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Original Article

Accuracy of Dental Calcification Stages in Predicting the Peak Pubertal Stage of Females

Maryam Mostafavi[1], Mohammed Hossein Razeghinejad[2], Saied Shahi[3], Elham Mortezapoor[3], Ahad Alizadeh[4], Roghieh Bardal[5]

[1]Urmia University of Medical Sciences Faculty of Dentistry, Department of Oral and Maxillofacial Radiology, Urmia, Iran
[2]Urmia University of Medical Sciences Faculty of Dentistry, Department of Orthodontics, Urmia, Iran
[3]Tabriz University of Medical Sciences Faculty of Dentistry, Tabriz, Iran
[4]Qazvin University of Medical Sciences, Medical Microbiology Research Center, Qazvin, Iran
[5]Qazvin University of Medical Sciences, Dental Caries Prevention Research Center, Department of Oral and Maxillofacial Radiology, Qazvin, Iran

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Main Points

- All four study teeth had high accuracy in predicting peak pubertal stage.
- The coinciding chance of peak pubertal stage with stage H in all studied teeth and with stage G in the second premolars and second molars was higher than in other stages.
- Stage G of the second molar is the best predictor of peak pubertal stage.

ABSTRACT

Objective: This study aimed to evaluate the accuracy of dental calcification stages in predicting the peak pubertal stage.

Methods: This retrospective study was conducted on panoramic and lateral cephalometric images of 406 female patients aged 9-14 years. The skeletal maturity and calcification stages of the mandibular canines, first premolars, second premolars, and second molars were determined using the Hassel-Farman and Demirjian (DI) methods, respectively. The prediction accuracy of the peak pubertal stage with the studied teeth was assessed using a receiver operating characteristic curve and the area under the curve (AUC). The DI stage of H was designated as the reference level, and Bayesian logistic regression analysis was used to assess the coinciding chance of each DI stage and peak pubertal stage.

Results: The AUC range of studied teeth was 0.84-0.92 in predicting peak pubertal stage (all $p<0.001$). In the canines and first premolars, the coinciding chance of peak pubertal stage and stage H was significantly higher than that in other stages [$p<0.05$, odds ratio (OR) ≤0.14]. In the second premolars and second molars, the chance of peak pubertal stage coinciding with stages H and G did not significantly differ ($p>0.05$); however, the chance of stage G coinciding with peak pubertal stage in the second molars was higher than in stage H (OR=4.59).

Conclusion: Stage H in all studied teeth and stage G in the second premolars and second molars predict peak pubertal stage with high accuracy. Considering that stage H is the end of tooth calcification stages and the accuracy of predicting stage G of second molar teeth is higher than the above stage, estimating the peak pubertal stage is recommended by the second case.

Keywords: Calcification, cervical vertebrae, puberty, tooth

Corresponding author: Roghieh Bardal, **e-mail:** r.bardal@yahoo.com
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INTRODUCTION

Developmental scheduling plays a vital role in orthopedic treatment outcomes for musculoskeletal disorders in developing patients.[1,2] The highest response to jaw functional appliances depends on their performance during the peak pubertal stage (PPS).[3,4] Chronological age is not a valid measure of growth, and biological age is more reliable. Bone maturity indices of the wrist and cervical vertebrae on radiographs are common methods for biological age definition.[5-7] The stages of dental development are considered a potential method to estimate skeletal age and can be examined from two aspects. The first is the eruption phases of the tooth, for which studies have shown a weak correlation between the eruption phases and skeletal maturation. The second is the dental calcification stage, which is a more reliable parameter. With a simple and reliable method based on the dental developmental stages, the routine use of panoramic and periapical radiography in most dental clinics can justify the evaluation of skeletal maturity without the need for additional radiographs, thus decreasing patient exposure according to the principle of as low as reasonably achievable principle.[2,5,8]

Most studies have shown a high correlation between the stages of tooth calcification and indicators of skeletal maturity.[1-3,5,6,8,9] However, some studies have shown a poor correlation.[10,11] To determine a reliable method instead of skeletal maturity, further studies with statistically more accurate methods than Pearson and Spearman's correlation coefficients are necessary. On the other hand, some studies have examined the relationship between the stages of dental calcification and PPS separately.[12] Therefore, despite evidence of a strong relationship between dental calcification and skeletal maturation, a practical recommendation based on dental calcification stages for PPS prediction is not possible.[12] This study aimed to assess the accuracy of dental calcification stages for predicting the peak pubertal growth stage compared with cervical vertebral maturation in females.

METHODS

This retrospective study involved panoramic and lateral cephalometric images of 406 female patients aged 9-14. According to the statistical power analysis, 5% of type one error, and Spearman's rank correlation tests, the sample size of the study (n=406) obtained 80% of the statistical power. The study protocol was approved by the Ethics Committee of Urmia University of Medical Sciences under the code IR.UMSU.REC.1397.420 and date 30.01.2019.

All panoramic and lateral cephalometric images were collected from the archives of orthodontic treatment centers. The inclusion criteria consisted of a) simultaneous preparation of both images (i.e., panoramic and lateral cephalograms), b) proper image quality, and c) the presence of all studied teeth. The exclusion criteria included a) radiographs of patients with a history of hormonal, developmental, and nutritional diseases, b) radiographs of patients with a history of trauma to the jaw and face, c) root canal treatment of the studied teeth, d) shape and size anomalies of the studied teeth, and d) history of orthodontic treatment. The images were saved in the Digital Imaging and Communications in Medicine format. All observations were performed using Romexis software (version 3.8.2) on a 14-inch LCD monitor (ASUS, China) with a resolution of 768 × 1366.

The calcification stages of the mandibular canines, first premolars, second premolars, and second molars were obtained by the Demirjian (DI) method on panoramic images (Figure 1).[13] In this method, there are eight stages of dental development:

- A: In single-rooted or multi-rooted teeth, the onset of calcification at the top of the crypt is observed as one or more inverted cones with no connections between them.
- B: By connecting the calcified areas, one or more cusps are formed, determining the morphology of the crown.
- C: Enamel formation is completed at the occlusal surface and extends to the cementoenamel junction (CEJ), the pulp chamber is formed, and dentin deposition begins.
- D: Crown formation is complete until CEJ, the pulp chamber becomes trapezoidal, and the roots begin to form.
- E: The formation of root divisions begins; nevertheless, the root is still shorter than the crown.
- F: The end of the root is funnel-shaped, and the length of the root is equal to or greater than that of the crown.
- G: The root canal walls are parallel, and the apex is open.
- H: The apex is completely closed, and the periodontal ligament has the same width around the apex and root.

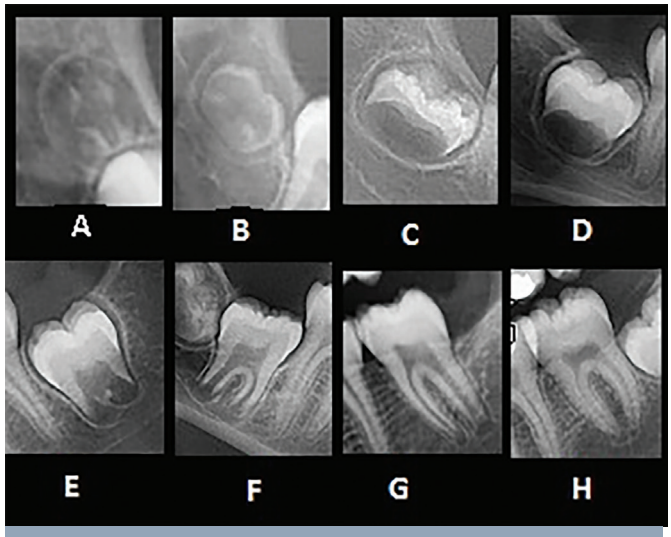

Figure 1. Demirjian (DI) tooth calcification stages: A, to H

The cervical vertebral maturation index (CVMI) for each patient was obtained by examining the morphology of the bodies of C2, C3, and C4 vertebrae on lateral cephalograms using the Hassel-Farman method[7] with no knowledge of the results of the dental calcification stage and without observing their panoramic images. (Figure 2). In this method, according to the presence or absence of concavity in the lower borders of the C2, C3, and C4 vertebrae and the difference in the shape of the body of the vertebrae, there are six stages:

• CVMI 1 (Initiation): The lower borders of C2, C3, and C4 are flat. The body shapes of C3 and C4 are trapezoidal, and their upper border converges from posterior to anterior.

• CVMI 2 (Acceleration): Concavity forms in the lower borders of C2 and C3, and the lower border of C4 remains flat. The shapes of the bodies of C3 and C4 are almost rectangular.

• CVMI 3 (Transition): A clear concavity is observed in the lower borders of C2 and C3, and a concavity is formed in the lower border of C4. The shapes of the C3 and C4 bodies are rectangular.

• CVMI 4 (Deceleration): A clear concavity is observed in the lower borders of C2, C3, and C4. C3 and C4 are close to square in shape.

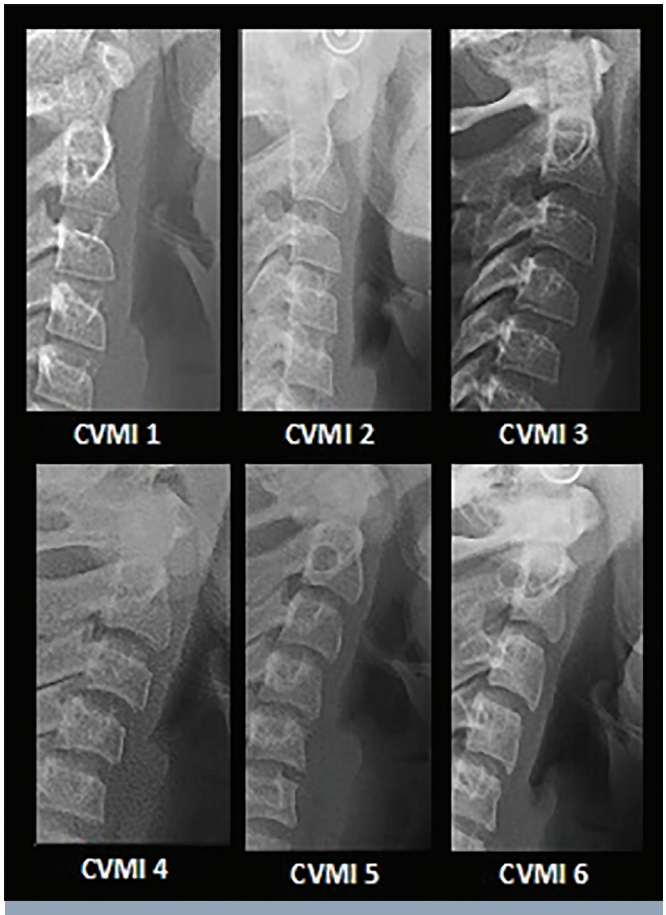

Figure 2. Cervical vertebral developmental stages, CVMI 1 to CVMI 6, proposed by Hassel-Farman
CVMI, cervical vertebral maturation index.

• CVMI 5 (Maturation): A clearer concavity is observed in the lower borders of C2, C3, and C4. The bodies of C3 and C4 are square.

• CVMI 6 (Completion): Deep concavity is observed in the lower borders of the C2, C3, and C4 vertebrae. The C3 and C4 bodies are vertical rectangles.

All observations were performed by an oral and maxillofacial radiologist with 14 years of experience. To ensure the reliability of the results and methods, 10% of the samples were examined 2 weeks later by the main observer (intra-observer) and an experienced orthodontist (inter-observer). ICC (CI 95%) in determining all stages of DI and CVMI was found as ≥0.942.

Statistical Analysis

Statistical analysis of data was performed using R software (version 3.6.3, Lucent Technologies, New Jersey, USA) and the "arm" package. Spearman's correlation coefficient was used to evaluate the correlation between DI stages and CVMI. The pre-pubertal stage was defined as the reference level. The coinciding chance of the PPS and DI stages was assessed using Bayesian logistic regression. For a more complete explanation, the science of statistics is generally divided into two concepts: classical and Bayesian. Most statistical methods in the classical concept require a large sample size and inference asymptotically. In contrast, methods based on the Bayesian concept are more efficient in small sample sizes. The Bayesian logistic regression method with a weak informative prior was used in this study to increase the robustness of the results. Multiple collinearity is a problematic case in statistical modeling, which is caused by the correlation of predictor variables. Performing multiple Bayesian logistic regression with the presence of correlated covariates leads to invalid results. In this study, univariate Bayesian models were used to avoid multiple collinearity problems. The DI stage of H was designated as the reference level because of the higher prevalence of the data. The first type error of 0.05 was considered to be a significance level. The prediction accuracy of the PPS for each tooth was evaluated in two steps. In the first step, PPS attainment probabilities were predicted. In the second step, the probability values were analyzed using the area under the curve (AUC).

RESULTS

The calcification stages of the canines were distributed in four stages from E to H, the first and second premolars in five stages from D to H, and the second molars in six stages from C to H (Table 1). Highest frequency of the DI stages in the CVMI 3 and 4 (i.e, PPS) was related to stage H of the canines, with the frequency of (75.3%) and (95.5%), respectively (Table 2). There was only one case of CVMI 6, and all four teeth were in stage H; therefore, these data were not included in Table 2.

The results of the Spearman test showed a good correlation between the DI stages of the studied teeth and CVMI.

Table 1. Distribution of stages of dental calcification with the Demirjian method

Stage	Number (%)			
	Canine	First premolar	Second premolar	Second molar
C	0 (0)	0 (0)	0 (0)	1 (0.2)
D	0 (0)	1 (0.2)	14 (3.4)	13 (3.2)
E	4 (1)	30 (7.4)	42 (10.3)	66 (16.3)
F	54 (13.3)	93 (22.9)	144 (35.5)	112 (27.6)
G	98 (24.1)	101 (24.9)	127 (31.3)	188 (46.3)
H	250 (61.6)	181 (44.6)	79 (19.5)	26 (6.4)
Total	406 (100)	406 (100)	406 (100)	406 (100)

Table 2. Distribution of DI stages of studied teeth with regard to CVMI stages, No. (%)

							CVMI, Number (%)
	CVMI 1 (Pre-pubertal)						**CVMI 1**
DI stage	C	D	E	F	G	H	
Canine	0 (0.0)	0 (0.0)	4 (5.9)	35 (51.5)	22 (32.4)	7 (10.3)	68 (16.7)
First premolar	0 (0.0)	1 (1.5)	27 (39.7)	34 (50.0)	6 (8.8)	0 (0.0)	
Second premolar	0 (0.0)	13 (19.1)	26 (38.2)	28 (41.2)	1 (1.5)	0 (0.0)	
Second molar	1 (1.5)	12 (17.6)	39 (57.4)*	16 (23.5)	0 (0.0)	0 (0.0)	
	CVMI 2 (Pre-pubertal)						**CVMI 2**
Canine	0 (0.0)	0 (0.0)	0 (0.0)	16 (18.2)	53 (60.2)	19 (21.6)	88 (21.7)
First premolar	0 (0.0)	0 (0.0)	3 (3.4)	47 (53.4)	29 (33.0)	9 (10.2)	
Second premolar	0 (0.0)	1 (1.1)	11 (12.5)	58 (65.9)*	16 (18.2)	2 (2.3)	
Second molar	0 (0.0)	1 (1.1)	25 (28.4)	54 (61.4)	8 (9.1)	0 (0.0)	
	CVMI 3 (Peak pubertal)						**CVMI 3**
Canine	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)	18 (22.2)	61 (75.3)*	81 (19.9)
First premolar	0 (0.0)	0 (0.0)	0 (0.0)	8 (9.9)	43 (53.1)	30 (37.0)	
Second premolar	0 (0.0)	0 (0.0)	2 (2.5)	33 (40.7)	37 (45.7)	9 (11.1)	
Second molar	0 (0.0)	0 (0.0)	2 (2.5)	34 (42.0)	45 (55.6)	(0)	
	CVMI 4 (Peak pubertal)						**CVMI 4**
Canine	0 (0.0)	0 (0.0)	0 (0)	1 (0.8)	5 (3.8)	127 (95.5)*	133 (32.6)
First premolar	0 (0.0)	0 (0.0)	0 (0)	4 (3.0)	23 (17.3)	106 (79.7)	
Second premolar	0 (0.0)	0 (0.0)	3 (2.3)	23 (17.3)	68 (51.1)	39 (29.3)	
Second molar	0 (0.0)	0 (0.0)	0 (0.0)	8 (6.0)	120 (90.2)	5 (3.8)	
	CVMI 5 (Post-pubertal)						CVMI 5
Canine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	35 (100)*	35 (8.5)
First premolar	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	35 (100)*	
Second premolar	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.7)	5 (14.3)	28 (80)	
Second molar	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	15 (42.9)	20 (57.1)	

*Represents the highest frequency of DI stages in each CVMI stage.
DI, Demirjian index; CVMI, cervical vertebral maturation index; No. (%), number (percent)

Table 3. Spearman correlation between CVMI stages and calcification stages of studied teeth

	Number (%)			
	Canine	First premolar	Second premolar	Second molar
Spearman correlation	0.732	0.793	0.716	0.847
p value	<0.001	<0.001	<0.001	<0.001

P value of 0.05 was considered to be a significance level
CVMI, cervical vertebral maturation index.

The highest correlation was related to the second molar (Table 3). Due to the high correlation between the DI stages of the studied teeth, leading to multicollinearity, multiple Bayesian logistic regression analysis results were not valid, and univariate analysis presented more acceptable and applicable results. The results of the univariate analysis (when each tooth was analyzed independently of the other teeth) are presented in Table 4.

In the canines and the first premolars, the coinciding chance of PPS and stage H was significantly higher than that in other stages [p<0.001, odds ratio (OR)≤0.14]. In the second premolars (p=0.14) and the second molars (p=0.09), there was no significant difference between stage G and stage H; however, the coinciding chance of the PPS and stage G of the second molars was insignificantly higher than stage H (OR=4.59) (Table 4).

According to the results of the receiver operating characteristic (ROC) analysis in Table 4 and the AUC in Figure 3, all four teeth had high accuracy in predicting PPS (AUC≥0.84, p<0.001). The highest prediction accuracy was related to the second molars (AUC=0.92, p<0.001).

DISCUSSION

In orthodontic patients, determining the skeletal maturity stage is of utmost importance before initiating developmental treatment. The common method used in this case is to examine the changes in the cervical vertebrae on lateral cephalograms. As panoramic radiography is a standard record before orthodontic treatment, it might reduce the need for additional radiographs if it is possible to determine the stage of skeletal maturation using panoramic views. This approach not only minimizes the patient's exposure to radiation but also reduces costs. The calcification stages of teeth, which can be examined through panoramic radiography, have shown a significant relationship with skeletal maturity indices in various studies.[1-3,5,6,8,9] Due to superimpositions in the maxillary area of panoramic radiographs, this study focused on examining mandibular canines, first premolars, second premolars, and second molars. DI was used to evaluate tooth calcification stages. According to Björk and Helm's[11] study, DI has the lowest inter-examiner and intra-examiner errors and exhibits the highest correlation with biological age. In orthodontic growth modification therapies, knowledge of the timing of the growth spurt is essential. The PPS occurs in CVMI 3 and 4, according to Baccetti et al.'s[4] study.[4]

One of the influential factors in the occurrence of growth mutations is gender.[13] According to studies, The PPS tends to start earlier in females, and the duration of puberty is generally shorter compared to males. Consequently, the timing of PPS holds greater clinical significance. In the present study, 74.3% of patients were in CVMI stages 2, 3, and 4, which are considered the most clinically important stages. This distribution indicates that the age range of 9-14

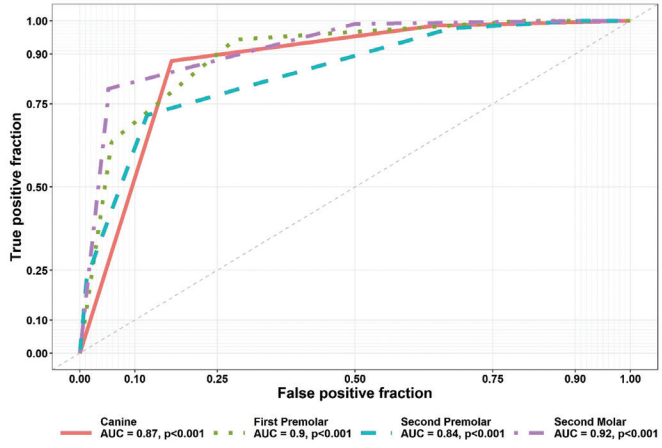

Figure 3. The surface area under the ROC curve for prediction of pubertal stage separately for each tooth
AUC, area under the curve; ROC, receiver operating characteristic.

Table 4. Bayesian logistic regression between DI stages and PPS

Tooth*		Univariate analysis			
		OR (95% CI)	p value	AUC	p value
Canine	F	0.009 (0.003,0.031)	<0.001	0.87	<0.001
	G	0.045 (0.025,0.084)	<0.001		
First premolar	F	0.012 (0.005,0.028)	<0.001	0.9	<0.001
	G	0.147 (0.07,0.311)	<0.001		
Second premolar	E	0.01 (0.003,0.039)	<0.001	0.84	<0.001
	F	0.045 (0.015,0.138)	<0.001		
	G	0.432 (0.137,1.358)	0.148		
Second molar	E	0.008 (0.001,0.068)	<0.001	0.92	<0.001
	F	0.141 (0.025,0.782)	0.026		
	G	4.599 (0.787,27.136)	0.093		

*The "H" stage was set as a reference category, stages without data were not entered in the table
P value of 0.05 was considered to be a significance level.
AUC, area under the curve; OR, odds ratio; CI, confidence interval; DI, Demirjian index; PPS, peak pubertal stage.

years was appropriately selected for the study. The accuracy of the studied teeth in predicting PPS was high (AUCs≥0.84, all p<0.001), and the second molars exhibited the highest accuracy. While there was no statistically significant difference between stages H and G in the second premolar and second molar (p>0.05); the chance of stage G coinciding with PPS in the second molar was higher than that of stage H (OR>1). As a result, stage H of the studied teeth and stage G of the second premolars and second molars were found to coincide with PPS with high accuracy.

Spearman's correlation coefficient was more than 0.7 for the studied teeth; with the highest coefficient being 0.847, observed in the second molar. Various studies have employed Spearman's correlation coefficient to establish the relationship between DI stages, skeletal maturity,[2,3] and PPS.[14-18] The results of these studies indicate a robust association between DI stages and skeletal maturation, aligning with the findings of this study. However, it's important to note that high Pearson and Spearman's correlation coefficients only indicate a strong relationship between the two variables and do not imply that the values obtained by both methods are identical. Therefore, studies such as Valizadeh et al.'s[8], Lopes et al.'s[1], and Rebouças et al.[19] utilized ordinal logistic regression models as a more accurate statistical method to designate the DI stages as indicators of pubertal stage. Nevertheless, due to the frequent occurrence of zero values in the early DI stages, the use of their data is prone to sparsity bias[20] leading to higher OR values than reality. On the other hand, the PPS stage cannot be evaluated separately, or it is impossible to analyze the relationship between individual DI stages and PPS with this analysis. Consequently, all three studies resorted to using the data frequency distribution to investigate this relationship.

Perinetti et al.[21] and Toodehzaeim et al.[22] investigated the diagnostic ability of the DI stages of the mandibular second molar to identify the pre-pubertal, pubertal, and post-pubertal stages using positive likelihood ratio (PLR) analysis with a threshold of ≥10 for satisfactory performance. Despite the high correlation coefficient between DI stage and skeletal maturity, they found DI stages reliable only for identifying the post-pubertal stage. In general, regression analysis is a stronger statistical method than PLR because of the PLR results' dependency on sample size. The PLR (sensitivity/1-specificity) requires a 2 × 2 table; the CVMI is considered the gold standard; each DI stage is considered the exposed cases, and the other stages are considered the unexposed cases.

Due to the sequence of calcification stages, the obtained PLR will not show the actual value. Nevertheless, the present study analyzed the data with the PLR analysis to compare with the above-mentioned study; the PLR of the DI stages in determining the pubertal stage was calculated with a confidence interval of 95%. Because stage H was the most frequent, stage H was considered the reference level (PLR=1), and PLR≥10 was considered clinically significant. 1<PLR<10 means that stage H predicts the stage of puberty better than the desired DI stage, however, the difference between stage H and the DI stage was not clinically significant. The results showed that, stage H in second premolars and second molars predicts PPS significantly better than stages E [$PLR_{second\ premolar}$ (CI 95%) =20.53 (5.14, 82.05); $PLR_{second\ molar}$ (CI 95%) = 46.20 (6.33, 336.94)] and F [$PLR_{second\ premolar}$ (CI 95%) = 20.53 (5.14, 82.05); $PLR_{second\ molar}$ (CI 95%) =10.08 (1.28, 79.40)]. Stage G in the second molars [PLR (CI 95%)=0.40 (0.05, 2.98)] predicts PPS non-significantly better than stage H. The difference between these results and results of Perinetti et al.'s[21] and Toodehzaeim et al.'s[22] studies could be attributed to the sample size. According to Spearman's correlation coefficients, univariate Bayesian logistic regression analysis, and ROC and PLR analyses, the second molar G stage has the highest chance of coincidence with PPS.

CONCLUSION

The H stage of the studied teeth estimates the peak pubertal stage with high accuracy; however, considering the end stage of the H stage and the higher prediction accuracy of the G stage of the second molar teeth, PPS estimation is more practical in the latter case.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Urmia University of Medical Sciences under the code IR.UMSU.REC.1397.420 and date 30.01.2019.

Informed Consent: Retrospective study.

Author Contributions: Concept - M.M.; Design - E.M.; Supervision - M.M.; Data Collection and/or Processing - S.S.; Analysis and/or Interpretation - A.A.; Literature Review - M.H.R.; Writing - R.B.; Critical Review - R.B.

Declaration of Interests: All authors declare that they have no conflict of interest.

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