Short Communication

Premarital screening of college students for carrier detection in thalassemia and sickle cell disease: need of the hour

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Abstract

Background: Hemoglobinopathies are a group of inherited conditions characterized by quantitative and qualitative abnormalities in the synthesis of hemoglobin. In India, the most prevalent hemoglobinopathies are thalassemia and sickle cell anemia. To reduce the burden of highly prevalent monogenic disorders, it is essential that disease progression be halted at the carrier stage. This can be done by carrier detection and genetic counseling in young individuals. In Central India, where prevalence of thalassemia and sickle cell anemia is high, premarital screening is being implemented for the first time in medical students for identification of asymptomatic carriers of these hemoglobinopathies and possible prevention of future high-risk marriages by genetic counseling.

Objectives: The objectives of this study were to (1) determine the prevalence of asymptomatic carriers of sickle cell disease and thalassemia in first-year MBBS students; and (2) know the frequency of hemoglobinopathy carriers in different ethnic groups of this study group.

Materials and Methods: This study was conducted at a Regional Hemoglobinopathy Detection and Management Centre of a tertiary-care hospital in central India in newly admitted medical students and was approved by the institutional ethics committee. Venous blood samples were analyzed for blood counts and solubility test positivity. Electrophoresis for pattern analysis and high-performance liquid chromatography for confirmation of diagnosis were used on each student. Results were analyzed with the help of statistical analysis.

Results: Overall prevalence of hemoglobinopathies was 10%. β-Thalassemia trait was the most prevalent hemoglobinopathy followed by sickle cell trait. Presence of hemoglobinopathies was seen in varied ethnic groups.

Conclusion: Importance of screening in young asymptomatic individuals is highlighted.

KEY WORDS: Hemoglobinopathies, sickle cell anemia, thalassemia, premarital screening

Introduction

India is an ethnically diverse country with an approximate population of 1.2 billion.[1] Hemoglobinopathies such as sickle cell anemia, thalassemias, and variant hemoglobins together are responsible for the largest number of genetic diseases. These genetic diseases are controlled by a single gene that is transmitted from parents to offspring from one generation to another.[2]

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World Health Organization figures estimate that 7% world population is carrier for hemoglobin disorders, leading to high degree of morbidity and mortality.[3] Thalassemia are a group of congenital anaemia that have defect of one or more of the globin subunits of human hemoglobin due to point mutation.[4] Population screening has identified the prevalence of β-thalassemia carrier state as high as 17% in certain communities in India.[5]

Sickle cell disorder is a group of disease caused by point mutation at sixth position in β globin chain substituting valine for glutamic acid. Shape of erythrocytes changes to sickle cell in deoxygenated state and also the fragility of cell membrane increases.[6]

The prevalence of hemoglobin S (HbS) is 4.3% in India.[7] Sickle cell disease is more common in central and southern parts of the country and is the second most common hemoglobinopathy next to thalassemia. In 1952, Lehman and Catbush[8] were the first to report the presence of the

disease in India among the tribals of Nilgiri hills, and Shukla and Solanki[9] reported the disease for the first time in Vidarbha region of Maharashtra with prevalence ranging from 9.4% to 22.2% in non-tribal population.[6]

Screening programs should aim to identify asymptomatic carriers of hemoglobin disorders in young population to assess the risk of having children with severe form of disease. In countries with high prevalence of hemoglobinopathies, premarital screening programs are essential for the identification and prevention of high-risk marriages.[10,11] With wide ethnic distribution of monogenic hemoglobinopathies, screening programs have to be based on age rather than ethnicity for carrier detection.

Materials and Methods

This study was conducted at a Regional Hemoglobinopathy Detection and Management Centre of a tertiary-care hospital in central India in newly admitted medical students and was approved by the institutional ethics committee.

Demographic data including age and caste were noted of the total 150 students. A detailed clinical history and family history were obtained from each student. History of major systemic illness or recent blood transfusion, if present, was noted. Blood samples (2 cc) anticoagulated in ethylenediaminetetraacetic acid (EDTA) were run in an automated hematology analyzer (Abacus) for counts and red cell indices.

Samples were then run on cellulose acetate electrophoresis at pH 8.9 for pattern analysis and HbA2, HbF, and other hemoglobin variants were quantified by high-performance liquid chromatography using the variant hemoglobin testing system (Bio-Rad Laboratories, Hercules, CA, USA).

A value more than 3.5% of HbA2 was taken as a cutoff point for determining the β-thalassemia trait and a value more than 10% was assumed to be hemoglobin E (HbE).

Statistics

Mean ± 2SD was used as the statistical value.

Results

The study group comprised 150 medical students. Age range of study group was 17–21 years. Among them, 80 were female and 70 were male students with female/male ratio of 1.14:1. None of the students gave positive history of blood transfusion or any major illness in the past. Personal or family history was non-contributory. Hematologic parameters were studied in all students.

On electrophoresis, normal Hb pattern was found in 135 students (90%). Disorders of hemoglobin was found in 10% students. The distribution of different Hemoglobin patterns in the study group is shown in Table 1 (n = 150).

As seen in Table 1, the most common hemoglobin abnormality detected was β-thalassemia trait found in eight students (5.36%) followed by sickle cell trait in five students (3.36%) with other variants such as HbE (heterozygous)and HbD (heterozygous) in one student each (0.67%). The profile of hemoglobinopathies in different ethnic groups is shown in Table 2.

Table 1: Distribution of different hemoglobin patterns

Patterns of hemoglobin	No. of students	Percentage
AA	135	90
β-Thalassemia trait	8	5.36
AS	5	3.36
AE	1	0.67
AD	1	0.67
Total	150	100

AA, Normal Hb pattern; AS, Sickle cell trait; AE, HbD Trait (heterozygous D); AD, HbE Trait (heterozygous E)

High prevalence of β-thalassemia trait was found in Gond caste (50%) followed by Chambhar (33.33%) and Kunbi (10.52%) castes. β-Thalassemia trait was also detected in four students (1.29%) belonging to Brahmin caste. High prevalence of sickle cell trait was seen in Pardhan and Pankya caste students (100%) followed by Halba (16.67%) and Mahar (11.76%) castes.

Hematological parameters of thalassemic and sickle cell trait students were analyzed further [Tables 3 and 4].

Mean values of Hb, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) among students with sickle cell trait were higher than those with β-thalassemia. Red blood cell (RBC) count was higher in students with β-thalassemia minor. Mean RBC of the students with sickle cell trait showed lesser value than that for students with β-thalassemia trait.

Discussion

Hemoglobinopathies constitute the most commonly inherited genetic disorders, the distribution of which varies geographically and by community.[12] High prevalence of these hemoglobinopathies was seen in some parts of central India and in some ethnic groups.

In India, sickle cell anemia and thalassemia are the most common hemoglobinopathies that present with varied clinical features and pose a great threat to population imbalance. These hemoglobinopathies are a serious public health problem in central India, reflecting genetic heterogeneity of population with burden on available medical facilities.[2]

Population-based screening programs for the detection of thalassemia and sickle cell anemia are implemented in this region.

The overall prevalence of hemoglobinopathies that included sickle trait (AS), β-thalassemia trait, HbD (heterozygous), and HbE (heterozygous) was 10%. Jain et al.[5] found the prevalence rate to be 10% in 276 premarital individual.

Table 2: Profile of hemoglobinopathies in different ethnic groups

Community	No	HBAA, *N* (%)	β Thal, *N* (%)	HbAS, *N* (%)	HbAD, *N* (%)	HbAE, *N* (%)
Brahmin	34	29 (83.87)	4 (1.29)	-	1 (3.22)	-
Muslim	8	8	-	-	-	-
Jain	5	5	-	-	-	-
Maheshwari	5	5	-	-	-	-
Rajput	4	4	-	-	-	-
Maratha	3	3	-	-	-	-
Kayastha	2	2	-	-	-	-
Christian	1	1	-	-	-	-
Sindhi	1	1	-	-	-	-
Panchal	1	1	-	-	-	-
Bhamti	2	2	-	-	-	-
NT1	2	2	-	-	-	-
Dhangar	5	5	-	-	-	-
Bhoi	3	3	-	-	-	-
Mahar	17	15 (88.23)	-	2 (11.76)	-	-
Chambhar	3	2 (66.67)	1 (33.33)	-	-	-
Mahadev Koli	1	1	-	-	-	-
Halba	6	5 (83.34)	-	1 (16.67)	-	-
Mana	1	1	-	-	-	-
Wanjari	3	3	-	-	-	-
Teli	7	6 (88.71)	-	-	-	1 (14.28)
Lodhi	1	1	-	-	-	-
Manik	1	1	-	-	-	-
Kushwaha	1	1	-	-	-	-
Sonar	1	1	-	-	-	-
Gond	2	1	1 (50)	-	-	-
Pankya	1	-	-	1 (100)	-	-
Thakur	1	1	-	-	-	-
Kunbi	20	18 (89.47)	2 (10.52)	-	-	-
Gujarati	1	1	-	-	-	-
Kalar	2	2	-	-	-	-
Banjara	2	2	-	-	-	-
Baniya	1	1	-	-	-	-
Sumi	1	1	-	-	-	-
Pardhan	1	-	-	1 (100%)	-	-
Total	150	135 (90)	8 (5.36)	5 (3.36)	1 (0.67)	1 (0.67)

Table 3: Hematological parameters of thalassemia minor students

Hematologic parameters	Mean	SD	Mean ±2SD
Hb (g/dl)	9.6	1.44	9.6 ± 2.88
HCT (%)	31.05	3.79	31.05 ± 7.58
MCV (fl)	58.02	4.89	58.02 ± 9.78
MCH (pg)	17.8	0.91	17.8 ± 1.82
MCHC (g/dl)	30.85	1.58	30.85 ± 3.16
RBC (millions/mm^3)	5.41	1.05	5.41 ± 2.1
RDW	15.95	0.99	15.45 ± 1.98
WBC (per mm^3)	10720	4073	10720 ± 8146
Platelets (lacs/mm^3)	3.225	0.61	3.225 ± 1.22

Hb, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RBC, red blood cell; RDW, red-cell distribution width; WBC, white blood cell

Table 4: Hematological parameters of sickle cell trait (AS) students

Hematological parameters	Mean	SD	Mean ± 2SD
Hb (g/dl)	11.73	1.89	11.73 ± 3.78
HCT (%)	35.2	3.89	35.2 ± 7.78
MCV (fl)	81.06	3.51	81.06 ± 7.02
MCH (pg)	26.83	0.3	26.83 ± 0.6
MCHC (g/dl)	33.16	1.789	33.16 ± 3.578
RBC (millions/mm^3)	4.19	0.5	4.19 ± 1
RDW	14.5	0.6	14.5 ± 1.2
WBC (per mm^3)	6668	5856	6668 ± 11712
Platelets (lacs/mm^3)	3.35	0.31	3.35 ± 0.62

In our study, we found β-thalassemia trait (5.36%) to be the most common hemoglobinopathy. Similar findings were observed by Mondal et al.[13] in their largest study carried out in West Bengal showing the prevalence to be 4.29%. Patel et al.[7] have reported 16.35% prevalence of thalassemia in their study in a district of Gujarat. A study by Bhukhanvala et al.[12], which was conducted in Surat city, found the prevalence to be 3.91%. In present study, the prevalence of sickle cell trait was found to be 3.4%. Urade[2] reported the prevalence of sickle cell trait to be 5.6%. Bhukhanvala et al.[12] found its prevalence to be 2.41%.

We detected four students with β-thalassemia trait belonging to general castes (including Brahmin) not already known. Hb S gene positivity was suggested by presence of sickle cell trait in Mahar and Halba caste. Very high frequency of Hbs gene among Pardhans is seen. All these findings are well correlated with those reported by Urade.[2]

Wide prevalence of thalassemias and hemoglobinopathies has been attributed to migration of people from one region to another and marriages between different communities.[13]

Screening of healthy population is required to determine the carrier rates and gene frequencies in this region.[2] If screening of premarital youths, such as in our study, is carried out on wider bases with vigorous genetic counseling, we can hope to reduce the disease burden in the society.

Conclusion

The need of the hour is to launch student-based mass screening programs for highly prevalent hemoglobinopathies on large scales. By targeting premarital population, detecting carriers by screening college students for hemoglobinopathies, and providing vigorous genetic counseling, we can hope to reduce the prevalence of hemoglobinopathies in coming years.

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