a vast public health problem. The basic defect is reduced globin chain synthesis. Clinically, thalassemia syndrome is divided into 3 groups: thalassemia major, intermedia and minor. Patients of Thalassemia minor usually have no complaints except mild anemia during pregnancy without splenomegaly. Previously, a child born with homozygous β thalassemia would die in the first few years of life from anemia, congestive cardiac failure and intercurrent infection. But now a day with adequate transfusion and chelation therapy, survival is prolonged into teens and early 20s and few successful pregnancies are possible. Thalassemia intermedia is a clinical designation, often used to characterize individuals who maintain their haemoglobin at 6-9 gm. / dl without regular transfusion. Pregnant patients with thalassemia intermedia may present with moderate to severe anemia requiring transfusion to avoid heart failure. Without transfusion, fetal loss is up to 50% compared with normal fetal loss if Hb% is maintained more thatn 9 gm. % through transfusion. Interaction of thalassemia with other Hb variants like pregnancy with sickle cell β (0) thalassemia usually have history of abortion or stillbirth, on the other hand patients with stckle cell β (+) thalassemia, pregnancy is well tolerated except few complications during last two trimesters in the form of painful crises before or just after delivery. Fetus of pregnant patients with Hb Bart's usually die in utero. Pregnant patients with HbH disease mainly present with anemia (Hb 4-6 gm. %) and some have miscarriages and some require transfusion. Thalassemia aggravates the hypercoagulable state of pregnancy requiring close maintoring during antepartum, interpartum, and post-partum periods.

OBJECTIVES

The study was conducted with an objective to determine the frequencies of different types of thalassemia in pregnancy, its effects on pregnancy, find out measures to reduce the complications attributable to it during pregnancy, and toimprove maternal and perintal outcome.

MATERIALS & METHODS

The study was conducted in the department of G&O, NRS Medical Colege, Kolkata over 2 years. Those with mild anemia, mild jaundice with or without splenomegaly with low or normal Hb%, decreased MCV and MCH were investigated for thalassemia. Cut off value of MCV and MCH were taken as 80fl and 27pg respectively. Further investigation included homoglobin electrophoresis on cellular acetate at alkaline Ph (8.2-8.6) which enabled the provisional indetification of HbS, A, F, S/G/D, A_2/C/E/O Arb, H, lepore and other less common variants. In electrophoresis, if HbF > 2%, and a split HbA_2 band appears – it is useful in differentiating a chain from a β chain variant. Secondary screening also included an estimation of HbA_2 level. An increased HbA_2 >3.7% with hypochromic microcytic red cell is virtually diagnostic of heterozygous β thalassemia. HbA_2 value of < 3.2 is usually considered normal, while those between 3.2 and 3.7 should be interpreted with care. Diagnostic work up included detailed history, clinical examination and laboratory tests. Laboratory tests included complete hemogram (Hb%, Hct, MCV, MCH, MCHC, total RBC count, platelet RBC morphology, reticulocyte count), Coomb's test (selected cases), serum iron, TIBC, serum ferritin, LFT routine examinations of urine, stool, bone marrow study (selected cased) chest x-ray, ECG, echocardiography (selected cases) and USG whole abdomen, including fetoplacental profile.

RESULT

Average age of patients was 22 year (20-32 yrs). Out of 31 patients, 8 (26.6%) were primigravida, 15 (48%) were 2nd gravid, & 8 (25.6%) were multigravida. Among 31 patients 4 (12.8%) had one 1st trime4ster miscarriage 2 (6.4%) had prior more than one 1st trimester miscarriage. 4 patients (12.8%) received regular blood transfusion at an interval of 1.2 months, total > 15 units. 9 patients (28.8) received irregular blood transfusion usually before delivery and in the post-partum period. 7 patients (22.4%) had family history of thalassemia. Out of 31, 17 (54.4%) had mild pallor, 4(12.8%) had modeate, and 10 (32%) had severe pallor. 12 (38.4%) had mild, 8 (25.6%) moderate, while 1 (3.2%) patient had severe jaundice. 10 (32%) mothers had no jaundice. Out of 31, 3 (9.6%) had mild splenomegaly (length< 2 cm below costal margin), 2 (6.4%) had moderate splenomegaly (2-10 cm), 8 (25.6%) had severe splenomegly (>10 cm below costal margin), whereas 18 patients (57.6%) had no splenomegaly. Total RBC count of 31 patients ranged between 2.8 million/ml to 4.4 million / ml with an average of 3.2 million / ml. 3 patients (9.6%) had mild elevation of serum bilirubin (2 β thalassemia trait, 1 HbE trait). 13 patients (41.6%) had moderate elevation of bilirubin (12 E- β thalassemia, 1 sickle β thalassemia). 15 patients had normal bilirubin level (8 HbE trait, 7 β thalassemia trait). Out of 31, 6 patients had cardiomegaly on chest x-ray (5 E β thalassemia, 1 β thalassemia trait) whereas 25 patients had no abnormality (9 HbE traits, 9 β thalasemia trait, 7 E β thalassemia). Out of 31 patients, 12 (38%) had ferritin level < 1000 ng/ml, 10 (32%) patients had ferritin level between 1000-2000 ng/ml, 4 (13%) had ferritin level>2000 ng/ml. 5 patients were unable to do ferritin level.

DISCUSSION

In two studies from Athens, Aessopos[1] (1999) and Daska lakis (1998) and their collegues reported a total 31 pregnancies without severe complication. Kumar[2] and associates (1998) from Manipur, India described 32 women who had successful pregnancies. All of them stressed that underlying cardiomyopathy should be excluded and

intensive surveillance is needed throughout pregnancy. Most of the patients were β-thalassemia major in their study. E hemoglobinopathy is more prevalent in this part of the country, so the patients in our study were mostly having E β thalassemia. In our study out of 31, 12 cases were E β thalassemia, 9 cases HbE trait, 9 cases were β thalassemia trait and 1 case was sickly β^+ thalassemia. Thalassemia minor patients presented only with mild anemia during pregnancy. White et al[3] (1985) and Landman, H[4]. (1988) found that these patients usually maintain Hb% around 10 gm. % and the lowest in 2nd trimester which is between 9.10 gm. %. In our study, thalassemia minor patients usually maintained Hb% >10 gm. % but 5 patients (27.5%) maintained Hb < 10 gm. % due to associated iron and folic acid deficientcy (as indicated by serum ferritin) in this study, out of 31 patients, only 4 patients (12.8%) had mild IUGR, and 7 patients (22.4%) had moderate IUGR, but in the study of Sheiner E, Levy A; Yerushalmi R. Katz M[5], only 4.2% had IUGR. In our study, IUGR noted is much higher than other published data, may be due to associated malnutrition, built, other environmental and genetic influences over the pregnancy. In our study, 4 (12.8%) out of 31 patients had preterm delivery. But in the study of Sheiner E, Levy A; Yerushalmi R. Katz M[5], only 4-6% went into preterm labor. This higher rate of preterm labor in our study may be due to malnutrition, unhygienic condition and associated infections. In this study, thalassemia minor patients usually had mild pallor, and maintained Hb % between 8-10 gm. % and MCV around 80 fl, but Gatto[6], Valentine and Neel[7] study (1942-48) showed MCV < 75 fl. Anemia in thalassemia is usually microcytic and hypochromic. In this stydy, 10 patients (32%) had MCV > 80. Pregnancy itself causes some degree of macrocytoses; increase is usually around 4 fl. This may be the cause of increased MCV in these patients. However, in 1 patients (3.2%), MCV was > 100 fl probably due to associated folate deficiency. In this study, thalassemia minor patients usually had no splenomegaly. Whipple and Bradford[8] (1936) found no splenomegaly in thalassemia minor patients. In β thalassemia minor, normally iron overload is not seen; however in some cases increased iron absorption from gut leading to hemosiderosis have been reported. In this study, ferritin level of β thalassemia minor is leading to hemosiderosis have been reported. In this study, ferritin level of β thalassemia minor is usually maintained < 1000 ng/dl and bilirubin is within normal range that correlated with the published data by Sheiner E, Levy A, Yerushalmi R. Katz M[5] on 2004 (January). In this study, course of pregnancy in patients with thalassemia minor including perinatal outcome is favourable, only 3% had PPH, and 12-13% had preterm delivery, but this is similar to the non-thalassemic patients. Similar results are seen in the study by Sheiner E, Katz M[5], 2004. Here we found that the rate of caesarean section is similar to that of non thalassemic pregnant patients whereas Sheiner E, Levy A, Yerushalmi R Katz Mm[5] 2004 showed that thalassemia minor patients were more likely to have caesarean section than non thalassemic parturient (16.9% vs. 12.2% respectively). But later it was found that thalassemia minor was not found as an independent risk factor for caesarean delivery. In our study, thalassemia minor patients maintained HbF level between 0.7-7% and that corresponds to published data (Wintrobe[9] & Damashek[10], 1940 – HbF maintaine4d between 1-5%). Patients with E β thalassemia usually present with moderate to severe anemia with splenomegaly (moderate to severe). In this study, they maintained their Hb% between 6-8 gm. %. We found that 40% patients required either antenatal, intranatal or post natal blood transfusion. In a multicentric trial by six north-eastern medical institutes in US it was shown that 32% patients required regular and 40% patients needed irregular transfusion. This disparity may be due to the fact that our study contained less number of patients and differences in the socio-economic status, built, environmental factor and availability of blood for transfusion. In our study, patients receivingregular blood transfusion maintained ferritin level > 1500 ng/dl and those who received irregular trandsfusion maintained their ferritin level > 1000 mg/dl. But the multicentric study mentioned earlier showed mean peak fertritin level was 2743 ng/dl nad 70% had ferritin level > 1000 ng/dl. We found that MCV in oursubjects were 70fl. In large Italian study, Mazza et al[11], 1976 found the MCV was < 83 fl in 75% of patients. In our study, E β thalassemia patients usually had moderateto severe splenomegaly in 10(32%) cases, and had raised bilirubin level in 11 (35%) cases, preterm deliveries in 6 (22%) cases, and PPH in 7 (22%) cases. In our study, E β thalassemia patients had moderate tosevere IUGR in 6 (20%) cases which is comparable (21%) with the multicentric study in United Stated. Mode of deliverty is not dependent upon these clinical and biochemical parameter of thalassemia as is evident from both our study and that multicentric study. In this study, we had only 1 patient of sickle β^+ thalassemia who maintained Hb% level 9.2 gm%, MCV>80 fl, HbF 23.9% and ferritin level of 732 ng/dl. She was mild anemic, with mild splenomegaly. She required blood transfusion in antenatal and intranatal periods. She had preterm labor, without PPH. She delivered a baby with moderate IUGR and had no crisis during labour of puerperium. In a study from Jamaica, Serjeant et al[12], 1973 found significant higher incidence of abortion and stillbirth in sickle β^0 thalassemia patients. Also they found painful crisis, before of just after delivery, severe PPH, eclampsia and convulsion secondary to subarachnoid haemorrhage.

CONCLUSION

From this study, we found that thalassemia trait and intermedia patients were fertile and conceived without aid. Pregnancy was uncomplicated in cases of thalassemia trait, and most of them did not require transfusion. E β thalassemia behaves like thalassemia intermedia. And successful pregnancy outcome is possible even with a baseline Hb% of 6-7gm/dl and pregnancy is not complicated with cardiac decompensation in spite of this low Hb value. Incidence of IUGR and preterm delivery is not increased when compared with non-thalassemia pregnancies.

Table 1. Hemogram (% of total number)

Hb%	Level	<7 gm.%	7-10 gm.%	>10gm%
	No. of patients	10 (32%)	12(38.4%)	9 (28.8%)
MCV	Level	<60 fl	60-80 fl	>80 fl
	No. of patients	3 (9.6%)	18(57.65%)	10 (32%)

Range of haemoglobin of these patients was 5.2 gm.& - 11 gm.%, with an average of 8.6 gm%, 10 patients had Hb% < 7 gm%, 12 had 7-10 gm. %, and 9 had > 10 gm. % MCV ranged between 50.8 to 101.4 fl. 3 had < 60fl, 18 patients had 60-80 fl, and 10 had > 80 fl.

Table 2: Hemogram (% of total number)

		Thalassemia minor		E-β Thalassemia	Sicke β+ Thalassemia
		β Thal Trait	Hb E Trait		
Hb (gm. %)					
Hb (gm%)	<7	0	1 (3.2%)	9 (38%)	0
	7-10	7 (22%)	2 (6.4%)	2 (6.4%)	1 (3.2%)
	>10	2 (6.4%)	7 (22.4%)	0	0
MCV (fl)					
MCV (fl)	<60	0	0	3 (9.6%)	0
	60-80	7 (22.4%)	4 (13%)	7 (22.4%)	0
	<80	2 (6.4%)	5 (16%)	1 (3.2%)	1 (3.2%)

Table 3: Clinico-biochemical profile (%of total number)

	Thalassemia minor		E- β thalassemia	Sickle β+ thalassemia
	B thal trait	HbE trait		
Hb % < 8 gm.%	0	1 (3.2%)	10 (32%)	0
Splenomegaly >6 cm	0	0	9 (29%)	0
Hb F	1.1-6.7 (28.8%)	0.7-1.3 (28.8%)	6-43 (35.2%)	23.9 (3.2%)
Transfusion requirement	0	1 (3.2%)	11 (35%)	1 (3.2%)

Out of 31,9 patients (28.8%) had β thalassemia trait, 9 (28.8%) were HbE trait, 12 (38.4%) were E-β thalassemia, 1 (3.2%) was sickle (β+) thalassemia. Amongst 31 patients, range of HbF was 0.7% to 43%. Patient with β thalassemia trait had HbE between 1.1% and 6.7%. those with HbE trait had HbF 0.7% - 1.3%. patients with E-β thalassemia had 6% - 43%, whereas, patients with sickle β+ thalassemia had HbF 23.9%.

Table 4: Pregnancy outcome

		B-Thalassemia trait	HbE trait	E- β Thalassemia	Sickle β+ Thalassemia
Fetal loss	3 (9.6%)	2 (6.4%)		1 (3.2%)	1 (3.2%)
IUGR	Mild	2 (6.4%)	2 (6.4%)	5 (16%)	0
	Moderate	3 (9.6%)	4 (12.8%)	4 (12.8%)	1 (3.2%)
	Severe	0	0	3 (9.6%)	0
Preterm birth		1 (3.2%)	3 (9.6%)	6 (19.2%)	1 (3.2%)
PPH		0	1 (3.2%)	8 (25.6%)	0

Postdated pregnancy	2 (6.4%)	0	0	0
Stillborn	0	0	2 (6.4%)	0

Out of 31 patients, 9 (28.8%) had mild IUGR. 12 (38.4%) patients among 31 had moderate IUGR. 3 (9.6%) had severe IUGR, all belonged to E- β thalassemia group. 7 (22.4%) patients had no IUGR. 18 among 31 patients delivered at term. Out of 18 patients, 7 (38.5%) were HbE trait, 6 (33%) were β thalassemia trait, and rest 5 (27.5%) were E β thalassemia. 11(35.2%) had preterm delivery. Among them, 3 (27.9%) were HbE trait, 1 (9.1%) was β thalassemia trait, and 6 (54.9%) had E β Thalassemia, 1 had sickle β thalassaemia. 2 patient had postdated pregnancy, both were β thalassemia trait. PPH occurred in 9 (28.8%) patients – 8 (88.8%) amongst them were E β thalassemia, 1 (11.1%) was HbE trait.

Table 5: IUGR (moderate to severe)

Patients	Hb %(gm)	Transfusion (unit)	Ferritin (ng/ml)	Type of thalassemia	IUGR	Associated features
1	6.4	2	2100	E β Thal	Severe	Malnutrition+ multiparity
2	6.4	2	1080	E β Thal	Severe	Malnutrition
3	5.8	13	1820	E β Thal	Severe	Malnutrition
4	8.2	3	1350	Hb E Trait	Moderate	Malnutrition
5	9.8	NO	320	Hb E Trait	Moderate	No
6	9.8	No	250	β Thal trait	Moderate	No
7	9.2	2	752	Sickle β+thal	Moderate	No
8	6.9	8	2132	E β Thal	Moderate	Malnutrition
9	9.8	No	356	B Thal trait	Moderate	No
10	5.7	6	825	E β Thal	Moderate	Malnutrition+ short stature
11	9.8	No	526	Hb E Trait	Moderate	No
12	10.2	No	494	Hb E Trait	Moderate	No
13	9.8	No	232	B Thal trait	Moderate	No
14	6.8	4	1650	E β Thal	Moderate	Malnutrition
15	8.4	2	-	E β Thal	Moderate	No

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