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ASSESSMENT OF CEPHALOMETRIC FEATURES, DENTAL ARCH DIMENSIONS, DENTAL AGE IN A GROUP OF PATIENTS WITH THALASSEMIA MAJOR

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ABSTRACT:

Introduction: *Thalassemia is one of the most common worldwide genetic disorders in which there are overgrowth of the skull, rodent face, protrusion and spacing of maxillary anterior teeth, open bite, progressive reduction of bone mass, retardation in general skeletal growth and teeth development are there (exists). Quantitative assessments of the skeletal morphology of patients with thalassemia major are rare therefore, the purpose of this study was to evaluate cephalometric skeletal and dental features, dental arch dimensions and teeth development in relation to bone mineral density and vitamin D in a group of Egyptian patients with thalassemia major relative to healthy control age and gender matched.* ***Patients and Methods:*** *This study was carried on 94 thalassemia patients (46 male and 48 female) compared with 120 subjects (age and gender matched healthy control 60 male and 60 female). Age ranged from 6 to 12 year. For each patient some cephalometric skeletal and dental measurements, dental arch dimensions, vitamin D, DXA scan to measure bone mineral density and dental age was done.* ***Results:*** *All thalassemic patients had a significant hyper-divergent growth pattern leading to steep mandibular plane, increased anterior facial height and decreased posterior facial height, Short mandibular body, short ramus length,*

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shorter arch width and shorter arch circumference when compared with healthy control, Class II malocclusion with an average ANB angle of 7.5 degree. The retardation of dental development in thalassemic male and female equal to (1.011 and 0.791 year) respectively. Thalassemic male showed significant negative correlation between (CA-DA) and BMD. ***Conclusions:*** *In all thalassemic patient skeletal Class II dental base relation, shorter dental arch dimensions significant retardation in dental age, very low level of vitamin D and reduced bone mineral density had found.*

Key Words: *thalassemia, cephalometric, dental age, DXA scan and BMD.*

INTRODUCTION

Thalassemia refers to a group of hemolytic anemia disorders that involve defects in the synthesis of hemoglobin α- or β-polypeptide chains (α- and β-thalassemia, respectively). It leads to decreased hemoglobin production and hypochromic microcytic anemia associated with erythrocyte dysplasia and destruction. Thalassemia is one of the most common genetic disorders worldwide and presents major public health and social challenges in areas of high incidence. About 3% of the world's population carries the thalassemia gene. Growth disturbances are a major clinical feature of untreated patients with thalassemia. [(1)] As thalassemic patients approach the age of puberty, many develop growth retardation and pubertal failure. [(2,3)]

Caffey and Baker described the appearance of these thalassemic patients as rodent face.[(4,5)] Dentition shows protrusion, flaring and spacing maxillary anterior teeth, open bite and other type of malocclusion Many authors found posterior rotation of the mandible and he found posterior (clock wise) mandibular rotation in the thalassemic children.[(6- 8)]

Dentition development is an integral aspect of craniofacial growth, even though it is only marginally related to other maturation processes and is less susceptible to environmental influences[(9)]. Dental maturity,

expressed as dental age (DA), is a method for estimating age. In both pediatric dentistry and orthodontics, child's growth and development status are especially important in diagnosis and treatment. In addition, assessment of dental development is one of the most reliable indicators of chronologic age (CA) and the most widely used in forensic and legal dentistry. Several methods of estimating dental maturity measure the degree of calcification in radiographs of permanent teeth. The most widely used method was developed by Demirjian et al.[10], based on observation of the seven left mandibular teeth in children of French-Canadian descent and has been subsequently used in a number of different populations.

Vitamin D deficiency (Deficiency is defined as a serum 25-hydroxyvitamin D level of less than 20 ng per mL, and insufficiency is defined as a serum 25-hydroxyvitamin D level of 20 to 30 ng per mL (50 to 75 nmol per L) causes bone to demineralize. In children, bones soften over time and become deformed, leading to growth retardation, enlargement of the epiphyses of the long bones, and leg deformities.[11] many studies reported that Vitamin D plays an important role in skeletal development, bone health maintenance[12]

Several sensitive techniques are now available for quantity assessment of the degree of osteoporosis and total bone mass. Bone density measurement by dual X-ray absorptiometry (DXA) of the lumbar spine, femoral neck, and forearm is recommended as one of the most reliable and non-invasive techniques.[13,14] Dual energy X-ray absorptiometry (DXA) is the most widely available method of measuring bone densitometry (X-rays are used, but the radiation dose is less than during a chest X-ray) and can be applied in different skeletal sites, though the lower spine and total body are mainly studied to evaluate respectively cancellous and cortical bone. Routinely DXA is frequently used for assessing BMD in pediatrics and many Authors have carried out BMD normality curves for the pediatric age[15,16].

Quantitative assessments of the skeletal morphology of patients with thalassemia major are rare[6,17]. Therefore, the purpose of this study was to identify the changes of cephalometric, dental arch and dental age in relation to bone mineral density and blood level of vitamin D in patients with β-thalassemia major and compare them with age and sex matched healthy controls of a group of Egyptian children with beta-thalassemia major.

PATIENTS AND METHODS

The present study was carried out in the Department of hematology in hospital of the faculty of medicine, Tanta University. Patients were regularly attending the Out Patient Department or blood bank for repeated blood transfusion. A written consent was taken from each patient that they agree to participate in this study.

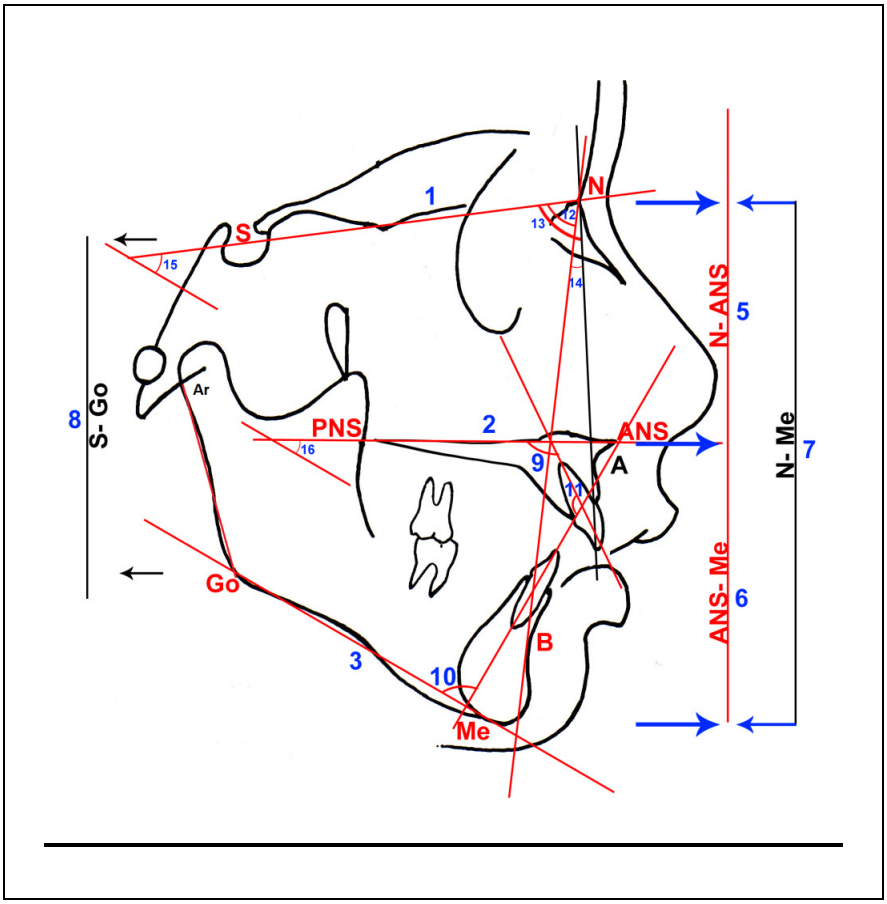
A sample of 94 thalassemic patient (46 male and 48 female) was compared with 120 healthy control group (60 male and 60 female) matched for age and sex. According to the following criteria:

- ❖ The age of all patients ranging from 6 to 12 year.
- ❖ All patients suffering from thalassemia major disease.
- ❖ Absence of any associated systemic disease.
- ❖ All patients did not have any previous orthodontic treatment.

For each patient the following was done:

- *panoramic x ray film.*
- *Lateral cephalometric x ray film.*
- *Study upper and lower models.*
- *laboratory test to measure the blood level of vitamin D.*
- *DXA scan to measure the bone mineral density.*

Cephalometric measurements : (figure 1)



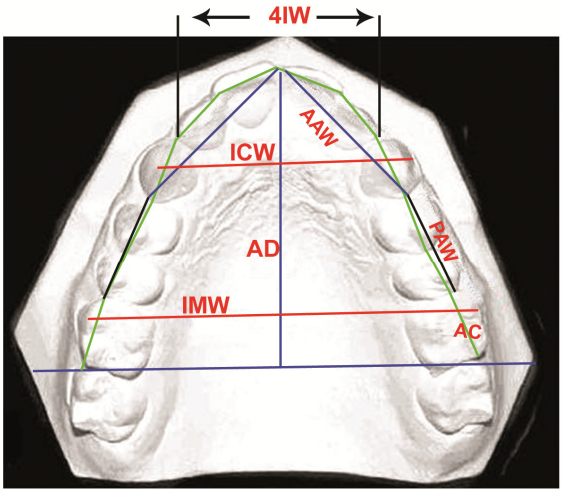
Cephalometric linear measurements:

Anterior cranial base (S-N), ANS-PNS, GO-Me, Ar-Go, N-ANS, ANS-Me, N-Me, S-Go, N-ANS/ANS-Me, S-Go/N-Me, U1- NA mm, Overjet.

Cephalometric angular measurements :

U1-NA DEGREE, U1 to PP, L1 to MP, Inter-incisal angle, SNA, SNB, ANB, SN-Mp, PP/MP.

Dental model measurements: (figure 2)



- Arch depth (AD): distance from the line connecting the distal surface of the first molars to the midpoint between the central incisors.
- Segmented arch length (AAW-PAW): anterior segment: distance between the mesial contact point of the central incisor and the distal contact point of the canine plus the posterior segment: distance between the distal contact point of the canine and the distal contact of the second premolar.
- Mesiodistal width of four incisors(4IW): distance between the distal contact point of the lateral incisor on one side to the distal contact point of the contra-lateral tooth.
- Inter-canine width (ICW): distance between the cusp tip of the canine on one side to the cusp tip of the contra-lateral canine.
- Inter-molar width (IMW): distance between the mesiobuccal cusp tip of the first molar on one side to the mesiobuccal cusp tip of the contra-lateral first molar.

- Arch circumference (AC): a line from the distal aspect of the first molar passing around the arch on the contact points and incisal edges to the distal aspect of the contra-lateral first molar.

For each subject from panoramic x ray the seven left mandibular teeth from the central incisor to the second molar were rated on eight stages scale using the method described by Demerjian et al[10]. The stage of each tooth was converted to the corresponding numerical value and then all values was added to obtain a maturity score which corresponded to a dental age. Dental and chronological ages were compared in both male and female in thalassemia and healthy control group and related it to blood level of vitamin D and bone mineral density obtained by DXA scan. BMD was measured by DXA scan using Z sore matched reference group Standard Deviation Measurement of BMD in grams/centimeter (g/cm2).[18-20]

All data (linear and angular cephalometric measurements, dental arch measurements, dental age, chronological age, Blood level of vitamin D, bone mineral density and gender difference in both thalassemia and healthy control groups) were compared using statistical package for the social science (SPSS V.16) with $p<0.05$ considered significant and $p<0.001$considered highly significant.

RESULTS

The following results were obtained:

Cephalometric findings

The mean linear distance of the mandibular body length, ramus length, upper anterior facial heights and posterior facial height had found to be shorter in thalassemia than healthy control matched in age and sex by 7 mm, 4 mm, 5 mm and 5 mm respectively. These differences were statistically significant ($P < 0.001$). Statistically significant difference ($P < 0.001$) regarding the mean linear distance of the lower anterior facial height, total anterior facial height overjet and U1 to NA mm which had found to be larger in thalassemia than healthy control by 4mm , 9 mm , 3.7 mm and 3.3 mm respectively.

SNA exhibited no significant difference between both groups while SNB in thalassemia group showed highly significant difference than healthy control group as it decreased by (3.1 degree). A statistically High significant difference was found between both groups regarding the following angular measurements which exhibited greater values in thalassemia than healthy control matched in age and sex: upper incisors to palatal plane (5 degree), lower incisor to mandibular plane (13 degree), ANB (4.1 degree), SN-Mp (9.7 degree), Ar-Go-Me (5 degree) and PP-Mp (11 degree).

Dental model findings

The segmental arch lengths (the sum of the anterior and posterior arch lengths) in the maxilla and mandible of the thalassemic group were reduced by an average of 2.23 and 2.21 mm, respectively, compared with the control group. The arch depths of the maxilla and mandible in thalassemic group were shorter than the controls by 2.99 and 3.1 mm, respectively. These differences were statistically significant ($P < 0.001$).

The width of four incisors in the thalassemic group was 1.2 mm shorter in the maxilla and 2.3 mm shorter in the mandible compared with the control group. These differences between the two groups were statistically significant ($P < 0.001$). The inter-canine and inter-molar widths in thalassemia were shorter than control group by 2.8 mm and 2.2 mm for upper arch and by 0.9 mm and 1.2 mm for lower arch respectively. These differences were statistically significant ($P < 0.001$) and ($p<0.05$) for upper and lower arch respectively.

Dental age findings

The difference between CA and DA shows highly significant difference in both male and female thalassemia groups. A highly significant difference in DA was found in both male and female groups. When comparing the difference between CA and DA in thalassemia and control group, a highly significant difference was found in both male and female groups with greater retardation of dental development in thalassemic male group 1.011 year than thalassemic female group 0.791 year. Male thalassemia group showed significant negative correlation between (CA-DA) and BMD.

Table (1): linear and angular cephalometric measurements for thalassemia and healthy Control.

Cephalometric linear measurements	Thlassemia		Healthy control		t	p
	mean± SD		mean± SD			
anterior cranial base (S-N_mm)	68	1.2	68.3	1.4	1.658	0.099
ANS-PNS	52	1.65	50.9	1.97	4.353	0.001**
Go-Me	69	2.1	76	3.5	17.123	0.001**
Ar-G0	42	3.2	46	3.6	8.469	0.001**
N-ANS	47	2.9	52	2.47	13.609	0.001**
ANS-Me	72	2.98	68	2.4	10.879	0.001**
N-Me	129	3.2	120	3.5	62.449	0.001**
S-Go	70	2.9	75	3.1	12.043	0.001**
N-ANS/ANS-Me	0.65	0.97	0.76	0.61	1.012	0.312
S-Go/N-Me	0.47	0.91	0.62	0.88	1.223	0.224
U1-NA mm	6.8	3.7	3.5	3.4	6.778	0.001**
overjet	6.9	3.1	3.2	3.5	8.069	0.001**
Cephalometric angular measurements						
U1-NA degree	15.6	2.1	15.4	2.7	0.594	0.555
U 1to PP	32	3.6	27	2.9	11.253	0.001**
L1 to Mp	106	4.2	93	3.1	26.039	0.001**
inter-incisor angle	118	2.5	123	2.8	13.579	0.001**
SNA	80	1.4	80	1.67	0.001	0.999
SNB	73.5	2.8	76.6	2.77	8.089	0.001**
ANB	7.5	2.6	3.4	1.5	14.477	0.001**
SN-Mp	47	2.9	37.3	1.6	31.103	0.001**
Ar-Go-Me	134	1.88	129	2.1	18.362	0.001**
PP/Mp	38	2.74	27	1.56	37.001	0.001**

P. value < 0.001** (highly significant)

Table (2): Comparison of dental arch dimensions in thalassemia and healthy control.

Upper dental arch measurements	Thlassemia		Healthy control		t	p
	mean	SD	mean	SD		
arch depth	37.9	3.1	40.89	2.4	7.948	0.001**
segmented arch length	35.7	2.8	37.95	1.68	7.219	0.001**
width of four incisors	26.8	2.1	28	2.4	3.834	0.001**
inter-canine width	32	3.6	34.8	3.2	5.469	0.001**
inter-molar width	48.8	2.76	51	3.8	4.723	0.001**
arch circumference	94.6	2.3	98.2	1.98	12.286	0.001**
Lower dental arch measurements						
arch depth	32.7	1.6	35.8	3.4	8.159	0.001**
segmented arch length	29.69	2.5	31.9	2.9	5.869	0.001**
width of four incisors	20.11	2.1	22.3	1.8	8.826	0.001**
inter-canine width	25.9	2.7	26.8	3.1	2.227	0.027*
inter-molar width	44.7	2.5	45.9	3.4	2.872	0.005*
arch circumference	85.9	2.3	89.97	2.6	11.947	0.001**

P. value < 0.05* (significant) P. value < 0.001**(highly significant)

Table (3): Comparison between chronological age and dental age for both male and female thalassemia group.

		N	CA		DA		t	p
			Mean	SD	Mean	SD		
Male thlassemia	6-6.99	7	6.431	0.264	5.374	0.385	5.418	0.001**
	7-7.99	9	7.375	0.237	6.212	0.338	7.734	0.001**
	8-8.99	8	8.446	0.252	7.362	0.279	7.403	0.001**
	9-9.99	8	9.367	0.285	8.310	0.281	7.469	0.001**
	10-10.99	7	10.414	0.272	9.422	0.258	7.004	0.001**
	11-11.99	7	11.531	0.269	10.513	0.201	8.017	0.001**
	Total	46	8.927	0.263	7.916	0.290	17.512	0.001**
Female thlassemia	6-6.99	8	6.322	0.216	5.500	0.284	6.359	0.001**
	7-7.99	7	7.461	0.280	6.639	0.263	5.657	0.001**
	8-8.99	9	8.413	0.221	7.796	0.278	7.718	0.001**
	9-9.99	8	9.502	0.361	8.706	0.262	5.352	0.001**
	10-10.99	7	10.498	0.251	9.688	0.312	5.348	0.001**
	11-11.99	9	11.477	0.298	10.598	0.321	6.021	0.001**
	Total	48	8.946	0.271	8.155	0.287	13.876	0.001**

P. value ≤ 0.001** (highly significant)

Table (4): Comparison between chronological age and dental age for both male and female healthy control group.

		N	CA		DA		t	p
			Mean	SD	Mean	SD		
Male control	6-6.99	10	6.406	0.236	6.521	0.247	1.058	0.301
	7-7.99	10	7.435	0.269	7.678	0.265	2.038	0.056
	8-8.99	10	8.387	0.248	8.512	0.292	1.032	0.316
	9-9.99	10	9.402	0.387	9.649	0.374	1.453	0.164
	10-10.99	10	10.523	0.288	10.730	0.311	1.542	0.139
	11-11.99	10	11.388	0.238	11.598	0.258	1.894	0.075
	Total	60	8.924	0.278	9.115	0.291	3.684	0.001**
Female Control	6-6.99	8	6.600	0.288	6.970	0.376	2.213	0.044*
	7-7.99	11	7.401	0.279	7.789	0.301	3.139	0.005*
	8-8.99	9	8.511	0.258	8.877	0.275	2.913	0.010*
	9-9.99	10	9.435	0.281	9.795	0.297	2.782	0.012*
	10-10.99	12	10.453	0.265	10.801	0.270	3.187	0.004*
	11-11.99	10	11.584	0.291	11.889	0.246	2.534	0.021*
	Total	60	8.997	0.277	9.354	0.294	6.849	0.001**

P. value ≤ 0.05* (significant) P. value ≤ 0.001** (highly significant)

Table (5): Comparison of dental age between thalassemia and healthy control for both male and female.

	AGE	N	Thlassemia DA		N	Control DA		t	p
			Mean	SD		Mean	SD		
Male	6-6.99	7	5.474	0.385	10	6.521	0.247	6.213	0.001**
	7-7.99	9	6.312	0.338	10	7.678	0.265	8.048	0.001**
	8-8.99	8	7.462	0.279	10	8.512	0.292	7.442	0.001**
	9-9.99	8	8.310	0.281	10	9.649	0.374	6.842	0.001**
	10-10.99	7	9.422	0.258	10	10.730	0.311	7.943	0.001**
	11-11.99	7	10.513	0.201	10	11.598	0.258	7.928	0.001**
	Total	46	7.916	0.290	60	9.115	0.291	18.193	0.001**
Female	6-6.99	8	5.500	0.284	8	6.970	0.376	8.192	0.001**
	7-7.99	7	6.639	0.263	11	7.789	0.301	5.771	0.001**
	8-8.99	9	7.796	0.278	9	8.877	0.275	5.659	0.001**
	9-9.99	8	8.706	0.262	10	9.795	0.297	5.628	0.001**
	10-10.99	7	9.688	0.312	12	10.801	0.270	5.693	0.001**
	11-11.99	9	10.598	0.321	10	11.889	0.246	7.017	0.001**
	Total	48	8.155	0.287	60	9.354	0.294	15.453	0.001**

P. value ≤ 0.001** (highly significant)

Table (6): Comparison of thalassemia and healthy control group regarding the difference between chronological age and dental age in both male and female

	AGE	N	Thlassemia(CA-DA)		N	Control (CA-DA)		t	p
			Mean	SD		Mean	SD		
Male	6-6.99	7	0.957	0.357	10	0.115	0.110	7.082	0.001**
	7-7.99	9	1.063	0.456	10	0.243	0.114	5.513	0.001**
	8-8.99	8	0.984	0.354	10	0.125	0.098	7.382	0.001**
	9-9.99	8	1.057	0.274	10	0.247	0.109	8.587	0.001**
	10-10.99	7	0.992	0.417	10	0.207	0.097	5.809	0.001**
	11-11.99	7	1.018	0.328	10	0.21	0.087	7.523	0.001**
	Total	46	1.011	0.441	60	0.191	0.795	6.294	0.001**
Female	6-6.99	8	0.822	0.124	8	0.37	0.125	7.263	0.001**
	7-7.99	7	0.822	0.153	11	0.388	0.174	5.387	0.001**
	8-8.99	9	0.617	0.114	9	0.366	0.154	3.393	0.002**
	9-9.99	8	0.796	0.214	10	0.36	0.165	4.894	0.001**
	10-10.99	7	0.81	0.225	12	0.348	0.108	6.089	0.001**
	11-11.99	9	0.879	0.198	10	0.305	0.112	7.889	0.001**
	Total	48	0.791	0.146	60	0.357	0.135	16.013	0.001**

P. value ≤ 0.001** (highly significant)

Table (7): Comparison of male and female regarding the difference between chronological age and dental age in thalassemia and healthy control group.

	AGE	N	male (CA-DA)		N	female (CA-DA)		t	p
			Mean	SD		Mean	SD		
Thlassemia	6-6.99	7	0.957	0.357	8	0.822	0.124	1.013	0.332
	7-7.99	9	1.063	0.456	7	0.822	0.153	1.334	0.204
	8-8.99	8	0.984	0.354	9	0.617	0.114	2.952	0.001**
	9-9.99	8	1.057	0.274	8	0.796	0.214	2.123	0.052
	10-10.99	7	0.992	0.417	7	0.81	0.225	1.019	0.329
	11-11.99	7	1.018	0.328	9	0.879	0.198	1.053	0.309
	Total	46	1.011	0.441	48	0.791	0.146	3.269	0.001**
Control	6-6.99	10	0.115	0.110	8	0.37	0.125	4.603	0.001**
	7-7.99	10	0.243	0.114	11	0.388	0.174	2.229	0.038*
	8-8.99	10	0.125	0.098	9	0.366	0.154	3.974	0.001**
	9-9.99	10	0.247	0.109	10	0.36	0.165	1.809	0.087
	10-10.99	10	0.207	0.097	12	0.348	0.108	3.192	0.005
	11-11.99	10	0.21	0.087	10	0.305	0.112	2.119	0.048*
	Total	60	0.191	0.795	60	0.357	0.135	1.593	0.113

P. value ≤ 0.05* (significant) P. value ≤ 0.001** (highly significant)

Table(8): Correlation between blood level of vitamin D and the difference between chronological and dental age in thalassemia and healthy control group for both male and female.

CA – DA / Blood level of Vit. D	Thalassemia CA – DA				Control CA – DA			
	Male		Female		Male		Female	
	r	p	r	p	r	p	r	p
	- 0.182	0.221	- 0.176	0.227	- 0.213	0.064	- 0.118	0.365

Table(9): Correlation between total body BMD , BMD at AP spine L1-L4 and the difference between chronological age and dental age in thalassemia and control group in both male and female.

CA – DA / BMD	Thalassemia CA – DA				Control CA – DA			
	Male		Female		Male		Female	
	r	p	r	p	r	p	r	p
AP spine L1-L4 BMD (Z score)	- 0.480	0.001*	- 0.171	0.215	- 0.188	0.150	- 0.036	0.784
Total body BMD (Z score)	- 0.285	0.055	- 0.076	0.609	- 0.145	0.270	- 0.023	0.862

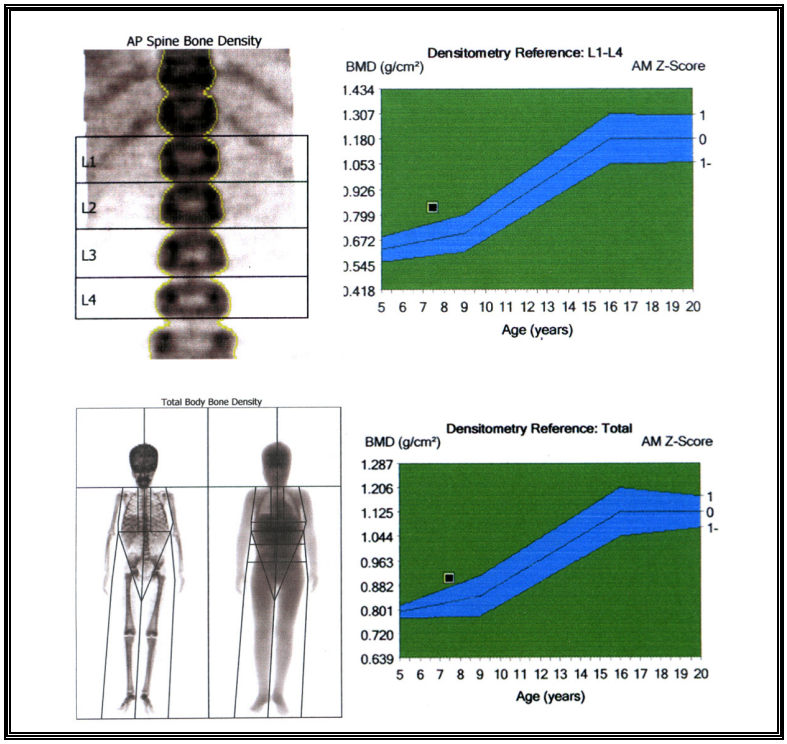


Figure (3): Healthy control BMD chart

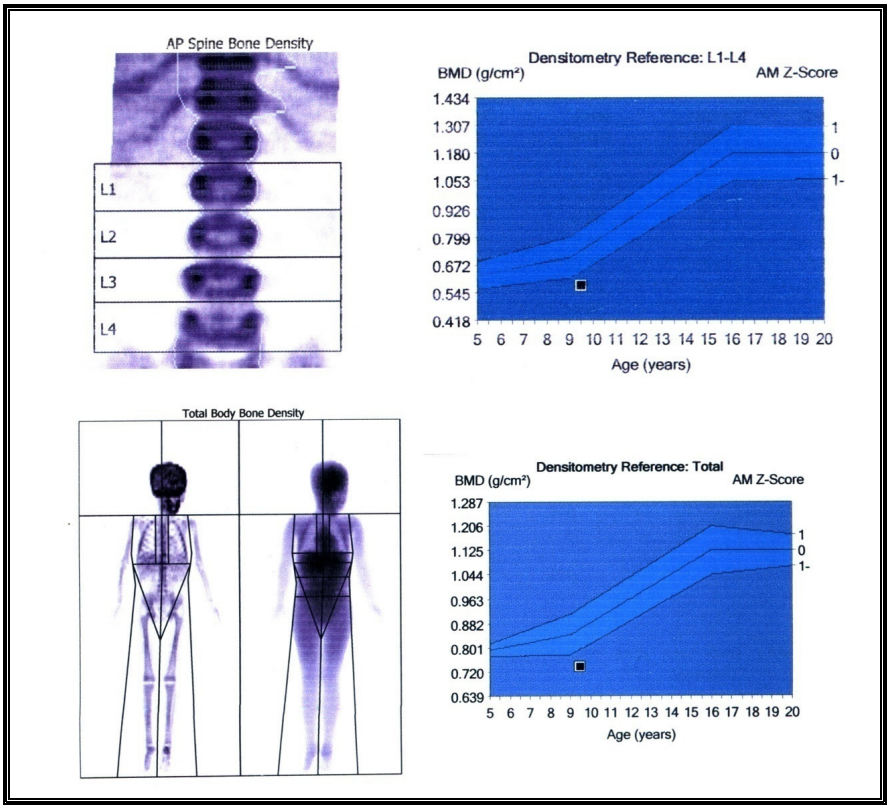


Figure (4): Thalassemic patient BMD chart

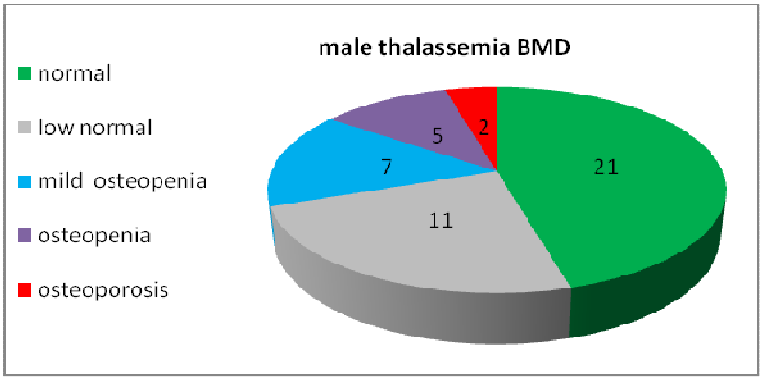


Figure (5): Distribution of osteopenia and osteoporosis among thalassemia male group.

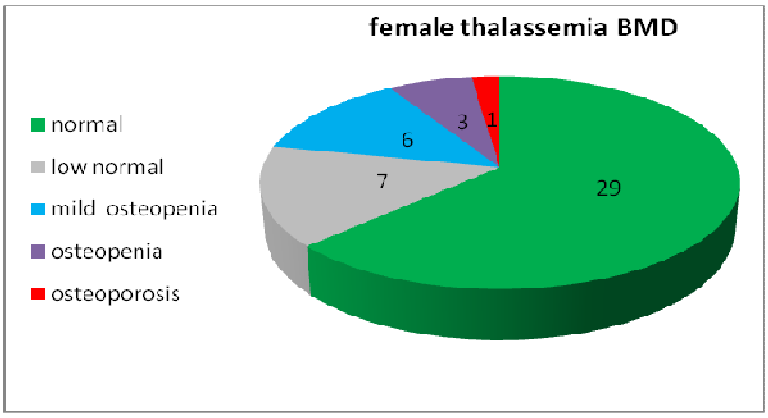


Figure (6): Distribution of osteopenia and osteoporosis among thalassemia female group.

Normal = Z score > -1, osteopenia = Z score from -1 to -2.5 and osteoporosis = Z score < -2.5

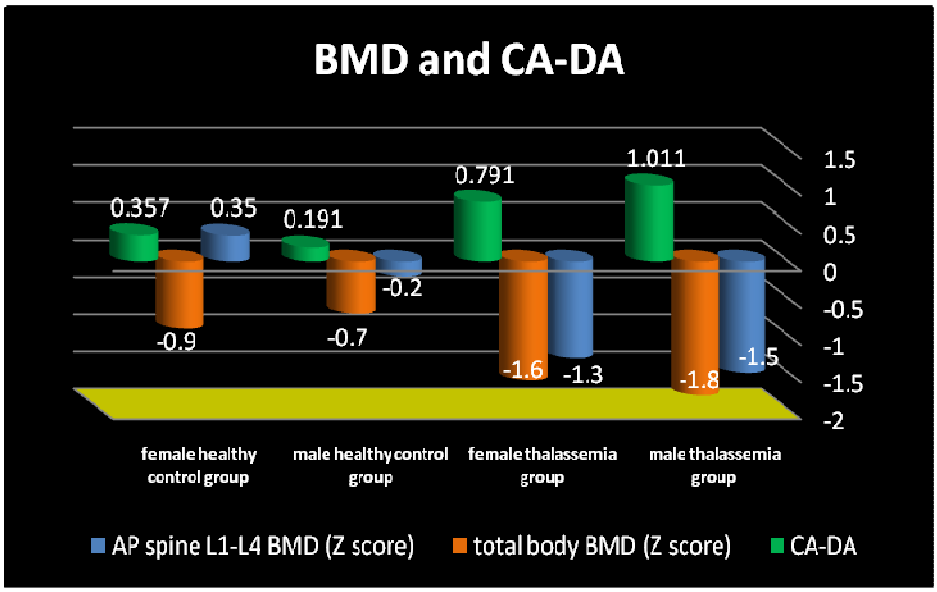


Figure (7): Mean values of total body BMD, BMD at AP spine L1-L4 and the difference between chronological age and dental age in thalassemia and control group in both male and female.

DISCUSSION

In the present study there is statistically significant reduction in SNB angle in thalassemic patient (73.5 degree) compared to controls (76.6 degree). This finding came in accordance with Zuccato et al, Altemus and Epps.[21,22] According to these findings, the thalassemic patients exhibited significantly retrognathia in the mandible, ANB Angle highly significant increase in thalassemic patients (7.5degree) compared to controls (3.4 degree). Amini et al.[23] reported a significant increase in ANB angle in thalassaemia major patients and attributed it to a short mandible.

No significant difference in SNA angle between thalassemic and healthy controls. According to this finding, the thalassemic patients exhibited Class II skeletal pattern.These finding coincides with the findings of Bassimitci[6] and Abu–AL Haija[17] and Moutaz[8]. who reported insignificant increase in tendency to sagittal maxillary over growth and the anterio-posterior position of the maxilla in relative to cranial base and significant increase in ANB angle. On the other hand our findings, however, are not in line with others, who have reported that because of more cancellous bone-containing marrow spaces in maxilla there is a dramatic maxillary prognathism [24-26].

A pronounced vertical growth direction of the mandible in these patients seemed to be a consistent finding in almost all publications[6,17]. Various explanations for this pronounced vertical growth direction have been reported such as muscular weakness mouth breathing pattern vertical decent of the posterior maxilla (due to enlargement of the maxillary marrow spaces) and probably a deficient ramus and condylar growth.[27,28]

Highly significant difference with longer total anterior facial height for thalassemic patients (129 mm) compared to controls (120 mm) was found. This finding disagreed with Bassimitci[6] and Abu– AL Haija[17] who found that thalassemic patients have a shorter total anterior facial height with no significant difference. The total posterior facial height significantly decreased in thalassemic patients (70 mm) compared to controls (75 mm). This finding partially coincides with Bassimitci, Abu–

AL Haija and Moutaz [6,7,18]; all found that thalassemic patients possess shorter posterior facial height but is not significantly different. The posterior facial height is largely determined by growth at the condyle, which is deficient probably due to anemia.

Dental arch size and shape are influenced by a variety of factors including genetic, environmental, pathological conditions, eruption, position, number of teeth, and ethnic diversity.[29,30] The present study showed that all arch dimensions, were reduced in the thalassemic group compared to the controls. The differences between the two groups were statistically significant. In thalassemic subjects, the arch length was (2. 1 mm) shorter in the maxilla and (3.1 mm) shorter in the mandible compared to the controls.

The shorter arch depth and length and the narrower arch width in this study could be a reflection of general growth retardation.[17,27], and skeletal changes in thalassemic patients. In addition, the reduced tooth size in this disorder may render the dento-alveolar bone housing the teeth to be more deficient. Evidence supporting the relation between reduced tooth size and smaller dental arches has come from studies in patients with Down's syndrome,[29] oligodontia,[30,31] and cleft lip and palate.[32]

Pediatric dentists and orthodontists must be mindful of both the growth patterns associated with thalassemia and the effects that delays dental development. Dental age estimation is considered as an additional diagnostic method when detecting possible growth or maturation changes in children. Age estimation studies was conducted by many researchers as Willems et al.[33], Eid et al[34], McKenna et al.[35] and Foti et al.[36]

Our results revealed that. in male control group, the dental age exceeded the chronological age by (0.191) years. This result came in accordance with Nystrom et al.[37] (0.29) years, Nykänen et al.[38] (0.20) years, Davidson and Rodd,[39] (0.19) years, Mckenna et al.[35] (0.30) years and Al-Emran,[40] (0.30) years. Where as the dental age in male group was delayed, in a study by Qudeimat and Behbehani, [41] (0.71) years and Chen et al.[42] (0.08) years.

Our study showed that, in female control group the dental age exceeded the chronological age by (0.357) years. This result agreed with Nykänen et al.[38] (0.30) years. Whereas the dental maturation in female group was delayed in a study by Qudeimat and Behbehani,[41] (0.67) years, Cruz-Landeira et al.[43] (0.10) years and Chen et al. [42] (0.15) years.

Our results revealed that dental maturation in Egyptian females were more rapid than Egyptian males. This came in accordance with the study of Al-Kholy,[44] on Egyptian children. He reported that there was more advancement in dental development in females than males by (0.1) years and Bagherian and Sadeghi,[45] (0.15) years and Feijoo et al.[46] (0.291) years. Whereas the dental age in male group exceeded the female group in a study by Eid et al.[34] (-0.04) years, Bagherpor et al.[47] (0.16) years and Baghdadi,[48] (-0.73) years.

On the other hand, our results disagree with Cruz-Landeira et al.[43] who studied Venezuelan children and they found that the difference between male and female dental age was 0.13 years delayed dental maturation and Qudeimat & Behbehani,[41] who studied Kuwaity children as they found that the difference between male and female dental age was 0.04 years.

Dental age may be overestimated as Leurs et al.[49], Koshy and Tandon,[50] or under estimated as Cruz-Landeira et al.[43]. So age estimation studies are needed in medicine and dentistry, being relevant to the timing of treatment procedures in endocrinology, pediatric dentistry, orthodontics, besides its importance in forensic science. Tooth formation is a reliable method for assessing dental maturation and generally used for estimating dental age (Demirjian et al.[10] and Bagherpour et al.[47]). In the current study the Demirjian method was used because it's the most commonly used to determine dental age (Demirjian et al.[51] Nystrom et al.[37] Chaillet et al.[52]) as it is simplest, most practical and widely reliable method to estimate dental age and maturity.

In accordance with our results, De Mattia D 1996[53] reported Delayed eruption of both deciduous and permanent teeth in patients with thalassemia. The cause of growth retardation in children with TM is multifactorial and includes chronic anemia and hypoxia, iron overload, endocrinopathies, low socioeconomic status, and racial factors [54].

In the present study a highly significant delay in dental development among the participants equal to 1.011 year in male and 0.791 in female had found with no significant differences between male and female. this results agreed with Faiez N. Hattab[55] who found stronger association between DA and CA and reported greater delay in male than female equal to (0.97 years and 0.31 years) respectively. Also Hazza.a AM et al[56] reported that the delay in dental development in thalassemia major varied according to the patients age. This positive correlation parallels the general growth of thalassemic children.

A similar significant delay in the development of thalassemic dentition with an average of 1.01 years was obtained by other studies as Flynn DM et al[57] and Saenger P et al[58] and another finding of significance was the correlation between the amount of delay and the chronologic age. An increase in delay of dental development results as the thalassemic patient gets older especially after the age of seven years the suggested causes of growth retardation and delay of bone maturation are chronic anemia,[4].

In accordance with the present study the low vitamin D and low BMD observed in thalassemia patient also reported by Lasco A et al[59], Soliman AT et al[60] and Umit Dundar et al[61]. The major pathogenetic factors for the development of low bone mineral density (BMD) in thalassemic subjects appear to be; chronic hypoxemia and medullary expansion, defective growth affecting both height and weight, abnormal calcium-phosphate homeostasis, delayed or lack of pubertal development and decreased sex steroid secretion and low plasma vitamin D concentration.

CONCLUSIONS

- All thalassemic patients had a Class II skeletal base relationship with an average ANB angle of 7.5 degree. The mandible is retruded and smaller in size, proclination of upper and lower incisors, significant hyper-divergent growth pattern leading to steep mandibular plane, increased anterior facial height and decreased posterior facial height, Short mandibular body, short ramus length, shorter arch width and shorter arch circumference when compared with healthy control matched in age and sex.

- A statistically high significant difference was found in both male and female thalassemia groups regarding the difference between the chronological and dental age with delay in dental development in male greater than female (1.011 year and 0.791 year) respectively.
- A high significant difference was found regarding dental age between thalassemia patient and healthy control of the same age and gender.
- The dental age in healthy control group exceed the chronological age by a greater value in female than male (0.357 year and 0.191 year) respectively .
- Egyptian healthy females are more advanced in their dental age development than chronological age which was greater than healthy Egyptian males (0.357 year and 0.191 year) respectively.
- Vitamin D in thalassemia patient recorded very low values when compared with age and sex matched healthy control and there were a negative non significant correlation between blood level of vitamin D and retardation in dental development.
- Low normal BMD and mild degree of osteopenia were found in thalassemia patients which was greater in male than female and had a negative significant correlation with retardation in dental development in male thalassemia group.

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