FREQUENCY OF SHORT STATURE IN - THALASSEMIA MAJOR PATIENTS

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ABSTRACT

Objective: To determine the frequency of short stature in children with thalassemia major receiving multiple transfusions at Military Hospital Rawalpindi.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: Study was conducted at Military Hospital from 1st January 2010 to 30th June 2010.

Subjects and Methods: Total 100 multi-transfused cases of -thalassemia major were included in the study. The height of every child was measured in centimeters using the same free-standing standard stadiometer, and the same technique by a single pediatrician.

Results: Out of 100 patients of -thalassemia major 57.0% (n=57) were male while 43% (n=43) were female. Mean age was 9.94 years (SD ± 2.93) with range of 6 to 14 years. Mean height was 115.77 cm (SD ± 13.79) with range of 72.00 to 148.00 cm. 57.0% (n=57) were found to be short statured while 43.0% (n=43) were with normal height. Mean age of short statured patients was 11.61 ± 2.34 years and mean age of patients with normal height was 7.73 ± 2.05 years.

Conclusion: The frequency of short stature in our patients with -thalassemia major receiving multiple transfusions is high. There is need to monitor the height of thalassemic children regularly and to improve the quality of care being provided to them so as to improve their quality of life.

Keywords: -thalassemia major, short stature, Transfusions

INTRODUCTION

-Thalassemia major is a genetic disorder of hemoglobin synthesis characterized by ineffective erythropoeisis and chronic anemia, requiring regular red blood cell transfusions to overcome the complications of anemia and compensatory bone marrow expansion[1]. Three precent of the world's population carries genes for -thalassemia[2]. The estimated prevalence in Pakistani population is 3-8%[3]. Transfusion related iron overload is among the primary complications seen in -thalassemia major individuals[2].

The use of iron chelating agents delays the development of iron-induced damage to cardiac and liver tissues, thus improving the overall survival[2]. Chronic transfusion regimen and chelating therapy has dramatically improved the life expectancy of thalassemic patients but at the same time it has predisposed the patients to endocrinal dysfunction[4].

Short stature is a frequent finding among patients with beta-thalassemia major, with a major impact on the quality of life[5]. Disproportionate truncal shortening which is common especially among adolescents with thalassemia, is due to platyspondyly resulting from a combination of factors like hemosiderosis, endocrinal dysfunction, desferroxamine toxicity or deficiency of trace elements[6]. Short stature, low weight and sex development delay are common in children with beta-thalassemia major[7]. In a study carried out in Karachi, 40% of the children suffering from beta thalassemia major were found to be 2.5 standard deviations below the mean[8]. Thus, thalassemia is an important cause of increased morbidity and mortality among Pakistani children[9].

The purpose of this study is to find the frequency of short stature among the children with thalassemia major, being managed at our

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facility. The importance of study of short stature in this group is that the affected children can be advised appropriately and monitored for growth alongside the management of thalassemia. Furthermore, the exact underlying cause of short stature like high iron over load, chelating practices, pre-transfusion hemoglobin, endocrinopathies etc can be subsequently looked for and treated appropriately.

MATERIAL AND METHODS

This descriptive – cross sectional study was conducted at out-patient department of paediatrics, Military Hospital, Rawalpindi, from 1st January 2010 to 30th June 2010. One hundred diagnosed cases of -thalassemia major were registered. The patients of both genders between the ages of 6 and 14 years who were receiving regular blood transfusions on monthly basis with pre-transfusion hemoglobin of more than 8 gm/dl were included in the study by non probability – convenience sampling.

Any thalassemia patient with short stature proven due to any disease or concomitant chronic illness other than -thalassemia major e.g familial short stature, constitutional growth delay, congenital heart disease, tuberculosis, celiac disease, immunodeficiency etc were excluded from the study.

Every child was assigned a serial number. Detailed history was taken and all the information was recorded. The height of every child was measured in centimeters using the same free-standing standard stadiometer, by the same pediatrician and using the same technique. Results were entered in the proforma and the height of every child was plotted on standard WHO growth charts. The children whose heights were two standard deviations below the 50th centile for their age and sex were considered to be short statured.

Data was entered and analyzed using SPSS version 17. Mean and standard deviation (SD) were calculated for quantitative variables like age and height. Frequencies and percentages were calculated for qualitative variables like gender and short stature.

RESULTS

Hundred patients were enrolled in the study. The age of the patients ranged from 6 to 14 years, mean age was 9.94 years (SD ± 2.93 years). The height of patients ranged from 72.0 cm to 148.0 cm, mean height was 115.77 cm and standard deviation ± 13.79. Out of 100 patients

Table-1: Frequency distribution of various height statures according to age group of patients.

Age (years)	Stature of patients		Total
	Short stature n (%)	Normal height n (%)	
6.1-8.0	10 (23.8 %)	32 (76.2%)	42
8.1-10.0	6 (50%)	6 (50%)	12
10.1-12.0	13 (86.6%)	2 (13.4%)	15
12.1-14.0	28 (90.3%)	3 (9.7%)	31
Total	57 (57%)	43 (43%)	100

$p = 0.01$

57.0% (n=57) were short statured as their height was two standard deviations below the mean for age and sex while 43.0% (n=43) patients were of normal height. Out of 100 patients there were 57.0% (n=57) male and 43.0% (n=43) female. Out of 57.0% (n=57) short stature patients 34.0% (n=34) were males and 23.0% (n=23) were females. Out of 43.0% (n=43) patients with normal height, 23% (n=23) were males and 20% (n=20) were females. Mean age of short statured patients was 11.61 ± 2.34 years and mean age of patients with normal height was 7.73 ± 2.05 years (Figure 1 and 2). There was statistically significant relation between the frequency of short stature and advancing age of the patients (*p* value 0.01). Frequency distribution of various height statures according to age group of patients is shown in table-1.

DISCUSSION

Beta thalassemia is the most common single

gene disorder in Pakistan with a gene frequency of 3-8% and about 8-10 million carriers in the country[8]. Thalassemia major is an autosomal recessive disorder, lack of awareness in general public and the culture of cousin marriages is resulting in increased number of patients in Pakistan. Over the past three decades, regular blood transfusions and iron chelation has significantly improved the quality of life and transformed thalassemia from a rapidly fatal disease in early childhood to a chronic disease compatible with prolonged life. However, with the dramatically improved survival of patients with beta thalassemia major, care providers face new clinical scenarios and new challenges associated with the longer life and aging of these patients. One of such challenges is the management of short stature in thalassemic patients. Growth impairment has long been recognized as an important cause of morbidity in patients with thalassemia.

Large data are now available on growth and pubertal development of thalassemic patients. A study conducted in 1993 by Pantelalakis SN et al showed a tendency for height and weight to fall off after the age of 8 years for boys and 11 years for girls[10]. Body growth was satisfactory but bone age was generally retarded, more so in boys than in girls. Similar results were seen in a study done by Kattamis et al in 1970 which reported normal growth in children with hemoglobin levels above 8g/dl[11]. In 1980, delay in growth as judged by standard deviations for height, weight and bone age was reported in a study by Karagiorga-Lagana et al on body growth in relation to hemoglobin and ferritin levels. In boys, retardation in height started at the age of 8 years, becoming prominent at 11 years; and in girls started at the age of 10 years, becoming more pronounced at the age of 12 years. Bone age retardation also increased with age, but characteristically started much earlier than the height and weight retardation[12].

In our study, out of 100 patients of transfusion dependent beta thalassemia, we found 57% patients to be short stature. This prevalence is higher compared to the prevalence amongst Greek patients (35.3%) and also amongst Italian patients, aged 10-25 years old (37%)[12]. The higher prevalence in our patients could be attributed to suboptimal chelation therapy since

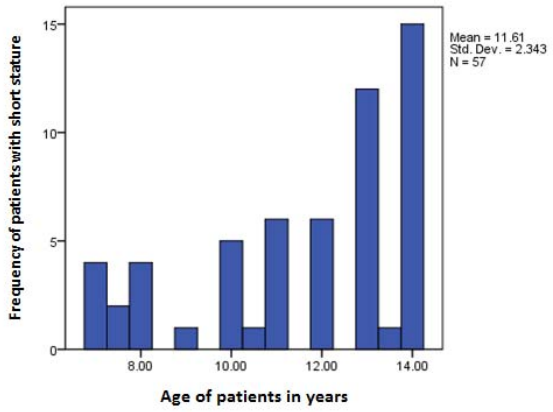

Figure-1: Distribution of short stature patients by age.

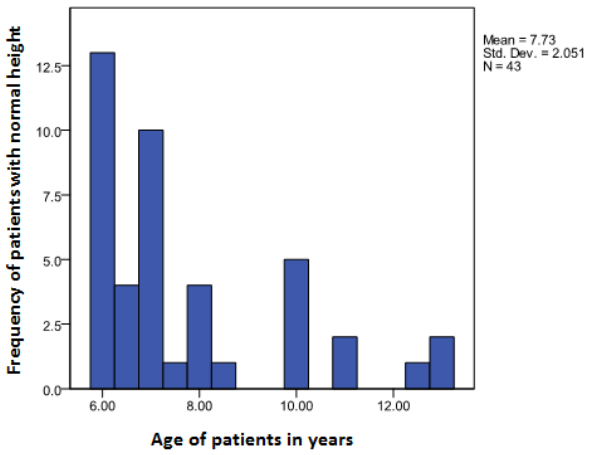

Figure-2: Distribution of patients with normal height by age.

the use of the desferrioxamine is limited to patients who can afford it. In addition, compliance is a major problem in many patients who are on chelation therapy.

Similar results were seen in a study done by A.Hamidah et al at Malaysia in 2001, they studied the growth status in 66 patients with beta-thalassemia major and Hb E - beta thalassemia who were transfusion dependent, aged from 2 to 24 years, and 66 controls matched for sex and age. The prevalence of short stature in transfusion-dependent thalassemics was 54.5% compared to 4.5% in control group (p<0.001). Short stature was more prevalent in those above the age of 10 years in this study group (83.3% vs 16.7% respectively)[5]. A study carried out by Fica S et al at Bucharest, Romania revealed a prevalence of 53.12% short statured beta thalassemia patients[1]. Also in a study done by Louis C.K Low in China, even a more high prevalence of 75% in girls and 62% in boys was reported[6].

A cross-sectional analysis of the growth patterns in Beta Thalassemia patients done by Pantelalakis SN et al in 1973 reported that growth retardation became more pronounced with advancing age[11]. It is likely that growth impairment in thalassemics commences at an earlier age, however further deceleration of growth probably takes place in the second decade[12]. Similar results were found in our study where short stature was more prevalent in those who were above 10 years compared to those who were below 10 years (41% vs 16% respectively). Similarly a multi-centric study done by Borgna - Pignati C et al in 1985 on thalassaemic patients in northern Italy also reported retarded growth in height and skeletal maturation in both the sexes, which was more pronounced after the age of 14 years. The results of multiple longitudinal growth studies showed that growth retardation was more pronounced between the age of 10 and 15 years in females and between 15 and 20 years in males[10,11,13].

In a study done by Anita Saxena in 2003, it has been reported that growth delay sets in after the age of 4 years in boys and 3 years in girls[14]. These studies show that patients of thalassemia major who are treated with frequent transfusions and chelation therapy, grow normally up to the age of 8-11 years, but thereafter show growth retardation most often coupled with delay in sexual maturation. Patients experienced short and delayed pubertal spurt in all the parameters[15].

Karagiorga-Lagana et al reported in 1980 that cause and effect relationship exists between hemoglobin and various body segments. Low hemoglobin levels were associated with slow growth and compromised height. Disproportion in body segments can be explained on the basis of following: (i) chronic anemia caused stunting effect on both long and trabecular bone and hence body disproportion, (ii) suboptimal chelation therapy lead to uncontrolled serum ferritin levels causing damage to hypothalamic - pituitary axis and hence growth failure and lack of normal pubertal spurt[12].

The pathogenesis of late impairment of growth and sexual maturation in transfused patients with thalassemia major is not yet well defined. It is generally believed that it is directly related to iron toxicity, especially of the endocrine glands. However, more studies are needed to clarify the pathogenetic mechanisms of growth retardation in thalassaemic patients and subsequently to assist in more adequate and efficient planning of a therapeutic approach, including perhaps hormonal therapy.

CONCLUSION

We conclude that the frequency of short stature in children with thalassemia major receiving multiple transfusions at Military Hospital Rawalpindi is very high. The frequency of short stature in older patients was significantly greater than the younger ones thus showing a clear association between advancing age and risk of acquiring short stature. Quality of care being provided to such patients including adequate blood transfusion, chelation practices and monitoring of complications of iron overload may be improved so as to improve their quality of life.

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