TOOTH CROWN SIZE OF THE PERMANENT DENTITION IN SUBJECTS WITH THALASSEMIA MAJOR

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ABSTRACT Thalassemia refers to a group of hereditary anemias resulting from defects in synthesis of either alpha or the beta polypeptide chains of hemoglobin. The homozygous form of beta thalassemia (thalassemia major) exhibits the most severe clinical symptoms. Odontometric analysis of subjects with thalassemia are lacking, despite the widely distribution of the disease and its orofacial characteristics. The aim of this study was to provide detailed description of tooth crown size in the permanent dentition of subjects with thalassemia major and to compare the findings with those of the same population.

Dental casts of 46 thalassemic subjects, 25 males and 21 females, aged 7.3 to 23.7 years, were measured for the mesiodistal and buccolingual crown diameters. Crown size variability, correlations, sexual dimorphism, and summary measurements are presented. All means for mesiodistal and buccolingual dimensions in males exceeded those in females, with 18 of the 28 comparisons were statistically significant (ranged from $P<0.05$ to $P<0.001$, ttest). With the exception of maxillary central and lateral incisors and mandibular first molars, all other teeth exhibited greater bucco-lingual diameters then mesiodistally. No specific pattern of percentages of sexual dimorphism was noted between the mesiodistal and buccolingual diameters. Comparison of the mesiodistal crown diameters in thalassemic subjects with unaffected control group showed that thalassemic males and females have significantly smaller dimensions than their controls, with 9 of the 24 comparisons being highly significant.

INTRODUCTION

Tooth crown size in human populations has been the subject of numerous studies because of its application in anthropological and forensic investigations, as well as in clinical dentistry. In addition, crown size provide a significant information on the genetic relation between populations and environmental adaptation (Garn et al., 1967; Margette and Brown, 1978; Haeussler et al., 1989).

Thalassemia is a group of inherited defects in the synthesis of either the alpha or beta polypeptide chains of hemoglobin, referred to as alpha and beta thalassemia, respectively. The beta thalassemia results from a wide variety of genetic defects and produce diverse clinical and hematological findings. Based on genotype, thalassemias are classified as homozygous, heterozygous, or compound heterozygous (Weatherall and Clegg, 1981). The heterozygous form of the disease (thalassemia minor) is mild,with minimal clinical expression. The homozygous form of beta thalassemia (also known as thalassemia major, Cooley's anemia, or Mediterranean anemia) exhibits severe clinical symptoms with marked orofacial malformation. Patients with severe beta thalassemia are usually diagnosed between 6 months and 2 years of age. Probands with untreated thalassemia major die in early childhood from the complication of anemia. With multiple transfusions, life is prolonged to age 15-25 years and growth and well-being are improved (Flynn et al., 1978). Growth retardation occurs invariably in the thalassemia major, particularly after the age of 7 (Lapatsanis et al., 1978).

The suggested causes of growth retardation and delay of bone maturation include chronic anemia (Caffey, 1957), hypoparathyroidism (Flynn et al., 1976), and somatomedin deficiency, a factor that is produced by the liver and stimulates cartilage growth (Saenger et al., 1980). Beta-thalassemia major occurs characteristically among populations bordering on the Mediterranean (*thalas* [Gr.]= the sea). The prevalence of thalassemia is as high as 15-20% in Greece, Turkey, Cyprus, and Southern Italy.

The condition is also prevalent in the Middle East and Far East (Weatherall and Clegg, 1981). In Jordan, approximately 1000 transfusion-dependent thalassemia major patients are registered (1:4600 of the total population) with annual increase of 80 cases and a carrier rate of 7-10% of the population. One-third of the country thalassemic subjects reside in Irbid, the largest city after the capital Amman with estimated population of 835,360 in year 1997.

Collectively thalassemias are among the commonest genetic disorders to cause a major public health problem in many populations. Surprisingly, detailed odontometric data of thalassemia are not available in the literature. The aim of the present study was to determine the tooth crown size of permanent dentition in subjects with thalassemia major and to compare the results with data of healthy Jordanian group (control).

MATERIALS AND METHODS

The sample comprised 46 subjects with beta-thalassemia major, 25 males and 21 females aged 7.3 to 23.7 years, with the mean age (±standard deviation) of 11.2±3.9 years. They were born of Jordanian parents and grew up in Irbid city, Jordan. Family history revealed that 72% of the probands were the product of first-cousin marriage, 13% of second-degree cousins, and only 15% of the parents without a history of consanguinity. The average heights and weights of the sample were within the third and tenth percentile, respectively, on the standard chart for the country population. Teeth were selected for measurements only if they were fully erupted, not noticeably effected by attrition or caries, had not been restored and did not display abnormal crown morphology.

Alginate impressions were taken in suitable perforated trays for the upper and lower dental arches of every patient. Impressions were cast in dental stone immediately to obviate problems with distortion of the casts. The mesiodistal and buccolingual crown diameters were registered for each maxillary and mandibular permanent tooth from the second molar on one side to the corresponding tooth on the contralateral side. The mesiodistal crown diameter of a tooth was obtained by measuring the greatest distance between the approximal surfaces of the crown using an electronic sliding caliper inserted from the buccal or labial aspect and held parallel to the occlusal and vestibular surfaces of the crown. The buccolingual crown diameter was taken as the greatest distance between the labial or buccal surface and the lingual surface of the tooth crown in a plane perpendicular to the mesiodistal crown diameter of the tooth. If a tooth was rotated or malpositioned in relation to the curvature of the dental arch, the mesiodistal measurements was taken between to points of the approximate surfaces of the crown where the observer considered that contact with adjacent teeth would normally occur. Intra- and inter-observers errors were 1.2% and 2.1% of the mean, respectively (Hattab et al., 1999a).

Descriptive statistics including the mean of the mesiodistal and the buccolingual crown size, standard deviation, standard error of the mean, and coefficient of variation (coefficient of variation as 100 times the standard deviation divided by the mean) were computed for each individual tooth. The data for males and females were analyzed separately and in combination when appropriate. Pearson's correlation coefficient (r) was used to express the degree of association among pairs of antimeric teeth. The differences between sets of data of antimeres were evaluated by analysis of variance (ANOVA). The Student's t-test for independent sample was performed for comparison of mean values between males and females. Sexual dimorphism in tooth size was quantified by expressing the percent to which the crown diameters of males exceeded those of females for each individual tooth: 100 (male mean divided by the female mean minus 1). Three derived summary measures, representing one side of the upper and lower dental arches were included: summations of 1) the 14 mesiodistal crown diameters; 2) the 14 buccolingual crown diameters; and 3) the products of mesiodistal times buccolingual dimensions of each tooth, known as crown area, summary tooth size, or robustness value and expressed in mm^2. Hereafter, we refer to the mesiodistal and buccolingual measurements of a tooth as crown diameters or size.

RESULTS

The mean mesiodistal diameters and percentage sexual dimorphism are shown in Table 1. The data for the buccolingual dimensions and percentage sexual dimorphism are presented in Table 2. With the exception of maxillary central and lateral incisors and mandibular first molars, all other teeth exhibited greater buccolingual diameters than mesiodistal. Statistical analysis using ANOVA revealed no significant differences in the mean mesiodistal and buccolingual diameters of the antimeres for both sexes. The degree of symmetry between pairs of antimeric teeth, used coefficient of correlation, showed that the r values for the mesiodistal diameters ranged from 0.61 to 0.80 and for the buccolingual from 0.60 to 0.86 (sexes pooled). The pattern and magnitude of the coefficient correlations varied at random between mesiodistal and buccolingual measurements. There was little evidence to indicate any trend towards sex differences in crown size variability. Mean variability coefficients for males were 5.9% in mesiodistal and 6.5% in buccolingual measurements. The corresponding values for females were 6.2% and 6.4%, respectively.

All means for crown size in males exceeded those in females (Tables 1 and 2). In 18 of the 28 comparisons (right and left sides pooled) the differences were statistically significant ranged from $P<0.05$ to $P<0.001$. In absolute terms, males had larger crown size than females with differences ranging between 0.12 mm and 0.54 mm; weighted average 0.31 mm. Ranking of sexual dimorphism percentages in crown size according to the morphological classes revealed the following order: canines (5.4%) > molars (4.6%) > incisors (3.3%) > premolars (2.5%). The total average of sexual dimorphism percentage was 3.7% for the mesiodistal and 3.8% for the buccolingual dimensions with no specific pattern of the percentages of sexual dimorphism between mesiodistal and buccolingual dimensions (Tables 1 and 2).

The three summary measures of size of the dentition, the summary of the mesiodistal, summary of the buccolingual, summary of the mesiodistal times the buccolingual diameters, are valuable data for groups of comparisons. The cumulative mesiodistal diameters of the 14 teeth (from the second molar to its antimere) in each arch was calculated. In males, the cumulative mesiodistal diameters of the maxillary and mandibular teeth were 112.5 and 105.1 mm, respectively. The corresponding mesiodistal diameters in females were 108.2 mm. and 101.2 mm. The cumulative buccolingual diameters of the maxillary and mandibular teeth in males were 120.9 mm. and 110.3 mm, respectively. The corresponding dimensions in females were 116.3 mm. and 105.7 mm. The total crown area of one side of the arch in males was 493.62 mm^2 for the maxilla and 431.64 mm^2 for mandible. The corresponding values in females were 454.46 mm^2 and 399.93 mm^2, respectively.

DISCUSSION

Studies have indicated that the final tooth morphology reflects interplay between the timing and rate of cellular proliferation in the developing tooth germ, together with the time of onset and spread of mineralization (Kraus and Jordan, 1965). Alvesalo (1971) analyzed male and female cousin groups, as well as siblings, and found evidence that both X and Y chromosomes carried genes that may effect sooth size. It has been proposed that growth retardation due to a general reduction in cellular mitotic activity affects dental development in Down syndrome (trisomy 21), leading to a reduction in size and an alteration in crown shape (Brown and Townsend, 1983; Townsend, 1983). The permanent teeth attain their definitive crown dimensions after birth and enamel completed by age of 4 to 8 years except the third molar. Evidence indicates that a variety of definable factors operating well before birth may effect crown dimensions ofboth deciduous and permanent teeth in both sexes (Garn et al., 1979).

Patients with beta-thalassemia major become symptomatic after birth. The condition is life threatening, characterized by a severe anemia, hepatosplenomegaly, growth retardation, endocrine dysfunction and skeletal changes due to hypertrophy and expansion of the hematopoietic marrow. The gross bone-marrow expansion consequent on severe ineffective erythropoiesis leads to most of the clinical features of the disease, through its effect on the bones and growth (Model, 1976). The best-known oral manifestations of the condition are the enlargement of the maxilla, frontal bones and zygomata due to bony expansion with depression of the bridge of the nose(knownas chipmunk faces), flaring and spacing of the maxillary anterior teeth (Kaplan et al., 1964; Van Dis and Langlais, 1986; Hes et al., 1990). Radiological changes include large bone marrow spaces, coarse trabeculae and osteoporosis in both jaws; thin lamina aura and crypts of teeth; short teeth roots (Poyton and Davey, 1968). Our cephalometric analysis revealed that the maxillary and mandibular lengths in thalassemic children were significantly less than in disease-free controls. Thalassemic subjects are at risk to caries and periodontal disease (Siamopoulou-Mavridou et al., 1992; Hattab et al., 2000). They exhibit yellowish dental discoloration as a result of bilirubin, a degraded product of hemoglobin, deposition during the formation of dental hard tissues (Hattab et al., 1999b).

Our results showed that males exhibit consistently larger crown size (mesiodistal and buccolingual diameters) than those of females, the largest differences being found in the canines ($P<0.001$ in three out of four comparisons, t-test). Numerous studies on normal population groups have confirmed such a trend for the mesiodistal dimensions, with evidence indicates that the magnitude and patterning of sexual dimorphism varies between populations (Garb et al., 1967; Perzigian, 1977; Kieser, 1990; Hattab et al., 1996).

The present findings were compared with apparently healthy controls comprised of 198 individuals (mean age of the male was 15 ± 2.6 years and females 15 ± 2.2 years), who were born of Jordanian parents and grew up in Jordan (Hattab et al., 1996). Comparison showed that the total average of mesiodistal diameters in thalassemic subjects (sexes pooled) was 4.0% (0.31 mm) less than healthy controls (Table 3). All means for mesiodistal diameters of thalassemic males and females were significantly smeller then their controls, with nine of the 24 comparisons being statistically significant at a level of $P< 0.001$.

Apparently, a variety of environmental factors including severe chronic agenda, endocrine dysfunction and somatomedin deficiency, affect crown dimensions in thalassemia as a part of their general effect on growth retardation. Strong evidence point to crown dimensions being genetically determined by factors acting during odontogenesis (Garn et al, 1967; Townsend and Brown, 1978; Dempsey et al, 1995). One may conclude that tooth size in thalassemia reflects a complex interaction between a variety of genetic and environmental factors, yet the relative contribution of these factors need to be determined.

In summary, the present study showed that crown size (mesiodistal and buccolingual diameters) of thalassemic males and females were significantly smaller than those of unaffected controls. A variety of genetic and environmental factors seem to underlie the reduced crown size in thalassemia.

TABLE 1. Mesiodistal crown diameters (in mm) and sexual dimorphism (%) of the permanent teeth in thalassemia (right- and left-side measurements pooled).

	Males					Females						
Tooth	N	Mean	SD	SEM	CV	N	Mean	SD	SEM	CV	Diff.	P-value	Di
Maxilla													
I^1	40	8.72	0.40	0.063	4.6	31	8.41	0.51	0.092	6.1	0.31	<0.01	3.1
I^2	38	6.69	0.38	0.062	5.8	29	6.42	0.47	0.087	7.3	0.27	<0.05	4.2
C	22	7.72	0.36	0.077	4.7	19	7.37	0.31	0.071	4.2	0.33	<0.001	4.5
P^1	33	6.89	0.45	0.078	6.5	30	6.75	0.49	0.089	7.3	0.14	NS	2.1
P^2	26	6.47	0.38	0.075	5.9	27	6.31	0.50	0.096	7.9	0.16	NS	2.5
M^1	50	10.34	0.52	0.073	5.1	38	9.86	0.53	0.086	5.4	0.48	<0.001	3.7
M^2	13	9.43	0.44	0.122	4.7	15	8.96	0.58	0.150	6.5	0.47	<0.05	5.2
Mandible													
I_1	37	5.45	0.34	0.056	6.2	30	5.35	0.37	0.068	6.9	0.20	<0.05	2.3
I_2	33	6.01	0.43	0.075	7.1	27	5.74	0.46	0.088	8.0	0.27	<0.05	4.7
C	24	6.86	0.30	0.059	4.4	22	6.44	0.31	0.066	4.8	0.42	<0.001	6.5
P_1	24	6.77	0.46	0.093	6.8	25	6.61	0.37	0.084	5.6	0.16	NS	2.9
P_2	19	6.92	0.44	0.101	6.4	19	6.80	0.42	0.096	6.2	0.12	NS	1.8
M_1	41	11.09	0.48	0.075	4.3	31	10.64	0.48	0.086	4.5	0.45	<0.01	4.2
M_2	12	9.46	0.62	0.179	6.6	13	9.13	0.51	0.141	5.6	0.33	NS	3.6

N= number of teeth measured. Mean = mean of mesiodistal diameters. SD = standard deviation. SEM = standard error of the mean. CV = coefficient of variation (%). Percentage sexual dimorphism = 100(male mean/female mean minus 1). Di= Dimorphism.

TABLE 2. Buccolingual crown width diameters and sexual dimorphism of the permanent teeth in thalassemia (right- and left-side measurements pooled).

	Males					Females						
Tooth	N	Mean	SD	SEM	CV	N	Mean	SD	SEM	CV	Diff	P-value	Di
Maxilla													
I^1	38	7.23	0.45	0.073	6.2	30	6.89	0.41	0.075	6.0	0.34	<0.01	4.9
I^2	34	6.22	0.53	0.091	8.5	29	6.07	0.50	0.093	8.2	0.15	NS	2.5
C	20	8.11	0.44	0.098	5.4	17	7.61	0.46	0.117	6.3	0.50	<0.001	6.7
P^1	32	8.82	0.57	0.101	6.5	29	8.55	0.44	0.082	5.1	0.27	NS	3.2
P^2	25	8.90	0.61	0.122	6.9	27	8.71	0.53	0.102	6.1	0.19	NS	2.2
M^1	50	10.96	0.68	0.096	6.2	41	10.42	0.55	0.086	5.3	0.54	0.001	5.2
M^2	13	10.22	0.75	0.208	7.3	15	9.71	0.74	0.191	7.6	0.51	<0.05	5.3
Mandible													
I_1	35	5.98	0.37	0.062	6.2	28	5.66	0.39	0.074	6.8	0.32	<0.01	2.7
I_2	31	6.23	0.49	0.088	7.9	27	6.09	0.45	0.087	7.4	0.14	NS	2.3
C	23	7.05	0.41	0084	5.8	21	6.76	0.39	0.085	5.7	0.29	<0.05	3.8
P_1	22	7.74	0.39	0.083	5.0	23	7.41	0.43	0.090	5.8	0.33	<0.05	3.3
P_2	19	8.04	0.55	0.126	6.8	18	7.88	0.44	0.103	5.6	0.16	NS	2.0
M_1	41	10.47	0.55	0.086	5.3	31	10.02	0.58	0.104	5.8	0.45	<0.01	4.5
M_2	12	9.65	0.39	0.113	4.0	14	9.17	0.52	0.139	5.7	0.48	<0.05	5.2

Abbreviations same as those in Table 1

TABLE 3. Mesiodistal crown diameters (in mm) and sexual dimorphism (%) of the permanent teeth in thalassemia subjects compared to healthy control group (right- and left-side measurements and sexes pooled)).

	Thalassemia			Control		
Tooth	N	Mean	CV	N	Mean	CV
Maxilla						
I^1	40	8.72	4.6	31	8.41	0.51
I^2	38	6.69	5.8	29	6.42	0.47
C	22	7.72	4.7	19	7.37	0.31
P^1	33	6.89	6.5	30	6.75	0.49
P^2	26	6.47	5.9	27	6.31	0.50
M^1	50	10.34	5.1	38	9.86	0.53
M^2	13	9.43	4.7	15	8.96	0.58
Mandible						
I_1	37	5.45	6.2	30	5.35	0.37
I_2	33	6.01	7.1	27	5.74	0.46
C	24	6.86	4.4	22	6.44	0.31
P_1	24	6.77	6.8	25	6.61	0.37
P_2	19	6.92	6.4	19	6.80	0.42
M_1	41	11.09	4.3	31	10.64	0.48
M_2	12	9.46	6.6	13	9.13	0.51

Source of Control: Hattab et al, 1996
Abbreviations same as those in Table 1.

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