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SHORT COMMUNICATION

Spectrum of Hemoglobinopathies: A New Revelation in a Tertiary Care Hospital of Odisha

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Abstract The prevalence of different types of hemoglobinopathies and its spectrum in Odisha state is believed to be high, but its exact prevalence is not known due to lack of large population based study. The present study was undertaken to know the magnitude and spectrum of hemoglobinopathies among the patients attending tertiary care centre for evaluation of anemia. All the patients of various age group without any history of blood transfusion preceding 3 months of period attending the Clinical Hematology Department of SCB Medical College, Cuttack for evaluation of anemia were included in this 10 year prospective study. Detail history, clinical examination followed by blood sample examination including by HPLC/CzE were done in all cases. Other investigations were done as per need of evaluation of anemia. Out of 21,371 patients with anemia, hemoglobinopathies was detected in 10,745 (50.2%) cases. The profile of hemoglobinopathy was as follows: HbS gene in 52.48% cases, betathalassemia in 54.06% and HbE hemoglobinopathies in 9.19% cases. Hemoglobinopathy was detected in very high percentage (50.2%) of cases in our centre. Various types of β-thalassemia and sickle cell hemoglobinopathies were two major types (54.06% and 52.48% respectively). This needs to be confirmed by large population based study.

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Introduction

Hemoglobinopathies and thalassemia are hereditary disorders of haemoglobin, caused by genetic mutation leading to the major public health problem in many parts of the world including India [1, 2]. It is observed that thalassemia is more prevalent in Mediterranean littoral and in south East Asia while Hb-S and Hb-C are more prevalent in tropical Africa [3]. There is a wide variation in the incidence of Beta thalassemia trait (TT) and sickle cell trait (SCT) in India which constitute about 3–17% and 1–44% respectively [4]. According to WHO, it is estimated that there are about 3 lakh babies born every year globally with severe hemoglobin disorder and 80% of these in developing countries [5, 6].

Proper management of these disorders is a huge socio-psycho-economical burden. The curative treatment like stem cell transplant is costly and not available to many patients due to various reasons. Thus its prevention is cost effective. Even if population based prevalence data is not available, Odisha is believed to have high prevalence of both HbS as well as β-thalassemia. A detailed scan of the literature revealed two studies of small sample size of two particular geographical areas as follows; Balgiri found SCT in 29.8% and TT 18.2% (n = 1015) while Alam found 68.3% hemoglobinopathy out of 331 anemia cases [7, 8]. Thus the present study was planned to assess the spectrum and magnitude of these hereditary disorder from a large sample size those were referred to Clinical Hematology department, SCB Medical college and Hospital, Cuttack for evaluation of annemia.

High Performance Liquid Chromatography (HPLC) and Capillary zone electrophoresis (CzE) are two equipments, based on different principles and are commonly used for diagnosis of these disorders [9].

Materials and Methods

This was a prospective study from January 2008 to December 2017 among the patients attending the Department of Clinical Hematology SCB MCH, Cuttack for evaluation of anemia. All these patients of various age groups and without history of any blood transfusion within 3 months of period were included in this study. Detail histories including any blood transfusion, family history, clinical examination were documented.

Two ml Blood sample was collected from all the patients in EDTA vial by following standard procedure. Complete blood count (CBC), Red Blood Cell indices and reticulocyte count were measured using automated—five part differential cell counter (SYSMEX 1000i). The results of haemoglobin (Hb) and other red cell indices were correlated with peripheral smear examination. The samples were analyzed for hemoglobin disorders by HPLC (BIORAD VARIANT) or CzE, (MINICAP SEBIA) randomly. Evaluation of Serum ferritin by chemiluminosense (ROCHE ECL) and HPLC/CzE of both parents were done of those patients where the definite diagnosis couldn't be achieved after evaluation of patients, i.e. to differentiate between HbSS with high HbF, HbS- β-thalassemia, HbS-HPFH; borderline range Hb variants (HbS, HbF, HbE, HbA2) with previous history of blood transfusion (3 months earlier) etc. Other investigations for anemia work up were done as per indication. Relevant demographic factors like age, sex, caste and district wise distribution was documented. Written consent was obtained in all the cases. The study was performed after approval by institutional ethical committee and carried out in accordance with the Declaration of Helisinki. All the data were analyzed by SPSS (trial) version 25.

Result

A total of 21,371 patients were enrolled during these 10 years of study period. Out of these 10,745 (50.2%) cases were diagnosed with different types of hemoglobinopathies those detail fractions are depicted in the Table 1. β-thalassemia (TDT + TT + Sickle-thal + E-thal) was determined in 5809 cases (54.06%), HbS (SCT + SCD + Sickle-thal) in 5639 cases (52.48%) and HbE in 988 cases (9.19%). Other hemoglobinopathies like α-thalassemia, HbD Punjab, Hb Lepore, HPFH were present in $< 1\%$ each.

The demographic distribution like age (median 11.4 ± 5.2 years, range 1 year to 54 years), gender, caste and domicile are depicted in the Fig. 1. Male sex, eastern part of Odisha state and patients of Other Backward Caste (OBC) were more common than their respective counter parts. There were 405 families (one member having Hb variant) constituting 965 members evaluated for hemoglobinopathies and of these 903 members were diagnosed with one type of hemoglobinopathies. In 579 cases (2.7%) no definite diagnosis could be done was considered as indeterminate group (Table 2).

Discussion

This largest prospective study in Odisha detecting hemoglobinopathies in 10,745 patients (50.2%, n = 21,371) certainly indicates its high prevalence even if not based on population screening. Distribution of HbS gene across the different parts of the state (other than western and tribal) and all types of caste (including General) are other new revelation in this study. Double heterozygous state like sickle-β-thalassemia constituting 14.99% of total hemoglobinopathies is another new observation which is considered unique to the Odisha state. HbE hemoglobinopathies (HbE trait/Homozygous/-β-thalassemia) was seen in 9.19% cases. Out of 988 cases, majority cases are inhabitants of districts like Balasore and Mayurbhanja who are adjacent to West-Bengal where its prevalence is high. Detection of few cases in other districts may be due to population migration during course of time. HbD-Punjab was detected in 8 cases who were not the origin of Punjab descent rather Odia.

Two studies in small population of a particular tribal areas of Odisha has documented TT in 6–14% and HbS hemoglobinopathy in 0.3–20.7% among general cast, 0-8.9% among scheduled cast and 0–5.5% among scheduled tribes [7, 10]. In other studies by different workers have reported hemoglobinopathy in 12.17% among general population and in 14.5–51% among cases referred to tertiary care centre for anemia evaluation [11–16].

The high prevalence of hemoglobinopathy in the present study was well explained by the fact that the study population was referred cases for evaluation of anemia in clinical hematology department of tertiary medical college hospital. The β-thalassemia and HbS genes were two most common and equally distributed. The unique high incidence of sickle-β-thalassemia (14.99%) and the wide spread distribution of HbS gene across all part of Odisha state and all types of caste could be explained by various

Table 1 Profile of hemoglobinopathies [total number of patients evaluated 21,371, total number of patients detected to have hemoglobinopathies 10,745 (50.2%)]

Disease	Number	% of total Hb-pathies (n = 10,745)	% of total anemia cases (n = 21,371)
SCD	1354	12.6	6.33
SCT	2675	24.8	12.51
TDT	1422	13.2	6.65
TT	2517	23.4	11.77
ßTHALintermedia	98	0.91	0.5
Sickle-thal	1610	14.99	7.53
HbE-disease	566	5.26	2.64
HbE-THAL	162	1.50	0.76
HbE-trait	260	2.41	1.22
α-Thalassemia	24	0.22	0.11
Hb D punjab	08	0.07	0.04
HPFH	48	0.44	0.22
HbLepore	01	0.008	0.005
Indeterminate	579	–	2.7%

SCD sickle cell disease (homozygous), *SCT* sickle cell trait, *TDT* transfusion dependent thalassemia, *TT* thalassemia trait, *HPFH* hereditary persistence of fetal haemoglobin

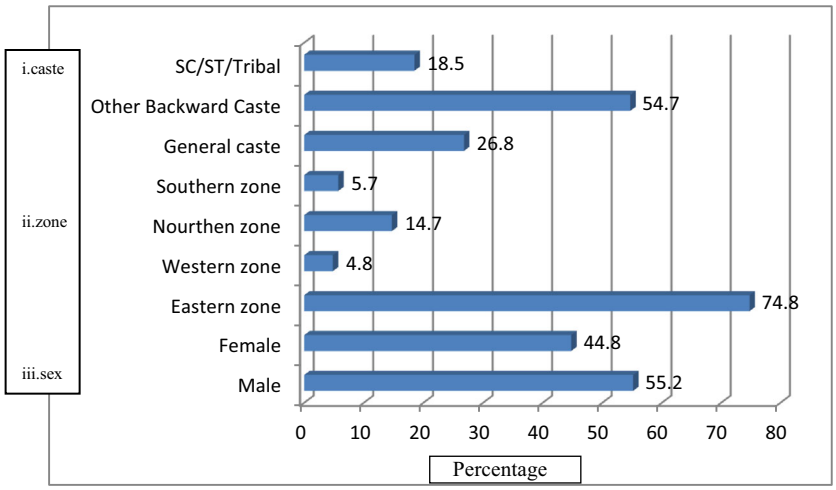

Fig. 1 Caste, zone, sex wise distribution of hemoglobinopathies in Odisha

i. General(Bramhin, Karan, Khandayat), Other Backward Caste, SC/ST/Tribal

ii. Eastern zone: Puri, Khurda, Nayagarh,Cuttack, Jagatsinghpur, Jajpur, Bhadrak,

Kendrapada, Balasore, Dhenkanal, Anugul (**The patients of these districts are usually treated in SCB medical college, Cuttack)

Western Zone: Sambalpur, Sonepur, Balangir, Baragada, Nuapada

Southern Zone: Ganjam, Gajapati, Boud, Kandhamal, Rayagada, Koraput, Nabarangpur,

Malakanagir, Kalahandi.

Northern Zone: Sundergad, Jharsuguda, Keonjhar, Deogada, Mayurbhanj.

iii. male & female distribution

Table 2 Correlation of red cell indices with haemoglobin variants

Hb variants	Cases %	Hb(g/dl)	MCV	MCH	MCHC	RBC count	RDW	HbA	HbA2	HbF	Varinat Hb
SCD	12.6	7.2 (1.3)	90.8 (10.2)	29.8 (3.4)	33.2 (1.2)	2.7 (0.4)	58.7 (6.4)	6.8 (5.6)	2.9 (0.7)	16.1 (6.7)	74.3 (4.6)
SCT	24.8	10.8 (1.7)	86.1 (3.8)	27.2 (3.4)	32.5 (2.4)	4.1 (0.6)	45.3 (14.9)	54.6 (3.8)	3.4 (0.3)	2.5 (3.2)	33.4 (3.2)
TM/intermedia	13.7	4.9 (1.6)	72.2 (6.7)	22.6 (3.7)	29.8 (2.5)	2.5 (0.7)	56.8 (11.3)	22.7 (13.8)	3.4 (0.9)	82.6 (27.6)	–
TT	23.4	10.2 (1.4)	69.7 (5.2)	20.8 (3.4)	27.2 (1.8)	4.4 (1.3)	33.9 (6.2)	87.4 (3.2)	5.2 (1.2)	2.1 (0.9)	–
Sickle-thal	14.99	6.9 (1.8)	76.2 (10.2)	22.9 (2.5)	30.2 (2.9)	2.9 (1.2)	50.6 (16.1)	4.4 (2.7)	4.7 (0.4)	22.7 (4.9)	61.8 (5.2)
HbE-disease	5.26	8.7 (1.9)	67.4 (3.2)	20.2 (2.6)	32.9 (2.7)	3.9 (0.6)	36.9 (3.1)	5.4 (1.4)		4.8 (2.9)	86.7 (12.2)
HbE-THAL	1.50	8.2 (1.2)	66.8 (5.9)	18.6 (3.3)	31.1 (1.8)	3.7 (0.9)	44.8 (5.8)	18.6 (10.5)	–	19.2 (8.7)	56.4 (4.2)
HbE-trait	2.41	11.2 (3.7)	82.4 (4.1)	26.2 (1.9)	32.8 (2.4)	3.8 (1.9)	41.1 (4.8)	67.2 (2.7)	–	1.8 (2.1)	27.4 (3.2)
α-Thal trait	0.22	7.2 (1.8)	66.2 (4.9)	16.3 (2.9)	25.9 (3.2)	4.7 (1.2)	39.1 (8.9)	86.2 (3.9)	2.5 (0.4)	0.4 (0.1)	–
Hb D punjab	0.07	8.7 (3.2)	70.9 (12.2)	20.1 (6.2)	29.2 (2.2)	4.1 (0.4)	44.6 (10.8)	57.2 (4.2)	1.5 (0.4)	0.6 (0.4)	33.4 (33.2)
HPFH	0.44	10.5 (2.9)	72.9 (5.4)	25.6 (3.1)	33.1 (2.1)	4.5 (1.3)	40.7 (8.9)	62.2 (2.7)	2.2 (1.1)	31.2 (1.2)	–
HbLepore	0.008	11.2 (2.4)	69.1 (6.1)	22.7 (2.5)	32.8 (2.4)	3.6 (1.2)	45.8 (2.1)	74.1 (4.2)	–	5.6 (2.7)	13.1 (2.3)

factors like coexistence of both HbS and β-thalassemia gene and marriage among themselves, population migration from western Odisha and tribal areas (where HbS gene was historically prevalent) to other parts of Odisha, intercaste marriage and spontaneous mutation in the globin gene.

The average HbF level in SCD (homozygous) was 16.1% which is in agreement with other studies done by Kar et al. [17] (16.64%) in Odisha and being considered to amelerioate the clinical severity in Arab-Indian haplotype of SCD. In Sickle-β-thalassemia its level was 30.1(11.8–41.4%). The average level of HbA2 were 3.5% (1.1–6.4%) and 3.2% (1.9–5.6%) in SCD and HbS-β-thalassemia respectively. The high level of HbA2 could be partly due to glycosylated HbS. Thus it is difficult to differentiate both the condition by the level of HbA2 and HbF. Microcytic red cells, significant splenomegaly and requirement of frequent blood transfusion favour the diagnosis of HbS-β-thalassemia where the evaluation of both the parents and mutation analysis could be confirmatory.

The variation in red cell indices were well explained in the literature and were consistent with other study conducted by Mandol et al. [11].

Conclusion

The reporting of high incidence of hemoglobinopathies in this institutional based study on referred cases probably indicates its high prevalence in Odisha state. β-thalassemia and HbS hemoglobinopathies are most common type (equal distribution). HbE hemoglobinopathy and others constitute 9.5% and $< 1\%$ cases respectively. This needs to be confirmed by large population based study.

Funding This study was not granted any fund.

Compliance with Ethical Standards

Conflict of interest There is no conflict of interest.

Statement of Human Rights The study was approved by institutional ethical committee and carried out in accordance with the Declaration of Helisinki.

Informed Consent Informed consent was obtained from all patients.

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