



## Original Article

# Clinical Profile of Thalassemia Syndrome in Children of Northern Bangladesh

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### Abstract

**Background:** 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:** Hundred cases were selected from Thalassemia patient admitted in department of pediatrics, on May 2012 to October 2012. A prescribed questionnaire was used to record the information. The methods were explained to the patients and consent was taken. Necessary physical examination was performed and investigations were done. The data was analyzed by standard procedure.

**Results:** Out of hundred (100) cases, most (61%) 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. 54% were male and 46% were female. The major presenting symptom was progressive pallor in 70% cases. Others presenting complaints were low grade fever (40%). Hemoglobin concentration at the time of diagnosis was below 5 gm/dl in 53.33% patients. In hemoglobin electrophoresis it was Hb-E ranged from  $54.64 \pm 13.02\%$ , Hb-F  $34.84 \pm 13.73\%$ , Hb-A  $23.32 \pm 18.15\%$  and Hb-A<sub>2</sub>  $3.5 \pm 70\%$ . Radiological findings revealed gross bony changes occur in long standing cases. Enlarged cardiac shadow was found in those cases having severe anemia with heart failure.

**Conclusion:** In countries with a high incidence of thalassemia, it is vitally important to offer prospective genetic counseling and to warn carriers about the risks of intramarriage. Nutritional and folic acid supplementation with regular blood transfusion along with iron chelation therapy is essential to improve the prognosis.

**Key words:** Thalassemia, clinical profile.

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## Introduction

Thalassemia is a common inherited hematological disorder in our country. It is characterized by the reduction or absence of synthesis of globin chains. Thalassemia may be alpha or beta. There is a wide array of genetic defects and a corresponding diversity of clinical syndromes.<sup>1,2,3</sup> Children with Beta thalassemia usually become symptomatic during 2<sup>nd</sup> 6 month of life. Fatigue, poor appetite and lethargy are late findings of severe anemia in an infant or children before transfusions 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. These classical findings are primarily seen in developing countries.

Many of these features became less severe and less frequent with blood transfusion. Endocrine and cardiac pathology is often associated with excessive iron stores in patients with thalassemia major who are chronically transfused. Common endocrine dysfunctions are hypothyroidism, gonadal failure, hypoparathyroidism, and diabetes mellitus. Most infants and children have cardiac decompensation when the hemoglobin is 4.0 g/dL or less.<sup>4</sup> The diagnosis of thalassemia is initially suggested by clinical findings, family history and the results of routine hematological profile and confirmed by Hb Electrophoresis.<sup>5</sup> Structural hemoglobinopathy have an impact on RBC indices e.g. Hb, MCV, RDW, RBC number are critical to diagnosis. Thalassaemic 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.<sup>6</sup> Normal haemoglobins are Hb-A > 95%, Hb-A<sub>2</sub> < 3.5% Hb F < 2.5%.<sup>4</sup>

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

Thalassemia syndrome. So this study is under taken to correlate between clinical presentation, hematological profile and Hb Electrophoresis of different types of Thalassemia for proper management and ensure better outcome in our setting. The present study was aimed to find out the clinical features of different types of Thalassemia in northern area of Bangladesh.

## Materials and Methods

This was a prospective type of study done in department of pediatrics, Rajshahi Medical College Hospital, Rajshahi. Study period was six months from May 2012 to October 2012. Total hundred Thalassemia patients 0-12 years admitted in pediatric ward of Rajshahi Medical College Hospital. Purposive sampling method was followed in this series. Written informed consent was obtained from parents, a prescribed questionnaire sheet was used to record the information. All necessary physical examination of the patient was performed. All necessary investigations were done. Main outcome variable: age, sex, weight, height, liver size, splenic size, jaundice, edema, Hb (gm/dl), Hb Electrophoresis (HbA, HbA<sub>2</sub>, HbF, Hb E), S. Iron level. Inclusion criteria was children under 12 yrs with thalassemia syndrome. Exclusion criteria were thalassemia with septicemia, thalassemia with meningitis. Ethical measures were taken. After all necessary correction, the data was compiled and analyzed in the computer based software, the statistical package for social science (SPSS) version 17.

## Results

A total 100 patients were included in this study Shows 61% Hb-E beta thalassemia. Onset before 6 months of age was 20%. Most cases present within one year (64%). Majority of the patients (70%) had complaints of progressive pallor. Out of 100 cases 46 cases had typical mongoloid facies, 68 cases had moderate pallor

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.

Almost all the cases had widened diploic spaces of the skull bones, widening or broadening of the posterior ends of the ribs and transverse processes of the vertebrae as well as metacarpals of the hands with thinned cortices. Few cases had enlarged heart shadow as well as pulmonary congestion. There were no bone changes in Hb-E trait and Hb-E disease cases, some thalassemia minor cases had only mild bone changes.

**Table 1: Types of Thalassemia syndrome in study population**

Types of disorder	Number of patients	Percentage
HbE-β thalassemia	61	61%
Thalassemia major	20	20%
Thalassemia minor/trait	17	17%
Hb-E disease	1	1%
Hb-E trait	1	1%

**Table 2: Presenting complaints of study subject**

Symptoms	Number	Percentage (%)
Progressive pallor	70	70%
Jaundice	21	21%
Anorexia	29	19%
Abdominal swelling	27	27%
Fever	40	40%
Abdominal pain	15	15%
Cough and cold	30	30%
Diarrhea	15	15%
Urinary complaints	13	13%
Growth failure	18	18%
Miscellaneous	13	13%

**Table 3: Physical signs at the time of study of the study subjects**

Physical signs	Number of patients	Percent age (%)		
Mongoloid facies	46	46%		
Frontal bossing	26	26%		
Pallor	Mild	13	13%	
	Moderate	68	68%	
	Severe	18	18%	
Jaundice	Mild	30	20%	
	Moderate	15	15%	
	Severe	-	-	
Not palpable	Not palpable	14	14%	
	Hepatomegaly	<5 cm	49	49%
		5-8 cm	27	27%
		>8 cm	10	10%
Not palpable	Not palpable	7	7%	
	Splénomegaly	<5 cm	23	23%
		5-8 cm	25	25%
>8 cm		34	34%	
Edema	12	12%		
Growth retardation	57	57%		
Splenectomy	5	5%		

**Table-4: Hb-electrophoresis of the study subjects**

Types of disorder	Hb A	Hb A <sub>2</sub>	Hb F	HbE
HbE-beta thalassemia	23.32±18.15	3.50±.70	34.84±13.73	54.64±13.02
Thalassemia major	22.52±20.78	10.97±13.94	69.20±22.19	-
Thalassemia minor/trait	83.00±4.49	4.15±2.97	13.10±4.24	-
Hb-E disease	50.00±5.00	-	-	50.00±5.00
Hb-E trait	70.00±0.00	-	-	24.1±

## Discussion

In an attempt to find clinical presentation different types of Thalassemia in northern Bangladeshi population, this study is carried out. 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.<sup>6</sup> 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.<sup>6-9</sup> 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.<sup>7, 10-12.</sup>

Clinical presentation of thalassemia might show a variable degree of expression.<sup>10,13</sup> 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. Three 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 4 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.

Five cases of thalassemia minor also manifested before 1 yr of age which also suggests that, it can manifest at early age especially if infection, stress and other stimulus act as precipitating factors. Physical findings of the patients were also consistent with another report.<sup>6</sup> Growth deficiency found in the vast majority of cases was also consistent with another report.<sup>7</sup> The major presenting symptom was progressive pallor in 70% cases. The next major complaint was low grade fever, 40% cases. Abdominal swelling was present in 27% of cases and diarrhea 15%. This finding is more common in 1 to 5 years of age and

coincides with the previous studies. History of jaundice was present in 21% 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. This can be present only during hemolytic crises.<sup>14</sup>

About 29% cases complained of anorexia, growth failure was noted in 18% of cases. This finding is more common in 5 to 10 years aged children due to anemia and anorexia. 15% presented with abdominal pain due to pressure effect by enlarged liver and spleen. Pain subsided after blood transfusion while liver and spleen became smaller.

Miscellaneous symptoms like headache, generalized weakness, vertigo, palpitation, respiratory distress, pain in the limbs were present in few cases. Random findings in few cases had pain in the limbs with gross deformity. This indicates excessive proliferation of bone marrow (marrow expansion) for increased growth of erythroid series which leads to deformity along with pain in the limbs due to pressure effect. Family history of thalassemia was positive in 23%. There was no history of consanguinity of marriage in this study. Majority of the patients came from poor socio-economic background.

Physical signs in this study were consistent with the signs of chronic hemolytic anemia. Signs vary according to the severity and duration. Eight cases of thalassemia minor, 1 cases of Hb-E disease and Hb-E trait each patients had no signs. Chronic hyperbilirubinemia, gall stone formation and gall-bladder disease are unusually common in people with HbE-beta thalassemia in Srilanka.<sup>15</sup> There was no such case in this study,

Definite growth retardation was present in 60%, out of which all the 20 cases of thalassemia major and 40 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.<sup>16</sup>

Hemoglobin concentration at the time of diagnosis was below 5 gm/dl (53.33% cases). These patients had severe clinical anemia. Only 7 patients out of these had sign & symptoms of heart failure.

Pre-transfusion hemoglobin concentration was between 6-8 gm/dl in most cases, and peripheral blood film showed anisocytosis, poikilocytosis, microcytosis, tear drop cells, target cells, fragmented RBC and polychromasia. Reticulocytes count was found to be increased. Higher count of reticulocyte was associated with increased size of the spleen.

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. Ribs and metacarpals showed broadening and enlarged ends with increased translucency as well as transverse processes of vertebrae. Enlarged cardiac shadow was found in those cases having severe anemia with heart failure.

### Conclusion

In countries with a high incidence of thalassemia, it is vitally important to offer prospective genetic counseling and to warn carriers about the risks of intra-marriage. To date, attempts at this approach have been relatively unsuccessful. Hence, considerable efforts have been directed towards prenatal diagnosis programs. As carrier states of the thalassemias are readily identifiable, affected fetuses can be diagnosed. Nutritional and folic acid supplementation with regular blood transfusion along with iron chelation therapy is essential to improve the prognosis.

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