

Present scenario of hemoglobinopathies in West Bengal, India: An analysis of a large population

Abstract

Background: To find out the prevalence of hemoglobinopathies by screening large population in West Bengal from Eastern India. **Materials and Methods:** A total of 50,487 subjects are screened for hemoglobinopathies from June 2010 to August 2013. A 2.5 ml of venous blood samples were collected in the tri-potassium EDTA vacuum container from each subject and tested with automated blood cell counter (Sysmex KX21) for red cell indices. Diagnosis of hemoglobinopathies was done by VARIANT™ (Bio-Rad Laboratories, Hercules, CA, USA) high performance liquid chromatography (HPLC). **Results:** Out of 50,487 cases, 44,620 (88.38%) had normal and 5,867(11.62%) showed abnormal hemoglobin fractions on HPLC. Of these, 5,180(10.26%) were heterozygotes (traits) and 687(1.36%) cases were either homozygotes or compound heterozygote for different types of hemoglobinopathies. The following hemoglobinopathies were present: β -thalassemia trait 6.61%, HbE trait 2.78%, sickle cell trait 0.56%, HbD-Punjab trait 0.21%, β -thalassemia major 0.73%, HbEE 0.05%, compound heterozygosity for HbE- β -thalassemia 0.42%, and HbS- β -thalassemia 0.15%. **Conclusion:** Among the hemoglobinopathies, β -thalassemia trait (6.61%) and HbE trait (2.78%) are prevalent in rural Bengal.

Key words: Hemoglobinopathies, HPLC, prevalence, West Bengal

Prakas Kumar Mandal,
Suman Kumar Maji¹,
Tuphan Kanti Dolai

Department of Hematology,
N.R.S. Medical College
and Hospital, Kolkata,
¹Department of Microbiology,
Vidyasagar University,
West Midnapore - 721 101,
West Bengal, India

Address for the Correspondence:

Dr. Prakas Kumar Mandal,
8c/1/N, Roy Para Road, First
Floor, Kolkata - 700 050, India.
E-mail:prakas70@gmail.com

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INTRODUCTION

Thalassemia and other hemoglobinopathies are genetic disorders of hemoglobin, which can be prevented by population screening and offering genetic counseling. In India it is estimated that there are over 25 million carriers of this disease.^[1] Beta-thalassemia (β -thalassemia), sickle cell anemia, E-beta thalassemia and hemoglobin D Punjab are the common hemoglobinopathies in the world including India. About 4.5% of world population is affected by hemoglobinopathies.^[2] The estimated prevalence of thalassemia in India is 3-8%.^[3] In a recent study, the carrier rate in rural West Bengal is shown to be around 16.23% in general population.^[4] It was recorded that yearly 10,000 children with β -thalassemia major are born in India which comprise 10% of the total number in the World.^[5] Another report has revealed that 7,500-12,000 babies would be born with β -thalassemia major in India each year.^[6] When different Hb variants are in heterozygous state, they can interact with others and may lead to serious homozygous or compound heterozygous Hb variants in the offspring. Double or compound heterozygous states between certain variants can lead to clinical manifestations. During the last few years a group of hematologists and geneticists including professional technical staff of the many countries endow with efforts for prevention and control of thalassemia to increase their good practice in the control and management of thalassemia in Asia for providing a central forum, interacting with governments and international health agencies to give support for this objective. The present work was carried out to evaluate the prevalence of β -thalassemia, HbS, HbD, HbE by generating awareness and successful screening programme for carrier detection which is important to identify asymptomatic carriers who have an increased risk of having a child with thalassemia. There is no sufficient data from rural Bengal from Eastern India. This will be the first epidemiological study on a vast population from rural Bengal.

MATERIALS AND METHODS

Thalassaemia Society of Midnapore District conducted this pilot study from June 2010 to August 2013. A total of 50,487 cases were subjected to study from different districts of rural areas of West Bengal by arranging camps and awareness programmes in the villages. The society served their services in schools, colleges and university also for screening of individuals for detection of different hemoglobinopathies. The technical staffs collected 2.5 ml of venous blood in the tri-potassium EDTA vacuum container from each subject. They were informed and written consent was collected in the presence of health personnel and community leaders. Collected samples were transported under cool conditions to the laboratory within 3-6 hrs of collection.

The blood samples were tested by automated blood cell counter (Sysmex KX21; Sysmex Corporation, Kobe, Japan) for red cell indices. Peripheral blood smear examination, red cell indices and other parameters are also considered for diagnosis of hemoglobinopathies. Diagnosis of hemoglobinopathies was done by VARIANT™ (Bio-Rad Laboratories, Hercules, CA, USA) high performance liquid chromatography (HPLC). HbA2 value of 3.3% to 3.8% was considered as borderline and a cut-off of over 3.9% was taken for diagnosis of β -thalassaemia trait.^[4,7-9] In very few cases, which were not interpreted by HPLC, were confirmed by amplification refractory mutation system, polymerase chain reaction (PCR-ARMS) technique.^[10]

RESULTS

A total 50,487 cases were studied. Of these, 44,620 (88.38%) had normal and 5,867 (11.62%) showed abnormal hemoglobin fractions on HPLC. The distributions of different traits and hemoglobinopathies are shown in Tables 1 and 2. After analysis, 5,180 cases (10.26%) were detected as carriers and 687 (1.36%) cases were either homozygotes or compound heterozygote for different kinds of hemoglobinopathies. Out of 5180 cases of traits; 5,132 cases had shown β -thalassaemia trait, 6.61%, HbE trait, 2.78%, sickle cell trait, 0.56%, HbD-Punjab trait, 0.21%. Thirty four cases (0.07%) had shown hereditary persistence of fetal hemoglobin (HPFH) traits and 14 cases (0.03%) had shown other rare hemoglobin variants which included 6 cases of Hb-Lepore trait. Amongst the homozygotes or compound heterozygotes, the distribution of cases was as follows: β -thalassaemia major (368 cases) 0.73%, HbEE (26 cases) 0.05% and compound heterozygosity for HbE- β -thalassaemia (213 cases) and HbS- β -thalassaemia (75 cases) were 0.42% and 0.15% respectively.

DISCUSSION

Hemoglobinopathies are a major health problem all over the world including India and Southeast Asian region.^[11] In the present study, out of 50,487 cases, 44,620 (88.38%) had normal and 5867 (11.62%) showed abnormal hemoglobin fractions on HPLC. In a recent study from Western India, out of 7261 cases, 1615 (22.24%) cases showed

Table 1: Distribution of different heterozygotes (traits) in the present study (n = 50,487)

Type	Number	Percentage
Beta trait	3339	6.61
E trait	1403	2.78
S trait	284	0.56
D trait	106	0.21
HPFH	34	0.07
Others	14	0.03
Total	5180	10.26

Table 2: Distribution of different homozygotes or compound heterozygotes in the present study (n = 50,487)

Types	Number	Percentage
β -thalassaemia major	368	0.73
HbE- β -thalassaemia	213	0.42
Hb E disease	26	0.05
HbD-Punjab disease	05	0.01
HbS- β -thalassaemia	75	0.15
Total	687	1.36

abnormal Hb fractions.^[12] Higher cases of abnormal hemoglobin fractions on HPLC from referral center in Western India probably does not reflect population-based data as shown in the present study with much lower overall prevalence, done in a rural population from Eastern India.

The largest screening programme for thalassaemia using the HPLC system in the population has been carried out in Gujarat, India by the Indian Red Cross Society in Ahmedabad and other cities. From 2004 to 2010, they screened 370,117 subjects for carrier status, among whom there were 173,112 students, 45,000 youths and 8,377 pregnant women. Carrier rate has varied from 4.3% to 5.0%.^[13]

In the present study, the prevalence of β -thalassaemia trait was 6.61% making this the major hemoglobinopathy in West Bengal, India. The high prevalence rate of β -thalassaemia trait is found in more than 60 countries with carrier population up to 150 million.^[11] The distribution of the β -thalassaemia gene is not uniform in Indian subcontinent.^[1,3] The prevalence of β -thalassaemia trait varies from 1% to 17% in different populations of India as revealed by many studies from India.^[14-16] The prevalence of β -thalassaemia trait was 5.5% in northern India, 2.7% in western India and the overall frequency was 4.05%.^[6] Another tertiary center study from western India reported incidence of β -thalassaemia trait was 11.55%.^[14] A study on college, university students and pregnant women from different cities of eastern India (Kolkata, West Bengal), north east India (Dibrugarh, Assam) and southern India (Bangalore, Karnataka) showed prevalence of β -thalassaemia carriers was 3.64%, 1.48% and 2.16%, respectively.^[17] Another study with 1726 cases on hemoglobinopathies in tribal population of Eastern and North-eastern India, including 463 cases from West Bengal showed the prevalence of β -thalassaemia carrier of 5.18%.^[18]

Worldwide, hemoglobin E thalassemia is one of the most important varieties of hemoglobinopathy.^[11] There were 1403 cases of HbE trait leading to a prevalence of 2.78% in the study population. Since its classic description by Chernoff *et al.*,^[19] it has been noted to be an important public health problem in the Indian subcontinent and Southeast Asia. In a recently published report of multicenter study conducted by the Indian Council of Medical Research including Kolkata in West Bengal in the east, Dibrugarh in Assam in the north east amongst six cities included in the study, done in tertiary care centers covering mostly city based population showed the prevalence of HbE trait as 3.92% in Kolkata and 23.90% in Dibrugarh;^[17] whereas the prevalence of HbE trait (2.78%) found in the present study conducted in rural areas was lower than the earlier study. The difference in prevalence of HbE trait between the two studies reflects the population heterogeneity in the studies.

A total of 248 cases (0.56%) of sickle cell trait were detected in the present study. Earlier studies by Mohanty *et al.*^[17] have shown a prevalence of 0.14% and 0.13% from Kolkata and Dibrugarh respectively. Recent published study from Kolkata showed only 39 cases (0.276%) of sickle cell trait amongst 14, 145 cases included in the study.^[20]

The prevalence of HbD-Punjab trait was 0.21% in the present study. Hemoglobin D (Hb D) was discovered in a family of mixed British and American-Indian origin from the Los Angeles area.^[21] Earlier studies from West Bengal by Mohanty *et al.*^[17] and Dolai *et al.*^[4] showed a prevalence of HbD-Punjab trait of 0.2% and 0.37%, respectively. Though mostly reported from Punjab and other northern states of India,^[6] the present study had shown the homozygous and heterozygous states of HbD-Punjab in 0.01% and 0.21% of cases in West Bengal.

Among the other less common variants found in the present study were 34 cases (0.07%) of HPFH traits and 14 cases (0.03%) of rare hemoglobin variants including 6 cases of Hb-Lepore trait. There are few studies on HPFH in India. Only a few cases have been reported from western India and Kolkata.^[22,23] Rao *et al.*,^[24] in a study of 800 samples, from north India reported one case each of Hb Lepore trait and HPFH trait. In a recent study from Kolkata, West Bengal, there was only one case of Hb Lepore trait and no HPFH reported.^[20]

β -thalassemia major was detected in 368 cases (0.73%) constituting majority in the group of homozygous thalassemia followed by 213 cases (0.42%) and 75 cases (0.15%) of HbE- β -thalassemia and HbS- β -thalassemia, respectively. The first case of HbE disease in India was reported by Chatterjee *et al.*^[25] Because of the extremely high frequency of HbE trait within the Indian subcontinent, it is very common for individuals in this region to inherit both hemoglobin E and β -thalassemia. Data collected over recent years indicate that HbE- β -thalassemia is causing an increasingly severe public health problem throughout the Indian subcontinent and parts of Southeast Asia.^[26] Among ethnic groups in which prevalence of HbE and β -thalassemia are known, there is a vast discrepancy between the reported number of cases of

HbE/ β -thalassemia and the number predicted by Hardy-Weinberg law.^[27] The first case of β -thalassemia/sickle cell disease in India was reported by Naik and colleagues.^[28] Though, a high prevalence of sickle cell trait (29.8%) is reported from Orissa,^[29] only a small number of cases (heterozygous, 0.56%) are observed in the present study giving rise to small number of compound heterozygotes (HbS- β -thalassemia, 0.15%) where β -thalassemia trait showed the highest prevalence of 6.61%.

Due to socio-cultural practices, marriages in India are usually among individuals of the same caste or ethnic group and this makes it important to know the prevalence of β -thalassemia and also HbE in different ethnic groups.^[17] Weatherall^[30] suggested that more detailed information on frequency and economic data is required to provide evidence for the health burden posed by thalassemias in the developing world. The programme of prevention through carrier screening and prenatal diagnosis should receive the highest priority in the future, in order to reduce drastically the birth of affected children.^[31] Diseases which are known to run in families and have high-risk of recurrence become a social stigma when nothing or very little is known about them. Illiterate populations are ignorant about the medical, social and financial burden of the disease. This further compounds the problem.^[1]

The present study conducted in large rural population in West Bengal arguably reflects the different types of hemoglobinopathies prevalent in eastern part of the country.

CONCLUSION

β -thalassemia is the most common hemoglobinopathy in rural Bengal followed by HbE. The heterogeneous population is harboring almost all major hemoglobinopathies. The prevention and control of hemoglobinopathies in the state is an uphill task for the planners, policy makers, medical and health care providers. This study, done in a large population, provides a comprehensive database on the spectrum of hemoglobinopathies in West Bengal.

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