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THALASSEMIA SYNDROME AND OTHER HEMOGLOBINOPATHIES: A SINGLE THALASSEMIA CENTRE EXPERIENCE FROM TERTIARY CARE HOSPITAL OF PURULIA

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ABSTRACT **Background:** Hemoglobinopathies are one of the major health burden globally including India and Southeast Asian region. This study was carried out to find out the prevalence of β-thalassemia, HbS, HbD, HbE as well as identification of asymptomatic carriers who have an increased risk of having a child with thalassemia in the western part of West Bengal.

Materials and methods: In this retrospective cohort study, the data was collected from all newly registered patients with anemia, referred from different outdoor patients in a tertiary care hospital, attending thalassemia clinic over a period of 3 years from January2018 to December2020. Detailed clinical history was taken and blood samples collected are tested with Sysmex automated blood cell counter for red cell indices. Diagnosis of hemoglobinopathy was done by G8 HPLC (high performance liquid chromatography) Analyzer by TOSOH Bioscience.

Results: A total 2297 cases were studied during the study period. The age of the patients ranged between 6 months to 60 years. Higher percentage of the study sample was at age of more than 10 years (93.8%). Among 2297 cases, 477 cases showed abnormal Hb fractions on HPLC. The following Hb abnormalities detected were following: β (beta) thalassemia trait 13.2%, β thalassemia major 2.3% followed by sickle cell trait 2.17%, HbE trait 1.8%, HbS disease 0.21%, Hb E disease 0.13%, hereditary persistence of fetal hemoglobin (HPFH) traits 0.17% and Hb D trait 0.08% along with HbE-β-thalassemia 0.30% and HbS-β-thalassemia 0.26%.

Conclusion: Among the hemoglobinopathies, β-thalassemia trait (12.9%) is prevalent in western part of Bengal.

KEYWORDS : Hemoglobinopathies, HPLC, prevalence, West Bengal

INTRODUCTION:

Hemoglobinopathies, inherited disorders of globin chain, including thalassemias and hemoglobin (Hb) variants, are the most common group of autosomal recessively inherited monogenic disorders of Hb production. [1] Apart from α- and β-thalassemia, the main structural Hb variants in hemoglobinopathies are HbS, HbE, and HbC.[2] Beta thalassemia and sickle cell disorders pose a major public health burden in India.[3]

Globally at least 60000 new patients are born with a severe form of thalassemia every year.[4] About 80% of these births occur in developing countries.5 Whereas in India, the overall prevalence of β-thalassemia is 3-4% with approximately 10,000-12,000 children are born with β-thalassemia major every year.

Mutations in globin genes may cause reduction or complete absence of synthesis of α or β globin chains, this gives rise to α or β thalassemia. When mutations in these genes cause changes in hemoglobin structure, the structural Hb variants are produced (e.g. Hb S, Hb D, Hb E).[6] When different Hb variants are inherited in heterozygous state, it can results in serious homozygous or compound heterozygous Hb variants in the offspring. Such double or compound heterozygous states between certain variants may lead to clinical manifestations.[7]

Although new clinical management including regular and safe blood transfusion based on severity of anemia along with adequate iron chelation therapy and bone marrow transplantation (BMT) as a definitive management have significantly enhanced the prognosis as well as the survival rates of the patients. Frequent hospital visits, drug intake, side effects of drugs and disease complications affects quality of life in great extent.[4]

Many government and non- government institutions endow with great efforts for prevention and control of thalassemia and other hemoglobinopathies, develop facilities for prenatal diagnosis and genetic counselling. The present study is intended to carry out to know the prevalence of β-thalassemia, HbS, HbD, HbE as well as identification of asymptomatic carriers who have an increased risk of having a child with thalassemia. As there is no sufficient data from Purulia till now, this study will help to assess the true burden of hemoglobinopathies within population of Purulia. Along with the information regarding socio-demographic condition, clinical presentations among the patients will help to formulate plan awareness programme and prevention strategies for such disease for the district of Purulia.

MATERIAL AND METHODS

This study was done in the department of Pathology of a tertiary care Hospital in Purulia in collaboration with Thalassemia clinic after getting ethical clearance. The data was collected from retrospectively in non-randomized method from all newly registered patients attending thalassemia clinic over a period of 3 years from January2018 to December2020. Patients with anaemia referred for screening of Hb disorders, patients who came up with premarital check up, antenatal mother referred for screening of Hb disorders and transfusion dependent patients were included in the study. However patient coming from area other than Purulia and patients with history of blood transfusion within 1 month are excluded from the study. A signed consent was taken from all the patients. Detailed clinical history including family history and past history of blood transfusion wherever present was obtained from each patient. Blood samples collected in ethylene diamine tetrachloride acetate (EDTA) vials were analyzed with Sysmex, automated cell counter for complete blood counts. Peripheral blood smear (PBS) examination is done to see red cells morphology for the supporting of diagnosis of hemoglobinopathies. Diagnosis of hemoglobinopathies was done by by G8 HPLC (high performance liquid chromatography) Analyzer by TOSOH Bioscience. Confirmatory tests such as sickling test, solubility test, brilliant cresyl blue test for HbH inclusions etc[21] were performed as and when required.

RESULTS

A total 2297 newly registered cases were studied during the study period of 3 years. The age of the patients ranged between 6months to 60 years. Table 1 shows the distribution of the sample according to their age groups and gender. The study showed that higher percentage of the study sample was at age of more than 10 years (93.8%). Predominant population in the study is female accounting for 1757 cases (76.4%) with male: female ratio 1:3. The distribution of different Hb patterns in the study population has been shown in Table 2. For each group of Hb

pattern, data on haematological parameters like haemoglobin (Hb), MCV (mean corpuscular volume) and MCH(mean corpuscular haemoglobin) are also recorded in Table 2. Among 2297 cases, 477 cases showed abnormal Hb fractions (19.4%) on HPLC. The most common Hb abnormality detected was β (beta) thalassemia trait present in 305(13.2%) patients. Patients with β thalassemia major/intermediate was found in 53 (2.3%) cases followed by sickle cell trait in 50 (2.17%), HbE trait in 42 (1.8%), HbS disease in 5(0.21%) and HbE disease in 3(0.13%) cases. Very few numbers of patients displayed hereditary persistence of fetal hemoglobin (HPFH) traits in 4(0.17%) cases and Hb D trait only in 2 (0.08%) cases. Amongst the compound heterozygotes, the distribution of cases was as follows: HbE-β-thalassemia 7 cases (0.30%) and HbS-β-thalassemia 6 (0.26%) cases.

Table 1- Distribution of patients according to Age groups and Gender

AGE GROUPS		NUMBERS	PERCENTAGES
	≤10 years	142	6%
	>10years	2155	93.8%
GENDER	Male	540	23.5%
	Female	1757	76.4%

Table -2 Distribution Of Haemoglobinopathies Along With Haematological Parameters Of Patients In The Present Study (n=477) (values Mentioned Are Mean ± Standard Deviation)

NAME OF HAEMOGLOBINOPATHY	NUMBERS / PERCENTAGES	Hb (g/dl)	MCV(fl)	MCH(pg)
Beta Thalassemia trait	305(13.2%)	9.7(1.5)	70.3(5.6)	20.8(3.0)
Beta Thalassemia major	53(2.3%)	5.8(1.5)	73.9(7.7)	24.5(3.3)
Sickle cell trait	50(2.17%)	10.7(1.1)	85.9(4.3)	27.1(3.3)
HbE trait	42 (1.8%)	10.4(3.4)	81.8(3.7)	26.0(1.8)
HbS disease	5(0.21%)	7.3(1.3)	82.3(7.8)	26.7(3.3)
Hb E disease	3(0.13%)	7.9(1.6)	65.8(3.1)	20.6(2.5)
HPFH trait	4(0.17%)	10.6(2.1)	72.8(5.4)	25.5(2.6)
HbE-β-thalassemia	7(0.30%)	6.1(1.4)	62.5(8.5)	17.3(2.0)
HbS-β-thalassemia	6(0.26%)	7.5(1.6)	78.3(7.4)	24.9(2.9)
Hb D trait	2(0.08%)	8.8(2.8)	72.7(13.7)	22.9(5.8)

DISCUSSION

Hemoglobinopathies are one of the major health concerns all over the world including India and Southeast Asian region.[6] The present study was conducted primarily with the patients attending Thalassemia clinic of medical college of Purulia. In this study, out of 2297 cases, 1820 cases had normal and 447 cases showed abnormal haemoglobin fraction in HPLC. So, in this present study, the prevalence of the Hb disorders was seen to be 19.4% which is more than the study conducted in West Bengal by Santosh et al[8] and lesser than another study done in the southern part of West Bengal where the prevalence of such disorders were found to be 25%[9]. In a study from Western India, out of 7261 cases, 1615 (22.24%) cases showed abnormal Hb fractions.[10] The largest screening programme for thalassemia in Gujrat among youth and pregnant women, showed prevalence of carrier rate varied from 4.3% to 5.0%, carried out by the Indian Red Cross Society from 2004 to 2010 over 370,117 subjects.[16] Results on haemoglobin parameters of different haemoglobin patterns are quite similar to the study of Santosh et al[8].

In the present study, β-thalassemia trait constitutes 13.2%% of the study population. The greater prevalence rate of β-thalassemia trait is seen in more than 60 countries accounting carrier population upto 150 million.[11] Around 1.5% of the world's population was carriers of β thalassemia as per report of Colah R *et al*.[12] In the Indian populations, the prevalence of β-thalassemia carriers is 3-4%. Some ethnic groups like Sindhis, Kutchis, Lohanas, Bengalese, Punjabis, few Muslim groups as well as few tribal populations have a higher prevalence (5-17%).[13,14] Madan *et al* reported in their study as the prevalence of β-thalassemia trait was 5.5% in northern India, 2.7% in western India and the overall frequency was 4.05%.[13] Another multicentre study conducted by the Indian Council of Medical Research on college, university students and pregnant women from different cities of eastern India (Kolkata, West Bengal), north east India (Dibrugarh, Assam) and southern India (Bangalore, Karnataka) showed prevalence of β-thalassemia carriers was 3.64%, 1.48% and 2.16%, respectively.[14] Whereas a study from West Bengal by Mondal *et al* shows the prevalence of β-thalassemia trait was 6.61%[7] and Dolai TK et al shows as high as 10.38% in the rural parts of West Bengal.[15] Another study with 1726 cases based on hemoglobinopathies in tribal population of Eastern and North-eastern India, including 463 cases from West Bengal showed the prevalence of β-thalassemia carrier of 5.18%.[16]

Another important variety of hemoglobinopathy throughout the world is Hemoglobin E thalassaemia. In a older study by Chernoff *et al* , there were 1403 cases of HbE trait having prevalence of 2.78% in their study population.[17] Whereas in a recent multicentre study conducted by the Indian Council of Medical Research covering mostly city based population showed the prevalence of HbE trait as 3.92% in Kolkata and 23.90% in Dibrugarh. Few patients with δβ-thalassemia, HPFH, HbS trait, HbD trait, HbE homozygous and HbE β-thalassemia as well as HbS homozygous and HbS-β-thalassemia (<1 %) were also identified in this study.[14] Whereas in the present study, the prevalence of HbE trait found was 1.7%, that of HbE β-thalassemia and HbE homozygous was 0.26% and 0.13% respectively.

In a comprehensive study from a larger population in West Bengal from Eastern India showed HbE trait 2.78%, sickle cell trait 0.56%, β-thalassemia major 0.73%, HbEE 0.05%, compound heterozygosity for HbE-β-thalassemia 0.42%, and HbS-β-thalassemia 0.15%.[7] A recent report on screening from rural areas in West Bengal showed that the prevalence of HbE carriers was 4.3 % and whereas HbS and HbD carriers was 1.12 % and 0.37 %, respectively.[15] Another study from rural areas of West Bengal showed the prevalence of HbE trait to be 3.86% and that of Eβ thalassemia to be 1.25%.[18] Whereas it has been noted in the present study that prevalence of sickle cell trait, sickle cell disease and HbS-β-thalassemia constitutes 2.17%, 0.21% and 0.26% % of study population respectively.

Other variants detected in very few numbers are hereditary persistence of fetal hemoglobin (HPFH) trait (0.17%) and HbD trait (0.08%) in this present study. Very few cases of HPFH have been reported from western India and Kolkata.[19] 0.18% of HPFH cases has been reported in ICMR multicenter study.

India has extremely diverse group of population comprising of more than 3,000 ethnic groups. [14] Due endogamous norms of marriages in India usually among individuals of the same caste or ethnic group, it becomes very important to know the prevalence of β-thalassemia and also HbE in different ethnic groups. Treatment of hemoglobinopathy especially thalassemia is a huge financial burden to society. Illiterate populations are ignorant about the medical, social and financial burden of the disease. This further compounds the problem. Very few patients are able to have a permanent cure in the form of blood and marrow transplants due to nonavailability of human leukocyte antigen-matched donors coupled with lack of infrastructure and financial resources in India like developing countries.[20]

So extensive screening programme and prenatal diagnosis should be done through nationally coordinated programmes in order to reduce drastically the birth of affected children. As the prevalence rate is variable even within small geographic regions and many ethnic groups have not been studied. This study should be done in a large population to provide a comprehensive database on the spectrum of hemoglobinopathies in Purulia.

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