

Growth Impairment and Dental Caries in Thalassemia Major Patients

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Abstract:

Background: The aim of present study was to determine whether beta-thalassemia major is associated with an increased risk of growth retardation and dental caries.

Methods: Anthropometric measurement were used to study the physical growth of 50 thalassemic patients and compared with 50 age- matched healthy controls from Jodhpur district of Rajasthan. DMFT and DMFS scores were also measured and compared with age- matched controls.

Results: Both thalassemic diseases of male and female patients were shown to have statistically significant lower height, weight, body mass index, mid arm circumference, chest circumference and head circumference (but not height and head circumference in age group 2-10years) as compared to normal patients with comparable sex and ages. A highly significant difference was observed when all anthropometric parameters of thalassemic males and healthy males were compared but a non-significant difference was seen between thalassemic females and healthy females of control group. Dental caries were significantly higher in thalassemics.

Conclusion: Thalassemia is associated with growth retardation and higher rates of dental caries.

Keywords: thalassemia major, dental caries.

Introduction

Beta thalassemia major (BTM) is a severe haemolytic anemia and it is the most common single gene abnormality. It has over 200 mutations; most of them are very rare. Approximately 20 common alleles constitute 80% of the known thalassemia worldwide. About 3% of the world population carries genes of beta thalassemia¹. Many complications of beta thalassemia are the result of increased iron deposition from repeated blood transfusion. The accumulation of iron in different tissues causes organ damage affecting mainly endocrine glands, heart and liver². The most prominent endocrine complication is failure of normal pubertal development and growth retardation³.

Growth retardation is commonly reported in children and adolescents with BTM. The child with BTM has a particular growth pattern, which is relatively normal until age 9-10 years; after this age a slowing down of growth velocity and a reduced or absent pubertal growth spurt are observed. The pathogenesis of growth failure is multifactorial^{4,5}. Key contributing factors to stunted growth in patients with TM may include chronic anaemia, transfusional iron overload, hypersplenism, and chelation toxicity. Other contributing factors include hypothyroidism, hypogonadism, GH deficiency/insufficiency, zinc deficiency, chronic liver disease, under nutrition and psycho-social stress⁶. Growth disturbance are a major clinical feature of untreated patient with thalassemia⁷.

The increasing mean survival age is indicative of the fact that modern therapies are generally safe and effective but it is becoming increasingly clear that as thalassemic patients approach the age of puberty, many develop growth retardation and pubertal failure⁸.

Thalassemia is widely distributed in Asian Indians with an average prevalence rate of 4 %⁹. Growth impairment is a common complication of homozygous b-thalassemia. There are very

few studies available on the growth patterns in thalassaemic children from this region¹⁰. Thus, this study was designed to evaluate the various growth parameters and to compare them with age and sex matched healthy controls.

Further, dental caries and oro-facial changes in thalassaemia major patients are reported by several investigators who have reported that dental caries were significantly higher in thalassaemia patients as compared to healthy controls¹¹⁻¹⁴. The aim of this study was also to assess whether beta-thalassaemia major is associated with an increased risk of dental caries.

Material and Methods

The present study was carried out in the Department of Anatomy, Dr. S.N. Medical College & Associated group of Hospitals, Jodhpur in association with Department of Paediatrics, Umaid Hospital for women and children Regional Institute of Maternal & Child Health Dr. Sampurnanand Medical College & Associated group of hospitals, Jodhpur and Central Academy School, Jodhpur.

Fifty (50) Healthy controls and fifty (50) Thalassaemic patients of both sex and varying age groups (2-20 years) were included in the present study and the patients were registered with Marwar Thalassaemia Society. These selected 50 Thalassaemic patients were regularly attending the Out Patient Department (OPD) or blood bank for repeated blood transfusion or were admitted in the wards of Department of Paediatrics, Umaid Hospital for women and children, Regional Institute of Maternal & Child Health, Dr. Sampurnanand Medical College & Associated group of hospitals, Jodhpur.

All diagnosed Thalassaemic patients and Healthy controls were further evaluated for present study by taking anthropometric parameters as well as dental diagnosis. This included 34 males and 16 females with thalassaemia major and 31 males and 19 females were healthy. These patients and healthy controls were categorized into two groups: 37 thalassaemic patients and 30 healthy controls (2-10 years) and 13 thalassaemic patients and 20 healthy controls (10-20 years) for anthropometric measurements. Patients were divided into three age groups according to their dentition (deciduous, mixed and permanent) for dental diagnosis.

Anthropometric measurements:

The anthropometric measurements were taken following the standard techniques¹⁵. 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 formula¹⁶.

$$\text{BMI (kg/m}^2\text{)} = \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$$

Dental diagnosis:

Decayed-Missing-Filled Teeth Index (DMFT Index)

‘D’- was used to describe decayed teeth.

‘M’- was used to describe missing teeth due to caries.

'F'- was used to describe teeth that have been previously filled.

Mouth mirror and a fine-pointed pig-tail explorer were used for determine the sum of how many tooth were:

"Decayed," "Missing" or extracted due to decay, and filled as a result of caries involvement.

It was calculated by adding each component, i.e. D, M, & F.

Decayed-Missing-Filled Tooth surfaces Index (DMFS)

Mouth mirror and a fine-pointed pig-tail explorer were used for determine the sum of how many tooth surfaces were:

"Decayed," "Missing" or extracted due to decay, and filled as a result of caries involvement. The surfaces examined were:

1. For Posterior teeth: Five surfaces were examined and recorded: facial, lingual, mesial, distal and occlusal.
2. For Anterior teeth: Four surfaces were examined and recorded facial, lingual, mesial and distal.

Individual DMFS Index was calculated by:

Total number of decayed surfaces = **D**

Total number of missing surfaces = **M**

Total number of filled surfaces = **F**

DMFS score = D+M+F

The data obtained for various parameters were subjected to essential statistical evaluations. Arithmetic mean and standard deviations were calculated for all parameters studied. 'p'-values (probability) were determined to make out the statistical significance of variance between the mean values of individual parameters between the two groups of the subjects studied.

Results

Growth retardation was found in most of the subjects with β -thalassemia. Data was compared in two age groups (2-10 and 10-20) and both the sex groups. The mean standing height, weight, mid arm circumference, chest circumference, head circumference and Body Mass Index for different age the sex groups are shown in **Table-1& 2**.

In the present study the mean height, body Weight, mid arm circumference, chest circumference, head circumference and body mass index values of thalassemic patients (age group 2-10 years) were 1.00 ± 0.16 , 15.85 ± 4.91 , 15.43 ± 1.57 , 54.51 ± 4.61 , 49.51 ± 2.43 , 15.45 ± 3.02 respectively and for the healthy controls belonged to same age group the values for above mentioned parameters were 1.07 ± 0.20 , 19.5 ± 7.73 , 17.2 ± 2.63 , 57.1 ± 7.68 , 50.0 ± 2.84 , 17.64 ± 4.06 respectively. When the mean values for all parameters of thalassemic patients and healthy controls were compared a significant difference ($p < 0.05$) is observed for all except for the mean height and head circumference ($p > 0.05$).

The mean height, body weight, mid arm circumference, chest circumference, head circumference and body mass index values of thalassemic patients (age group 10-20 years) were 1.33 ± 0.14 , 29.37 ± 6.26 , 18.84 ± 2.47 , 67.15 ± 4.70 , 52.92 ± 2.21 , 21.75 ± 2.84 respectively and for the healthy controls belonged to same age group the values for above mentioned parameters were 1.52 ± 0.5 , 43.65 ± 14.15 , 25.45 ± 6.15 , 74.95 ± 12.24 , 54.25 ± 1.33 , 28.20 ± 7.11 respectively.

When the mean values for all parameters of thalassemic patients and healthy controls were compared a significant difference ($p < 0.05$) is observed for all the parameters. (**Table 1**)

Table 1: Anthropometric measurements of subjects according to age

Anthropometric measurements	Age (years)					
	2-10			10-17		
	TM(n=37) Mean±SD	HC(n=30) Mean±SD	t values	TM(n=13) Mean±SD	HC(n=20) Mean±SD	t values
Height (meters)	1.00±0.16	1.07±0.20	1.59	1.33±0.14	1.52±0.5	1.32
Weight(kg)	15.85±4.91	19.5±7.73	2.34	29.37±6.26	43.65±14.15	3.41
Mid arm circumference (cm)	15.43±1.57	17.2±2.63	3.41	18.84±2.47	25.45±6.15	3.67
Chest circumference (cm)	54.51±4.61	57.1±7.68	1.70	67.15±4.70	74.95±12.24	2.18
Head circumference (cm)	49.51±2.43	50±2.84	0.760	52.92±2.21	54.25±1.33	2.16
Body Mass Index(kg/m ²)	15.45±3.02	17.64±4.06	2.53	21.75±2.84	28.20±7.11	3.10

Similarly the mean height, body Weight, mid arm circumference, chest circumference, head circumference and body mass index values of thalassemic males were 1.10±0.21, 19.77±7.68, 16.23±2.27, 58.35±6.74, 50.94±2.70, 17.32±3.94 respectively and values for same parameters of healthy controls males were 1.36±0.27, 35.12±16.15, 22.61±6.20, 68.58±12.98, 52.81±2.90, 24.65±7.55 respectively.

The mean height, body weight, mid arm circumference, chest circumference, head circumference and body mass index values of thalassemic females were 1.06±0.23, 18.52±8.68, 16.50±2.63, 56.62±8.32, 49.25±2.74, 16.59±4.38 respectively and values for same parameters of healthy controls females were 1.07±0.22, 19.42±10.02, 17.05±3.47, 57.15±9.99, 49.89±2.70, 17.32±4.93 respectively.

A highly significant difference ($p < 0.001$) is observed in the mean height, body weight, mid arm circumference, chest circumference, head circumference and body mass index values of thalassemic males and healthy males but a non-significant difference ($p > 0.05$) is observed in the mean height, body weight, mid arm circumference, chest circumference, head circumference and body mass index values of thalassemic females and the females of control group. (**Table 2**)

Table 2: Anthropometric measurements of subjects according to sex

Anthropometric measurements	Males			female		
	TM(n=34) Mean±SD	HC(n=31) Mean±SD	t values	TM(n=16) Mean±SD	HC(n=19) Mean±SD	t values
Height(meters)	1.10±0.21	1.36±0.27	4.35	1.06±0.23	1.07±0.22	0.13
Weight(kg)	19.77±7.68	35.12±16.15	4.96	18.52±8.68	19.42±10.02	0.28
Mid arm circumference(cm)	16.23±2.27	22.61±6.20	5.60	16.50±2.63	17.05±3.47	0.52
Chest circumference(cm)	58.35±6.74	68.58±12.98	4.03	56.62±8.32	57.15±9.99	0.16
Head circumference(cm)	50.94±2.70	52.81±2.90	2.69	49.25±2.74	49.89±2.70	0.69
Body Mass Index(kg/m ²)	17.32±3.94	24.65±7.55	4.96	16.59±4.38	17.32±4.93	0.45

DMFT and DMFS indices of thalassemia major patients and control groups are shown in **Table-3**. The indices were higher in thalassemic patients as compared to healthy controls of the same age groups. Its difference was statistically highly significant ($p < 0.001$) in the all age groups.

Table 3: DMFT and DMFS index in BTM and control groups

Age (years)	DMFT			DMFS		
	BTM (n=50) Mean±SD	HC(n=50) Mean±SD	t value	BTM(n=50) Mean±SD	HC(n=50) Mean±SD	t value
2-6	2.84±3.74	0.47±0.83	4.39	5.10±7.72	1.13±1.99	3.52
6-12	3.42±2.52	0.58±1.07	7.36	7.90±6.97	1.26±2.13	6.44
12-17	3.90±2.64	.53±0.74	8.69	4.80±3.58	1.53±2.10	5.58

Discussion

Growth disturbances are a major clinical feature of untreated patients with thalassemia⁷. The results of the anthropometric measurements of age and sex matched thalassemia major patients and healthy controls. Thalassemia major patients (both male and female) showed statistically significant lower values of all the measurements (except for height and head circumference of age group 2-10 years) as compared to healthy controls of the same age and sex groups. BMI values were also found to be significantly lower among the thalassemia major male and female patients than the normal. Sex wise distribution of different anthropometric measurements showed significant decreased mean values of all the measurements in the males than the females in thalassemia major patients as compared to the healthy controls.

Our study in accordance with the studies of George A *et al* as they reported among head, chest and mid arm circumference, the mid arm circumference was more affected than head and chest circumference¹⁰. In the present study growth retardation became more pronounced with increasing age which is in agreement with a few studies¹⁷⁻²². Gomber S *et al* measured the weight, standing height, sitting height and subischial leg length in 65 thalassemic children at a tertiary hospital Delhi. They concluded that weight, standing height, sitting height and subischial leg length in children $> \text{ or } = 10$ years of age were significantly lower than those of children < 6 years or those 6-10 years of age²³.

Table 2 illustrates the mean, standard deviation and statistical difference between BTM and control groups of (DMFS and DMFT), The BTM group had higher DMFT and DMFS compared to control group with statistically highly significant difference ($P < 0.001$). The present study showed that DMFT and DMFS was significantly higher in thalassemic patients than in age matched healthy controls. In recent studies, Al-Wahadni showed a higher rate of dental caries in thalassemic patients⁹. and De Mattia found a mean DMFT index of 5.12 ± 4.76 in thalassemic patients, which was correlated with age and splenectomy¹⁰. These results are same with our results. Leonardi *et al.* also found caries in 90% of thalassemic males and 60% of thalassemic females²⁴. Similarly, Mehdizadeh performed their study on 50 patients (21 male and 29 female) with thalassemia major. Dental caries were significantly higher in thalassemic patients ($p < 0.001$) in comparison with healthy control group. It was concluded that thalassemia is associated with higher rates of dental carries and malocclusion¹³. Hattab also proposed their study on 54 thalassemic patients. The prevalence of dental caries in the thalassemic patients was considerably higher (22.7%) than that reported in a normal Jordanian sample (DMFT 6.26 vs. 4.84). it was also observed that more than half of patients had poor oral hygiene¹². Similarly Al-Jobouri conducted their study on 41 Beta thalassemia

major patients (31 male, 10 female) and 41 healthy control subjects. This study showed that Beta thalassemia group had higher DMFS. The DMFS score for thalassemic major group was 9.29 ± 7.66 and for control group DMFS was 2.54 ± 2.44 ²⁵.

Conclusion

Growth retardation in patients with BTM is evident especially in patients with males of older age. Growth retardation in our patients with BTM is mainly due to chronic anemia. The aetiology of growth retardation in BTM patients is likely to be multifactorial although delay in onset of puberty, iron overload, the toxic effects of Desferrioxamine or the development of other endocrinopathies such as growth hormone insufficiency or primary hypothyroidism may be contributory factors.

Patients with BTM showed highly significant differences in DMFT and DMFS indices as compared to control group especially in older patients. This can be due to poor oral hygiene, poor motivation, malocclusion, endocrine problems such as diabetes mellitus and hypocalcaemia and finally, subclinical immune deficiency, which has been claimed in iron overload status and splenectomized patients. A low IgA level in saliva has also been shown in thalassemic subjects, which may contribute to an increased rate of caries.

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