

Original Research Article

Pattern of hemoglobinopathies and thalassemia in Manipur, India

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ABSTRACT

Background: Hemoglobinopathies are the commonest genetic disorders worldwide. Thalassemia Major, Thalassemia Intermedia and Sickle Cell Disease are the major disorders that require lifelong management and are to be considered for prevention. In India, Beta-Thalassemia is prevalent across the country, with an average frequency of carriers being 3-4%.

Methods: This is a cross sectional study conducted between June 2016 - May 2017 in the Department of Medicine, RIMS Imphal in 453 patients as a workup for anemia and clinically suspected cases of Hemoglobinopathy or beta thalassemia. Blood samples were collected and sent for Haemoglobin Electrophoresis using cellulose alkaline technique.

Results: Among the 453 cases of the population surveyed, 35% showed the presence of abnormal hemoglobin. 16% were found to be beta thalassemia carrier, 11.69% HbE trait, 6.62% Homozygous HbE, 0.4% beta thalassemia and 0.7% had Hereditary persistence of HbF.

Conclusions: High prevalence of Beta Thalassemia trait occurred more frequently than other Hemoglobinopathies. The study concludes that it is immensely important epidemiologically to explore the haemoglobin variants in Manipur so that the carriers can be detected for prevention of more serious disorder in the future generations.

Keywords: Beta-Thalassemia, Haemoglobinopathies, Hemoglobin electrophoresis, Hereditary persistence of HbF

INTRODUCTION

Hemoglobinopathies are the most common genetic disorders reported in the World.^{1,2} WHO figures estimate that 5% of the world population is a carrier for hemoglobinopathies.³ The frequency of β -thalassemia in India ranges from 3.5% to 15%, in general, population.⁴ A higher frequency has been observed in certain communities, such as Sindhis, Punjabis, Gujaratis, Bengalis, Mahars, Kolis, Saraswats, Lohanas and Gaur.^{5,6} HbS is highly prevalent in the tribal populations of Southern, Central and Western states reaching as high as 48% in some communities. HbE is common in the North Eastern states, and has a carrier frequency as high

as 50%, in some areas. It is found in lower frequencies in the Eastern states of West Bengal, Bihar and Uttar Pradesh, while HbD is present in about 2% of people in Punjab.⁷ Three types of Hemoglobin are present in a normal individual-HbA, HbF (Fetal Hemoglobin), and HbA2.

At birth HbF is the predominant hemoglobin comprising approximately 80% of total hemoglobin and slowly reduces with rise in HbA. The HbA makes up the major component, comprising 96-98% of the total hemoglobin in an adult. Adult levels of all hemoglobin's are reached by approximately one year of age and finally stabilize by two years of age.

Hemoglobinopathies may be either qualitative or quantitative defects of hemoglobin. The major hemoglobinopathies consist of thalassemia (mainly α and β thalassemia) and variant hemoglobin's (HbS, HbE, HbD Punjab etc.). In India, the major symptomatic hemoglobinopathy disorders are β (beta) thalassemia and Sickle Cell Anemia. They result in clinical syndromes known as Thalassemia Major (TM), Thalassemia Intermedia (TI) and Sickle Cell Disease (SCD). The prevalence of haemoglobinopathies varies with the geographic location and ethnic groups. Among the common Hb variants HbE and β thalassemia are commonly found in the North Eastern states of India i.e Assam, Arunachal Pradesh, Nagaland, Manipur, Tripura and Meghalaya and the average allele frequency of HbE in north east region is 10.90%.^{6,8} Hemoglobin electrophoresis is a blood test that can detect different types of haemoglobin based on the principle of gel electrophoresis.⁹

METHODS

A cross sectional study was conducted for a period of one year from June 2016 to May 2017 in the Department of Medicine, Regional Institute of Medical Sciences, Imphal. A total of 453 patients attending Medicine OPD or admitted in Medicine ward with microcytic hypochromic anemia (MCV <80 fl, MCH <27 pg) and a clinically suspicion of hemoglobinopathy were included in the present study. Patients with recent blood transfusion (<3 months) were excluded. From each patient 8ml of blood was collected in EDTA tubes for complete haemogram and electrophoresis and was run in Sysmex autoanalyzer for hemogram and red cell indices.

Hb electrophoresis uses an electric current to separate normal and abnormal types of haemoglobin with different charges and moving at different speeds. Cellulose alkaline Hb Electrophoresis of Genios Company was used for the study. At alkaline pH haemoglobin is a negatively charged protein and when subjected to electrophoresis will migrate towards anode. Structural variants of haemoglobin that have a charge on the surface of the molecule at alkaline pH will separate from HbA.

The value of HbA2 in beta -thalassemia trait ranges between 3.5 to 9%. For diagnosing beta-thalassemia major, hemoglobin F (HbF) values of 30% to 90% or more of the total haemoglobin were considered. For diagnosing delta/beta thalassemia the HbF concentration considered was 5-15% of the total Hb value.

RESULTS

A total of 453 cases were included in the present study. Out of which 125 were male and 328 females. The age group ranged from 1 to 80 years. 160(35%) cases were found to have abnormal haemoglobin on Haemoglobin Electrophoresis and out of 160 cases, 45 were male and 115 were female with a female to male ratio of 2.5:1. The

most prevalent age group was 21-30 years (Table 1). The pattern of haemoglobin distribution is shown in (Table 2) with 198(43.7%) having severe anemia and 25.38% having a haemoglobin of >10gm.

Table 1: Age distribution.

Age group	No. of cases	Percentage (%)
11-20	74	16.33%
21-30	125	28%
31-40	116	26%
41-50	70	15.45%
51-60	33	7.28%
61-70	19	4.19%
71-80	16	3.53%
Total	453	100%

Table 2: Haemoglobin level among study population.

Haemoglobin(g m%)	No. of patients	Percentage (%)
<7	198	43.7%
7-10	140	30.9%
>10	115	25.38%
Total	453	100%

In this study, 16% had beta thalassemia trait, 11.69% had HbE trait, 6.62% had HbE thalassemia and 0.7% had Hereditary persistence of HbF (HPHF). In all these haemoglobinopathies the prevalence amongst female was found to be more than male (Figure 1).

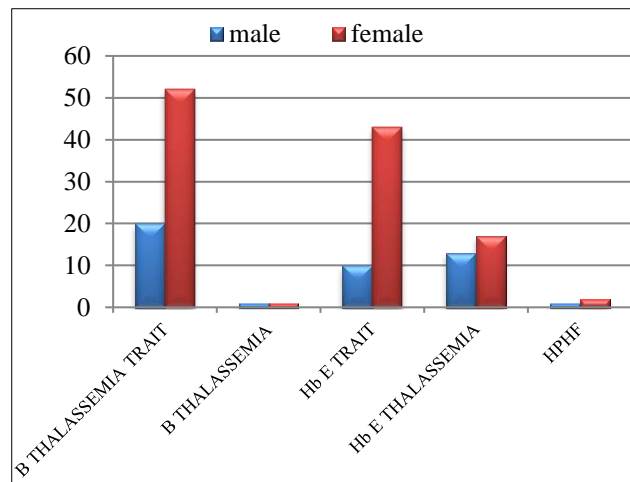


Figure 1: Prevalence of hemoglobinopathy.

DISCUSSION

Disorders of haemoglobin and thalassemia are autosomal recessive genetic disorders, mainly affecting the globin moiety of the Haemoglobin molecule. Thalassemia's and other haemoglobin variants were restricted to some particular geographical areas, caste, tribes and religion especially where marriages were confined to the same

community and regions. However, now they are prevalent throughout the globe. The probable explanation to this is following increased migration of people from one place to other. Inter caste marriages are another reason for increase in the incidence and prevalence rates of hemoglobinopathies. The Indian population is composed of various castes and tribal groups, each with different genetic traits.

There are numerous haemoglobin variants in the Indian population many of which remain undetected due to lack of available infrastructure. Depending on the area of distribution, different hemoglobinopathies have been detected. Beta-Thalassemia trait is the commonest hemoglobin abnormality in the Indian subcontinent which is a similar finding in our study. In beta-thalassemia trait, the Hemoglobin A2 (HbA2) values range between 3.5 to 9%. Low Hemoglobin, reduced MCV, MCH and raised RBC count suggest Beta thalassemia trait.

For diagnosing Beta-thalassemia major the HbF values of equal to or more than 90% of the total Hb are considered. For diagnosing delta / beta thalassemia trait (F-Thalassemia) the concentration of HbF should be between 5-15% of the total Hb values. In hemoglobin S (Hb S)/beta zero-thalassemia, higher concentrations of Hb F do occur.

The most prevalent Haemoglobinopathy is Beta Thalassemia Trait in 72 (16%) followed by HbE Trait in 53 (11.69%). HbE is most common in South East Asia and second most prevalent haemoglobin variant worldwide. Its high frequency in South East Asia is attributed to its mild thalasemic phenotype, which may impart positive selection in area where malaria is endemic.¹⁰ High prevalence of haemoglobin E (>50%) were observed among the Soui, Thai Khmer, So, Yor and Puthai populations inhabiting the region near Cambodia and Laos, higher frequency of HbE in the Phayeng (a Chakpa) of Manipur can be taken as a favour on the hypothesis of association of Austroasiatic race and HbE.

In the study conducted by Maishnam Rustam Singh et al. the greatest frequency of allele Hb β E, 0.101, is found among the Meitei population of Manipur.¹¹ Kishore B et al, made a study of haemoglobin E in north India, report of 11 cases and stated that in India, it is prevalent in Bengal and the north-eastern region, but relatively rare in the rest of the country.¹² Prevalence of Hb E is also associated with the linguistic affiliation of various Tibeto-Burman linguistic families inhabiting in malaria endemic northeast India.¹³

CONCLUSION

Manipur being a state with diverse tribal groups, it is therefore mandatory to screen for hemoglobinopathies, especially in severe anemia who most of the time are treated with Iron supplements that would worsen the condition in Thalassemia due to iron overload.

Identification of these individuals is of crucial importance as they may be transmitters of abnormal genes giving rise to various combination of Hemoglobinopathies and Thalassemia in their progeny which can be symptomatic and associated with high morbidity. They are not curable but can be prevented by population screening, genetic counselling and prenatal diagnosis.

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