บทวิทยาการ
Original article

A Study of Mandibular Third Molar Dental Age and Cervical Vertebral Maturation in Thai Cleft Lip and Palate Patients

นพปฎล จันทร์ผ่องแสง*
Noppadon Chanpongsaeng*

Abstract

Background: Cervical vertebral maturation (CVM) and dental age assessment are two common growth prediction methods. Even though the development of cervical vertebrae and dentition in cleft lip and palate (CLP) patients was reported to be different from non-cleft patients, both of CVM and dental age has never been investigated in Thai cleft patients. **Objective:** This study aimed to compare the mandibular third molar dental age and CVM stage between Thai cleft and non-cleft patients. **Materials and methods:** Two hundred and eighty-four orthodontic patients aged 7-13 years old were divided into two groups: (1) non-syndromic unilateral or bilateral complete CLP patients and (2) non-cleft patients as the control group. The panoramic and lateral cephalometric radiographs were examined. Dental ages from either the left or right mandibular third molar, CVM in cervical stages, and chronological ages of the subjects were recorded. Descriptive statistics were used to describe the demographic data and the independent t-test was used to compare the dental ages and chronological ages at each stage of CVM between the cleft and non-cleft groups. **Results:** All patients, male and female, demonstrated a statistically significantly younger chronological age at cervical stage 2 and 4 (CS2 and CS4) than the non-cleft group. The female cleft group and all patients in the cleft group at 7-8 years old had statistically significantly younger third molar age than the non-cleft group.**Conclusion:** At 7-8 years old, the cleft patients showed statistically significantly delayed development of mandibular third molars and faster CVM at CS2 and CS4 than the non-cleft group.

Keywords: Cervical vertebral maturation, Complete cleft lip and palate, Dental age, Mandibular third molar

Received: 30-Sep-2023 **Revised:** 13-Oct-2023 **Accepted:** 16-Oct-2023

Corresponding author: Noppadon Chanpongsaeng
E-mail: doiji.fern@gmail.com
ผู้ติดต่อบทความ นพปฎล จันทร์ผ่องแสง
อีเมล doiji.fern@gmail.com

* Dentist, Senior professional level, Queen Sirikit National Institute of Child Health, Ratchathewi, Bangkok, Thailand
* ทันตแพทย์เชี่ยวชาญ สถาบันสุขภาพเด็กแห่งชาติมหาราชินี เขตราชเทวี จังหวัดกรุงเทพมหานคร ประเทศไทย

Introduction

Cleft lip and palate (CLP) is a congenital anomaly with a prevalence of 1.4:1000 newborns in Thailand.[1] From the time of birth, CLP patients require multidisciplinary and comprehensive treatment. The orthodontic treatment protocol for cleft patients starts with obturators in severe newborn cases, arch preparation for alveolar bone graft, and growth modification in mixed dentition. Finally, correction of all deformities by only orthodontic or combined orthodontic and surgical treatment is performed in adults.[2]

Because the maxilla is underdeveloped due to scars from several surgeries, timing is a crucial factor in promoting the growth of the maxilla. The growth status of a patient can be determined by many techniques that include Fishman's hand and wrist radiograph,[3] Baccetti et al.'s cervical vertebral maturation (CVM) method from a lateral cephalometric radiograph,[4] and the developmental stage of a third molar.[5] Although third molars are recognized to have variations in the crown and root development,[6] it was interesting because of its delayed development while other teeth have already matured.[7] Previous studies reported an association between the development of the mandibular third molars and the cervical vertebrae (CV) and the growth status in both non-cleft[8-10] and cleft patients.[11] Another study investigated the third molars in predicting chronological age.[12] Although many studies reported that CLP patients demonstrated delayed development of all permanent teeth, especially the teeth approximating the cleft sites,[13-18] some studies reported that the development of all teeth was normal.[19-21] Furthermore, various results were proposed by studies of CVM in CLP patients that showed delayed development[22-24] and accelerated development of CV.[25] Delayed CV development also affects the accuracy of CVM in identifying the patient's growth status. Even though race has been shown to affect the delayed development of the third molar[26] and CV,[27] no study has been performed in Thai patients. Therefore, the objective of this study was to compare the dental ages of the mandibular third molar and the CVM stages between Thai CLP and non-cleft patients.

Materials and methods

The study protocol was approved by the Ethics Committee of Queen Sirikit National Institute of Child Health (REC.042/2566). All lateral cephalometric radiographs (Vatech, USA, dosage 84 kVp, 9.00 mA) and panoramic radiographs were taken by the same x-ray machine (Vatech, USA, dosage 74 kVp, 9.00 mA) from January 2018 to January 2023.

The samples were divided into two groups: the cleft lip and palate group (CLP-G) and the non-cleft group (NC-G) as the control group. The sample size was calculated using the following formula according to Ngamjarus and Pattanittum,[28] where Z (0.975) = 1.96, σ = 3.0, and d = 0.5.

$$n = z(1 - \frac{\propto}{2})^2 \frac{\sigma^2}{d^2}$$

The calculation revealed that 139 CLP patients were required in this study. A total of 142 radiographs of CLP patients were obtained for the CLP-G, which were divided into six age groups of one-year intervals . Another 142 subjects for the NC-G were then selected according to age-sex matching to stratify the subjects with an equal number of sex and third molar (tooth 38 or 48). The collected data were divided into two parts: a study on the dental age of the mandibular third molars and a study on the maturation stage of the CV.

The inclusion criteria for the CLP-G were 1) complete unilateral or bilateral CLP patients, 2) either male or female aged 7-13 years old, 3) the presence of panoramic and lateral cephalometric radiographs taken on the same date, 4) no history of fixed orthodontic treatment in the mandibular arch, and 5) the presence of either or both left and right mandibular third molar (tooth 38 or 48) on the

panoramic radiographs. The inclusion criteria for the NC-G were 1) non-cleft male or female patients aged 7-13 years old, 2) skeletal Class I with normal maxilla, mandible, and their relationship, as showed by SNA (84 ± 3°), SNB (81 ± 3°), and ANB (3 ± 2°), otherwise the same inclusion criteria were used as 3) through 5) in the CLP group. The exclusion criteria for both groups were 1) an unclear outline of the mandibular third molar and CV from the second to fourth cervical vertebrae (C2-C4) and 2) a recognizable occlusal table of the mandibular third molar that indicated buccoversion or linguoversion of the tooth on the panoramic radiographs.

Development of the left mandibular third molar (tooth 38) from the panoramic radiographs was interpreted by two orthodontists into nine stages of tooth development (1, A, B, C, D, E, F, G, H) including stages A-H from the Demirjian guideline.[29] Stage 1 was added by the author to describe a stage with a radiolucent tooth bud. In the case of a missing tooth number 38, the right mandibular third molar (tooth 48) was evaluated instead. The nine stages (1, A, B, C, D, E, F, G, H) of tooth development were calculated into dental scores of 1, 2, 3, 4, 5, 6, 7, 8, and 9 respectively. Each score was put in an equation formulated by Duangto et al.[30] to predict the age of the third molar. The formula for each sex is different (Table 1). The mean values for all subjects in the CLP group (TCLP-G) and all subjects in the non-cleft group (TNC-G) were calculated from the mean values of the male and female groups. The statistical analysis was conducted within the age groups to compare the CLP-G with the NC-G (Table 2).

The same orthodontists also interpreted the stage of CVM in both groups using the guideline by Baccetti et al.,[4] which describes the maturation stages of the C2-C4 vertebrae in six cervical stages (CS1-CS6). The subjects were divided into age groups, according to Batwa et al.,[23] 7-10 years old and >10-13 years old, to observe the differences in the CVM. In the case of any radiographic interpretation disagreement, both orthodontists reviewed the interpretations until a consensus was reached.

One week after the data were recorded, 10% of the panoramic and lateral cephalometric radiographs (28 radiographs each) were re-interpreted by the same investigators. Interobserver and intraobserver reliability were analyzed with weighted kappa statistics. Descriptive statistics were used to report the distribution of subjects in groups divided into six age groups and six CVM stages. Mean values were used to report the dental age and chronological age of each sex and the whole study population. The Kolmogorov-Smirnov test showed a normal distribution at $P < 0.01$. The independent samples t-test was used to compare the differences in the third molar age of each age group, the chronological age of each CV stage, and the differences between the CLP and control groups.

Table 1 Formulas used for calculation of dental age of the third molars (teeth 38 and 48)

Gender	Tooth	Model
Male	38	$y = 7.648 + 0.753x_1 + 0.093\ x_1^2$
	48	$y = 7.535 + 0.799x_2 + 0.088\ x_2^2$
Female	38	$y = 6.421 + 1.256x_1 + 0.055\ x_1^2$
	48	$y = 6.522 + 1.243x_2 + 0.055\ x_2^2$

y = dental age, x_1 = development score for tooth 38, x_2 = development score for tooth 48

Table 2 Distribution of subjects allocated by age, sex, and mandibular third molar (tooth 38 or 48) in both the CLP-G and NC-G

Age group (years)	Gender	CLP-G			NC-G			Total (Sex)	Total (Age)
		38	48	Total	38	48	Total		
7 to 8	M	2	0	2	2	0	2	4	28
	F	12	0	12	12	0	12	24	
>8 to 9	M	13	2	15	13	2	15	30	60
	F	14	1	15	14	1	15	30	
>9 to 10	M	18	1	19	18	1	19	38	68
	F	14	1	15	14	1	15	30	
>10 to 11	M	12	2	14	12	2	14	28	52
	F	11	1	12	11	1	12	24	
>11 to 12	M	14	3	17	14	3	17	34	52
	F	9	0	9	9	0	9	18	
>12 to 13	M	8	0	8	8	0	8	16	24
	F	4	0	4	4	0	4	8	

CLP-G = cleft lip and palate group, NC-G = non-cleft group

Results

Interobserver and intraobserver reliability results were between 0.8-1.0, which demonstrated substantial agreement to almost perfect or perfect agreement. Table 2 shows the numbers of participants according to age, sex, and tooth number distributed into each group. The highest number of subjects in both groups (34 subjects, each) fell into the >9 to 10-year-old age group, while the age group with the least number of subjects (12 subjects, each) fell into the >12 to 13-year-old age group.

Table 3 shows the mean third molar age and chronological age by sex. The CLP-G and NC-G exhibited an older mean value of third molar ages than chronological ages. Meanwhile, most age groups in the NC-G showed older mean ages of the third molar than the CLP-G. However, the male CLP-G (MCLP-G) 7-8 years old and the female CLP-G (FCLP-G) >12-13 years old were older than the NC-G. Furthermore, the TCLP-G and TNC-G of ages >12-13 years showed an equal third molar age. Nevertheless, an independent samples t-test showed no statistical significance between the CLP-G and NC-G in all ages. However, the FCLP-G ($P < 0.01$) and TCLP-G ($P < 0.05$) of 7-8 years old showed a younger third molar age than the NC-G.

The data to compare CVM between the CLP-G and NC-G are shown in Table 4. A mode analysis of CVM staging revealed that the highest occurrences of CS3 were in the FCLP-G, MCLP-G, and TCLP-G of the 7- to 10-year-old group, which also accounted for 53.8% (42 subjects) and 59.0% (46 subjects) in the TCLP-G and NC-G, respectively. CS3 and CS4 were found at similar percentages of 37.5% (24 subjects) and 35.9% (23 subjects), respectively, in the TCLP-G of the >10- to 13-year-old group. In the NC-G, 45.3% of the subjects were found to be in CS3 (29 subjects). A comparison of the mean differences in the chronological ages between the CLP-G and NC-G are presented in Table 5. Significant differences were found at CS2 and CS4 between the TCLP-G and TNC-G at $P < 0.05$.

Table 3 Comparison of mandibular third molar dental age between the CLP-G and NC-G using the independent t-test

Age group (years)	CLP-G (Mean ± SD)			NC-G (Mean ± SD)			P-values (Between-group difference)		
	FCLP-G	MCLP-G	TCLP-G	FNC-G	MNC-G	TNC-G	Female	Male	Total
7-8									
Number (n)	12	2	14	12	2	14			
Chronological age (years)	7.68 ± 0.24	7.79 ± 0.06	7.68 ± 0.23	7.63 ± 0.23	7.75 ±0.35	7.64 ± 0.23			
3rd molar age (years)	7.85 ± 0.41	9.01 ± 0.73	8.02 ± 0.60	8.68 ± 0.70	8.49 ± 0.00	8.65 ± 0.60	0.002*	0.423	0.012**
>8-9									
Number (n)	15	15	30	15	15	30			
Chronological age (years)	8.48 ± 0.26	8.66 ± 0.24	8.57 ± 0.26	8.61 ± 0.33	8.69 ± 0.26	8.65 ± 0.29			
3rd molar age (years)	8.82 ± 1.54	9.22 ± 1.06	9.02 ± 1.30	9.11 ± 1.44	9.66 ± 1.00	9.38 ± 1.20	0.606	0.265	0.284
>9-10									
Number (n)	15	19	34	15	19	34			
Chronological age (years)	9.48 ± 0.32	9.53 ± 0.31	9.50 ± 0.31	9.61 ± 0.32	9.51 ± 0.25	9.55 ± 0.28			
3rd molar age (years)	9.94 ± 1.90	10.28 ± 1.60	10.13 ± 1.70	10.81 ± 2.40	10.73 ± 1.50	10.76 ± 1.90	0.281	0.381	0.156
>10-11									
Number (n)	12	14	26	12	14	26			
Chronological age (years)	10.44 ± 0.28	10.48 ± 0.21	10.46 ± 0.24	10.67 ± 0.29	10.64 ± 0.31	10.65 ± 0.30			
3rd molar age (years)	11.23 ± 2.02	11.23 ± 2.63	11.23 ± 2.20	12.44 ± 2.38	12.15 ± 1.60	12.28 ± 1.90	0.248	0.195	0.079
>11-12									
Number (n)	9	17	26	9	17	26			
Chronological age (years)	11.52 ± 0.22	11.57 ± 0.28	11.55 ± 0.26	11.56 ± 0.28	11.52 ± 0.27	11.54 ± 0.27			
3rd molar age (years)	12.76 ± 1.95	12.43 ± 1.54	12.55 ± 1.60	13.15 ± 1.81	12.80 ± 1.60	12.92 ± 1.00	0.667	0.501	0.418

Table 3 Continued

Age group (years)	CLP-G (Mean ± SD)			NC-G (Mean ± SD)			P-values (Between-group difference)		
	FCLP-G	MCLP-G	TCLP-G	FNC-G	MNC-G	TNC-G	Female	Male	Total
>12-13									
Number (n)	4	8	12	4	8	12			
Chronological age (years)	12.65 ± 0.17	12.42 ± 0.28	12.49 ± 0.27	12.29 ± 0.24	12.48 ± 0.40	12.42 ± 0.36			
3rd molar age (years)	13.64 ± 1.70	13.17 ± 1.13	13.32 ± 1.00	13.23 ± 0.84	13.36 ± 1.00	13.32 ± 1.20	0.682	0.721	0.993

CLP-G = cleft lip palate group, NC-G = non-cleft group, FCLP-G = female cleft lip palate group, MCLP-G = male cleft lip palate group, TCLP-G = total cleft lip palate group, FNC-G = female non-cleft group, MNC-G = male non-cleft group, TNC-G = total non-cleft group.
*P < 0.05, **P < 0.01

Table 4 Distribution of subjects allocated according to their cervical vertebral maturation stages CS1-CS6 in the CLP-G and NC-G allocated by age and sex

Age (years)	Group	Sex	CS1	CS2	CS3	CS4	CS5	CS6	Total (n)
7-10	CLP-G	M	7 (19.4)	11 (30.6)	17 (47.2)	1 (2.8)	0 (0.0)	0 (0.0)	36
		F	2 (4.8)	9 (21.4)	25 (59.5)	5 (11.9)	1 (2.4)	0 (0.0)	42
		Total	9 (11.5)	20 (25.6)	42 (53.8)	6 (7.7)	1 (1.3)	0 (0.0)	78
	NC-G	M	6 (16.7)	5 (13.9)	23 (63.9)	2 (5.6)	0 (0.0)	0 (0.0)	36
		F	1 (2.4)	12 (28.6)	23 (54.8)	4 (9.5)	2 (4.8)	0 (0.0)	42
		Total	7 (9.0)	17 (21.8)	46 (59.0)	6 (7.7)	2 (2.6)	0 (0.0)	78
>10-13	CLP-G	M	1 (2.6)	3 (7.7)	18 (46.2)	15 (38.5)	1 (2.6)	1 (2.6)	39
		F	0 (0.0)	2 (8.0)	6 (24.0)	8 (32.0)	5 (20.0)	4 (16.0)	25
		Total	1 (1.6)	5 (7.8)	24 (37.5)	23 (35.9)	6 (9.4)	5 (7.8)	64
	NC-G	M	0 (0.0)	3 (7.7)	22 (56.4)	12 (30.8)	1 (2.6)	1 (2.6)	39
		F	0 (0.0)	0 (0.0)	7 (28.0)	10 (40.0)	4 (16.0)	4 (16.0)	25
		Total	0 (0.0)	3 (4.7)	29 (45.3)	22 (34.4)	5 (7.8)	5 (7.8)	64

Data are presented as n (%) unless otherwise indicated.

Table 5 Comparisons of cervical vertebral maturation stage (CS1-CS6) between CLP-G and NC-G and sub-groups by independent t-test

CVM (stage)	CLP-G (Mean ± SD)			NC-G (Mean ± SD)			P-value		
	FCLP-G	MCLP-G	TCLP-G	FNC-G	MNC-G	TNC-G	Female	Male	Total
CS1									
Number (n)	2	8	10	1	6	7			
Chronological age (years)	9.20 ± 2.08	9.18 ± 1.20	9.20 ± 1.10	7.73 ± 0.00	9.39 ± 0.80	9.15 ± 0.99	0.667	0.697	0.945
CS2									
Number (n)	11	14	25	12	8	20			
Chronological age (years)	8.26 ± 0.98	9.23 ± 1.30	8.80 ± 1.20	9.34 ± 1.70	10.41 ± 1.80	9.77 ± 1.79	0.079	0.092	0.030 *
CS3									
Number (n)	31	35	66	30	45	75			
Chronological age (years)	10.05 ± 2.31	11.55 ± 1.70	10.85 ± 2.10	10.38 ± 2.20)	11.41 ± 1.90	11.00 ± 2.14	0.579	0.740	0.679
CS4									
Number (n)	13	16	29	14	14	28			
Chronological age (years)	10.48 ± 2.80	12.04 ± 1.90	11.35 ± 2.40	12.32 ± 2.40	12.84 ± 1.00	12.58 ± 1.85	0.082	0.164	0.037*
CS5									
Number (n)	6	1	7	6	1	7			
Chronological age (years)	12.45 ± 2.68	13.73 ± 0.00	12.64 ± 2.50	11.14 ± 3.20	13.74 ± 0.00	11.51 ± 3.13	0.464	-	0.472
CS6									
Number (n)	4	1	5	4	1	5			
Chronological age (years)	11.97 ± 2.05	12.15 ± 0.00	12.00 ± 1.70	13.23 ± 1.70	13.74 ± 0.00	13.33 ± 1.49	0.381	-	0.237

CLP-G = cleft lip palate group, NC-G = non-cleft group, CVM = cervical vertebral maturation, FCLP-G = female cleft lip palate group, MCLP-G = male cleft lip palate group, TCLP-G = total cleft lip palate group, FNC-G = female non-cleft group, MNC-G = male non-cleft group, TNC-G = total non-cleft group.
*P < 0.05

Discussion

A guideline has been widely used in assessing the age of the maxillary and mandibular third molars.[31-33] Following the guideline by Demirjian et al.,[29] initial mineralization of the third molar was reported to start at 8 years of age.[34] Therefore, the starting age of the subjects recruited in this study was 7 years old. From a previous study,[30] the left mandibular third molar was chosen for assessment because of greater accuracy in predicting the dental age than the contralateral tooth (tooth 48). The formulas used to calculate the dental age in this study were from the same study that also investigated mandibular third molars in a similar age range (8-23 years old).

The speed of dental development can be assessed by comparing the dental age between groups. After translating the third molar developmental stage into dental age, we found that most CLP-G showed younger dental ages than the NC-G within the same age group and sex. However, only FCLP-G and TCLP-G in the 7- to 8-year-old group showed statistical significance. The CLP-G tended to have delayed dental development compared to the NC-G, which agrees with the results from previous studies.[13-17] At the same chronological age, the CLP-G had a younger dental age, or slower development of the third molars compared to the NC-G.

Growth assessment is essential in planning the right treatment timing for CLP patients. Assessing the CVM is one method to evaluate a child's growth status, which was described in previous studies by Hassel and Farman[35] and Baccetti et al.[4] We chose the method by Baccetti et al., which classifies the stages of CVM in cervical vertebrae C2-C4 into six stages, because it has been extensively used in previous studies of CLP patients.[22-24] Another study stated that CS1 was the appropriate stage to start facemask therapy with rapid maxillary expansion because midface development would have the greatest response to treatment owing to an incomplete fusion of facial sutures. Furthermore, peak growth would be reached within two years.[36] One year after a child has reached CS2, the start of peak mandibular growth can be expected. Peak craniofacial growth can be anticipated at CS3. Some growth remains at CS4 but to a lesser extent than at CS3. At CS5 and CS6, most of the substantial growth has already passed, which makes it a suitable time to start orthodontic treatment for patients who require orthognathic surgery.[37]

The chronological ages between CLP-G and NC-G (CS1-CS6) were compared. At CS2 and CS4, TCLP-G was found to be 0.97 and 1.23 years younger than the TNC-G, respectively ($P < 0.05$), which meant the same maturation stage of CV in the CLP-G was reached at a younger age than the NC-G. A common practice to stimulate a forward movement of the maxilla in NC patients is done during CS1 and CS2, while movement of the mandible is done during CS3. Our findings indicated that orthodontists should be aware that CLP patients will reach CS2 and CS4 before non-cleft patients. Therefore, the optimal treatment period for the maxilla is at CS1 and CS2 and the mandible at CS3, which will also end faster. Orthodontists should discuss this issue with the patients and their guardians since the optimal time period is short and requires the best compliance possible to achieve the expected results. Despite that, other studies have reported conflicting results that were possibly caused by dissimilarity in race and sex, which was also found between the females[24] and males[22,23] in our study. Another study that investigated the Thai population of all sexes also found faster CV maturation in all maturation stages except for cervical vertebral maturation index stage 4 (CVMI 4).[25] The reason for inconsistency in the results could be different indexes used to evaluate the CVM and the age range of the participants in both cleft and non-cleft patients. A different growth index may result in a different growth status, which is why orthodontists should be aware of this variation. Other growth assessment methods should be used in addition to the CVM guideline, for example, the hand-wrist radiograph. Even so, the hand-wrist radiograph also

showed variation in CLP patients. One study reported an older bony age than the chronological age in females with unilateral CLP and a younger bony age than the chronological age in males with bilateral CLP.[38]

The limitation of this study was that the ages of the participants were quite young because the mission of Queen Sirikit National Institute of Child Health is to provide care to young children with complicated medical conditions. Treatment in CLP patients often starts at birth with an obturator, followed by nasoalveolar molding and orthodontic treatment preparation for alveolar bone graft. Most patients are treated at the age range recruited, which is 7-13 years old. A more comprehensive age range would result in more extensive results. This study was conducted at a single-center and the results cannot represent all cleft patients. Therefore, a multi-center study is recommended. A longitudinal study to explore the relationship between the mandibular third molar development and CVM is also recommended.

Conclusion

Compared to non-cleft patients, the FCLP-G and TCLP-G at 7-8 years old showed statistically significantly delayed development of mandibular third molars, and the TCLP-G showed a faster maturation of cervical vertebrae at CS2 and CS4.

References

1. Virarat P, Ritthagol W, Limpattamapanee K. Epidemiologic study of oral cleft in Maharatnakornratchasima hospital between 2005-2009. J Thai Assoc Orthod 2010(9):3-13.
2. Mercado AM, Vig KWL. Orthodontic principles in the management of orofacial cleft. In: Losee JE, Kirschner RE, editors. Comprehensive Cleft care. 2nd ed. New York: CRC Press; 2016. p.1253-98.
3. Fishman LS. Radiographic evaluation of skeletal maturation. A clinically oriented method based on hand-wrist films. Angle Orthod 1982;52(2):88-112.
4. Baccetti T, Franchi L, McNamara JA. The Cervical Vertebral Maturation (CVM) Method for the Assessment of Optimal Treatment Timing in Dentofacial Orthopedics. Semin Orthod 2005;11(3):119-29.
5. Mauricio-Vilchez C, Mauricio F, Vilchez L, Cadenillas A, Medina J, Mayta-Tovalino F. Radiographic Correlation of Skeletal Maturation Using the Stages of Dental Calcification in a Peruvian Population. Scientifica (Cairo) 2020;2020:4052619.
6. Lewis JM, Senn DR. Dental age estimation utilizing third molar development: A review of principles, methods, and population studies used in the United States. Forensic Sci Int 2010;201(1-3):79-83.
7. Sisman Y, Uysal T, Yagmur F, Ramoglu SI. Third-molar development in relation to chronologic age in Turkish children and young adults. Angle Orthod 2007;77(6):1040-5.
8. Cho SM, Hwang CJ. Skeletal maturation evaluation using mandibular third molar development in adolescents. Korean J Orthod 2009;39(2):120-9.
9. Felemban NH. Third Molar Maturation Stages in Correlation with Cervical Vertebra Maturation Stages in a Saudi Sample. Adv Dent & Oral Health 2017;5(5):555675.
10. Al-Balbeesi HO, Al-Nahas NW, Baidas LF, Bin Huraib SM, Alhaidari R, Alwadai G. Correlation between skeletal maturation and developmental stages of canines and third molars among Saudi subjects. Saudi Dent J 2018;30(1): 74-84.
11. Chongcharueyskul P, Wangsrimonkol T, Pisek P, Pisek A, Manosudprasit M. Correlations between Cervical Vertebral Maturation (CVM) and Dental Development in Thai Cleft Patients. J Med Assoc Thai 2015;98:S92-100.
12. De Salvia A, Calzetta C, Orrico M, De Leo D. Third mandibular molar radiological development as an indicator of chronological age in a European population. Forensic Sci Int 2004;146:S9-12.
13. Van Dyck J, Begnoni G, Willems G, Laenen A, Thevissen P, Verdonck A, et al. Dental development in patients with and without unilateral cleft lip and palate (UCLP): a case control study. Clin Oral Investig 2021;25(5):2619-31.
14. Hermann NV, Zargham M, Darvann TA, Christensen IJ, Kreiborg S. Early postnatal development of the mandibular permanent first molar in infants with isolated cleft palate. Int J Paediatr Dent 2012;22(4):280-5.
15. Bindayel NA, Alsultan M, Hayek SE, Almoammer K. Comparison between Chronological Age and Dental Ages of Saudi Patients with Cleft Lip and Palate. J Contemp Dent Pract 2019;20(5):603-8.

16. Hazza'a AM, Rawashdeh MA, Al-Jamal G, Al-Nimri KS. Dental development in children with cleft lip and palate: a comparison between unilateral and bilateral clefts. Eur J Paediatr Dent 2009;10(2):90-4.
17. Van Dyck J, Cadenas de Llano-Pérula M, Willems G, Verdonck A. Dental development in cleft lip and palate patients: A systematic review. Forensic Sci Int 2019;300:63-74.
18. Tan EL, Yow M, Kuek MC, Wong HC. Dental maturation of unilateral cleft lip and palate. Ann Maxillofac Surg 2012;2(2):158-62.
19. Topolski F, Souza RB de, Franco A, Cuoghi OA, Assunção LR da S, Fernandes Â. Dental development of children and adolescents with cleft lip and palate. Braz J Oral Sci 2014;13(4):319–24.
20. Borodkin AF, Feigal RJ, Beiraghi S, Moller KT, Hodges JS. Permanent tooth development in children with cleft lip and palate. Pediatr Dent 2008;30(5):408-13.
21. Thevissen PW, Alqerban A, Asaumi J, Kahveci F, Kaur J, Kim YK, et al. Human dental age estimation using third molar developmental stages: Accuracy of age predictions not using country specific information. Forensic Sci Int 2010;201(1-3):106-11.
22. Sun L, Li WR. Cervical vertebral maturation of children with orofacial clefts. Cleft Palate Craniofac J 2012;49(6):683-8.
23. Batwa W, Almoammar K, Aljohar A, Alhussein A, Almujel S, Zawawi KH. The Difference in Cervical Vertebral Skeletal Maturation between Cleft Lip/Palate and Non-Cleft Lip/Palate Orthodontic Patients. Biomed Res Int 2018;2018:5405376.
24. Sun L, Li WR. Cervical vertebral maturation of female children with orofacial clefts. Cleft Palate Craniofac J 2013;50(5):535-41.
25. Pisek P, Godfrey K, Manosudprasit M, Wangsrimongkol T, Leelasinjaroen P. A comparison of cervical vertebral maturation assessment of skeletal growth stages with chronological age in Thai between cleft lip and palate and non-cleft patients. J Med Assoc Thai 2013;96:S9-18.
26. Thevissen PW, Fieuws S, Willems G. Human third molars development: Comparison of 9 country specific populations. Forensic Sci Int 2010;201(1-3):102-5.
27. Soegiharto BM, Cunningham SJ, Moles DR. Skeletal maturation in Indonesian and white children assessed with hand-wrist and cervical vertebrae methods. Am J Orthod Dentofacial Orthop 2008;134(2):217-26.
28. Ngamjarus C, Chongsuvivatwong V, McNeil E. n4Studies: Sample Size Calculation for an Epidemiological Study on a Smart Device. Siriraj Med J 2016;68(3):160-70.
29. Demirjian A, Goldstein H, Tanner JM. A new system of dental age assessment. Hum Biol 1973;45(2):211-27.
30. Duangto P, Iamaroon A, Prasitwattanaseree S, Mahakkanukrauh P, Janhom A. New models for age estimation and assessment of their accuracy using developing mandibular third molar teeth in a Thai population. Int J Legal Med 2017;131(2):559-68.
31. Kasper KA, Austin D, Kvanli AH, Rios TR, Senn DR. Reliability of third molar development for age estimation in a Texas Hispanic population: a comparison study. J Forensic Sci 2009;54(3):651-7.
32. Streckbein P, Reichert I, Verhoff MA, Bödeker RH, Kähling C, Wilbrand JF, et al. Estimation of legal age using calcification stages of third molars in living individuals. Sci Justice 2014;54(6):447-50.
33. Soares CB, Figueiroa JN, Dantas RM, Kurita LM, Pontual Ados A, Ramos-Perez FM, et al. Evaluation of third molar development in the estimation of chronological age. Forensic Sci Int 2015;254:13-7.
34. Liversidge HM. Timing of human mandibular third molar formation. Ann Hum Biol 2008;35(3):294-321.
35. Hassel B, Farman AG. Skeletal maturation evaluation using cervical vertebrae. Am J Orthod Dentofacial Orthop 1995;107(1):58-66.
36. Franchi L, Baccetti T, McNamara JA. Postpubertal assessment of treatment timing for maxillary expansion and protraction therapy followed by fixed appliances. Am J Orthod Dentofacial Orthop 2004;126(5):555-68.
37. McNamara JA, McClatchey LM, Graber LW. Optimizing orthodontics and dentofacial orthopedics: treatment timing and mixed dentition therapy. In: Graber LW, Vanarsdall RL, Vig KWL, Huang GJ, editors. Orthodontics Current Principles and Techniques. 6th ed. St. Louis: Elsevier; 2017.p.403-36.
38. Bowers EJ. Growth in children with clefts: serial hand-wrist x-ray evidence. Cleft Palate Craniofac J 2011;48(6): 762-72.