A study of physical growth parameters in patients of Thalassemia major.

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Abstract:

Introduction: Thalassemia is the most common genetic disorder all over the world as per WHO and so pose a major public health burden in this millennium affecting the growth and the general well being of a large number of children**. Aims & Objectives:** To analyze physical growth in patients of thalassemia major and to determine association between pre blood transfusion haemoglobin levels and serum ferritin with the growth parameters. **Materials and Methods:** Cross sectional study including 72 children with B-thalassemia major under the age of 12 years coming to civil hospital for regular blood transfusion. Height and weight of the child were measured using standard techniques every time the child came for blood transfusion along with pre transfusion haemoglobin. Serum ferritin was repeated every 3months.The effect of serum ferritin and pre transfusion haemoglobin on physical growth was studied. **Results:** Out of total 72 patients, there was a slight preponderance of males (54.1%) compared with females (46.9%).Of total 31 short statured, 15(48.3%) were females and 16(41.7%) were males. 20 out of total 31(64.5%) short statured patients had serum ferritin >2000ng/ml. The patients with a mean transfusion haemoglobin <9g/dl were 40 (55.5%), out of which 20 patients have short stature (64.5% of the total short stature). **Conclusion:** Regular blood transfusions can maintain pre transfusion haemoglobin levels, but if serum ferritin levels are higher than the desired levels, patients' physical growth can be affected. Thus, along with maintaining haemoglobin levels, it is important to have effective iron chelation therapy to minimize retardation of growth in patients with transfusion-dependent thalassemia. Thalassemia patients requiring regular blood transfusions need better strategies for removing excess iron.

Key words: Physical growth, Pre transfusion haemoglobin, Serum ferritin, Thalassemia.

Introduction:

Thalassemia is an inherited hemoglobinopathy characterised by ineffective erythropoiesis. Patients with thalassemia major require blood transfusions every 2-4 weeks. Blood transfusion corrects anaemia, enables normal growth and physical activity along with inhibiting marrow expansion. But the benefits of transfusion are accompanied by iron overload. Iron overload results in endocrinopathies, cardiac and liver dysfunction, disorders of growth and puberty.[1] Physical growth is affected in a large number of the patients with transfusion-dependent thalassemia. The etiological factors leading to growth retardation in transfusion-

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dependent thalassemia are varied, with iron overload-induced endocrinopathies, chronic anaemia, and folate and zinc deficiencies having been implicated in this complication.[2,3] A close monitoring of growth may lead to early identification and treatment of these complications to ensure that patients achieve near normal adult height. India has a large number of young patients with transfusion-dependent thalassemia, and very few studies have reported the issues related to physical growth in these children. [4, 5]

Materials and Methods:

This is a cross sectional study involving 72 patients conducted in civil hospital Ahmedabad (thalassemia clinic).The subjects included in the study are already enrolled over the past few years and are taking regular blood transfusions.

At the time of registration, all patients had a detailed clinical examination and laboratory tests, including a hemogram, liver function test, and screening for hepatitis B, hepatitis C, and human immunodeficiency virus (HIV). Most of the patients visited the thalassemia clinic at civil hospital Ahmedabad every 3–4 weeks for blood (packed cell) transfusion. At this time, in addition to clinical data, a hemogram was done for all patients. Serum ferritin and calcium levels were recorded at the time of registration and every 3 months. Screening for hepatitis B, hepatitis C, and HIV was repeated every 6 months. The first ferritin level was measured after 15 blood transfusions, and deferasirox (20–40 mg/kg/day) was started when the patient's s. ferritin >1000. Serum ferritin levels were tested every 3 months.

The anthropometric measurements were taken following the standard techniques. Weight measurement was taken on a balance scale. Weight was recorded to the nearest 0.1kg. Height was measured using a stadiometer with the subject standing erect with heels together. Chest circumference was measured by using a measuring tape. The tape was held horizontally at the level of nipple passing over the lower subscapular angle. Using measuring tape, mid arm circumference was taken at maximum girth of arm. Head circumference (cm) was measured by using measuring tape. The tape was wrapped snugly around the widest possible circumference from most prominent part of forehead (Often 1-2 fingers above the eyebrow) around to the widest part of the back of head.

BMI was calculated by using following formula:

$$\textbf{BMI (kg/m}^2\textbf{) =weight (kg)/ height (m}^2\textbf{)}$$

Results:

Table 1 Comparison of weight of thalassemic children with normal population:

Age group	Mean Weight of thalassemia major subjects	Mean Weight (50^{th} percentile) IAP standards
1-4 years	12.7 kg	15.16 kg
5-8 years	17.6 kg	21.65 kg
9-12 years	23.71 kg	30.84 kg

Table 2 Comparison of height of thalassemic children with normal population:

Age group	Mean height of thalassemia major subjects	Height (50th percentile) IAP standards
1-4 years	86.7 cm	99.39 cm
5-8 years	103.21 cm	118.13 cm
9-12 years	123.01 cm	138.9 cm

Age ranges of the subjects were from 10 months to12 years. Mean age was 7.507 years. There was an almost equal distribution of patients from infancy to adolescence, with a slight preponderance of childhood over toddlers owing to age at diagnosis. There was a slight preponderance of males (54.1%) compared with females (46.9%).

Table 3 Clinical parameters of patients undergoing regular blood transfusion: (n=72)

Clinical Parameter	Number of Patients	Percentage (%)
Hepatosplenomegaly	47	65.2
Splenectomised	5	6.9
Iron chelation therapy	68	94.4
No of patient with weight <2 SD	8	11.1
No of patients with height <2 SD	31	42.4
HBsAg reactive	5	6.94
HCV Reactive	7	9.72

Table 4 Clinical correlation between Pre transfusion Hemoglobin levels with stunting:

Pre transfusion Hemoglobin	Number of patients (%)	Height <2SD
<7g/dl	5	4 (80%)
7-9g/dl	35	15 (42.8%)
9-11g/dl	32	12 (36.6%)

Pre transfusion haemoglobin levels were well maintained, with mean levels being 9.16 g/dl. Almost 2/5th (40.10%) of the patients had pre transfusion Hemoglobin levels above 9.5 g/dl, and only one patient presented with a mean pre-transfusion haemoglobin <7. Hemoglobin 4.96 g/dl. Lower pre transfusion haemoglobin is associated with stunting. 4 out 5(80 %) of patients with pre transfusion haemoglobin<7 had stunting height < 2 SD and 15(42.8%) out of total 35 with pre transfusion haemoglobin between 9-11 had stunting with height <2 SD.

Table 5 Clinical correlation between ferritin levels with stunting:

Mean serum ferritin	Number of patients (%)	Height <2SD
<2000 ng/dl	38 (54.10%)	11 (28.90%)
2000-5000 ng/dl	30 (38.91%)	16 (53.30%)
>5000 ng/dl	4 (06.60%)	4 (100%)

Mean ferritin level was 3112 ng/ml. The minimum value (385 ng/ml) was observed in a new patient, and the maximum value (5211ng/ml) was observed in a 12-year-old boy. Almost all patients (94.4%) were on chelation therapy; the remaining four patients were

considered to be too young for iron chelation therapy and had serum ferritin levels less than 1000 ng/ml. None of the patients was overweight or obese .Although minor variations were found in these parameters between males and female.

The relationship of height *z*-scores with mean serum ferritin levels and mean pre transfusion Hemoglobin was further substantiated by comparing these parameters in patients with height *z*-scores <2 with those with scores >2. Mean ferritin levels were significantly higher in short-statured (height *z*-score, 31/72) patients in comparison with pat0ients with normal heights.20 out of total 31(64.5%) short statured patients had serum ferritin >2000ng/ml. The prevalence of hepatitis B, C, and HIV was low in our patients, as they receive properly tested blood. Only a minority (9.73%) of patients required splenectomy(because of their socioeconomic and family constraints)

Discussion:

Physical growth is affected in a large number of the patients with transfusion-dependent thalassemia. A study of patients aged 10–27 years with thalassemia major found short stature in 70% of the males and in 73% of the females. [8] Another study found short stature in 29.7% of patients.[9)]The mean levels of serum ferritin depend on several factors, including age at presentation, age at beginning regular PRBC transfusion, age at starting iron chelation therapy, efficacy of the iron chelation drug and its compliance, and the age group of the reported series of patients. Our observed high ferritin levels among our thalassemic patients are consistent with serum ferritin levels of 2729 ng/ml (6579 pmol/L) observed in 11–19-year-old transfusion-dependent thalassemia major patients in Hong Kong.[9] However, low levels (2013 ng/ml or 4525 pmol/L)were found in patients younger than 11 years of age in this series. Observation of non-transplanted thalassemia major patients in the national registry of France indicates that better-managed patients may have lower serum ferritin levels (1240 ng/ml).[10] In one study, Mean haemoglobin pre transfusion levels can be maintained at; 8 mg/dl [10], the remainder [5] has an average haemoglobin below 8 mg/dl. Four children with serum ferritin over 3000 ng/ml, all with short stature.[11]

This excess iron store, as shown by increased ferritin values, seems to mediate several of the complications of thalassemia. In well-transfused patients, poor compliance to chelation treatment and subsequent iron overload remain the main causes of poor growth.

Conclusion:

Physical growth is very commonly affected in children with thalassemia major. The common predisposing factors are lower pre transfusion haemoglobin and higher mean serum ferritin levels. Height seems to be more commonly affected than weight. Regular blood transfusions can maintain pre transfusion Hemoglobin levels, but if serum ferritin levels are higher than the desired levels, patients' physical growth can be affected. Thus, along with maintaining Hemoglobin levels, it is important to have effective iron chelation therapy to minimize retardation of growth in patients with transfusion-dependent thalassemia. Thalassemia patients requiring regular blood transfusions need better strategies for removing excess iron.

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