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Prevalence of Crown Resorption in Amelogenesis Imperfecta due to Junctional Epidermolysis Bullosa

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ABSTRACT

Introduction: Junctional epidermolysis bullosa (JEB) is a rare genetic disease manifesting with skin and mucosal blistering. As part of the JEB, patients present with syndromic amelogenesis imperfecta (AI). Reports have described external crown resorption (ECR) in the teeth of patients with JEB, but its prevalence is unknown.

Objective: To determine the prevalence of ECR in patients with JEB.

Methods: A longitudinal retrospective cohort study was performed at the Special Care Dentistry Clinic, University of Chile. Clinical records of patients with JEB between 2005 and 2024 were analysed. Prevalence of ECR per patient, per type of tooth and per tooth was calculated.

Results: Of the 20 patients examined, 90% presented ECR in at least one tooth, with an average of 4.8 primary and 6.8 permanent teeth affected. The most affected type of teeth were the incisors. 57.5% of primary incisors and 68% of permanent incisors had resorption. The most affected tooth was #82 in primary dentition (75%) and #32 in the permanent dentition (88.9%).

Conclusions: The prevalence of ECR in patients with AI due to JEB caused by variants in *LAMB3* was 90%. Establishing clinical and radiographic dental protocols for the early detection of ECR is essential to prevent extensive tooth destruction.

1 | Introduction

Epidermolysis bullosa (EB) is a rare genetic disease characterised by blistering of skin and mucosal membranes as a manifestation of a disruption in the basement membrane zone (BMZ). EB is classified into four types: EB simplex (EBS), junctional EB (JEB), dystrophic EB (DEB) and kindler EB (KEB) (Has, Bauer, et al. 2020). The incidence of JEB in the United States has been described as 2.68 per 1 million live births, while its reported prevalence has been 0.49 per 1 million population (Fine 2016).

JEB is caused by biallelic recessive variants in one of the seven genes that encode for structural proteins of the lamina lucida in the BMZ (*LAMA3, LAMB3, LAMC2, ITGA6, ITGB4, ITGA3* and *COL17A1*). Clinically, nine different subtypes are recognised. The two major subtypes are severe JEB, associated with early lethality in the first 6–24 months of life, and intermediate JEB, which can be associated to variants in the genes coding laminin 332 and type XVII collagen (Has, Bauer, et al. 2020). *LAMB3* encodes for the laminin subunit beta 3 of the protein Laminin 332 and is responsible for all cases of JEB

in Chile (Fuentes et al. 2017). It has been reported that 100% of the patients diagnosed with JEB present abnormal dental enamel, representing a syndromic amelogenesis imperfecta (SAI) (Bardhan et al. 2020; Gostyńska et al. 2017). Patients with JEB can present different phenotypes of syndromic AI, such as generalised enamel hypoplasia or pitted and fissured enamel (Wright, Johnson, and Fine 1993). Crown resorptions, delayed eruption, agenesis, taurodontism and pulp calcifications are some of the dental anomalies that coexist within AI (Collins et al. 1999). External crown resorption (ECR) related to AI has been reported, but its aetiology is yet to be elucidated (Morrier et al. 2008; Urzúa et al. 2021; Lee et al. 2011; Lindemeyer, Gibson, and Wright 2010).

The aim of this study was to determine the prevalence of ECR per patient, per type of tooth and per tooth in the Chilean cohort of JEB between 2005 and 2024, based on clinical and radiographic findings.

2 | Materials and Methods

This longitudinal cohort study was performed at the Special Care Dentistry Clinic, University of Chile, Santiago, Chile, in association with DEBRA Chile (2005–2024). A retrospective analysis of dental records, clinical pictures and radiographs available from 2005 to 2024 was performed by three clinicians during a series of diagnostic meetings (S.K., S.V. and C.B.) to reduce the risk of bias. This convenience sample included all patients diagnosed with JEB living in Chile, who attended the Faculty of Dentistry, University of Chile (FOUCH), national reference centre for EB, for assessment and clinical treatment between 2005 and 2024. Ethical approval was obtained from the University of Chile (FOUCH, 2015/02 and 2023/13) and informed consent was obtained from patients or legal tutors.

Inclusion criteria: patients with a genetic diagnosis of JEB living in Chile between 2005 and 2024, who had at least one tooth partially or fully erupted during clinical assessment (photographic register or clinical examination) and/or adequate radiographic assessment. Edentulous patients, deceased patients without photographic or radiographic registers and patients without consent were excluded from the study.

2.1 | Clinical-Radiographic Diagnostic Criteria for ECR

A. Unerupted tooth with a radiographic image compatible with coronary resorption. That is to say, successive radiological controls show a tooth cavity with sharp radiographic limits whose size increases over time.

B. Partially erupted tooth with gingival tissue adhered to the tooth (it is not possible to separate with the periodontal probe) and radiographic image compatible with coronary resorption.

C. Erupted tooth described as a tooth cavity with regular edges and a hard surface, but not related to caries. For example, incisors with semilunar incisal loss. Ideally, a radiographic image compatible with crown resorption.

All teeth assessed clinically were coded: 0 = absence of ECR; 1 = presence of ECR; or NE = not evaluated, when it was not possible to diagnose. The codes used for radiographic assessment were as follows: 0 = absence of ECR; 1 = presence of ECR, described as a radiolucent area with defined edges in the crown surface, not related to caries, including semilunar edges in anterior teeth (Figures 1a–g and 2a–d); and NE = not evaluated

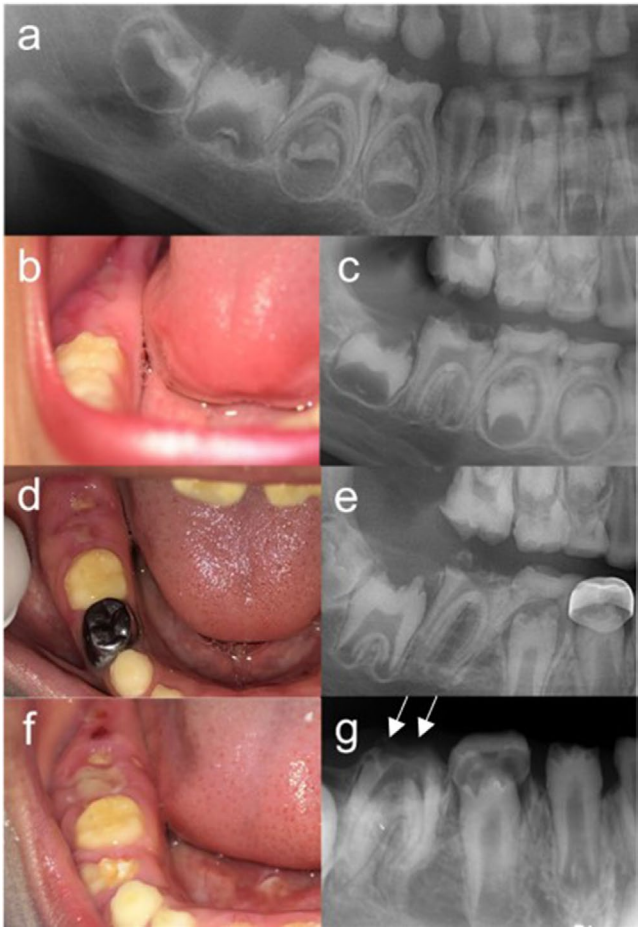

FIGURE 1 | Long-term radiographic and clinical follow-up of external crown resorption on the first right lower molar (#46) of a patient with junctional epidermolysis bullosa and amelogenesis imperfecta. (a) Radiographic image of Patient 16 showing unerupted #46 at the age of 4 years and 7 months: complete crown formation. No contrast between enamel and dentin can be seen, compatible with generalised hypoplastic syndromic AI. (b) Same patient at the age of 7 years, 5 months: clinical image shows very early signs of eruption. (c) Radiographic image at 7 years, 10 months showing resorption of the unerupted mesial cusps. (d) Clinical picture at the age of 9 years: The molar does not erupt; the gingival tissue looks fibrous. (e) Radiographic image at the age of 9 years and 6 months showing severe crown resorption. (f) Clinical picture at the age of 9 years and 11 months, fibrotic gingival tissue in the area of tooth #46, that has not erupted. (g) Radiographic image at 10 years old, complete crown resorption of tooth #46. Only a thin layer of dentin covers the pulp chamber: 'perichamberal resorption-resistant sheet' (white arrows). Radicular dentin is unaffected.

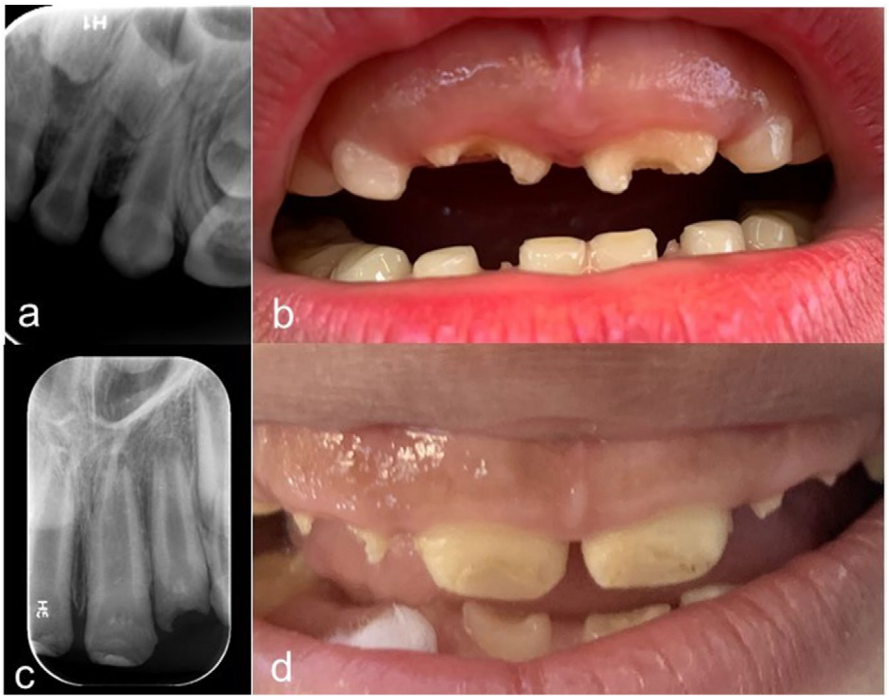

FIGURE 2 | Long-term radiographic and clinical follow-up of external crown resorption on the central and lateral incisors resulting in semilunar edges on a patient with junctional epidermolysis bullosa and amelogenesis imperfecta. (a) Periapical radiograph of primary teeth 63 and 62 of patient 16 at the age of 4 years and 7 months: The incisal edges of the upper permanent incisors 21 and 22 have a normal shape. (b) Same patient at the age of 8 years, 4 months: Clinical image shows crown resorption of both central incisors, with a semilunar shape. (c) Periapical radiograph taken at the age of 9 years and 6 months showing restored edge of central incisor 21 and external crown resorption (ECR) of unerupted lateral incisor 22. (d) Clinical picture at the age of 11 years: 22 erupting with a semilunar edge due to ECR.

(unerupted teeth, uncooperative behaviour, not possible to assess). The final diagnosis was established by combining clinical and radiographic assessments. A descriptive statistical analysis of the sample was carried out, including absolute and relative frequency, central tendency (average) and dispersion (range). We used Excel software version 2021 (Microsoft) to manage the data. The report follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (von Elm et al. 2007) reporting guideline for cohort studies.

3 | Results

3.1 | Sample Description

From 2005 to 2024, a total of 32 patients with JEB were registered at Debra Chile. Of those, 20 patients were included in the study: 17 were assessed while having primary teeth in their mouths and 11 while having permanent teeth. All presented recessive variants in the *LAMB3* gene. The subtypes of JEB in the cohort were as follows: intermediate JEB1A (OMIM #226650): 10 patients; and severe JEB1B (OMIM #226700): 10 patients (Table 1). Considering the clinical and radiographic diagnoses of these 20 patients, a total of 482 teeth were analysed. Twelve patients were excluded from the study: 5 were edentulous at the time of the first examination and passed away prior to the second examination (age of death range 4–16 months, average 10 months) and 7 died before the first examination (age of death range 3–25 months, average 8 months).

3.2 | Prevalence of Crown Resorption per Patient

On clinical examination, 13 of 16 patients with primary teeth (81.3%) presented ECR in at least one tooth. The average number of teeth affected was 4.6, ranging from 0 to 12. While all 11 patients with permanent teeth (100%) presented ECR in at least one tooth, the average number of teeth affected was 5.5, ranging from 1 to 9.

On radiographic examination, 10 of 13 patients with primary teeth (76.9%) presented ECR in at least one tooth, with an average of 3 affected teeth per patient (range 0–6). On permanent teeth, all 8 patients (100%) presented radiographic signs of ECR in at least one tooth. The average number of affected teeth was 8.3, ranging from 4 to 13.

Combining the clinical and radiographic findings, the prevalence of ECR per patient was 90% ($n = 18/20$) (Table 2).

3.3 | Prevalence of Crown Resorption per Type of Tooth

In primary teeth, the incisors were the most affected type of teeth, with an ECR prevalence of 57.5%, followed by canines and molars, with a prevalence of 30.6% and 1.2%, respectively. Similarly, in permanent teeth, the most affected type of teeth were also the incisors, with 68%, followed by canines (28.1%), molars (12.5%) and premolars (10.9%) (Figure 3a,b). In molars

TABLE 1 | Patients' characterisation.

Patient ID	Age of examination		Sex	Subtype of JEB	Gene affected	*LAMB3* pathogenic variants at coding DNA level	Type of AI	Affected teeth
	First	Last						
1	8 mo	3 y	Female[d]	Severe JEB	*LAMB3*	c.823-1G>A/c.3228+1G>A	Generalised hypoplastic AI	52, 51, 61, 62, 71, 81
2	9 mo	13 y	Female	Severe JEB	*LAMB3*	c.823-1G>A/c.3228+1G>A	Generalised hypoplastic AI	61, 71, 81, 82, 13, 12, 11, 23, 28, 33, 32, 42
3	10 mo	10 mo	Female[d]	Severe JEB	*LAMB3*	c.282G>A/c.3228+1G>A	Generalised hypoplastic AI	51, 61
4	10 mo	3 y	Male	Intermediate JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	51, 71, 81, 82
5	10 mo	8 y	Male	Intermediate JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	51, 61, 72, 71, 81, 82, 83, 12, 11, 21, 26, 32, 31, 41, 42, 44
6	1 y	1 y	Male	Severe JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	—
7	1 y	1 y	Female[d]	Severe JEB	*LAMB3*	c.2975delT/c.3228+1G>A	Generalised hypoplastic AI	72, 71, 81
8	1 y	1 y	Female[d]	Severe JEB	*LAMB3*	c.823-1G>A/c.3228+1G>A	Generalised hypoplastic AI	—
9	1 y	2 y	Female	Intermediate JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	52, 51, 61, 72, 71, 81, 82, 83
10	1 y	2 y	Female	Intermediate JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	53, 52, 51, 61, 62, 63, 73, 72, 71, 81, 82, 83
11	1 y	13 y	Male	Intermediate JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	61, 72, 82, 14, 12, 11, 21, 22, 24, 33, 32, 31, 41, 44
12	1 y	16 y	Male	Intermediate JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	52, 51, 61, 62, 72, 13, 12, 21, 22, 33
13	2 y	4 y	Female	Intermediate JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	51, 61, 73, 72, 81, 82
14	2 y	5 y	Male[d]	Severe JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	31, 62, 72
15	3 y	10 y	Female[d]	Severe JEB	*LAMB3*	c.957_958dup77/c.3228+1G>A	Generalised hypoplastic AI	55, 62, 72, 82, 11, 21, 36, 46
16	4 y	12 y	Female	Intermediate JEB	*LAMB3*	c.939C>A/c.973T>C	Generalised hypoplastic AI	82, 12, 11, 21, 22, 34, 32, 31, 41, 42, 46
17	7 y	7 y	Female[d]	Intermediate JEB	*LAMB3*	c.3268del5/c.3228+1G>A	Generalised hypoplastic AI	11, 32, 42
18	7 y	9 y	Female	Severe JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	73, 12, 11, 21, 22, 32, 41
19	11 y	14 y	Male	Severe JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	11, 21, 37, 33, 32, 31, 41, 42, 43
20	22 y	27 y	Female[d]	Intermediate JEB	*LAMB3*	c.3228+1G>A	Generalised hypoplastic AI	22

Note: If only one variant is indicated, then it is homozygous; mo: months; y: years; d: deceased.

TABLE 2 | Prevalence of external crown resorption in patients with junctional epidermolysis bullosa and amelogenesis imperfecta.

	Clinical diagnosis		Radiographic diagnosis		Combined clinical and radiographic diagnosis	
	Prevalence per patient (number of patients)	Average teeth affected per patient (range)	Prevalence per patient (number of patients)	Average teeth affected per patient (range)	Prevalence per patient (number of patients)	Average teeth affected per patient (range)
Primary teeth	81.3% ($n = 13/16$)	4.6 (0–12)	76.9% ($n = 10/13$)	3 (0–6)	88.2% ($n = 15/17$)	4.8 (0–12)
Permanent teeth	100% ($n = 11/11$)	5.5 (1–9)	100% ($n = 8/8$)	8.3 (4–13)	100% ($n = 11/11$)	6.8 (1–13)
Overall prevalence per patient	94.7% ($n = 18/19$)	7 (0–15)	100% ($n = 14/14$)	7.5 (0–15)	90% ($n = 18/20$)	7.8 (0–19)

with advanced resorption a 'perichamberal resorption-resistant sheet' (Figure 1g) could be seen.

3.4 | Prevalence of Crown Resorption per Tooth

Combining clinical and radiographic findings, 13 of the 20 primary teeth presented ECR. The lower right lateral incisor (#82) presented the highest prevalence of ECR (75%), followed by the lower left lateral incisor (#72), presenting a prevalence of 71.4%. No evidence of ECR was found in teeth #54, #64, #65, #75, #74, #84 and #85. On the other hand, 24 of the 32 permanent teeth presented ECR in at least one case. The highest prevalence (88.9%) was observed in the lower left lateral incisor (#32), followed by the upper right central incisor (#11), with a prevalence of 80%. No evidence of ECR was found in teeth #18, #17, #15, #25, #27, #38, #47 and #48 (Figure 4a,b).

4 | Discussion

The present study highlights the high prevalence of external crown resorption in patients with generalised hypoplastic syndromic AI due to JEB caused by variants in *LAMB3*. In our cohort, ECR was present in 90% of the 20 patients examined, more precisely, in all 11 patients whose permanent teeth were examined (100%). ECR was diagnosed by combining clinical and radiographic findings, the latter being very important during the eruptive process. The average number of teeth affected per patient, combining clinical and radiographic diagnosis, was 4.8 in primary teeth and 6.8 in permanent teeth. Incisors were the most affected type of tooth, both in primary and permanent teeth. The highest prevalence was shown on the primary lower lateral incisors (right 75%, left 71.4%) and in permanent teeth; more than 70% of the examined lower lateral incisors and upper central incisors presented crown resorption.

4.1 | Type of AI

ECRs have been described both in isolated and syndromic AI (Urzúa et al. 2021; Lindemeyer, Gibson, and Wright 2010). Comparing our data to the available literature is difficult, as no studies on the prevalence of ECR in AI have been found by the authors. It is possible, however, to compare the newly obtained data to the previously described case reports. Korbmacher, Lemke, and Kahl-Nieke (Korbmacher, Lemke, and Kahl-Nieke 2007) reported one patient with isolated generalised hypoplastic AI and crown resorption/radiolucencies on at least 6 permanent teeth with different degrees of severity. This number of teeth affected is very similar to the 6.8 average obtained in our study. Lindemeyer, Gibson, and Wright (Lindemeyer, Gibson, and Wright 2010) reported the case of a 9-year-old patient with isolated hypoplastic AI and unerupted first permanent molars. The radiographic evaluation showed ECR of teeth #16, #26 and #46. In Lee et al. (2011) published the case of a 12-year-old male patient with X-linked isolated hypoplastic AI due to variant in *AMELX* in whom clinical examination revealed 9 posterior permanent teeth with crown resorptions. These two examples, with 3 and 9 teeth affected, reflect the range of teeth that can be affected in different patients. In our cohort, the range of affected

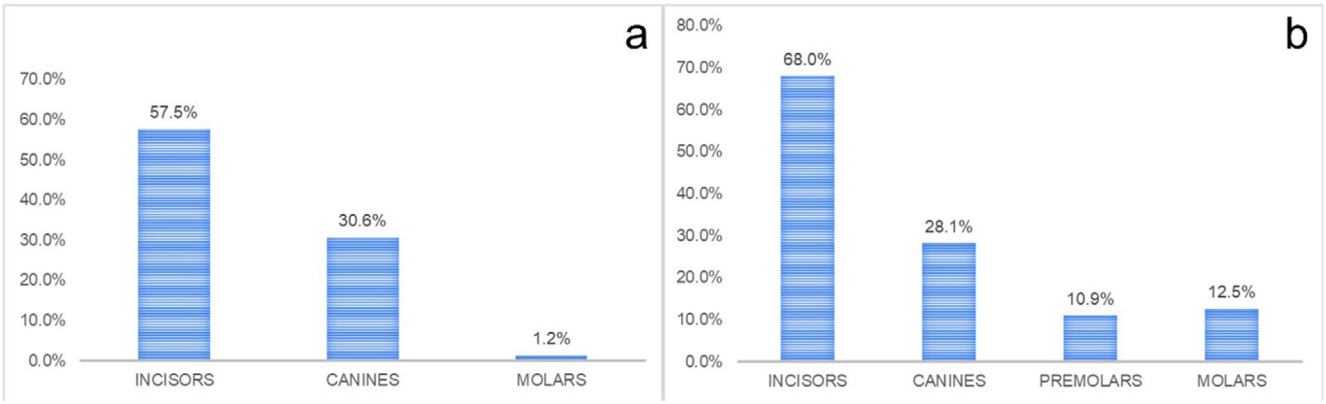

FIGURE 3 | Prevalence of external crown resorption (ECR) per tooth type. (a) Bar chart describing the prevalence of ECR per tooth type in the primary dentition (incisors/canines and molars). (b) Prevalence of ECR per tooth type in the permanent dentition (incisors/canines/premolars and molars).

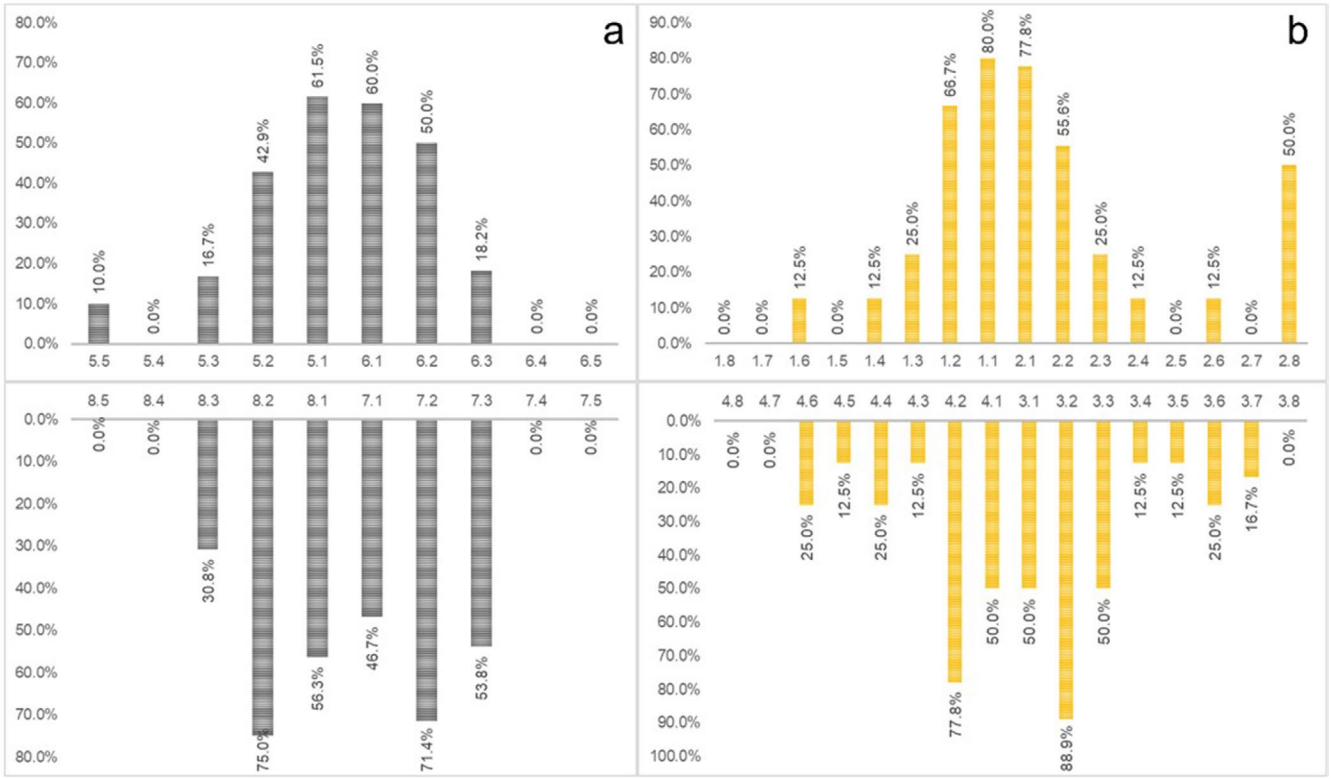

FIGURE 4 | Prevalence of external crown resorption (ECR) per tooth. (a) Bar chart describing the prevalence of ECR per tooth in the primary dentition (all upper and lower teeth). (b) Prevalence of ECR per tooth in the permanent dentition (all upper and lower teeth).

teeth combining clinical and radiographic diagnosis was 1–13. Reports of ECR in syndromic AI include the cases reported by Urzúa et al. (2021) describing ECR in a patient with generalised hypoplastic AI due to JEB; and Morrier et al. (2008) reporting ECR on the permanent mandibular first molars on a 10-year-old patient with syndromic hypoplastic AI and pseudoxanthoma elasticum. Another condition presenting with syndromic AI is enamel renal syndrome (OMIM # 204690), caused by recessive variants in *FAM20A*. Dental phenotype includes severe enamel hypoplasia affecting both primary and permanent dentition, with semi lunar shapes of the upper central incisors, delayed eruption and ECR as associated feature, similar to the findings of the present study (De La Dure-Molla et al. 2014).

Noteworthy, all patients included in our cohort and all patients reported in the previous paragraph presented a generalised hypoplastic type of AI. Bhatia, Hunter, and Ashley (2015) on the other hand, reported three patients with coronary resorption: two with hypoplastic AI and one with hypocalcified AI. In all cases, asymptomatic permanent molars were covered by hyperplastic gingiva.

JEB is a rare skin blistering disease caused by recessive pathogenic variants in one of the genes codifying proteins of the lamina lucida: *LAMA3*, *LAMB3*, *LAMC2*, *COL17A1*, *ITGB4* and *ITGA3* (Has, Bauer, et al. 2020). The clinical presentation of AI varies among patients with JEB into two main groups: (1)

generalised, rough pitted enamel hypoplasia and (2) generalised thinning and/or furrowing of the enamel (Wright, Johnson, and Fine 1993). The distribution of affected genes varies in different countries. In Germany, the most commonly altered genes are *LAMB3*, *COL17A1* (Has, Liu, et al. 2020), and while in Brazil, pathogenic variants for JEB have been found in the genes *LAMB3*, *LAMC2* and *COL17A1* (Mariath et al. 2019). In our study, all participants presented variants in the *LAMB3* gene, coinciding with the molecular epidemiology study by Fuentes et al. (2017) carried out with data between 1998 and 2015 in Chile. Considering this important fact, the prevalence of ECR should be explored in larger, multicentric studies in patients with (i) different types of AI, and (ii) AI due to variants in other genes; to establish precise phenotype–genotype correlations.

4.2 | Type of Teeth

On anterior teeth, ECR is presented clinically as a tooth with a semilunar edge. In the pre-eruptive phase, this can be diagnosed with radiographs. During the eruption process, a conical fragment of the tooth first erupts into the mouth, later resulting in the tip of a semilunar edge (Reference: article under review). This can be easily identified on clinical examination; however, it is often diagnosed as an abnormal shape and not recognised as the result of a resorptive process and therefore underdiagnosed. Our cohort presents a high prevalence of affected incisors (57.5% in primary and 68% in permanent teeth). The literature is scarce in describing this type of resorption, which can be explained by the underdiagnosis (de La Dure-Molla et al. 2019).

4.3 | Differential Diagnosis

The main differential diagnosis of ECR is dental caries and tooth structural anomalies. Time of diagnosis is important. ECR occurs mainly during pre-eruptive and peri-eruptive stages, while the enamel is in close contact with gingival tissue. In partially erupted teeth with ECR, it is important to differentiate the soft tissue on the crown from a gingival polyp on a tooth with caries. It is important to emphasise that in teeth with coronary resorption, the gingival tissue is strongly adhered to the dental crown, and the radiograph shows a tooth cavity with clear limits, unlike caries, in which a gradient of radiolucency is seen. Radiographic follow-up allows identification of changes in the tooth shape and radiopacity (Abbott and Lin 2022).

During the eruption process, the posterior teeth with ECR are covered with a fibrous gingival tissue, and eruption is delayed. In the anterior teeth, a conical fragment emerging into the cavity is observed, making the differential diagnosis with caries simple. At later ages, the differential diagnosis becomes more challenging, as severely broken posterior teeth can be misdiagnosed with caries, and anterior teeth suffer attrition, with a smoothing of the semilunar shape of the incisal edge. On the other hand, on restored teeth, a differential diagnosis is challenging, as clinicians only get to see the sequelae of the diseases but do not have the full clinical information to establish a diagnosis.

The differential diagnosis with tooth structural anomalies, such as Hutchinson's teeth, can be established based on a series of radiographs. Teeth with structural anomalies do not change their shape during the eruption process, while in ECR the tooth begins with a normal crown shape and loses mineralised tissue during eruption (de La Dure-Molla et al. 2019).

4.4 | Time of Diagnosis

The present study demonstrates that ECR takes place during the eruption process and can be diagnosed with imaging studies before the teeth emerge into the mouth. During our study, a 10-month-old patient had a periapical radiograph taken when a conical fragment of the primary lower right central incisor became visible. Periapical radiographs confirmed the diagnosis of ECR and allowed the finding of severe ECR with complete crown resorption of the crown in two other unerupted incisors. This radiographic finding allowed development of a specific treatment plan to protect and preserve the integrity of the affected teeth. Therefore, although taking x-rays in young children is complex, protocols should be proposed to obtain an accurate and early diagnosis.

4.5 | Radiographic Techniques

Radiographs analysed in our study included bisecting and paralleling periapical radiographs, bite-wings, orthopantomographs (OPG) and cone-beam computed tomographies (CBCT). Generally, the radiograph of choice for detecting dental resorptions (cervical or root) is the periapical radiograph (Lima et al. 2016). Within the periapical techniques, as the type of resorption presented in this article affects the crown and not the cervical and root areas, our team highly suggests preferring the paralleling technique over the bisecting-angle technique, as the former allows a better view of the proximity of the resorptive lesion and the pulp chamber.

Once the resorptive lesion is detected, periapical techniques are inaccurate for determining the location, nature and severity of the resorption (Lima et al. 2016). For this reason, several authors recommend the use of CBCT once the lesion is detected to determine crucial parameters for the success of the treatment, such as extension and proximity to the pulp chamber (Lima et al. 2016; Gunst et al. 2013; Chen, Huang, and Deng 2021). As a standard of care, due to radiation and costs, CBCT can not be requested at every follow-up appointment. However, we recognise that there are cases in which conventional x-rays do not have sufficient sensitivity to detect ECR. In the present study, we had patients in whom OPG showed no ECR, and CBCTs taken at the same time revealed several resorptive lesions.

4.6 | ECR in AI as a New Type of Tooth Resorption

Abbott and Lin (2022) published a classification for tooth resorptions, grouping them into internal and external. Although it is mentioned that external invasive resorption can be developed in unerupted teeth with enamel defects, the type of resorption described does not resemble the one observed in patients with AI, either in the present study or in the cases reported by other authors (Morrier et al. 2008; Urzúa et al. 2021; Lee et al. 2011;

Lindemeyer, Gibson, and Wright 2010; Korbmacher, Lemke, and Kahl-Nieke 2007; Bhatia, Hunter, and Ashley 2015). Altogether, as this pattern of crown resorption presented specifically in AI patients is not included in Abbott's classification, our group suggests that it should be included in a new classification of tooth resorptions.

4.7 | Possible Aetiopathogenesis of ECR

Mechanisms of pathological external tooth resorption have been proposed mainly for the root in the cervical area (Gold and Hasselgren 1992; Mavridou et al. 2016). These consider three stages: *initiation stage* developed after injury to the periodontal ligament on the cementum under the gingival epithelium attachment, *resorption stage* with destruction of the cementum and dentin with persistence of a thin layer of dentin recognised as 'pericanalar resorption-resistant sheet' (PRRS) and a *repair stage* with apposition of bonelike tissue over the resorbed surface (Mavridou et al. 2016; Ricucci et al. 2023). In the case of coronal resorption, the dentin is covered by enamel and not by cementum, as occurs in the root. ECRs have been observed in both isolated and syndromic hypoplastic AI, in which the enamel layer over the dentin is very thin or even absent (Morrier et al. 2008; Urzúa et al. 2021; Lee et al. 2011; Lindemeyer, Gibson, and Wright 2010; Korbmacher, Lemke, and Kahl-Nieke 2007; Bhatia, Hunter, and Ashley 2015). The triggering mechanism for initiating the crown resorption still needs to be elucidated. Theories include that in the absence of reduced enamel epithelium, the connective tissue fails to recognise the nature of the dentinal tissue and triggers the resorptive process. Another theory is that mechanical trauma on the dental follicle of these teeth with very thin or absent enamel could destroy or separate the reduced epithelium of the dental organ and leave the dentin exposed to the connective tissue, triggering the resorptive process.

An important finding of the present study is that teeth with crown resorption also present a thin dentin layer covering the pulp cavity, similar to the PRRS described in external root resorption (Mavridou et al. 2016; Ricucci et al. 2023). We propose to call this layer 'perichamberal resorption-resistant sheet'.

4.8 | Limitations of the Study

The present study includes only patients with JEB due to variants in *LAMB3*, as this is the only gene detected in the Chilean cohort (Palisson et al. 2024). Therefore, the results of the present study cannot be generalised to all patients with AI due to JEB. Further studies in other countries with patients with JEB caused by variants in other genes would help determine this phenomenon in patients with other JEB-associated variants, who could present different AI phenotypes, such as hypoplastic AI with pits and/or pitting.

For a differential diagnosis with caries and tooth shape anomalies, continuous follow-up to identify ECR during the eruption process and having a series of radiographs taken over time to compare tooth shape changes is crucial. The advantage of our study is the 19-year-follow-up time of this cohort. Most diagnoses were established during the eruptive process, with a series of radiographs available where the loss of tooth structure during the eruption process could be confirmed. However, patients with JEB due to variants in *LAMB3* have a short life expectancy, (Fine 2016; Kelly-Mancuso et al. 2014) making long term follow-up challenging. For example, five patients were edentulous at the first examination, and passed away before having a second dental appointment, not being eligible for this study. In Chile, the mean age of death is at the age of 7 years old, which explains why there were more primary than permanent teeth examined (Palisson et al. 2024).

5 | Conclusion

This study demonstrates the magnitude of ECR in patients with generalised hypoplastic syndromic AI due to JEB caused by variants in *LAMB3*, with 90% of the patients presenting at least one tooth affected by crown resorption. The incisors were the type of teeth with the highest prevalence of ECR. As this study only includes JEB and generalised hypoplastic syndromic AI due to variants in *LAMB3*, the results cannot be generalised to all patients with JEB or AI. Further studies should explore the prevalence of resorption in patients with other types of AI and propose clinical and radiographic follow-up protocols aimed at early detection and treatment of these lesions.

Author Contributions

Colomba Besa-Witto: conceptualization, investigation, writing – original draft, writing – review and editing, methodology, data curation, project administration, formal analysis. **Ana Ortega-Pinto:** conceptualization, methodology, data curation, supervision, formal analysis, investigation, writing – original draft, writing – review and editing. **Sebastián Véliz:** conceptualization, methodology, data curation, supervision, formal analysis, investigation, writing – original draft, writing – review and editing. **Marco Cornejo:** methodology, software, formal analysis, writing – review and editing. **Ignacia Fuentes:** investigation, data curation, writing – review and editing, validation. **Francis Palisson:** conceptualization, writing – review and editing, investigation, supervision. **Susanne Krämer:** conceptualization, methodology, data curation, supervision, resources, formal analysis, validation, investigation, project administration, writing – review and editing, writing – original draft.

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Ethics Statement

Ethical approval was obtained from the University of Chile (FOUCH, 2015/02 and 2023/13).

Consent

Informed consent was obtained from patients or legal tutors.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

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