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# Alarming Rise of Haemoglobinopathies in Jammu Division

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## Abstract

**Introduction:** Haemoglobinopathies are major public health problems in India. Haemoglobinopathies are inherited single gene disorders having abnormal globin protein. Genes in α-globin and β-globin genes clusters (on chromosomes 16 and 11) control globin chain production. Due to spontaneous mutation in globin genes haemoglobin variants are produced.

Disorders range from thalassemia to many hemoglobin variants with no, mild or severe consequences for the carrier.

**Materials and Method:** The present laboratory-based retrospective study was conducted for a period of two years from January 1, 2013 to December 31, 2014 in the Government Medical College, Jammu. Data of 543 patients who had come to the laboratory for their hemoglobin electrophoresis was compiled and studied. Complete blood count was carried out on HMX (Beckman Coulter) and hemoglobin electrophoresis for diagnosing any abnormal hemoglobin disorder was done on D10 (BIO RAD).

**Results:** Out of 543 patients, 368 (67.77%) were normal and 175 (32.23%) had abnormal hemoglobin pattern. Spectrum of haemoglobinopathies prevalent in descending order were 13.99% β-thalassemic trait, 6.26% α-thalassemic trait, 4.6% elevated fetal haemoglobin, 2.57% false elevation of hemoglobin A2 because of mean corpuscular volume, 1.29% β-thalassemic major, 0.93% haemoglobin S homozygous, 0.74% borderline hemoglobin A2, 0.55% patients were with other type of hemoglobinopathies.

**Conclusion:** High prevalence of haemoglobinopathies in Jammu division makes the disease a major public health problem in our population. Population screening, genetic counseling and prenatal diagnosis can prevent these genetic disorders.

**Keywords:** Haemoglobinopathies, Thalassemia, Anaemia, beta thalassemia, Jammu.

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## Introduction

Among all the inherited disorders of blood, haemoglobinopathies are the major public health problem in the world. Inherited haemoglobin disorders were originally characteristic of tropics and sub-tropics but are now common worldwide due to migration. World Health Organisation estimates that globally at least 5% of adults are carriers for a haemoglobinopathies: approximately 2.9% for thalassemia.(1) There is a tremendous amount of burden of haemoglobinopathies in India. It has been estimated that there would be about 45 million carriers and about 15,000 infants born each year with haemoglobinopathies in India. Major haemoglobin variant, i.e. HbA ranges from 15 to 45% of the total haemoglobin in the red cells. More than 100 alpha-chain variants have been described in the world.(2) The cumulative gene frequency of haemoglobinopathies in India is 4.2%.(3) The cumulative gene frequency of the three most predominant abnormal haemoglobins, i.e. sickle cell, haemoglobin D and haemoglobin E has been found to be 5.35% in India. Every year 10,000 children with thalassemia major are born in India, which constitute 10% of the total numbers in the world.(4)

Haemoglobinopathies are characterized by production of structurally defective haemoglobin because of abnormal globin moiety formation. Hemoglobinopathy is the condition in which there is mutation in haemoglobin which leads to alteration of its biological behaviour. It leads to moderate to severe haemolytic anaemia among vulnerable segments of society like infants, children and adults. It leads to high degree of morbidity.

There are two forms of beta thalassemia:

- Thalassemia minor
- Thalassemia major (also called Cooley's anemia).

The most familiar type of thalassemia is beta thalassemia:

Thalassemia syndromes particularly beta thalassemia major and certain alpha thalassemia are serious and a major cause of morbidity.(3) In India, 10,000 thalassemic children are born every year. In Gujarat, about 6000 thalassemic children are born every year.(5)

Individuals with thalassemia major usually present within the first two years of life with severe anemia, requiring regular red blood cell (RBC) transfusions. Findings in untreated or poorly transfused individuals with thalassemia major, as seen in some developing countries, are growth retardation, pallor, jaundice, poor musculature, hepatosplenomegaly, leg ulcers, development of masses from extramedullary hematopoiesis, and skeletal changes that result from expansion of the bone marrow. Regular transfusion therapy leads to iron overload-related complications including endocrine complication (growth retardation,

failure of sexual maturation, diabetes mellitus, and insufficiency of the parathyroid, thyroid, pituitary, and less commonly, adrenal glands), dilated myocardiopathy, liver fibrosis and cirrhosis). Patients with thalassemia intermedia present later in life with moderate anemia and do not require regular transfusions.[6]

Beta (β) - thalassemia and sickle cell disease represents the most frequent haemoglobinopathies. The prevalence of beta Thalassemia trait and sickle cell in India varies between 3-17% and 1-44% respectively.[7] Hgb S causes red blood cells to become stiff and abnormally shaped. Instead of having a normal round, disk shape, these red blood cells become sickle-shaped, or crescent-shaped. These cells don't live as long as normal red blood cells. Because of their shape, they get stuck inside small blood vessels. These problems cause symptoms of sickle cell disease. About 3% of the world's populations (150 million people) carry beta-thalassemia genes.[8]

Parents who are both carriers have a one in four chance in each pregnancy of giving birth to a child affected with the disease. Carriers can be identified by simple blood tests [Hb-electrophoresis or High Performance Liquid Chromatography (HPLC)]. Couples could then be informed about their risk, preferably before pregnancy.[9]

Epidemiologic studies have shown that the Knowledge of the molecular defects in each country allows the development and improvement of diagnostic tests and management protocols for these disorders.[10] In India, average frequency of sickle cell gene is around 5%. The highest frequency of sickle cell gene in India is reported in Orissa (9%), followed by Assam (8.3%), Madhya Pradesh (7.4%), Uttar Pradesh (7.1%), Tamil Nadu (7.1%) and Gujarat (6.4%) .The distribution of beta thalassemia is not uniform in Indian subcontinent. The highest frequency of beta thalassemia trait is reported in Gujarat (10-15%), followed by Sindh (10%), Punjab (6.5%), Tamil Nadu (8.4%) and Maharashtra.[11]

## Materials and Method

A retrospective laboratory based analysis of blood samples from the patients was designed with an objective to find out the prevalence of haemoglobinopathies in Jammu division. A total number of 543 anaemic patients referred by various practitioners for the diagnosis of haemoglobinopathies were included in the study from Jan 2013 to Dec 2014. Using ethylene diamine tetra acetic acid (EDTA) as anticoagulant, intravenous blood samples were collected by disposable syringes. Age, sex and date of investigations were obtained.

Complete blood count (CBC) including hemoglobin was carried out on HMX (Beckman Coulter) fully automated five part differential cell counter for measuring various hematological indices. Haemoglobin electrophoresis was done on D10 (BIO RAD) by High performance liquid chromatography (HPLC).

HPLC is an excellent diagnostic tool and is suitable for the investigation of haemoglobin variants and thalassemias. Further reports of patients for CBC and Haemoglobin electrophoresis were interpreted for prevalence.

**Statistical Analysis:** The data was categorized in n(%).

## Results

Out of 543 patients, 368 (67.77%) cases were found normal and 175 (32.22%) had one or the other form of haemoglobinopathies. Table 1 & Fig. 1 represents the spectrum of haemoglobinopathies encountered during two years of study and Fig. 2 depicts the electrophoretogram of different types of haemoglobinopathies. It is important to note here that β-thalassemia minor was the most common form of haemoglobinopathies (13.99%), followed by α-thalassemia trait (6.26%), Hb F elevated (4.60%), Hb A2 false elevation (2.57%), β-thalassemia major (1.29%), Hb S homozygous (0.93%), Hb A2 borderline (0.74%), Hb E trait, and Hb F with β-/major thalassemia (0.37% each), Hb A2 reduced, α/β-thalassemia intermedia, Hb S trait and Hb S/D double heterozygous (0.18% each).

Table 2 depicts the hematological parameters in different groups of heamoglobinopathies. Hb value was very low in case of β-thalassemia major (4.3+1.6) and HbF with β-/major thalassemia(4.7+0.5). In most of the cases of β-thalassemia trait RBC count was raised.

Though the study was lab based research, the data represents an overall picture of the Jammu and Kashmir State.

**Table 1: Spectrum of Haemoglobinopathies**

| Type of manifestation | No. of patients | %age of patients |
|---|---|---|
| Normal | 368 | 67.77 |
| β-thalassemia minor | 76 | 13.99 |
| α-thalassemia trait | 34 | 6.26 |
| Hb F elevated | 25 | 4.60 |
| Hb A2 false elevation | 14 | 2.57 |
| β-thalassemia major | 7 | 1.29 |
| Hb S homozygous | 5 | 0.93 |
| Hb A2 borderline | 4 | 0.74 |
| Hb E trait | 2 | 0.37 |
| Hb F with β-/major thalassemia | 2 | 0.37 |
| Hb A2 reduced | 1 | 0.18 |
| α/β-thalassemia intermedia | 1 | 0.18 |
| Hb S trait | 1 | 0.18 |
| Hb S/D double heterozygous | 1 | 0.18 |

**Table 2: Haematological parameters in different group of hemoglobinopathies -**

| Haemoglobinopathies | Hb | RBC Count | PCV | MCV | MCH | RDW |
|---|---|---|---|---|---|---|
| β-thalassemia trait | 10.1±2.0 | 5.1±0.9 | 34.4±7.7 | 66.1±8.8 | 19.9±2.7 | 16.7±3.7 |
| α-thalassemia trait | 6.4±1.7 | 4.04±0.8 | 23.3±5.6 | 57.4±13.7 | 16.1±3.5 | 22.1±5.1 |
| Hb F elevated | 6.5±2.2 | 2.5±1.3 | 20.7±7.8 | 90.1±20.1 | 29.6±8.7 | 25.6±8.0 |
| Hb A2 false elevation | 6.6±1.9 | 1.7±0.4 | 20.5±5.7 | 114.9±12. | 37.3±4.7 | 23.1±6.2 |
| β-thalassemia major | 4.3±1.6 | 1.9±0.8 | 13.8±5.9 | 72.8±2.3 | 23.3±3.2 | 36.6±5.2 |
| Hb S homozygous | 7.3±1.9 | 2.6±0.7 | 23.6±6.5 | 91.2±5.07 | 28.3±2.0 | 22.1±1.8 |
| Hb A2 borderline | 10.9±3.8 | 4.3±1.5 | 35.1±12.6 | 81.0±3.0 | 25.4±1.0 | 15.8±5.9 |
| Hb E trait | 9.4±5.4 | 3.5±2.5 | 30.1±18.3 | 89.9±13.4 | 28.8±5.7 | 17.05±4.1 |
| Hb F with β-/major thalassemia | 4.7±0.5 | 2.3±0.5 | 15.6±2.6 | 66.4±3.8 | 20.1±2.1 | 38.3±2.0 |

## Discussion

Haemoglobinopathies are the most common disorders of erythrocytes. Haemoglobinopathies consist of thalassemia and variant haemoglobins. In India, they are responsible for the largest number of genetic disorders and hence are of great public health importance. Clinically important thalassemic disorder in India is β-thalassemia? While α-thalassemia, although more common in tribal population, is free from morbidity. Of the several abnormal haemoglobin molecules, three which are widely prevalent in India include: Hb S, Hb E and Hb D.[3] Recent surveys suggest that between 300,000 and 400,000 babies are born with a serious hemoglobin disorder each year and that up to 90% of these births occur in low- or middle-income countries.[12] Hb E is widely distributed in north-eastern states of India. The prevalence of Hb E carrier state is below 1% in Mizoram. In West Bengal it varies from 3-33% while it is almost non-existing in southern India. Hb D is predominantly seen in Punjab, Uttar Pradesh, Gujarat and Jammu and Kashmir. Hb D in both heterozygous and homozygous form is clinically asymptomatic. Even when co-inherited with β-thalassemia, the presentation is similar to thalassemia minor. The only clinically significant form of Hb D is when it is co-inherited with Hb S producing a severe sickle cell disease. The overall gene frequency of Hb D in India is below 1%.[13] The presence of thalassemia and Hb E, Hb S in this part of the country has great historical importance as it is based on the migration or flow of different population from different regions of India through marriages.[14] The Indian population comprises numerous casts and tribal groups, each revealing different genetic traits(15).

In our study beta thalassemia was present in 15.4% patients, hemoglobin S trait in 0.18% and Hemoglobin S homozygous in 0.93%. while comparing the incidence it was found that in Oman a national study revealed that approximately 10% patients are having Sickle Cell Anemia and 4% are having beta-thalassemia major.[16] *A study in Karnataka reported that* 30% of the children were victims of beta thalassemia, 40% were carriers of beta thalassemia, 4% were cases of sickle cell trait, and one was a compound heterozygote of HbS/beta thalassemia.[3,11]

According to study done by Indian red cross society, Gujrat state branch prevalence of beta thal trait is 3.4% and sickle cell trait is 0.7% in Ahmedabad.[17] This shows that prevalence of thalassemia and sickle cell disease varies from region to region and it is very high in Jammu and Kashmir as compared to other cities. This may be because our patients had low hemoglobin, MCV, MCH and raised RBC count pointing towards beta thal trait.[18]

While studying thalassemia incidence 22.09% cases were found to be having thalassemia similar findings were observed in a longitudinal study done by Kohne and Kleihaeur (2009) thalassemia syndromes were the largest group (25.6%) in Germany.[19] A retrospective cross sectional study done in eight capital cities of Columbia.[20] The most frequent abnormal hemoglobin found was HbS(43%), HbC(9%). For quantitative hemoglobins, HbA2 was 3.7% and HbA kept slightly elevated in 14.7% of cases. Almost similar findings were observed by Marull A et al[21] during 10 years (2005 -2015) study of hemoglobinopathy in the area of Girona, Spain.

One more study done by Sachdev et al for Indian population 13 cases of Hb D- Punjab heterozygous were found[22] while only one case (0.18%) was present in our study. But percentage of other traits is very similar to our study. alpha thalassemia trait of 5.48%,[23] elevated Hb F (25 cases) and Hb E (2 cases) were seen in study in Indian population.[22] In our study alpha thalassemia is reported in 6.26%, HbF is seen in 25 cases and HbE is seen in only 2 cases.

In our study Low haemoglobin concentration is a result of many factors such as malnutrition, haemorrhagic conditions are by hereditary factors such as haemoglobinopathis.[24,25] These facts help us in using new techniques for early detections prevention and treatment of this disease. It is of paramount importance of increase awareness of this rare disorder among clinicians and patients to assist in prenatal diagnosis. In our study two cases (one of 3 months and another of 7 months) were with very low Hb (1.5 & 2.5).

A study conducted in Bengal shows borderline Hb $A_2$value in 0.73%cases and low Hb $A_2$ value in 0.68%

cases.[26] In our study low HbA2 values were seen in 0.18% cases and border line in 0.74% cases.

Generally in anemic patients first line of treatment is giving iron but if hemoglobinopathy is ruled out before giving iron therapy then it will not lead to unnecessary iron overload in patients of hemoglobinopathies.Person having positive report for carrier stste should be couselledfor the nature of the disease and implications of being carrier.

## Conclusion

The patients in the present study were referred from peripheral regions of Jammu and Kashmir State where the diagnostic facility is not much available. The data of this study can be foreseen as representative of overall prevalence of haemoglobinopathies and thalassemia in the State of J&K. The majority of cases detected were of thalassemia but Detection of other variants becomes important due to complex interactions in cases with double heterozygous and homozygous states, which may lead to severe hematological abnormalities. An effective strategy of preventing the progression of the disease might be employing more sophisticated techniques like polymerase chain reaction (PCR) followed by direct sequencing, genetic counseling, prenatal diagnosis and creating public awareness. High prevalence of haemoglobinopathies in Jammu division makes the disease a major public health problem in our population.

Studies such as ours are required to better understand the social, demographic and medical attributes of thalassemics in this region to develop better health management strategies for the future.

## References


1. WHO- Executive Board, EB118/5, 118th Session Report by the Secretariat on Thalassemia and other haemoglobinopathies: Prevalence of Haemoglobinopathies. 11 May 2006; 1-8.
2. Balgir R S. The burden of haemoglobinopathies in India. ICMR.10 Dec 2000;79:11.
3. Sarnaik SA. Thalassaemia and related haemoglobinopathies. Indian J Pediatrics 2005;72:319-24.
4. Selvaraj B, Swaminathan R. Studies on Beta Thalassemia and other Hemoglobinopathies in Metropolitan City of Chennai, Tamil Nadu, India. International journal. 2016;7-19.
5. Bodarya V, Makwana H, Lakum N, et al. A study of thalassemia screening of 1000 medical students and comparison of various screening methods. Int J. 2016:5;272-275.
6. Shrivastav A, Patel U, Joshi J R, et al. Study of hemoglobinopathies and Hb variants in population of Western India using HPLC: A report of 7,000 cases. 2013;4:104-109.
7. Bhalodial J N, Voza H, Modi P J, et al. Study of hemoglobinopathies in patients of anemia using high performance liquid chromatography(HPLC) in western India. National Journal. 2015;6.
8. Bhanvadia V M, Chavda A, Mehta D, et al. Study of prevalence of hemoglobinopathy in Sindhi community of Jamnagar, Gujarat. International Journal. 2015;5:349-352.
9. Jans S M, Van C, et al. A case study of haemoglobinopathy screening in the Netherlands: witnessing the past, lessons for the future. Ethn Health. 2012;17(3):217-239.
10. Hamany h, Allawi N. Epidemiological profile of common hemoglobinopathies in Arab Countries. J Coommunity Genet. 2013 Apr;4(2):147-167.
11. Shivashankara A R, Jailkhani R Hemoglobinopathies in Dharwad, North Karnataka2008;2:593-599.
12. Williams T N, Weatherall D J. World Distribution, Population Genetics, and Health Burden of the Hemoglobinopathies. 2012;2:9.
13. Agarwal MB. The burden of haemoglobinopathies in India - Time to wake up? JAPI 2005; 1017-18.
14. Patne S C U, Shukla J. Hemoglobin E disorders in Eastern Uttar Pradesh. Indian Journal of Pathology and Microbiology. Jan-March 2009;52(1):110-112.
15. Patel A G, Shah A P, Sorathiya S M, Gupte S C. Hemoglobinopathies in South Gujrat Population and incidence of anemia in them. Indian Journal of Hum Genet. Sep-Dec 2012;18(3):294-298.
16. Rajab G, Patton M A.Study of hemoglobinopathies in Oman through a national register.2000;21.
17. Patel A P, Naik M R, Shah N M, Sharma N P, Parmar P H. Prevalence of common hemoglobinopathies in Gujrat: An analysis of a large population screening programme. National Journal of Community Medicine. Jan- March 2012: Vol 3(1):112-116.
18. Jignasa N Bhalodia, Haren v oza, Palak J Modi, Kinara A Patel, Himani B Patel. Study of hemoglobinopathies in patients of anemia using HPLC in Western India. National Journal of Community Medicine. 2015;Jan-March: Vol 6(1);35-40.
19. Kohne D E, Kleihauer E. Hemoglobinopathies: A Longitudinal Study Over Four Decades.2009;August.
20. Sandra J E C, Claudia C C M, Zuli X Y M, Oscar M N, Mario A. Hemoglobinopathy detection through an institutional neonatal screening program in Columbia. J Bras Patol Med Lab. 2016; vol 52(5):299-306.
21. Marull A, Ramirez J M et al. Epidemiological distribution of hemoglobinopathies in the area of Girona over 10 years. Intl J Lab Hem. 17 March 2017.
22. Sachdev R, Dam A R, Tyagi G. Detection of Hb variants and hemoglobinopathies in Indian population using HPLC: Report of 2600 cases.2010;53 :57-62.
23. Clinique S,Enfants H. Hemoglobinopathies in Tunisia. An updated review of the epidemiologic and molecular data.2006;84:687-696.
24. Ahmed A, Naser A, Talib Hassan A, Moayed Naji M. Detection of hemoglobinopathies in hypochromic, microcytic and sickle cell blood films by hemoglobin electrophoresis. Thi-Qar Medical Journal (TQMJ):2011; vol 5(1):139-148.
25. Aziz B, Abolghasem P, Reza E. Discrimination of beta thalassemia minor and iron deficiency anemia by screening test for blood cell indices. Turk J Med Sci. 2012; 42(2): 275-280.
26. Dolai T K, Dutta S, et al. Prevalence of Hemoglobinopathies in Rural Bengal, India.2011; 57-63.