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Spectrum of hemoglobinopathies in the state of Madhya Pradesh, India

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ABSTRACT

Background: Hemoglobinopathies are common genetic disorders of hemoglobin (Hb). Identification of these disorders is immensely important epidemiologically, and they can be prevented by population screening. Inherited abnormalities of hemoglobin synthesis include a myriad of disorders ranging from thalassemia syndromes to structurally abnormal hemoglobin variants. Identification of these disorders is immensely important epidemiologically and aid in prevention of more serious hemoglobin disorders. The present study was carried out to evaluate the spectrum of hemoglobinopathies in the state of Madhya Pradesh. In this study, the hemoglobinopathies were detected by fully automated electrophoretic Apparatus of Interlab Genio S.

Materials and Methods: In our study, screening of all anemia cases was done initially by clinical history including family history, cast, and ethnicity of the patients. All cases were subjected to physical examination, a blood count and peripheral blood examination. In addition, sickle cell phenomenon and alkali denaturation for fetal Hb were also carried out. The more confirmatory test by Cellulose Acetate Membrane electrophoresis at alkaline pH (CAM) was followed in all cases of suspected hemolytic anemia.

Results: The study confirmed that hemoglobinopathies were prevalent in 10.17% in a cohort of anemic patients. Prevalence of sickle cell β thalassemia was 4.33%, sickle cell trait 1.50%, β thalassemia trait 2.44%, sickle cell disease 0.94%, and β thalassemia major 0.94% was observed. The prevalence of sickle cell-β thalassemia was significantly higher and prevalence of sickle cell disease and β thalassemia major was equal and lowest.

Conclusion: This study provides for the first time comprehensive databases on the spectrum and pattern of hemoglobinopathies in a rural tertiary care center. Significance of these observations has been discussed, and necessity for extensive survey work with improved techniques in future is proposed.

Key words: Electrophoresis, hemoglobinopathy, hemolytic anemia, sickle cell disease, sickle cell trait, thalassemia

INTRODUCTION

At present, approximately 250 million people constituting 4.5% of the world population carry a potentially pathological hemoglobinopathy gene. Each year about 3,00,000 infants are born with a major hemoglobinopathy.[1-3] Accurate and timely detection of various hemoglobin (Hb) variants including β-thalassemia trait (BTT) can prevent the occurrence of more serious disorders like thalassemia major in newborns.[3] Until recently the identification and quantification of Hb variants required a sequence of tests each with inherent problems of reproducibility, accuracy, labor intensity, and cost.

Thalassemia and other structural hemoglobinopathies are the major genetic disorders prevalent in certain parts of the world including India. The general incidence of thalassemia trait and sickle cell hemoglobinopathy in India varies between 3–17% and 1–44%, respectively,[4] but, because of consanguinity, caste, and area endogamy, some communities show a very high incidence, making the disease a major public health problem in our country.[4,5] Inherited disorders of Hb synthesis are an important cause of morbidity and mortality worldwide. They place a large burden on the patients, their families, and even the community.

Alpha-thalassemia is primarily due to gene deletion directly causing reduced α globin chain synthesis. β-thalassemia is usually caused by point mutation rather than large deletion. Sign of thalassemia develops after 6 months of age because this is the time when Hb synthesis switches from Hb F to Hb A. Mediterranean people with both parents heterozygous for β-thalassemia are at risk of producing homozygous child. The true genetic character of the disorder became fully appreciated after 1940. The disease described by Cooley and Lee in the homozygous state of an autosomal gene. Sever homozygous condition became known as thalassemia major. The heterozygous state and thalassemia trait were designated according to their severity as thalassemia minor,[6] later the term thalassemia intermedia was used to describe disorder that was milder than major form but more severe than the trait.

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The countries where thalassemia register is maintained for surveillance purpose are United Kingdom, Iran, and Oman.[6,7] In the eastern oases of Saudi Arabia, more than 50% of population appears to have a clinically silent form of α-thalassemia, and Hb H disease is recognized with increasing frequency of about 3% of world population (150 million people) carry β-thalassemia gene.[8] It has been described in high frequency in Indians 3.5%–14.9%.[9]

Sickle Hb is a mutant Hb in which valine has been substituted for glutamic acid normally at the sixth amino acid of β globin chain. Sickle cell disease is occurred when an individual is homozygous for sickle cell mutation or is a compound heterozygote for sickle Hb and β-thalassemia and Hb C and less common β globin mutation. Disease is characterized by hemolytic anemia and by three types of crises - painful (vaso-occlusive), sequestration, and aplastic. Treatment with hydroxyurea results in amelioration of crises. It has been found that the area where the disease is most prevalent also showed the higher frequency of malaria. The disorder has its onset during the 1st year of life when Hb F level falls. DNA from fetal cells can be directly examined, and the presence of sickle cell mutation can be accurately diagnosed. Emmel[10] demonstrated that red cells sickled when blood from such patient was sealed under glass and allow to stand at room temperature for several days. However, the fact that the transformation to sickled cells occurs in response to a fall in oxygen tension was not recognized until the classic studies of Hahn and Gillespie in 1927.[11]

All cases of anemia referred to the Department of Pathology Index Medical College were subjected to Hb electrophoresis followed by quantitative analysis of the abnormal Hb. This provided a definitive diagnosis of anemic patients. Affected persons and their families with hemoglobinopathies were offered appropriate management, advice, and genetic counseling. This study also revealed the incidence and types of hemoglobinopathies among the rural population in patients of the area, which will cover approximately 85000 people of 65 villages in and around the area of this tertiary care hospital.

Aim

The aim of the study was to know the incidence and prevalence of hemoglobinopathy in anemic rural population in the area covered by tertiary care hospital Index Medical College.

Objectives

The objectives of the study were as follows:

1. To find the types of Hb abnormalities among all cases of hemolytic anemia.
2. To find the clinical presentation of hemoglobinopathy in adults and pediatric patients.
3. To compare the incidence of hemoglobinopathies between adults and pediatric population.
4. To explore possibility of screening and counseling and suggest protocol to prevent and reduced the incidence of disease in affected population.

MATERIALS AND METHODS

In this study, 510 cases of anemia that attended the outpatient department of the hospital or admitted inward from October 2011 to October 2013 were included. These cases were routinely investigated for anemia. Cases that were suspected of hemolytic anemia on routine complete blood count (CBC), red blood cell (RBC) indices and peripheral smear, and on special investigation were analyzed for Hb abnormality. These 510 cases were randomly selected and included in this study. In every case, 2–5 ml blood was collected by venepuncture under aseptic condition. All cases were subjected to clinical examination and laboratory investigation. History and physical examinations of the patients were recorded in pro forma enclosed. A great emphasis was laid in eliciting family history to find out any familial tendency or affection of sibling or other relations. A detailed physical examination was done with special reference to the presence of jaundice and hepatosplenomegaly.

The following investigations were done: CBC, peripheral blood smear study, reticulocyte counts, osmotic fragility test, sickling test, and alkali denaturation test for HbF.

Hb Electrophoresis

Inclusion criteria

The following criteria were included in this study:

1. Patient of all age group except newborn.
2. Patients who had Hb level below 10 GM/dl or who had evidence of hemolytic disease on clinical examination.
3. Patient who had hemolytic picture on peripheral blood smear.

Exclusion criteria

The following criteria were excluded from the study:

1. All newborns.
2. Patients who do not have hemolytic picture on peripheral blood smear.

CBC

CBC performed by an automated analyzer that counts the number and type of different cells within the blood. Cellenium 19 and Sysmex XS 800i fully automated Cell counter were used for CBC [Figure 1]. Mean corpuscular volume (MCV) is a key diagnostic indicator. An important factor, namely, iron deficiency anemia (IDA) coexisting with BTT can have very low value for MCV. For all practical purposes MCV of ≤65 fl, indicates possibility of coexistence of β-thalassemia trait and iron deficiency.

Red cell distribution width (RDW) is a measure of the degree of variation in red cell size. IDA is characterized by an increase in RDW and thalassemia trait in contrast tends to produce a uniform microcytic red cell population without a concomitant increase in RDW. Therefore, RDW may provide information useful as an adjunct to diagnosis, but it is not useful as alone indicator. RBC counts are a useful diagnostic adjunct because thalassemias produce ineffective erythropoiesis with microcytic hypochromic anemia with an increase in RBC numbers.[4]

Peripheral Blood Smear Study

The polychromatic staining solution (Wright, Leishman, and Giemsa) contain methylene blue and eosin. These basic and acidic dyes induce multiple colors when applied to cells. The acidic component (nucleus with nucleic acid) takes blue-purple shades by the basic dye and they are called as basophilic. The neutral component of the cells is stained by both the dyes.[5]

Reticulocyte Counts

Brilliant cresyl blue in an isotonic medium selectively stains nucleic material of erythrocytes called reticulocytes which can be seen under a microscope directly or with a counterstain.[12]

Table 1: Interpret of electrophoresis result as follows[15]

Condition	HbF %
Normal	<1% Adults
β-Thalassemia major	10–98%
α-Thalassemia	Reduced
Sickle cell trait	Normal
Sickle cell anemia	1–20%

Hb: Hemoglobin

Table 2: Spectrum of hemoglobinopathies among all anemia cases

Total patients seen during study period	531
Total number of patients with sickle cell disease	05
Prevalence of sickle cell disease	0.94%
Total number of patients with sickle cell trait	08
Prevalence of sickle cell trait	1.50%
Total number of β-Thalassemia patients	05
Prevalence of β-Thalassemia	0.94%
Total number of sickle cell β-Thalassemia patients	23
Prevalence of sickle cell β-Thalassemia patients	4.33%
Total number of β-Thalassemia carriers	13
Prevalence of β-Thalassemia carrier	2.44%

Osmotic Fragility Test

In this study we had used the method for osmotic fragility test as described by Parpart *et al*.[13] The principle of method is a small volume of blood is mixed with a large excess of buffered saline solutions of varying concentration. The fraction of red cells lysed at each saline concentration is determined calorimetrically. The test is normally carried out at room temperature (15–25°C).

Sickling Test

When red cells containing Hb S are subjected to deoxygenation, they become sickle-shaped while cells that do not contain Hb S remain normal. Certain reducing chemical agents such as 2% sodium metabisulfite or sodium dithionite can deprive red cells of oxygen. Blood and 2% sodium metabisulfite reducing agent in equal proportion was mixed on a glass slide and a coverslip was placed over it then it was sealed with petroleum jelly or paraffin wax mixture. Amount of HbS in red cells and degree of deoxygenation influenced the speed and extent of sickling. Sickling is usually evident after 30 min; if it is not then the slide is re-examined after allowing it to stand overnight. The sickled cells have minimum of two pointed projections.[6]

Alkali Denaturation Test for Hb F

HbF may be estimated by several method based on its resistance to denaturation at alkaline pH, by high-performance liquid chromatography or by an immunological method.[7] Of the alkaline denaturation methods, that of Betke *et al*.[8] are reliable for small amounts (<10–15%) of Hb F, whereas for levels of more than 50% and in cord blood, the method of Jonxis and Visser[9] is preferable; however, this method is not reliable at levels of <10%.

Hb Electrophoresis

Cellulose acetate electrophoresis at alkaline pH

At alkaline pH, Hb is a negatively charged protein and when subjected to electrophoresis will migrate toward the anode (+). Structural variants that have a change in the charge on the surface of the molecule at alkaline pH will separate from Hb A. Hb 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 separate by electrophoresis [Table 1, Figure 2].

RESULTS

In the present study, 531 patients of anemia have been investigated for abnormal Hb. The study was carried out between October 2011 and September 2013. All cases were subjected to CBC and peripheral smear examination. All suspected cases of hemolytic anemia were investigated for hemoglobinopathy. In this study, maximum number of cases was of sickle cell β-thalassemia, i.e., 4.33% and minimum number of cases were of sickle cell disease and β-thalassemia major, i.e., 0.94% [Table 2].

In the hemoglobinopathy cases, maximum number of males (68.9%) belonged to the pediatric age group, i.e., 0–18 years, while there was nearly equal (17.8%) distribution in the age groups 18–45 years and >45 years. Maximum number of female patients (60%) belonged to the age group 18–45 years, followed by 36% in pediatric age group, i.e., 0–18 years and only 4% belonged to the age group >45 years [Table 3].

The study showed that maximum 269 (50.65%) patients belonged to the age group 18–45 years, followed by 142 (26.74%) in the age group 0–18 years and 120 (22.59%) patients belonged to the >45 years age group. Maximum number of patients in our study group was females 314 (59.13%), followed by 217 (40.87%) males.

Distribution of various clinical presentations is shown in Table 4. It can be clearly seen that maximum number of patients in both the groups had pallor as the most common symptom. Other symptoms that were seen are icterus, edema, lymphadenopathy, bone pain, splenomegaly, and hepatomegaly. Maximum 483 (90.96%) patients had pallor, followed by cyanosis 102 (19.21%) and then icterus 78 (14.69%).

Table 5 shows the clinical presentation in the positive cases (n = 102). Bone pain 21 (20.60%) was seen in majority of the patients, followed by splenomegaly 10 (9.80%) and then hepatomegaly 7 (6.90%).

Table 7 shows the hemolytic facies in the positive cases. The hemolytic facies were present in 35 (64.81%) of the cases.

Table 8 shows the distribution of positive cases according to their gender with respect to hemoglobinopathy presentation. In our study, most common hemoglobinopathy was sickle cell β-Thalassemia 4.33% followed by β-Thalassemia trait 2.44% and then sickle cell trait 1.5%. The prevalence of sickle cell disease and β-Thalassemia major was equal 0.94% and lowest.

Table 9 shows the distribution of various hemoglobinopathies in 54 positive cases. In the age group 0–18 years, maximum patients 8 males' belonged sickle cell β-thalassemia, followed by 4 males in β-thalassemia trait, and 3 males each in sickle cell disease, sickle cell trait and β-thalassemia major, respectively, while maximum 5 females belonged to sickle cell β-thalassemia and 3 females belonged to β-thalassemia trait [Table 6, Figure 3].

Table 3: Analysis of patients age and sex distribution in all cases of anemia (*n*=531)

Age group (years)	*n* (%)			
	Non-hemolytic cases (*n*=477)		Hemoglobinopathy cases (*n*=54)	
	Male (*n*=187)	Female (*n*=290)	Male (*n*=29)	Female (*n*=25)
0–18	66 (35.3)	48 (16.5)	20 (68.9)	9 (36.0)
18–45	55 (29.4)	193 (66.5)	5 (17.3)	15 (60.0)
>45	66 (35.3)	49 (16.9)	4 (13.8)	1 (4.00)
Total	187 (100.0)	290 (100)	29 (100.0)	25 (100)

Table 4: Clinical presentation in all cases (*n* (%)=531)

Clinical presentation	*n* (%)	
	Non-hemolytic cases (*n*=477)	Hemoglobinopathy cases (*n*=54)
Pallor	458 (96.02)	49 (90.74)
Icterus	69 (14.47)	12 (22.22)
Edema	96 (20.13)	10 (18.51)
Lymphadenopathy	17 (3.56)	2 (3.7)
Bone Pain	87 (18.24)	25 (46.29)
Splenomegaly	20 (4.19)	8 (14.81)
Hepatomegaly	16 (3.35)	3 (5.56)
Hepatosplenomegaly	70 (14.67)	14 (25.92)

The mean HbF value in the positive cases was found to be 20.03. The mean of all hematological parameters showed significantly lower level of fetal hemoglobin and HbS. The percent of HbF ranges 0.3%–>50% [Table 10]. The mean in sickle cell trait shows higher than the mean value for β-Thalassemia trait. The mean RBCs of sickle cell trait show lesser value than the mean for β-Thalassemia. The mean value of Hb, MCV, mean corpuscular Hb, and mean corpuscular Hb concentration among sickle cell trait of both male and female shows higher frequency than β-Thalassemia trait.

The mean Hb S value in the positive cases was found to be 45.91 [Table 11]. In our study, Hb S seen 5.56% in Bilalas, 3.70% in Thakurs, and 5.56% in Muslims and Jharias, Ahirs, Banjaras, Patelias and Balais, each has got 1.85%, whereas β Thalassemia was seen 7.40% in Muslims, 9.25% in Bilalas (including 3.70% of Bheels), 5.56% in Thakurs, and 3.70 % in Jharias and Sindhis, Malis, Rajputs and Banjaras, each has got 1.85%.

DISCUSSION

Hemoglobinopathies are most common single gene disorder in man. There are several hundred of these disorders, though the thalassemias - alpha and beta and sickling disorders make up the vast majority. Hemoglobinopathies are a diverse group of inherited disorder of Hb production and synthesis. Hemoglobinopathies are of worldwide occurrence though some geographical areas have high prevalence of these disorders.[14] This is well-established fact that socioeconomic status and cultural norms have direct impact on all types of anemia.

The present study was conducted on 531 individual who was referred to hospital lab from various clinical departments of the hospital with an established diagnosis of anemia based on low Hb content and suspicion of hemoglobinopathies. 89.83% (*n* = 477) of these cases did not reveal any abnormality on detailed investigations and electrophoresis, hence where labeled as non-hemolytic anemia. In the present study during past 2 years, the prevalence of hemoglobinopathies was found to be 10.17%.

In India average frequency of sickle cell gene is around 5% with highest reported from Orissa (9%), Assam with 8.3%, and Madhya Pradesh 7.4%. The distribution of β-Thalassemia is not uniform in Indian subcontinent. The highest frequency of β-Thalassemia trait is reported in Gujarat (10–15%), followed by Sindh (10%), Punjab (6.5%), and Tamil Nadu (8.4%).[16]

Hemoglobinopathies are inherited disorder of globin chain synthesis. It is either reduced rate of synthesis or structurally abnormal globin chain leading to abnormal Hb molecule synthesis. The diagnosis of hemoglobinopathy including thalassemia can result from either clinical suspicion or from follow-up of an abnormality detected during screening.[17]

Various Indian studies have reported that many variants of Hb are prevalent and these are very common in rural Indian population. Hemoglobinopathies are one of the major public health problems in our country. On the basis of analysis of reports published in past 20 years, it is observed that several tribes in various parts of India have been identified as high-risk groups of hemoglobinopathies. In India, about 4635 ethnic communities have shown 05 common and 12 rare mutations.[18]

The sickle cell anemia and thalassemia are the most severe form of genetic disorders and hence are of great importance to be dealt with from public health point of view in India. These two forms of Hb variants prevalent at higher magnitude pose a great threat to population imbalance. Therefore, these inherited abnormalities of Hb synthesis are the most serious public health problem in central India, in particular, and India, in general, reflecting the genetic heterogeneity of the population.[19]

Colah *et al*., 2007,[20] in their recent study have screened 18651 individuals for hemoglobinopathies and mutation were characterized in 1334 β-Thalassemia heterozygotes. In our study, we did not study gene mutation for the prevalent hemoglobinopathies in our area. In most studies, pallor was found to be the most common presenting complaint in patients with

hemoglobinopathies as high as 87%.[21] This result is consistent with our study revealing 95.48% had pallor as presenting feature. Other symptoms such as bone pain, cough, fatigue, and headache also seen but the magnitude of these features are different from Chopra *et al*. Fever has been reported in hemoglobinopathy following an acute crisis or any associated infections.

In the present study out of 54 cases, 35 cases, i.e., (64.81%) showed the hemolytic facies. Hemolytic facies are also known as thalassemia facies as due to marked erythroid hyperplasia in thalassemia resulting in expansion of the skull vault and maxillary bones. This is because of short RBCs life resulting in excessive hemolysis. It stimulates EPO (erythropoietin) production by kidney. EPO acts on bone marrow leading to marked erythroid hyperplasia. There is an expansion of medullary cavities of the bones resulting in widening of diploe of the skull and also long bones. In our study, one of the thalassemia major cases showed Sun Ray or hair end on appearance on skull X-ray.[22]

The Indian Council of Medical Research did the first multicentric study in the mid-1980s on high school children from Mumbai in the West, Delhi in the North, and Kolkata in the East. The study showed the prevalence of β-Thalassemia trait was 2.7% in Mumbai, 5.5% in Delhi, and 10.2% in Kolkata (Madan *et al*., 2010). However, a follow-up of heterozygote's done for 20 years after screening. In Mumbai group, it was found that counseling children at the school going age did not have the desired impact.[23]

Table 5: Clinical presentation in the positive cases (*n*=102)

Clinical presentation	*n* (%)
Bone pain	21 (20.60)
Splenomegaly	10 (9.80)
Hepatomegaly	7 (6.90)
Total	38 (37.25)

Table 6: Anemia typing in all cases (*n*=531)

Clinical presentation	*n* (%)
Normocytic normochromic	7 (12.96)
Normocytic hypochromic	3 (5.55)
Microcytic hypochromic	42 (77.77)
Macrocytic hypochromic	1 (1.85)
Dimorphic	1 (1.85)
Total	54 (100.00)

Table 7: Hemolytic facies in hemoglobinopathy cases (*n*=54)

Hemolytic facies	*n* (%)
Present	35 (64.81)
Absent	19 (35.11)
Total	54 (100.00)

Table 8: Type of hemoglobinopathy according to gender in positive cases (*n*=54)

Hemoglobinopathy	*n* (%)	
	Female (*n*=25)	Male (*n*=29)
Sickle cell trait	1 (4.0)	7 (24.1)
Sickle cell disease	1 (4.0)	4 (13.8)
Sickle cell beta-thalassemia	15 (60.0)	8 (27.6)
Thalassemia trait	7 (28.0)	6 (20.7)
Thalassemia major	1 (4.0)	4 (13.8)

Figure 1: Cellenium 19 and Sysmex XS 800i fully automated cell counter

Figure 2: Interlab Genio S electrophoresis apparatus and Interlab master kit of reagents (buffer, staining solution, destaining solution, and clearing solution)

Table 9: Analysis of hemoglobinopathy in different age groups and gender

Hemoglobinopathy	0–18 years		18–45 years		>45 years		Grand Total
	Male	Female	Male	Female	Male	Female	
Sickle cell disease	3	0	1	1	0	0	5
Sickle cell trait	3	0	1	1	3	0	8
Sickle cell β-thalassemia	8	5	1	8	0	1	23
β-thalassemia major	3	0	0	1	1	0	5
β-thalassemia trait	4	3	3	3	0	0	13
Grand total	21	8	6	14	4	1	54

Studies which have been done previously showed that the hemoglobinopathies are more prevalent among pediatric age group patients (0–15 years), in which it is 35%. This prevalence is much higher 53.7% in the children in our study.[21] The range for osmotic fragility test for hemolysis of RBCs is 0.1% NaCl to 0.85 % NaCl. The mean of osmotic fragility test is 0.239% NaCl. The range for HbF in thalassemia patients and Sickle cell β-thalassemia is 0.3% to 73.5%. The mean for HbF is 26.74%.

Agarwal and Mehta revealed at least in Orissa, sickle cell gene is prevalent even in general caste, unlike the reports from other parts of the countries where the problem is chiefly confined to schedule caste or tribes. In our study, though gene frequency was not studied, we have seen the presence of hemoglobinopathies in general population. Sindhis, Punjabis, Gujarati, Bengalis, and Muslims account for most of the β-thalassemia. Carrier state for β-thalassemia in India varies from 1 to 17% with an average of 3.2%.[24]

Table 10: Hb F value in thalassemia patients (*n*=18)

HbF range	Number of cases
0.3–25.0	13
25.1–50.0	0
>50.0	5

Table 11: Hb S value in sickle cell anemia + sickle cell trait patients (*n*=13)

HbS range	Number of cases
1.9–25.0	4
25.1–50.0	2
>50.0	7

In a recent study, the prevalence of hemoglobinopathy has been reported as high as 42.2%, with most common hemoglobinopathy observed was β-thalassemia trait 21.3%.[28] In the present study, we encountered total hemoglobinopathy 10.17% and β-thalassemia 3.39%. Many studied also reported a very high incidence of hemoglobinopathies in pediatric age group (0–18 years) as 55.7%.[28] This is very well correlated with our study which has revealed maximum prevalence of hemoglobinopathies in this age group 53.70%. Patients having sickle cell trait and sickle cell disease are mostly from Central Eastern India where this disease is prevalent.[29,30]

In our study, the prevalence of β-thalassemia major was low (0.94%), and all their families were given genetic counseling. The prevalence of sickle cell trait was 1.5% in our study. Our result was consistent with Chopra *et al.*,[21] our result was higher than that of Mohanti *et al.* in which it was 0.70%.[23] Probable reason may be for this as; our study was conducted in Central India, where the prevalence of HbS is high. However, our result was low when compared to Balgir[26] 29.8%, Chhotray *et al.*[27] 25.19%, and Urade[19] 5.6%. The prevalence of sickle cell disease was 0.94% in our study. This is consistent with Chopra *et al.* study 1.7%.[23] In this study, we found higher value than Patra[25] 0.21% and Urade[19] 0.15%. Our result showed a lower value than Balgir[26] 7.5% and Chhotray *et al.* 9.42% [Table 12].[27]

CONCLUSION

Hemoglobinopathies are the most common monogenic disorder of erythrocytes. India is the home of several Hb variants causing much suffering to afflicted individuals and imposes considerable financial, genetic and psycho-social burden on family, society, and nation at large. Out of all 531 cases of anemia common hemoglobinopathies observed: Sickle cell β-thalassemia 4.33%,

Table 12: Prevalence of hemoglobinopathies compared with other studies

Hemoglobinopathy	Our study	Mohanti *et al.*[23]	Patra *et al.*[25]	Chopra *et al.*[21]	Balgir[26]	Chhotray *et al.*[27]	Urade[19]
Sickle cell trait (%)	1.5	0.70	9.30	2.30	29.8	25.19	5.6
Sickle cell disease (%)	0.94	0.04	0.21	1.70	7.50	9.42	0.15
Sickle cell β-Thalassemia (%)	4.33	0.02	8.10	0.60	1.70	3.26	0.12
β-Thalassemia trait (%)	2.44	2.78	6.00	17.0	18.2	19.8	2.01
β-Thalassemia major (%)	0.94	-	-	0.40	5.30	8.84	-

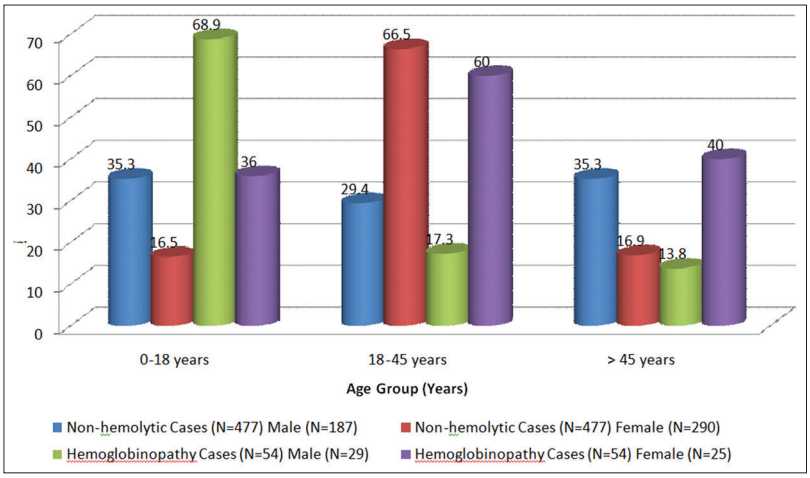

Figure 3: Analysis of patient's age and sex distribution in all cases of anemia (*n* = 531)

β-thalassemia trait 2.44%, sickle cell trait 1.5%, sickle cell disease, and β-thalassemia major both 0.94%. Male preponderance was seen in early childhood up to early adolescents in case of sickle cell disease and sickle cell trait followed by sickle cell β-thalassemia. Pediatric age group including early adolescents comprises most of the hemoglobinopathies 53.7% followed by 18–45 age group 37.03%. Pallor (90.74%) was the most common clinical presentation followed by bone pain (46.29%) in both adult and pediatric age group.

This study provides for the first time comprehensive databases on the spectrum and pattern of hemoglobinopathies in a rural tertiary care centre. Significance of these observations has been discussed, and necessity for extensive survey work with improved techniques in future is proposed.

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