Brief Reports

Physical Growth Patterns and Dental Caries in Thalassemia

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This study was conducted to assess the effect of age, ferritin level, hemoglobin level and chelating agents on the physical growth in thalassemic children and to determine the prevalence of dental caries in thalassemic children. Weight, standing height, sitting height and subischial leg length were measured in 65 children attending the Thalassemia day care center at a tertiary hospital in Delhi. Their mean pre transfusion hemoglobin and ferritin levels over the previous two years were calculated. Dental caries indices, DMFT and DMFS were measured and compared with age-matched controls. Weight, standing height, sitting height and subischial leg length expressed as percentage for age in children ≥ 10 y were significantly lower than those of children < 6 y, and those 6-10 y. Mean hemoglobin and ferritin did not affect growth significantly. Sitting height% for age in children receiving Desferrioxamine alone or Desferrioxamine with Deferiprone was significantly lower than that of children receiving Deferiprone alone or no chelating agent. Dental caries were significantly higher in thalassemics.

Key words: *Chelation, Dental caries, Growth, Truncal shortening.*

THALASSEMIA is widely distributed in Asian Indians with an average prevalence rate of 4%(1). Growth impairment is a common complication of homozygous β-thalassemia. There are very few studies available on the growth patterns in thalassemic children from this region(2). Thus, this study was undertaken to assess the physical growth in thalassemic children in relation to their age, iron stores, hemoglobin level and chelating agents.

Few studies have reported a higher frequency of periodontal diseases and dental caries in thalassemics(3). The aim of this study was also to determine the prevalence of dental caries in thalassemics and to compare them with age matched healthy controls.

Subjects and Methods

This study was conducted in 65 thalassemic children (37 males and 28 females) ranging between 9 months to 22 years of age with a mean age of 7.2 years, receiving regular blood transfusions at the thalassemia day care center at a tertiary hospital in Delhi. We intended to study the effect of age, iron stores, hemoglobin level and type of chelation on the physical growth in thalassemic children. The physical growth parameters of the thalassemic children viz, weight, standing height, sitting height, and subischial leg length, were measured using standard anthropometric techniques. Complete physical examination was conducted while recording the anthropometric parameters on a specially designed

proforma. Measurements were expressed as percentage of expected for age using 50th centile for age as per the standards of physical growth of affluent Indian children given by Aggarwal and others(4). Since corresponding standard measurements for sitting height and subischial leg length for affluent Indian children below 6 years age are not available, their analysis could not be done for the same parameters. A mean level of pretransfusion hemoglobin and mean serum ferritin, over the preceding two years was calculated for each child from his/her transfusion records maintained at the center. Mean protein and caloric intake was calculated for subjects after dietary recall and found to be adequate in majority (92%) of subjects.

Dental examination was done in 53 out of the 65 enrolled thalassemic children. Dental examination was omitted in children below two years of age. Dental caries was diagnosed by visual examination using dental mirror, explorer and periodontal probe as per the criteria recommended by the World Health Organization(5). Dental caries indices *viz.*, DMFT index and DMFS index, were calculated and recorded for the subjects and for age-matched controls seeking treatment from the pediatric out-patient department for illnesses other than dental diseases.

The data was analyzed after making suitable categories for age, mean serum ferritin and mean pretransfusion hemoglobin. The effect of chelating agent used was detected by grouping subjects into three categories, *viz.*, those who received daily oral deferiprone, those receiving subcutaneous desferrioxamine alone or along with daily deferiprone and those who did not receive any chelating agent. The subjects were given chelation if their serum ferritin was more than 1500 ng/mL. Desferrioxamine was administered to subjects subcutaneously using an infusion pump at doses ranging from 30 to 50 mg/kg/day five times per week at home. For patients who could not be administered desferrioxamine in the above-mentioned protocol, daily oral chelation with deferiprone along with biweekly desferrioxamine was given. Deferiprone was administered orally in capsule form at a dose ranging between 50 to 100 mg/kg/day. Serum ferritin values were measured every six months to monitor chelation. All statistical analysis was done using one-way ANOVA, Tukey's test or Student's 't' test at 5% significance level.

Results

Growth retardation was found in most of the subjects with β-thalassemia. Patient data was analyzed in three age groups (0-6 years, 6-10 years and ≥ 10 years). All the three groups were comparable with respect to sex distribution. The mean weight, standing height, sitting height and subischial leg length, expressed as percentage of expected for age, for the different age groups is shown in *Table I*.

30.8% of subjects had a weight less than 3rd centile and 35.4% of subjects had standing height below 3rd centile. 75% of subjects ≥ 10 years were short statured. The mean weight percent, standing height percent, sitting height percent and subischial leg length percent in children ≥10 years were significantly lesser than those in children <6 years or 6-10 years. However, children <6 years and 6-10 years were comparable for the same parameters. Thus, growth retardation was more evident with increasing age.

The effect of iron load, as measured by mean serum ferritin level, on physical growth was analyzed after grouping subjects according to their mean ferritin level (<1500 ng/mL, 1500-3000 ng/mL and ≥ 3000 ng/mL). Physical growth was also correlated with the mean pretransfusion hemoglobin level. 13.8%

TABLE I–*Physical Growth with Respect to Age Group*

Growth parameter	< 6 years (n = 29)	6-10 years (n = 20)	≥10 years (n = 16)
Mean weight %*	87.63	89.39	73.04
Mean standing height %*	95.90	95.78	89.17
Mean sitting height %*	–	95.27	89.10
Mean subischial leg length %*	–	96.71	88.85

* 50th centile values as per standards given by Agarwal, *et al.* for affluent Indian children represent the mean expected value for age(7).

TABLE II–*Physical Growth With Respect To Mean Serum Ferritin And Pretransfusion Hemoglobin*

Growth parameter	Serum ferritin			Pretransfusion hemoglobin		
	<1500 ng/mL (n =13)	1500-3000 ng/mL (n =24)	≥3000 ng/mL (n =20)	Hb < 7 g/dL (n = 9)	Hb 7-9 g/dL (n = 43)	Hb ≥ 9 g/dl (n = 13)
Mean weight %*	88.61	85.91%	78.60	84.19	84.17	86.08
Mean standing-height %*	95.67	95.37	92.21	94.86	94.24	93.69
Mean sitting height %*	–#	93.44%	91.69	91.76	92.30	97.44
Mean subischial leg length %*	–#	95.42%	90.67	94.78	92.51	97.13

* 50th centile values as per standards given by Agarwal, *et al*. for affluent Indian children represent the mean expected value for age(7).

\# Since all children with mean serum ferritin <1500 ng/mL were below 6 years in age, the mean sitting height per cent and subischial leg length per cent for age could not be calculated for the same.

Serum ferritin could be carried out in 57/ 65 children.

of subjects (n = 9) had pretransfusion hemoglobin <7 g/dL, 66.1% of subjects (n = 43) had pre-transfusion hemoglobin 7-9 g/dL and 20.1% (n = 13) of subjects had pre-transfusion hemoglobin ≥9 g/dL. No significant relationship was observed between mean serum ferritin and physical growth or between pretransfusion hemoglobin level and physical growth as seen in *Table II.*

Subjects were also analyzed by grouping them with respect to the chelating agent received by them into three groups, *viz.*, those on deferiprone alone, those receiving desferrioxamine alone or in combination with deferiprone and those who did not receive any chelating agent, as shown in *Table III.* Mean sitting height percent for age, in children receiving desferrioxamine alone or along with deferiprone was significantly lower than that of children receiving deferiprone alone or no chelating agent ($P < 0.05$).

Dental caries indices were calculated in 53 thalassemic subjects. The mean composite DMFT and mean composite DMFS for

TABLE III–*Physical Growth with Respect to Chelating Agent*

Growth parameter	Deferiprone (n =35)	Desferrioxamine/ Both (n =12)	Nil (n =18)
Mean weight %*	85.66	74.83	88.98
Mean standing height %*	94.63	91.55	95.06
Mean sitting height %*	93.81	88.55	–#
Mean subischial leg length %*	94.32	90.13	–#

* 50th centile values as per standards given by Agarwal, *et al*. for affluent Indian children represent the mean expected value for age(7).

\# Since all children who did not receive any chelating agent were below 6 years in age, the mean sitting height percent and subischial leg length per for age could not be calculated for the same.

thalassemic children were 6.604 and 8.308 respectively against 0.79 and 1.06 in the controls which were significantly higher in thalassemics. Mean DMFT and mean DMFS in thalassemics <6 years, were 2.77 and 10.84 respectively, against 0.55 and 0.68 in age-matched controls (P = 0.007 and P = 0.009). Mean DMFT and mean DMFS in thalassemics 6-10 years, were 4.17 and 6.11 respectively, against 1.05 and 1.57 in age-matched controls (P = 0.003 and P = 0.006). Likewise, mean DMFT and mean DMFS in thalassemics ≥10 years, were 5.54 and 9.31 respectively, against 1.00 and 1.20 in age-matched controls (P = 0.003 and P = 0.006). No significant effect of chelating agent, serum ferritin or pre-transfusion hemoglobin was found on the dental caries indices.

Discussion

We conducted this study as there are not enough studies on physical growth in thalassemics from the Indian subcontinent. Also the effect of mean pretransfusion haemoglobin level and chelating agents on physical growth has not been studied from this region before(2). Growth retardation in thalassemics can occur as early as the first or second year of life but these abnormalities are more apparent after 6 to 8 years(6,7). In our study growth was adversely affected in thalassemics and the prevalence and severity of short stature was higher in thalassemics ≥10 years. The advent of growth deficit at young age along with the association of prevalence and severity of short stature and wasting with advancing age is consistent with the hypothesis of some chronic process underlying the etiology of growth retardation in thalassemics.

Further, our study showed that growth retardation was only inconsistently associated with the degree of anemia as also reported by Tienboon and collegues(8). This is contrary to the findings of some other studies, which showed a correlation between growth retardation and low pretransfusion hemoglobin levels, implicating chronic hypoxia as a cause of growth retardation(9,10). Thus, growth retardation in thalassemics could have a multifactorial etiology.

No significant association could be found between serum ferritin levels and growth retardation, as also seen in certain other studies(9,11). However, iron overload has been implicated for contributing to growth failure in thalassemics(12).

It is true that physical growth retardation in

Key Messages

- Physical growth is adversely affected in thalassemic children especially with increasing age.
- Desferrioxamine on chronic administration causes truncal shortening, therefore its judicious use is of paramount importance.
- Prevalence of dental caries is significantly higher in thalassemics.

thalassemics is mainly due to chronic anemia and iron overload. However, growth is influenced by other factors also like ethnicity, genetic composition and hormonal milieu which we did not undertake in our study.

Our study also investigated the effect of iron chelators on body proportions in thalassemics. We found a significant relation between desferrioxamine and reduced sitting height. Previous studies also showed that use of desferrioxamine was associated with platyspondyly(12,13). The pathogenesis of skeletal abnormalities associated with the use of desferrioxamine is not clear. Various mechanisms have been postulated: chelation of trace elements(14), inhibition of cellular proliferation(15) and a direct effect of the drug and its metabolites on bones, due to its slow clearance(16).

The present study also showed that prevalence of dental caries was significantly higher in thalassemic patients than in age-matched healthy controls, suggesting a need for restorative dental care in thalassemics. Certain oral structural changes that take place in thalassemic patients due to maxillary enlargement result in protrusion of anterior teeth, increased space between teeth, over-bite or open-bite and varying degrees of malocclusion, which further predispose to caries(3). A lower IgA level in saliva of thalassemic children has been reported in children which may lead to increased predisposition to caries in thalassemics(17). An earlier study also theorized endocrine dysfunction in thalassemics to be responsible for dental caries(18). Colonization with Streptococcus mutans in thalassemics has been found to be higher which may also have a role in the higher caries incidence seen in them(19). These patients are so preoccupied with their main life-threatening illness that they neglect basic and preventive dental care. A higher caries incidence in thalassemics can also be attributed to poor oral hygiene, improper dietary habits and lack of motivation of these patients.

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