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Screening for Hemoglobinopathies in Pregnant Women of Haroti Region: A Guide for Surveillance, Diagnosis and Prevention

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Abstract: ***Thalassemia is the most common inherited blood disorder in India. Anemia is the major health disease in the world, affecting 24.8% of the world population which corresponds to 1.62 billion people. (1) The average carrier rate of thalassemia in India is 3.3% which differs from 1% to 17 % in different region of country (2). In India the high cost of t/t creates economic burden to the family, therefore screening for the beta - thalassemia is a viable option. With the help of thalassemia screening during the antenatal period followed by prenatal diagnosis, couples "at risk" can avoid having affected children and are spared from months of anxiety awaiting the outcome of pregnancy. (4, 5) The various methods available for mass population screening are red cells indices and Hemoglobin A2 estimation by HPLC (high performance liquid chromatography) (6). Hb A2 estimation is the gold standard for the diagnosis of b - thalassemia trait. Recent studies have used mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) to screen b - thalassemia trait. This study was planned to determine the frequency of carrier status of thalassemia in pregnant females visiting our hospital to identify at risk couples and to prevent birth of new cases of thalassemia major. The study was conducted over 18 months in department of pathology and obstetrics& gynecology, J. K Loan hospital, GMC Kota. Pregnant women in 1st trimester and early second trimester (<16 weeks), who were willing for carrier screening, were screened by hematological indices after an informed consent. Women who attended the antenatal clinics in late second trimester and third trimester or those who did not consent were excluded. In this study, 130 anemic antenatal women are screened for the detection of b - thalassemia, out of which 21 women screened out to be thalassemia trait.***

Keywords: Thallassemia, anemia, screening, women, antenatal

1. Introduction

Thalassemia is the most common inherited blood disorder in India. It is characterized by a defective formation of hemoglobin chains which leads to severe anemia requiring repeated blood transfusions. Anemia is the major health disease in the world, affecting 24.8% of the world population which corresponds to 1.62 billion people. (1)

Almost 10% of all the world's thalassemia patients are born in India every year. The average carrier rate of thalassemia in India is 3.3% which differs from 1% to 17 % in different region of country (2)

Every year, about 800 babies with thalassemia major are born in India. Since thalassemia carrier are clinically normal and healthy, they are ignorant of their carrier status. If both the patients have thalassemia trait as per Mendelian law of Inheritance, there is 25% probability of having a child with thalassemia major, 25% chance of having a normal child and 50% chance of a child with thalassemia trait. In India the high cost of treatment creates economic burden to the family, therefore screening for the beta - thalassemia is a viable option. Pre - marital screening is one of the successful methods to diagnose thalassemia in early age, but premarital screening in a country like India is not possible due to social reasons; so screening antenatal woman is the more feasible and acceptable alternative (3).

With the help of thalassemia screening during the antenatal period followed by prenatal diagnosis, couples "at risk" can avoid having affected children and are spared from months of anxiety awaiting the outcome of pregnancy. (4, 5).

The various methods available for mass population screening are red cells indices andHemoglobin A2 estimation by HPLC (high performance liquid chromatography) (6).

Hb A2 estimation is the gold standard for the diagnosis ofbeta - thalassemiatrait. Recent studies have used mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) to screen b - thalassemia trait. Thementzer index can be used for a thalassemia carrier screening test, is an MCV /RBC ratio calculation in which patients with a value of < 13 is diagnosed as thalassemia carrier while a value of > 13 is found in patients with iron deficiency (7, 8)

The most effective and feasible approach to reduce the Incidence of thalassemia major is implementation of carrier screening program to test the mothers antenatally as early as

8 - 12 weeks of pregnancy, offering genetic counseling, prenatal diagnosis and selective termination of affected fetuses.

This study was planned to determine the frequency of carrier status of thalassemia in pregnant females visiting our hospital to identify at risk couples and to prevent birth of new cases of thalassemia major.

The RDWI (Red cell Distribution width Index) is noble in screening of beta - thalassemia trait (BTT) specially to differentiate it from Iron deficiency anemia. It is calculated as (MCV X RDW / RBC) (9). Its cut off value for screening of BTT< 220.

2. Methods

The study was conducted over 18 months in department of pathology and obstetrics & gynecology, J. K Loan hospital, GMC Kota. Pregnant women in 1st trimester and early second trimester (<16 weeks), who were willing for carrier screening, were screened by hematological indices after an informed consent. The detailed history to ascertain the ethnic descent and any h/o blood transfusion was obtained. Complete blood count was done on automated cell counter (XN - 1000 Sysmex, 6 - part) and hematological parameters were recorded for 130 women. HbA2 estimation was done in female with (D - 10 BioRad). The value of RDWI was calculated from parameter provided by automated analyzer.

Inclusion criteria:

Exclusion criteria: Women who attended the antenatal clinics in late second trimester and third trimester or those who did not consent were excluded. HbA2 estimation was performed using HPLC. The value of HbA2 > 3.5 confirmed the diagnosis of beta thalassemia trait. Out of 130 pregnant women with anemia 21 (16.15%) were diagnosed as beta thalassemia trait.

3. Results

In this study, 130 anemic antenatal women are screened for the detection of b - thalassemia. The Red blood cell indices – MCV, MCH, MCHC, RBC count, Hb, RDW, RDWI and HbA2 of all women were measured to detect b - thalassemia. The mean age of women in the study group was 27 years. The Hb level of women ranged from 6 – 12 g/dl with mean Hb level of 8.8 g/dl. The maximum number of women had Hb range from 8 - 10 gm% in both thalassemia trait (BTT) & non thalassemia trait (non BTTgroups) (Table 1). The maximum number of women had MCV < 70 in BTT (n= 16) and 71 – 85 in non BTT (n=56) The mean MCV (Table2) for women with BTT differed significantly from women without BTT cases.

The mean RBC count for BTT 4.7millions/l (Table 2)

In our study maximum number of BTT case are < 5 million/l

The mean MCV (Table3) for women with BTT differed significantly from women without BTT cases.

Out of total 21 patients of BTT, 13 (61.9 %). Patients have M. I <13: non BTT cases 105 out of 109 patients are >13 (96.3 %) Table 7

Table 8 shows that Hb, MCV, MCH, MCHC and PCV in the BTT cases had lower than in non BTT cases, but higher values of RBC count the value of RDWI.

The husbands of 21 women who were diagnosed as thalassemia trait carrier with HbA2 > 3.5 were also analyzed by HPLC. Only 2 were diagnosed thalassemia trait.

4. Discussion

In the present study thalassemia trait was found to be prevalent among antenatal women with anemia (MCV<70). Both MCV and MCH were significantly low in BTT cases. In India, 3.3 % of population is carrier of thalassemia and 6000–8000 children are born every year with thalassemia major (10, 11).

Anemia is common in antenatal women in Indian population. More than half of the 21 thalassemia trait cases had moderate anemia Hb (8 - 10) and MCV (<70). Similar study was done by Tunkyietal. in South African urban population (12))

In the present study 21 out of 130 (16.1%) antenatal women with anemia were identified to have b - thalassemia trait. b–thalassemia carrier state varies from 1 to 17% with an average of 3.3 % carrier rate in India (13)

In a study by Bhukhanvala et al. (14), in Gujarat, the prevalence of BTT was 3.38 %. In Madhya Pradesh, Baxi et al. (15) reported the rate of BTT as 2.7 % among 1006 pregnant women.

Gosh et al. (16) in their study on the Indian population have also suggested that the typical beta - thalassemia carriers may have a normal MCV and/or MCH sometimes, and these individuals may be missed while screening for betathalassemia. The method of choice for the hemoglobinanalysis is automated cation - exchange HPLC. This gives an accurate estimate of HbA2. The use of HPLC is more appropriate as screening test in all antenatal anemic women in South Asian region where due to associated iron deficiency anemia, the sensitivity and specificity of RBC indices as screening test are low. If the facility for HPLC does not exist, the new cut - off 74 pg for MCV and 28 fl for MCH should be used.

5. Conclusions

This approach will help in appropriate screening and detection of women who are carriers. Spouse testing and counseling of couples at risk will reduce the morbidity and mortality from a potential homozygous offspring. This investigation can be implemented in private and government tertiary care centers, and they can cater samples from primary and secondary health centers.

Table 1: Comparison of Hb values in women with B thalassemia trait (BTT) and without BTT cases of study group

Hb level (g/dl)	BTT (n=21)		Non BTT (n=109)	
	Count N	%	Count N	%
6 - 7	6	28.5	17	15.5
8 - 10	12	57.1	76	69.7
11 - 12	3	14.2	15	13.7
>12	-		1	0.9
Total	21		109	

P= 0.704

Table 2: Comparison of MCV values in women with B Thalassemia trait (BTT) and without BTT cases of study group

MCV (fl)	BTT (n=21)		Non BTT (n=109)	
	Count N	%	Count N	%
<70	16	76.2	28	25.7
71 - 85	3	14.3	56	51.4
>85	2	9.5	24	22.01
Total	21		109	

P=0.261

Table 3: Comparison of RBCs values in women with B thalassemia trait (BTT) and without BTT cases of study group

RBCs count (mill/L)	BTT (n=21)		Non BTT (n=109)	
	Count N	%	Count N	%
<5	17	80.9	108	99
>5	4	19.0	1	0.9
Total	21		109	

P< 0.001

Table 4: Comparison of MCH values in women with B thalassemia trait (BTT) and without BTT cases of study group

MCH (pg)	BTT (n=21)		Non BTT (n=109)	
	Count N	%	Count N	%
<27	19	90.4	82	75.2
28 - 31	2	9.5	20	18.3
>31	-		7	6.4
Total	21		109	

P< 0.001

	Count N	%	Count N	%
<29	19	90.4	82	75.2
30 - 33	2	9.5	20	18.3
>33	-		7	6.4
Total	21		109	

Table 5: Comparison of MCHC values in women with B thalassemia trait (BTT) and without

MCHC (g/dl)	BTT (n=21)	Non BTT (n=109)

BTT cases of study group
P=0.261

Table 6: Comparison of Mentzer index values in women with B thalassemia trait (BTT) and without BTT cases of study group

MI	BTT (n=21)		Non BTT (n=109)	
	Count N	%	Count N	%
<13	13	61.9	4	3.6
>13	8	38.1	105	96.3
Total	21		109	

Table 7: Comparison of RDWI values in women with B thalassemia trait (BTT) and without BTT cases of study group

RDWI= MCVxRDW/RBC	BTT (n=21)		Non BTT (n=109)	
	Count N	%	Count N	%
<220	13	61.9	1	0.9
>220	8	38.1	108	99.1
Total	21		109	

P< 0.001

Table 8: Comparison of mean hematological values in women with B thalassemia trait (BTT) and without BTT cases of study group

Hematological parameters	Mean value in BTT (n=21)	Mean value in non BTT (n=109)	P value
Hb	8.68+/ - 1.25	8.91=/ - 1.21	0.429
RBCs count	4.20+/ - 0.72	3.72+/ - 0.66	0.003
MCV	68.23+/ - 12.14	78.04+/ - 11.47	0.0001
MCH	21.30+/ - 4.56	24.74+/ - 4.21	0.0001
MCHC	31.31+/ - 1.82	31.34+/ - 1.82	0.945
HbA2	5.15+/ - 1.16	2.62+/ - 1.04	0.0001

Disclosures

Compliance with Ethical Standards
Conflict of interest: There is no potential conflict of interest among authors.

Human Participants and Informed Consent:
The research involved human participants. Informed consent was taken before the study.

Ethical Standard:
Ethical clearance was taken before the study

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