International Journal of Paediatric Dentistry 2005; **15:** 98–104

Dental arch morphological and dimensional characteristics in Jordanian children and young adults with β-thalassaemia major

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Summary. *Objective.* The aim of this study was to examine the arch dimensions of Jordanian patients with β-thalassaemia major in comparison with an unaffected control group.
Methods. The sample consisted of 24 patients who suffered from β-thalassaemia major (mean age = 13·9 ± 3·1 years) and an unaffected control group (mean age = 13·5 ± 2·9 years) matched for dental age, sex, and incisor and molar relationships. The unaffected control group was randomly selected from four public schools in the Governate of Irbid-Jordan. Alginate impressions were taken of the maxillary and mandibular dental arches of all participants. All measurements of the arch dimensions were made on the casts using an electronic digital sliding calliper.
Results. In the mandibular arch, when compared with the patients with thalassaemia, the unaffected control group subjects showed a (statistically) significantly larger incisor width, larger arch depth, and larger left and right anterior arch lengths (1·18, 2·58, and 1·85 and 1·12 mm, respectively). In the maxillary arch, there was a statistically significant difference in the mean incisor width (± 2·16 mm), arch depth (± 3·14 mm), intermolar width (± 1·21 mm) and in the left anterior arch length (± 1·97 mm). The canine widths, premolar widths, left and right posterior arch length, and curve of Spee of both arches showed no statistically significant differences between the two groups.
Conclusion. When compared to unaffected subjects, patients with β-thalassaemia major exhibited: a narrower maxilla; a shorter maxilla and mandible; and smaller incisor widths for the maxillary and mandibular arches.

Introduction

The condition β-thalassaemia (sometimes referred to as Cooley's anaemia or Mediterranean anaemia) is a hereditary blood disorder that results in a failure to produce β-globin chains, and as a consequence, normal haemoglobin cannot be synthesized. In addition, there is ineffective erythropoiesis because of an excess of α-globin chains; these damage the red cell membrane, resulting in cell lysis and an increased breakdown of red cells, which leads to severe anaemia [1]. There are two β-genes. Deficiency of one β-gene essentially leads to significant haemolysis (β-thalassaemia trait/thalassaemia minor); deficiency of both genes leads to significant haemolytic anaemia (thalassaemia major). Thalassaemia intermedia represents a condition in which the degree of haemolysis is milder even though the affected patient may have a deficiency of both β-genes. Therefore, thalassaemia intermedia is an essentially descriptive term that indicates minimal or no need for transfusions in affected patients [2]

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Although relatively uncommon in North America, thalassaemia is the second most common cause of anaemia in children world-wide after iron deficiency anaemia [3]. In the USA, thalassaemia most often affects children of Mediterranean descent; 3–10% of those of Greek or Italian ancestry are affected with β-thalassaemia trait [3]. In the UK, approximately 2800 (0·44%) children are born annually who carry the β-thalassaemia trait, with approximately 43 (0·07 per 1000) suffering β-thalassaemia major/intermedia [4]. In Northern Jordan, the overall prevalence of β-thalassaemia is 5·93% [5], while that of β-thalassaemia major is 0·1% [6].

It has been reported in the literature that the major oral change in thalassaemic patients is enlargement of the maxilla caused by bone marrow expansion. This results in a characteristic appearance known as chipmunk facies [1,7]. Affected patients usually suffer from spacing of the teeth and forward drift of the maxillary incisors, so that orthodontic treatment may be indicated [7]. Although β-thalassaemia major is considered to be a common genetic disorder in Jordan, there are few up-to-date research reports in the literature with regard to the morphological and dimensional characteristics of the dental arch in affected patients world-wide. Therefore, the aim of this study was to investigate dental arch parameters in β-thalassaemia major patients and to compare measurements with corresponding values in a group of unaffected subjects.

Subjects and methods

All subjects with β-thalassaemia major included in this study were patients attending a specialist care at a thalassaemia centre at Basma Hospital, Irbid, Jordan.

Written consent was obtained from the adult subjects and the parents of all the children included prior to dental examination. For both the study and unaffected control groups, subjects were excluded from this research if they had any of the following:
1 clinically evident interproximal dental caries;
2 an alteration in the number or shape of the teeth that might affect the diameter of the dental arch (e.g. congenitally missing teeth or Turner's tooth);
3 any oral habit that might influence the dental arches (e.g. digit sucking habits);
4 any hereditary or acquired dental or facial deformity; or
5 experience of orthodontic treatment prior to the start of the examination.

After applying the exclusion criteria, a total of 24 Jordanian patients (12 males and 12 females) affected with β-thalassaemia major were included in this study. As part of their medical care at the centre for subjects with thalassaemia, all patients were treated with a transfusion regimen (Hb levels = 6–10 g dL^{-1}), an iron chelating agent (desferrioxamine, 35–50 mg kg^{-1}) to control iron overloading and folic acid supplements. None of the patients included in this study had a medical history of bone marrow transplantation procedures prior to the study date.

To select the subjects for the control group, a list of the primary and secondary schools attended by children of equivalent age and sex to the patients in the study group was obtained from the Jordanian Ministry of Education. Four schools were randomly selected and a series of computer generated random numbers were used to select classes in these schools. The first pupil on the class list who fitted the inclusion criteria and was matched to a study subject was selected for this study. Using this method, a control group of 24 unaffected Jordanian subjects (12 males and 12 females) matched for dental age, sex, incisor relationship (according to the British Standard Classification) and Angle's molar relationship was selected. Alginate impressions were taken of the maxillary and mandibular dental arches of all participants. In order to standardize the dental models as much as possible, all impressions were cast in hard stone on the same day as the impression was taken.

All measurements of arch dimensions were made on the casts using an electronic digital sliding calliper (JOCAL, C. E. Johansson, Eskilstuna, Sweden). The following measurements were made by one examiner (A.A.-W.) (Fig. 1):

- *Inter-incisor width* was measured from the distal contact point of the permanent lateral incisor on one side to the distal contact point of the contralateral permanent lateral incisor.
- *Inter-canine width* was measured from the cusp tip of the permanent canine on one side to the cusp tip of the contralateral permanent canine.
- *Inter-premolar width* was measured from the cusp tip of the second premolar on one side to the cusp tip of the contralateral second premolar.
- *Inter-molar width* was measured from the mesiobuccal cusp tip of the first permanent molar on one side to the mesiobuccal cusp tip of the contralateral first permanent molar.

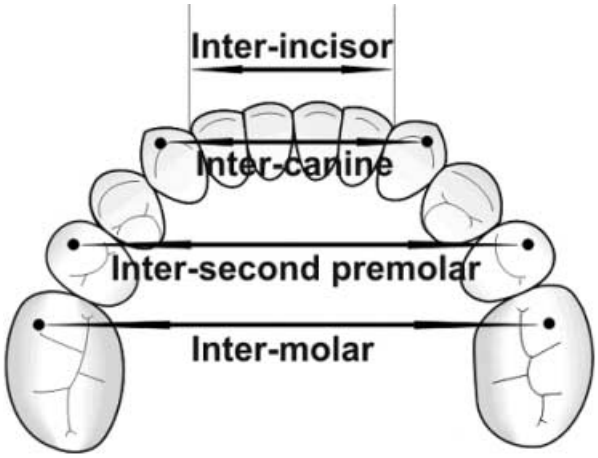

Fig. 1. Diagram of the upper arch showing the measurements of the inter-incisor, inter-canine, inter-premolar and inter-molar widths.

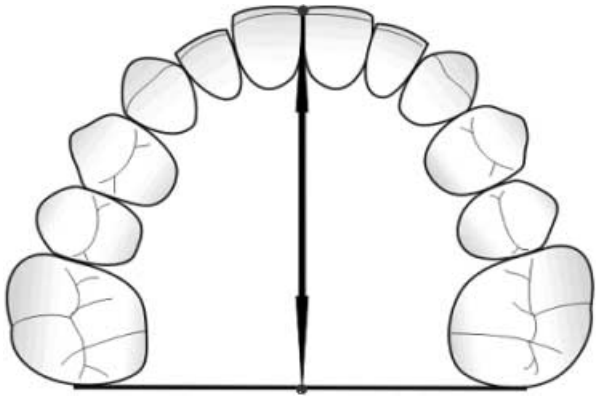

Fig. 2. Diagram of the upper arch showing the measurement of the arch depth.

- *Arch depth* was measured as the shortest distance connecting the distal surface of the first permanent molars to the labial surface of the most anterior tooth in the arch (Fig. 2).
- *Anterior arch length* was measured between the mesial contact point of the permanent central incisor, and the point between the permanent canine and the first premolar (Fig. 3).
- *Posterior arch length* was measured between the mesial contact point of the permanent canine and the distal contact point of the second premolar.
- *The curve of Spee* was measured as the perpendicular line from the cusp tip of the second premolar to a line connecting the distal cusp tip of the first permanent molar and the incisal edge of the most anterior tooth (Fig. 4) [8]. If an individual tooth was erupted to a position above the plane of occlusion, the interference was disregarded.

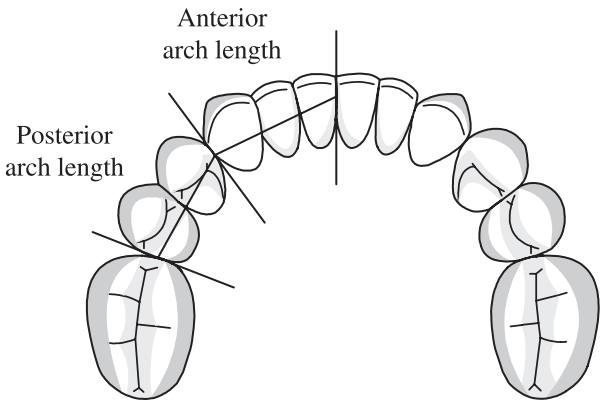

Fig. 3. Diagram of the upper arch showing the measurements of the anterior and posterior arch lengths.

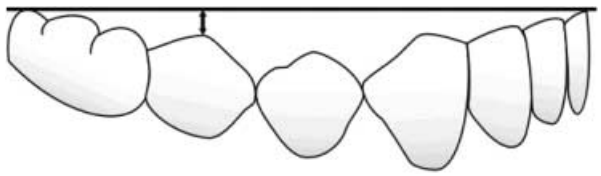

Fig. 4. Diagram of the lower arch showing the measurement of the curve of Spee.

Statistical analysis

A period of training was completed by the assessor to ensure compliance with the measurement criteria and improve reproducibility. The reproducibility was evaluated by analysing the differences between 10 double measurements taken at different times for all variables investigated. The error of measurement, or mean square error (SE^2), was assessed by Dahlberg's formula [9]:

$$(1)\ SE^2 = \Sigma\, d^2/2n,$$

where d is the difference between duplicate measurements and n is the number of double determinations. The errors ranged from 0·10 to 0·47 for the mandibular arch and from 0·15 to 0·48 for the maxillary arch (Table 1).

The data were then entered onto a computer and tabulated using the SPSS computer program. Means and standard deviations were calculated, and a two-tailed t-test was used to determine statistically significant differences using $P < 0{\cdot}05$ as the level of significance.

Table 1. Reproducibility of the measurements was evaluated analysing 10 double measurements. The error of measurement was assessed as recommended by Dahlberg [9].

Measurement	Maxillary arch (mm)	Mandibular arch (mm)
Inter-incisor width	0·46	0·10
Inter-canine width	0·16	0·25
Inter-premolar width	0·24	0·33
Inter-molar width	0·22	0·47
Arch depth	0·24	0·12
Left anterior arch length	0·33	0·22
Right anterior arch length	0·22	0·15
Left posterior arch length	0·20	0·25
Right posterior arch length	0·15	0·14
Curve of Spee	–	0·48

Results

Fifty-six patients with β-thalassaemia major and 576 subjects in the unaffected control group were examined initially. Twenty-four affected individuals fulfilled the inclusion criteria for this study and these subjects were then matched for dental age, sex, and incisor and molar relationships with unaffected control cases. The ages of the patients with β-thalassaemia major and the unaffected control group ranged from 9·5 to 23·4 years (mean age = 13·9 ± 3·1 years) and from 9·1 to 22·9 years (mean age = 13·5 ± 2·9 years), respectively. Using the British Standard Classification, one patient in both groups had a Class I incisor relationship, while 20 had Class II, Division 1 malocclusions and three had Class II, Division 2 malocclusions.

Tables 2 and 3 detail the findings of this study for the mandibular and maxillary arch measurements in both the β-thalassaemia major and unaffected groups. Incisor widths for the maxillary and mandibular arches were greater in the unaffected control group than the β-thalassaemia group (2·16 mm and 1·18 mm, respectively; $P < 0·05$). In the maxillary

Table 2. Means, standard deviations (SDs) and difference between means of the width and length of the lower dental arch in the β-thalassaemia major and unaffected control groups: (d.f.) degree of freedom.

	Control group (mm)		β-Thalassaemia group (mm)		Difference between		
Variable	Mean	SD	Mean	SD	means	d.f.	*P*-value
Inter-incisor width	22·36	1·35	21·18	2·88	1·18	22	0·042*
Inter-canine width	27·41	2·09	26·36	2·74	1·05	15	0·237
Inter-premolar width	40·33	2·14	38·88	2·89	1·44	12	0·179
Inter-molar width	44·80	3·02	43·91	2·75	0·89	23	0·143
Arch depth	35·58	2·63	33·00	2·95	2·58	22	0·001*
Left anterior arch length	18·22	2·19	16·38	1·37	1·85	15	0·017*
Right anterior arch length	17·85	1·58	16·72	0·89	1·12	15	0·018*
Left posterior arch length	14·39	1·31	13·42	4·08	0·96	13	0·383
Right posterior arch length	14·67	2·11	14·08	1·49	0·59	12	0·465
Curve of Spee	1·44	0·60	1·06	0·65	0·37	12	0·169

*Statistically significant.

Table 3. Means, standard deviations (SDs) and difference between means of the width and length of the upper dental arch in the β-thalassaemia major and unaffected control groups: (d.f.) degree of freedom.

	Control group (mm)		β-Thalassaemia group (mm)		Difference between		
Variable	Mean	SD	Mean	SD	means	d.f.	*P*-value
Inter-incisor width	29·52	1·60	27·37	2·83	2·16	22	0·004*
Inter-canine width	34·04	3·03	32·34	2·59	1·70	14	0·115
Inter-premolar width	45·45	3·07	44·75	2·79	0·69	15	0·423
Inter-molar width	50·89	2·41	49·68	3·04	1·21	23	0·049*
Arch depth	42·06	3·31	38·92	2·62	3·14	22	0·000*
Left anterior arch length	23·54	2·49	21·57	1·89	1·97	14	0·035*
Right anterior arch length	23·48	2·52	21·84	1·74	1·64	14	0·060
Left posterior arch length	14·76	1·95	14·04	1·86	0·71	16	0·336
Right posterior arch length	14·52	1·99	14·49	2·21	0·04	15	0·967

*Statistically significant.

arch, inter-molar width was 50·89 mm (± 2·41) in the unaffected control group and 49·68 mm (± 3·04) in the study group, demonstrating a statistically significant difference of 1·21 mm ($P < 0·05$).

In the unaffected control group, the maxillary arch depth was 3·14 mm larger than in the study group ($P < 0·05$). A statistically significant difference was also found between the mean values for mandibular arch depth, which was 2·58 mm larger in the unaffected control group ($P < 0·05$).

The canine widths, premolar widths, left and right posterior arch lengths, and curve of Spee of both arches showed no statistically significant differences between the study and control groups.

Discussion

There have been previous anecdotal reports of the dimensional changes of the dental arch in patients with β-thalassaemia major disease, but none has biometrically quantified these changes.

Patients suffering β-thalassaemia major show great clinical variability in the systemic signs and symptoms with which they present. Because of the severe anaemia they suffer in early childhood, bony changes, retardation in growth, splenomegaly, and iron overload and consequent deposition in tissues all occur [10]. It has been stated that the effects of thalassaemia on bones depend on the severity of the anaemia, the patient's age, the duration of the clinical symptoms, and the timing of both therapeutic blood transfusion and splenectomy [11–13]. It has also been reported that transfusion therapy may diminish or, indeed, prevent development of bony abnormalities in growing patients [12,14]. To reduce the variables which might affect the outcome results, all patients selected for this study had received treatment in the same way (including regular transfusions).

It has been stated previously that bone marrow hyperplasia caused by rapid red cell turnover results in changes in the bony structure in patients with β-thalassaemia major [15]. The hyperplasia of bone marrow in the maxilla exceeds that of the mandible, which may help to explain the absence of Class III occlusion in thalassaemia [15]. Numbers of subjects included were small, but this may be supported by the current study, in which no Class III malocclusions were seen and where the majority had a Class II incisor relationship.

Other authors have suggested that the larger arch depth in the maxilla found in patients affected with β-thalassaemia major may be attributed to the protrusion of maxillary anterior teeth [10,15,16]. This results in an increase in overjet and overbite, which allows the lower lip to be trapped between upper and lower incisors. Consequently, the growth of the mandible tends to be inhibited and protrusion of the maxilla becomes more pronounced [15]. One study reported that there was only a small and statistically insignificant increase in sagittal maxillary overgrowth in a group with β-thalassaemia major in comparison with a control group [10]. This is contrary to the findings in this study for the maxillary arch, where arch depths were shorter in the β-thalassaemia major group than in the unaffected control group. One possible explanation for this may be derived from findings in a cephalometric study carried out in 37 patients affected with β-thalassaemia major, where the authors concluded that the maxillary incisors in subjects with β-thalassaemia tended to be upright or even retroclined [17]. The shorter mandibular arch found in this study is in agreement with the findings of other studies of patients affected with β-thalassaemia major [15,17,18].

No significant differences in the distance between the most prominent maxillary molars for patients with β-thalassaemia major have been reported previously [10]. In this study, however, inter-molar width in the upper arch was significantly smaller in the group with β-thalassaemia major. This could have been a result of the difference in the first permanent molar position, inclination or bucco-lingual size between affected and non-affected subjects, a factor which was not explored.

The inter-incisor width, the anterior arch length for the maxillary left side, and the mandibular left and right sides were significantly smaller in the β-thalassaemia group. This could be explained by a decrease in the mesiodistal size of the permanent teeth for the thalassaemic patients reported in a previous study [19]. Another explanation might be the presence of more anterior crowding in the thalassaemic group; however, anterior crowding was not evaluated in this study.

It can be concluded from this research that the dental arch parameter characteristics of patients with β-thalassaemia major include a narrower maxilla, a shorter maxilla and mandible, and smaller incisor widths for the maxillary and mandibular arches. Therefore, it is important to understand the changes associated with thalassaemia and their implications for orthodontic treatment.

Finally, the findings of this study should be interpreted with caution because of the small sample size involved. Increasing the sample size would have provided a greater probability of establishing statistical significance for the trends seen in the measurements of maxillary and mandibular arch width if these were real. Further research using a larger sample is needed if these findings are to be confirmed.

Conclusions

When compared to an unaffected control group matched for sex, dental age, and incisor and molar relationships, patients with β-thalassaemia major had:

1 a narrower maxilla;
2 a shorter maxilla and mandible; and
3 smaller incisor widths for the maxillary and mandibular arches.

Acknowledgements

We are grateful to Dr Wesam Al-Saqa for her assistance with the drawings.

Résumé. *Objectif.* Cette étude a eu pour objectif d'examiner les dimensions d'arcade de patients porteurs de β-thalassémie majeure en comparaison avec un groupe témoin d'enfants jordaniens non affectés. *Méthodes.* L'échantillon a consisté en 24 patients souffrant de β-thalassémie majeure (âge moyen 13,9 ± 3,1 ans), et un groupe témoin non affecté (âge moyen 13,5 ± 2,9 ans) apparié en âge, en sexe et en interrelations incisive et molaire. Le groupe non affecté a été sélectionné au hasard dans quatre écoles publiques choisies au hasard dans la zone de Irbid, Jordanie. Des empreintes à l'alginate des arcades maxillaires et mandibulaires de tous les participants ont été prises. Toutes les mesures de dimension d'arcade ont été effectuées sur les modèles par curseur électronique digitalisé.
Résultats. Les sujets du groupe témoin ont montré, à l'arcade mandibulaire, une plus grande largeur incisive, plus grande profondeur d'arcade et de plus grandes longueurs d'arcade antérieure droite et gauche (1,18 mm, 2,58 mm et 1,85 mm et 1,12 mm respectivement), toutes statistiquement significatives. Au maxillaire, il y avait une différence significative au niveau de la largeur moyenne incisive (+2,16 mm), profondeur d'arcade (+3,14 mm), largeur intermolaire (+1,21 mm) et dans la longueur antérieure d'arcade gauche (+1,97 mm). Il n'y avait pas de différence significative entre les groupes pour les largeurs canines, prémolaires, la longueur d'arcade postérieure droite et gauche, la courbe de Spee.
Conclusion. Comparés à des patients non affectés, les sujets porteurs de β-thalassémie majeure présentaient un maxillaire plus étroit, un maxillaire et une mandibule plus petits et des largeurs d'incisives plus petites aux deux arcades.

Zusammenfassung. *Ziele.* Diese Studie wurde durchgeführt, um die Zahnbogendimensionen von Patienten mit ß-Thalassämia major mit einer nicht betroffenen Kontrollgruppe zu vergleichen.
Methoden. Die Stichprobe bestand aus 24 Patienten, welche an ß-Thalassämia major litten (mittleres Alter 13.9 +/– 3.1 Jahre), und einer Kontrollgruppe (mittleres Alter 13.5 +/– 2.9 Jahre) diese wurde gematcht hinsichtlich Alter, Geschlecht und Kieferrelation. Die Kontrollgruppe wurde zufällig ausgewählt aus den Schülern von vier Schulen, welche ihrerseits ebenfalls zufällig innerhalb des Regierungsbezirkes Irbid, Jordanien, ausgewählt worden waren. Alginatabformungen wurden von Ober- und Unterkiefer aller Teilnehmer genommen. Alle Messungen der Kieferdimensionen wurden mit einem digitalen Calliper elektronisch registriert.
Ergebnisse. Im Unterkiefer zeigte die Kontrollgruppe im Vergleich zur Studiengruppe eine signifikant größere Schneidezahnbreite, eine größere Zahnbogentiefe und eine Vergrößerung der rechten und linken Zahnbogenlängen (1.18 mm, 2.58 mm, 1.85 mm, 1.12 mm). Im Oberkiefer zeigte sich eine statistisch signifikante Abweichung der mittleren Schneidenzahnbreite (+2.16 mm), Bogentiefe (+3.14 mm), Intermolarenbreite (+1.21 mm) und der Zahnbogenlängen beidseits (+1.97 mm). Keine statistisch signifikanten Unterschiede zwischen beiden Gruppen wiesen auf die Eckzahn- und Prämolaren-Zahnbogenweiten, die hinteren Zahnbogenlängen beidseits und die Speekurve.
Schlussfolgerung. Im Vergleich zu nicht betroffenen Kontrollen zeigten Patienten mit ß-Thalassämia major folgendes: Engere Oberkiefer, kürzere Ober- und Unterkiefer sowie schmalere Schneidezahnbreiten in beiden Kiefern.

Resumen. *Objetivo.* El objetivo de este estudio fue examinar las dimensiones de la arcada de pacientes β-talasémicos major en comparación a un grupo control de jordanos no afectados.

Métodos. La muestra consistió en 24 pacientes afectados de β-talasemia major (edad media 13,9 ± 3,1 años), y un grupo control no afectado (edad media 13,5 ± 2,9 años) emparejados por edad dental, sexo, y relación molar y de incisivos. El grupo control no afectado se seleccionó aleatoriamente de cuatro escuelas públicas escogidas al azar en la Gobernación de Irbid-Jordan. Se tomaron impresiones de alginato en las arcadas dentarias maxilares y mandibulares de todos los participantes. Todas las medidas de las dimensiones de la arcada se hicieron sobre moldes usando un calibrador deslizante digital electrónico.

Resultados. En la arcada mandibular, cuando se compararon los pacientes con talasemia, los sujetos del grupo control no afectado mostraron una anchura de los incisivos significativamente (estadísticamente) más ancha, mayor profundidad de arcada y mayor longitud de arcada anterior derecha e izquierda (1,18 mm, 2,58 mm, 1,85 mm y 1,12 mm respectivamente). En la arcada maxilar superior, hubo una diferencia estadísticamente significativa en la anchura media de los incisivos (+2,16 mm), la profundidad de arcada (+3,14 mm), la anchura intermolar (+1,21 mm) y en la longitud de arcada anterior izquierda (+1,97 mm). La anchura de los caninos, la anchura de los premolares, la longitud de arcada posterior derecha e izquierda y la curva de Spee de ambas arcadas no mostró diferencias significativas entre los dos grupos.

Conclusión. Cuando se compararon los sujetos no afectados, los pacientes con β-talasemia major mostraron un maxilar más estrecho, un maxilar superior y una mandíbula más cortas y una anchura de incisivos más pequeña, tanto en la arcada del maxilar superior como en la mandibular.

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