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Comparative effectiveness of cervical vertebral maturation and hand-wrist radiography in assessing bone age in patients with amelogenesis imperfecta: a retrospective analysis

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Abstract

Objective Amelogenesis imperfecta (AI) is a hereditary enamel disorder whose potential impact on skeletal development remains unclear. Accurate assessment of skeletal maturation is essential for optimizing treatment timing in these individuals. This study aimed to investigate the agreement between cervical vertebral maturation (CVM) and hand-wrist radiography (HWR) in determining skeletal age in patients with AI.

Methods This retrospective study included 28 AI patients (16 females, 12 males; mean age: 9.65 ± 2.92 years) and 30 age- and sex-matched healthy controls. This retrospective study analyzed 58 participants: 28 patients with AI (16 females, 12 males; mean age 9.65 ± 2.92 years) and 30 healthy controls matched for age and sex (15 females, mean age 10.4 ± 2.09 years and 15 males, mean age 10.93 ± 2.4 years). Skeletal maturation was assessed via CVM stages from lateral cephalometric radiographs and Björk's hand-wrist maturation stages. For comparative analysis, Björk's nine stages were condensed into five developmental categories. Agreement between methods was evaluated via weighted kappa statistics. Gender-based subgroup analyses and intermethod correlations were also performed. Statistical significance was set at $p < 0.05$.

Results Moderate agreement was observed between the CVM and HWM stages in both groups (AI group: $\kappa = 0.440$; control group: $\kappa = 0.556$; total: $\kappa = 0.525$; $p < 0.05$). The lowest agreement was found among males with AI ($\kappa = 0.221$; $p < 0.05$), whereas the highest agreement occurred among control group males ($\kappa = 0.623$; $p < 0.05$). Despite moderate overall agreement, the findings suggest possible discrepancies in skeletal maturation assessment among AI patients, particularly in male subgroups.

Conclusion The CVM and HWM methods demonstrated moderate overall agreement in assessing skeletal age. However, the reduced agreement in male AI patients indicates the need for careful interpretation of skeletal

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maturation in this subgroup. The results highlight the importance of using both methods complementarily to optimize growth assessment and treatment planning in AI patients.

Keywords Amelogenesis imperfecta, CVM, Maturation

Introduction

Amelogenesis imperfecta (AI) is a hereditary form of enamel dysplasia characterized by quantitative and qualitative defects in the enamel structure [1]. Its prevalence varies from 1:700 to 1:14,000, according to population studies [2]. Although numerous studies have focused on dental anomalies and maturation patterns in patients with AI, skeletal development in these individuals remains largely unexplored [3, 4]. However, accurate assessment of skeletal maturation and remaining growth potential is critical for determining the ideal timing of orthodontic or orthopedic interventions.

Amelogenesis imperfecta is a genetically determined disorder primarily affecting enamel formation; however, increasing evidence suggests that it may also be associated with systemic alterations, including growth hormone irregularities and altered bone metabolism. These systemic effects may influence skeletal development and maturation patterns. For this reason, evaluating skeletal maturation methods specifically in patients with amelogenesis imperfecta is clinically important, as growth assessment findings derived from healthy populations may not always be directly applicable to this unique group.

Traditionally, hand-wrist radiographs have been considered the gold standard for assessing bone age and are based on the ossification stages of the hand and wrist bones [5–7]. Several studies have demonstrated a strong correlation between hand-wrist maturation (HWM) and cervical vertebral maturation (CVM) stages, with reported correlation coefficients ranging between $r = 0.80$ and $r = 0.95$ [8–10]. The CVM has gained popularity as an alternative to the HWM because of its ability to estimate skeletal age via routine lateral cephalograms, thus avoiding additional radiation exposure. Nevertheless, concerns have been raised regarding its interobserver reliability, particularly in subjective stage determination [11].

Recently, objective formula-based CVM methods have been developed to improve the reproducibility and accuracy of skeletal age assessment [12, 13]. Studies conducted in different populations have demonstrated high agreement between CVM-derived skeletal age and the Tanner-Whitehouse 3 (TW3) method, which is based on hand-wrist radiographs [12, 14].

In AI patients, dental age has been reported to be consistent with chronological age [15]; however, limited information is available regarding their skeletal maturation status. The absence of studies exploring possible

skeletal development delays or discrepancies in this group represents a significant gap in the literature. Such discrepancies, if present, could lead to misinterpretation of growth potential and suboptimal treatment timing.

Although amelogenesis imperfecta primarily affects enamel formation, increasing evidence suggests that it may also be associated with systemic conditions and altered growth patterns, indicating that its effects may extend beyond the dentition [3, 16].

Recent systematic reviews and meta-analyses have confirmed a generally good correlation between cervical vertebral maturation and hand-wrist radiography in healthy populations; however, variability between methods still exists, particularly in specific patient groups [17].

Although cervical vertebral maturation and hand-wrist radiography have been widely compared in healthy pediatric populations, their agreement has never been specifically investigated in patients with amelogenesis imperfecta [18]. Unlike the general population, children with AI may present with systemic conditions such as growth hormone irregularities and altered bone metabolism, which could influence their overall growth and skeletal maturation [19, 20]. For this reason, assuming that skeletal maturation patterns in AI patients follow the same trajectory as those of healthy individuals may be misleading. Exploring potential differences in this unique population is therefore essential not only to justify the present study but also to ensure accurate growth assessment and optimal timing of orthodontic treatment in patients with amelogenesis imperfecta.

A comprehensive review of the literature revealed no prior comparative analyses of CVM and HWM for skeletal maturation assessment in AI patients. The findings of this study will contribute to optimizing treatment planning and may help reduce unnecessary radiographic exposure in this patient population.

This study aimed to investigate the agreement between cervical vertebral maturation (CVM) and hand-wrist radiography (HWR) in determining skeletal age in patients with AI. The null hypothesis is that there is no significant difference between cervical vertebral maturation (CVM) and hand-wrist radiography methods in assessing bone age in patients with amelogenesis imperfecta.

Materials and methods

Ethical approval for this retrospective study was granted by the Ethics Committee of Istanbul University (Approval No: 2023/27), ensuring compliance with the principles

of the Declaration of Helsinki. Prior to data collection, a priori power analysis was conducted via G*Power software (version 3.1.9.2) to determine the minimum required sample size. The analysis indicated that at least 26 participants per group were necessary to achieve a statistical power of 80% at a significance level of $\alpha = 0.05$. This calculation guided the recruitment process and ensured that the study was adequately powered to detect clinically meaningful differences between the groups.

Eligible patients who presented to the Department of Pediatric Dentistry at Aydın University were retrospectively screened for inclusion. The diagnosis of amelogenesis imperfecta (AI) was confirmed through a combination of clinical evaluation and radiographic findings, such as reduced enamel thickness, taurodontism, and short root morphology observed on panoramic radiographs. For the purpose of this investigation, patients with different AI subtypes were analyzed collectively, without stratification into subgroups, to obtain a representative cohort.

The participants were allocated into two study groups: the AI group ($n=28$) and an age- and sex-matched healthy control group ($n=30$) with no systemic or craniofacial anomalies. Although the number of participants in the control group was slightly higher than that in the AI group, matching was based on age and sex distribution rather than strict numerical equivalence. This difference reflects the retrospective nature of the study and the limited availability of eligible AI patients compared with the larger pool of healthy controls in the archives.

The inclusion criterion was individuals between 6 and 14 years of age, a developmental period characterized by active craniofacial and skeletal growth. Preexisting diagnostic records, including both hand-wrist radiographs and lateral cephalometric radiographs, were retrieved from the archives and used for skeletal maturation assessment.

Skeletal maturation was assessed via both hand-wrist radiographs and cervical vertebral maturation (CVM) via lateral cephalometric radiographs. CVM stages were determined on the basis of the morphology of the second, third, and fourth cervical vertebrae (C2, C3, and C4), following the method described by Baccetti et al.

[21]. Hand-wrist radiographs were evaluated according to the nine developmental stages defined by Björk et al. [19], which reflect the ossification and maturation of the wrist and hand bones.

For comparative analysis between the two methods, the nine Björk stages were condensed into five stages, as proposed by Hoseini et al. [20]. This simplified staging system allows for effective comparisons while preserving key developmental markers.

Cervical vertebral maturation (CVM) was assessed on lateral cephalometric radiographs according to the method described by Baccetti et al., based on the morphological changes of the second, third, and fourth cervical vertebrae (C2–C4). The evaluation was performed by observing the progressive development of concavities at the inferior borders of the vertebral bodies and the changes in vertebral body shape from trapezoidal to rectangular and square forms.

For statistical comparison with the CVM stages and to ensure methodological compatibility between the two systems, Björk's original nine stages were condensed into five developmental stages (A–E) according to the modification proposed by Hoseini et al. [20]. The Hoseini modification condenses Björk's nine radiographic indicators into five clinically meaningful developmental phases by focusing on epiphyseal widening, capping, and fusion in the phalangeal, metacarpal, and radial growth plates. Each phase corresponds to a major biological growth period, ranging from prepubertal status to full epiphyseal union, thereby allowing direct comparison with CVM stages.

The conversion of Björk's stages into the Hoseini classification is presented in Table 1.

All radiographs were independently assessed by two calibrated researchers (İŞ, ED). Both researchers underwent standardization training for the measurement procedures prior to data collection. All radiographs were independently evaluated by two calibrated examiners (İŞ, ED). For intraobserver reliability assessment, the first examiner re-evaluated all radiographs after a two-week interval under identical conditions. For interobserver reliability assessment, all radiographs were independently analyzed by the second examiner. Intra- and interobserver agreement was assessed using the intraclass correlation coefficient (ICC). The intra- and interobserver reliability analyses demonstrated excellent agreement.

The correlations between skeletal maturation stages assessed by the hand-wrist and CVM methods were statistically analyzed, and comparisons between the AI and control groups were performed.

Statistical methods

Statistical analyses were performed using SPSS software (version 29.0; IBM Corp., Armonk, NY, USA).

Table 1 Condensation of Björk's hand-wrist maturation stages into five developmental stages according to Hoseini et al

Hoseini Stage	Corresponding Björk Stages	Clinical Growth Period
A	Björk 1–2	Prepubertal
B	Björk 3	Early pubertal
C	Björk 4–5	Peak pubertal growth
D	Björk 6–7	Late pubertal
E	Björk 8–9	Growth completion

The distribution of continuous variables (chronological age) was assessed using the Shapiro–Wilk test to determine conformity with normality assumptions. Variables that showed normal distribution were analyzed using independent-samples *t*-tests, whereas non-normally distributed variables would have been analyzed using the Mann–Whitney *U* test. Sex distribution between groups was compared using the chi-square test.

Agreement between the cervical vertebral maturation (CVM) stages and the hand–wrist maturation stages was evaluated using the contingency coefficient and weighted kappa statistics. Interpretation of kappa values followed Altman’s classification system [22].

Interobserver and intraobserver reliability for CVM scoring were assessed using Intraclass Correlation Coefficients (ICC), calculated using a two-way mixed-effects model with absolute agreement (ICC(3,1)), which is appropriate for fixed raters evaluating all samples. ICC values were reported with 95% confidence intervals and interpreted according to established thresholds for reliability.

Descriptive statistics (mean, standard deviation, and frequency distributions) were used to summarize demographic characteristics and maturation stages. The significance level was set at $\alpha = 0.05$ for all statistical tests.

Results

A total of 58 patients were included in the current study. The amelogenesis imperfecta (AI) group consisted of 28 patients, including 16 females (mean age: 10.19 ± 3.12 years) and 12 males (mean age: 9.00 ± 2.62 years). The control group comprised 30 patients, with 15 females (mean age: 10.40 ± 2.09 years) and 15 males (mean age: 10.93 ± 2.40 years). Independent-samples *t*-test demonstrated no statistically significant difference in chronological age between the AI and control groups ($p = 0.257$). This confirms that baseline age distribution was comparable between groups. Chi-square analysis showed no significant difference in sex distribution between the AI and control groups ($p = 0.586$), confirming that gender matching was successfully achieved. Subgroup analyses conducted separately for males and females demonstrated no significant age differences between the AI and control groups for either sex (male: $p = 0.176$; female:

Table 2 Demographic characteristics of the study population

Variable	AI group	Control group	<i>p</i> -value
Age, years (mean \pm SD)	9.63 \pm 2.97*	10.67 \pm 2.25*	0.257†
Age – Females (mean \pm SD)	10.19 \pm 3.12	10.40 \pm 2.09	0.501‡
Age – Males (mean \pm SD)	9.00 \pm 2.62	10.93 \pm 2.40	0.176‡
Sex, n (%)			0.586§
Female	16 (57.1%)	15 (50.0%)	
Male	12 (42.9%)	15 (50.0%)	

*Group mean values calculated based on provided female and male subgroup means

†Independent-samples *t*-test for overall age comparison

‡Independent-samples *t*-test for age comparison within sex subgroups

§Chi-square test for sex distribution

$p = 0.501$), confirming that age matching was achieved across both genders (Table 2).

Intraobserver reliability for Observer 1 showed an ICC of 0.972 (95% CI: 0.952–0.983), while Observer 2 demonstrated an ICC of 0.978 (95% CI: 0.963–0.987). Interobserver agreement between the two observers was also excellent, with an ICC of 0.972 (95% CI: 0.952–0.983). All ICC values were statistically significant ($p < 0.001$), indicating highly consistent and reproducible measurements across and within observers.

The distributions of patients across the cervical vertebral maturation (CVM) stages and Björk hand–wrist maturation stages for both groups are presented in Tables 3 and 4.

The agreement between the CVM and Björk stages was moderate for both groups (AI group: $\kappa = 0.440$, SE = 0.112; control group: $\kappa = 0.556$, SE = 0.101; $p < 0.001$) (Table 5).

The overall kappa coefficient for the entire study population was $\kappa = 0.525$ (SE = 0.074) ($p < 0.001$), reflecting a moderate level of agreement according to Altman’s classification. (Table 5)

Table 6 presents the gender-based kappa statistics for both the AI and control groups. The highest agreement was observed among male participants in the control group ($\kappa = 0.623$, $p < 0.05$), indicating good agreement. Conversely, male participants in the AI group demonstrated significantly lower agreement ($\kappa = 0.221$, $p < 0.05$), corresponding to a fair agreement category.

Table 3 The frequency distribution of the maturation stage of hand and wrist bones in the amelogenesis imperfecta and control groups

Interval	AI group		Control group		Total number	Total Percentage
	Number	Percentage	Number	Percentage		
A	20	66.6	10	33.4	30	51.8
B	0	0	4	100	4	6.89
C	2	18.18	9	81.82	11	18.9
D	1	20	4	80	5	8.62
E	5	62.5	3	37.5	8	13.79

Table 4 The frequency distribution of CVMS in the amelogenesis imperfecta and control groups

Interval	AI group		Control group		Total number	Total Percentage
	Number	Percentage	Number	Percentage		
1	13	46.4	10	33.4	23	39.65
2	8	28.5	8	26.6	16	27.58
3	1	3.57	9	30	10	17.24
4	2	7.14	3	10	5	8.62
5	4	14.39	0	0	4	6.91

Table 5 Kappa coefficient between the hand-wrist bone maturation stage and CVMS score in both groups

	Kappa measurement	Asymptotic Standard Error	Approximate T	Approximate Significance
AI Group	0.44	0.112	4.847	<0.001
Control Group	0.556	0.101	5.583	<0.001
Total	0.525	0.074	7.772	<0.001

Table 6 Kappa coefficient between the hand-wrist bone maturation stage and CVMS in both groups across genders

	AI group		Control group	
	Female (n = 16)	Male (n = 12)	Female (n = 15)	Male (n = 15)
Kappa measurement	0.538	0.221	0.474	0.623
P value	<0.001	0.021	<0.001	<0.001

Discussion

Understanding when a patient reaches key stages of skeletal growth is fundamental for making the right treatment decisions in orthodontic treatment. In particular, for children with developmental conditions such as amelogenesis imperfecta (AI), skeletal growth assessment becomes crucial. Traditionally, hand-wrist radiography has been accepted as the most reliable method for assessing skeletal age [5]. However, with increasing concerns about radiation exposure, especially in young patients, the cervical vertebral maturation (CVM) method has gained popularity as a safer, more convenient alternative since it relies on lateral cephalograms often taken for orthodontic purposes [8, 10].

In our study, we aimed to explore whether CVM provides results comparable to those of the classic hand-wrist method in children with AI—a group whose skeletal development remains poorly understood. Overall, we found moderate agreement between the two methods, both in AI patients and in healthy controls ($\kappa = 0.525$). These findings echo those of previous studies that reported a relatively strong correlation between CVM and hand-wrist assessments, although the two are not entirely interchangeable [8, 9].

When the results were evaluated deeply at the subgroup level, particularly by sex, male AI patients showed

considerably lower agreement between the CVM and hand-wrist assessments than the other groups did ($\kappa = 0.221$), whereas healthy males actually showed the highest agreement ($\kappa = 0.623$). This suggests that for boys with AI, skeletal maturation might not follow typical patterns, standard assessment tools may not reflect the real developmental status, and findings should be reinforced with alternative assessment methods such as hand wrist radiographies. Although statistically significant, the reduced agreement in this subgroup may be partially explained by the smaller sample size of males in the AI group ($n = 12$) than females ($n = 16$).

Although AI is mainly known as a condition affecting enamel, the possibility that it may subtly influence broader skeletal development cannot be ignored. Research, such as that by Santos et al. [14, 15], reported that dental age tends to align with chronological age in AI patients. However, our results suggest that skeletal age—assessed with standard tools—may not be so straightforward, especially for boys.

In some AI patients, we observed that cervical vertebral maturation reflected more advanced developmental stages, whereas hand-wrist assessments indicated earlier skeletal development, suggesting ongoing growth potential. Therefore, relying solely on CVM in these individuals may lead to premature conclusions regarding growth completion. In contrast, CVM assessments in the control group demonstrated greater consistency, supporting their reliability in healthy individuals. This discrepancy in AI patients may be partially explained by altered growth patterns, possibly influenced by systemic factors such as growth hormone dysregulation [23, 24].

Therefore, relying solely on cervical vertebral maturation assessment may not be sufficient for accurate growth evaluation in patients with amelogenesis imperfecta, and complementary assessment methods such as hand-wrist radiography should be considered, especially in male patients.

The lower agreement observed in male patients compared with females may be partly related to well-known differences in growth patterns and the timing of pubertal maturation between the sexes. In general, boys tend to experience a later but more pronounced pubertal growth spurt than girls, which can result in greater variability in skeletal maturation findings within the same age range

[25, 26]. In this context, the relatively wide age range included in the present study may have contributed to the observed sex-related differences and may also help explain the reduced concordance found in male patients with amelogenesis imperfecta.

From a clinical standpoint, this finding indicates that growth-modifying orthodontic treatments in male patients with amelogenesis imperfecta should be planned with particular caution, and the combined use of multiple skeletal maturity indicators may help to avoid inaccurate treatment timing.

Another factor to consider is the method itself. While the CVM is practical, it is not without limitations. Its subjective nature has been criticized for leading to inconsistent results, even among trained professionals [11]. Despite careful calibration in our study, the reduced agreement—most notably in male AI patients—highlights that relying solely on the CVM might not be ideal in every case.

Fortunately, more objective, formula-driven approaches to CVM have emerged in recent years, showing promise in improving accuracy and consistency [12]. Future studies applying these methods specifically to AI patients could help clarify whether the variability we observed reflects genuine biological differences or if it is simply a matter of how the measurements are being made.

From a clinical standpoint, these findings serve as a reminder that no single method is perfect—especially for unique patient groups such as those with AI. Using both CVM and hand-wrist assessments together and interpreting the results carefully appear to be the most reliable strategy to avoid mistiming growth-related interventions, which is further supported by a 2025 study reporting that the combined use of CVM and hand-wrist staging enhances the accuracy of skeletal age estimation in forensic applications [27].

Limitations

While this study offers valuable early insight into how skeletal maturation may differ in AI patients, several limitations should be considered when interpreting the results. First, our sample size was relatively small, especially within the male AI subgroup, which may have affected both the statistical power and the variability we observed. This limited number of male AI patients is due to the rarity of amelogenesis imperfecta, which makes recruiting large and balanced study groups challenging. Second, because of the retrospective nature of the study, we could not follow patients over time to track their growth patterns more comprehensively.

Another limitation of the present study is that some maturation stages contained zero observations in certain groups (e.g., hand-wrist maturation stage B in the AI group and CVM stage 5 in the control group), which may

have influenced the interpretation of stage distribution and agreement analyses.

Finally, even though we followed strict calibration protocols, the CVM staging method we used is still largely based on visual interpretation, which naturally carries some degree of subjectivity.

Conclusion

This study demonstrated moderate overall agreement between the cervical vertebral maturation (CVM) and hand-wrist maturation (HWM) methods for assessing skeletal age in both amelogenesis imperfecta (AI) patients and healthy controls. However, male AI patients showed notably reduced agreement between the two methods, suggesting that skeletal maturation patterns in this subgroup may deviate from typical growth trajectories. Given these findings, clinicians should exercise caution when relying solely on CVM for growth assessment in AI patients—particularly in males—and consider the complementary use of both CVM and HWM to increase diagnostic accuracy. Further prospective research with larger sample sizes and objective CVM assessment techniques is recommended to clarify the biological and methodological factors underlying these discrepancies and to optimize growth-related treatment planning in AI.

Abbreviations

AI	Amelogenesis Imperfekta
CVM	Cervical vertebra Maturation
HWM	Hand wrist maturation

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Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by authors. The first draft of the manuscript was written by I.Ş. and E.D. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval for this retrospective study was obtained from the Ethics Committee of Istanbul University (Approval No: 2023/27), and all procedures were conducted in accordance with the principles of the Declaration of Helsinki. As only anonymized retrospective data were used, the requirement for individual consent to participate was waived by the Ethics Committee.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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