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Review

The Pathology of the First Permanent Molar during the Mixed Dentition Stage—Review

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Abstract: Background: The eruption of the first permanent molar (FPM) marks the beginning of the mixed dentition, which is one of the most dynamic periods in the development and growth of the stomatognathic system. Aim: The purpose of the study was to investigate the pathology of the first permanent molar (FPM) during the transition stage between the primary and permanent dentition. Materials and Methods: A literature search was performed in Clarivate Web of Science, Google Scholar, and PubMed databases. Cohort and cross-sectional studies, reviews, case reports, background information, and expert opinion were included. Results: Ectopic eruption is one of the most frequent pathologies during the mixed dentition period, and ectopic eruption of the maxillary FPM is the most encountered. Hypomineralization is currently the most prevalent pathology of the hard dental tissue in FPM, often in association with the same type of damage on the incisors in the context of the so-called molar incisor hypomineralization (MIH). FPM particular vulnerability to caries is due to its posteruptive enamel maturation, which is accomplished during the mixed dentition stage. Conclusions: Proper clinical management of FPM pathology is a demanding task for the pediatric dentist and is of great importance for the development of a healthy permanent dentition and stable occlusion.

Keywords: stomatognathic system; mixed dentition; ectopic eruption; molar incisor hypomineralization; dental caries; functional occlusion

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1. Introduction

Mixed dentition, characterized by the coexistence of deciduous and permanent teeth in the oral cavity, is one of the most active periods in the development and growth of the stomatognathic system [1]. This stage extends between the ages of 6 to 13 years, and it is further divided into early mixed and late mixed dentition [2]. The dynamic biological and functional events that mark the mixed dentition phase include not only the teeth but also the alveolar process, which remodels to accommodate the newly erupted permanent teeth, and the relationships that are established between the maxillary and mandibular teeth (the dental occlusion).

The onset of mixed dentition is marked at around the age of six by the eruption of the first permanent molar (FPM), called accessional tooth because it emerges posterior to the primary teeth, different from the so-called successional teeth, which replace the previous deciduous ones.

The transition from primary to permanent dentition includes three stages [3]:

- The first stage corresponds to the first transition in which the FPMs erupt, the primary incisors exfoliate, and the permanent incisors erupt.

- When the permanent incisors have reached the plane of occlusion, the first transition ends, and we move to the second stage, called the intertransitional stage, in which intense remodeling of the alveolar process occurs simultaneously with the continuation of the development of the permanent teeth and with the resorption of the roots of the deciduous canines and molars. During the intertransitional period, the permanent incisors, primary canines, primary molars, and the FPMs cohabit in the oral cavity.
- The third stage corresponds to the second transition in which the deciduous molars and canines exfoliate, and their successors erupt (the permanent premolars and canines), whereupon the permanent second molars erupt.

The development of the FPM begins in intrauterine life [4]. As radiographic investigations have shown, the crypts of the FPMs can be seen at birth in the territory of the second primary molars, in addition to the germs of the deciduous teeth [5]. At first, the crypts of the maxillary FPMs are oriented high in the maxilla, above and behind the germ of the second deciduous molar, and the crypts of the mandibular ones are found below the anterior border of the ramus of the mandible [5]. Osseous growth occurs through the apposition of bone to the maxillary tuberosity and resorption of the anterior border of the mandibular ramus, providing space for the FPMs to erupt [5]. Consequently, the FPMs perform intramaxillary and intramandibular movements, traverse the bone and end up taking the form of two plateaus covered by the gingiva, which can be observed behind the deciduous dental arches at around three to five years of age [5]. Once the occlusal surface is free of gingiva, the path of eruption is guided by the terminal plane (the relationships of the distal surfaces of the second primary molars, when viewed from the side). The FPMs erupt almost perpendicular to the occlusal plane [3].

The FPM plays a dominant role in the development of dental arches and occlusion during the mixed dentition period:

- The eruption of the FPM is a unique morphological and functional event because it simultaneously establishes the distal limit of the canine and premolar segment and the mesial limit of the molar teeth [6]. It not only achieves the only stable posterior occlusal stops, but it contributes to accomplishing the consistency between the anterior determinant (the teeth) and the posterior determinant (the temporomandibular joint) of occlusion [7].
- Being the first permanent tooth that erupts, the FPM pushes the jaws apart, increasing the height of the lower third of the face [8].
- It changes its vertical position to compensate for the mandibular rotation pattern, thus establishing the vertical dimension of occlusion [9,10].
- As an accessional tooth, during the transition between the primary and permanent dentition, the FPM shifts mesially, exploiting any anteriorly existing space, like the primate diastemata (spaces between primary teeth) and the leeway space of Nance, which is the result of the difference between the sum of the widths of the deciduous canine and molars and that of their successors, the permanent canine and premolars [3,4,11,12]. Closing of the primate diastemata is accomplished through the early mesial shift, while the leeway space of Nance is used through the late mesial shift [12]. As the leeway space of Nance is greater in the mandible than in the maxilla, through the late mesial shift, the mandibular FPM changes its sagittal position in relation to the maxillary FPM [12]. This is considered the last mechanism of permanent molar occlusion development [12].

The relative position of the antagonistic first molars was appreciated by Angle as the key to occlusion and is the criterion for classifying malocclusion [13]. The FPMs are the biggest and strongest teeth in each arch [14]. Their final anteroposterior position is near the center of each permanent dental arch [14]. The FPM occupies a strategic position in the dental arch, where it bears the greatest masticatory load, which has the possibility to harmoniously disperse to the surrounding bone through its wide root spread [14].

Important as it is, the FPM is also a vulnerable tooth. This aspect is explained by the following risk factors:

- The formation and mineralization of the FPM take place during difficult periods of human development, namely at the time of birth and immediately after, until the age of three [7].
- During the transition period between primary and permanent dentition, it coexists with the deciduous teeth, which are mobile at the time of the physiological resorption of their roots and sometimes decayed, thus favoring dental plaque retention [7].

This study aims at reviewing the literature covering the pathology of the FPM during the mixed dentition period, with a focus on the particular challenges posed to the child's oral health and well-being.

2. Materials and Methods

2.1. Data Collection

References were collected by two authors from the Clarivate Web of Science, Google Scholar, and PubMed databases. The search terms used were: "mixed dentition AND first permanent molar", "ectopic eruption of first permanent molar" OR "ectopic eruption AND first permanent molar", "delayed eruption AND first permanent molar", "molar incisor hypomineralization" OR "MIH", "mixed dentition AND dental caries", "first permanent molar AND dental caries".

2.2. Eligibility Criteria

Articles and book chapters were included in the current research if they met the following criteria:

- published in a peer-reviewed scientific journal
- available in full-text
- related to children in the mixed dentition stage
- fit in the following type of study: cohort and cross-sectional studies, reviews (narrative or systematic), case reports, background information, and expert opinion.

The exclusion criteria were:

- published in a language other than English
- conference proceedings
- editorials
- letters

2.3. Search Strategy

The titles and abstracts of the identified papers were manually screened by the first and the third author. The corresponding and the last author carried out a manual selection on the reference list of initially found articles with the aim of including other relevant works in the study. Some references of the initially found papers (either articles or books) were also added to the study. Therefore, a total of 12 book chapters referring to the pathology of mixed dentition were also included. Ultimately, the corresponding author comprehensively assessed the final reference list. All the selected papers were analyzed in full-text versions. The study is based on relevant articles published up to October 2022, as the time frame of the data collection and analysis ranged from March to October 2022.

Finally, a total of 124 publications were identified and selected: 112 articles and 12 book chapters. The comprehensive analysis is based on references with a wide publication time frame (1899–2022), containing mostly papers published in the last decade.

3. Results and Discussion

3.1. Eruption Pathology

Eruption was defined by Massler and Schour as "the process whereby the forming tooth migrates from its intraosseous location in the jaw to its functional position within the oral cavity" [15]. Eruption is the third stage of tooth development, following the periods of growth and calcification [15]. The emergence of a tooth in the oral cavity occurs when about

three-fourths of its root is completed [4]. Eruption comprises two phases, an intraosseous phase until the tooth penetrates the oral epithelium, and the second stage, finalized when the tooth reaches the level of the occlusal plane. All disturbances in the normal way of the tooth coming into firm contact with its antagonist are brought together under the term eruption pathology.

3.1.1. Ectopic Eruption

Ectopic eruption is one of the most frequent pathologies encountered during the mixed dentition period. Eruption is considered to be ectopic when a tooth erupts in an abnormal position or with an abnormal orientation [16].

The maxillary FPM is reported to be the tooth most affected by ectopy in the pediatric patient, followed by the maxillary canine [16,17].

In the case of FPM, ectopic eruption is distinguished by a mesial shift from the normal path [18]. Therefore, the FPM is blocked from complete eruption by the primary second molar due to the close contact between the two teeth and becomes locked under the distal aspect of the deciduous molar [18–20]. When this happens, space loss has already occurred [21].

The etiology is multifactorial, with both genetic and local factors being involved. The high frequency in siblings [19] suggests a hereditary component. The increased prevalence of cleft children could be evidence of the contribution of genetic and local causes [22]. Ectopic eruption of the FPM is encountered in patients with a small maxilla, reduced arch length, a retruded position of the maxilla in relation to the cranial base [21], and when there is a lack of synchronization between the eruption moment of the FPM and tuberosity growth [23]. A steeper angle of eruption and a larger FPM width are also found [19]. Early eruption of the FPM could be another cause [24].

Diagnosis

Ectopic eruption is diagnosed by radiographic examination, either following clinical suspicion or as an incidental finding detected during the evaluation for a different dental complaint.

Clinical suspicion is raised when there is a delay of at least six months, or there is asymmetry in the eruption of one or more FPM as compared to other FPMs already erupted into the oral cavity [20,25]. Another clinical situation that suggests the pathology is when the distal cusps are emerging into the oral cavity before the mesial cusps [17]. The first clinical sign that indicates the ectopic eruption of the FPM is a canting of the occlusal plane of the second deciduous molar [21].

On the radiograph, the ectopically erupted FPM appears in a superposed image and is impacted in the distobuccal root of the primary second molar [17]. Because the FPM has no deciduous predecessor, it is accommodated in the dental arch by the development of the jaw bones in the posterior regions as the tooth forms [24]. Under normal conditions, the FPM assumes its position behind the primary second molar without initiating resorption [24]. When the FPM ectopically erupts, resorption of the primary second molar occurs, this being an important radiological finding. Barberia-Leache et al., 2005, defined four grades of severity based on the resorption rate of the primary second molar [17]:

- grade I (mild)—resorption limited to cementum or with minimum dentin penetration
- grade II (moderate)—resorption of the dentin without pulp exposure
- grade III (severe)—resorption of the distal root resulting in pulp exposure
- grade IV (very severe)—resorption extended to the mesial root of the primary second molar.

Another radiological finding is the magnitude of impaction (MOI), described by Barberia-Leache et al. as being the distance from the maximum mesial convexity of the FPM to a tangential line drawn to the distal contour of the primary second molar perpendicular to the occlusal plane [17].

In 1983, Bjerklin and Kurol described the two categories of FPM ectopic eruption according to its evolution: the reversible type, when the FPM breaks free, and the irre-

versible type, when the FPM remains in a locked position [19]. The authors showed that the type of ectopic eruption could be reliably established between the ages of 7 to 8 years because most of the FPMs had freed themselves in 7-year-old patients with reversible ectopic eruption [19]. Interestingly, in a 2017 study by Dabbagh et al., one-third of the forty-six self-corrected ectopic eruptions of the maxillary FPM occurred after the age of nine [26].

Prevalence and Characteristics in Different Populations

FPM ectopic eruption was investigated by many researchers in different population samples.

Chintakanon and Boonpinon, 1998, in a group of 3612 Thai pediatric population 6–9 years old, determined a prevalence of 0.75% for FPM ectopic eruption (27 children) [27]. Ectopic eruption in the maxilla was present in 0.39% of the studied cases (14 subjects) and in the mandible in 0.36% (13 subjects). The majority of the ectopic eruptions in the maxilla were severe, with subsequent root resorption of the primary second molar, while those in the mandible were minimal [27]. Concerning the correlations with the type of malocclusion, the ectopic eruption of the maxillary FPMs was mostly found in patients with Class I, but also in Class II and III malocclusions, while the ectopic eruption of the mandibular FPMs was predominantly found in Class I and not at all in subjects with Class III malocclusion [27].

Barberia-Leache et al., 2005, carried out an extensive retrospective study concerning ectopically erupted maxillary FPM on a group of 509 consecutive Spanish patients in the early mixed dentition stage, aged six to nine, who were reviewed every six months, from January 1998 up to December 2002 [17]. The criterion for including the subjects in the study was that the mandibular FPM had to have emerged [17]. Twenty-two patients, representing 4.3% of the total, and having an average age of seven years and six months, showed ectopic eruption of the maxillary FPM. Bilateral location was found in 63.6% of the cases and unilateral in 36.4% of the cases, but no statistically significant differences were determined between one side vs. two sides located ectopic eruptions ($p > 0.05$). The unilateral locations were predominant on the right side (75%); statistically significant differences were found between right/left localizations ($p < 0.05$). The difference between the average impaction on the right (2.91 mm) versus the left side (1.6 mm) was statistically significant ($p < 0.05$). In addition, 69.4% of the total 36 ectopic molars self-corrected, and the rest remained impacted [17].

In a sample of British children (aged 7.0–11.4 years, mean 8.5 years $\pm$ 1.2) with radiographic evidence of ectopic eruption of one or more FPMs, Mooney et al., 2007, recorded 49 affected molars [20]. The prevalence was higher in the maxilla (n = 45; 91.8%) than in the mandible (n = 4; 8.2%), with an almost equal distribution between the left/right sides [20]. A similar number of reversible and irreversible ectopic eruptions was registered (24 and 25, respectively) [20].

In another 2017 study investigating 1052 Italian individuals in the early mixed dentition stage, the prevalence of maxillary FPM ectopic eruption was 2.5% (26 subjects), and the ratio between unilateral and bilateral locations was 1:5 (in 6 and in 20 subjects, respectively) [18]. The distribution of patients according to gender was 14 boys and 12 girls. No differentiations were carried out between the reversible and irreversible types due to the early mean age of the sample [18].

In their study conducted on ectopic eruption over a group of 505 Spanish children aged between 5 and 8 years, Mendoza-Mendoza et al., 2014, identified the pathology in 34 patients (6.7% of the cases) [28]. The distribution according to gender was 18 males (52.9%) and 16 females (47.1%), with no statistically significant differences ($p > 0.05$). The highest prevalence of FPM ectopic eruption was among the eight-year-old children (41.2%), followed by the seven-year-old children (32.4%), six-year-old group (20.6%), and five-year-old group (5.9%). This study pointed out a higher incidence of bilateral occurrence (67.6%) as compared to unilateral occurrence (32.4%) [28]. The reversible type of ectopic eruption was diagnosed in 58.8% of the cases, and the irreversible type in 41.2% of the cases [28].

In his study on a sample of the Turkish population (7649 subjects), Güven, 2018 determined a prevalence of 2.65%, with a distribution of FPM ectopic eruption between the two dental arches of 57.5% for the maxilla and of 42.5% for the mandible [29]. A higher incidence of severe and very severe degrees of ectopic eruptions was registered in the maxilla as compared to the mandible [29].

In the study by Aldowsari et al., 2021, on a sample of the population in Saudi Arabia with a mean age of 6.90 ± 0.985 years, 60 FPMs were found with an ectopic eruption in 45 of the 2014 investigated subjects [25]. The prevalence was higher in males (2.9%) than in females (1.6%), but with no statistically significant differences ($p = 0.59$). Forty-seven (78.4%) of the ectopic FPMs were in the maxilla and 13 (21.6%) in the mandible, with statistically significant differences between the two dental arches ($p = 0.000$). Similar rates between the right and left sides were determined [25].

In a sample of 772 Iranian children aged 5–8, Hali et al., 2021, identified 79 subjects with an ectopic eruption of FPM, of which 61% were girls and 39% were boys [30]. The prevalence was 10.2%, the highest reported among all studies considered for this review. A mild ectopic eruption was found in 25.6% of the patients, a moderate one in 60.3%, and a severe one in 14.1%. The authors reported a higher frequency of ectopic eruption in the mandible (59.5%) as compared to the maxilla (19%) [30]. Of the subjects, 21.5% presented FPM ectopic eruptions in both the maxilla and the mandible [30].

In their 2021 study analyzing 11,403 Chinese patients aged 4–11, Chen et al. found 409 children (3.6%) with 634 ectopically erupted FPMs, out of which 89.7% occurred in the maxilla. Two hundred sixty-five boys and 144 girls presented FPM ectopy [31]. The male-to-female ratio was 1.79:1 in the group exhibiting self-corrected ectopic eruption and 1.53:1 in the group exhibiting the irreversible type. Correlating the pathology with the subjects' age, the highest prevalence was seen in six-seven-year-old children [31].

As can be seen from the listed papers, a higher prevalence of ectopically erupted maxillary FPMs, as compared to the mandibular ones, was determined by all studies investigating the anomaly in both dental arches. The severe ectopic eruption was also more prevalent in the maxilla than in the mandible. Since the eruption of the maxillary FPM is of interest, certain studies have analyzed the anomaly only regarding the upper dental arch. It is appreciated that the maxillary FPM is at risk for developing the anomaly due to its particular pattern of eruption, namely, not vertical, but in a forward and downward direction, through a rotary movement having the apices of the roots as a center [24].

Table 1 summarizes the main studies regarding the occurrence of FPM ectopic eruption.

Table 1. Occurrence of FPM ectopic eruption as described by different authors. F—female; M—male; Mx—maxilla; m—mandible; B—bilateral; U—unilateral; R—right; L—left; NS—not specified.

Study	Year	Sample	Number of Subjects with Ectopic Eruption	Prevalence in Relation to Age	Gender Distribution	Number of Ectopic Molars	Prevalence in Relation to Dental Arch	Prevalence in Relation to Side
Barberia-Leache et al. [17]	2005	509	22 (4.3%)	average age in the affected group: 7 y 6 mo	F-9 (41%) M-13 (59%)	36	Only maxillary FPM was assessed	B-63.6% U-36.4% •R-75% • L-25%
Mucedero et al. [18]	2015	1052	26 (2.5%)	average age in the affected group: 8 y 2 mo ± 9 mo	F-12 (46.2) M-14 (53.8)	NS	Only maxillary FPM was assessed	B-20 U-6
Mooney et al. [20]	2007	48	28	average age in the affected group: 8.5 y	NS	49	Mx-45 (91.8%) m-4 (8.2%)	Equal R/L distribution
Aldowsari et al. [25]	2021	2014	45 (2.2%)	5 y-10.4% 6 y-22.6% 7 y-33.3% 8 y-33.7%	F-17 (37.7%) M-28 (62.3%)	60	Mx-47 FPMs (78.4%) m-13 FPMs (21.6%)	Similar R/L rates
Chintakanon et al. [27]	1998	3612	27 (0.75%)	6–9 y	F-7 (25.9%) M-20 (74.1%)	NS	NS	NS
Mendoza-Mendoza et al. [28]	2014	505	34 (6.7%)	5 y-5.9% 6 y-20.6% 7 y-32.4% 8 y-41.2%	F-16 (47.1%) M-18 (52.9%)	NS	Only maxillary FPM was assessed	B-67.6% U-32.4%

Table 1. *Cont.*

Study	Year	Sample	Number of Subjects with Ectopic Eruption	Prevalence in Relation to Age	Gender Distribution	Number of Ectopic Molars	Prevalence in Relation to Dental Arch	Prevalence in Relation to Side
Guven [29]	2018	7649	203 (2.65%)	average age in the affected group: 6.82 ± 1.25	F-85 (41.9%) M-118 (58.1%)	273	Mx-157 (57.5%) m-116 (42.5%)	B-59 (29.1%) U-144 (70.9%)
Hali et al. [30]	2021	772	79 (10.2%)	5 y-0.9% 6 y-9.3% 7 y-13% 8 y-12.9%	F-48 (61%) M-31 (39%)	145	Mx-19% m-59.5% Both Mx and m: 21.5%	NS
Chen et al. [31]	2021	11,403	409 (3.6%)	mostly in 6–7 y	F-144 (35.2) M-265 (64.8)	634	Mx-89.7% m-10.3%	mostly symmetrically

Predictive Factors for Irreversible Outcome

Differentiation between the reversible and irreversible types is important for the therapeutic approach. The irreversible type can cause premature exfoliation of the primary second molar, which, in turn, leads to the mesial shift of the FPM and reduced space for the eruption of the second premolar [17,21], deficiency in quadrant arch length and overeruption of the opposing permanent molar [25]. In the reversible type, the primary second molar, even presenting an atypical resorption, remains mesial to the erupted FPM until normal exfoliation [19]. Therefore, several researchers were preoccupied with assessing the predicting factors for the irreversible outcome.

The irreversible type has been significantly correlated with a larger FPM width and a more mesial angle of eruption; a tendency toward a shorter maxilla has also been associated with the irreversible category [19].

Barberia-Leache et al., 2005, determined a ratio of reversible versus irreversible ectopic eruption of 2.27:1 [17]. Significant correlations were found between spontaneous self-correction and bilateral locations ($p < 0.05$). The average magnitude of impaction (MOI) was 2.91 mm on the right side and 1.6 mm on the left side, and this difference was found to be statistically significant ($p < 0.05$). The MOI was higher in the irreversible group than in the reversible one. Therefore an increasing value of MOI was considered a reliable predictor for the irreversible outcome, although the correlation between the MOI and the type of ectopy (reversible versus irreversible) was not assessed. Classes I and II resorption cases got self-corrected, and classes III and IV resorption cases remained impacted. No statistically significant correlation was found between the degree of resorption of the primary second molar and the MOI of the FPM [17].

In another study that evaluated the predicting factors for the irreversible outcome of ectopic eruption of maxillary FPM, Dabbagh et al., 2017, identified positive correlations between increased MOI, resorption class of the primary second molar, severe lock, bilateral location, and irreversible ectopic eruption [26]. The authors showed that increased MOI was the most reliable predictor for irreversible outcomes [26].

In their 2021 research on 419 teeth, out of which 257 (61.3%) presented reversible and 162 (38.7%) irreversible ectopic eruptions, Chen et al. found Class III resorption in the majority (84.2%) of the cases [31]. A statistically significant difference was determined between the reversible and irreversible groups ($p = 0.022$). The more severe the root resorption, the more inclined the outcome was toward the irreversible type [31]. The mean value for the magnitude of the impaction index (MOII) was calculated by dividing the value of FPM impaction magnitude by the value representing the crown width of the second primary molar. The mean value of MOII was 0.198 ± 0.077 in the reversible group and 0.282 ± 0.115 in the irreversible group. A statistically significant difference was found between the two groups ($p < 0.001$) [31]. Concerning the eruption angulation, the critical value determined was 73.05°. Therefore a greater value was correlated with an irreversible outcome. No statistically significant difference was found between the groups [31].

Associated Anomalies

Canut and Raga found a posteriorly positioned maxilla relative to the cranial base, a tendency to dolichocephaly, and a posterior rotation of the chin in cases of ectopic eruption of the maxillary FPM [32].

Bjerklin et al., 1992, assessing the association between ectopic eruption of the maxillary FPM and three other dental and developmental anomalies (ankylosis and infraocclusion of primary molars, ectopic eruption of maxillary canines, and aplasia of premolars), characterized the four conditions studied as "different manifestations of one syndrome, each manifestation having an incomplete penetrance" [33]. The authors identified one additional disturbance in 18–28% and two additional disturbances in 2–3% of the children primarily diagnosed with only one dental or developmental disturbance [33].

Bektor et al., 2005, concluded that ectopic eruption of the maxillary FPM associated with root resorption of the second primary molar could be an early indicator of later ectopic eruption of the maxillary canine causing incisors root resorption [34].

Mooney et al., 2007, reported a high prevalence of other dental anomalies in patients with ectopic eruption compared to controls (60.7% vs. 25%, $p = 0.01$) [20]. The most frequently occurring other dental anomalies were: primary molar infraocclusion (32.1%), hypodontia (28.6%), cleft lip and/or palate (25%), and supernumerary teeth (17.9%) [20].

Salbach et al., 2012, showed that FPM ectopic eruption is statistically significantly associated with crowding, lateral crossbite, and a tendency towards Class III malocclusion [35]. Other findings were faulty occlusion between individual teeth and Class II malocclusion division I. The prevalence of Class III malocclusion in children with ectopic eruption was almost three times higher than in the overall group (5.9% vs. 2.1%, $p = 0.009$) [35].

Mucedero et al., 2015, found significantly increased widths of the primary second molars and maxillary FPMs ($p < 0.01$) and smaller maxillary arch length ($p < 0.01$) in the group presenting ectopic eruption as compared to the control group [18]. Anterior and posterior transverse interarch discrepancies, with small maxillary intercanine and intermolar widths, were determined, which suggested that ectopic eruption is associated with severe maxillary hypoplasia [18]. Another finding was the significant maxillary and mandibular tooth crowding in cases with ectopic eruption compared to controls ($p < 0.01$) [18]. The authors postulated that the combination of maxillary macrodontia and maxillary arch constriction plays a role in dental crowding, pointing to the involvement of dentoskeletal factors in the etiology of ectopic eruption [18].

In another recent study (2021), Helm et al. [36] determined that the most prevalent dentoskeletal characteristics of the Spanish pediatric population affected by maxillary FPM ectopic eruption were: a shortened anterior cranial base, a retroposition of the maxilla and a more distal position of the affected tooth in relation to the pterygoid vertical. In children with bilateral ectopic eruption, decreased palatal plane values and a more posterior position of the upper incisor was registered [36].

Clinical Management of FPM Ectopic Eruption

Early diagnosis of FPM ectopic eruption is the most important step in its clinical management. If the disturbance is diagnosed in five- to six-year-olds, an observational strategy of "watchful waiting" is indicated, taking into consideration that self-correction is reported to occur in two-thirds of the cases [25,37]. In cases when locked eruption persists for six months and the resorption of the primary second molar continues to increase, orthodontic intervention is necessary [25,37] in order to intercept the active phase of FPM eruption [23,38]. Timing and case selection are the most important aspects in the clinical management of FPM ectopic eruption [31].

The goals of the treatment are:

- obtaining a normal eruptive pathway [17]
- preserving the primary second molar [17,39]
- increasing the arch perimeter [39].

Proper clinical management of FPM ectopic eruption is a demanding task for the pediatric dentist and is of great importance for the development of a stable occlusion [23,38].

3.2. Pathology of the Dental Hard Tissues

The FPM starts to develop from the posterior extensions of the dental epithelium behind the second primary molar during the first half of the fourth prenatal month [40]. Environmental, systemic, and local factors during odontogenesis or later can permanently impair the dental hard tissues since these, once formed, do not undergo remodeling [41].

FPM dental hard tissues serve as a "kymograph" that records prenatal, perinatal, and postnatal health and diseases [42].

Premature damage of the FPM dental hard tissues leads to compromising the posterior occlusal supporting areas and imbalances the stomatognathic system homeostasis.

Particular challenges in the treatment are generated by age-related behavioral characteristics, the morphological peculiarities of the dentoalveolar structures, and sometimes by the necessity for long-term therapeutic approaches.

3.2.1. Molar Incisor Hypomineralization

Molar incisor hypomineralization (MIH) is the name assigned by Weerheijm, Jälevik, and Alaluusua in 2001 to a pathologic condition characterized by "a hypomineralisation of systemic origin of one to four FPMs frequently associated with affected incisors" [43]. Mandibular incisors are more rarely involved than maxillary ones [43,44].

The condition was first reported in the late 1970s by Swedish dentists, worried because of its particular, destructive behavior and its increasing incidence [42]. From then until the consensus adopted in 2001 [43], large defects in FPMs during or soon after the eruption were referred to in the literature as non-fluoride enamel opacities, idiopathic enamel opacities, internal enamel hypoplasia, mottling of enamel, cheese molars, etc. [45].

MIH represents a major concern for the child's oral health due to the rapid destruction of the dental tissue it generates soon after the eruption of FPM.

Etiology

Enamel is formed through the process called amelogenesis, carried out by ameloblasts [46]. Amelogenesis comprises two sequential stages, the matrix secretion stage and the calcification (maturation) stage [47–49]. Disturbances during the maturation stage are responsible for enamel hypomineralisation [47,49–51]. Amelogenesis is completed at the time of tooth eruption, and the ameloblasts die after the end of this process [46]. Therefore, no secondary or regenerative enamel is produced afterward [46], no metabolic activity exists once the enamel is formed, and disturbances during enamel formation are expressed as permanent defects in the erupted tooth [50].

Enamel formation is a sensitive process; thereby, systemic and environmental factors can affect it [44,47,49–51].

The unique combination of affected molars and incisors indicates that a specific influence on enamel development during a limited period of time is responsible for MIH lesion occurrence [44]. The period of amelogenesis of the FPM starts from the eighth month of intrauterine life and continues until the age of four; the risk factors associated with MIH act during this period, the first ten months of life being critical [52,53].

Prenatal, perinatal, and postnatal medical conditions were associated with MIH lesions.

Among prenatal medical conditions, Jälevik and Noren, 2000, found the mother's chronic diseases like syphilis, high blood pressure, hyperglycemia, and prolonged use of drugs to be related to MIH [42]. Hypocalcemia due to maternal diabetes and vitamin D deficiency can also be associated with MIH occurrence [51]. Lygidakis et al., 2008 identified multiple maternal episodes of high fever due to cold and infections during the last pregnancy months in association with MIH and emphasized on the harmful influence of maternal pyrexia on amelogenesis, ranging from dysfunction to complete degeneration of the ameloblasts [54]. Other maternal medical conditions reported by Lygidakis et al.,

2008, were diabetes, prolonged vomiting, and use of spasmolytic medication in late pregnancy [54]. Sönmez et al., 2013, found no association between maternal health problems during the third trimester of pregnancy and MIH [49]. Bagattoni et al., 2022, identified significant correlations between smoking during pregnancy and MIH ($p = 0.0005$) [55].

Perinatal medical conditions include premature birth, prolonged delivery, and low birth weight. All these generate hypoxia, and lack of oxygen in active ameloblasts seems to be one of the most plausible causative factors for MIH [51]. Sönmez et al., 2013, determined correlations between MIH occurrence and prematurity and no associations of MIH with low and very low birth weights [49]. Lygidakis et al., 2008 determined cesarean section, prolonged delivery, premature birth, and twining in association with MIH [54]. Thakur et al., 2020, ascertained significant correlations between low birth weight and MIH [56].

Alaluusua et al., 1996, first suggested that prolonged breastfeeding can generate enamel mineralization defects, possibly because of environmental contaminants such as dioxin and dioxin-like compounds that hamper amelogenesis [57,58]. There are also researchers who found no correlations between the duration of breastfeeding and the presence of enamel defects [49,59]. Laisi et al., 2008, showed no statistically significant correlation between the exposure of the child to dioxins via mother's milk and the occurrence of MIH lesions [60]. Furthermore, Thakur et al., 2020, reported a high prevalence of MIH in cases of early weaning, showing that the nutritional status of the child is compromised in this situation, with unfavorable consequences on enamel development [56].

Scientific evidence shows a strong link between many medical conditions in the first years of life and MIH. Respiratory diseases such as pneumonia, lung and airway infections, and asthma can generate metabolic disturbances with further impact on dental hard tissues [56]. These conditions trigger the phenomenon of hypoventilation that favors tissue acidosis [56]. As a result of the pH changes in the enamel matrix, an inhibition of proteolytic enzymes and of hydroxyapatite crystals development occurs, ultimately leading to the hypomineralization of dental hard tissues [56].

Thakur et al., in their study (2020), found a strong correlation between MIH with postnatal acute ailments like unexplained fever and chest infections other than pneumonia and pneumonia [56]. Ahmadi et al., 2012, showed that chicken pox, renal failure, asthma, and allergic reactions were more common in children with MIH than in controls [61]. In another study, the prevalence of MIH was positively correlated with asthma, adenoid infections, tonsillitis, and fever in the first four years of life [62]. A positive correlation between the prevalence of MIH and otitis in the first three years of life and atopic dermatitis was demonstrated by Ilczuk-Rypuła et al., 2022 [63]. Upper respiratory infections and their complications, such as otitis media, bronchitis, bronchiolitis, laryngitis, tonsillitis, repeated episodes of high fever due to common cold/coryza, neonatal illness, and viral gastroenteritis were the most commonly encountered conditions by Lygidakis et al., 2008, in the postnatal period [54]. The correlation between MIH and viral gastroenteritis is explained by the hypocalcemia the disease generates in infants [54]. The latter authors identified more than one medical condition in MIH subjects [54]. Significant correlations between MIH and both chickenpox and measles before the age of four were found by Sönmez et al., 2013 [49]. The same authors also reported pneumonia and gastrointestinal diseases to be associated with MIH lesions [49]. Bagattoni et al., 2022, found a positive association between genetic syndromes and MIH [55].

Correlations between prolonged use of corticosteroids and antibiotics due to respiratory or urinary tract problems and MIH were reported by Lygidakis et al., 2008 [54]. Antibiotic intake during the second year of life was also found to be positively correlated with MIH lesions in the study by Bagattoni et al., 2022 [55]. The role of antibiotics in MIH occurrence is still controversial because it is not possible to establish if the childhood illness itself or the medication intake is the causative factor or if both are responsible [51].

MIH etiology is subject to controversy, and no consensus exists in the scientific literature. Fatturi et al., 2019 and Garot et al. 2021, by their systematic reviews and meta-analyses, emphasized on the multifactorial etiology of MIH [64,65].

MIH Diagnosis

Hypomineralization is a qualitative defect that is clinically identified as a disturbance in the enamel translucency (opacity) [42,43]. It is characterized by the presence of creamy-white, yellow, or brown enamel opacities, which have distinct margins with the adjacent normal enamel, hence the name "demarcated opacities" [42].

Histologically, the affected enamel shows varying degrees of porosity [42,43] and contains higher carbon and lower calcium and phosphorus concentrations [42,43]. Compared to healthy teeth, MIH-affected ones show less distinct prism sheaths and a lack of arrangement of the hydroxylapatite crystals [66]. Increased amounts of serum albumin, type I collagen, ameloblastin, α1-antitrypsin, and antithrombin III are found in the hypo-mineralized enamel [66]. The presence of these proteins inhibits the growth of hydroxylapatite crystals and influences the enzymatic activity during enamel maturation, thus leading to the reduction of mineral content and explaining the structural deficiencies of teeth affected by MIH [66–68].

Due to its porous structure, the enamel is very fragile and disintegrates under masticatory forces [45,69]. A particular pattern of enamel destruction involving the occlusal surfaces and the cusps is a characteristic of MIH. Sometimes the enamel loss can be so rapid after the eruption that it looks like the enamel was not initially formed [45]. The destruction generates sensitivity, even pain which further determines the child to avoid oral hygiene practices. Plaque accumulates, caries rapidly develop, and even a subclinical inflammation of the dental pulp cells is reported [69]. As a consequence, dental fear and anxiety are more common in children with MIH than in non-affected children [69]. The severity of MIH lesions can differ between the four FPMs. Within one patient, only enamel opacities, without loss of hard dental tissue, can be present on one molar, while in another molar, large parts of the enamel are already broken down [45]. The risk for the onset of MIH lesions on upper incisors is higher when more FPMs are affected [45].

MIH case definition:

- was introduced by the 6th Congress of the European Academy of Paediatric Dentistry (EAPD) in 2002 [70].
- eight years of age was considered as the appropriate time for any examination for the condition because, at this age, in most children, all four FPMs and the majority of the incisors will be erupted [70].

Judgements related to individual teeth should include [70]:

- absence or presence of demarcated opacities;
- posteruptive enamel breakdown;
- atypical restorations (extended to the palatal surface and buccal surfaces; an opacity is frequently present at the border of the restoration);
- extraction of molars due to MIH.

Extraction of molars due to MIH is suspected when the absence of an FPM is associated with opacities or atypical restorations in other FPMs [70]. When the absence of an FPM in a sound dentition is associated with demarcated opacities on the incisors, it is also suspected for MIH [70].

According to severity, MIH lesions fall into three categories [71]:

Mild:

- Demarcated opacities in non-stress-bearing area of molar.
- Normal dental sensitivity

Moderate:

- Intact atypical restoration present
- Occlusal/incisal third of teeth without initial posteruptive enamel breakdown.
- Posteruptive enamel breakdown/caries limited to one or two surfaces without cuspal involvement.
- Normal dental sensitivity.

Severe:

- Rapid posteruptive enamel breakdown on erupting tooth
- Often develop widespread caries associated with affected enamel
- History of dental sensitivity.

Differential diagnoses include:

- Amelogenesis imperfecta, a hereditary abnormality characterized by quantitative and structural disturbances of the enamel, without structural modifications of the dentine; it affects all teeth in the permanent dentition [52].
- Enamel hypoplasia, a quantitative abnormality identified as an external defect involving the enamel surface [42] and a localized reduction in the enamel thickness [52]. The damage occurs during the secretory phase of amelogenesis [52]. The margins of the lesion are smooth and round [42].
- Dental fluorosis is the result of excessive fluoride absorption during the mineralization stage and is characterized by diffuse white opacities affecting homologous teeth [42,52]. Decay-resistance is a distinguishing feature [52].

The Burden of MIH

Due to MIH's rapid increase in incidence and the large geographic area covered, numerous researchers have focused on this pathology, even considered an "emerging disease" [72]. The prevalence, the patterns of distribution in relation to gender and age groups, and the MIH clinical picture were the preoccupations of many investigators.

Martínez Gómez et al., 2012, in a group of 505 Spanish pediatric population aged 6–14 years old, determined a prevalence of 17.85% for MIH (90 children) [73]. An equal distribution was found regarding gender. The authors showed that 57.7% of all MIH-type lesions were located in the maxillary FPMs and 42.4% in the mandibular FPMs. Of the subjects, 16% presented more than one affected FPM. Of the cases, 58.88% had both molars and incisors affected, 8.88% of the cases had four affected FPMs, 11.11% had three affected FPMs, 11.11% had two affected FPMs, and 10% had one affected molar. Most of the lesions encountered were mild forms (50%), 28.89% were moderate, and 21.11% were severe. The most frequently affected was the maxillary right FPM [73].

In the study by Ghanim et al., 2014, 164 (20.2%) of the 810 Iranian children, 9- to 11 years old, had MIH lesions, and over half of them (53.7%) presented developmental defects on all four FPMs [74]. Furthermore, the authors showed that the subjects with all molars affected were over three times more likely to have four to seven incisors affected than those presenting MIH lesions on one FPM [74]. Regarding the severity of MIH lesions, the most common type was the mild form, with creamy/white lesions in 17.1% and yellow/brown defects in 41.6%, followed by moderate lesions (31.3%) and severe defects (10.0%) [74].

In another study on 1511 children aged between 8–11 years in Istanbul, MIH lesions registered a prevalence of 14.2% [75]. Out of 215 patients diagnosed with MIH, 102 were boys (47.4%) and 113 girls (52.6%) [75]. Regarding the distribution of MIH defects in relation to age, a higher percentage was found in 11-year-old children (n = 144; 18.2%) than in 8-year-old children (n = 71; 9.9%), showing statistically significant differences [75].

On a sample of 705 Spanish children aged 6–14 years and 11 months, MIH defects were found in 56 of them, representing a prevalence of 7.94% [76]. Regarding gender distribution, MIH lesions were more frequently found in females (9.41%) than in male subjects (6.39%), representing a ratio of 1:1.54 between males and females. The maxillary teeth were more commonly affected (n = 137) than the mandibular ones (n = 78) from a total of 215 teeth (both FPMs and incisors) with MIH lesions [76].

In a sample of 686 Mexican children, Villanueva-Gutierrez et al. reported a prevalence of 35.4% for MIH lesions (in 243 subjects) [77]. In what concerns the severity of the MIH lesions found, the moderate category was the most frequent (n = 163; 67.1%), followed by mild lesions (n = 45; 18.5%) and severe lesions (n = 35; 14.4%) [77].

Davenport et al., 2019, investigating a group of 375 children aged 7–12 years in Milwaukee, Wisconsin, determined an MIH prevalence of 9.6% (n = 36), with a higher

distribution upon the maxillary FPMs (n = 26) in comparison to the mandibular FPMs (n = 18) [78]. The authors reported a higher distribution in females (n = 25, representing 11.1% of the 226 female participants) than in males (n = 11, representing 7.7% of the 142 male participants). Mild lesions were found in 69.4% (n = 25) and severe forms in only 30.6% (n = 11) of the total MIH cases investigated. A higher frequency of severe defects was registered in the mandibular FPMs (n = 13) than in the maxillary FPMs (n = 5). Another aspect highlighted by the study was that over half of the subjects diagnosed with MIH (n = 19; 52.8%) had one FPM affected, whereas all four FPMs with MIH lesions were found only in 8.3% of cases (n = 3) [78].

Thakur et al. carried out a cross-sectional study concerning MIH prevalence on 2000 Indian patients aged 8–16 years [56]. MIH cases were found in 58 children examined, resulting in an overall prevalence of 2.9% (1.65% in male and 1.25% in female patients) [56]. The most common lesions found were demarcated opacities (71.5%), followed by posteruptive enamel breakdown (19.6%) and atypical restorations (8.9%). The highest prevalence was found in the youngest group of age, eight-year-olds (n = 19; 32.8%), followed by 12-year-old children (n = 12; 20.7%) and nine-year-olds (n = 10; 17.2%) [56].

In another study investigating 659 Lebanon children 7–9 years old, the MIH recorded prevalence was 26.7% (176 subjects) [79]. The distribution of MIH patients according to gender was 80 boys (45.45%) and 96 girls (54.55%). In what concerns the distribution of MIH lesions in relation to age, a higher percentage was found in nine-year-old patients (29.8%), followed by the eight-year-old group (20.7%) and seven-year-old group (25%). The majority of cases (52.8%) showed only FPM affection, while in 47.2% of cases, both molars and incisors were involved [79].

Emmatty et al., in a group of 5318 Indian children, revealed a number of 216 patients with MIH defects, representing a prevalence of 4.1% [80]. MIH lesions were found more frequently in males (120 subjects) than in females (96 subjects), but no statistically significant differences were determined. The majority of MIH lesions were in the maxilla (619 teeth) compared to the mandible (589 teeth) [80].

In another 2020 study investigating 407 Brazilian children aged 7–14 years old by Silva et al., MIH prevalence was 14.5% (59 subjects), with a higher distribution among male patients (n = 33; 55.9%) compared to female patients (n = 26; 44.1%), but no statistically significant difference was found [81]. Most of the MIH teeth presented mild defects (n = 202; 77.4%). Of the 261 MIH affected teeth, the maxillary FPMs represented 33% (n = 86) and the mandibular FPMs 28.3% (n = 74) [81].

Table 2 summarizes the main studies regarding the occurrence of MIH.

Table 2. Occurrence of MIH as described by different authors. F—female; M—male; NS—not specified; C/W—creamy/white; Y/B—yellow/brown.

Study	Year	Sample	Prevalence of MIH	Gender Distribution	Degree of Severity of Affected Molars		
					Mild	Moderate	Severe
Martínez Gómez et al. [73]	2012	505	90 (17.85%)	F-45 (50%) M-45 (50%)	45 (50%)	26 (28.89%)	19 (21.11%)
Ghanim et al. [74]	2014	810	164 (20.2%)	F-96 (58.5%) M-68 (41.5%)	17.1% C/W 41.6% Y/B	31.3%	10%
Koruyucu et al. [75]	2018	1511	215 (14.2%)	F-113 (52.6% M-102 (47.4%)	NS	NS	NS
Hernández et al. [76]	2018	705	56 (7.94%)	F-34 (60.7%) M-22 (39.3%)	NS	NS	NS
Villanueva-Gutierrez et al. [77]	2019	686	243 (35.4%)	F-120 (49.4%) M-123 (50.6%)	45 (18.5%)	163 (67.1%)	35 (14.4%)
Thakur et al. [56]	2020	2000	58 (2.9%)	NS	70,8%	20.6%	8.6%

Table 2. *Cont.*

Study	Year	Sample	Prevalence of MIH	Gender Distribution	Degree of Severity of Affected Molars		
					Mild	Moderate	Severe
Elzein et al. [79]	2020	659	176 (26.7%)	F-96 (54.55%) M-80 (45.45%)	74.45%	23.04%	2.51%
Emmatty et al. [80]	2020	5318	216 (4.1%)	F-96 M-120	361 (53.5%)	103 (15.3%)	210 (31.2%)
Silva et al. [81]	2020	407	59 (14.5%)	F-26 (44.1%) M-33 (55.9%)	68.75%	-	31.25%

In a 2017 systematic review of 61 publications, the overall prevalence of MIH was 11.24%, with a high degree of geographic variations and mild variation according to gender [82]. A higher prevalence in European and South American countries than in Asian countries was found. The highest prevalence estimate was for middle social class school children in Brazil, and the lowest prevalence estimate was for urban school children in India [82].

In another 2018 systematic review and meta-analysis of 99 studies on 113,144 participants from 43 countries, the number of prevalent cases in 2015 was 878 (791–971) million, and the number of incident cases in 2016 was 17.5 (15.8–19.4) million [83]. The mean prevalence identified by meta-analysis was 13.1%. The burden of MIH was driven by the country-specific demographics: heavily populated countries like India, China, and the United States significantly contributed to the number of prevalent cases, while growing countries like India, Pakistan, and Indonesia ranked first with respect to the number of incident cases. The authors determined that 27.4% of the cases were or will be in need of therapy due to MIH pathology [83].

Many researchers highlighted the high prevalence of dental caries and high caries scores (decayed, missing, and filled primary teeth—dmft and Decayed, Missing, and Filled permanent Teeth—DMFT) in association with MIH.

Ghanim et al., 2013, investigating 152 Iraqi, 7 to 9-year-old children diagnosed with molar hypomineralization (MH), found statistically significantly higher caries mean scores for both primary and permanent teeth in the MH-affected group than in control one (dmft 4.82 $\pm$ 2.73 vs. 3.36 $\pm$ 2.30 and DMFT 2.79 $\pm$ 1.39 vs. 1.28 $\pm$ 1.39) [84].

In a 2017 systematic review, a significant correlation between MIH and dental caries was found, with both DMF index and caries prevalence being higher in MIH-affected children than in non-affected ones [85].

In a 2017 case-control study on a pediatric sample, 9.63 $\pm$ 1.29 years, a large difference was noticed between MIH cases and controls in what concerns DMFT score (more than six times higher in MIH cases than in controls), given that dmft score was similar for the two groups [86]. Since the latter indicated that the patients were exposed to the same caries risk factors, it follows that the high caries prevalence in the permanent teeth was the consequence of the presence of MIH lesions [86]. Further investigating only the FPMs of MIH cases, the same authors noticed that MIH-affected FPMs presented a higher number of dentine carious lesions than the non-affected ones [86].

In another case-control study, Jalevik et al., 2002, showed that by the age of nine, children diagnosed with severe MIH had undergone dental treatment of their FPMs ten times more frequently than the unaffected controls, and on average, each affected tooth had been treated twice [69].

The management of MIH-affected children is a real challenge for the pediatric dentist. Enamel hypomineralization is a dynamic defect [84]; therefore, treatment should intercept it. It is recommended that children with poor general health in the first four years of life be considered at risk for MIH and to be monitored more frequently during eruption of FPMs [45]. The therapeutic approach should be oriented toward controlling post-eruptive enamel breakdown, dental caries, and associated symptoms like sensitivity and pain and improving the long-term prognosis of the affected teeth [45]. In cases of enamel breakdown,

severe restorative problems arise [45]. The margins of the restoration should be placed in sound enamel, and it is very difficult to find where the boundary between hypomineralized and sound enamel is [45]. Taking into consideration the altered prismatic morphology in the hypomineralized enamel, the bonding to it is unachievable [69]. Therefore, failure of direct restorations and continuing breakdown of the enamel occurs [69]. Full coronal coverage restorations, especially preformed stainless steel crowns, can be a better alternative to direct restorations [45,87]. FPM extraction, followed by early orthodontics, could be the treatment of choice in cases of severely hypomineralized FPMs [87].

3.2.2. Dental Caries

Caries is a chronic infectious disease that leads to destruction by demineralization of the hard dental tissues [88]. The etiology of dental caries is multifactorial and involves the interaction between the host, the oral microflora, the metabolic substrate represented by the diet, and a long period of time in which these factors coexist [88]. It is the result of the imbalance between the demineralization produced by acids and the remineralization carried out, especially by saliva and its components [89].

Although preventable and in increasing decline worldwide, dental caries still represent a serious trait of a child's oral health [90].

FPM Vulnerability to Caries during the Mixed Dentition Stage

FPM is considered the most caries-sensitive tooth in permanent dentition [91,92].

After the completion of the increase in enamel thickness, the maturation stage of its development begins, comprising a pre-eruptive and a post-eruptive stage [93]. Post-eruptive maturation of the enamel is characterized by chemical and physical changes in the surface layers of the enamel as a consequence of exposure to the oral environment [94]. Post-eruptive enamel maturation of the FPM takes place during the mixt dentition period, when the FPM cohabits with deciduous teeth, mobile at the time of their exfoliation and sometimes decayed, features which favor biofilm retention and disadvantage self-cleaning [7].

Posteruptive age is considered a predictor for caries on permanent teeth, the FPM being at higher risk of occlusal caries within the first year post-eruption [95,96]. Therefore, the FPM can serve as "the first indicator of dental caries activity during the phase of initial mixed dentition" [97]. Furthermore, the fact that the FPM reveals the progress of caries with high sensitivity determines the use of this tooth as an important tool for establishing programs of preventive maintenance and evaluating their outcome [97]. Its caries status in childhood can reveal the permanent dentition caries distribution in adulthood [98].

From the moment of FPM arising from the oral mucosa until it contacts its antagonist in the occlusal plane, an average time between six months and one year is necessary, which means the existence of a long period without functionality, characterized by occlusal surface massive plaque accumulation [7]. Many authors showed that considerably higher amounts of biofilm accumulate on the occlusal surface of partially erupted FPMs compared to fully erupted FPMs [95,99–101]. Moreover, Carvalho et al. found that lesions initiated during eruption arrest in FPMs which had been in full occlusion for more than one year, due to functional usage and improved conditions for tooth brushing [99].

Llena et al., 2020, showed that FPM's particular vulnerability to caries is due to the eruption age and the position in the dental arch, lack of brushing skills, and parents' ignorance of the permanent nature of this molar [102].

Dental caries of the FPM have a specific profile during the mixed dentition stage: the occlusal surface is the first exposed to risk factors and remains vulnerable until the age of eight, after which the lesions are mostly located on the mesial surface [7]. Researchers showed that mesial surface decay on FPM accounts for the majority of caries experienced in 12-year-old children [91,103]. Other authors consider that the occlusal surfaces of FPMs and the buccal pit in mandibular FPMs are the most frequent locations for the occurrence of caries during the mixed dentition stage [102,104].

Epidemiology of FPM Caries in the Mixed Dentition Stage

Many researchers were concerned with the epidemiology of dental caries on FPM during the mixed dentition phase, focusing on its prevalence, incidence, distribution, associated risk factors, treatment needs, and effectiveness of preventive and curative measures.

Llena et al. 2020, and Llena and Calabuig 2018, showed that the risk factors associated with the occurrence of caries in FPM are represented by the retentive occlusal morphology, caries antecedents in primary teeth, the experience and educational level of the parents, dietary habits (daily sweets, pastries, soft drinks intake), the frequency of tooth brushing and the presence of MIH syndrome [102,105].

In a study on the prevalence of Saudi Arabia children, 7–10 years old, the DMFT for FPM increased with age, having values of 1.88, 2.48, 2.88, and 3.04 for 7, 8, 9, and 10 years age groups, respectively [106]. Mandibular FPMs exhibited statistically significant higher Decayed and Filled components of the DMFT index than their maxillary homologues [106]. This was explained by the particular morphology of the occlusal surface of the mandibular molar, with more pits and supplementary grooves which serve as food retentive areas facilitating caries and by the slightly earlier eruption of the mandibular FPM as compared to the maxillary FPM in the majority of the children [106]. The DMFT index was higher among public school children than in private school children, with a statistically significant difference in what concerns the Decayed and Filled component of DMFT between public school and private school children. This aspect highlights the impact of social factors on caries pathology and the lack of access to oral health education, preventive programs, and school dental services for public school children [106].

Phipps et al., 2013, investigated FPM caries patterns in 15,611 American Indian and Alaska Native children in kindergarten, first, second, and third grade from 186 schools in 19 states [107]. Results showed that 7% of kindergarten children, 21% of first grade, 31% of second grade, and 38% of third-grade children had decayed, missing, or filled (DMF) FPMs [107]. The largest increase in the prevalence of FPM dental caries was registered between kindergarten and first grade [107]. The mean number of DMF molars ranged from 0.10 in kindergarten children to 0.81 in third-graders [107].

In a 2021 cross-sectional study on a group of 1510 Indian school children, 7–10 years old, Wasnik et al. determined a prevalence of 47.48% for FPM dental caries [108]. Both prevalences of caries in FPMs and DMFT increased with age. Government school children were more affected than private school children (57.90% vs. 35.71%) [108].

Alwayli et al., 2017, researched caries prevalence among a group of 17,891 female children aged 6–9 years from public schools in Riyadh, Saudi Arabia [109]. Caries were present in 6338 subjects, representing an overall prevalence of 35.4% [109]. Regarding age distribution of caries lesions, the 8–9-year-old group was the most affected (31.2%, n = 7110), followed by 7–8-year-old children (23.5%, n = 4833) and 6–7 year-olds (16.1%, n = 2370). From the total of 14,313 decayed molars, the highest prevalence was registered in the mandibular FPMs (33%) in comparison to the maxillary FPMs (18.2%) [109]. The decayed FPM counted for 24.6% (n = 14,313) of the total number of examined teeth, and fillings were only found in 1.0% (n = 573) of the FPMs. Only 1.3% of the children presented fissure sealants, demonstrating the underutilization of the procedure in caries prevention in public schools [109].

Aldossary et al., 2018, studied caries prevalence in a group of 1844 male children from 17 public primary schools in Saudi Arabia aged between 6 and 9 years [90]. In the sample examined, decay was only present in 305 children representing a total prevalence of 16.5%, leaving the other 83.5% of the patients examined (n = 1539) caries free. From a total of 5394 FPMs examined, cavities were found in 574 teeth (10.6%), and only 27 FPMs (0.5%) were treated. Caries on FPM were more prevalent in the mandible (14.4%) than in the maxilla (7.7%). Decay incidence increased with patients' age, such as the group of 8–9-year-old children examined presented the highest percentage (14.1%; n = 282), followed by the 7–8-year-old group (10.2%; n = 191) and 6–7-year-old group (6.6%; n = 101). The use of fissure sealants revealed a low distribution in the sample examined (0.8%, 0.3%, and

0.4%, respectively). From the total of 27 filled first permanent molars (0.5%), the highest prevalence was found in the third-grade children (n = 23; 1.1%), followed by the first-grade children (n = 3; 0.2%) and the second-grade children (n = 1; 0.05%) [90].

In a 2020 study by Aras and Dogan, 398 (51.2%) of the 778 Turkish children, 7- to 9- years old, had caries experience in the FPM [110]. The age distribution of caries lesions in the sample examined was 41.2% (n = 96) in the seven-year-old children, followed by 51.6% (n = 160) in the eight-year-olds and 60.4% (n = 142) in the nine-year-olds. These results highlighted that caries prevalence increased with age. Carious lesions were more common in the mandibular FPMs (51.6%) than in the maxillary FPMs (48.4%). The mean DMFTs were 1.35 in girls and 1.05 in boys, and sex-based statistically significant differences were found ($p < 0.01$ by independent t-test). Of real concern was the finding that 10% of the FPMs exhibited extensive caries within two–three years after eruption [110]. Extensive-stage caries were more prevalent in mandibular FPMs than in maxillary FPMs, with statistical significance ($p < 0.05$) [110].

In the study by Alraqiq et al., the high prevalence of dental caries in the mixed dentition stage was associated with low socio-economic status and several behavioral factors, including the duration of tooth brushing and previous dental treatments and emergency visits [111]. Therefore, efforts should be made to address these factors, to improve oral health behavior and the use of oral health care services [111].

A cohort study on a group of children seven to eight years old from Tehran (Iran) showed that 53% of the subjects developed at least one new dental caries at the level of the FPMs within two years, and according to the CAST (Caries Assessment Spectrum and Treatment) index and OHI-S (Oral Hygiene Index-Simplified), this finding was associated with socio-economic status and mother's education but was not associated with sweets consumption and oral hygiene [112]. The study also revealed no statistically significant correlations between caries occurrence and gender [112].

Duman and Duruk, 2021, in their study carried out on a community in the Eastern Anatolia region of Turkey, showed that the FPMs are among the teeth most affected by caries during childhood, and the prevalence of these lesions increases with age [113]. Mandibular FPMs were more frequently affected than their maxillary counterparts, without significant left/right differences. The authors also showed that the prevalence of dental caries in the FPM, according to gender, was higher among girls compared to boys, and the fact that tooth eruption occurs earlier in girls compared to boys could explain this result due to the time of longer exposure of the FPM to cariogenic agents [113].

There are authors who showed that it is possible to identify the risk of dental caries in FPMs based on primary molar carious experience, the condition of deciduous second molar being of particular importance on caries development in adjacent FPM.

Vanderas et al., 2004, showed that dental caries were frequently located on the mesial surface of the FPMs and found strong correlations between the presence of caries on the distal surface of the primary second molar and the occurrence of the disease in the mesial surface of the adjacent FPM [114].

Mejàre et al., 2001, investigating 374 children during their mean ages of 6.7 to 11.5 years, showed that there is a close correlation between the caries status of the distal surface of the second primary molar and the caries rate for the mesial surface of the FPM and that FPM caries rate was 15 times higher in cases of enamel/enamel-dentin border caries on the second primary molars compared to cases of sound deciduous molars [115].

Leroy et al., examining annually 4468 children during their primary school time, identified that cavity formation in FPMs was strongly influenced by the status of the adjacent primary molars, the effect of the second deciduous molar being the most pronounced [116]. In cases where both primary molars were affected by dental caries, in association with a poor oral environment, a peak in cavity formation in the FPM one to two years after emerging from the mucosa was registered [116].

In a recent (2021) cross-sectional study that assessed 413 children 7- and 8-year-old, Jafari et al. found that in cases of sound primary first molars, 22.9% of the adjacent FPMs

were also sound, and in cases of sound primary second molars, 25.7% of the FPMs in the same quadrant were also sound [117]. A stronger correlation between a carious primary second molar and the development of dentin caries in the adjacent FPM than in cases of a carious primary first molar was noticed ($p < 0.001$) [117].

Particularities of Approaching the Child with FPM Caries

The preservation of FPM health is an important determining factor for future oral health [102].

Risk assessment is the first step in caries management because multiple risk factors for caries attack on FPM are related to the challenging and dynamic period of mixed dentition [118]. The interval between the initiation of tooth eruption and the tooth coming into full functional occlusion is considered an important time for FPM caries prevention intervention [100]. Preventive care is implemented throughout the entire period of transition between the primary and permanent dentition and continues afterward. The prevention strategy includes oral health education, fluoride administration, use of pit and fissure sealants, and risk-oriented timing of recall visits [118]. Pit and fissure sealants are the preferred methods for the prevention of FPM occlusal caries in children who are at high risk and have barriers to accessing dental care [119]. School-based sealant programs should target kindergarten children and first graders, with follow-up programs for second-grade children [107].

When operative intervention is necessary, the principles of preserving healthy hard dental tissues and pulp vitality are applied [118,120]. The life-long need for restoration replacement has also to be taken into consideration [91].

Cases of teeth with extensive caries must be carefully assessed as heavily restored teeth enter a restorative cycle leading to dental extraction [121]. Late extraction of FPM generates the need to restore the edentulous space [121]. Therefore, in order to avoid the occlusal and prosthetic complications determined by FPM extraction later in life, Gill et al. recommend that extraction during the mixed dentition stage could be the treatment of choice for FPMs with poor prognosis, making space for the second permanent molars to favorably erupt in the place of FPMs [121].

According to Eichenberger et al., 2015, extraction of the mandibular FPM during the mixed dentition stage has a favorable outcome because the maxillary FPM on the opposing dental arch remains in contact with the primary second molar and vertical migrations are minor [122].

In a 2018 systematic review concerning the consequences of FPM early extraction, Saber et al. concluded that the ideal time for FPM extraction to achieve complete closure of the edentulous span is when the second permanent molar is at the early bifurcation stage of its development [123].

Teo et al., 2013 reported higher rates of space closure in the maxilla than in the mandible (92% vs. 66%) [92]. The authors also showed that spontaneous space closure was independent of the type of malocclusion [92].

Teo et al., 2016, investigating 66 patients five years after the mandibular FPM extraction, illustrated that together with the ideal developmental stage of the second permanent molar, three other factors influence spontaneous space closure: the second premolar engaged in the bifurcation of the primary second molar, a mesial angulation of the second permanent molar in relation to the FPM and the presence of the third molar [124]. Because the third molar cannot be radiographically identified before the age of eight, it is reasonable to delay the extraction until its presence is confirmed, but before half the root of the second permanent molar is fully developed, with equal and even more beneficial outcomes than the early extraction [124]. The authors also highlighted the need for orthodontic evaluation in any cases of FPM early extraction [124].

4. Conclusions

The maxillary FPM is reported to be the tooth most affected by ectopic eruption in the pediatric patient. Differentiation between reversible and irreversible ectopic types is an important step in its clinical management.

Hypomineralization is currently the most prevalent structural disturbance in FPM, which must be considered a public health problem due to the rapid destruction of the hard dental tissues it generates. MIH represents a high-risk factor for the onset of dental caries, as well.

FPM particular vulnerability to caries is due to its posteruptive enamel maturation, which is accomplished during the mixed dentition stage. There are regional variations in the prevalence of FPM dental caries stemming from social, economic, cultural, and dietary differences and from oral health preventive programs that differ among countries.

Early, even pre-eruptive FPM monitoring and early diagnosis of FPM pathology help in the provision of preventive and interceptive interventions to minimize long-term imbalances of the stomatognathic system homeostasis.

Proper clinical management of FPM pathology is a demanding task for the pediatric dentist and is of great importance for the development of a healthy permanent dentition and stable occlusion.

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