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Carrier Screening For Thalassemia And Related Haemoglobinopathies In Antenatal Women In A Tertiary Care Hospital

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Abstract

Background: Thalassemias are an important cause of morbidity and mortality worldwide. Thalassemia is an incurable disease till now and producing thalassemic children only enhances the disease burden both for the society and family. However, severely symptomatic disease can be prevented by education, general public awareness, screening, premarriage counseling and prenatal diagnosis.

Aims: The present study was undertaken with an aim to find the prevalence of carriers of thalassemia and other hemoglobinopathies in pregnant females and their husbands so as to identify the couples at risk of having severely affected children.

Materials and Methods: The study included 585 antenatal patients of anemia detected on routine hematological examination. Serum ferritin levels were performed on study population , and cases with normal or high serum ferritin were analyzed for hemoglobin variants by high-performance liquid chromatography using Bio-Rad D10 hemoglobin testing system-beta thalassemia short program.

Results and Conclusion: 20 of the 585 women screened (3.4%) were identified as carriers of beta thalassemia trait and other hemoglobinopathies. Most of them were beta thalassemia trait 16/20 (80%) followed by HbD 2/20 (10%), HbS 1/20 (5%) and HbE Beta TT 1/20 (5%)

Keywords: Hemoglobinopathies, microcytic hypochromic anemia, thalassemia

Introduction

Thalassemias and related hemoglobinopathies are autosomal recessive conditions affecting the quantity and quality of hemoglobin molecules in red blood cells[1]. It is commonest monogenetic disease worldwide. It is more common in certain ethnic group.[2] It is characterised by a defective formation of hemoglobin chains which leads to severe anemia and requires repeat blood transfusions.[3] it is a major health problem in many Mediterranean countrie, South East Asia, the Middle East and the Indian subcontinent. Homozygous β-thalassemia is usually a severe transfusion dependent disorder from early childhood. Interaction of β-thalassemia with other hemoglobins variants like HbS and HbE can also result in severe manifestation of the disease.[4] Beta thalassemia is the most common single gene disorder in our country. The incidence of thalassemia is very high, with over 30 million people carrying the defective gene. Carrier frequency varies from 3 to 17% in different populations.[5]

Diagnosis of thalassemia is done by the identification of an abnormal hemoglobin or elevated level of HbA2 (≥3.5%) for beta thalassemia carriers and identification of H bodies for alpha thalassemia carries. High performance liquid chromatography (HPLC) is most commonly used method for detection and quantitative estimation of hemoglobin variants.[6]

As India is a vast country ,where over 4000 ethnic groups with diverse cultural background are residing, several communities have not been screened so far and so micro mapping is required at least at district level, to get an accurate estimate of β-thalassemia gene in the population.[7] This severe disorder can be prevented by education, general public awareness, screening, premarriage counseling and prenatal diagnosis.[8] Antenatal screening is the best approach to identify carriers and couple at risk.[9]

We will evaluate the outcome of screening and counseling pregnant women for hemoglobinopathies during their first antenatal visit.This study will provide prevalence of carriers of thalassemia and other hemoglobinopathies in pregnant women and their husbands, so that those couples at high risk of having severely affected children may be identified. The goal would be to prevent the birth of affected individuals; thereby decrease emotional and financial stress and decrease morbidity and mortality.

Material And Methods

Type of study:- An observational study

Study design:-Cross section study

Duration of study:- March 2020 – feburary 2021 or till desired sample size is reached and 2 month for data compilation and statistical analysis.

Place of study:- Department of Obstetrics and Gynaecology, and Advance Haematology and HLA Lab, SMS Medical College, Jaipur

Inclusion criteria

1. Pregnant anemic women (Hb <10.9 gm%) .
2. Women giving written informed consent.

Exclusion criteria

1. Women with iron deficiency anemia
2. History of blood transfusion in past one month
3. Participating in any other study

Methodology:

This observational study was conducted in the Department of Obstetrics and Gynaecology in collaboration with Advance haematology and HLA Lab (Departmemt of Pathology) in SMS Medical College Jaipur from 2020 to 2021.The study included 585 patients with anemia (Hb<10.9gm%) , attending the antenatal clinic of this hospital .

Blood samples were collected in ethylenediaminetetraacetic acid and plain vacutainers from each patient after informed consent . Erythrocyte indices were assessed using Sysmex1000 XT1800i.All cases with microcytosis(MCV<77fl) and hypochromia (MCH<27pg) were tested for serum ferretin levels using MAGLUMI FERRITIN sandwich immunoluminometric Assay kit . Cases with low serum ferritin level (norml value: women-10-200ng/ml) were tested again after a course of iron replacement therapy for 4 week and reassessed for MCV ,MCH , and serum ferritin values . Microcytic hypochromic anemia cases with normal or raised serum ferritin levels were analyzed for hemoglobin variants by HPLC using Bio-Rad D10 hemoglobin testing system , beta thalassemia short program. A diagnosis of beta thalassemia carrier was made when HbA2 is more than or equal to 3.5% . Carriers of other hemoglobinopathies were detected by the presence of the particular abnormal hemoglobin.

Husbands of carriers of thalassemia and related hemoglobinopathies were assessed for haemoglobin variants.Data so collected was statistically analysed .

Result

This cross sectional study, consisted of 585 pregnant anemic women (hb <10.9) women with red cell microcytosis (MCV <77) and hypochromic (MCH <27) and serum ferritin normal (10-200) or higher (>200) value and was designed to pick up possible beta thalassemia traits and case of other hemoglobinopathies by gold standard method HPLC. Their husbands were further screened for disease and couple at risk were identified and counselled.

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Demographic Profile of Women with Hemoglobinopathies

S. No.	Variables			No of Cases	Percentage
1	**Age (year)**	18-28		15	75
		29-38		5	25
		39-48		0	0
		Mean ± SD		26.50 ± 4.17	
2	**Caste**	HINDU	Bramhim	3	15.00
			Kumhar	1	5.00
			Modi	1	5.00
			Panjabi	2	10.00
			Rajput	2	10.00
			Saini	2	10.00
			Scheduled Caste (SC)	5	25.0
		MUSLIM		4	20.00
3	**Residence**	Rural		12	60.00
		Urban		8	40.00

We observed that most of pregnant women with BTT and other hemoglobinopathies were in age group of 18-28 years (75%) followed by 29-38 years (5%) with Mean ± SD of 26.50 ± 4.17. The prevalence of BTT and other hemoglobinopathies was more in rural residents (60%) compared to urban residents (40%). The highest prevalence of BTT and other hemoglobinopathies was observed in Scheduled Caste (SC) 5/20 followed by Muslims 4/20, Brahmin 3/20 and Punjabi, Rajput, Saini each 2/20. Accurate information regarding caste distribution was not possible to elicit. Therefore, an attempt to categorize women according to caste was made more often from family names.

All cases with hemoglobin <10.9 gm% were included in study population (n=585). . Hemoglobin value was less in BTT and other hemoglobinopathy group Mean ± SD 8.57 ± 1.16 compared to normal individual Mean ± SD 9.20 ± 1.45, which is statistically significant. BTT and other hemoglobinopathies cases present with moderate anemia (7.0- 10.0). MCHC value was slightly low in BTT and other hemoglobinopathy group Mean ± SD 31.47 ± 2.69 compared to normal individual group Mean ± SD 31.55 ± 11.85, though not significant. RBC count was slightly higher in BTT and other hemoglobinopathy group Mean ± SD 3.75 ± 0.75 compared to normal individual group Mean ± SD 3.66 ± 0.70, though not significant.

Women with microcytic hypochromic anemia (190) were further followed by serum ferritin level.

Distribution of IFA Deficiency and Hemoglobinopathies in Case with Microcytic Hypochromic Anemia (n=190)

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S. No.	Microcytic Hypochromic Anemia Cause	Number of Cases	Percentage
1.	**IFA Deficiency**	153	80.52
2.	**BTT and Other Hemoglonopathies**	20	10.52
3.	**Other Cause**	17	8.94
	Total	**190**	**100.00**

(IFA – iron folic acid , BTT- Beta thalassemia trait)

Above table show that iron folic acid deficiency is main cause of microcytic hypochromic anemia (80.52%), as it is more prevalent in India mainly in pregnant women. BTT and other hemoglobinopathies account for 10.52% cases of microcytic hypochromic anemia. There were many other cause (8.94%) like Anemia of chronic diseases, Sideroblastic anemia. Of the 190 cases, 37 whose serum ferritin level was normal or rised, were sent for HPLC. A value of more than 3.5% of HbA2 fraction was taken as positive for BTT. A total of 20 cases were found to be BTT and other hemoglobinopathies. In present study mean ± SD of HbA2 is 4.79 ± 0.75 for BTT and 5.02 ± 2.18 for other hemoglobinopathies .

Types of Hemoglobinopathy

S.No.	Hemoglobinopathy	Number of Cases (n=20)	Percentage
1.	**BETA TT**	16	80.00
2	**HBS**	1	5.00
3	**HBD**	2	10.00
4.	**HBE**	0	0.00
5.	**HBE BETATT**	1	5.00

(BETA TT- beta thalassemia trait, HBS -Hemoglobin S, HBD -Hemoglobin D, HBE -Hemoglobin E)

The highest prevalence was observed for beta thalassemia trait 16/20 (80%) followed by HbD 2/20 (10%), HbS 1/20 (5%), HbE Beta TT 1/20 (5%) and no case observed for HbE.

Identification of Couple at Risk

S. No.	Screening Done	Number of Case
1.	**Women with BTT and Other Hemoglobinopathies**	20
2.	**Husbands Screened**	17
3.	**Couple at Risk**	2

Husbands of all women who were found positive (20) for BTT and other hemoglobinopathies, were counseled for screening. Out of 20, 17 patient's husband agreed for screening, and three refused for screening. Out of 17, two patient's husband found positive for BTT.Two couples were found at risk of having children affected with hemoglobinopathies. Both Couples were counseled for molecular diagnosis.

Discussion

Thalassaemia is the most common monogenetic disease worldwide. Antenatal screening is effective and simple, and accurate genetic prenatal diagnosis

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can be achieved in early gestation.[2] Once we find out the prevalence of carriers of thalassemia and other hemoglobinopathies in pregnant women and their husbands, couples at high risk of having severely affected children may be identified. Early diagnosis can facilitate implementation of proper preventive health measures, education of the parents regarding their carrier status, and provide the child with ongoing comprehensive care. The goal would be to prevent the birth of affected individuals; thereby decrease emotional and financial stress and decrease morbidity and mortality.[9]

We observed that most of pregnant women with BTT and other hemoglobinopathies were in age group of 18-28 years (75%) followed by 29-38 years (5%) with Mean ± SD of 26.50 ± 4.17. The prevalence of BTT and other hemoglobinopathies was more in rural residents (60%) compared to urban residents (40%) Present study result comparable to **Chauhan A et al (2018)**[12].. The highest prevalence of BTT and other hemoglobinopathies was observed in Scheduled Caste (SC) 5/20 followed by Muslim (4/20), Brahmin (3/20) and Punjabi, Rajput, Saini each (2/20). **Baxi A et al (2013)**[5] found highest prevlance in Brahmin and Punjabi each with 6/28 and Scheduled caste (SC) 1/28. **Madan N et al (2010)**[10] found highest >5% prevalence in scheduled caste.

We observed that Hemoglobin value in BTT and other hemoglobinopathy group 8.57 ± 1.16 (Mean ± SD),result was similar to the observation by **Sharma A et al (2020)**[11](8.7 ± 2.1). MCHC value in BTT and other hemoglobinopathy group Mean ± SD 31.47 ± 2.69 ,similar result obtained by **Sharma A et al (2020)**[11] (31.2 ± 1.42) **Mehandiratta SL et al (2015)**[3](31.5), **Madan N et al (2010)**[10] (31.7 ± 2.5 in mumbai,32.4 ± 1.9 in delhi). RBC count in BTT and other hemoglobinopathy group Mean ± SD 3.75 ± 0.75,this result was slightly lower than observation by **Sharma A et al (2020)**[11] **(**5.52 ± 0.62),**Mehandiratta SL et al (2015)**[3] (4.6),**Madan N et al (2010)**[10](5.5 ± 0.6 in mumbai, 5.25 ± 0.7 in delhi) as in present study mean RBC Count of study population is below 5 million/ul.

The prevalence of beta thalassemia trait and other hemoglobinopathies was 3.4% in present study. The highest prevalence was observed for Beta thalassemia trait 16/20 (80%). In present study mean ± SD of HbA2 is 4.29 ± 0.75. Finding of present study were comparable with **Sharma A et al (2020)**[11](4.3 ± 1.8), **Madan N et al (2010)**[10](5.21 ± 0.68 in mumbai, 4.6 ± 0.9 in delhi), **Gorakshakar AC et al (2009)**[7](4.99 ± 0.64). The overall prevalence of BTT in India is about 3.3% to 4.05%, however the distribution of β thalassemia gene is not uniform in the Indian sub-continent and therefore has varying frequency in different regions.

Conclusion

The study included 585 patients with microcytic hypochromic anemia, attending the antenatal clinic of this hospital.Majority of women were in the age group of 18-28 year (79.14%) Followed by 29-38 (20.68%), 39-48 (0.17%) respectively with Mean ± SD 25.54 ± 4.08.The highest prevalence of BTT & and other hemoglobinopathies was observed in Scheduled castes 5/20 followed by Muslims 4/20.The prevalence of beta thalassemia trait and other hemoglobinopathies was more in rural residents 12/20 (60%) compared to urban residents 8/20 (40%).Prevalence of BTT & and other hemoglobinopathies was found to be 3.4% in pregnant women with Microcytic hypochromic anemia.Based on auto analyzer readings, the mean Hb was 8.57 ± 1.16 g/dl in BTT and other hemoglobinopathies and 9.20 ± 1.45 g/dl in normal individual. Hence Hb value was low in BTT and other hemoglobinopathies (p-value< 0.001) (S). Mean RBC count was 3.75 ± 0.75 million/uL in BTT & other hemoglobinopathies and 3.66 ± 0.66 million/uL in normal individuals. Hence RBC count was slightly high in BTT and other hemoglobinopathies, (p-value = 0.836) though not significant.Mean MCHC was 31.47 ± 2.69 g/dl in BTT and other hemoglobinopathies as compared to 31.55 ± 11.85 g/dl in normal individuals. Hence MCHC was slightly low in BTT and other hemoglobinopathies, (p-value = 0.212) though not significant.Mean HbA2 was found to be 4.79 ± 0.75 for BTT, and 5.02 ± 2.18 for other hemoglobinopathies on HPLC BIO RAD variant 2 hemoglobin testing system. Hence from this study we found out the prevalence of carriers of thalassemia and other hemoglobinopathies in pregnant women and their husbands, so that those couples at high risk of having severely affected children may be identified. The goal would be to prevent the birth of

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affected individuals; thereby decrease emotional and financial stress and decrease morbidity and mortality.

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