

A Study on Anthropometry of Transfusion-Dependent Thalassemia Major Children and its Correlation with Pretransfusion Hemoglobin and Serum Ferritin

Shivani C. Rampure¹, Sneha Patil²

¹Assistant Professor, Dept. of General Surgery, Mahadevappa Rampure Medical College, Kalaburgi

²Dept. of Pediatrics

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Corresponding Author: Dr. Sneha Patil

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Abstract:

Introduction: In India prevalence of thalassemia ranges between 3-18%, particularly in certain communities like sindhi, Lohanas, gouda, etc. Regular blood transfusion with chelation is the main treatment since most patients cannot afford bone marrow transplants. Growth failure is the major complication in children with transfusion-dependent thalassemia major (TM) children even after giving chelation.

Material and Methods: In the study. weight, height, and BMI were measured and z scores of less than 2 were taken as underweight, stunted, and thin respectively. Z- scores were correlated with pretransfusion hemoglobin and serum ferritin. children having pretransfusion hemoglobin between 9-10.5 gm/dl was taken as adequately transfused. Growth parameters were also compared between adequately and inadequately transfused children.

Results: 36(56%) were Underweight (weight z score below 2), 28(43%) children had stunting (Height z score below 2) and according to BMI 24(36%) (BMI z score below 2) children were classified as thin. All the stunted children were in the 6-8 age group. correlation for PTHB with height for age z-score was positive and significant (spearman's $r=0.345$, $p=0.005$), with weight for age z score was positive but insignificant and with BMI was negative and insignificant. Correlation of serum ferritin with height for age z score and weight for age z score was positive but insignificant and with BMI was negative and insignificant.

Conclusion: Growth failure in children with thalassemia major requiring regular blood transfusions, in first decade is possibly due to inadequate transfusion rather than inadequate chelation. It is recommended to maintain pretransfusion haemoglobin in range of 9-10.5gm/dl to reduce the severity of growth failure.

Keywords: Anthropometry, Transfusion Dependant Thalassemia Major (TDTM), Growth Failure Pretransfusion Haemoglobin, Serum Ferritin.

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Introduction

Of the genetic disorders worldwide, thalassemia is the most common. Prevalence was previously more in the Mediterranean region, Africa, Southeast Asia, India, Southern China, middle east but it is increasing more even in north America and Europe. [1] 20 million Indians are carriers of thalassemia with the prevalence ranging between 1-18%. [2] Northern Indian communities like sindhi, lohanas and kutchi are more likely to carry the gene. (3-18%). It is also seen more in south Indian communities like gouda, Lingayat (1-3%). Bone marrow transplant is the definitive treatment for thalassemia but seldom children can afford it in low-income countries like India. So, patients of severe thalassemia like beta thalassemia major (TM) are dependent mainly on regular packed cell volume (PCV) transfusion [3,4]. Patients given regular PCV transfusions must be monitored Comprehensively

for complications like growth retardation, iron overload in the liver and heart, bone pathologies, and endocrinal issues like short stature diabetes mellitus, delayed puberty, and hypothyroidism. [5]

Growth retardation (GR) is a common complication in TM worldwide. [6] Prevalence of GR has been noted to be as high as 25-65%. Many factors have been implicated in GR of transfusion dependant TM patients. In the first decade of life factors like chronic hypoxia due to anaemia or irregular transfusion are one of the major issues. [3,7] other factors are trace element deficiencies like zinc and folate and the overloading of iron. Whereas during the adolescent age group, iron overload causing endocrinal dysfunction, liver Dysfunction, or inadequate chelation has been implicated as causative factors in GR [7] oral iron chelators have been considered as safe and efficient as

deferroxamine. [8,9,10]. TM is also more prevalent in the north Karnataka region in Certain communities like goudas, Lingayats, and tribal areas where consanguinity is common. So, we took up this study to determine the growth profile of these children and its correlation with anemia and/or iron overload. We used IAP-modified WHO growth charts for Indian children for measuring anthropometry. [11]

Material and Methods

All children diagnosed as TM by haemoglobin electrophoresis on regular blood transfusion and oral chelation therapy with deferasirox (DFX) for at least 5 years were included in the study.

Exclusion criteria: Children receiving transfusion for other hemolytic anemia, nutritional anemia, and suffering from chronic disorders needing a transfusion. Informed consent was taken from parents. Information regarding age, sex, age at diagnosis, PCV transfusion history, chelation duration, pre-transfusion haemoglobin, and serum ferritin levels were taken from departmental documents. Blood was collected for pretransfusion hemoglobin and Serum Ferritin in ethylenediaminetetraacetic acid and plain vacutainers respectively under all aseptic precautions. Haemoglobin was done on sysmex XN 1000 automated blood analysis machine and serum ferritin was estimated with the electro-chemiluminescence method. Anthropometry including weight in kg, and height in centimeters were recorded for all the sixty-four children who consented and plotted on IAP-modified WHO growth charts. BMI was calculated from measured weight and height with the formula weight in kg/

height in square meters. Z-Score of height, weight, and BMI were calculated by $x - \mu / \sigma$. A z-score of < -2 for weight was Considered as underweight, height < -2 as stunted, and BMI < -2 was considered thin for age. Versions 22 of the statistical package for the social sciences (SPSS) and STATA13 were used to gather, manage, edit, enter, and analyse the data (Stata Corp, College Station, TX, U.S.A.). For each patient in the study, a descriptive analysis was conducted. Frequency tables for categorical variables such (as gender and age group) were developed in order to examine the profile of the sample in relation to the variables analysed. In the case of parametric data, the mean, standard deviation, minimum, and maximum values were computed; in the case of non-parametric data, the median and interquartile range were determined. The growth parameters between groups that received adequate and inadequate transfusion were compared using the Chi-square method.

Relationships between the non-parametric variables were examined using Spearman rho correlation. A p-value of < 0.05 was used as the level of significance for all statistical tests. The connection between pre-transfusion hemoglobin in children with stunted vs. normal height was confirmed using the Mann-Whitney test.

Results

Total 64 children met the inclusion criteria. 38(59.4%) were male and 26(40.6%) were Female. Most children were between 6-8 years, as shown in table no.1 & 2. The median age was 7.5 years (10-7). Consanguinity was seen in 32(50%) children attending the thalassemia clinic.

Table 1: Demographic parameters of TDTM

Parameters	Category	Frequency(percent)
Age	6-8	44(68.8)
	9-11	6(9.4)
	12-14	14(21.8)
Sex	Male	38(59.4%)
	Female	26(40.6%)
Consanguineous	Male	13(20.3)
	Female	19(29.7)
Non-consanguineous	Male	25(39%)

Table 2: anthropometric parameters of TDTM

Parameter	Median/mean*	IQ /Standard deviation*
Age in years	7.5	10-7
Weight in kg	17	25-15
Height in cm	118*	15.55*
BMI in kg/sq. m	15.2	16.1-13
Z-score weight median	-4.7	4.98- (-7.1)
Z-score height mean	0.00	8.00
Z-score BMI median	15.2	16.1-13

All children were on oral chelation for the last 5 years. Compliance with chelation therapy with oral deferasirox was ensured Orally and checking for any remaining dose from parents during issuing the next

monthly dose each month. Median serum ferritin levels were 2000(2397-1614) ng/ml with the Median deferasirox dose being 20 (30-15) mg/kg.

Table 3: Clinical parameters of TDTM

Parameter	Category	Number
Blood transfusions	12 /year	44
	18/year	18
	24/year	2
Chelation	Total	64
	Regular (missed dose <4 days/month)	56
	Irregular (missed dose >4 days but <8 days/month)	08

Median pretransfusion hemoglobin was 6(9-5), which was much below the recommendation of the international thalassemia society i.e., 9-10.5 gm/dl.[12]. 44(69%) children were receiving only 12 transfusions per year, 18(28%) children were receiving 18 transfusions per year, and the Remaining 2 (3%) children 24 per year. Splenectomy was done in 8 children receiving 12

transfusions per Year and in 6 out of 18 children receiving 18 per year. Anthropometry of these children noted as 36(56%) were Underweight (weight z score below 2), 28(43%) children had stunting (Height z score below 2), and according to BMI 24(36%), children were classified as thin. All the stunted children were in the 6-8 age group.

Table 4: laboratory parameters of TDTM:

Parameter	Median	IQ
serum ferritin ng/ml	2000	2397-1614
Pretransfusion hemoglobin mg/dl	6	9-5
DFX mg/kg	20	30-15
Years on DFX	5	8-5

Those children having pretransfusion hemoglobin (PTHB) less than 9 were classified as inadequately transfused (IT) and those having above 9 were considered adequately transfused (AT). Out of the 36 underweight children, 31 were IT and only 5 were AT and the chi-square was significant ($p < 0.009$) among 28 stunted children all were IT. Chi-square being highly significant ($p = 0.00$). out of the 24 thin 18 were IT and 6 were AT ($P = 0.00$). The correlation coefficient of PTHB with weight for age z-score was positive but insignificant (Spearman's $r = 0.203$, $p = 0.107$). correlation for PTHB with height for age z-score was positive and significant (spearman's $r = 0.345$, $p = 0.005$), and with BMI was negative and insignificant (spearman's $r = -0.154$, $p = 0.224$). correlation of serum ferritin with height for age z score was positive but insignificant (spearman's $r = 0.138$, $p = 0.276$) And with weight for age z score was also positive but insignificant (spearman's $r = 0.14$, $p = 0.280$). The correlation of serum ferritin with BMI z score was negative and insignificant. ($r = -0.17$, $p = 0.177$)

Discussion:

The majority of children were in the 6-8 years age group. All these children were on regular but inadequate transfusion as the mean pre-transfusion haemoglobin was less than the recommendation of the international thalassemia society. [3,12] Male

preponderance was seen. 59.4% male as against 40.6% females. These findings were like seen in other studies. [2,3]. Consanguinity was 50%. [2] Basic anthropometric measurements of these children revealed significant growth retardation (GR). [6] stunting was mainly seen in 6-8 age group. This was due to chronic hypoxia due to anaemia. These findings were like those found in other studies [13]. Underweight and stunting were both seen more significantly in inadequately transfused children than in adequately transfused children [3,14]. Stunting was highly significant and this was like the study by other authors [2,15]. GR of these children was correlated with low pretransfusion hemoglobin which was significantly less than the recommendation of the international thalassemia society. These results were like the results of other studies [2,7,13,14]. The growth failure was not correlating with serum ferritin levels Which were seen in other studies like [16,17]. Growth failure in TM children is multifactorial [7]. We found weight and stature to be affected significantly due to decreased PTHB in the first decade of life. But in another study [18] serum ferritin was found to be the final predictor of stature during the first decade of life. Another study revealed that serum ferritin becomes a more relevant predictor of growth retardation after the adolescent age group as the number of transfusions increases [19]. The role of

zinc in growth retardation needs to be further evaluated [7,21]. Other factors which are known to affect growth are genetic factors, endocrinopathies, and nutritional status which were not evaluated in the present study. Our study was done by using 2015 IAP growth charts. These revised 2015 IAP growth charts have been compiled in such a way that the weight and height of the child can be plotted from 5-15 years in a single chart and these charts have been more relevant for Indian children above 5 years rather than WHO charts. [11]

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