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Original Research Article

Spectrum of Hereditary Hemolytic Anemia-A Tertiary Care Hospital Based Study

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Abstract: Hereditary hemolytic anemias are broad category of hematological disorders that include hemoglobinopathies, enzymopathies and membrane disorders. Though most of the cases are clinically in apparent still hereditary hemolytic anemias particularly hemoglobin disorders are a considerable health problems in India and contributes significantly to morbidity and motality. These group of anemias have various clinical presentations with symptoms and signs. Failure to thrive, anemia, prostration, jaundice, spleenomegaly, cholelithiasis, cardiomegaly, severe life threatening infections and chronic disabilities leading to distress in the families. An analysis of 135 cases of hereditary hemolytic anemias were done in the present study. On the basis of clinical presentation physical findings, routine hematological investigations and hemoglobin electrophoresis pattern in hemoglobin defects were carried out to identify the type of hemolytic anemias. This clinicohematological study of hereditary hemolytic anemias showed 34(25.1%)cases of G6PD deficiency. The remaining 101(74.9%) cases were having diseases affecting hemoglobin molecule which included 58cases of sickle cell trait,17cases of sickle cell disease,4() cases of sickle beta thalassemias, 2 cases of Hbs/HPFH,16 cases of thalassemia trait and 4 cases of HbEdisorders. Out of 135 patients 75(55.5%) were males and 60 (44.5%)were females(M:F - 1.9:1). All the patients were from Eastern ODISHA. Family history was positive in 15 patients. Hereditary Hemolytic anemias with membrane defects were not observed in this study. Majority of the patients presented with progressive pallor and hepatospeenomegaly. Peripheral blood smear examination showed varied picture like microcytic hypochromic and normocytic normochromic anemias. Majority of the cases were associated with reticulocytosis. Hemoglobin electrophoresis confirmed the diagnosis in majority of cases. The basic hematological investigations remain the first panel or step towards the approach to diagnose hereditary hemolytic anemia in spite of advanced diagnostic investigations. Hemoglobin electrophoresis will help in confirming the diagnosis. In many cases the hematological findings may be subtle and need careful evaluation including family studies.
Keywords: Hereditary hemolytic anemia, clinicohematological study , hemoglobin electrophoresis.

INTRODUCTION:

Hereditary hemolytic anemias are group of disorders characterized by intrinsic defect in red blood cells associated with accelerated erythrocyte destruction, hyper bilirubinemia and erythroid hyperplasia. These group of disorders includes defect in red cell membrane such as hereditary spherocytosis, elliptocytosis, presence of abnormal hemoglobin synthesis- sickle cell a naemia, impaired globin synthesis- Thalassemia and defect in erythrocyte enzymes such as G6PD, pyruvate kinase deficiency[1].

The pattern of prevalence of different genetic hemolytic anemias have been studied extensively world wide as well as different states and communities in our country. Previous studies have identified that particular abnormal gene is more prevalent in particular region like β thalassemia in north- west (Sindhis, Gujaratis and Punjabis) and for far East (Bengalis and Muslims),

alpha thalessemia in tribal population of Andhra Pradesh and Gujurat, Sickle cell anemias predominantly in central India, HbE disease in North east part of India and HbD in Punjabi population of north india[2-5].

Hereditary hemolytic anaemias constitute important cause of mortality and morbidity in developing countries next only to infection and malnutrition. These group ofanaemias have various clinical presentations with symptoms and signs of failure to thrive, anaemia, prostration, jaundice, spleenomegaly, cholelithiasis, cardiomegaly, congestive cardiac failure, severe life threatening infections and chronic disabilities leading to distress in the families. The world health organization(WHO) has estimated that about 5% of the world population are carriers for different inherited disorders of hemoglobin[6].

These group of patients have preliminary hematological, biochemical and laboratory findings which help in deciding the further diagnostic work-up for accurate diagnosis. In many cases the hematological findings may be subtle and need careful evaluations including family studies.

MATERIAL AND METHODS

The study was carried out in patients presenting to department of medicine and pediatrics,kalinga institute of medical sciences with clinical diagnosis suggestive of hereditary hemolytic anemia. The study included patients mostly from Eastern part of ODISHA. The period of study was 2and1/2yrs.Patients with history of recent transfusion(previous three months)and children less than 6 months of age were excluded from the study. Informed consent was obtained in each case.

Detail history of the patient including Name, Age, Sex, Address, Presenting complaints, past history, family history, transfusion history was taken. EDTA anticoagulated blood was drawn from all the patients with proper aseptic procedure. Samples were analysed in fully automated counter in the hematology Laboratory of department of pathology. Multiparameter hemogram including hemoglobin, hematocrit, MCV, MCH, MCHC, RDW, RBC count, WBC count, Platelet count and Manual reticulocyte count using supravital stain were done. Leishman stained peripheral blood smears were analysed. Differential count, redcell morphological alteration (hypochromasia, anisopoikilocytosis, sicklecells, targetcells, spherocytes, polychromasia, nucleated red cells)were noted. On the basis of clinical history, examination findings and preliminary laboratory results further investigations were carried out for diagnosis of various hereditary hemolytic anemias. Special diagnostic tests like sickling test was done by using sodium metabisulfatesolution as a reducing substance.

Type and quantification of various hemoglobin variants was performed by fully automated cation exchange high performance liquid chromatography(HPLC)using BIORAD VARIANT II(manufactured by BIO-RAD laboratories, USA) . 4 ml of EDTA anticoagulated blood was collected from each case. The samples were stored at 2-8 degree C and tested within one week of collection. Sample was loaded in the instrument and analysis was carried out. The printed chromatogram showed all hemoglobin fractions eluted according to retention times. The areas under the peak showed the value of different hemoglobin components. Avaule more than 3.5% of A2 fraction of hemoglobin was taken as cut off point for diagnosing thalassemia trait. Associated iron and Vit-B12 deficiency were ruled out. Patient who had peak identified at S window were diagnosed as sickle cell trait, sickle cell disease or sickle cell β thalassemia. Results of HPLC were correlated with clinical profile and family studies.

Red cell enzyme assays were performed in selected cases.

Serum Bilirubin (Direct and indirect) estimation was done in all the cases clinically presented with jaundice and correlated accordingly.

Data collected in this study was organized, tabulated and analysed. The data analysis was done with the help of SPSS 16.0 softwere.

RESULT AND DISCUSSION:

Clinicohematological study of hereditary hemolytic anemias was done on 135 cases during the period of 2 and 1/2 years. Out of 135 cases 87 (64.4%) were in the pediatric age group (0-18yrs) and remaining 48 (35.6%) were in adult age group (>18 years). The distribution of cases among male and female were of 55.5% and 44.5% respectively (M:F- 1.9:1). In the pediatric age group as well as in adult age group sickling syndrome was of highest number approximately $3/5^{th}$ of the total cases. Proportion of cases with G6PD defect were 34(25.1%). Thalassemia syndrome were 16(11.9%).Only 4(3%) cases of other haemoglobinopathies were reported. (Table-1).Some of the other hospital based studies have also shown higher propertion of sickle cell trait cases in comparison to other hemoglobin disorders. In a previous study by

Balgir et al[7]which included predominantly symptomatic patients from same part of the country, Sickle cell trait was found to be the most common hemoglobin disorder followed by sickle cell disease and sickle beta thalassemia.

Table-1: distribution of Hereditary Haemolytic Anaemia by Age and Gender

Age group	Hereditary Hemolytic Anaemia	SEX					
		Male		Female		Total	
Child		No.	%	No.	%	No.	%
	Thalassemia Syndrome	10	19.2	5	14.3	15	17.3
	Sickling Syndrome	33	63.5	20	57.1	53	60.9
	Other Haemoglobinopathy	0	0.0	0	0.0	0	0.0
	G6PD Deficiency	9	17.3	10	28.6	19	21.8
	Total	52	100.0	35	100.0	87	100.0
	Cho Square- 3.101, p= 0.376						
Adult	Thalassemia Syndrome	0	0.0	1	4.0	1	2.1
	Sickling Syndrome	14	60.9	14	56.0	28	58.3
	Other Haemoglobinopathy	2	8.7	2	8.0	4	8.3
	G6PD Deficiency	7	30.4	8	32.0	15	31.3
	Total	23	100.0	25	100.0	48	100.0
	History of Pregnancy			5	20.0	25	100.0
	Chi Square- 1.379, p=0.710						
Total	Thalassemia Syndrome	10	13.3	6	10.0	16	11.9
	Sickling Syndrome	47	62.7	34	56.7	81	60.0
	Other Haemoglobinopathy	2	2.7	2	3.3	4	3.0
	G6PD Deficiency	16	21.3	18	30.0	34	25.1
	Total	75	100.0	60	100.0	135	100.0

58(71.6%) cases of sickle cell trait, 17(21%) cases of sickle cell disease, 4(4.9%) cases of sickle β thalassemia and 2(2.5%) cases of HBS/ HPFH were diagnosed. This group of patients had variable clinical profile. Positive sickling test was observed in all the cases. Peripheral smear examination revealed presence of occasional to numerous sickle cells.

Differential diagnosis of sickle cell disease and HBS/HPFH could not be conclusively made based on hematological parameters and needs complete family study.

Differential diagnosis of sickle cell disease and Sickle cell beta thalassemia could not be conclusively made based on presence of increased HbA2 level and needs complete family study and coexistant deficiency anemias.

All the thalassemia trait patients (16 cases,11.9%) had moderately reduced hemoglobin. peripheral smear examination showed marked anisopoikilocytosis and microcytic hyperchromic blood picture. Thalassemia trait patients in the present study had lower hemoglobin and higher. RDW as compared to other studies in India. This can be explained by presence of other associated health related problems, especially Iron deficiency in this group of patients.

Table 2: Hematological findings in Thalessemia Syndrome.

Parameter (n=16)	Mean	S.D	Min	Max
Hb	8.2	2.2	5.1	12.1
Hct	26.0	6.3	17.2	36.8
MCV	69.1	12.9	51.1	86.4
MCH	22.1	5.2	13.9	31.2
MCHC	31.5	2.1	26.7	35.1
RDW	23.2	7.5	14.0	37.0
Reticulocyte Counts Percentage	2.2	1.1	0.5	4.2

HbE disease can present in 4(3%) cases which included 1 case of HbE disease. 1 case of HbE trait, 1 case of HbE β Thalassemia and 1 case of double heterozygous for HBS and HBE disease. The hemoglobin ranged from 9.3g/dl to 12.5g/dl.).This is in accordance with previous studies which demonstrated that hemoglobin E trait cases are usually asymptomatic with normal to slightly decreased hemoglobin level. 34(25.1%) cases of G6PD deficiency were diagnosed. Most of the patient presented with pallor.25 patients had drug history like primaquine and nitrofurantoine.

There were no cases of membrane defects which are described in some studies were not done.

CONCLUSION

Hematological investigations are though useful for differentiating hereditary hemolytic anemia but hemoglobin electrophoresis establishes the disease in hemoglobinopathies.

Though various recent encouraging initiative are taken in the underdeveloped countries but screening test, counselling before marriage for control of hereditary hemolytic anemias are generally not given importance it deserves.

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