Ethnic distribution in empirically treated cases of haemoglobin disorders at Sir Takhtasinhji General Hospital, Bhavnagar – A study of 50 cases

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ABSTRACT

Background: In Sir Takhtasinhji Hospital, Bhavnagar, a large number of anaemic patients are seen in outpatient department. Many of these have haemoglobin disorders and on some kind of empirical therapy for years The present study was carried out with the objective of determining the prevalence of haemoglobin disorders in these cases, Gender-wise distribution, family history and most importantly their ethnic distribution. **Materials & Method:** The study was conducted on total of 50 outdoor & indoor unlabelled cases of haemoglobin disorders detected at Central laboratory, Department of Pathology, Sir T. Hospital, Bhavnagar. The cases selected on basis of detailed clinical history and physical examination had been on iron / folic acid / blood transfusion therapy of ≥ 1 month. The samples were analysed using RBC indices, Discriminant functions, Cellulose Acetate & Agarose Gel Electrophoresis and HPLC and conclusive diagnosis was given. A religionwise & castewise distribution was made and analysed. **Results:** Out of 50 cases studied, 33 cases were eventually diagnosed thalassaemia major, 1 thalassaemia intermedia, 11 thalassaemia trait & 5 sickle cell anaemia. Family history was positive in 74% cases and females were more frequently affected. Religionwise majority were Hindus(74%) and castewise majority belonged to the Koli community(28%). Ethnic diversity was also observed.

Keywords: Ethnic diversity,Haemoglobin disorders,Thalassemia major, Thalassemia minor, Sickle cell anemia

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Introduction

Disorders of haemoglobin are acquired and inherited. There are two main groups of inherited disorders of haemoglobins: Structural variants / Haemoglobinopathies & Thalassaemias

with defects in the synthesis of a globin chain. Several cases show an overlap between these groups. The haemoglobinopathies may be divided further into functionally distinctive groups including (a) functionally normal clinically silent cases, (b) polymer / crystal forming cases with picture of haemolytic disease and (c) unstable ones showing chronic or intermittent haemolysis.[1]

Haemoglobinopathies affect 4.5% of the world population. In India, they are responsible for the largest number of genetic disorders and hence are of great public health importance. The prevalence of β- thalassemia trait and sickle cell in India varies between 3-17% and 1-44% respectively because of consanguinity and caste and area endogamy. Every year, ten thousand children with β-thalassemia major are born in India, which constitutes 10% of the total number in the world[2]. The average frequency of haemoglobin S (Hb S) is 4.3 % in India. Sickle gene in India is mostly found amongst Dravidian and predravidian tribes.[3] The carrier rate for β-thalassemia gene varies from 1-3% in Southern India to 3-15% in Northern India. Certain communities in India, such as Sindhi and Khatri/Arora from Northern India, Bhanushali, Kutchi, Lohana from Gujarat, Mahar, Neobuddhist, Koli and Agri from Maharashtra, Gowda and Lingayat from Karnataka, Brahmin, Khandayat, Karan, Chasa, Teli, and Gauda from the state of Orissa, etc. having comparatively a higher carrier rate.[4] The highest frequency of sickle cell gene in India is reported in Orissa followed by Assam, Madhya Pradesh, Uttar Pradesh, Tamil Nadu and Gujarat.[2] Inherited hemoglobin disorders are an important cause of morbidity and mortality.

Investigations of a person suspected to have a haemoglobin disorder encompasses a complete blood count and film, reticulocyte preparation, RBC indices & its discriminant functions, tests to exclude iron deficiency, tests for HbS, cellulose acetate electrophoresis at pH 8.5, citrate agar electrophoresis at pH 6.0, acid & alkaline agarose gel electrophoresis, quantitation of HbA_2 & HbF, automated HPLC, FPLC, differentiation of common structural variants, IEF, globin chain electrophoresis at pH 8 & pH 6.3, detection of unstable haemoglobins, detection of methaemoglobins, detection of altered affinity haemoglobins, neonatal screening and molecular techniques.[5]

This study was undertaken to analyse the religionwise and castewise distribution of haemoglobin disorders in cases visiting Sir T. General Hospital, Bhavnagar and

detect the presence of ethnic diversity in these disorders.

Materials & Method

The present study has been conducted on unlabelled cases of haemoglobin disorders detected at Central laboratory, Department of Pathology, Sir T. Hospital, Bhavnagar during a period of 9 months from November 2007 to July 2008. A total of 50 outdoor & indoor cases including 43 paediatric and adult patients with chronic anaemia on empirical treatment were chosen for the study. Another 7 cases were either parents or siblings of few of the above cases included to reach a final diagnosis. The cases selected had been on iron / folic acid / blood transfusion therapy of ≥ 1 month.

Detailed history was taken. Blood samples of these cases were collected in EDTA vacuettes. The samples were run on automated cell analyzer Nihon Kohden Celtac α 1640 for Hb, RBC indices i.e. MCV, MCH, RDW & RBC count and based on these, 6 discriminant functions were calculated Shine & Lal index, Mentzer index, Srivastava index, England & Fraser index, Ricerca index and Green & King index. Peripheral blood films were examined under high power and oil immersion lens for various morphological changes in RBCs. Reticulocyte count was assessed & Sickling solubility test performed. Based on the history, clinical features and all the above tests a probable diagnosis was made. The sensitivity, specificity, positive predictive value and negative predictive value of these indices and discriminate functions were also calculated. Haemolysates were prepared within 1 hour of collection of sample using distilled water and washed packed cells adjusting the haemoglobin to 10 g / dl. The haemolysates were then subjected to cellulose acetate electrophoresis at pH 8.5 with Tris buffer, alkaline agarose gel electrophoresis also at pH 8.5 with Tris buffer using the ready – to – use strips SAS – MX Alkaline Hb – 10 Cat. No. 100800, Helena Biosciences Europe and HPLC, BioRad Variant analyser β Thalassaemia short program. A final diagnosis was attempted based on these techniques with special attention to the limitations that were faced due to the effect of empirical therapy especially blood transfusion on the peripheral blood film picture, RBC indices & HbA, HbA_2, HbF and HbS levels. Standard Reference values were used for analysis and diagnosis.[5,6]

Results

A total of 50 cases were studied. 33 cases were eventually diagnosed

thalassaemia major, 1 thalassaemia intermedia, 11 thalassaemia trait & 5 sickle cell anaemia. Relation of family history, Gender-wise distribution and religion wise & caste wise distribution of haemoglobinopathies were tabulated as follows:

Table 1: Relation of positive family history with haemoglobin disorders

Family History	TM (%)	TI (%)	TT (%)	SCA (%)	Total
+ve	27 (81.8)	0	8 (72.7)	2 (40)	37(74)
-ve	6 (18.2)	1 (100)	3 (27.3)	3 (60)	13(26)
Total	**33 (100)**	**1 (100)**	**11 (100)**	**5 (100)**	**50**

TM –Thalassemia Major, TI- Thalassemia Intermedia, TT-Thalassemia Trait, SCA-Sickle Cell Anaemia

Family history was positive in 81.8 % , 72.7 % and 40 % cases of thalassaemia major, thalassaemia trait and sickle cell anaemia respectively.

Table 2: Gender- wise distribution of haemoglobin disorders

Gender	TM (%)	TI (%)	TT (%)	SCA (%)	Total (%)
Male	17 (51.5)	0	5 (45.5)	2 (40)	24 (48)
Female	16 (48.5)	1 (100)	6 (54.5)	3 (60)	26 (52)
Total	**33**	**1**	**11**	**5**	**50 (100)**

TM –Thalassemia Major, TI- Thalassemia Intermedia, TT-Thalassemia Trait, SCA-Sickle Cell Anaemia

In all groups, females appeared to be more commonly affected. However, this is a hospital based study and may not be representative of the actual community scenario.

Table 3: Religion wise & Caste wise distribution:

Religion & Caste	TM (%)	TI (%)	TT (%)	SCA (%)	Total (%)
Hindus	**22(66.7)**	**1(100)**	**9(81.8)**	**5(100)**	**37(74)**
Koli	8 (24.2)	0	4 (36.4)	2 (40)	14 (28)
Lohana	8 (24.2)	0	3 (27.3)	1 (20)	12 (24)
Devipujak	2 (6.1)	0	1 (9.1)	0	3 (6)
Rajput	2 (6.1)	0	0	0	2 (4)
Ahir	1 (3.0)	0	0	1 (20)	2 (4)
Brahmin	0	1 (100)	0	1 (20)	2 (4)
Darji	0	0	1 (9.1)	0	1 (2)
Bhil	1 (3.0)	0	0	0	1 (2)

Muslims	**11(33.3)**	**0**	**2(18.2)**	**0**	**13(26)**
Memon	6 (18.2)	0	2 (18.2)	0	8 (16)
Khatri	4 (12.1)	0	0	0	4 (8)
Ghanchi	1 (3.0)	0	0	0	1 (2)
Total	**33 (100)**	**1(100)**	**11 (100)**	**5 (100)**	**50 (100)**

TM –Thalassemia Major, TI- Thalassemia Intermedia, TT-Thalassemia Trait, SCA-Sickle Cell Anaemia

Out of 50 cases of haemoglobin disorders, 74% Hindus and 26% Muslims were affected. Amongst the Hindus, the Koli community (Scheduled Tribe) was the most commonly affected followed by the Lohanas(24%); whilst amongst the Muslims, Memons were the most commonly affected(16%).

Discussion

In the present study, the incidence of Thalassemia major and trait are 66% and 22% respectively which do not match with the standard data. This is because empirically treated cases were included in the study of which most were those with anaemia on repeated blood transfusions and having history suspicious of haemoglobinopathy. The prevalence of sickle cell gene in Western India varies from 0-33.5% and in the present study is 10% which is relevant. Wide variability in the prevalence of Hb-S trait is observed in population groups within small geographical areas. Apart from malaria, factors like endogamy, ethnicity and inbreeding are responsible for this variability.[7]

Majority of the patients studied were Gujaratis by origin. However, the study consisted mainly of hospital based case reports, which cannot be regarded as representative of a community or population.

As seen in **Table 1**, a high positive family history was noted in Thalassaemia trait as this category included 7 parents / siblings of thalassaemia major patients. Negative family history noted in the case of thalassaemia intermedia could be due to the fact that this condition was diagnosed in a Brahmin patient in which this is very rare and a rare mutation could have occurred. Further positive family history suggests the possibility of individual spontaneous mutations and requirement of further genetic evaluations for the same.

Table 2 shown that in the present study, the male: female ratio is 0.9:1 indicating that in more female patients were affected.

Further, Wintrobe stated that sickle cell trait is more common in females.[1] But no such correlation could be found in the small data of this study. Studies by P. Deshmukh et al also did not find any such correlation.[8] However, studies by Shah Sejal J et al[9] and Preethi BP et al[10] show higher incidence in males. Study by Patel Ashwin P et al[2] shows slightly higher prevalence of thalassemia trait in males and sicke cell trait in females in non-tribal areas.

In Table 3 represents the ethnic diversity of haemoglobinopathies detected in the study with the Koli community, a tribal population showing more cases of Thalassemia major and non-tribal communities like Brahmin and Lohana showing sickle cell. The distribution of beta thalassemia is not uniform in the Indian subcontinent. Though certain communities are identified to have high prevalence, it has been detected in almost every Indian population. Also though sickle cell gene is considered as a 'tribal' gene, with migration and mixing between the trials and non-tribals, HbS is now documented from most caste groups and states. Sujata Sinha et al also found maximum occurence of sickle cell disease & HbS β Thalassaemia in Brahmins, Thakur, Bania, Marwari and Kayasth communities in her study in Uttar Pradesh.[11] These changes in community distribution and ethnic diversity are supported by studies by Patel Ashwin P et al, Gorakshakar Ajit C., Shah Sejal J et al, Preethi BP et al and Iyer SR et al.[2,7,9,10,12]

Conclusion

Beta-thalassemia is no longer confined to specific ethnic groups; instead it is widely distributed in all castes and communities native to the corresponding states. All the sickle gene has no longer remained a pure'tribal' gene. Knowledge of this ethnic diversity can further aid in suspicion of thalassemias and sickle cell disorders which get hidden amongst the widely prevalent nutritional anaemias.

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