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HIGH PREVALENCE OF DELTA BETA THALASSEMIA AND HEREDITARY PERSISTENCE OF FETAL HEMOGLOBIN (HPFH) IN THE SATWARA COMMUNITY IN GUJARAT: AN OBSERVATIONAL STUDY

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ABSTRACT

Background & Objectives: Delta beta (δβ) thalassaemia and hereditary persistence of fetal hemoglobin are the two inherited conditions generally due to large deletions in the beta globin cluster leading to elevated levels of fetal hemoglobin (HbF) in adult life. An observational study on screening for hemoglobinopathies showed a high prevalence of δβ thalassaemia and/or hereditary persistence of fetal hemoglobin (HPFH) in a specific community at Jamnagar, Gujarat. **Materials & Methods:** Samples were analyzed on a cell counter to measure the red cell indices and hemoglobin analysis was done by automated high performance liquid chromatography (HPLC). **Result:** Of the 716 individuals, 34 (4.75%) had beta thalassemia trait, and 31 (4.33%) had other hemoglobinopathies which included six with Hb D Punjab trait ***(HBB: c.364G>C)*** (0.84%), three with Hb E trait ***(HBB: c.79G>A)*** (0.42%), two with Hb S trait ***(HBB: c.20A>T)*** (0.28%) and one with Hb Q India trait ***(HBB: c.293G>C)*** (0.14%). There were 13 individuals (1.82%) with δβ thalassemia trait, four individuals (0.56%) with HPFH, and two individuals (0.28%) had homozygous δβ thalassemia. Co-incidentally, 17 of these 19 students with δβ thalassemia or HPFH belonged to a specific community named Satwara community residing in the western part of Gujarat, India. **Conclusion:** Awareness and screening of thalassemia syndromes along with counseling in specific population is needed to reduce the burden of disease.

INTRODUCTION:

The inherited hemoglobin disorders include the thalassemias due to impaired synthesis of one of the globin chains of the hemoglobin (Hb) molecule and the structural hemoglobin variants due to amino acid substitutions. The delta beta (δβ) thalassemias are characterized by reduction in synthesis of both δ and β-globin chains, usually due to large deletions covering both the δ and β globin genes on chromosome 11. [1] Hereditary persistence of fetal hemoglobin (HPFH) is caused by at least 25 different mutations, either large deletions in the β globin gene cluster or point mutations in the γ-gene promoter regions. These two groups of disorders are sometimes difficult to differentiate due to overlapping phenotypes in heterozygous individuals. Heterozygotes of delta beta thalassemia have hypochromic, microcytic red cell indices with HbF levels usually varying from 5% to 20% which is heterocellularly distributed in red cells, whereas heterozygotes of HPFH usually have near normal red cell indices with slightly higher HbF levels ranging from 17% to 30%, with a pancellular distribution. In addition, homozygotes of HPFH are asymptomatic, whereas delta beta thalassemia homozygotes have thalassemia intermedia-like features.[2]

MATERIAL & METHODS:

A total of 716 students were screened during a thalassaemia screening camp at an Industrial Training Institute at Jamnagar in western Gujarat. The study was cleared by the Institutional Ethics Committee. Two ml of an intravenous blood sample was collected in EDTA vials after an informed consent. The RBC indices were measured on a semi-automated three-part hematology cell counter whereas screening for hemoglobinopathies was done by automated HPLC in all the individuals.

A cut off of HbA2 >3.5% was taken as a diagnostic level for β thalassaemia trait, whereas HbA2 of <4% with elevated HbF between 10-30% and normal RBC indices were considered as HPFH carriers and those with HbF between 5-20% and reduced Hb and MCV ≤80; MCH≤ 27 were considered to be heterozygous for δβ thalassaemia. A level of HbF exceeding 90 %, was considered as homozygous for delta beta thalassemia or HPFH. Mild anemia with hemolytic features favored a diagnosis of homozygous delta beta thalassaemia.

Statistical analysis was carried out in Microsoft Excel version 10.0 powered by Microsoft Corporation Pvt. Ltd.

RESULTS:

Among the 716 students screened, 576 (80.45%) were males and 140 (19.55%) were females. The age group ranged from 15-33 years. They were all unrelated individuals. The Hb A2 levels in beta thalassaemia traits ranged between 3.6 to 9% with reduced red cell indices. 65 individuals with different hemoglobinopathies were identified, the predominant one being β thalassaemia trait in 34 individuals (4.75%). The other hemoglobin abnormalities detected were HbD Punjab trait in six individuals (0.84%), Hb E trait in three individuals (0.42%), HbS trait in two individuals (0.28%) and HbQ India trait in one individual (0.14%). Also identified were 19 individuals with high HbF determinants (2.6%). Their hematological and hemoglobin findings are shown in Table-1.

Table 1: The Hematological And Hemoglobin Profile In Individuals With Elevated HbF Levels

Sr. No.	Age (years)	Caste	Hb (g/dl)	RBC ($x10^6$/µl)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)	RDW (%)	HbF (%)	HbAo (%)	HbA2 (%)
1	18	Ahir	11.3	4.9	34.8	70.4	22.9	32.5	20.1	14.9	74.4	3.0
2	19	Satwara	10.5	4.6	32.9	70.9	22.6	31.9	19.7	11.7	77.3	2.4
3	18	Satwara	13.7	5.6	42.1	75.9	24.7	32.5	16.6	14.2	74.9	2.6
4	16	Satwara	13.5	6.2	42.3	68.2	21.8	31.9	18.4	14.7	73.6	2.4
5	17	Satwara	14.4	6.0	44.6	74.6	24.1	32.3	18.2	16.9	71.9	2.9
6	19	Satwara	14.4	5.4	43.1	79.4	26.5	33.4	17.0	11.5	77.8	2.5
7	39	Satwara	12.6	4.9	37.7	76.9	25.7	33.4	14.0	20.4	69.0	2.6
8	17	Satwara	12.2	4.7	36.3	76.7	25.8	33.6	17.2	16.9	72.0	2.9
9	16	Satwara	14.0	5.9	43.2	73.3	23.8	32.4	17.4	17.2	71.6	2.6
10	19	Dalwadi	13.8	5.4	40.1	74.3	25.6	34.4	16.0	16.8	72.8	2.3
11	20	Satwara	12.1	6.0	39.5	66.3	20.3	30.6	20.2	10.9	76.8	2.3
12	18	Satwara	12.5	5.3	37.2	69.8	23.5	33.6	18.8	12.3	77.2	2.5
13	17	Satwara	13.9	5.4	42.0	77.3	25.6	33.1	17.8	18.6	71.0	2.8
14	20	Satwara	12.1	6.6	43.7	66.1	18.3	27.7	25.5	99.0	0.2	-
15	17	Satwara	9.8	4.6	32.8	70.7	21.1	29.9	23.2	99.1	-	-
16	20	Satwara	13.2	4.7	40.3	86.3	28.3	32.8	17.5	14.7	74.1	3.0
17	18	Satwara	12.6	4.5	37.9	83.5	27.8	33.2	17.7	18.4	71.0	2.6
18	17	Satwara	13.3	4.9	39.8	81.4	27.2	33.4	16.4	18.4	71.4	2.5
19	17	Satwara	14.6	5.5	43.3	78.7	26.5	33.7	18.0	22.6	67.1	2.4

Hb: hemoglobin; RBC: red blood cell count; PCV: packed cell volume; MCV: mean corpuscular volume; MCH: mean corpuscular Hb; RDW: red blood cell distribution width.

Of these 19 individuals, 13 were considered to be δβ thalassemia carriers (Sr. no. 1-13), four individuals as carriers of HPFH (Sr. no. 16-19) and two individuals as homozygous δβ thalassemia (Sr. no. 14-15) based on the red cell indices and HbF levels. The two cases of homozygous delta beta thalassaemia had mild anemia with hemolytic features.

Coincidentally, 17 of the 19 individuals of δβ thalassemia/ HPFH, were from the Satwara community. Of the total students screened, 200 of them were from the Satwara community giving a prevalence of 8.5 % of δβ thalassemia and/or HPFH in this community. Apart from this, six students (3.0%) from this community also had b thalassemia trait.

DISCUSSION:

Delta beta thalassemia and HPFH are due to a delayed switch in fetal to adult hemoglobin synthesis leading to elevated fetal Hb levels in adult life. There are only a few case reports and occasional series of cases reported from different regions in India which have shown a low prevalence of these disorders. [3-12] Molecular analysis helps to arrive at a definitive diagnosis but is not always possible at all centers and δβ thalassemia carriers are often differentiated from HPFH carriers based on phenotypic analysis. Molecular analysis done at a few referral centers have shown that the Asian Indian Inversion deletion Gg(Agδβ)^0 thalassemia was the commonest mutation followed by the HPFH-3 deletion.

In the present study the prevalence of beta thalassaemia trait was 4.75% which is somewhat higher than in our earlier study from Rajkot which is also in this region. Of the hemoglobinopathies found in the western region of Gujarat, δβ thalassemia is the fourth most commonly observed hemoglobinopathy after β thalassemia, Hb D trait and HbS trait. [13]

Two of our 19 students with high HbF determinants had mild anemia and HbF of ≥99 % with reduced RBC indices and hence they were categorized as homozygous δβ thalassemia. An earlier case report by Gupta *et al.* [4] also showed elevated HbF levels (>95%) to be the cause of homozygous delta beta thalassemia. Co-inheritance of δβ thalassemia or HPFH with a or β thalassemia mutations has also been reported from India with variable clinical phenotypes. [9, 11] Parental studies are important in such cases when molecular analysis is not possible.

In the present study, the differentiation between δβ thalassemia and HPFH was made on the basis of the percentage of fetal hemoglobin (HbF), mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH). The ICMR multicenter study in six states showed a low prevalence of δβ thalassemia and HPFH carriers (< 0.5%) [8] while a large screening survey from West Bengal found an incidence of 0.73% of δβ thalassemia and 0.18% of HPFH [5], as compared to 1.82% δβ thalassemia carriers and 0.56% HPFH carriers in our study. We observed that 200 students screened were from a single community named Satwara and 17 of them had δβ thalassemia or HPFH giving an overall unexpectedly high prevalence of 8.5% of high HbF determinants in this community.

Unlike classical β thalassemia, the clinical presentation of δβ thalassemia is mild in both heterozygotes and the uncommonly seen homozygous patients while HPFH is a benign asymptomatic condition. Nevertheless, accurate molecular diagnosis is important for prevention programmes especially when one of the partners is a carrier of β thalassemia.

In adults, the variation in HbF levels could also be associated with other disease states, including leukemias and bone marrow failure syndromes and it is important to distinguish between these other causes of elevated HbF. [14-15]

Our present study emphasizes the need for community specific screening to reduce the overall burden of hemoglobinopathies in the western part of India.

CONCLUSION:

Community based large screening programs are of utmost importance to know the prevalence of different hemoglobinopathies. Apart from commonly known communities like Sindhi, Lohana and Vankar known to have high prevalence of beta thalassemia, the present study was able to highlight the high prevalence of δβ thalassemia/HPFH in the Satwara community residing in the Saurashtra belt of Gujarat with an overall population of 81000 individuals in India.

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