Int J Hum Genet, 3(4): 237-246 (2003)
PRINT: ISSN 0972-3757 ONLINE: 2456-6360 **DOI: 10.31901/24566330.2003/03.04.08**

Growth Retardation in Thalassemia Major Patients

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KEYWORDS Growth; puberty; thalassemia; iron; chelation; deferoxamine; deferiprone

ABSTRACT Regular blood transfusion followed by iron chelation therapy is just a supportive treatment for thalassemia major which is associated with serious complications. Growth disturbances are a major clinical feature of untreated patients with thalassemia. 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 failure. The main objective of present study was to examine longitudinally the growth pattern of thalassemic patients on hyper-transfusion regimen over a period of three years and to document disproportion in body segments. Material and Methods: Height, weight, sitting height vertex, trunk and leg length of 90 patients (57 male, 33 female) aged between 2 and 18 years were measured every two months over a period of 3 years. Results: This study supports the fact that thalassemic patients are short, have low rate of growth and BMI and have either delayed or absent pubertal spurt, which is related to low hemoglobin and high ferritin levels and sub-optimal iron chelation therapy. Growth faltering sets in at a much younger age and becomes apparent by 8 years of age. Poor socio-economic background compounds the problem.

INTRODUCTION

β-thalassemia major has a spectrum of clinical severity which is associated with ineffective erythropoeisis, bone marrow expansion and rapid destruction of erythrocytes. Anemia demands frequent blood transfusion to maintain life while hemosiderosis and other complications of the disease require a continuous and distressing treatment regime that includes iron chelation treatment, regular medical supervision, frequent admissions to the hospital and on many occasions surgery. This autosomal recessive anemia is fatal in infancy without transfusions and is fatal in adolescence even with them. The only curative treatment for this disease is bone marrow transplantation (BMT) which is expensive and has a variable success rate of 60-70%.

Regular blood transfusion followed by iron chelation therapy is just a supportive treatment for this disease which is associated with serious complications. The beneficial effects of regular transfusions on growth and bone disorders in patients with thalassemia were first reported in 1965 (Weatherall and Clegg 1981) and have been subsequently confirmed by additional studies (Bronspiegel-Weintrob et al. 1990; Johnson et al. 1966; Logothetis et al. 1972). In India the cost of treating a thalassemic child varies from few thousand rupees to Rs 100,000 a year depending upon the kind of treatment opted by the family. The excess iron causes diffuse organ damage, usually resulting in fatal cardiac toxicity. In supportive treatment, because the magnitude of the body iron burden seems to be the principal determinant of clinical outcome (Brittenham et al. 1994; Olivieri et al. 1994, 1995), the prime goal of iron-chelating therapy in patients with thalassemia major is to control body iron. The optimal body iron should minimize both the risk of adverse effects from the iron-chelating agent and the risk of complications from iron overload. With stable transfusion requirements and in the absence of other confounding factors, the lower the level of body iron desired, the higher the dose of iron chelator needed. With effective chelation using DFO, normal growth and sexual maturation can be expected.

Growth disturbances are a major clinical feature of untreated patients with thalassemia (Kattamis and Kattamis 1995). 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 failure (Borgna-Pignatti et al. 1985; De Sanctis et al. 1994; Kattamis et al.1990). The objective of present study was to examine longitudinally

MATERIAL AND METHODS

Patient based longitudinal study was

conducted over a period of 3 years at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow on 90 thalassemia major patients (57 male, 33 female) aged between 2 and 18 years. Patients visited the hospital for blood transfusion once every three to four weeks.

Routine Tests: Pre-transfusion hemoglobin was tested on every visit and serum ferritin levels every six months. Yearly evaluation of patients included liver function test (serum bilirubin, AST, ALT) complete blood count, HIV I & II antibodies, TSH, T4, ACTH stimulated serum cortisol, GTT, calcium and phosphorus.

Chelation Therapy: Eight patients were taking subcutaneous deferoxamine, 62 patients were on deferiprone and 20 patients were not taking chelation therapy due to financial constraints.

Auxological Assessment: Height vertex, span, sitting height vertex (SHV), trunk length, lower limb length, and body weight were measured every two months using standard anthropometric techniques (Lohman et al.1988). Quality control of the measurements (intra-observer and instrument error) was checked by taking repeat measurements. Internationally accepted index trunk*100/height (Giuffrida-Ruggeri, 1980) was used for documenting the size of trunk length with respect to height (Male: X-51: short, 51.1-53: medium; 53.1-X large; Female: X-52: short, 52.1-54: medium; 54.1-X large). Upper segment lower segment ratio was also calculated. Growth pattern of each child was recorded on growth charts prepared from Indian growth data (Agarwal et al. 1992). Z scores and

Fig. 1a. Patient's height compared to Indian Standards

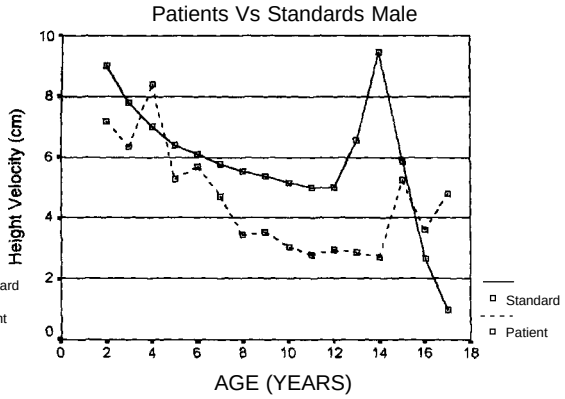

Fig. 1c. Height velocity Curve

Fig. 1b. Patient's height compared to Indian Standards

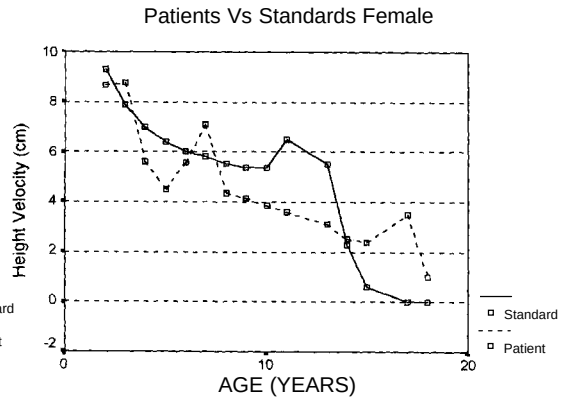

Fig. 1d. Height velocity curve

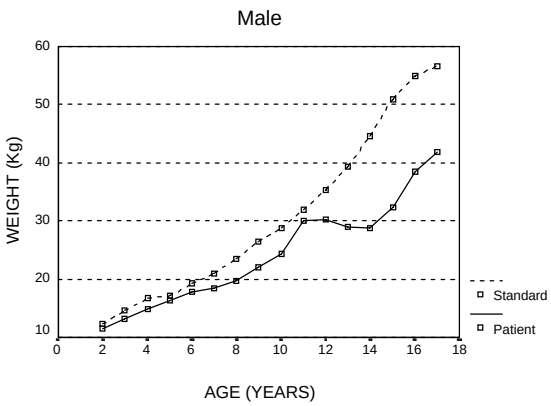

Fig. 2a. Patient's weight compared to Indian Standards

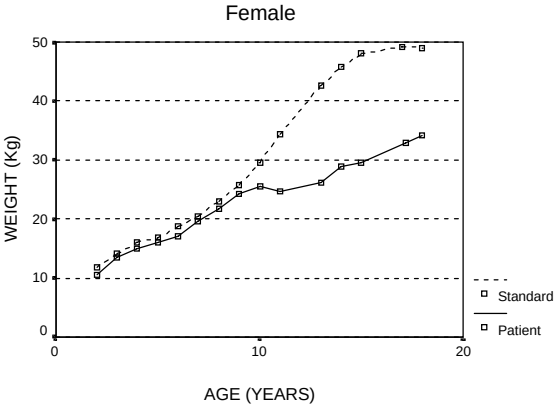

Fig. 2b. Patient's weight compared to Indian Standards

Fig. 3a. Patient's sitting height vertex compared to Indian Standards

Fig. 3b. Patient's sitting height vertex compared to Indian Standards

body mass index (BMI) were calculated (WHO 1983). Bone age of 60 patients was estimated from hand (with wrist) radiographs. Pubertal assessment was done every six months according to Tanner Stages (Tanner and Whitehouse, 1976). Data were analyzed using SPSS 6.0 for Windows. Students independent t test was used for testing differences in variables. Correlation analysis was used to find out cause and effect association between variables. Z-scores were also calculated.

RESULTS

Growth of Body Segments: Growth curves of patients for all the parameters ran below Indian Growth Standards (Figs. 1-3). Differences between the two became more pronounced with increasing age. Significant difference existed in the mean values of various parameters of patients

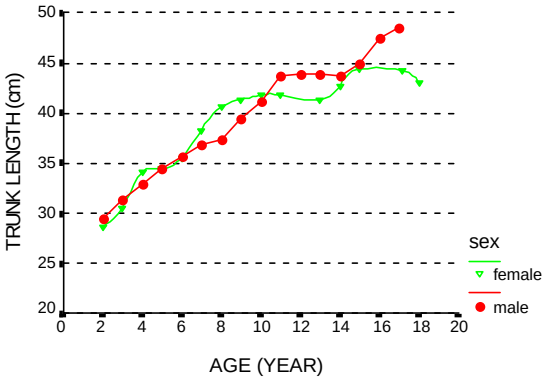

Fig. 4. Patient's Trunk length

and Indian Standards (independent t test boys height P<.007, weight P<.002, sitting height vertex P <.000, leg length P<.000; girls P<.011, P< .001, P<.000, P<.000). On comparing patient data with George et al's data (1997) on thalassemic patients,

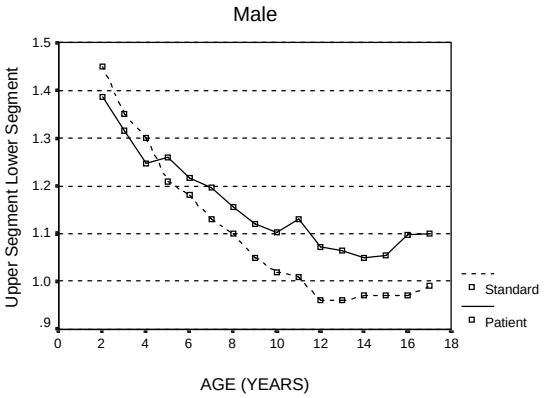

Fig. 5a. Patient's upper segment lower segment ratio compared to Indian Standards

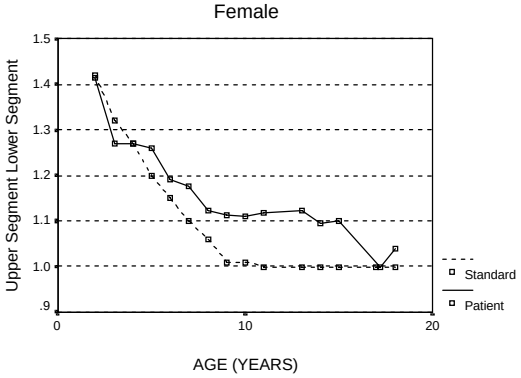

Fig. 5b. Upper segment lower segment ratio Patients Vs Standards Female

no significant difference in height and weight was observed.

Growth curves depicted gradual increase in height and weight till 11 years in boys and till the age of 8 years and 10 years for both the parameters in girls . After initiation of blood transfusions, catch-up growth was evident between 2 and 3 years. Growth curves showed pronounced growth retardation in height and weight after 11 years of age in boys and after 9 years in girls. Small but delayed pubertal spurt was seen at the age of 16 years in boys and 15 years in girls. As per the absolute mean values, there was no difference in the height and weight of boys and girls till 6 years of age (Tables 1 and 2). Patients had normal span. Growth curve for sitting height vertex (Table 3, Fig. 3) were low compared to Indian Standards till the age of 10 and 6 years in boys and girls respectively. The difference in the data became marked after the age of 11 years in boys and 9 years in girls showing considerably slow growth of upper segment. At 15 years of age, the patients experienced short growth spurt. Although trunk length (Table 4, Fig. 4) followed similar pattern as SHV, no distinct growth spurt was visible in boys. It was, however, apparent between 12 and 13 years in girls. Both boys and girls had short trunk with respect to height.

In boys, although mean values for leg length increased gradually throughout growth period, a distinct adolescent spurt was absent (Table 3). Girls experienced growth spurt after the age of 15 years. Difference between patient and Standards

Table 1a: Mean weight and height of patients, George et al. 1997, Agarwal et al. 1992 (Standard), and NCHS Data (Boys)

Age	*Height (CM)*				*Weight (KG)*			
(in years)	*Patients*	*Agarwal*	*George*	*NCHS*	*Patient*	*Agarwal*	*George*	*NCHS*
2	84.6	85.6	85.5	86.8	11.50	12.3	11	12.34
3	91.6	94.9	91.3	94.9	12.86	14.6	13	14.62
4	102.43	102.9	102.	102.9	18.17	16.7	15.8	16.69
5	106.83	109.9	103	109.9	17	17.1	16	18.67
6	108.60	113.7	107.5	116.1	17.66	19.2	17.4	20.69
7	111.81	118.6	111.8	121.7	18.56	21	17.2	22.85
8	119.50	124.1	119.3	127	20.46	3.5	20.4	25.30
9	125	130.4	116.8	132.2	23	26.5	19.5	28.13
10	130.60	134.7	124.1	137.5	27.17	28.7	22.1	31.44
11	127.70	139.6	130	148.3	27.50	31.9	24.6	35.30
12	134.90	144.7	132	149.6	28.33	35.4	26.6	39.78
13	127.48	150.3	136.5	156.5	25.75	39.4	26.3	44.95
14	138.1	158	136.3	163.1	27	44.7	27.5	50.77
15	139.67	164.3	142	169	32.67	51	29.5	56.71
16	142.5	167.1	141	173.5	38	55	26.8	62.10
17	-	168.5	144	176.2	-	56.6	33	66.31
18	145.0	168.5	156.9	176.0	40	56.6	37.2	68.8

Table 1b: Mean weight and height of patients, George et al. 1997, Agarwal et al. 1992 (Standard) and NCHS data (Girls)

Age	*Height*				*Weight*			
(in years)	*Patients*	*Agarwal*	*George*	*NCHS*	*Patient*	*Agarwal*	*George*	*NCHS*
2	84.4	85.7	81.5	86.8	10	11.8	10.8	11.80
3	92.2	94.1	93.5	94.1	13.5	14.1	13.5	24.10
4	99.4	101.6	98.5	101.6	15.2	16	16.1	15.96
5	103.8	108.4	100.8	108.4	15.3	16.8	14.9	17.66
6	111.5	113	99.5	114.6	18.5	18.7	14.7	19.52
7	116.5	118.2	114.5	120.6	18.8	20.5	18.3	21.84
8	124	122.7	117.5	126.4	22.1	23	19.2	24.84
9	125.8	128.6	119.5	132.2	25.1	25.8	19.7	28.46
10	126.9	134.8	125.2	138.3	23.5	29.6	22.8	32.55
11	-	141.3	131	144.8	-	34.3	20.6	36.95
12	-	146.7	131	15.5	-	38.7	26.6	41.53
13	125.6	151.4	134.6	157.1	25.5	42.6	26.9	46.10
14	-	153.6	138	160.4	-	45.7	32.2	50.28
15	-	155	124	161.8	-	48	25.7	53.68
16	-	155.1	137.5	162.4	-	49.2	30.6	55.89
17	141.7	157.1	131.5	163.1	31	49	29.7	56.69
18	142.0	157.6	147	165.0	32	49	36.4	57.0

Table 2: Mean and standard deviation for sitting height vertex and trunk length

Age	*Sitting height vertex (cm)*				*Trunk length (cm)*			
(in year)	*Male*		*Female*		*Male*		*Female*	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
2	49.1	1.7	49.7	2.98	29.4	1.2	28.7	2.6
3	52.9	2.3	52.7	1.86	31.3	1.7	30.5	2.8
4	55.0	3.3	55.3	2.37	32.8	2.0	34.1	4.8
5	58.1	5.0	58.0	2.07	34.5	2.8	34.4	1.3
6	60.1	5.5	59.2	3.13	35.6	2.5	35.5	1.66
7	61.0	3.5	63.0	3.01	36.8	2.2	38.2	1.9
8	62.0	2.8	65.7	22.55	37.2	2.0	40.6	1.8
9	65.1	2.4	66.7	2.98	39.4	1.7	41.3	2.2
10	67.1	3.4	66.8	3.42	41.1	2.2	41.8	2.1
11	71.5	2.1	67.6	3.12	44.3	2.3	41.8	2.2
12	71.6	2.5	-	-	43.8	1.67	-	-
13	71.0	1.68	66.5	0.36	43.9	1.44	40.3	1.6
14	71.2	1.74	67.9	.70	43.8	1.38	42.7	1.9
15	72.6	2.27	68.8	0.84	44.8	1.53	44.4	1.1
16	76.8	3.74	-	-	47.5	1.95	-	-
17	77.6	0.88	70.4	0.84	48.4	1.95	44.9	0.42
18	-	-	69.9	5.31	-	-	43.0	3.5

became pronounced after the age of 8 years in girls and 12 years in boys. Z scores for height for age and weight for age (reference data WHO, 1983) ranged between + 0.03 to –5 SD and +0.94 SD to -5 SD, respectively.

Upper segment/lower segment ratio (Fig. 5) was low compared to Standards till the age of 4 years depicting rapid growth in the leg length compared to trunk length. In the rest of the growth period, the ratio was high suggesting disproportion in body segments of patients. Table 4 shows mean values of BMI of the patients. Initially the BMI of patients tracked along the 75th percentile, depicting catch-up growth, but after 5 years of age rapid crossing over of percentiles towards lower position was observed, depicting relatively decreased growth.

Pre-transfusion Haemoglobin and Its Association with Physical Parameters: Patients had low pre-transfusion haemoglobin levels 8.0 and 7.4 for girls and boys respectively (boys mean 8.0, 7.2–9.3 and girls mean 7.4, 5.5–9.4). Significant differences ($P<0.01$) were observed in hemoglobin level of boys and girls (Table 5). Pre-transfusion haemoglobin was significantly associated with height, and leg length at the age of 2 years (which

Table 3: Mean and standard deviation for leg length

Age	*Male*		*Female*	
(in year)	*Mean*	*SD*	*Mean*	*SD*
2	35.5	0.2	35.1	4.6
3	40.2	2.6	41.5	2.7
4	44.1	3.5	43.5	2.9
5	46.0	4.3	46.0	3.0
6	49.4	3.5	49.7	3.3
7	50.9	3.1	53.6	3.3
8	53.7	3.7	58.6	4.6
9	58.0	3.8	60.0	4.6
10	60.9	2.67	60.2	4.2
11	63.6	4.2	60.5	3.2
12	66.7	3.74	-	
13	66.5	1.66	59.7	0.95
14	67.8	2.24	62.0	0.58
15	68.8	2.89	62.6	1.13
16	70.0	2.88	-	4.88
17	70.6	1.88	71.6	1.13
18	-	-	67.3	4.88

Table 4: Mean and SD of body mass index

Age	*Male*		*Female*	
(in year)	*Mean*	*SD*	*Mean*	*SD*
2	16.06	0.40	14.31	1.04
3	15.05	1.0	15.15	1.37
4	15.37	1.17	15.30	1.37
5	14.91	1.41	14.93	1.18
6	14.77	1.48	14.34	1.34
7	14.71	1.39	14.37	1.57
8	14.72	1.10	14.06	1.53
9	14.49	0.65	15.06	1.40
10	14.80	1.00	15.66	1.79
11	16.37	1.27	14.98	1.31
12	15.77	0.81	16.46	
13	15.28	0.87	17.19	1.02
14	14.84	0.86	17.09	0.54
15	16.11	1.15	15.86	
16	17.80	1.42	-	
17	18.93	0.20	16.09	0.64
18			18.32	2.42

is also a period of catch-up growth after initiation of blood transfusions), and at 12 and 13 years with height, SHV, trunk, and leg length indicating that increase in pre-transfusion hemoglobin caused increase (spurt) in the body segments. Similar association was observed between hemoglobin and height, SHV, and leg length at the age of 16 years. Serum ferritin levels ranged from 2000 to > 10,000 ng/dl.

Pubertal Development: None of the boys showed pubertal changes. Only one girl attained spontaneous sexual maturity. X-rays of 4 patients (1 deferoxamine and 3 without chelation) depicted delayed bone age.

Table 5: Pretransfusion hemoglobin levels of patients

Age	*Male*		*Female*	
(in year)	*Mean*	*SD*	*Mean*	*SD*
2	8.05	1.48	9.41	1.30
3	8.65	1.03	8.97	2.17
4	7.73	1.39	8.28	1.47
5	7.97	1.39	8.30	1.12
6	7.96	1.25	8.08	1.62
7	7.82	1.67	8.42	1.34
8	7.64	1.43	8.67	1.24
9	7.98	1.52	8.35	1.48
10	7.33	1.54	8.97	1.08
11	8.18	1.41	7.81	1.87
12	7.96	1.82	-	-
13	7.21	0.84	5.57	0.68
14	8.42	1.32	6.82	0.26
15	7.87	1.03	8.80	0.00
16	9.13	0.68	-	-
17	9.38	1.39	7.62	0.00
18			7.99	0.00

DISCUSSION

Evidence for Retardation of Growth: Large data are now available on growth and pubertal development of thalassemic patients. First such data were presented in 1977 (Pantelakis et al. 1977) which showed a tendency for height and weight gain to fall off after the age of 8 years for boys and 11 years for girls (observed in this study also). Body growth was satisfactory but bone age was generally retarded, more so in boys than in girls. The results were also in agreement with other studies (Kattamis et al. 1970) which reported normal growth in children with hemoglobin levels above 8g/dl. In 1980, delay in growth as judged by SDS for height, weight and bone age was reported in a study on body growth in relation to hemoglobin and ferritin levels (Karagiorga-Lagana, et al.1980). 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. A cross-sectional analysis of the growth patterns reported that growth retardation became more pronounced with advancing age (Pantelakis et al.1973). A multi-centric study 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 (Borgna-Pignati et al.1985). The

results of longitudinal growth study (Borgna-Pignati et al.1985; Kattamis et al.1990; Pantelakis et al.1993) 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. Delayed growth and sexual maturation was observed in most of the patients who had received transfusion (Pantelakis et al.1993).

In the present study growth retardation became pronounced with increasing age which is in agreement with these studies (Borgna-Pignati et al.1985; Kattamis et al.1990; Karagiorga-Lagana et al.1980; Pantelakis et al.1973, 1993). Although catch-up growth was observed after initiation of blood transfusions, later on, rate of growth became slow and growth retardation became obvious in the rest of the growth period. Bone age was delayed in 4 out of 60 patients. Thalassemic patients were between 5th(and below) and 25th percentile (Indian Standards) for height, weight and leg length. In other words, thalassemic children were short compared to Standards. It has been reported that growth delay sets in after the age of 4 years in boys and 3 years in girls (Saxena et al. 2002). 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. In this study, out of 90 patients, only one girl attained spontaneous sexual maturation, although, her height and weight SDS was –3.

Patients experienced short and delayed pubertal spurt in all the parameters. It has been reported that the trunk length of thalassemic patients is short since it is more vulnerable to toxic or damaging effects of chelating agent (desferoxamine) (Rodda et al.1995) but the leg length is preserved. In this study also patients had short trunk with respect to height and distinct spurt in the trunk length was absent in boys. Upper segment/lower segment ratio was low till the age of 4 years depicting rapid growth in the leg length compared to trunk length, followed by relatively high ratio suggesting gross disproportion of body segments in patients. Except in early childhood, patients had low BMI.

Although the patients were on hyper-transfusion therapy, they were maintaining low hemoglobin levels which is evident from positive association with physical parameters and slow rate of growth. There was significant difference in the hemoglobin levels of girls and boys. High hemoglobin levels in early years of growth in girls compared to boys explains better growth observed in girls till 10 years of age. Also, girls came from better socio-economic status, which implies better nutrition, hygiene and social atmosphere. However, improved hemoglobin levels during adolescence (after the age of 10 years compared to younger age) in boys explains better growth during this period. These associations show that cause and effect relationship exists between hemoglobin and various body segments which supports the finding of other studies (Karagiorga-Lagana et al.1980). Low hemoglobin levels were associated with slow growth and compromised height.

Negative correlation between ferritin levels and height is established (Karagiorga-Lagana et al.1980). In this study, 8 patients were taking deferoxamine, 62 patients were on deferiprone and 20 patients were not taking chelation therapy. Only 20% of the patients were taking optimum chelation dose. Serum ferritin levels were very high. Therefore, in this study 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.

There was no significant difference in the parameters of this study and that reported from Delhi (George et al. 1997). Although, Z scores for both height and weight for age for young patients ranged between -1 SD and -2 SD, with advancing age regression in these scores was obvious (fall in values was more prominent in height compared to weight). Overall, Z scores for height for age and weight for age were low. Genetic potential seems to explain the reason why some patients had z scores in the range of + 0.99 and +1. Parents of these patients were tall and well built. It does not, however, imply that the parents of the rest of the patients were very short. Secondly, these patients (with high z-scroes) came from privileged families (high socio-economic status).

Possible Mechanisms of Growth Retardation: No consensus has so far been reached on mechanisms leading to growth retardation in thalassaemics. Most patients with thalassemia have delayed growth and sexual maturation. The

pubertal growth spurt is often absent or delayed, and even patients with normal growth spurts can have delayed sexual maturation. In patients with growth retardation, hypogonadism is often present. The reduced growth rate is associated with prolongation of the period of growth in many (as also observed in this study). Prolongation of growth at a lower velocity explains the higher prevalence of growth retardation in the younger age groups, both for boys and girls, compared with young adults.

The pathogenesis of late impairment of growth and sexual maturation in transfused patients with thalassemia major is not yet well classified. It is generally believed that it is directly related to iron toxicity, especially of the endocrine glands (Gabutti et al. 1989; Merkel et al. 1988; Tsitoura et al. 1978). It has been postulated that intensive chelation with high doses may have toxic effects in patients under 10 years of age, resulting in a reduction in growth velocity and final height (De Virgillis et al. 1988). There is direct relationship between ferritin levels and degree of growth retardation in height velocity (Gabutti et al. 1985). Intensive chelation therapy has beneficial effects in restoring height velocity, promoting the development of sexual characteristics, and inducing acceleration of growth and sexual maturity after several years of pubertal delay and stunted growth. However, comparison of different studies is often difficult because of different degrees of success in chelation therapy. Exact mechanism through which iron overload or the chelating agent produces growth retardation is not known. The physiological role of growth hormone (GH) secretion on growth retardation remains to be elucidated (Kattamis 1990; Model and Berdoukas 1984; Oerter et al. 1993; Sinaniotis et al.1973). In thalassemic patients lower IGF-1 circulating levels appear to be negatively correlated with both aspartate aminotransferase and alanine amino-transferase as well as with ferritin circulating levels indicating a probable role of hepatic hemosiderosis in IGF-1 production (Vannasaeng et al. 1991). However, reduced IGF-1 secretion is not the main cause of growth retardation since this would have elicited an enhanced response of growth hormone release hormone (GHRH) in the presence of a normal hypothalamic pituitary axis[36]. In contrast GH response to GHRH has been reported to be low in thalassemic patients compared to controls) but the circadian secretory pattern of GH in these patients is preserved although the amplitude of the rhythm is reduced (Pasqualetti et al. 1992). Growth hormone neurosecretory dysfunction is not a universal finding in children with thalassemia major but might depend on the degree of iron deposit in the pituitary.

Nutrition is an important factor in proper growth and development. Zinc deficiency exists as a growth-limiting factor in thalassemia major. Short stature, low weight, anorexia, and hypogonadism found in the zinc deficiency, has been found in most of the patients with thalassaemia (Arcasoy and Cavadar 1981; Arcasoy et al. 1983). 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.

Effectiveness of Different Treatment Regimes: Although modern hypertransfusion and chelation regimens have had a radical impact on growth and skeletal formation of patients with thalassemia major, growth failure has persisted despite major treatment advances. Conventional treatment of the Thalassemia Syndromes is directed to control the main symptoms of anemia, stunting of growth, skeletal deformities, iron overload and hyper-splenism. Abnormal growth and delayed puberty can be partly overcome by early initiation of chelating therapy. Patients who begin treatment at a young age can be protected from the lethal complications of iron overload for at least two decades, but chelation therapy may not always prevent or ameliorate late growth failure and/or delayed or absent puberty (Chan et al. 2000; de Sanctis et al. 2000). Those with iron damage to the heart and other organs may experience stability or improvement in function with intense chelation. In the present study, only 20% of the patients were taking optimal chelation therapy, as a consequence of which, they suffered from growth retardation.

CONCLUSION

This study supports the fact that thalassemic patients are short, have low rate of growth and BMI and have either delayed or absent pubertal spurt, which is related to low hemoglobin and high ferritin levels and sub-optimal iron chelation therapy. Growth faltering sets in much earlier

but becomes obvious after the age of 8 years. In developing countries, poor socio-economic background compounds the problem.

ACKNOWLEDGEMENT

I thank Prof. SS Agarwal, former Head Department of Medical Genetics, SGPGI, for his guidance and help in completing the project which was funded by CSIR, New Delhi, India.

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