Cephalometric Aspects of Thalassemic Children in the Indian Subcontinent: A Cross-sectional Study

Abstract

Objectives: To compare the cephalometric characteristics of thalassemic children in the Indian subcontinent with the controls, matched for sex and dental age. Methodology: A total of 31 thalassemic children were a part of the study. Cephalometric readings were recorded for the study and the control group. Results: Within the Group I stage, the anterior cranial base length was 68.40±2.93 mm, shorter when compared to the control group. In the Group II stage, the maxillary/mandibular angle was 31.58º for the case group and the mandibular length was shorter in comparison to the controls. In the Group III stage, the SNB angle was 76.42º, lesser than the control group. A relative maxillary prognathism of 9.88 mm and 12.85 mm was observed in thalassemic males and females respectively through the Wiley’s analysis. Conclusion: The overall picture depicted a retruded position of the maxilla and a retrognathic mandible within the study group. A class II profile has also been observed among the study subjects.

Keywords: Cephalometry, craniofacial growth, thalassemia

Introduction

Thalassemias are a group of inherited disorders in the synthesis of the alpha or the beta polypeptide chain of hemoglobin, referred to as alpha beta-thalassemia.[1] Thalassemias are classified into major (homozygous) and minor (heterozygous).

Thalassemia minor (alpha-thalassemia) is considered to be mild and is clinically asymptomatic. Homozygous beta-thalassemia exhibits a severe clinical presentation; it is transfusion dependent and is manifested during the 1st year of life.[1] Affected infants are severely anemic, fail to thrive, and become progressively weaker. Feeding problems, diarrhea, recurrent fever, spontaneous fractures, and retardation of growth are the common presenting symptoms.[1]

The documented orofacial manifestations of beta-thalassemia are prominent cheek bones with a protrusive maxilla due to erythroid hyperplasia with the depression of the bridge of the nose.[2] The dentition exhibits signs of protrusion, flaring and spacing of the maxillary anterior teeth, open bite with varying degrees of malocclusion.[2-5]

The tooth crown size and the tooth length in these patients are significantly altered in comparison to the unaffected groups.[6,7] Thalassemias are considered to be a major public health issue in the South East Asian countries, where the carrier state reaches a prevalence of up to 60%.[8] This disease is also distributed across Africa, the Middle East, the Mediterranean region, South East Asia, and in the Indian subcontinent.[9,10] In the Indian subcontinent, there are approximately 30 million carriers of beta-thalassemias, with an estimated 10,000 babies born each year with severe defects in the beta chain of the hemoglobin molecule.[11]

A few researchers have investigated the cephalometric characteristics of these children,[12-15] and no scientific research had been attempted to assess the cephalometric aspects of these unfortunate children in the Indian subcontinent. Thus, the aim of the present study is to study the cephalometric characteristics of the beta-thalassemic children and to compare the measurements with normal healthy controls of the similar age group.

Methods

This cross-sectional study had been cleared by the Institutional Review Board of Sri Sai

How to cite this article: Samba AA, Bhoopathi PH, Sundaram RM, Patil AK, Gupta BV, Rao VT. Cephalometric aspects of thalassemic children in the Indian subcontinent: A cross-sectional study. Indian J Dent Res 2018;29:286-90.
College of Dental Surgery, Vikarabad, India (SSCDS/13/C/b/012), and conducted in accordance with the guidelines laid down by the World Medical Association and Helsinki Declaration. This research was a collaborative study between the Thalassemia and Sickle Cell Society of Hyderabad (Reg no: 5359), India.

All participants were diagnosed to be suffering from beta-thalassemia major and were registered under Thalassemia and Sickle Cell Society of Hyderabad, Telangana. The children visit the society for regular screening and blood transfusion as a part of their treatment regimen. Out of 200 patients examined during a period of 6 months, 31 patients who gave their consent were included in the study. The control group consisted of 41 healthy children with similar socioeconomic characteristics. The participants in both the groups were in the age group between 8 and 16 years.

The exclusion criteria for both the groups are as follows:
1. Alteration in the number or shape of the teeth that might affect the diameter of the dental arch
2. Any oral habit that might influence the dental arch (e.g., digit sucking)
3. Any hereditary or acquired dental or facial deformity
4. Experience of orthodontic treatment before the start of the examination.

Lateral cephalograms were taken for the participants at a diagnostic center with the posterior teeth in maximum intercusption and the anode-mid-sagittal plane distance fixed. All radiographs were taken on the same machine (Villa Rotograph Plus). The ×10 magnification was corrected to standardize all radiographs. The lateral skull radiographs were traced on matte acetate paper using 0.5 mm lead pencil, and 14 cephalometric points were registered. Measurements were performed manually using a ruler and protractor and recorded to the nearest 0.1 mm or 1°.

The linear and the angular measurements were recorded and analyzed accordingly. In addition to the cephalometric assessment, Wiley’s analysis was performed to assess the horizontal discrepancies between the maxilla and the mandible, with the Frankfort horizontal plane taken as the reference. The cranial base measurements such as the length of the maxilla and mandible were noted and compared with the standard values.

The maxillary/mandibular values if exceeding the standard values indicated maxillary or the mandibular prognathism. If the maxillary length was less than standard, the deficit was added to mandibular prognathism and vice versa. If the effective length of the cranial base element exceeded the standard, the excess contributed to maxillary prognathism; if it was less than the standard, the deficit contributed to mandibular prognathism.

The results thus obtained were tabulated and subjected to statistical analysis using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Mean, standard deviation, and difference between means for each group were calculated using independent t-test to find out the significance in means between the study group and the control group for all the parameters. P < 0.05 was taken as the level of significance. Student’s independent or unpaired t-test is used when two separate sets of independent and identically distributed samples are obtained, one from each of the populations being compared.

**Results**

The study comprised of 31 children distributed into three groups based on the eruption status of their teeth. The Group I consisted of children with erupted permanent first molars and incisors, the Group II with permanent canine and at least two premolars erupted, and the Group III had children with all erupted permanent teeth with the exception of the third molars [Tables 1-3].

**Group I stage**

In the Group I stage, the SNB of the thalassemic group was lesser than the control group and was statistically significant. The upper incisor inclination angle was 104 ± 13.78 for the thalassemic patients and 112.67 for the control group. Regarding the linear measurements, the anterior cranial base length (S-N) was 68.40 ± 2.93 mm, shorter marginally when compared with the control group. The mandibular length was much shorter in the thalassemic group than the control, though the difference was not statistically different.

**Group II stage**

The maxillary/mandibular angle was 31.58 for the case group, greater than the control group and was statistically significant. The mandibular length was much shorter in the case group, and this difference was statistically significant.

**Group III stage**

The SNB angle for the case group was less than that of the control group and is statistically significant. The maxillary/mandibular angle was higher in the case group, with this difference being statistically significant. The SNB for the case group was lower than the control, and was statistically insignificant.

For the thalassemic males and females, a relative maxillary prognathism of 12.85 and 9.88 mm was observed through the Wiley’s analysis [Tables 4 and 5].

**Discussion**

Thalassemia poses a grave challenge to the health of these unfortunate children and drastically decreases the health-related quality of life. It is suggested to have an improved understanding of the craniofacial features of these participants to render better clinical, psychological, and social support programs for these participants. [16] In a
country as large as India, with significant thalassemic cases being diagnosed each year, there has not been a single scientific investigation to assess the cephalometric aspects of these children in the Indian subcontinent and thus warrants further investigation.

The cranial and the linear measurements of the thalassemic children were marginally lower in comparison to the controls, although not statistically significant. An exception was seen among the children in the Group III stage, which had significantly lower linear and angular measurements, and similar results had been found in studies carried out by Bassimitci et al.\cite{17} and Alhaija et al.\cite{12} However, studies conducted by Amini et al. and Takriti and Dashash found no significant differences among the thalassemia children and controls.

This present study showed a retruded position of the maxilla in comparison to the controls, which is evident by the decreased SNA angle and is similar to the data reported by Bassimitci et al.\cite{17} and Alhaija et al.\cite{12} Other studies have found a protrusive maxilla which was obviously due

| Variable | Mean±SD | Difference between means | t | P |
|----------|---------|--------------------------|---|---|
| N-S-Ar   | 124.57±4.57 | 124.71±5.76 | 0.14 | 0.05 | 0.96 |
| SNA      | 83.14±2.54 | 79.00±4.08 | 4.14 | 2.27 | 0.04 |
| SNB      | 77.86±3.07 | 71.71±3.49 | 6.15 | 3.48 | <0.05 |
| ANB      | 5.29±1.25 | 7.29±2.62 | 2.00 | 1.81 | 0.09 |
| Maxillary/mandibular | 24.00±4.16 | 30.00±6.13 | 6.00 | 2.14 | 0.05 |
| Upper incisor/maxillary | 112.67±4.36 | 104.29±13.78 | 8.38 | 1.46 | 0.17 |
| Lower incisor/mandibular | 99.29±9.56 | 99.86±5.36 | 0.57 | 0.13 | 0.89 |

| Variable | Mean±SD | Difference between means | t | P |
|----------|---------|--------------------------|---|---|
| N-S-Ar   | 123.67±5.91 | 120.50±4.54 | 3.17 | 1.47 | 0.15 |
| SNA      | 83.17±3.73 | 80.58±3.26 | 2.59 | 1.80 | 0.08 |
| SNB      | 78.92±4.03 | 75.83±3.92 | 3.34 | 1.89 | 0.07 |
| ANB      | 4.25±1.35 | 4.75±2.34 | 0.50 | 0.64 | 0.52 |
| Maxillary/mandibular | 24.08±4.14 | 31.58±2.87 | 7.50 | 5.15 | <0.05 |
| Upper incisor/maxillary | 115.92±5.63 | 111.75±6.78 | 4.17 | 1.63 | 0.11 |
| Lower incisor/mandibular | 102.92±6.51 | 101.17±4.40 | 1.75 | 0.77 | 0.44 |

SD=Standard deviation
to the maxillary erythroid hyperplasia commonly seen in these classes of participants,\cite{2,12,14,18,19} but the drawbacks of these studies are that a few of these are only case reports.

The reasons for not appreciating the classical maxillary prognathism could be the blood transfusion regimes that these participants are exposed to, thereby partially negating the negative consequences.

The results of this present study portray a picture of a retrognathic mandible as suggested by the reduced SNB angle in all the three groups. Similar results were seen in studies carried out by Bassimitci et al.,\cite{17} Amini et al.,\cite{13} and Takriti and Dashash;\cite{15} however, Alhaija et al.,\cite{12} found a normally positioned mandible in comparison to the controls in his study.

A casual glance into the length of the maxilla and the mandible with respect to all the three age groups indicates general growth retardation in these thalassemic patients. This delay in growth especially in the mandible can be explained by the fact that the subperiosteal growth of the ramus as well as the secondary cartilage of the mandible are sensitive to severe anemia, endocrine dysfunction, and growth hormone insensitivity.

### Table 3: Descriptive statistics of the children in the dental Group III versus the controls

| Variables | Control group (n=7) | Case group (n=7) | Difference between means | t | P |
|-----------|---------------------|------------------|--------------------------|---|---|
| Angular measurements | | | | | |
| N-S-Ar | 122.92±4.54 | 122.08±3.42 | 0.84 | 0.50 | 0.61 |
| SNA | 84.58±3.60 | 81.33±3.91 | 3.25 | 2.11 | 0.04 |
| SNB | 81.25±3.16 | 76.42±4.23 | 4.83 | 3.16 | 0.00 |
| ANB | 3.33±3.65 | 4.92±4.50 | 1.59 | 0.94 | 0.35 |
| Maxillary/mandibular | 24.33±4.63 | 31.75±3.44 | 7.42 | 4.44 | <0.05 |
| Upper incisor/maxillary | 110.00±27.71 | 108.08±8.14 | 1.92 | 0.23 | 0.82 |
| Lower incisor/mandibular | 104.08±7.23 | 102.58±4.89 | 1.5 | 1.25 | 0.35 |
| Linear measurements | | | | | |
| S-N | 72.15±3.73 | 71.40±3.68 | 0.75 | 0.49 | 0.62 |
| S-Ar | 35.02±2.93 | 32.70±2.34 | 2.32 | 2.14 | 0.04 |
| PNS-ANS | 51.45±2.54 | 47.77±2.77 | 3.67 | 3.38 | 0.00 |
| Ar-Gn | 107.03±7.44 | 101.62±6.99 | 5.40 | 1.8 | 0.08 |
| Na-Me | 111.08±7.94 | 111.30±6.81 | 0.22 | 0.07 | 0.94 |
| ANS-Me | 65.40±3.64 | 67.20±6.45 | 1.80 | 0.84 | 0.41 |
| Ar-Go | 44.40±3.50 | 43.12±6.80 | 1.27 | 0.57 | 0.57 |
| S-Go | 71.62±8.60 | 70.95±5.77 | 0.67 | 0.22 | 0.82 |

SD=Standard deviation

### Table 4: Wiley’s analysis for the thalassemic male participants

| Measurement | Wylie’s standard (mm) | Sample (case) Mean±SD | Maxillary prognathism (mm) | Mandibular prognathism (mm) |
|-------------|-----------------------|------------------------|---------------------------|----------------------------|
| Ar-S | 18 | 13.35±2.56 | 4.65 |
| S-Ptm | 18 | 21.03±2.92 | 3.03 |
| Ptm-ANS | 52 | 49.92±3.56 | 2.08 |
| Ar-P | 103 | 90.61±6.49 | 12.39 |
| Prognathism totals | | 17.5 | 4.65 |

Prognathism total=17.5-4.65=12.85 mm maxillary prognathism. In males, there is a relative maxillary prognathism of 12.85 mm.

SD=Standard deviation

### Table 5: Wiley’s analysis for the thalassemic female participants

| Measurement | Wylie’s standard (mm) | Sample (case) Mean±SD | Maxillary prognathism (mm) | Mandibular prognathism (mm) |
|-------------|-----------------------|------------------------|---------------------------|----------------------------|
| Ar-S | 17 | 12.67±2.83 | 4.33 |
| S-Ptm | 17 | 20.85±2.99 | 3.85 |
| Ptm-ANS | 52 | 50.92±1.97 | 1.08 |
| Ar-P | 101 | 91.72±4.44 | 9.28 |
| Prognathism totals | | 14.21 | 4.33 |

Prognathism total=14.21-4.33=9.88 mm maxillary prognathism. In females, there is a relative maxillary prognathism of 9.88 mm.

SD=Standard deviation
A vertical growth pattern can be appreciated in this study which can be attributed to a combination of increased anterior facial height and short posterior facial height which ultimately culminates in an increase in maxillary/ mandibular plane angle. Studies carried out by Bassimitci et al.,[17] Alhaija et al.,[12] Takriti and Dashash[15] and Amini et al.[13] have found similar results.

Another prominent feature is the maxillo-mandibular discrepancy represented by the increased ANB angle seen among the study participants in this study and this is because of a smaller mandible/short ramus. The posterior cranial base (S-Ar) is shorter in all the three groups of thalassemic patients in comparison with the controls, and the resultant effect is the development of a class II profile. Amini et al.,[13] Alhaija et al.,[12] Takriti and Dashash[15] and Bassimitci et al.[17] had in the past also reported similar results. One of the other factors for a class II relationship could be blamed on the slower growth of the mandible in comparison to the maxilla, and thereby, the growth of the mandible is hindered by the excessive vertical maxillary growth.

The study entailed the utilization of Wiley’s analysis to detect horizontal relationship between maxilla and the mandible. A relative maxillary prognathism of 9.88 and 12.85 mm was observed in thalassemic males and females, respectively. The reasons for such a finding could be attributed to a short cranial base and short mandible seen among the thalassemia patients.

The classic midface prominences in thalassemic patients have not been investigated in this study and can be a subject of investigations at a later date. The effect of blood transfusions on the growth retardation definitely needs a thorough investigation, the life course epidemiological concepts could be utilized to assess the effect of blood transfusion on growth retardation in future studies. However, for this to happen, these participants have to be followed up at regular intervals and this is the need of the hour.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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