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Prevalence of Hemoglobinopathies and Thalassemia Carriers in Women of Reproductive Age Group Especially the Prospective Mothers: A Single Center Study at West Bengal

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Abstract

Background: Hemoglobinopathies are group of diseases characterized by abnormalities both quantitative and qualitative in the production of hemoglobin. In India, major concerned hemoglobinopathic disorders are sickle cell anemia and β-thalassemia. The aim of the study was to prevent the birth of first thalassemic child by screening pregnant women before 17 weeks of gestation and offering prenatal diagnosis if needed and to increase the awareness among general population about prevention of birth of genetically abnormal child.

Methods: Blood samples were tested for complete blood count and hemoglobin electrophoresis.

Results: During the study period, a total of 1,083 women were screened; among them 50 women who carried abnormal pattern (β-thalassemia) were detected. The prevalence of carriers was 4.61%. Apart from β-thalassemia and hemoglobin E carrier (1.10%), two additional variants were encountered.

Conclusion: The data regarding prevalence and distribution can be useful in prevention and management of various hemoglobinopathies.

Keywords: β-thalassemia trait; Pregnancy; Thalassemia; Hemoglobinopathies

Introduction

The genetic disorders of hemoglobin, particularly the β-thalassemias and their interaction with hemoglobin E (HbE) and hemoglobin S (HbS), are a considerable health problem in India and contribute significantly to morbidity and mortality. Identification of these disorders is immensely important epidemiologically and they can be prevented by population screening. Approximately 250 million people constituting 4.5% of the world population carry a potentially pathological hemoglobinopathy gene. Each year about 0.3 million infants are born with a major hemoglobinopathy [1]. Proper identification of various hemoglobin variants including β-thalassemia trait can prevent occurrence of more serious disorders like thalassemia major in newborns [2]. Earlier studies have shown that the overall prevalence of β-thalassemia is 3-4% with an estimate of around 8,000 - 10,000 new births with major disease each year [3, 4]. Thus preventing the birth of affected children is the best option for India. A prerequisite for this is the knowledge of the prevalence of β-thalassemia and other hemoglobinopathies in different regions of the country and in particular in different ethnic groups. In various parts of India, the prevalence of β-thalassemia is different: 6.5% in Punjab, 8.4% in Tamilnadu, 4.3% in south India, and 3.5% in Bengal. β-thalassemia has a high prevalence in some communities, such as Sindhi, Luvana, Tribes, and Rajputs. The incidence of β-thalassemia in Gujarat is 10-15% [5]. In the studies from north India, major groups of thalassemics from Uttar Pradesh (UP) are the migrant ethnic populations of Punjab and Sindh origin [6-10].

The high incidence of β-thalassemia and abnormal HbE in normal populations of Eastern India including the heterogeneous population of Kolkata has already been reported in our previous studies [11-13].

The present study was conducted to evaluate the variety and frequency of various hemoglobinopathies and thalassemia carriers in pregnant women at the state of West Bengal and to prevent the birth of first thalassemic child by screening pregnant women before 17 weeks of gestation.

Materials and Methods

Target population

A total of 1,083 pregnant women attending the prenatal clinic of ILS Hospital, Kolkata were screened during the period of

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Table 1. Distribution of Patients According to Type of Hemoglobinopathies

Hemoglobinopathy	No. of patients
β-thalassemia trait	50
Thalassemia trait HbE	12
HbD Iran	1
HbD Punjab	1

2010 - 1015. Those who referred from other units, pregnant with anemia and those referred with history of one or more thalassemic child were also considered. Pregnant women age ranged from 17 to 45 years. All pregnant women along with their husband were offered counseling for thalassemia. Counseling was done regarding method for screening thalassemia, reason for performing test, including social aspects, and various tests available for prenatal diagnosis. Various medical and ethical issues involved with this were also discussed. A non-directive approach was used when presenting women with various options. Ethical committee approval was taken. Informed consent was taken from all regarding use of screening and further implications.

Blood samples

About 2 - 3 mL intravenous blood samples were collected after obtaining informed consent using ethylene diamine tetra acetic acid (EDTA) as anticoagulants by disposable syringes and needles from each individual free of blood transfusions.

Hematological analysis

The hematology analyzer (Sysmex Corporation, Kobe, Japan) was used to determine peripheral cell count and red blood cell indices using standard procedure.

Hemoglobin electrophoresis

Hemoglobin fractionation was carried out by high performance liquid chromatography (HPLC).

Details about previous pregnancies and family history of thalassemia were enquired. All the women were examined for anemia, hepatosplenomegaly, and other signs of thalassemia. Individuals who were positive were investigated further for diagnosis of β-thalassemia and other abnormal hemoglobin. If woman was found to have thalassemia trait, husband's blood sample was taken for HPLC. Then the couple was subjected to genetic counseling. Couples at risk were counseled about thalassemia disease and given the option of prenatal diagnosis and possibilities were explained. Maternal medical records were reviewed for several demographic and clinical variables. In cases with HbA2 > 3.5%, or with variant hemoglobin, mutation screen was done by amplification refractory mutation system polymerase chain reaction (ARMS-PCR).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were presented as frequencies and percentages. All the analyses were done using IBM SPSS statistics software, version 20.0 and MedCalc software, version 12.3.0.0.

Results

Total pregnant women who accepted screening test were 1,083 while 211 refused. Early acceptability was significantly associated with a higher education level. Common cause for no acceptance was cost for the test and further invasive test if test reports positive.

During the study period out of 1,083 women who underwent screening, 50 patients were found to be having β-thalassemia trait, 12 had HbE carrier and two had other hemoglobin variants (HbD Iran, HbD Punjab) (Table 1). Mean age of the study group was 21.6 ± 8.7 years (Table 2). Out of 50 β-thalassemia trait, 52% were Bengali, 20% were Muslim, and 16% were Marwari (Table 2). Population comprises 4.61% of women with β-thalassemia, 1.10% HbE carrier and 0.18% with other variants hemoglobin. Screening of partner of these 50 women was offered. In 48 out of them it was found normal. Two couple was found to have β-thalassemia trait. So, chorion villus sampling (CVS) was done to exclude thalassemia major. Pregnancy was continued as the result of CVS showed thalassemia trait. The β-thalassemia group showed high mean corpuscular volume (MCV 62.4 ± 4.18 fL) and low (Hb 9.7 ± 1.9 g/L) (Table 3).

Discussion

The sickle cell anemia and thalassemia are the most severe forms of genetic disorders and hence are of great importance to be dealt with from public health point of view in India. These two forms of hemoglobin variants prevalent at higher magnitude pose a great threat to population imbalance. Therefore, these inherited abnormalities of hemoglobin synthesis are the most serious public health problem in central India in particular and in India in general reflecting the genetic heterogeneity of the population. Thalassemia is classified according to globin chain that is deficient. Two major forms involve impaired production or stability of either α or β peptide chains, causing α-thalassemia or of β chains causing β-thalassemia. In β-thalassemia minor hemoglobin A2 (composed of two α and two δ chains) is more than 3.5%. There is usually pregnancy-induced increase of erythropoiesis. There is no specific therapy for β-thalassemia minor during pregnancy. Prophylactic iron and folic acid supplementation are given. Women who are carrier for β-thalassemia minor appear perfectly healthy, other than a mild anemia. However, where two carriers decide a family there is one in four chances that their child could inherit β-thalassemia major, one in four of a child being normal and one in two chance of the child also being a carrier.

Table 2. Distribution of the Study Population (n = 1,083) Depending on Various Demographic Factors

Parameters	All (n = 1,083)	β-thalassemia trait (n = 50)	HbE carrier (n = 12)	Other hemoglobinopathy (n = 2)
Year of study				
2010	102 (9.41%)	8 (16%)	4 (33.33%)	-
2011	157 (14.49%)	11 (22%)	-	-
2012	197 (18.19%)	7 (14%)	1 (8.33%)	-
2013	168 (15.51%)	9 (18%)	1 (8.33%)	1 (50%)
2014	253 (23.34%)	10 (20%)	4 (33.33%)	1 (50%)
2015	206 (19.02%)	5 (10%)	2 (16.66%)	-
Age (years)	21.6 ± 8.7	23.55 ± 9.10	24.7 ± 10.71	20.65 ± 8.4
Caste				
Bengali	714 (65.92%)	26 (52%)	8 (66.66%)	-
Muslim	184 (16.98%)	10 (20%)	2 (16.66%)	-
Marwari	153 (14.12%)	8 (16%)	-	1 (50%)
Punjabi	18 (1.66%)	4 (8%)	-	-
Others	14 (1.29%)	2 (4%)	2 (16.66%)	1 (50%)

A simple blood test often employed called HPLC will tell about the carrier or a trait of thalassemia minor. Hemoglobinopathies are the only genetic disease where it is possible to detect carriers using hematological findings rather than DNA analysis. However, hematological diagnosis is sometimes presumptive, and in these cases, DNA analysis becomes necessary. Complete screening is based on the detection of red cell indices, HbA2, and hemoglobin variant values. In particular, HbA2 determination plays a key role in screening programs for β-thalassemia because a small increase in this fraction is one of the most important markers of β-thalassemia heterozygous carriers [14]. Heterozygous β-thalassemia is usually silent at the clinical level. His phenotype is characterized by microcytosis and hypochromia with increased hemoglobin A2 value. The state of β-thalassemia could be alarming as consanguinity is high and the literacy rate is low. A thalassemia prevention program is the need of the hour in India. The approach to deal with the thalassemic problem is to prevent and control births of the new cases. Emphasis is given on selective screening for β-thalassemia minor in pregnant women who belong to ethnic population having high prevalence for thalassemia. In the present study, β-thalassemia minor was diagnosed.

Colah et al [15] reported that antenatal screening is acceptable in India; however, awareness generation is still a primary requisite. Several programs, with the aim of preventing homozygous β-thalassemia, based on carrier screening and counseling of couples at marriage, preconception or early pregnancy, are operating in several at-risk populations in Mediterranean areas [16].

Reduction of the birth rate of thalassemia major from 1:250 live births to 1:4,000 in Turkey was reported after execution of comprehensive genetic preventive program based on voluntary screening and non-directive counseling [17]. ACOG recommends screening for β-thalassemia in couples of Mediterranean society [18].

While conducting this study our experience was that most of the couples readily agreed for screening and this test can be included as essential test. The most feasible option in our view is to screen the mother prenatally in early pregnancy preferably in the first trimester. In present study as our main aim was to find out prevalence of thalassemia trait, we offered test to all pregnant women who came for prenatal care of their gestational age.

Countries like Pakistan, Iran, Saudi Arabia, and Lebanon which initially practiced only premarital screening to disallow marriage where both partners were carriers have now reinterpreted religion to include prenatal diagnosis and abortion till a particular gestation [19].

Carrier screening by premarital screening followed by prenatal diagnosis and medical termination of pregnancy is acceptable to our communities. This approach is safe without significant marital, social, maternal, and fetal adverse events. Screening program can be made successful in India by increasing awareness not only among population but also among

Table 3. Assessment of Hematological Parameters in Different Groups of Patients

Diagnosis (n = 1,083)	No. of cases (%)	Hb (g/dL)	MCV (fL)	RBC (× 10^6/mm^3)	MCHC (g/dL)	Hematocrit (%)	MCH (pg)
β-thalassemia trait	50 (4.61)	9.7 ± 1.9	62.4 ± 4.18	6.13 ± 1.01	28.2 ± 1.9	34.2 ± 4.8	22.4 ± 3.1
HbE carrier	12 (1.10)	10.8 ± 1.3	75.2 ± 4.9	4.27 ± 0.54	30.9 ± 2.1	37.7 ± 6.1	25.8 ± 2.7
Others carrier	02 (0.18)	11.6 ± 0.9	797 ± 5.0	4.78 ± 0.82	32.1 ± 0.9	38.1 ± 7.4	26.9 ± 2.9

health care professionals so that they can offer screening test on correct time and can improve detection rates.

Conclusion

Universal screening is better in diagnosing woman with hemoglobinopathies. Ideally, this screening should be done pre-conceptionally or as early as possible in the pregnancy. Implementation of a simple carrier screening in pregnancy is practicable in India. Prenatal screening during the first termination was found to be very useful as short term program which includes identification of carriers, prenatal diagnosis for the couples "at risk" and termination of pregnancies if needed to prevent the birth of thalassemic children. β-thalassemia trait and HbE carrier are the most prevalent abnormalities in this region and more screening program should be established to find out these hidden carriers.

Competing Interests

The authors declare that they have no competing interests.

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