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Original Article

Clinico-Pathological Profile of Thalassemia Patients in A Tertiary Care Hospital

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ABSTRACT

Introduction: *Thalassemia is a common hematological disorder in our country having wide spectrum of clinical presentation. The frequency and severity of the several types of thalassemia depend on the racial background of the population. Hb-E Beta thalassemia is prevalent in our country.* ***Objective:*** *To see the clinical features of different types of Thalassemia in northern area of Bangladesh.* ***Methods and Material:*** *Hundred cases were selected from Thalassemia patients admitted in department of pediatrics, from January 2020 to October 2020. A prescribed questionnaire was used to record the information. Necessary physical examination was performed and investigations were done. The data was analyzed by standard procedure.* ***Results:*** *Out of hundred (100) cases, most (67%) were Hb-E beta Thalassemia, less common (1%) was Hb-E disease, and 1 % case was Hb-E trait. Majority (64%) manifested clinically under one year of age. 53% were male and 47% were female. The major presenting symptom was progressive pallor in 83% cases. Others presenting complaints were low grade fever (45%). Hemoglobin concentration at the time of diagnosis was below 5 gm/dl in 18% patients.* ***Conclusion:*** *In countries with a high incidence of thalassemia carrier identification, genetic counseling, and prenatal diagnosis among high-risk groups carrying thalassemia traits for minimizing its incidence is of paramount importance.*

Key words: *Hemoglobinopathies, Thalassemia, clinical profile*

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INTRODUCTION

Thalassemia is the most common genetic blood disease in the world and varies in different population group in the world. World Health Organization (WHO) estimates that at least 6.5% of the world

populations are carries of different inherited disorders of hemoglobin. Thalassemia syndromes are caused by inherited mutations that decrease the synthesis of either alpha or beta globin chains of hemoglobin. Imbalance in globin chain synthesis results in anemia, tissue hypoxia, and red cell hemolysis.

In the normal children, hemoglobin A, which is composed of two alpha and two beta globins (α2β2), is the most prevalent, comprising about 95% of all hemoglobin. Hemoglobin A2, composed of two alpha and two delta globins (α2 δ2) which comprises 2-3.5% of hemoglobin, while hemoglobin F, composed of two alpha and two gamma globins (α2 γ2) which comprises less than 2% of hemoglobin. The genes controlling globin production are on chromosome 16 (alpha-globin genes: "α"), and chromosome 11 (beta: "β", gamma: "γ", and delta: "δ" genes). [1]

Their clinical severity widely varies, ranging from asymptomatic forms to severe or even fatal entities. Individuals with beta-thalassemia major or homozygous type manifest with severe Transfusion dependent anemia. Those with beta-thalassemia minor or heterozygous genotype present with mild asymptomatic anemia. The heterogeneous variant of moderate severity is called beta-thalassemia intermedia. [2, 3, 4]

Children with Beta thalassemia usually become symptomatic during 6-12 month of life. Initially they present with Fatigue, poor appetite and lethargy; Thereafter becoming severely anemic and ultimately become transfusion dependent therapy. The findings in severe thalassemia includes typical facies (maxillary hyperplasia, flat nasal bridge, frontal bossing), pathologic bone fractures, marked hepatosplenomegaly, and cachexia. The spleen may become so enlarged that it causes mechanical discomfort and secondary hypersplenism. They also suffer from psychological depression and recurrent infections. These classical findings are primarily seen in developing countries.

Many children get improved physically following a proper regimen of blood transfusion. But patients who get regular long-term transfusion may suffer from significant endocrine and cardiac resulting from excessive iron stores. Common endocrine dysfunctions are hypothyroidism, gonadal failure, hypoparathyroidism, and diabetes mellitus. Irregularly and improperly transfused children with severe pallor (Hb< 4gm/dl) may suffer from cardiac decompensation.[4] The diagnosis of thalassemia is initially suggested by clinical findings, family history and the results of routine hematological profile and confirmed by Hb Electrophoresis.[5] Structural hemoglobinopathy have an impact on RBC indices e.g., Hb, MCV, RDW, RBC number are critical to diagnosis. Thalassemic individual have a reduced MCV. One study suggested that an MCV of 72 fL is maximally sensitive and specific for presumptive diagnosis of thalassemia syndrome.[6] Normal hemoglobins are Hb-A > 95%, Hb-A_2 < 3.5% Hb F <2.5%.[5]

Management of a patient with Thalassemia syndrome depends not only on but also on an in depth understanding of the understanding of clinical expression of the defect along with an accurate diagnosis is paramount in the proper management of Thalassemia patient. In addition, there is an obligation for screening and genetic counseling of population with any increased prevalence of a Thalassemia syndrome.

So, we intend to have a clear understand of the correlation between clinical presentation, hematological profile and Hb

Electrophoresis of different types of Thalassemia with an aim to get a good outcome for the patient. With this background, this study was done in Sher-E-Bangla Medical College Hospital.

The objectives of this study were to assess the pattern clinical, epidemiological and biochemical profile of different types of Thalassemia patients.

METHODS AND MATERIALS

This prospective study was done in the inpatient department of Pediatrics, Sher-E-Bangla Medical College Hospital, Barishal. Study period was ten months from January 2020 to October 2020. Total one hundred Thalassemia patients 0-12 years admitted in pediatric ward of Sher-E-Bangla Medical College Hospital was included in this study. Purposive sampling method was followed in this series. Written informed consent was obtained from parents, a preformed questionnaire was used to record the information. After enrollment, detailed history and thorough physical examination were done in all patients. Relevant investigations were done. Main outcome variables were age, gender, weight, height, liver size, splenic size, jaundice, edema, Hb (gm/dl), Hb Electrophoresis, S. Iron level. Inclusion criteria was children under 12 yrs with thalassemia syndrome. Exclusion criteria were thalassemia with septicemia, thalassemia with meningitis. Ethical clearance was obtained with institutional review board. After all necessary correction, the data was compiled and analyzed by Statistical Package for Social Science (SPSS) version 17.

RESULTS

The mean age of cases was 5.6 years. The age at diagnosis ranged from 3 months to 11 years. The majority of cases were under-fives (61%) and were male (53%). The family history of thalassemia was positive among 11(11%) cases. History of consanguineous marriage was positive among 5(5%) cases. Most of the patients belonged to below poverty line (69%) and from urban areas (79%) [Table 1]. A total 100 patients were included in this study Shows 67% Hb-E beta thalassemia [Table 2]. Onset before 6 months of age was 20%. Most cases present within one year (64%). Majority of the patients (83%) had complaints of progressive pallor. [Table 3]. Out of 100 cases 55 cases had typical mongoloid facies, 70 cases had moderate pallor. [Table 4] Radiology shows bony changes which are consistent with the thalassemia syndrome. Typical hair on ends with osteopenic changes were present almost all the cases of thalassemia major and few cases in HbE-beta thalassemia cases who were suffering from the disease for a long period.

Table 1: Epidemiological profile of thalassemia patients (n=100)

Age group(yrs)	<1	19
	1->5	42
	5-<10	23
	>10	16
Gender	Male	53
	Female	47
Socioeconomic status	Above poverty line	69
	Below poverty line	31
Residence	Urban	79
	Rural	21

Table 2: Types of Thalassemia syndrome in study population (n=100)

Types of disorder	Number of patients	Percentage
HbE-β thalassemia	67	73%
Thalassemia major	16	20%
Thalassemia minor/trait	15	17%
Hb-E disease	1	1%
Hb-E trait	1	1%

Table 3: Presenting complaints of study subject (n=100)

Symptoms	Number	Percentage (%)
Progressive pallor	83	83%
Jaundice	25	25%
Anorexia	30	30%
Abdominal swelling	44	44%
Fever	45	45%
Abdominal pain	10	10%
Cough and cold	15	15%
Diarrhea	15	15%
Urinary complaints	13	13%
Growth failure	33	33%

Table 4: Physical signs at the time of study of the study subjects

Physical signs	Number of patients		Percentage (%)
Mongoloid facies	55		55%
Frontal bossing	22		22%
Pallor	Mild	12	13%
	Moderate	70	68%
	Severe	18	18%
Jaundice	Mild	30	30%
	Moderate	10	15%
	Severe	-	0%
Hepatomegaly	Not palpable	14	14%
	<5 cm	51	51%
	5-8 cm	25	25%
	>8 cm	10	10%
Splenomegaly	Not palpable	5	5%
	<5 cm	25	25%
	5-8 cm	37	37%
	>8 cm	33	33%
Edema	12		12%

Growth retardation	65	65%
Splenectomy	3	3%

DISCUSSION

Among thalassemias, beta-Thalassemia gene has a widespread prevalence extending from Mediterranean zone, Middle East, Indian sub- continent including Bengal and parts of Southeast Asia.[7] 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.[7-10] So, the interaction of Hb-E and beta-Thalassemia, HbE-beta-Thalassemia is the most important type of congenital hemolytic anemia in this region. A study was carried out in BSMMU (2002) also demonstrate same type of result. This study found that 61% cases were HbE-beta-Thalassemia which is consistent with other studies.[8, 11-13]

Clinical presentation of thalassemia might show a variable degree of expression.[11,14] This study also found many variations in the clinical expression of disease. The reason behind this late diagnosis may be late referral of patients to pediatricians or hematologist. This might be a reflection of less awareness or less alertness of the people and general physicians about the disease.

All cases of thalassemia major and most of the cases of HbE-beta thalassemia cases can manifest before one year of age and both groups may present with similar clinical features. Two cases of HbE-beta thalassemia presented at 3 months of age, 1 beta thalassemia major presented at 2 months of age and another 2 thalassemia major cases presented at 5 months of age. This indicates that Hb-E beta thalassemia or a double heterozygous condition can be as severe as a homozygous condition like thalassemia major.

Growth deficiency found in the vast majority of cases. George E et al found similar picture in his study done in Malaysia.[8] The major presenting symptom was progressive pallor in 83% cases. The next major complaint was low grade fever, 45% cases. Abdominal swelling was present in 44% of cases, anorexia 30% cases and diarrhea 15%. This finding is more common in 1 to 5 years of age and coincides with the previous studies.[11] History of jaundice was present in 25% cases which varied from mild to moderate severity clinically. This indicates that though jaundice was present in many cases, this is not a constant feature of hemolytic anemia due to thalassemia syndrome.[15]

About 30% cases complained of anorexia, growth failure was noted in 33% of cases. Chattopadhyay et al found that 23.6% patients [16] and Hashemi et al found that 45.7 % patients[17] had growth failure. This finding is more common in 5 to 10 years aged children due to anemia and anorexia. 10% presented with abdominal pain due to pressure effect by enlarged liver and spleen. Pain subsided after blood transfusion while liver and spleen became smaller.

Definite growth retardation was present in 65%, out of which all the 20 cases of thalassemia major and 37 cases were HbE-beta thalassemia. This indicates growth retardation is invariably present in thalassemia major cases and not invariably present in HbE-beta thalassemia patients, though chronic hemolytic anemia is one of the causes of growth retardation. This is probably because many parents in this study followed advices of regular blood transfusion but properly not maintained. Growth retardation is more pronounced in terms of Height for age rather than Weight for age and more in case of thalassemia major than HbE-beta thalassemia. Nutritional support may enhance growth in

thalassemia major if timed approach is made.[17]

Hemoglobin concentration at the time of diagnosis was below 5 gm/dl (18% cases). These patients had severe clinical anemia. Only 5 patients out of these had sign & symptoms of heart failure. Pre-transfusion hemoglobin concentration was between 6.5-8.2 gm/dl in most cases, and peripheral blood film showed anisocytosis, poikilocytosis, microcytosis, tear drop cells, target cells, fragmented RBC and polychromasia.

Radiological findings revealed hair on end appearance of the skull bone in several cases of the thalassemia major and HbE-beta thalassemia cases who had been suffering from early period of life. Gross bony changes are noted in long standing cases. Enlarged cardiac shadow was found in those cases having severe anemia with heart failure

CONCLUSION

In countries such as ours with a high incidence of thalassemia, carrier identification, genetic counseling, and prenatal diagnosis among high-risk groups carrying thalassemia traits for minimizing its incidence is of paramount importance. Nutritional and folic acid supplementation with regular blood transfusion along with iron chelation therapy is essential to improve the prognosis among the affected individuals.

REFERENCES

1. *Kumar V, Abbasi AK, Aster JC. Red blood cells and bleeding disorders. In: Robbins and Cotran, Pathologic basis of Disease. 10th ed. Gurgaon: Reed Elsevier India Private Limited; 2015.p.638,639,641.].*
2. *Khan WA. Thalassaemia in Bangladesh. Dhaka Shishu (Children) Hospital Journal. 1999; 15: 42-44.*
3. *Lanzkowsky P. Manual of Pediatrics Hematology and oncology. 2nd ed. New York: Churchill Living stone, 1995.*
4. *Lukens JH. Wintrobes Clinical Hematology. 9th ed. Philadephia: LWW, 1993.*
5. *DeBaun MR, Frei-Jones M, Vichinsky E. Thalassemia syndromes. In: Kliegman RM, Geme III JWS, Behrman RE. Editors. Nelson Textbook of Pediatrics, 21st Edition. New Delhi: Elsevier; 2020. 1674–7.*
6. *Panich V. Problems of thalassemia in Thailand. South east Asian Journal of Tropical medicine public health. 1992; 23:1-6.*
7. *Olivieri NF, Weatherall DJ. Thalassemias. In: Pediatric Hematology. 2nd edition, Churchill Livingstone, London. 1999; pp 307-327.*
8. *George E, Wong HB. Hb E Beta-Thalassemia in West Malaysia: Clinical features in the most common beta-thalassaemia mutation of the Malays. Singapore Med J. 1993; 34: 500-503.*
9. *Marwaha RK, Lal A. Present status of Hemoglobinopathies in India. Indian Pediatr. 1994; 31: 267-271.*
10. *Krishnamurti L. Few Reports of Hemoglobin E/beta-Thalassemia in Northeast India: Under-diagnosis or complete exclusion of beta-Thalassemia by Hemoglobin E. J Pediatrics Hematol Oncol. 2000; 22: 558-563.*
11. *Fucharoen S, Ketvichit P, Pootrakul P, Siritanaratkul N, Piankijagum A, Prawase W. Clinical manifestation of beta-Thalassemia /hemolgobin E disease. J Pediatr Hematol Oncol. 2000; 22: 552-557.*
12. *Rahman SA, Jamal CY. Congenital hemolytic Anemia in Bangladesh: types and clinical manifestation. Indian Pediatrics. 2002; 39: 574-577.*
13. *Chatterjee JB. Hemoglobinopathis, Glucose-6 Phosphatase dehydrogenase deficiency and allied problems in the Indian sub-continent. Bull World Health Organization. 1996; 35: 837-839.*
14. *Honig GR. Hemoglobin disorders. In: Nelson Textbook of Pediatrics, 15th edition, Philadelphia: Elsevier Sanders; 2000; pp 1478-1488.*
15. *Saxena R, Pati HP, Mahapatra M, Firkin F, Chesterman C. de Gruchy clinical Hematology in Medical practice. 6th ed. Wiley, London. 2012.*
16. *Chattopadhyay K, Biswas R, Bhattacherjee S, Bandyopadhyay R. An epidemiological study on the clinic-*

hematological profile of patients with congenital hemolytic anemia in a tertiary care hospital of Kolkata. Indian J Prev Soc Med 2012; 43:372-377.

17. *Hashemi AS, Ghilian R, Golestan M, Akhavan Ghalibaf M, Zare Z, Dehghani MA. The study of growth in thalassemic patients and its correlation with serum ferritin level. Iranian J Pediatr Hematol Oncol. 2011; 1(4):147-151*
18. *Fuchs GJ, Tienboon P, Khaled MA, Nimsakul S, Linpisarn S, Faruque ASG et al. Nutritional support and growth in thalassemia major. Archives of Disease in Childhood.1997; 76:509–512.*