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The Spectrum of Different Types of Hemoglobinopathies and its Distribution in Various Communities Attending the Pathology Department of a District Hospital- a Study Based on HPLC Done on Tribal and Non-Tribal Patients

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Abstract

Aim: Hemoglobinopathies are a group of disorders caused by the presence of variant hemoglobin in the red blood cells. Although over 700 structural hemoglobin variants have been identified only three reach high frequencies HbS, HbC, and HbE. The tribes are vulnerable to many hereditary disorders including thalassemia. Which affect adversely the general health of an individual. This study investigates trends in hemoglobinopathies using HPLC in the tribal population where they are considered highly predominant.

Materials and Methods: A cross-sectional study with 180 patients was undertaken to study the prevalence of different types of hemoglobinopathies in tribal patients using High-Performance Liquid Chromatography in the Pathology Department of the district hospital for a period of one year.

Results: Out of 180 patients diagnosed with hemoglobinopathies using HPLC, 46 cases (25.6%) belonged to the Tribal population and 134 cases (74.4%) belonged to the non-Tribal population. The different types of hemoglobinopathies observed in the non-tribal study group were β thalassemia major (27.2%), sickle cell disease (17.7%), β -Thalassemia major (11.1%), and sickle cell trait (8.3%). The different types of hemoglobinopathies observed in the tribal study group were β thalassemia trait (10.6%), sickle β thalassemia (5%), β thalassemia major (3.9%), and sickle cell disease (3.9%).

Conclusion: The tribes are vulnerable to many hereditary disorders including thalassemia. These genetic disorders adversely affect the general health of an individual. Concerted efforts are therefore required to identify their health issues. This study for the first time provides data on the pattern of the spectrum of hemoglobinopathies in the tribal population of eastern countries of India.

Keywords: HbS; HbC; HbE; Tribal population

Introduction

Hemoglobinopathies are disorders in which the hemoglobin molecule is abnormally created or structured. The disease is inherited through families [1]. These genetic disorders are considered a very important healthcare threat in many tropical countries. Inherited hemoglobin disorders fall into two main groups: structural hemoglobin variants and thalassemia [2]. In most cases, structural hemoglobin variants are the result of a single amino acid substitution in the alpha or beta chains. Thalassemia is classified according to globin chains that are ineffectively synthesized. Although over 700 structural haemoglobin variants have been identified only three have high frequencies: HbS, HbC, and HbE [3]. More than 200 different mutations have been identified to date, resulting in significant variations in the molecular basis of β-thalassemia. However, population studies suggest that only about 20 β-thalassemia alleles likely account for more than 80% of β-thalassemia mutations worldwide [4]. Hemoglobinopathies are more common in the rural population of India. Because of unknown reasons, some geographical areas & races show very high incidences making hemoglobinopathies, a major public health problem in our country. The average prevalence of β thalassemia carriers is 3–4%, meaning there are between 35 to 45 million carriers in our diverse population of 1.21 billion people, which includes 8% approximately belonging to tribal groups according to the 2011 Census of India. Certain ethnic groups exhibit even higher prevalence rates, ranging from 4% to 17% [5,6].

India has the highest number of children with thalassemia Major globally, nearly 150,000, and sees an additional 10,000-15,000 new cases each year. Moreover, the country hosts approximately 42 million ß-thalassemia carriers, with an average prevalence rate of 3–4%. Certain hemoglobin (Hb) variants, such as HbE and HbE-beta thalassemia, are primarily concentrated in specific regions like West Bengal and the northeastern parts of India. However, due to population migration and mixing, the full spectrum of thalassemia and Hb variants is now present across the entire country [7]. The tribal population of India constitutes approximately 8.5% of the total population of India and different tribal populations have distinctive genetic makeup. These tribal populations have migrated to different areas of India because of industrial growth and job opportunities [8]. A study of hemoglobinopathies in tribal populations of India can help in deciding whether to provide hemoglobinopathy care in the tribal belt of India. Jharkhand is a state in the North Eastern part of India with several tribal groups and it is important to study the hemoglobinopathies in this region. This study aims to explore the haemoglobin variants incidence in Jharkhand.

A total of 32 tribes inhabit the state of Jharkhand in India. The tribes in Jharkhand were originally classified based on their cultural types by the Indian anthropologist, Lalita Prasad Vidyarthi.

Her classification was as follows:

- Hunter-gatherer type - Birhor, Korwa, Hill Kharia
- Shifting Agriculture - Sauria Paharia
- Simple artisans - Mahli, Lohra, Karmali, Chik Baraik
- Settled agriculturists - Santhal, Munda, Oraon, Ho, Bhumij, etc.

The Scheduled Tribe (ST) population of Jharkhand State as per the 2001 census 7,087,068 constituting 26.3 percent of the total population (26,945,829) of the State. The Scheduled Tribes are primarily rural as 91.7 percent of them reside in villages. District-wise distribution of the ST population shows that Gumla district has the highest proportion of STs (68.4 percent). The STs constitute more than half of the total population in Lohardaga and Pashchimi Singhbhum districts whereas Ranchi and Pakur districts have 41.8 – 44.6 percent tribal population. Kodarma district (0.8 percent) preceded by Chatra (3.8 percent) has the lowest proportion of the STs Population. Jharkhand has 32 tribal groups:

• Munda	• Chero
• Santhal	• Chick-Baraik
• Oraon	• Gorait
• Kharia	• Ho
• Gond	• Karmali
• Kol	• Kharwar
• Kanwar	• Khond
• Savar	• Kisan
• Asur	• Kora
• Baiga	• Korwa
• Banjara	• Lohra
• Bathudi	• Mahli
• Bedia	• Mal-Paharia
• Binjhia	• Parhaiya
• Birhor	• Sauria-Paharia
• Birjia	• Bhumij

Table 1: Carriers of β thalassemia have high levels of hemoglobin A2 and F which can be greater than 3.5% and 2% of the total hemoglobin, respectively.

The VARIANT II is a fully automated HPLC system that can be used to separate and determine area percentages for hemoglobin A2 and F and to provide qualitative determinations of abnormal hemoglobin.

The most commonly occurring hemoglobin variants include hemoglobin D, S, C, and E. Presumptive identification of these hemoglobin variants is made using retention time windows, such as “D-Window,” “S Window,” and “C-Window.”

Hemoglobin E elutes within the hemoglobin A2 retention time window using the VARIANT II β thalassemia Short Program. Differentiation from hemoglobin A2 can be made with the observation of the area percent calculation on the sample report. Hemoglobin E in the heterozygous condition (phenotype AE) is typically present in the 30 to 35% range. The VARIANT II β thalassemia Short Program also offers an automatic sampling from primary whole blood tubes, followed by sample dilution and an analysis time of 6.5 minutes per sample.

Analyte Identification Windows

Analyte Name	Retention Time (Minutes)	Band (Minutes)	Window (Minutes)
F	1.10	0.12	0.98-1.22
P2	1.39	0.11	1.28-1.50
P3	1.70	0.20	1.50-1.90
A0	2.50	0.60	1.90-3.10
A2	3.60	0.30	3.30-3.90
D-WINDOW	4.10	0.20	3.90-4.30
S-WINDOW	4.50	0.20	4.30-4.70
C-WINDOW	5.10	0.20	4.90-5.30

Table 2: P2 and P3 are minor peaks associated with haemoglobin A.

One of the major deficits in the studies of hemoglobinopathies in India among tribal populations is (i) the lack of integrated hierarchical management and diagnostic facilities for hemoglobinopathies in remote areas where the majority of the tribal populations reside, and (ii) the lack of a hemoglobinopathies registry for the country as this would be a major tool for the state and central governments to concentrate efforts to develop facilities for care and diagnosis where they are needed most.

Materials and Methods

The present study entitled "Incidence of Hemoglobinopathies in various patients using High-Performance Liquid Chromatography" was carried out in the Department of Pathology, in a tertiary center hospital over a period of one year (Dec, 2016-Nov, 2017). The study was approved by the Institutional Ethics Committee.

Inclusion Criteria

All patients diagnosed with thalassemia based on High-Performance Liquid Chromatography (HPLC) will be included in the study. It includes β-thalassemia trait, β-thalassemia major, double heterozygous conditions like Sickle-β-thalassemia, HbE-βthalassemia and HbD-β-thalassemia, sickle cell trait, sickle cell disease, and HbE trait.

Exclusion Criteria

All patients with inconclusive HPLC results will be excluded from the study. The patients have recent blood transfusions. HPLC will not be able to distinguish between the patient's cells and transfused cells.

Method Used

Cation-exchange HPLC is the method of choice for the initial screening of Hb variants and accurate quantification of Hb A2 and HbF concentrations. Bio-Rad Variant II (Bio-Rad Laboratories) is an automated cation exchange HPLC instrument that has been used to quantify HbA 2, Hb F, and HbA along with screening hemoglobin variants like HbS, HbD, HbE, and HbC in a single, highly reproducible system.

Results

Distribution of hemoglobinopathies in Tribal and Non-Tribal Patients based on HPLC.

Diagnosis based on HPLC

B-Thalassemia trait shows an incidence of 10.6% in tribals and 27.2% in non-tribals. In tribals 5% had sickle β- thalassemia and in non-tribals, 3.9% had sickle β-Thalassemia, HbE trait, HbE thalassemia, and HbE-β thalassemia and β thalassemia intermedia were not reported in the tribals.

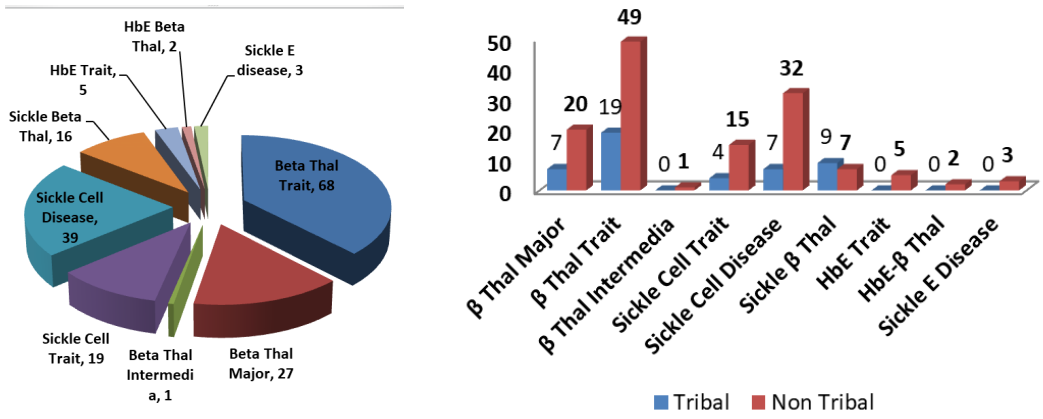
Community	No. of patients	Percentage
Non-Tribal	134	74.4%
Tribal	46	25.6%
Total	180	100%

Table 3: Distribution of hemoglobinopathies in Tribal and Non-Tribal Patients based on HPLC.

Diagnosis Based on HPLC

Diagnosis	No. of patients (Tribal + non-Tribal)	No. of patients (Tribal)	No. of patients (non-Tribal)	% Incidence in Tribals	% Incidence in Non Tribals
Thalassemia β Major	27	07	20	3.9%	11.1%
Thalassemia β Trait	68	19	49	10.6%	27.2%
Thalassemia β Intermedia	01	00	01	00%	0.6%
Sickle Cell Trait	19	04	15	2.2%	8.3%
Sickle Cell Disease	39	07	32	3.9%	17.7%
Sickle β Thalassemia	16	09	07	5%	3.9%
HbE Trait	05	00	05	00%	2.8%
HbE β Thalassemia	02	00	02	00%	1.2%
Sickle E Disease	03	00	03	00%	1.6%
Total	N=180	N=46	N=134		

Table 4: Diagnosis based on HPLC (n=180).



Figures 1&2: Diagnosis based on HPLC and incidence of hemoglobinopathies of Tribal and Non-Tribal patients.

Out of 180 patients diagnosed with hemoglobinopathies using HPLC, 46 cases (25.6%) belonged to the Tribal population and 134 cases (74.4%) belonged to the non-Tribal population. In tribal populations β thalassemia trait (10.6%) is the most common followed by Sickle β Thalassemia (5%) followed by β -Thalassemia major (3.9%) and sickle cell disease (3.9%). HbE trait, HbE thalassemia, and HbE-β thalassemia and β thalassemia intermedia were not reported in the tribals. In the non-tribal population, β thalassemia trait (27.2%) is the commonest followed by Sickle cell disease (17.7%) followed by β -Thalassemia major (11.1%), and sickle cell trait (8.3%) and minor.

Discussion

There are some studies conducted in various regions of India on the prevalence and distribution of hemoglobinopathies depicted closely match those of ours. In our study using the HPLC method in one year, 180 new patients were diagnosed with various hemoglobinopathies. In tribal and non-tribal populations β thalassemia trait (10.6% and 27.2% respectively) is the most common. Sachdev, et al. [9] found a beta thalassemia trait with a prevalence rate of 8.9% in northern India while Dolai, et al. [10] also found a prevalence of beta thalassemia trait of 10.38%. Similar findings were seen in a study done by Mondal SK, et al. [11] in which the overall beta thalassemia trait was the commonest abnormality (4.60%).

Nigam N, et al. [12] also showed that β thalassemia trait is the most common hemoglobinopathies (12.98%) in Uttar Pradesh. Nagar R, et al. [13] also reported that β thalassemia trait (3.4%) is the common hemoglobinopathies reported. Similar findings were seen in the study done by Kavitha A,

et al. [14] with the highest frequency of β thalassemia trait (69.13%). Although all these previous studies pointed to the second prevalent hemoglobinopathy to be HbE-Beta thalassemia (6.87%), which was not reported in our study. It could be because of the small sample size. In contrast, Saha S, et al. [7] study reported prevalence of the HbE trait was higher as compared to the beta thalassemia trait which could be because of the increased regional prevalence of HbE in Eastern India. Also, in contrast, Iyer S, et al. [4] study showed the HbS trait at the highest frequency (33.03%) [13] Which could be because the study included population from all over India. None of these studies were conducted on tribal and nontribal populations separately. This study has a few limitations. A major one is it took into record the cases who were symptomatic and visited the OPD. Cases that can be diagnosed on screening were not taken into consideration.

Conclusion

The results of our study showed a high prevalence of beta thalassemia trait hemoglobinopathies in both tribal and non-tribal populations. The second most common hemoglobinopathy is sickle beta-thalassemia in the tribal population and sickle cell anemia in the nontribal population. The results of our study enrich epidemiological data in our population and aid families in obtaining the most efficient genetic counselling possible. Unfortunately, our study is not without limitations and these should be mentioned: First, the sample size is limited. Second, the study was conducted in a limited geographic area, so the results may not apply to other regions. Additionally, some of the participants who were identified as carriers may have been misclassified due to the use of a single test to screen for beta thalassemia trait hemoglobinopathies. Further research is needed to better understand the prevalence of beta thalassemia trait hemoglobinopathies in different populations. Larger studies should be conducted to obtain more reliable results. It is also important to use multiple tests to accurately identify carriers of beta thalassemia trait hemoglobinopathies, as well as to include a wider geographic area to better represent different populations. Additional information that could be collected in future studies includes the socioeconomic background of the participants, as well as their family history of thalassemia or other genetic diseases. This could help to identify factors that may increase the risk of having a beta thalassemia trait hemoglobinopathies. Additionally, it would be useful to monitor the health of participants over time in order to assess the long-term effects of the condition.

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