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β-THALASSEMIA MAJOR;

FREQUENCY OF SHORT STATURE IN CHILDREN WITH β-THALASSEMIA MAJOR RECEIVING MULTIPLE BLOOD TRANSFUSION

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ABSTRACT… Background: B-thalassemia is a common single genetic disorder in Pakistan with about 8% gene frequency and roughly 10 million carriers. Growth impairment leading to short stature in thalassemic patients is an important cause of morbidity. **Objectives:** To determine the frequency of short stature in children with muti-transfused β-Thalassemia major. **Study Design:** Descriptive cross sectional study. **Place and Duration of Study:** Pediatric Department, Allied Hospital, Faisalabad from December 2015 to May 2016. **Patient & Methods:** Ninety multi-transfused β-thalassemia major patients diagnosed by hemoglobin electrophoresis between 06 to 10 years of age of either gender were included. Patients with β-thalassemia major with a concomitant chronic illness like congenital heart disease, tuberculosis, celiac disease and immunodeficiency and those with familial short stature as determined by history and mid-parental height were excluded. **Results:** Out of 90 cases, 56.67% (n=51) were between 6-8 years of age while 43.33% (n=39) between 9-10 years of age, mean ± SD was 7.85+1.50 years, 51.11%(n=46) male and 48.89%(n=44) were females. Frequency of short stature in children with β-thalassemia major receiving multiple transfusion was 41.11% (n=37) while 58.89% (n=53) had normal stature. **Conclusion:** The frequency of short stature is high among β-thalassemic multi-transfused children. It is recommended that every patient with β-Thalassemia major, should be sort out for short stature. However, surveillance of growth and development in these patients is important.

Key words: β-Thalassemia Major, Multiple Transfusion, Short Stature, Growth and Development.

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INTRODUCTION

Thalassemia is one of the major types of hereditary anemia resulting from defective hemoglobin production. Main etiology behind is reduced or absent production of one or more globin chains, thus disrupting the ratio of α or β globin chains in adult hemoglobin A. In minor varieties of α or β-Thalassemia maximum patients are asymptomatic and are mostly diagnosed incidentally on investigation as mild anemia with microcytic hypochromic red cells in peripheral smear. B-Thalassemia major patients with either absence or severe deficiency of β-globin chain synthesis have severe anemia and need frequent blood transfusions.[1] Target hemoglobin level > 9gm/dl should be maintained along with iron chelation therapy to avoid various complications of iron overload. With iron deposition and free radicals generated after iron metabolism damage membrane lipids and lead to cell death and end-organ damage. Most commonly, endocrine glands like pituitary gland, are more affected by iron overload leading to endocrinopathies. Early recognition and prompt treatment of these endocrine dysfunctions can decrease the morbidity associated with thalassemic patients.[1,2] These include hypogonadotrophic hypogonadism, deficiency of growth hormone and diabetes.[3,4]

Growth failure is one of the major recognized complications of thalassemia major seen almost in all patients. Growth failure is due to multiple causes like anemia, hypoxia, chronic liver disease, zinc and folate deficiency, iron overload, over-chelation, endocrine

dysfunctions (hypogonadism, delayed puberty, hypothyroidism) and dysregulation of GH–IGF–1 axis.[2] Insulin-like-growth-factor-1 (IGF-1) produce the growth effects of GH by acting on the growth plate and promoting anabolic reactions leading to increase in body mass and bone density. Thus, deficiency of growth hormone due to dysfunction of pituitary gland end up in short stature.[5]

In a study carried out in Sydney, frequency of short stature in Thalassemia patients was found to be 34.5%.[1] Roughly 6000 new cases of thalassemia are reported every year in Pakistan for treatment.[6]

The purpose of this study is to determine the frequency of β-thalassemia major muti-transfused patients with short stature, so that we can detect those children and monitor their growth velocity and then treat them accordingly. Prevention and early detection of endocrine dysfunctions in these patients can decrease the disease morbidity and improve the life Furthermore other associated endocrinological disorders can also be detected early if one disorder is detected.

We planned this study with the view to determine the frequency of children with β-thalassemia major with history of multiple blood transfusions and also having short stature, so that we can identify and later monitor their growth velocity while managing them properly.

PATIENTS & METHOD

Ninety β-thalassemia major patients diagnosed by hemoglobin electrophoresis between 06 to 10 years of age of either gender with past history of more than 20 blood transfusions coming for follow-up in emergency or pediatric ward, Pediatrics Department Unit – I, Allied Hospital Faisalabad between December 2015 to May 2016 were included in this Descriptive - cross sectional study after approval from the Punjab Medical College ethical committee through non-probability purposive sampling. A child was labeled as having β-thalassemia if he or she received multiple transfusions before 2nd birth day with splenomegaly clinically seen on clinical examination along with elevated fetal hemoglobin (Hb-F) on Hb electrophoresis. Those thalassemia patients who had received more than 20 blood transfusions were labeled as multi-transfused beta thalassemia patients. Children with height below 3rd percentile for the age and sex measured by growth chart were labeled as having short stature.

Sample size of 90 patients was calculated by using absolute precision 10%, confidence level at 95% and prevalence of short stature 34.5%.

Patients with β-thalassemia major with a concomitant chronic illness like congenital heart disease, tuberculosis, celiac disease and immunodeficiency and those with familial short stature as determined by history and mid-parental height were excluded.

After getting permission from hospital ethical review committee and taking informed written consent from parents/guardian of 90 Children meeting the inclusion criteria were selected. Every child was assigned a serial number. Detailed history was taken and all the information entered in the proforma. The height of every child was measured in centimeter using the same free standing standard stadiometer and using the same technique in the department of Pediatrics, Allied Hospital, Faisalabad. Results were entered in the proforma for each patient.

Data was entered and analyzed using SPSS v.19. Mean and standard deviation was calculated for quantitative variables like age and height. Frequency and percentages were calculated for qualitative variables like gender and short stature. Effect modifiers like age and gender were stratified. Post stratification chi-square was applied p-Value < 0.05 was taken as significant.

RESULTS

A total of 90 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the frequency of short stature in children with β-Thalassemia major receiving multiple transfusion at department of Pediatrics Allied Hospital, Faisalabad.

Age distribution of the patients shows that 56.67% (n=51) were between 6-8 years of age while 43.33% (n=39) were between 9-10 years of age,

mean + sd was calculated as 7.85+1.50 years. (Table-I) Patients were distributed according to gender showing 51.11% (n=46) male and 48.89% (n=44) were females. (Table-II) Height of the children (cm) was calculated as 129.52+16.43. (Table-III) Frequency of short stature in children with β-thalassemia major receiving multiple transfusion was recorded in 41.11% (n=37) while 58.89% (n=53) had no findings of the morbidity. (Table-IV) Stratification for short stature with regards to age shows that out of 37 cases 22 were between 6-8 years of age while 15 were between 9-10 years of age, p value was calculated as 0.65. (Table-V) Stratification for short stature with regards to gender shows that out of 37 cases 18 were male while 19 were females; p value was calculated as 0.69. (Table-VI)

Age(in years)	No. of patients	%
6-8	51	56.67
9-10	39	43.33
Total	90	100
Mean+sd	7.85±1.50	

Table-I. Age distribution (n=90)

Gender	No. of patients	%
Male	46	51.11
Female	44	48.89
Total	90	100

Table-II. Gender distribution (n=90)

Height of the Children (cm)	Mean	SD
	129.52	16.43

Table-III. Mean height (n=90)

Short stature	No. of patients	%
Yes	37	41.11
No	53	58.89
Total	90	100

Table-IV. Frequency of short stature in children with β-thalassemia major receiving multiple transfusion (n=90)

Age (in Years)	Short Stature		P value
	Yes	No	
6-8	22	29	0.65
9-10	15	24	

Table-V. Stratification for frequency of with regards to age (n=37)

Gender	Short Stature		P value
	Yes	No	
Male	18	28	0.69
Female	19	25	

Table-VI. Stratification for frequency of with regards to gender (n=37)

DISCUSSION

B-thalassemia is a most common single genetic disorder in Pakistan with an incidence of about 8% and roughly 10 million are carriers of this disease. In the last half century, multiple transfusions and chelation therapy has improved the quality of living and decreased morbidity from this disease. Early control and management of multiple endocrinopathies and complications of thalassemia during the childhood has improved the survival of these patients. But still health care providers daily face new challenges and cases requiring research and clinical consultations for better outcome. Growth impairment associated with multi-transfused thalassemia major seen in almost all patients.

In our study, out of 90 cases, 56.67%(n=51) were between 6-8 years of age while 43.33% (n=39) were between 9-10 years of age, mean±SD was calculated as 7.85+1.50 years, 51.11%(n=46) male and 48.89%(n=44) were females, frequency of short stature in children with β-thalassemia major receiving multiple transfusion was recorded in 41.11% (n=37) while 58.89% (n=53) had no findings of the morbidity.

The findings of a similar study carried out in Sydney revealed that the frequency of short stature in Thalassemia patients was 34.5%.[1]

Another study by Muhammad Shahid Aslam et al. determined the frequency of short stature in thalassemic patients at Military Hospital Rawalpindi and recorded that out of 100 patients of β-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, man height was 115.77 cm (SD ± 13.79) with range of 72.00 to 148.00 cm, our findings are in agreement with this study. He reported 57.0% (n=57) with short stature while 43.0%

(n=43) were having normal height, slightly higher common age was due to inclusion of patients between 6-14 years of age while the frequency of short stature was also higher and the probable reason may be the inclusion of up to 14 years of age of the patients, which is different from our study i.e. up to 10 years.[7]

The limitation of our study was that we included the children up to 10 years of age the frequency of this morbidity is more prone in children with 11-18 years of age; similarly in a cross-sectional analysis on beta-thalassemic patients, Pantelalakis SN, et al. reported that growth retardation became more pronounced with advancing age.[9] Probably growth retardation occurs at an earlier age, but further decrease is seen in the second decade of life along with other complications.[10]

After a multi-centric study done by Borgna - Pignati C, et al[11] in northern Italy, authers concluded that decrease in height and disturbed skeletal maturation in both the genders occurred and was more after the age of 14 years. Similar studies reported that growth retardation was more among the thalassemia patients between the age of 10 - 15 years in females and between 15 to 20 years in males.[8,10,11,13] Some more clinical trials are required in the age between 11-18 years to see the exact pattern and frequency of short stature in these patients.

LIMITATIONS

The limitation of our study was that we included the children up to 10 years of age the frequency of this morbidity is more prone in children with 11-18 years of age. Patients belonged to different socioeconomic background which affects the health care, growth, development and follow-up visits of these patients.

CONCLUSION

The frequency of short stature is high among β-thalassemic children receiving multiple transfusions. So, it is recommended that every patient who present with β-Thalassemia major, should be sort out for short stature. However, it is also required that every setup should have their surveillance in order to know the frequency of the problem.

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Never quit;
struggle for higher objective.

– Prof. Dr. Muhammad Shuja Tahir –

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Muhammad Shamaoon	Article writing, Data collection, Data analysis, Supervision and coordination.	
2	Junaid Nawaz	Data collection, Article writing, Data analysis.	
3	Muhammad Ahsan	Data collection, Article writing, Data analysis.	