Original Article

Dental and Skeletal Age Estimations in Lebanese Children: A Retrospective Cross-sectional Study

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Abstract

Aims and Objectives: Assessing dental and bone ages is frequently required in a wide range of fields such as odontology, forensic science, as well as orthopedics. The aim of this study was to evaluate applicability of two methods of bone age assessment and two methods of dental age (DA) assessment for Lebanese children.

Materials and Methods: Skeletal age (SA) of 260 orthodontic patients (124 males, 136 females divided into four groups each) was consecutively assessed using Greulich and Pyle and Fishman's SMI methods. DA was evaluated using both Demirjian's and Willem's methods. Mean age was 11.89 ± 1.38 years for males and 11.75 ± 1.58 years for females. Data were collected and statistically analyzed using the SPSS software (IBM SPSS Statistics, version 21, USA). The differences between estimated DA, estimated SA, and chronological age (CA) were compared by gender and age group.

Results: Greulich and Pyle method showed nonsignificant difference with CA in male sample, while in both assessment methods, the difference between skeletal and CAs is significant in female sample. Results of Willem's method in the whole sample suggested a statistically nonsignificant difference, when compared to CA. Demirjian's method delivered higher mean value than Willem's assessment in both genders.

Conclusions: Greulich and Pyle method is accurate for SA assessment in males and only in one group of females, while it significantly overestimates age in all other female groups. Willem's method is more suitable to assess DA in both genders. A strong correlation exists between both dental and skeletal assessment methods and CA.

Keywords: *Dental age, hand-wrist radiograph, Lebanese children, skeletal age*

Introduction

Evaluation of chronological age (CA) is an essential step of diagnosis and treatment planning in pediatrics, dentofacial orthopedics, and pediatric dentistry. In forensic science, age determination is needed for identification of human remains. CA is linked solely to the scale of time and printed on civil registry or family status. However, the information might be lacking in certain circumstances, hence leading to consider a different way for age evaluation based on growth. If growth is a continuous phenomenon throughout the years, huge modifications occur in almost the first two decades of life with great variations among individuals. Some children start their growth and finish their maturation early, compared to others with same age, depicting a delayed growth but showing later, greater amount of growth.[1]

Among all the possible means of assessment, hand-wrist radiograph is the most commonly used indicator to evaluate bone age or bone maturation of a patient, for its simple, little irradiant, and inexpensive aspects.

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This radiograph provides precious information on hand bones' ossification, based on the shape and volume of metacarpal bones,[2,3] and the presence of epiphyseal plates at certain age.[4,5]

However, if bone age assessment has reached a consensus to predict patient maturation, one more tool has to be considered on dental side leading to evaluate dental age (DA) of an individual.

Multiple radiological approaches (e.g., periapical radiograph, cone-beam computed tomography, or panoramic radiographs) will allow an accurate view on the whole dental system, the latter being the most commonly used for this purpose. Different methods of DA assessment were elaborated by several workers and frequently found in literature.[6-8] However, Demirjian's method,[9] readapted by Willems *et al*.,[10] has been widely used since its inception although several studies currently compare the applicability of two or more methods on populations from different origins. In Lebanon, the different methods of skeletal and dental assessments cited above are used without a prior testing regarding their accuracy. Thus, verifying applicability of the traditionally used methods and their correction (when necessary) is a must. The present study sheds light on the problem faced during orthodontic treatment of Lebanese children and proposes the optimal assessment tool to be applied on Lebanese individuals.

Herein, we aim to:

1. Evaluate the applicability of Greulich and Pyle (1959) and Fishman (1982) methods of bone age assessment for Lebanese children
2. Evaluate the applicability of Demirjian (1973) and Willems (2001) methods of DA assessment for Lebanese children.

Materials and Methods

Participants

In this retrospective cross-sectional study, all files of growing patients who have undergone orthodontic treatment for jaw discrepancies (known as orthopedic correction), between 2002 and 2015, were selected among 1427 orthodontic files from the database of the Department of Orthodontics and Dentofacial Orthopedics of the Lebanese University, School of Dentistry, Beirut, Lebanon. Prior to the orthodontic treatment, each patient (or his/her legal representative) was required to sign an informed consent form allowing dental staff to use the records obtained from potential patients. This study had obtained approval of Ethical Committee at Lebanese University (CUEMB 51/2016).

Criteria

Inclusion criteria were as follows:

- Healthy patients from Lebanese lineage, with age ranging between 8 and 17 years, without any syndrome or systemic pathology that might affect growth or dental formula (dental agenesis, dental impaction, or supernumerary teeth).
- Patients whose presence in the orthodontic file of both orthopantomogram (OPG) and left hand-wrist radiograph taken at the same date during the same month following the first orthodontic consultation were included in the sample.

Patients with extracted or absent teeth or with a history of orthodontic treatment were excluded from the sample (orthodontic treatment might involve teeth extraction or affect apex shape).

After file selection, the name, gender, and CA of each individual were recorded.

The sample of 260 individuals included 124 males and 136 females [Table 1].

Both male and female samples were divided into four groups, according to CA, as follows:

- Group 1: 8 to <10 years
- Group 2: 10 to <12 years
- Group 3: 12 to <14 years
- Group 4: 14 years and above.

For males, ages ranged from 8.7 to 16.5 years with a mean age of 11.89 years and standard deviation of 1.38 years, whereas for females, ages ranged from 8.1 to 14.9 years, with a mean age of 11.75 years and standard deviation of 1.58 years.

Methods

All OPGs and hand-wrist radiographs were scored separately by two observers to assess DAs and skeletal ages (SAs) according to:

- Demirjian and Willems methods for DA assessment [Figure 1]
- Greulich and Pyle and Fishman methods for SA assessment [Figure 2].

Table 1: Sample distribution by age and gender

Age (years)	Gender		Total
	Males	Females	
8-<10	9	16	25
10-<12	58	61	119
12-<14	49	47	96
14 years and above	8	12	20
Total	124	136	260

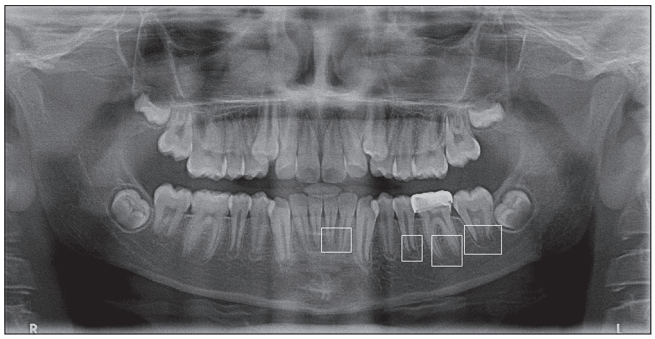

Figure 1: Panoramic radiograph of patient aged 11 years, 3 months. Demirjian's method rates each of the lower seven left teeth on a maturity scale from A to H. Here, apex of incisors and first molar are closed, which corresponds to the last stage of dental formation (H), while the second premolar is on Stage G, and the second molar is on Stage F. Dental age is 12.9 years according to Demirjian's method, and 12.38 years following Willem's method

Assessment of dental age by Demirjian's method

Each of the seven mandibular left-side teeth (excluding third molar) were rated on a maturity scale of A to H (A corresponding to the beginning of tooth calcification and H to the closure of apical end of the root canal). Each scale is translated into score. The sum of the seven allocated scores corresponds to the DA of the patient.[9]

Assessment of dental age by Willems method

The developmental tooth stages of each of the seven mandibular left teeth according to Demirjian's method with corresponding age scores were expressed directly in years. The Willem's estimation method is a modified Demirjian method.[10]

Assessment of skeletal maturity using Greulich and Pyle's atlas

The radiograph of the patient's left hand and wrist was compared with the images listed in the Radiographic Atlas of Greulich and Pyle (1959)[2] in the corresponding section (males and females). The matching image in the Atlas will provide the SA (as recorded by authors on the top of the Atlas page).

Assessment of skeletal maturity using the Fishman SMI method

Eleven skeletal maturity indicator (SMIs) were consecutively depicted in a stable sequence on selected epiphyseal plates of left hand radiograph, leading to gradual bone maturation.[5] At SMI 11 (ossification of radius bone), complete ossification is considered to be reached. Localization of an SMI step on patient's radiograph gives corresponding age as listed in Fishman's tables.

Statistical analysis

Data were collected and statistically analyzed using the Statistical Package for Social Sciences computer software (IBM SPSS Statistics, version 21, USA). The differences between estimated DA, estimated SA, and

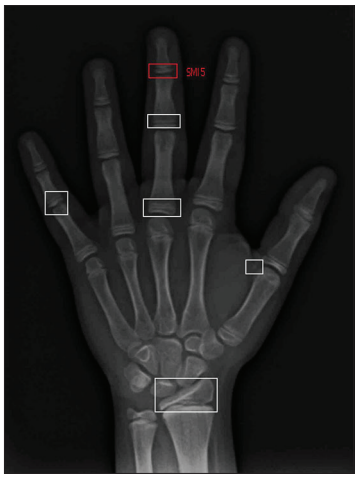

Figure 2: Hand wrist of the same patient showing different sites (in white and red) of skeletal maturity indicator (SMI) at epiphyseal plates assessed in Fishman's method. Skeletal age according to Greulich and Pyle Atlas is 13 years, 6 months. For Fishman's method, SMI 5 (in red) is depicted here, with capping of distal phalanx epiphysis of third finger, and skeletal age is 13 years

CA were compared by gender and age group with paired *t*-test and Wilcoxon signed-rank test. The nonparametric test (Wilcoxon signed-rank test) was used for groups with size <30. For all tests, $P < 0.05$ was considered statistically significant. Spearman's rank correlation test was used to assess the relation between estimated DA, estimated SA, and CA.

Intraclass correlation coefficient values were above 0.95 for both examiners, for the four methods, showing a high reliability.

Results

Statistical results and comparisons between groups and methods are shown in Tables 1-5. The sample of 260 individuals was distributed into 124 males and 136 females.

Mean CA was 11.90 ± 1.39 years for male sample and 11.76 ± 1.59 years for female sample. Groups 2 and 3 included higher number of patients in comparison to Groups 1 and 4, due to the ideal age of orthodontic treatment, frequently occurring between age 10 and 14.

Comparison between chronological age and different methods of skeletal age estimation in males [Tables 2 and 3]

The SA as recorded by both Fishman or Greulich and Pyle methods, compared to CA, delivers higher mean values for the whole male sample, the latter method being closer to the mean CA of the sample (12.69 ± 1.38 years for Fishman and 11.94 ± 1.79 years for Greulich and Pyle). Statistically, the difference between CA and SA as provided by Greulich and Pyle method is not significant.

Table 2: Comparison between Fishman's estimation of skeletal age and chronological age in males and females (*P* significant if <0.05)

Gender	Age (years)	*n*	Mean (SD)			95% CI of the difference	*t* statistics	df	*t*-test (*P*)	Wilcoxon (*P*)
			CA	Fishman	Fishman-CA					
Males	8-<10	9	9.41±0.40	11.66±1.10	2.25±0.93	1.54-2.96	7.27	8	0.000	0.008
	10-<12	58	11.11±0.52	12.09±0.82	0.99±0.81	0.78-1.20	9.34	57	0.000	0.000
	12-<14	49	12.83±0.57	13.20±1.34	0.36±1.17	0.03-0.70	2.17	48	0.035	0.063
	14 years and above	8	14.74±0.87	15.02±1.46	0.28±0.87	−0.44-1.01	0.92	7	0.388	0.401
	Total	124	11.90±1.39	12.69±1.38	0.79±1.09	0.59-0.98	8.02	123	0.000	0.000
Females	8-<10	16	9.11±0.58	10.95±0.53	1.84±0.84	1.39-2.28	8.74	15	0.000	0.000
	10-<12	61	11.02±0.60	11.98±0.86	0.95±0.75	0.76-1.14	9.99	60	0.000	0.000
	12-<14	47	12.93±0.55	13.29±1.14	0.37±1.07	0.05-0.68	2.34	46	0.023	0.044
	14 years and above	12	14.47±0.35	14.99±0.51	0.52±0.71	0.07-0.97	2.52	11	0.028	0.019
	Total	136	11.76±1.59	12.58±1.41	0.82±0.98	0.65-0.98	9.68	135	0.000	0.000

SD=Standard deviation, CI=Confidence interval, CA=Chronological age

Table 3: Comparison between Greulich and Pyle's estimation of skeletal age and chronological age in males and females

Gender	Age (years)	*n*	Mean (SD)			95% CI of the difference	*t* statistics	df	*t*-test (*P*)	Wilcoxon (*P*)
			CA	Greulich and Pyle	Greulich and Pyle-CA					
Males	8-<10	9	9.41±0.40	9.28±1.60	−0.13±1.41	−1.21-0.95	−0.27	8	0.791	0.213
	10-<12	58	11.11±0.52	11.37±1.14	0.26±1.01	0.00-0.53	1.99	57	0.052	0.135
	12-<14	49	12.83±0.57	12.63±1.53	−0.21±1.35	−0.59-0.18	−1.07	48	0.290	0.315
	14 years and above	8	14.74±0.87	14.94±1.15	0.20±0.61	−0.31-0.71	0.92	7	0.390	0.398
	Total	124	11.90±1.39	11.94±1.79	0.05±1.18	−0.16-0.25	0.43	123	0.670	0.670
Females	8-<10	16	9.11±0.58	9.69±0.93	0.58±1.14	−0.03-1.18	2.02	15	0.062	0.118
	10-<12	61	11.02±0.60	11.65±1.38	0.63±1.19	0.33-0.94	4.13	60	0.000	0.000
	12-<14	47	12.93±0.55	13.70±1.17	0.78±1.00	0.48-1.07	5.29	46	0.000	0.000
	14 years and above	12	14.47±0.35	15.42±0.79	0.95±0.80	0.44-1.45	4.12	11	0.002	0.004
	Total	136	11.76±1.59	12.46±1.99	0.70±1.09	0.52-0.89	7.53	135	0.000	0.000

SD=Standard deviation, CI=Confidence interval, CA=Chronological age

Table 4: Comparison between Demirjian's estimation of dental age and chronological age in males and females

Gender	Age (years)	*n*	Mean (SD)			95% CI of the difference	*t* statistics	df	*t*-test (*P*)	Wilcoxon (*P*)
			CA	Demirjian	Demirjian-CA					
Males	8-<10	9	9.41±0.40	10.93±2.35	1.53±2.09	−0.08-3.13	2.19	8	0.060	0.138
	10-<12	58	11.11±0.52	11.78±1.20	0.68±1.10	0.39-0.96	4.69	57	0.000	0.000
	12-<14	49	12.83±0.57	13.59±1.63	0.75±1.51	0.32-1.19	3.48	48	0.001	0.003
	14 years and above	8	14.74±0.87	15.04±1.24	0.30±1.44	−0.91-1.50	0.58	7	0.577	0.674
	Total	124	11.90±1.39	12.64±1.86	0.74±1.38	0.50-0.99	5.99	123	0.000	0.000
Females	8-<10	16	9.11±0.58	10.15±1.05	1.04±1.19	0.40-1.68	3.48	15	0.003	0.009
	10-<12	61	11.02±0.60	12.07±1.20	1.05±1.08	0.78-1.33	7.62	60	0.000	0.000
	12-<14	47	12.93±0.55	13.55±1.05	0.62±0.90	0.36-0.89	4.73	46	0.000	0.000
	14 years and above	12	14.47±0.35	15.03±0.91	0.56±0.97	−0.05-1.18	2.01	11	0.069	0.116
	Total	136	11.76±1.59	12.62±1.70	0.86±1.04	0.68-1.04	9.66	135	0.000	0.000

SD=Standard deviation, CI=Confidence interval, CA=Chronological age

Statistical results were found to be similar (nonsignificant difference for Greulich and Pyle, compared to CA) in Groups 1, 2, and 3, while in Group 4, results of the two methods, Fishman and Greulich and Pyle, suggest that difference is not significant between CA and SA.

Comparison between chronological age and different methods of skeletal age estimation in females [Tables 2 and 3]

Both methods of SA exhibit higher mean values for the whole sample with higher value for Fishman's, as

Table 5: Comparison between Willem's estimation of dental age and chronological age in males and females

Gender	Age (years)	*n*	Mean (SD)			95% CI of the difference	*t* statistics	df	*t*-test (*P*)	Wilcoxon (*P*)
			CA	Willems	Willems-CA					
Males	8-<10	9	9.41±0.40	10.62±2.00	1.22±1.69	−0.08-2.52	2.16	8	0.063	0.051
	10-<12	58	11.11±0.52	11.30±1.14	0.20±1.01	−0.07-0.46	1.49	57	0.143	0.117
	12-<14	49	12.83±0.57	12.89±1.37	0.06±1.26	−0.30-0.42	0.33	48	0.746	0.538
	14 years and above	8	14.74±0.87	14.39±1.32	−0.35±1.69	−1.76-1.06	−0.59	7	0.577	0.401
	Total	124	11.90±1.39	12.08±1.66	0.18±1.24	−0.04-0.40	1.62	123	0.108	0.081
Females	8-<10	16	9.11±0.58	9.47±0.91	0.36±1.17	−0.27-0.98	1.22	15	0.241	0.224
	10-<12	61	11.02±0.60	11.25±1.29	0.22±1.17	−0.08-0.53	1.49	60	0.141	0.416
	12-<14	47	12.93±0.55	12.75±1.17	−0.18±0.98	−0.47-0.11	−1.26	46	0.215	0.137
	14 years and above	12	14.47±0.35	14.49±1.20	0.02±1.24	−0.77-0.81	0.06	11	0.953	0.875
	Total	136	11.76±1.59	11.84±1.77	0.08±1.12	−0.11-0.27	0.85	135	0.395	0.900

SD=Standard deviation, CI=Confidence interval, CA=Chronological age

Table 6: Correlations (Spearman's rho) between chronological age and skeletal age (Fishman–Greulich and Pyle) and between chronological age and dental age (Demirjian–Willem's method)

	ρ		
	Males	Females	Both
Fishman	0.659**	0.833**	0.768**
Greulich and Pyle	0.696**	0.843**	0.776**
Demirjian	0.680**	0.805**	0.748**
Willems	0.684**	0.792**	0.740**

**Correlation is significant at the 0.01 level (two tailed)

compared to CA (12.46 ± 1.99 years for Greulich and Pyle and 12.58 ± 1.41 years for Fishman). In both assessment methods, the difference between SA and CA is significant.

Only in the 1st group (8–10 years), statistical difference was not significant when comparing CA to SA as assessed with Greulich and Pyle's method.

Comparison between chronological age and different methods of dental age estimation in males [Tables 4 and 5]

In the whole male sample, both methods of DA estimation provided higher mean value. However, DA assessment, according to Demirjian, showed higher difference (12.64 ± 1.86 years) with CA, than Willem's mean value (12.08 ± 1.66 years). Difference between CA and Willem's DA was statistically insignificant. As for age groups, the results of Willem's method in all groups suggested a statistically insignificant difference when compared to CA; in Groups 1 and 4, Demirjian's method as well as Willem's method showed insignificant difference with CA.

Comparison between chronological age and different methods of dental age estimation in females [Tables 4 and 5]

DA assessment according to both Demirjian (12.62 ± 1.70 years) and Willem's (11.84 ± 1.77 years) methods

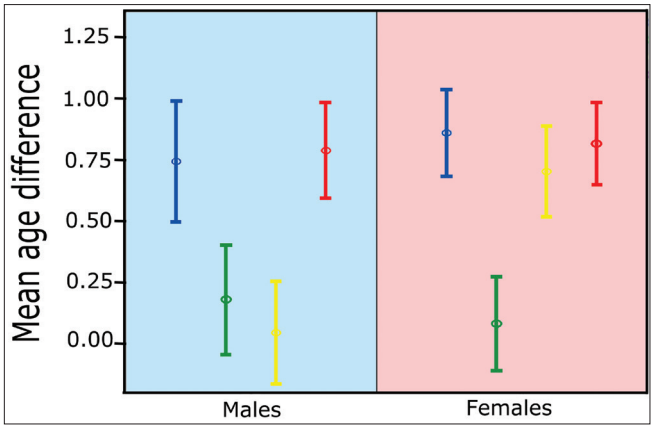

Figure 3: Mean age difference (at 95% confidence interval) of the four estimation methods for both males and females. Chronological age: blue for Demirjian, green for Willem's, yellow for Greulich and Pyle, and red for Fishman's methods

overestimated age in the female sample, but the mean difference with CA as reported by Willem's method is more reduced (+0.082 for Willems and +0.86 for Demirjian), and the statistical difference in the latter was insignificant. In all age groups, results of the Willem's method provided statistically insignificant difference with CA, whereas only in the Group 4, Demirjian's method showed insignificant difference.

Results are summarized graphically in Figure 3, showing mean age differences (using the four methods of dental and skeletal estimations for both genders).

Spearman's correlation coefficient (Rho) between CA and SA (Fishman and Greulich Pyle) and between CA and DA (Demirjian and Willems) was calculated for male and female samples and for the whole sample which is shown in Table 6. It shows a strong statistically significant correlation of the two SAs and the two DAs with the CA.

Discussion

SA assessment allows the clinician to determinate relative maturity of patients, hence to evaluate those

with advanced or delayed stages of puberty. In normal individuals, SA varies from CA on a ±10% average.[11] Some factors might lead to growth deficiency or delay, such as nutritional or metabolic alterations. Similarly, large variations in dental development have prevented the use of DA as an overall measure of maturation.

In this study, two methods of DA evaluation (Demirjian and Willems) and two methods of SA evaluation (Greulich and Pyle and Fishman) were used to assess their applicability in a sample of Lebanese growing population. Greulich and Pyle's method is widely used for evaluation of patients' SA in Lebanese individuals, thus the need to test its accuracy. No specific DA method is reported as reference for the same population.

Skeletal assessment

Both methods delivered overestimated results in male sample; however, Greulich and Pyle assessment is closer (11.94 ± 1.79 years) to mean CA (11.90 ± 1.39 years), in comparison to Fishman's values for the whole sample. In all age groups, Greulich and Pyle method showed nonsignificant difference.

Overestimation with significant differences to mean CA (11.76 ± 1.59 years) were shown in results of female sample for the two methods as well, with the exception of Group 1 for Greulich and Pyle; higher mean value was recorded in Fishman's assessment (12.58 ± 1.41 years) than that of Greulich and Pyle's method (12.46 ± 1.99 years).

Different ways of bone age prediction are found in literature such as the Roche–Wainer–Thissen method,[12] assessing SA on a radiograph of knee joint, or Sauvegrain method,[13] based on elbow radiograph. Some authors[11,14,15] developed methods based on examination of standard radiographs of left hand and wrist. Skeletal maturity depicts several ossification centers in a specific order in the hand and the wrist, which is clearly described in Fishman's method.

Although none of these described methods is uniformly accepted or used in clinical practice, the Greulich and Pyle method is one of the most popular and routinely used methods. A recent survey of the Society for Pediatric Radiology found that 27% of respondents were using a hemiskeleton method for infants, while 70% used the Greulich and Pyle method.[16] Percentage of the latter grows up to 97% when assessment is made on 3–18-year-old patients.

A study conducted on a multiethnic sample of 2614 individuals concluded that Greulich and Pyle method is reproducible and accurate with small difference between bone age and CA.[17] Similar results with significant correlation (r = 0.86) between skeletal and CAs were found by Mohammed *et al*. in a population of South Indian (Andhra) children.[18]

In opposition, this method overpredicted SA in South Turkish children from 10 to 15 years in males and 10 to 18 in females, as reported by Gungor *et al*.[19] Recently, ultrasonography and MRI were preconized for successful replacement of radiography in bone age assessment as presented by Greulich and Pyle.[20,21] The aim of such procedures was to avoid irradiation during this examination.

A study performed by Bagherpour *et al*.[22] found a significant correlation only in males between dental development stages of mandibular left and right canines as prescribed by Demirjian and skeletal maturity index (Fishman's SMI 4) corresponding to ossification of sesamoid bone. The author concluded that different skeletal maturity patterns between genders might be perceptible. Camacho-Basallo *et al*.[23] tested two hand wrist methods and showed that correlation coefficients for CA were statistically significant only for Fishman's method.

Fishman's method has been successfully applied on a sample of South Indian population. The study's results concluded that it can be used as a reliable choice for predicting biological age.[24] Mean age difference was minimal, hence 0.4 year in males and 0.3 year in females, indicating that SA is underestimated with this method. These results were not concordant with those of this study with mean age difference of 0.79 year in males and 0.82 year in females, indicating that SA is overestimated when Fishman's method is used.

Dental assessment

In male sample, Demirjian's method delivered higher mean value (12.64 ± 1.86 years) and significant difference in comparison to CA (11.90 ± 1.39 years), whereas the mean value obtained from Willem's method was 12.08 ± 1.66 years. The mean age difference was 0.18 year for Willem's method.

Similar overestimations were observed in female sample, but more reduced in Willem's method (11.84 ± 1.77 years) than in Demirjian's results (12.62 ± 1.70 years) with significant difference in the latter. The mean age difference was 0.08 years for Willem's method.

For males and females, statistical difference was insignificant in all age groups.

Pratyusha *et al*.[25] studied the applicability of Demirjian's method and modified Cameriere's method in children

aged from 9 to 14 years. Estimation age with the latter method was closer to CA. These results were not similar in a research[26] assessing the same methods. Demirjian's method showed more appropriate results for the investigated population.

Several studies on applicability of Demirjian or Willem's methods on Middle Eastern populations have been published. Nour El Deen *et al*. found a consistent overestimation using Demirjian method on Saudi population.[27] Another study tested the applicability of this method on a sample of Tunisian children.[28] It concluded that Demirjian's method underestimates age between 9 and 16 years.

A meta-analysis based on 26 studies using Demirjian method concluded that CA was overestimated, thus "the need of population-specific standard for better estimation"[29] while Willem's method was found less accurate than Demirjian's one for DA estimation in Thai children.[30]

However, different conclusions were found in a comparison between Willem's and Demirjian's methods conducted on a Chinese sample.[31]

These findings were in accordance with the results of the present study and those of Ambarkova[32] on a Macedonian sample with bigger overestimation in Demirjian's method.

All the above results should be analyzed cautiously, in light of ethnical specificity, multiple disparities into the same population, and sample size that might affect research interpretation.

Conclusions

Results of the present study suggest that a strong correlation exists between both dental and skeletal assessment methods and CA; Willem's method is more suitable to assess DA in both genders for Lebanese population; Greulich and Pyle method is accurate for SA assessment in males and females between 8 and 10 years, while it significantly overestimates age in all the other female groups.

Contemporary history of Lebanon witnessed periodical conflicts and violence that left behind numerous unknown and/or unidentified victims. Consequently, the present study is needed to evaluate CA of human remains, in addition to its application in odontology and pediatrics. It contributes as well as widens our knowledge on growth variability and dental maturity on Lebanese population, in comparison to neighboring ones.

Further investigations with larger sample would improve these findings and suggest specific charts applicable to Lebanese individuals.

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Conflicts of interest

There are no conflicts of interest.

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