Original Article

A Study on Thalassaemia from Different Types of Hemoglobinopathies in Sylhet

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Abstract:

Thalassaemia is an inherited impairment of haemoglobin production, in which there is partial or complete failure to synthesis a specific type of globin chain. In Bangladesh, there is no definite data regarding identification of thalassaemia . For this purpose this cross sectional study was performed to find out the electrophoretic pattern of thalassaemia in hereditary hemolytic anaemic patients by Hb electrophoresis that was conducted in the department of Biochemistry Sylhet M.A.G. Osmani medical college between the period of 1st January 2010 to 30th June 2011.Total 60 diagnosed hereditary hemolytic anaemic patients were selected, age ranging from 6 months to 50 years of both sex. This clinoco-haematological study of haemolytic anaemia showed that HbE-â thalassaemia were 43.34%, â thalassaemia trait 25%, HbE trait 25%, Sickle cell anaemia 3.34%, â thalassaemia major 1.67% and HbE disease 1.67%. In this study, it is evident that HbE-â thalassaemia is the most common hereditary hemolytic anemia followed by â thalassaemia trait & HbE trait.

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Introduction:

Haemoglobinopathies are characterized by the production of structurally defective Hb due to abnormalities in the formation of the globin moiety of the molecule. It can be classified into qualitative and quantitative abnormalities. Qualitative abnormal Hb is due to alteration in the amino acid structure of polypeptide chains or globin chains (HbS, HbC, HbD & HbE) in which there is substitution of normal amino acid by another amino acid resulting in impaired function of Hb. Quantitative abnormalities are thalassaemia in which one or other globin chain production is reduced.[1]

The thalasseamias are characterized by reduced rate of production of normal Hb due to absent or decresed synthesis of one or more types of normal globin polyperptide chains. There are two main groups of thalasseamia one affecting the synthesis of á chains which is called á thalasseamia and the other affecting the synthesis of â chains that is called â thalasseamia.[2] In â thalassaemia, the inadequate production of beta chains lead to reduction in the amount of Hb A in the red cell and microcytic hypochromic anaemia results. The total Hb is maintained in part by the production of gamma and delta chain and thus

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increased Hb F or Hb A_2 is usually formed. In á thalasseamia, the levels of Hb A, Hb F and Hb A_2 are equally depressed since they all have alpha chains. There is usually microcytic hypochromic anaemia. In absence of sufficient alpha chains excess beta chains or gama chains aggregate to from Hb H or Hb Bart's.[2] The thalassemia syndromes are a heterogeneous group of inherited disorders of hemoglobin synthesis which are the result of deletion or mutation of one or more of the genes that code for the alpha globin chains or the beta globin chains, which causes an imbalance in the rates of globin chain production. Normally, alpha and beta globin chains are produced at an identical rate. A mutated gene cannot produce as many globins as a non mutated chain, resulting in a build- up of non mutated gene chains within the cells and impaired hemoglobin production. The thalasseamia syndromes are endemic to the Mediterranean region, the Middle East, India, Southeast Asia, Oceania and sub-Saharan Africa.[3] With global improvement in childhood diseases, thalassaemia will become a major health issue in millennium. The â thalassaemia is the most common type of thalassaemia because they occur widely in a broad belt ranging from Mediterranean and parts of North and west Africa through the Middle East, Bangladesh, India, Srilanka and other countries of South East Asia.[4]

World Health Organization (WHO) estimates that at least 7% of the world population are carriers of different inherited disorder of Hb. The world population of carrier of â thalassaemia trait is reported to be more than 100 millions and about 1,00,000 children with thalassaemia major are born each year. In Bangladesh, there is no definite data regarding electrophoresis pattern of hereditary haemoglobin disorders. No nationwide screening program has yet been undertaken in any population group. A conservative world health report estimates that 3% are carriers of â thalassaemia and 4% are carriers of Hb E in Bangladesh.[5]

Diagnostic approach to hemolytic anemia include history of presenting symptoms, clinical examination, peripheral blood smear picture. Investigation for all hemolytic anemia are full blood examination including morphology of RBC, reticulocyte count, plasma haptoglobin, serum bilirubin, osmotic fragility test, direct antiglobulin test, antibody screening & urine for urobilinogen & haemosiderin.[6]

Hemoglobin electrophoresis is the most common initial screening method for detection and preliminary identification of hemoglobinopathis. The most common pattern of hemoglobin abnormalities that can be determined by electrophoresis are- (1) Sickle Cell Trait. (2) Sickle Cell Anemia. (3) Sickle-C Disease. (4) Sickle Cell-Thalassemia Disease. (5) Thalassemia-C Disease. (6)HbC Disease. (7) Thalassemia Major. (8) HbE-beta thalassaemia. (9) HBE Trait. (10) Beta thalassaemia Trait.[7]

Materials & Methods:

Calculated sample size was about 100, calculated by $n=z^2pq/d^2$, where p was 0.07 (7%). But we have taken 60 samples due to limitation of time and cost. A total number of 60 anaemic subjects with age range from 6 month to 50 years of both sex were included in the study. The study was conducted in the department of Biochemistry, Sylhet MAG Osmani Medical College. Patients were taken from both indoor and outdoor patients of Sylhet MAG Osmani Medical College and Hospital between the period of 1st January 2010 to 30th June 2011. The anaemic patients were selected on the basis of clinical, haematological and biochemical parameters. As haematological parameter, complete blood count, peripheral blood film and reticulocyte count were done. As biochemical marker, serum bilirubin was done. Whole blood had been collected by venous puncture and 2 milliliter blood was collected into a test tube containing EDTA. This sample was used for CBC, peripheral blood smear examination, bilirubin, reticulocyte count and Hb electrophoresis. In this study, anaemic patients were included whose blood haemoglobin level were 10 gm/dl or below it. Peripheral blood smear showed microcytic hypochromic red cells, anisocytosis, poikilocytosis, polychromatia, fragmented red cells, increased reticulocyte, eliptocyte,

teardrops etc. Biochemical finding were mild uncongugated hyperbilirubinaemia, decrease haptoglobin & increase LDH. When all the results indicate haemolytic anaemia, then agarose-gel haemoglobin electrophoresis was done. All data were checked and analyzed with the help of statistical package for social science (SPSS) for windows version 12.0. Quantitative data were analyzed by Mean and Standard Deviation. Qualitative data were analyzed by rate, ratio, and percentage; and comparison had been done by Chi-Square (χ^2) test. A probability (p) value of < 0.05 was considered statistically significant.

Result:

Out of the 60 subjects, 38 (63.33 %) were males and 22 (36.66 %) were females. Majority of the study subjects (38.33%) were between the age of 5-10 years. The Mean (± SD) age of the study subjects were 12.00 (± 10.472). Mean (± SD) age of male was 11.36 (± 9.93) and female was 13.10 (± 11.50).

Pattern of haemoglobin disorders was identified on the basis of different mobility of band on an electric field. Among the 60 subjects 26(43.34%)were diagnosed as Hb E â thalasseamia, (1.67%) was â thalasseamia major, 15(25%) were â thalassemia trait. 25% were Hb E trait and (1.67%) was Hb E disease. Out of 38 male study subjects, Hb E â thalassaemia was present 50%, â thalassemia major 00%. Â thalassaemia trait 18.42%. Out of 22 female study subjects, Hb E â thalassaemia was present 31.81%, â thalassaemia major 4.54%. Â thalassaemia trait 36.36%. In between male and female, the p value in Hb E â thalassaemia was 0.302, in â thalassaemia major was 0.0001, in â thalassaemia trait was 0.0001.

In this study population, highest number of 46.15% Hb E β thalassemia was present in the

Table-I

Distribution of different pattern of Hb in male and female study subjects

Hb pattern	Male (n=38)	Female (n=22)	χ2	P value
Hb E β thalassaemia	50%	31.81%	1.067	0.302
β thalassaemia major	00%	4.54%	56.067	0.0001
β thalassaemia trait	18.42%	36.36%	15.00	0.0001
Sickle cell anaemia	2.63%	4.54%	52.26	0.0001
Hb E trait	26.31%	22.72%	15.00	0.0001
Hb E disease	2.63%	00%	56.067	0.0001

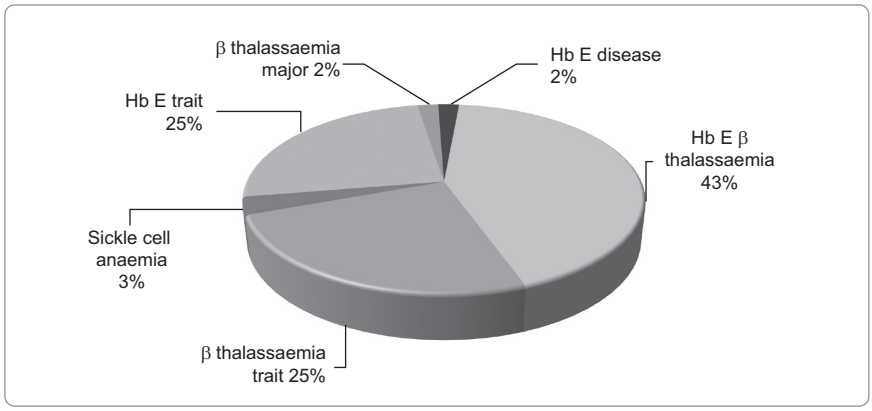

Figure-1: *Pie chart showing pattern of hereditary haemoglobin disorders*

age group of 5-10 years.30.76% Hb E â thalassemia was present in the age group<5 years.19.23% was present in age group 11-20 years. Only one case of â thalassemia major was found among the sample cases. Highest number 26.66% of â thalassemia trait was present in the age group 5-10 yeasr and 21-30 years, 20% was present in the age group 11-20>30 years.

Table-II

Distribution of Hb E beta thalassaemia in different age groups

Age(years)	Hb E beta thalassaemia	Percentage
<5	8	30.76
5-10	12	46.15
11-20	5	19.23
21-30	0	00
>30	1	3.84

Table-III

Distribution of beta thalasseamia trait in different age groups

Age(years)	Beta thalasseamia trait	Percentage
<5	1	6.66
5-10	4	26.66
11-20	3	20.0
21-30	4	26.66
>30	3	20.0

Discussion:

The purpose of this cross sectional study was to estimate the frequency of thalassaemia in patients of haemolytic anaemia. A total number of 60 patients of both sexes were included in that study based on clinical, haematological and biochemical parameter. Among Thalassaemias, â thalassaemia gene has a widespread prevalence extending from Mediterranean zone, Middle east, Indian subcontinent including Bengal and parts of Southeast Asia.[8] Several demographic studies have documented the remarkably high gene frequency of Hb E, particularly in eastern part of India including Bengal, Burma and Southeast Asia.[9] So, the interaction of Hb E and â thalassaemia, Hb E â thalassaemia is the most important type of congenital hemolytic anaemia in this region. This study found that 43.34% of congenital haemolytic anaemia cases were Hb E â thalassaemia which is consistent with other studies where Hb E â thalassaemia is reported as the commonest form of Thalassaemias in the neighboring and Southeast Asian countries.[10] In this study, Hb E beta thalassaemia was found most common. Hb E trait and beta thalassaemia trait were next most common which were similar to the findings observed in the study of khan et al. A large number of haemoglobin variants prevalent in the population indicate that haemoglobinopathies are not uncommon amongst our population. The inherited disorders of haemoglobin synthesis are one of the important public health problems in Bangladesh.[11] In our country, data regarding the hereditary haemoglobin disorder are not available so far, but in our neighboring countries in Myanmar and India, they have got their prevalence rate .Bangladesh is in geographical continuity with Myanmar , Assam (India), West Bengal (India), Tripura and also same belt of Thailand and Combodia.[12]

In one study in West Bengal (Kolkata) showed that the prevalence of beta thalassaemia trait alone to be 7.5% and it is much higher12.6% in Orissa (India).[13] It can compare this observation regarding the incidence as it also correlates well with some of the small studies done in Sylhet on hereditary haemolytic anaemia.[14] Within this small study group, Hb E beta thalassaemia and Hb E trait have taken a place. It is observed from other studies that double heterozygous Hb-E beta thalassaemia was the commonest thalassaemia syndrome in the region of Sylhet.[15.16.17.18] It is evident from this study that the hereditary haemoglobin disorders are quite common in Bangladesh and these disorders are inherited as autosomal recessive mendelian pattern affecting both male & female. So we can not avoid these diseases. In this study, we got heterozygous (trait) like both heterozygous thalassaemia and heterozygous HbE trait significant number in camouflage.

Conclusion: It is evident from the present study that hemoglobinopathies are mainly a disease of the pediatric groups, adolescents and young adults.Both genders are equally affected.Hb E and â thalassaemia occurred in relatively high frequency among the patients.When Hb E co-exisits with â thalassaemia in the same individual, severe anaemia manifested.We also got a good number of asymptomatic heterozyous trait. Which do not need treatment, but they are dangerous because of possibility of homozygous or double heterozygous inheritance through marraige. So it is mandatory to detect the traits in general population with large scale screening program, followed by proper genetic counseling.It is time to think about the molecular and prenatal diagnosis to start and to prevent further spread of the disease.

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