

Prevalence of Hemoglobinopathies in Manipur

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Abstract: Background : Hemoglobinopathies are the world wide prevalent monogenic genetic disorder affecting the structure, function, or production of hemoglobin with variable geographic distribution. In the southeast asia and Indian subcontinent, this has been considered as common disorder of blood posing a major genetic and public health problem.

Materials and Methods: This is a Cross Sectional study conducted in the Department Of Physiology, Department Of Pathology, RIMS between Jan 2014 – Feb 2015. A total of 400 from Manipur were included in the study. Interlab Genio Instrument For Alkali and acid Hemoglobin Electrophoresis was used. Data Entry And Analysis Was Done Using SPSS Version-16. Approval Was Taken From The Rims Institutional Ethics Committee.

Results: Among 400 of population surveyed 12.75% of the study population shows the presence of abnormal hemoglobin. 7% were found to be beta thalassaemia carrier, 0.5% homozygous thalassemia, 4% HbE trait, 1% Homozygous HbE, 0.25% Hereditary persistence of hemoglobin F

Conclusion: High prevalence of hemoglobinopathies where Beta thalassaemia in heterozygous state occurred more frequent than other hemoglobinopathies. The study concludes that it is important to explore the hemoglobin variants in Manipur so that the carriers can be detected and the serious damage to the future generation can be prevented.

I. Introduction

Hemoglobinopathies are the group of disorders caused by the presence of variant haemoglobin in the red blood cells. Hemoglobinopathies are the most studied and frequent pathologies. These genetic disorders are considered a very important health care threat in many tropical countries.¹

Inherited hemoglobin disorders fall into two main groups: the structural hemoglobin variants and the thalassemias. The structural hemoglobin variants mostly results from single amino acid substitutions in the alpha or beta chains. The thalassemias are classified according to particular globin chains that are ineffectively synthesised.² In many cases the variants are innocuous but in others they may alter the stability or functional properties of the hemoglobin and lead to clinical disorder. Premature cell destruction may occur due to precipitation of the unstable haemoglobin. The unstable haemoglobin also have greater tendency to spontaneously oxidise to methemoglobin when exposed to oxidative substances and increased temperature during infections. Although over 700 structural hemoglobin variants have been identified only three reach high frequencies HbS, HbC and HbE. The sickle cell gene is widely distributed in the sub Saharan Africa, the middle east and parts of the Indian sub continent. The HbC is relatively common among African blacks living north of Niger River and is found in two to three percent of blacks in United States. The HbE is found in the eastern half of the Indian subcontinent and throughout southeast Asia.^{3,4}

HbE is an abnormal hemoglobin with a single point mutation in the beta chain in which glutamic acid is substituted by lysine at position 26. The HbE variant causes a structural defect in the hemoglobin. The mutation affects beta gene expression creating an alternate splicing site in the mRNA at codons 25-27 of the beta globin chain.⁵ Homozygosity for HbE results in an asymptomatic condition similar to thalassemia minor with microcytic RBC, large numbers of target cells, normal or slightly reduced hematocrit and greater than 90 percent HbE. People heterozygous for HbE are asymptomatic and have hematologic findings similar to thalassemia minor with slightly reduced or low normal MCV and 25 to 35 percent HbE.⁶ Those with hemoglobin E-beta-thalassemia had severe anemia and required long-term transfusion therapy.⁷

Hemoglobinopathies are more common in the rural population of India. They are highly vulnerable to many hereditary disorders causing high degree of morbidity & mortality. Haemolytic anaemia are one of such disease and due to unknown reason some geographical area & races show very high incidence making the haemoglobinopathies, a major public health problem in our country. Manipur is a state in North Eastern part of India with several tribal groups and it is important to study the hemoglobinopathies in this region. In this study we would like to explore the hemoglobin variants in Manipur so that the carriers can be detected and the serious damage to the future generation can be prevented.

II. Methods

A total of 400 were examined in the last two years. 3ml of blood was collected by venepuncture from each subject. The sample is collected in a vial containing EDTA as anticoagulant. The hemosylate is prepared fresh on the same day the electrophoresis is performed. The sample is prepared by washing the red blood cells lysing the cells and pipetting the hemosylate. The hemosylate is made to run on cellulose acetate strips. INTERLAB GENIO instrument for Acid and alkali Hemoglobin Electrophoresis is used for the study. At alkaline PH haemoglobin is negatively charged protein and when subjected to electrophoresis will migrate towards anode. Structural variants that have a change on the surface of the molecule at alkaline PH will separate from HbA. Haemoglobin variants that have an amino acid substitution that is internally sited may not separate and those that have an amino acid substitution that has no effect on overall charge will not be separated by electrophoresis. The individuals who had recent blood transfusions are excluded as it is difficult to distinguish between patients own cells and transfused cells.

III. Results

354 (88.5%) out of all 400 cases were detected to have anemia whereas 51 cases had shown presence of abnormal haemoglobin bands on electrophoresis. Out of 51 cases 47 were found to have pallor. The 51 cases consisted of 29 males (56.86%) and 22 females (43.13%). Thus there is male prepondence. Table 1 shows the distribution of hemoglobinopathies in adult and pediatric age group. The analysis shown in Table 1, reveals prevalence of disease in pediatric age group to be 68.63%. The onset of disease was most prominent in Neonatal to pediatric age group including early adolescent (0-18 years) followed by reproductive age group (19-45Years). Only few cases of old age (46+ years) were detected. Clinical presentation of 51 people with hemoglobinopathies are listed in Table 2. 47 out of 51 who were found to have hemoglobinopathies showed presence of pallor. Pallor was the most prevalent manifestation and was found in 92.15% of the study population. Icterus and splenomegaly were found in 9.8%. This study found many variations in the clinical presentation. Patients belonging to beta thalassaemia minor group had mild anaemia. Haemoglobin electrophoresis showed a slight increase in HbA2 and HbF. They are either asymptomatic or develop mild to moderate anaemia.⁸ The spectrum of hemoglobinopathies prevalent in the study group is shown in Table 3, during the study period of 2 years. Beta thalassaemia carrier is the most common hemoglobinopathy seen in 28 (7%), followed by Hb E trait 16 (4%). Other hemoglobinopathies in decreasing order were Hb E 4(1%), beta thalassaemia 2(0.5%) and Hereditary persistence of fetal haemoglobin 1(0.25%). A value more than 3.5% of HbA2 fraction of Hb was taken as cut off point for determining the β thalassaemia trait & more than 10% was assumed to be HbE.⁹

Table 1: Adult and pediatric age group (Including early adolescents) distribution of different hemoglobinopathies

AGE	MALE (n=29)	percentage	FEMALE(n=22)	percentage	TOTAL(n=51)	Percentage
0-18	18	62.06	17	77.27	35	68.63
19-45	8	27.58	2	9.09	10	19.61
46 and above	3	10.34	3	13.63	6	11.76

Table 2: Pattern of clinical presentation in people with hemoglobinopathies (n=51)

Features	number	percentage
Pallor	47	92.15
Icterus	5	9.80
Splenomegaly	5	9.80
Hepatomegaly	6	11.76
Ascites	1	1.96

Table 3: Spectrum of haemoglobinopathy

	Male	Female	Frequency	Percentage
beta-Thalassaemia trait	12	16	28	7
Thalassaemia major	2	0	2	0.5
Hb E trait	12	4	16	4
Homozygous Hb E	3	1	4	1
Hereditary persistence of Hb F	0	1	1	0.25
Abnormal Hb	29	22	51	12.75
Normal	171	178	349	87.25
Total	200	200	400	100

IV. Discussion

Hemoglobinopathies are the group of disorders caused by the presence of variant haemoglobin in the red blood cells. Haemoglobin disorders fall into two main groups: the structural hemoglobin variants and the thalassemias. The structural hemoglobin variants results from single amino acid substitution and the thalassemias are classified according to particular globin chains that are ineffectively synthesised.

The diagnosis of haemoglobinopathy including thalassaemia can result from either clinical suspicion or from follow up of an abnormality detected during screening. In our study screening of 400 people was done. Clinical history including family history, cast & ethnicity of the patients were recorded and they were subjected to physical examination & peripheral blood examination. The more confirmatory test by Cellulose Acetate Membrane electrophoresis at alkaline and acid PH was done.

Various Indian studies have reported that many variants of haemoglobin are prevalent and very common in rural Indian population. Haemoglobinopathies are one of the major public health problems in our country. On the basis of reports published in last 20 years it is observed that several tribes in various parts of India have been identified as high risk groups of Haemoglobinopathies.

In India different ethnic communities have shown 5 common & 12 rare mutations of haemoglobin. Suprio Ray Chaudhury et al conducted a study on 14,145 to find out the spectrum of hemoglobin variants in eastern Indian population. Out of 14,145 cases 74.35% (10,518 cases) showed normal Hb pattern on HPLC and rest 26.65% (3627 cases) showed some abnormality. Common hemoglobinopathies included beta thal trait, E trait, E beta thal, persistent fetalHb, thal major, thal minor, HbS trait.¹⁰ 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 country¹¹. Prevalence of Hb E is also associated with the linguistic affiliation of various Tibeto-Burman linguistic families inhabiting in malaria endemic northeast India¹²

The frequency of hemoglobinopathy is increased by consanguinity & endogenous mating and the tribal community in India are facing the problem at large scale. Studies have shown that there is very high incidence of haemoglobinopathies in paediatric age group (0-18 years) as 55.7%.¹³ This is very well correlated with our study which has revealed maximum prevalence of 68.63% in pediatric age group. There are so many disorders of Red blood cells but haemoglobinopathy are most common disorder. In our study Beta thalassaemia carrier is found to be the most common hemoglobinopathy 28 (7%), followed by Hb E trait 16 (4%). Other hemoglobinopathies in decreasing order were Hb E 4(1%), beta thalassaemia 2(0.5%) and Hereditary persistence of fetal haemoglobin 1(0.25%).

HbE is the most popular haemoglobin variant in Southeast Asia as well as in Northeast India. 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 Manipur¹⁰.

Manipur is a state in northeastern part of india with several tribal groups and it is important to study the hemoglobinopathies in this region. We have done this study to explore the hemoglobin variants in Manipur so that the carriers can be detected and the serious damage to the future generation can be prevented.

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