Clinical Presentation and Electrophoretic Patterns of Hereditary Haemoglobin Disorders in Adults, a Study at Dinajpur Medical College Hospital

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Genetic defects of haemoglobin are the most common genetic disorders and affect around 7% of world's population. Thalassaemias and haemoglobinopathies have been sporadically found in every ethnic group and geographic region. They occur with particularly high frequency from the shores of the Mediterranean and Africa through the Middle East, Bangladesh, India, Sri Lanka, Myanmar, Thailand and other countries of Southeast Asia. The study was designed to find out the clinical presentation and electrophoretic patterns of hereditary haemoglobin disorders among adult patients admitted at Dinajpur Medical College Hospital. A total number of 60 adult patients of either sex irrespective of age having evidence of haemolysis in the peripheral blood were included in this observational study from July 2011 to July 2012. Patients were diagnosed by complete blood count, morphological blood film examination and haemoglobin electrophoresis on cellulose acetate at pH 8.6. Detailed history was taken along with thorough physical examination. Other relevant investigations like serum bilirubin, ALT, HBsAg, Anti-HCV, Ultrasonography of whole abdomen were done when indicated. Among 60 patients, Hb E trait was (41.67%), HbE disease (30%), HbE-beta thalassaemia was (23.33%), beta thalassaemia minor (3.33%) and Hb H disease (1.67%). It is evident that, hereditary haemoglobin disorders are quite common in Bangladesh and these disorders are inherited in an autosomal recessive Mendelian pattern affecting both males and females. Since these disorders are incurable, emphasis must shift from treatment of the affected child to prevention of such births in future.

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Introduction

Hereditary haemoglobin disorders are a heterogeneous group of Mendelian disorders. It includes haemoglobinopathies, characterized by structurally abnormal haemoglobin variants and thalassaemias by partial or total suppression of normal peptide chains of haemoglobin molecules.

More than hundreds of structural haemoglobin variants have been identified in the last three decades. Majority of these results from single amino acid substitution in one or other of the globin chains. The simple system of presumptive identification of these variants by simple electrophoresis still remain an extremely useful procedure though it does

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not discriminate between different mutants, which carry the same electrophoretic mobility. The inheritance of haemoglobin disorders follows a simple Mendelian pattern. The heterozygous state for a disorder is called "trait", while the homozygous or genetic compound is called "disease". It is estimated that in excess of 300,000 children are born each year with a severe inherited disorder of haemoglobin and that approximately 80% of these occur in low or middle income countries,[1] where their control and management is hampered by a lack of knowledge of their true prevalence, adequate services for their management and control, and support by their governments and international health agencies.[2] World Health Organization (WHO) estimates that at least 7% of the world population are carriers of different inherited disorders of haemoglobin[3] and couples in which both partners are carriers have a 1 in 4 risk in every pregnancy of having a child with a serious inherited anaemia.[4] In Bangladesh there is no definite data regarding electrophoretic pattern of hereditary haemoglobin disorders. No screening programme has yet been taken in any population group here.[5] A conservative WHO report estimates that about 3.0% of population are carriers of Beta Thalassaemia and 4.0% are carriers of Hb-E in Bangladesh, which means that there are about 3.6 million carriers of Beta Thalassaemia and 4.8 million carriers of Hb-E.[5,6] The expected births of thalassaemic children in Bangladesh are about 6000 to 7000 per year.[7] Most of the thalassaemic patients need frequent blood transfusions at about every 2 – 3 week intervals. As a result they utilize good percentage of blood, which is a major burden to the family and ultimately to the community. At the same time it is associated with hazards of repeated transfusions and other complications. There is every chance of transmission of infections like HBV, HCV, HIV, and Syphilis etc.

Methods

The present study was conducted at Dinajpur Medical College Hospital (DjMCH) among patients admitted under different Medical units from July 2011 to July 2012. Patients of either sex, irrespective of age with morphological evidence of haemolytic anaemia in peripheral blood film and haemoglobin electrophoresis on cellulose agar acetate at pH 8.6 were included in the study. Paediatric patients below 12 years of age were not included in the present study. Detailed history including family history and thorough physical examination of every patient was done and data was collected in pre-tested questionnaires. A total no. of 60 cases of hereditary haemoglobin disorders was studied.

Results

Among 60 patients Hb E trait was (41.67%), Hb E disease was (30%), Hb E-β thalassaemia was (23.33%), beta thalassaemia minor was (3.33%), and Hb H disease was (1.67%).

Table I: Distribution of patients by age (n=60)

Age (years)	No. of patients	Percentage %
12 – 20	24	40%
21 – 30	19	31.67%
31 – 40	11	18.33%
> 40	6	10%
Total	60	100%

Table I shows distribution of patients by age. Age range was 12 to 60 years. Mean age was 26.01 years. Majority of the patients were in the age groups 12 – 20 years (40%) and 21 – 30 years (31.67%) followed by age group 31 – 40 years (18.33%).

Table II: Sex distribution (n=60)

Sex	No. of patients	Percentage %
Male	34	56.67%
Female	26	43.33%
Total	60	100%

Table II shows distribution of the patients by sex. Out of 60 patients 34 were males (56.67%) and 26 females (43.33%) with male: female ratio 1.7: 1.3.

Table III: Presenting clinical manifestations

Symptoms & signs	No. of patients	Percentage %
Weakness	50	83.33%
Pallor	40	66.7%
Anorexia	33	55%
Jaundice	31	51.67%
Fever	21	35%
Splenomegaly	15	25%
Hepatomegaly	8	13.33%
Hepatosplenomegaly	15	25%
Growth retardation	9	15%
Splenectomy	2	3.33%
Leg ulcer	2	3.33%
Asymptomatic	3	5%

Table IV: Patterns of hereditary haemoglobin disorders (n=60)

Hereditary haemoglobin disorders	No. of patients	Percentage %
Hb E trait	25	41.67%
Hb E disease	18	30%
Hb E- β Thalassaemia	14	23.33%
β -Thalassaemia minor	2	3.33%
Hb H disease	1	1.67%

Table III shows distribution of patients by clinical presentations. Majority of the patients present with weakness (83.33%) followed by pallor (66.7%), anorexia (55%) and Jaundice (51.67%) respectively. Splenomegaly was found in 25% and hepatosplenomegaly in 25% of patients. Only 3.33% of patients had leg ulcer and 5% patients were asymptomatic

Table IV shows distribution of patients by Electrophoretic patterns. Majority of the patients present with Hb E trait (41.67%), followed by Hb E disease (30%), Hb E beta thalassaemia (23.33%) respectively. Only 3.33% patients present with Beta Thalassaemia minor and 1.67% patients with Hb H disease.

Table V: Distribution of Patients by severity of anaemia (n=60)

Electrophoretic Patterns	Severe (<6 gm/dl) No.(%)	Moderate (6-10 gm/dl) No.(%)	Mild (>10 gm/dl) No.(%)
Hb E -β thalassaemia	9(15%)	5(8.33%)	0(0%)
Hb E disease	4(6.67%)	11(18.33%)	3(5%)
Hb E trait	9(15%)	13(21.67%)	3(5%)
β-thalassaemia minor	1(1.67%)	1(1.67%)	0(0%)
Hb-H disease	1(1.67%)	0(0%)	0(0%)

Table shows distribution of patients by severity of anaemia. Majority of the patients (50%) were moderately anaemic, 40% were severely anaemic and 10% were mildly anaemic.

Table VI: Distribution of patients by Transfusion dependence (n=60)

Electrophoretic Patterns	Transfusion needed No.(%)	Transfusion not needed No.(%)
Hb E- β thalassaemia	14(23.33%)	0(0%)
Hb E disease	8(13.33%)	10(16.67%)
Hb E trait	18(30%)	7(11.67%)
β-thalassaemia minor	2(3.33%)	0(0%)
Hb H disease	1(1.67%)	0(0%)

Table VI shows distribution of patients by transfusion dependence. Majority of the patients (71.67%) needed transfusion and 28.33% patients didn't.

Discussion

The incidence of hereditary haemoglobin disorders in Bangladesh is not known. However data regarding the incidence of hereditary haemolytic anaemia in some neighboring countries is available. In India, the highest incidence of HbE trait has been reported from West Bengal and it is also prevalent in Assam and Tripura states. HbE-beta-thalassaemia is the commonest of the thalassaemia syndrome in Myanmar.[8] Bangladesh is in geographical continuity with West Bengal, Assam, Tripura states of India and with Myanmar. The population in West Bengal shares the common ethnic ancestry with the people of our country. In our study HbE was the most common haemoglobin disorder constituting 95% and other Hb variants constitute only 5%. Hb E is the most common haemoglobin variant in Southeast Asia. More over the percentage of HbE patients are increasing day by day because a dynamic model of three genes (involving Hb A, HbE and thalassaemia) suggest that the HbE gene is replacing the thalassaemia gene in most Southeast Asian populations.[5] HbE disorders include HbE trait, Hb E disease, Hb E/β thalassaemia, sickle cell/Hb E disease. In our study, Hb E trait was the most common finding. Hb E/β Thalassaemia and Hb E disease were next most common. In our study HbE trait constitutes 41.67% and HbE disease constitutes 30% which differs from the study of Uddin MK et al, who found these to constitute 13.33% and 5.71% respectively, this may be due to exclusion of children below 12 years in our study. However, HbE-beta thalassaemia constitutes 23.33%, which is similar to the study of Uddin MK et al.[3] Rahman SA et al. in a study done in Dhaka found HbE-β thalassaemia in 67% of cases.[9] Khan WA in a study from Dhaka Shishu (Children) Thalassaemia center reported 85% of cases were HbE β-thalassaemia.[7] The difference of these studies from our study may be due to exclusion of paediatric patients. However all these studies show the very high incidence of HbE disorders in Bangladesh, which correlates well with our study. In another study Khan WA et al. found prevalence of Hb E trait to be highest in Rajshahi division (16.5%), and the prevalence was 41.7% in tribal school children.[10] Farhana DT et al. in a study in Bangladesh Institute of Rehabilitation in Diabetes Endocrine and Metabolic disorders (BIRDEM) found Hb E trait 17.39% and Hb E disease 13.04%.[11] Haemoglobin E trait is most common abnormal haemoglobin in Bangladesh.[7] Hb E is found in the eastern half of Indian sub-continent and throughout South-East Asia, where in some areas, carrier rates may exceed 60% of the population.[12] All these data indicate the very high frequency of Hb E disorders in Southeast Asian countries including Bangladesh.

Clinical presentation of congenital haemolytic anaemia might show a variable degree of expression.[9] This study also found many variations in the clinical expression of disease. There was a big gap between the presentation and the diagnosis of the patients. Most authorities have described that patient of haemoglobin E trait is an asymptomatic with no clinical relevance, except for the risk of compound heterozygous states with a thalassaemia in the offspring and individuals with the genotype EE (homozygous state) are usually also completely asymptomatic. There is usually no anaemia and rarely any evidence of haemolysis. The spleen is not usually enlarged. The severity of patients with Hb E/B-thalassaemia is variable, ranging from that of beta-thalassaemia minor through thalassaemia intermedia to thalassaemia major.[5] However our study differs from this markedly especially in cases of Hb E trait and Hb

E disease (vide Table-V & Table- VI).
Examination of haemoglobin level in hereditary haemoglobin disorders is a very good indicator of measurement of severity of the disease.[8] In this study (Table-V) among 60 patients; 30 patients (50%) were moderately anaemic (Hb level 6-10 gm/dl), 24 (40%) patients were severely anaemic (Hb level >6gm/dl) and 6 (10%) patients were mildly anaemic (Hb level >10 gm/dl). These findings correlate well with the findings of Aziz et al.[8]

Another parameter of measurement of severity of the disease is transfusion dependency and frequency of transfusion.[8] In our study (Table-VI) out of 60 patients; 43 patients (71.67%) needed transfusion. These findings also differ markedly from usual descriptions of these diseases.

Conclusion
It is evident that the hereditary haemoglobin disorders are quite common in Bangladesh and these disorders are inherited as autosomal recessive Mendelian pattern affecting both males and females. So we can not avoid these diseases. The care of thalassaemia patients in Bangladesh is very poor. Ninety percent of patients can not afford adequate treatment. Since these disorders are incurable, emphasis must shift from treatment of the affected child to prevention of such births in future. In Bangladesh prevention of thalassaemia can successfully be done by developing premarital screening through the primary health care system and mandatory blood test before marriage registration and counseling. At the same time, prenatal diagnosis to prevent the births of thalassaemic children should also be made available nationwide and improving treatment strategy of thalassaemic patients within our limited resources. Ethical issues governing the genetic counseling need to be addressed and uniform policy should be made taking in account the local, social and religious structures.

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