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Clinical Study Of Haemoglobinopathies In Anaemic Patients Admitted In Rajendra Institute Of Medical Science ,Ranchi.

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Abstract
Background : In India ,major cause of anaemia is nutritional which is treatable with medicines. The inherited disorders of haemoglobin synthesis are one of the important public health problems in India and anaemia in general population. Identifying these disorders in anaemic patient is immensely important epidemiologically and for the prevention of these disorders.
Methods : A hospital based cross sectional study was undertaken in which 50 anaemic patients with Hb level <10 gm/dl admitted in Paediatrics Department of Rajendra Institute of Medical Science , Ranchi over a period of one year, with no previous history of known haemoglobinopathies and no history of blood transfusion within 45 days were selected as cases and their venous blood sample was sent for complete blood count and high performance liquid chromatography(HPLC).
Results : Normal haemoglobin pattern was seen in 21(42%) cases and abnormalities was detected in 29(68%) patients. β (beta) thalassemia trait was most common hemoglobinopathies found in 7 patients(14%). It is then followed by sickle β(beta) thalassemia in 7 patients(14%) ,then sickle cell disease in 6 patients(12%), β(beta) thalassemia major/intermedia in 5 patients(10%) ,sickle cell trait in 3 patients(6%) and Hb E β(beta)thalassemia in 1 patient(2%).
Conclusions : Premarital and antenatal screenings are important measure to prevent these haemoglobinopathies in children. Identification of trait is important for future counselling. Early diagnosis of inherited haemoglobinopathies is useful for initiation of treatment and preventing early morbidity and mortality.
Keywords: *Haemoglobinopathy ,High Performance Liquid Chromatography ,Thalassemia ,Sickle cell disease, Prevalence.*

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I. Introduction :

Haemoglobinopathies are group of genetic disorders characterized by quantitative or qualitative defect in haemoglobin synthesis. These inherited disorders of haemoglobin synthesis are one of the important public health problems in India and anaemia in general population. Haemoglobin is a tetramer consisting of 2 pairs of globin chain. Abnormalities of these proteins are referred to as haemoglobinopathies. These are the major cause for haemolytic anaemia. The Beta(β)-thalassemia and sickle cell disease represents the most frequent haemoglobinopathies. The clinical spectrum can vary from asymptomatic to more serious disorders requiring regular blood transfusion and require medical care. Thalassemia is a group of genetic disorders of globin-chain production in which there is an imbalance between the α-globin and β-globin chain production. B thalassemia major is a worldwide disease. About 3%of the world's population carries alleles for β-thalassemia and in Southeast Asia 5-10%of the population carry alleles for α-thalassemia. Sickle cell disease is the result of a single base-pair change, thymine for adenine, at the 6^{th} codon of the β-globin gene. This change encodes valine instead of glutamine in the 6^{th} residue in the β-globin molecule. The simplest method to detect these hemoglobinopathies is to study the different types of haemoglobin concentration by high performance liquid chromatography. As anaemia is one of the major public health problem in India this study was conducted to know the spectrum of hemoglobinopathies in anaemic patient.

AIM: To study the spectrum of haemoglobinopathies in anaemic patient admitted in Rajendra Institute Of Medical Sciences, Ranchi.
OBJECTIVES : To determine the prevalence of different haemoglobinopathies like thalassemia ,sickle cell anaemia and others in anaemic patients admitted in Rajendra Institute Of Medical Sciences, Ranchi.

II. Materials And Methods :

A hospital based cross sectional study was carried on 100 anaemic patients with Hb <10 gm/dl admitted in Department of Paediatrics , RIMS , Ranchi during the period August 19 to July 20.

INCLUSION CRITERIA :

1. Anaemic patient with Hb <10gm/dl between 12 months to 17 years admitted in Department of Paediatrics RIMS ,Ranchi.
2. Patient whose parents are willing to give consent.

EXCLUSION CRITERIA :

1. Patient who received blood transfusion within 45 days.
2. Patient who are already diagnosed with thalassemia ,sickle cell disease or other hemoglobinopathies and admitted for blood transfusion.
3. Patient whose parents are not giving consent.

Method of data collection :

In this study ,target group admitted in Department of Paediatrics ,RIMS Ranchi , 2ml sample was collected form each patient in EDTA vial and sent to pathology lab for complete blood count and HPLC. Details of clinical examination , history of any blood transfusion ,family history and written consent was taken in all cases. The results of Haemoglobin(Hb) ,Mean Corpuscular volume(MCV) ,Mean Corpuscular Haemoglobin(MCH) ,Mean Corpuscular Haemoglobin Concentration(MCHC) ,Red Blood Cell (RBC) count and Red Cell Distribution Width(RDW) was correlated with peripheral blood smear and High Performance Liquid Chromatography(HPLC) reports. HPLC is done using BIORAD 'VARIANT' II HPLC machine is based on exchange of charged groups on an ion exchange material for charged groups on Hb molecule . The printed report shows all the haemoglobin fractions eluted ,the retention times ,the areas of the peaks and the values(%) of different haemoglobin components.

III. Results :

HAEMOGLOBIN PATTERN	NO OF CASES	%
NORMAL	21	42%
B(beta) thalassemia trait	7	14%
Sickle cell disease	6	12%
Sickle β(beta) thalassemia	7	14%
B(beta) thalassemia Major / intermedia	5	10%
Sickle cell trait	3	6%
Hb E β(beta) thalassemia	1	2%

Table 1 : Type of Haemoglobin Pattern among Study Subjects.

Gender	No of cases	%
Male	32	64%
Female	18	36%
Total	50	100

Table 2 : Sex Wise Distribution of Cases .

Age (in years)	No of cases	%
12months – 5years	39	78%
6years – 10years	06	12%
11years – 17years	05	10%
Total	50	100

Table 3 : Age Wise Distribution of Cases.

HPLC Dx	Hb(g/dl) ±SD	RBC(mill /mm3 ±SD	PCV (%) ±SD	MCV (fl) ±SD	MCH(pg) ±SD	MCHC(g/dl) ±SD	RDW ±SD	HbA	HbA2/E	HbF	HbS	others
N	8.3±3.3	3.4±1.4	27.3± 11.5	80±13.8	26.5±8.8	32.1±3.0	16.3± 4.2	87±4. 8	2.4±0.5	0.8±0. 7		9.5±2.0
SCT	6.2±3.4	2.8±2.5	20±10	78±17	25.1±5.7	32.7±2.9	20±5. 1	57.5	4±3.0	2.6±2. 6	30.5± 5.9	6.1±3.1
SCD	6±2.1	2.6±2.7	19.3± 6.6	83.1±12 .4	26.1±3.1	31.6±4.1	21.7± 4.4	3.3±0. 7	3.3±0.7	19.3± 7.3	72±8. 3	6.1±3.1
SBT	5.5±3.1	2.4±2.2	18±6. 7	77±11.7	24.6±4.0	31.2±3.7	21.2± 4.8	4.6±2. 0	6.1±0.9	18.4± 8.7	69.9± 8.3	2.1±2.3
BTT	7.5±3.4	3.5±1.5	25±8. 3	71.7±11 .1	22.4±4.3	32.5±2.7	18±4. 9	83.2± 5.3	5.1±1.0	1.5±1. 3		9±5.0
BTM	3.4±2.1	1.8±1.1	12.3± 6.7	66.2±8. 5	20.3±3.4	32.2±3.5	26.2± 3.6	6.9±2. 5	4.5±1.5	88±6. 2		4.5±3.4
EBT	5.4±2.6	2.8±1.3	18.7± 8.0	67±9.9	20.2±3.9	31.5±3.2	23.3± 4.6	3.5±1. 7	56±9.6	30.7± 10.1		9±5.0

Table 4: RBC Indices and Haemoglobin fractions in various haemoglobinopathies RBC Indices and Haemoglobin Fractions In Various Haemoglobinopathies.

SCT – Sickle Cell Trait , SCD – Sickle Cell Disease , SBT – Sickle Beta Trait , BTT- Beta Thalassaemia Trait. BTM – Beta Thalassaemia Major , EBT – E Beta Thalassaemia

A total of 50 anaemic patients was included in the study over a period of one year. Among them 32 were males and 18 were females. Ratio of Male : Female was 1.7:1. The age of the patient ranged from 12 months to 17 years. Normal haemoglobin was found in 21 patients. Disorder of haemoglobin were noted in 29 patients. The most common haemoglobin abnormality detected was beta(β) thalassemia trait and Sickle beta(β)thalassemia present in 7 patients(14%). It is then followed by Sickle cell disease present in 6 patients(12%) ,then beta(β) thalassemia major/intermedia in 5 patients(10%) ,Sickle cell trait in 3 patients(6%) and Hb E beta(β)thalassemia in one patient(2%). In table 2 showing different haemoglobin patterns distribution has been shown. HPLC reports of different patient shows increase Hb F level in beta(β) thal major/intermedia , Hb E beta(β) thalassemia , Sickle beta(β) thalassemia and Sickle cell disease. Increased Hb A2 levels were found in Sickle beta(β)thalassemia , beta(β) thalassemia major/intermedia and Hb E beta(β) thalassemia. Increased HbS levels were found in Sickle cell trait, Sickle cell disease and Sickle beta(β)thalassemia.

IV. Discussion:

Inherited haemoglobinopathies are diseases, which can only be prevented or controlled by creating awareness regarding these diseases in the community, i.e. premarital counselling, pre-conceptional diagnosis and antenatal diagnosis for which the prevalence of the disease should be known in a particular region. The wide prevalence of thalassemia and other haemoglobinopathies has been attributed to migration of people from one region to another and marriages between different communities. With increasing awareness, detection of these disorders in countries like India ,Bangladesh mostly occurs during premarital screening. In Western European countries ,detection of these disorders usually occurs through pre-conceptional and neonatal screening programs. In the present study , the prevalence of haemoglobinopathies were studied in 50 anaemic patients who are admitted in the Department Of Pediatrics , RIMS ,Ranchi, and was found to be present in 29 patients. This figure is on the higher side as only anaemic patients are selected and haemoglobinopathies is one of the important cause of anaemia in this age group mainly after nutritional. In the north Indian population the incidence of haemoglobinopathies was found to be 12.5%. The prevalence rate in Bhopal is 7%. In this study the results show that the important cause of anaemia in this age group is haemoglobinopathy is due to as the study is conducted at tertiary level. The most common haemoglobin abnormality detected is beta(β) thalassemia trait and sickle beta(β) thalassemia estimated to be about 14%. Colah et al reported it to be nearly 1.5% of the world's population is carriers of beta thalassemia. In northern and western India the estimation is 4.05%. In Central India, the prevalence is of beta thalassemia is estimated to be 9.59%. These data reveals that in most part of india ,beta- thalassemia trait is the commonest Hb disorder which is commensurate with our findings. In Orissa, sickle cell trait was the most common abnormality found. In the present study , sickle cell disease was found in 6 patients(12%) and sickle cell trait was found in 3 patients(6%). In this study Hb E beta thalassemia was found in one patient. A study conducted in the rural areas of West Bengal reported the prevalence of Hb E trait be 3.86% and that of Hb E beta thalassemia 1.25%. Due to the high prevalence of haemoglobinopathies in various regions of Jharkhand, premarital screening must be routinely done for prevention of high risk marriages. High performance liquid chromatography has been established as a sensitive ,specific and accurate technique for the identification of different Hb fractions quantitatively and qualitativelty. It has always been emphasised that HPLC should be done only after clinical ,family history and complete blood counts and finding the PBS.

During interpretation of chromatograms ,nutritional anaemia must always be taken into account. A low level of Hb A2 may be induced by iron deficiency and can mask βthalassemia trait. Similarly cobalamine and folate deficiency may raise HbA2 levels leading to false diagnosis of thalassemia trait. HPLC is limited by its inability to detect beta thalassemia and normal HbA2 beta-thalassemia. Hb variants that elute the same retention time also cannot be separately identified by HPLC. Ideally HPLC must be used as a screening tool followed by molecular studies like PCR, amplification refractory mutation system and other tests.

V. Conclusion:

The importance of screening programs for Hb disorders in countries with high prevalence cannot be overemphasized. It is a common practise to give iron therapy to all anaemic patients which can lead to unneccesary iron overload in thalassemic and other haemoglobin variants patients. In India premarital screening is still considered a taboo. So the best approach would be to target those patients attending the haematology OPD ,antenatal population and extended family members. Persons having positive reports for carrier state should be counselled regarding the nature of the disease and implications of being carrier ,which help in preventing birth of child with homozygous inheritance of haemoglobinopathies. So , Jharkhand were beta thalassemia trait ,sickle beta thalassemia and others is so rampant ,premarital and antenatal screening should be mandatory to prevent birth of off-springs with beta thalassemia major and sickle cell disese. Moreover early detection of these disorders is usefull for formulating appropriate treating strategies and decreasing the morbidity and mortality associated with these disorders.

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