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DISTRIBUTION OF HEMOGLOBINOPATHIES AMONG PATIENTS ATTENDING HAEMATOLOGY UNIT OF A RURAL GOVERNMENT MEDICAL COLLEGE OF WEST BENGAL, INDIA-A SINGLE CENTRE BASED STUDY

Pathology

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ABSTRACT

B-thalassaemia is a heterogeneous group of inherited disorder of haemoglobin synthesis, characterized by a reduction of (β^+) or absence (β^0) of synthesis of beta globin chains of haemoglobin .Haemoglobinopathies are a group of genetic disorders of haemoglobin (Hb). Thalassemia syndromes are a heterogeneous group of single gene disorders, inherited in an autosomal recessive manner, prevalent in many parts of the world. Worldwide, 15 million people have clinically apparent thalassemic disorders.Prevalence of Hemoglobinopathies in West Bengal, India, is around 3.3%, although there are marked regional differences in incidence. The carrier rate for the β-thal gene varies from 1 to 3% in Southern India to 3 to 15% in Northern India.In this background of scientific knowledge the present study was conducted with aim to find out distribution of thalassaemia and other haemoglobinopathies in patients with anaemia attending haematology unit of a medical college. The present study analysed different fractions of hemoglobin of 2650 subjects attending the Haematology of a rural Medical College. It was seen that 22.71% of subjects had haemoglobin disorder and 77.29% of subjects were normal out of total 2650 subjects studied. Among screening group, the number of parental screening is maximum (44.52%) followed by suspect screening (30.74%) and then antenatal screening group(9.46%). In the 1yr to10yrs age group, the distribution of Beta thalassaemia major was 82%, that of HbE-Beta thalassaemia (47.70%) and HbS-Beta thalassaemia was found to be 47.06%. A high prevalence of Beta thalassaemia trait(42.29%) was noted in 20 yrs-30yrs age group followed by (23.60%) in 30yrs -40yrs age group.

KEYWORDS

Haemoglobinopathies, Thalassemia, suspect screening.

Haemoglobinopathies are a group of genetic disorders of haemoglobin (Hb). Defects in genes of haemoglobin can produce abnormal haemoglobins and anaemia, which leads to conditions, termed as "haemoglobinopathies"[1,2,3].B-thalassaemia is a heterogeneous group of inherited disorder of haemoglobin synthesis, characterized by a reduction of (β^+) or absence (β^0) of synthesis of beta globin chains of haemoglobin[4].

These hereditary disorders of haemoglobin pose a massive health problem in many countries including India[5,6]. WHO figures estimate that 5% of the world population is carrier for haemoglobin disorders [7]. The frequency of β-thalassaemia in India ranges from 3.5 to 15 % in general population. Every year 10,000 children with thalassaemia major are born in India, which constitutes 10 % of the total numbers in the world [8,9,10] . The average frequency of haemoglobin S (Hb S) is 4.3 % in India. Haemoglobin E (Hb E) is mostly present in the northeastern states of India [11,12] . Frequency of Hb E in Assam is 52 %, 7 % in Manipuris and 3.33% in West Bengal [9,13] . The frequency of Haemoglobin D (Hb D) has been reported to be 0.5 to 3.1% in different castes of Uttar Pradesh and Punjab [14,15,16] . Hb D has also been reported from Bengal, Bihar, South India and Gujarat [17] . The coexistence of β and HbE gene makes the population of our state west Bengal vulnerable to get both β thalassemia and HbE β thalassemia.

In this background of scientific information the present study was conducted with aim to find out distribution of thalassemia and other hemoglobinopathies in those with patients who presented themselves with anemia in the OPDs of a a Government run medical college of West Bengal.

MATERIALS AND METHODS :

This study was conducted at the Haematology Unit of the Department of Pathology, of a government run Medical College of west Bengal after receiving approval from the Institutional Ethical Committee. The study included 2650 participants referred for screening of Haemoglobinopathies for a period of one year. All the patients in the age group 6months to >50 years who presented in the OPD with anemia during the period of one year were considered for this study. Total number of cases was 2650 and known cases of thalassemia and hemoglobinopathies among them were 602.

Following Parameters were studied: History and clinical examination, Hemoglobin level, Total count of RBC, Red cell indices (PCV MCV,MCH,MCHC,RDW),Total count of WBC, Platelet count, Peripheral Blood Smear (stained by Leishman's stain), Reticulocyte count, High performance liquid chromatography for Hemoglobin (HPLC) ,Serum ferritin estimation as and when required.

Following Study tools were used : Clinical examination sheet , Measuring tape ,Weighing machine , Growth chart recommended by Indian Association of Pediatrics, Hemoglobin estimation by cyanmethemoglobin method , SYSMEX KX21 automated blood cell counter , For peripheral blood smear – glass slides, leishman's stain ,For Reticulocyte count – glass slides, new methylene blue stain and glass wares , BIORAD variant hemoglobin testing system .

First of all, history regarding age, sex, religion, address, family history of any illness was taken. They were inquired for onset of symptoms, weakness or lethargy, poor feeding, jaundice, recurrent fever, cough and cold, diarrhoea, painful crises and ulcers. History of blood transfusion and splenectomy also were taken. Height and weight of the child (1-12years) were measured. Detailed clinical examination was done. 3ml of EDTA blood and 2ml of clotted blood was collected from selected patients with prior written consent. A blood slide was drawn from the fresh blood.

RESULTS :

Our study showed high incidences β-thalassaemia major(82%) in the

age group of 1 yr-10yrs and high incidences β-thalassaemia heterozygous (42.29%) in the age group20-30yrs, BTT with raised HbF(50%) in the age group 10-20 yrs.Age group wise breakup showed (1-10yrs) age group with high incidence of HbE- βthalassaemia(41, 47.70%)followed by 10-20yrs group(32,37.20%). Hb E trait is maximum(39.14%) in 20-30yrs age group.

The present study clearly shows that most of the patients of severe hemoglobin disorders were from the age-group 1yr-10 yrs with comparatively less number of patients from the age-group 10-20 yrs and 20-30 yrs respectively and rarely from older age-groups.

Present study showed patients with HbE β thalassaemia were suffering from very low haemoglobin value(6.25 gm%) and high RDW(cv) 30.31. Patients with HbE disease had mild anaemia(Hb 9.96gm%) and had low MCV(59.22).It was also seen that mean HbA2 was 3.69 and HbF 26.78 in beta thalassaemia major & child were symptomatic, in beta thalassaemia minor or carrier state HbF was 1.03 &only mean HbA2 was 4.95.

Results of the study are tabulated and presented below.

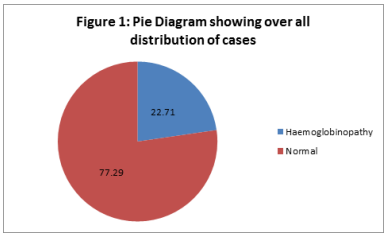

Figure 1: Pie Diagram showing 22.71% (n=602) total haemoglobi nopathy and normal subjects 77.29% (2048) out of Total subjects (N=2650).

Table 1: Age-wise distribution of subjects of β-Thalassaemia Major, β-Thalassaemia trait &β thalassaemia trait↑HbF

Age in years	β-thalassemia Major(BTM) No.(%)	BTT(β thalassaemia trait) No. (%)	BTT+raised HbF No. (%)
½- 1	02 (04)	0	0
1 yr – 10 yrs	41 (82)	23 (7.54)	0
10 yr – 20yrs	07 (14)	44 (14.42)	03 (50)
20 yrs – 30 yrs	0	129 (42.29)	02 (33.34)
30 yrs – 40 yrs	0	72 (23.60)	01 (16.66)
40 yrs – 50 yrs	0	23 (7.54)	0
≥50 yrs.	0	14 (4.59)	0
Total	**50**	**305**	**06**

Table No. 1 shows high incidences β-thalassaemia major(82%) in the age group of 1 yr-10yrs and high incidences β-thalassaemia heterozygous (42.29%) in the age group20-30yrs, BTT with raised HbF(50%) in the age group 10-20 yrs.

Table No. 2: Age wise distribution of subjects of HbE-β Thalassa emia, HbE trait, HbE trait with ↑HbF, HbE homozygous, HbE homozygous with↑HbF.

Age in years	E Beta thalassae mia No.(%)	HbE trait No.(%)	HbE trait+rai sed HbF No.(%)	HbE homozygo us No.(%)	HbEE+ raised HbF No.(%)
½- 1	02(2.32)	0	0	0	0
1 yr – 10 yrs	41 (47.70)	08 (10.12)	0	0	0
10 yr – 20yrs	32 (37.20)	17 (21.42)	01(100)	01(33.33)	01(50)
20 yrs – 30 yrs	08 (9.30)	31 (39.14)	0	01 (33.33)	0
30 yrs – 40 yrs	02 (2.32)	17 (21.78)	0	01(33.33)	0
40 yrs – 50 yrs	01 (1.16)	05 (6.32)	0	0	0
≥50 yrs.	0	01(1.22)	0	0	01(50)
Total	**86**	**79**	**01**	**03**	**02**

Table no.2 shows (1-10yrs) age groupwith high incidence of HbE-β thalassaemia(41, 47.70%)followed by 10-20yrs group(32,37.20%). Hb E trait is maximum(39.14%) in 20-30yrs age group.

Table no. 3: Incidences of different thalassaemias at different age groups

		Age in years						
	Sex	0.5-1	1-10	10-20	20-30	30-40	40-50	>50
Thal Major(50)	Male	3	24	2	-	-	-	-
	Female	3	16	2	-	-	-	-
	Total	6	40	4				
E-Beta thalassae mia (86)	Male	01	22	15	02	01	00	00
	Female	02	22	14	05	01	01	00
	Total	03	44	29	07	02	01	00
S-β thalassae mia (18)	Male	00	07	02	01	00	01	00
	Female	00	02	04	01	00	00	00
	Total	00	09	06	02	00	01	00

Table no. 3 clearly shows that most of the patients of severe hemoglobin disorders were from the age-group 1yr-10 yrs with comparatively less no. of patients from the age-group 10-20 yrs and 20-30 yrs respectively and rarely from older age-groups.

Table no. 4: Red cell indices of β-thalassaemia major(BTM), β-thalassaemia trait(BTT), β-thalassaemia trait with↑ed HbF(BTT with ↑ed HbF)

Laboratory parameters	B-thalassaemia major (mean)	B-thalassaemia trait (mean)	B-thalassaemia trait ↑ed HbF(mean)
Haemoglobin(g m %)	5.79	10.98	8.89
Total count of RBC	2.43	5.35	4.24
PCV (ml/ml)	17.44	37.46	29.88
MCV	76.46	67.16	68.56
MCH	24.99	20.5	20.71
MCHC	32.44	30.38	29.61
RDW(cv)	23.84	16.64	18.23

Above table 4 shows patients are suffering from severe anaemia(Hb 5.79%) and value of RDW(cv) is markedly increased(23.84).

Table no. 5: Red cell indices of HbE thalassaemia syndrome

Laboratory parameters	HbE thalassaemia trait(mean)	HbE-β Thalass aemia (mean)	HbEE diseas e (mean)	HbE thalassaemi a trait with ↑ed HbF(mean)	HbEE disease with ↑ed HbF(mea n)
Haemoglobin (gm%)	11.80	6.25	9.96	12.7	7.90
Total count of RBC	5.19	3.31	5.45	4.95	5.02
PCV(ml/ml)	36.8	22.7	31.5	38.00	28.00
MCV(fl)	76.47	67.43	59.22	76.80	55.80
MCH	24.54	18.93	18.70	25.70	15.70
MCHC	32.09	28.07	31.56	33.40	28.20
RDW(cv)	14.74	30.31	18.92	15.20	25.00

The above table 5 shows patients with HbE β thalassaemia are suffering from very low haemoglobin value(6.25 gm%) and high RDW(cv) 30.31. Patients with HbEE disease have mild anaemia(Hb 9.96gm%) and have low MCV(59.22).

Table No. 6: HPLC diagnosis of β thalassaemia major (BTM), β thalassaemia trait(BTT) &BTT with ↑edHbF

Presumptive HPLC diagnosis	B thalassaemia major (mean)	B thalassaemia minor (mean)	BTTwith ↑ed HbF (mean)
HbA2(%)	3.69	4.95	81.4
HbF(%)	26.78	1.03	5.1
HbA(%)	59.74	84.44	5.30

Table no.6 shows HbA2 3.69 and HbF 26.78 in beta thalassaemia major & child is symptomatic, in beta thalassaemia minoror carrier state HbF is 1.03 &only HbA2 is4.95.Patient is not symptomatic.In BTT with ↑HbF HbA is very low only 5.30%

DISCUSSION :

Thalassemia syndromes are a heterogeneous group of single gene disorders, inherited in an autosomal recessive manner, prevalent in

many parts of the world. Worldwide, 15 million people have clinically apparent thalassemia disorders (3). The estimated prevalence of carriers of β-thal Prevalence of Hemoglobinopathies in Bengal, is around 3.3% (1), although there are marked regional differences in incidence. The carrier rate for the β-thal gene varies from 1 to 3% in Southern India to 3 to 15% in Northern India[18,19].The distribution and prevalence rates of different hemoglobinopathies within the state of West Bengal, especially the rural areas where the majority of the population reside, are not known with certainty due to lack of comprehensive surveys. The current study addresses this burning issue.

As the thalassemia carrier rate inWest Bengal is high but varies from area to area, knowledge of local prevalence data will help in planning and implementing appropriate screening procedures.

Our study shows high incidences β-thalassaemia major(82%) in the age group of 1 yr-10yrs and high incidences β-thalassaemia heterozygous (42.29%) in the age group20-30yrs, BTT with raised HbF(50%) in the age group 10-20 yrs. Also the study obviates (1-10yrs) age group with high incidence of HbE-β thalassaemia(41, 47.70%)followed by 10-20yrs group(32,37.20%). Hb E trait is maximum(39.14%) in 20-30yrs age group.The study also clearly shows that most of the patients of severe hemoglobin disorders were from the age-group 1yr-10 yrs with comparatively less no. of patients from the age-group 10-20 yrs and 20-30 yrs respectively and rarely from older age-groups.The study also reveals patients with HbE β thalassaemia are suffering from very low haemoglobin value(6.25 gm%) and high RDW(cv) 30.31. Patients with HbEE disease have mild anaemia(Hb 9.96gm%) and have low MCV(59.22).Furthermore the study elaborates HbA2 3.69 and HbF 26.78 in beta thalassaemia major & child is symptomatic, in beta thalassaemia minoror carrier state HbF is 1.03 &only HbA2 is4.95.Patient is not symptomatic.In BTT with ↑HbF HbA is very low only 5.30%

An impressive number of 796 cases of thalassemic syndrome were investigated by J.B Chatterjee in the School of Tropical Medicine[18]. It was reported that 190 out of 796(24%) cases had β thalassaemia, 526(66%) had HbE β thalassaemia and 12(1%) Hb- β-thalassaemia. So thalassaemia was the major public heath problem in west Bengal. So recent data indicate that about 10% of the population is carrier of Hb disorder, commonly found in the heterozygous state of β-thalassaemia. Major form and symptomatic thalassaemia is Hb E β-thalassaemia.

In a study[19] in 2009 SK Dutta, A Chatterjee and AK Manna showed β-thalassaemia Major 30%, E-β Thalassaemia 5.3% and other small proportion of cases were Sickle –β thalassaemia HbS and HbD.

Our study showed E-β thalassaemia 14.28% which is higher than the above study and β thalassaemia Major is 8.30% that does not coincide with the study before.

S.K. Dutta et al.[20] showed 10.73% β-thal minor, 0.35% HbE heterozygous, 0.18% were sickle cell trait and 0.12% was HbS/HbE diseases , 0.6% HbD/HbE.

Our studies showed 50.66% β-thal. Heterozygous or carrier and HbE heterozygous was 13.12% & sickle cell heterozygous 5.48%, which are very high values than the other studies.

BM Das , MR Chakraborty H Delbruck et al[21] examined 2 groups of tribal communities in Assam, India. Among 80 Khasi (Bhoy subgroup showed 41% HbE heterozygous), who are austroasiatic tribal group and in 82 Ahom group , a group related to thai population , 58% of HbE carriers were found.

The present study showed 13.12% HbE heterozygous, 14.28% had Hb-E-β-thal & 0.49% HbE homozygous. So this study presents low prevalence in comparison to above study.

Chatterjee JB , Saha TK, RN Ghosh et al[22]studied 796 cases of thal syndrome in the School of Trop. Med. , Kolkata. It was reported that 24% cases had β-thal(BT), 66% had HbE-β-thal, 1% HbS-β-thal.

The present study showed incidence β thalassaemia minor or heterozygous state in Burdwan and Birbhum , Bankura, smaller area of Murshidabad district of West Bengal about 50.66% and β thalassaemia major 8.30%. This study indicates higher prevalence of β thalassaemia minor in these districts specially Burdwan , one of most populated district town .

It is worthwhile carrying out appropriate screening programs designed to detect most carriers, according to prevalence rates of the different carrier states in the region being screened.

Increasing awareness of the disease by education of not only the public but also the medical fraternity is mandatory for adequate control of these genetic disorders.

CONCLUSION

The present study was carried out and analysis of 2650 subjects of symptomatic or asymptomatic anaemia attending to the Thalassaemia wing ,Haematology Unit in the department of Pathology, Burdwan Medical College was done. It had been seen that 22.71% of subjects had haemoglobin disorder and 77.29% of subjects were normal out of total 2650 subjects studied . Among screening group, the number of parental screening is maximum (44.52%) followed by suspect screening (30.74%) and then antenatal screening group(9.46%), family member , sibling, premarital and other screening in decreasing order.

About age wise distribution in the present study, the distribution of Beta thalassaemia major is 82%, that of HbE-Beta thalassaemia (47.70%) and distribution of HbS-Beta thalassaemia as 47.06% were observed in the 1yr to10yrs age group.There was high prevalence of Beta thalassaemia trait(42.29%) in 20 yrs-30yrs age group followed by (23.60%) in 30yrs -40yrs age group in the present study.

The present study provides the broad overview of the burden and spectrum of hemoglobinopathies in this region of country. We emphasize that a routine premarital screening program is necessary.

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