Epidemiological profile of different hemoglobinopathies in pediatric age group (6 months-14 years) in south Odisha

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Abstract---This hospital based cross-sectional study describes the number of hemoglobinopathies in the population of southern Odisha during the study period and distribution of each group of hemoglobinopathy found in the study according to their age, sex, clinical signs & symptoms, history of consanguinity of marriage of parents, history of previous blood transfusion, history of siblings, socioeconomic status of the family, blood groups & hematological parameters.

Keywords---epidemiological profile, different hemoglobinopathies, pediatric age.

Introduction

The hemoglobinopathies refer to a diverse group of inherited disorders characterized by a reduced synthesis of one or more globin chains (thalassemias) or the synthesis of structurally abnormal hemoglobin (Hb).Thalassaemia and other structural haemoglobinopathies are the major genetic disorders prevalent in certain parts of the world including India. While the general incidence of thalassemia trait and sickle cell hemoglobinopathy in India varies between 3-17% and 1-44%, respectively because of consanguinity, caste and area endogamy, some communities show a very high incidence, making the disease as a major

public health problem in our country (1,2). Inherited disorders of hemoglobin synthesis are an important cause of morbidity and mortality worldwide. They place a large burden on the patients, their families and even their communities. They are generally not curable but can be prevented by population screening, genetic counseling and prenatal diagnosis.The state of Orissa inhabits 36.7 million of population,comprising 22.4% scheduled tribes and 16.2% scheduled caste people. They have their own socio-cultural customs, traditions, breeding practices and life-styles quite distinct from each other, which affect their breeding structures and vulnerability towards hereditary diseases in Orissa.(1)

Inherited disorders of hemoglobin are extremely common in Indian population ranging from near structurally normal hemoglobins to severe transfusion dependant hemoglobinopathies. Their detection is important epidemiologically and to prevent other more serious hemoglobinopathies in future generations.(5) In Odisha HbS is very common while in West Bengal Commonest Hemoglobinopathy is HbE Disease.2,3 Hb D Punjab occurs with greatest prevalence in Sikhs (2%) in Punjab.4 ICMR study showed that that the HbE was mainly seen in Assam (23.9%) and Kolkata in West Bengal (3.92%).(4).

The hemoglobinopathies encompass all genetic diseases of hemoglobin. They fall into two main groups:thalassemia syndromes and structural hemoglobin variants (abnormal hemoglobins). α and β-thalassemia are the main types of thalassemia; the main structural hemoglobin variants are HbS, HbE and HbC. There are many subtypes and combined types in each group. The highly variable clinical manifestations of the hemoglobinopathies range from mild hypochromic anemia to moderate hematological disease to severe, lifelong, transfusion dependent anemia with multiorgan involvement.(6) The objectives of this study are to describe the epidemiological profile of different hemoglobinopathies in pediatric age group (6 months-14 years) in south Odisha.

Methodology

Study Design : A hospital based analytical cross sectional study.
Study Setting : Department of Pediatrics, MKCG Medical College & Hospital, Berhampur, Ganjam.
Study Period : November 2016 – October 2018
Source Of Data : Children of age from 6 months to 14 years , presented to the MKCG Medical College hospital with hemoglobinopathies.
Sampling Technique : Purposive sampling method.
Sample Size : 278 cases satisfying our inclusion & exclusion criteria.
Inclusion Criteria : All the patients from 6 months to 14 yrs of age showing suggestive clinical features and various stigmata of hemoglobinopathies in haematological investigations and who have not received blood transfusion in past 3 months.

Exclusion Criteria

Apart from the patients & the parents who refused to be included in the study, all the patients found to have the following diagnosis in haematological investigations:

1. Iron Defficiency anemia.
2. Leukemia
3. Other causes of haemolytic anemia.(Acquired,Autoimmune,G-6-PD Defficiency)

Before taking as sample,written informed consent was taken from the parents on a pre structured proforma. Approval by institutional ethical committee was taken prior to the start of the study. A pre structured proforma was used for detailed history taking,clinical examination and haematological investigations.When a patient was presented to us & included in our study group according to our inclusion & exclusion criteria, first a detailed history taking was done followed by thorough clinical examination and then relevant haematological investigations.

Sickling test was done in all relevant cases as HbS prevalence is high in Odisha. The sickling phenomenon was simply demonstrated in a thin wet film of blood sealed between slide and cover glass by means of petroleum jelly- paraffin mixture. This was followed by gel electrophoresis and high performance liquid chromatography using standard procedures provided bby manufacturers of the equipment used.

Statistical Analysis

The data is analysed by SPSS free version 16 in the Paediatric department of MKCG Medical College. Continuous variables were expressed as mean SD. Categorical variables were expressed as frequencies and percentages. Chi- square test was used to compare the proportion of different haemoglobinopathies among different blood groups and among males & females.

Results

Our study included 278 cases among whom 51.4% were male and 48.6% female. The mean age was 7.29 yrs with SD of 3.875. In our study population, maximum no of cases i.e, 40.3% belong to >5yrs-10 yrs age group followed by 32.4% cases in >1 yr-5yrs of age group. O +VE blood group is most prevalent i.e, 35.3% in our study population followed by B +VE (27.7%), A +VE (21.6%), AB +VE (12.9%), O– VE (1.4%), B –VE (0.7%), A –VE (0.4%) blood groups. The patients mostly belong to Lower Middle class of socioeconomic status (34.9%) followed by Lower (23.7%), Upper Middle (21.6%), Upper Lower (15.5%) & Upper (4.3%) classes of socioeconomic status.

In our study population of hemoglobinopathies, Sickle cell homozygous is most prevalent i.e, 37.8% followed by β Thalassemia major (35.6%), Sickle cell trait (11.5%), Sickle β thalassemia syndrome (5.7%), β Thalassemia minor (2.9%), β Thalassemia intermedia (2.9%), Other Sickle cell disease (2.9%) , HbE-β thalassemia (0.7%)., α-thalassemia (0.7%), Hereditary persistence of fetal hemoglobin (0.7%), δ-β thalassemia (0.4%). The difference of proportions of haemoglobinopathies among male and female is found to be statistically significantly different. In our study group females are more affected in Thalassemia intermedia (75%),Sickle cell trait (71.9%)), Sickle cell homozygous

(59%) patients whereas males are more affected in β Thalassemia major (67.7%), β Thalassemia minor (62.5%), δ-β Thalassemia (100%) & HPFH (100%) & Other sickle cell disease (100%) patients. Males & females are equally affected in Sickle thalassemia syndrome, HbE-β Thalassemia & Alpha Thalassemia patients.

Table-1. Distribution of different hemoglobinopathies with relation to their blood group								
Hemoglobinopathies	O +VE	O –VE	A +VE	A -VE	B +VE	B –VE	AB +VE	AB -VE	TOTAL
Thalassemia major	38(40.4%)	1(1.1%)	8(8.5%)	0	31(33%)	0	16(17%)	0	94
Thalassemia minor	1(12.5%)	0	4(50%)	1(12.5%)	1(12.5%)	0	1(12.5%)	0	08
Thalassemia intermedia	1(12.5%)	0	5(62.5%)	0	2(25%)	0	0	0	08
Sickle cell homozygous	30(28.6%)	2(1.9%)	24(22.9%)	0	31(29.5%)	1(0.9%)	17(16.2%)	0	105
Sickle cell trait	23(71.9%)	1(3.1%)	0	0	7(21.9%)	1(3.1%)	0	0	32
Sickle cell – b Thalassemia syndrome	1(6.3%)	0	13(81.2%)	0	2(12.5%)	0	0	0	16
Other sickle Cell disease	1(12.5%)	0	6(75%)	0	0	0	1(12.5%)	0	08
Hbe-B THALASSEMIA	1(50%)	0	0	0	0	0	1(50%)	0	02
Alpha thalassemia	1(50%)	0	0	0	1(50%)	0	0	0	02
Delta-B thalassemia	0	0	0	0	1(100%)	0	0	0	01
HPFH	1(50%)	0	0	0	1(50%)	0	0	0	02
TOTAL	98	04	60	01	77	02	36	0	278

In our study among the β thalassemia major patients, O +VE (40.4%) blood group is most prevalent followed by B+VE(34.3%), AB +VE(16.2%), A +VE(8.1%), O –VE(1%) blood groups as detailed in table-1. Out of total 278 patients, 76 patients had history of consanguinity of marriage of parents, 208 patients had history of blood transfusion before presenting to us & 76 patients had positive history of siblings affected with hemoglobinopathies. Weakness (84.2%) was the chief complain of most of the patients followed by fever (77%), bone & joint pain (43.9%), loss of apetite (36.7%), abdominal pain (23%), respiratory symptoms (18.7%) and leg ulcer (2.9%). Most of the patients presented with more than one symptoms as shown in table-2.

Table-2. Hemoglobinopathies and common presenting complaints							
HEMOGLOBINOPATHIES	FEVER	WEAKNESS	LOSS OF APETITE	ABDOMINAL PAIN	BONE & JOINT PAIN	RESPIRATO-RY SYMPTOMS	LEG ULCER
β THALASSEMIA MAJOR	75.8%	88.9%	43.4%	8.1%	8.1%	18.2%	0%
β THALASSEMIA MINOR	100%	100%	75%	0%	0%	12.5%	12.5%
β THALASSEMIA INTERMEDIA	87.5%	100%	100%	0%	0%	12.5%	0%
SICKLE CELL HOMOZYGOUS	61.9%	84.8%	31.4%	46.7%	84.8%	16.2%	7.6%
SICKLE CELL TRAIT	100%	100%	25%	25%	34.4%	25%	0%
SICKLE- β THALASSEMIA	100%	100%	12.5%	18.8%	50%	0%	0%

SYNDROME							
OTHER SICKLE CELL DISEASE	100%	25%	37.5%	25%	100%	62.5%	0%
HbE-β THALASSEMIA	50%	100%	0%	0%	50%	100%	0%
ALPHA THALASSEMIA	100%	100%	50%	0%	0%	50%	0%
DELTA-β THALASSEMIA	100%	100%	0%	0%	0%	0%	0%
HPFH	100%	100%	50%	0%	0%	50%	0%

Anemia (97.1%) was the most common clinical finding in our study population followed by splenomegaly (94.2%), hepatomegaly (91.4%), hemolytic facies (46%), jaundice (43.2%), chest signs (31.7%), other signs (31.7%), hand foot syndrome (29.5%), oedema (11.5%) & CNS signs (5.8%).Most of the patients were found to have multiple clinical signs. The Mean Hb was found to be 5.61 gm% with SD of 1.21. 35.3% cases of our study group had pre transfusion Hb range of 5.1-6 gm% followed by 23.7% in 4.1-5 gm% range, 15.1% in 6.1-7 gm% range, 13% in 7.1-8 gm% range, 8.6% in 3.1-4 gm% range & 4.3% in 8.1-9 gm% range.

Discussion

India is an ethnically diverse country with marked regional variation. This diversity is reflected in the presence of different hemoglobin variants in different ethnic groups. Moreover due to migration,there is constant mixing of people from different regions. Many of these abnormal variants are of little clinical significance in heterozygous state,but when in the homozygous state or combined with other variants,they may give rise to severe disease. In any given population,it is the children that are both most vulnerable as well as most suitable for timely intervention and efficacious treatment.It is also this pediatric age group that genuinely reflects the challenges we are facing as a society from hemoglobinopathies.Our study on hemoglobinopathies in 6 months-14yrs of age group in southern Odisha was carried out in the Dept of Pediatric, MKCG Medical College and Hospital,Berhampur during the period from November 2016 to October 2018.

Table 1,2 & 3 :

Out of total 278 study population, 143(51.4%) cases are males and 135(48.6%) cases are females.There is not much difference in the no. of male & female patients. The male:female ratio is M:F= 1.1:1.This may be due to the increase awareness in the population that male & female children should be taken care of equally. This also shows that both males and females might have equal risk of developing hemoglobinopathies.

The no. of Sickle cell homozygous patients is maximum i.e, 105(37.8%) followed by β Thalassemia major 94(35.6%), Sickle cell trait 32(11.5%), Sickle β thalassemia syndrome 16(5.7%), β Thalassemia minor 8(2.9%), β Thalassemia intermedia 8(2.9%), Other Sickle cell disease 8(2.9%), HbE-β thalassemia 2(0.7%)., α-thalassemia 2(0.7%), Hereditary persistence of fetal hemoglobin 2(0.7%), δ-β thalassemia 1(0.4%). This finding differs from the results of the study conducted by others which showed that Sickle cell trait(29.8%) was most prevalent followed by β-Thalassemia trait(18.2%), Sickle cell disease(7.6%), β

Thalassemia major(5.3%), Sickle β- Thalassemia(1.7%), , β Thalassemia intermedia(0.9%), HbE trait(0.9%), , E-β Thalassemia(0.3%), HbE disease(0.3%), HbD trait(0.2%) and SD disease(0.2%).(1) The study by Deb T. et al. showed that HbE trait(26%) was most prevalent followed by HbE disease(21%), HbE Thalassemia(17%), Thalassemia minor(21%), HbS Trait(11%), HbS Disease(4%) & Thalassemia major(0%) in their study population.(4) Another study by Chopra Brig BS. Et al. in the Department of Laboratory sciences, Army Hospital(R&R), New Delhi showed that β-Thalassemia trait(17%) was most prevalent followed by Sickle cell trait(2.3%), Sickle cell disease(1.7%), HbD trait(1%), HbE trait(0.8%), Sickle cell β Thalassemia(0.6%), HbE disease(0.6%), E-β Thalassemia(0.6%) & Thalassemia major(0.4%).(2)

The difference in the prevalence of hemoglobinopathies between our study and some other studies may be due to the different geographical distribution of the hemoglobinopathies & population diversity. Our study represents exclusively population from southern Odisha. As our study was a hospital based study which depends upon presenting complaints and signs and symptoms, number of children affected with sickle cell disease catastrophe outnumbered other hemoglobin disorders and thalassemia cases in this study. In contrast, population based studies would show the actual prevalence of various Hb disorders.

In our study, out of total 278 patients, 76(27.3%) cases had history of consanguinity of marriage of parents. Out of the total 278 patients, 208(74.8%) cases had history of blood transfusion before presenting to us. 76(25.9%) cases had history of siblings positive for hemoglobinopathies, 146(52.5%) cases had negative history & 56 cases had no conclusive or definite history regarding this. Similar to this result, studies by Patel D.K et al. and Tariq H.A et al.shows that main reason for increased incidence of double heterozygous cases in particular communities like SC and Muslims is consanguinity. (6)

Out of total 278 cases, weakness was the chief complain of most of the cases i.e, 234(84.2%) followed by fever 214(77%), bone & joint pain 122(43.9%), loss of apetite 102(36.7%), abdominal pain 64(23%), respiratory symptoms 52(18.7%) and leg ulcer 08(2.9%). Most of the patients presented with more than one symptoms. This result may be due to the fact that almost all hemoglobinopthies present with anemia which normally presents with fever & weakness.This result is similar to the results of the study done by Deb T. et al. which shows that generalized weakness with easy fatiguability was the commonest presenting symptom being present in all 100% of patients with haemoglobinopathies. (4)

In our study, maximum patients had anemia i.e, 270(97.1%) out of total 278 as the clinical finding. This is followed by splenomegaly in 262(94.2%) patients, hepatomegaly in 254(91.4%) patients, hemolytic facies in 128(46%) patients, jaundice in 120(43.2%) patients, chest signs in 88(31.7%) patients, other signs in 88(31.7%) patients, hand foot syndrome in 82(29.5%) patients, oedema in 32(11.5%) patients & CNS signs in 16(5.8%) patients.Most of the patients were found to have multiple clinical signs. These results are similar to the result of the study conducted by Deb T. et al in Silchar Medical College & Hospital which showed that pallor was present in all the 47 cases of Hemoglobinopathies(100%).

Similarly in another study conducted by Chopra Brig GS et al. in the Army Hospital(R&R), New Delhi, pallor was the most common manifestation and was present in 87% of the patients. (2)

Conclusion

This hospital based cross-sectional study describes the number of hemoglobinopathies in the population of southern Odisha during the study period and distribution of each group of hemoglobinopathy found in the study according to their age, sex, clinical signs & symptoms, history of consanguinity of marriage of parents, history of previous blood transfusion, history of siblings, socioeconomic status of the family, blood groups & hematological parameters.

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