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SYSTEMATIC REVIEW

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Association between molar-incisor hypomineralization and dental developmental anomalies: a systematic review and meta-analysis

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Abstract

Background: Molar-incisor hypomineralization (MIH) is a common developmental enamel defect, and its potential association with developmental dental anomalies (DDAs) has been suggested but remains inconclusive. This systematic review and meta-analysis aimed to evaluate the association between MIH and DDAs in children and adolescents. **Methods**: A comprehensive search was performed in PubMed, Web of Science, Scopus, and Embase. Studies comparing the occurrence of DDAs between individuals with and without MIH were included. The quality of each study was assessed using the modified Newcastle-Ottawa Scale (NOS). Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and the certainty of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. **Results**: A total of 2343 records were identified, and 6 studies were included. According to the modified NOS, the methodological quality of the included studies ranged from moderate to very high. Analysis by anomaly type indicated that children with MIH had higher odds of hypodontia than those without MIH (OR = 1.63, 95% CI: 1.03–2.59, $p = 0.04$, $I^2 = 67\%$); however, this CI was wide, with its lower bound close to unity. No significant association was identified for hyperdontia (OR = 0.79, 95% CI: 0.47–1.33, $p = 0.37$, $I^2 = 0\%$), microdontia (OR = 1.79, 95% CI: 0.96–3.36, $p = 0.07$, $I^2 = 18\%$), or positional and morphological anomalies. An exploratory meta-analysis of overall DDAs showed no significant association between MIH and overall DDAs (OR = 1.71, 95% CI: 0.96–3.07, $p = 0.07$, $I^2 = 71\%$). The certainty of evidence was rated as very low for all outcomes as per the GRADE framework. **Conclusions**: MIH is weakly associated with hypodontia, while no clear associations were identified for other DDAs. The certainty of the evidence was very low, and the findings should be interpreted with caution. **The PROSPERO Registration**: CRD420261294642.

Keywords

Developmental dental anomalies; Molar-incisor hypomineralization; Hypodontia

1. Introduction

Molar-incisor hypomineralization (MIH) is a prevalent developmental defect of the dental enamel. It is characterized by demarcated hypomineralized lesions affecting one or more first permanent molars, occasionally involving permanent incisors, or restricted to molars alone [1]. The affected enamel exhibits reduced mineral density and compromised mechanical properties, predisposing teeth to post-eruptive breakdown under masticatory forces, with subsequent exposure of the dentin, increased susceptibility to dental caries, hypersensitivity, and restoration failure [2–4]. Epidemiological studies indicate considerable variability in the prevalence of MIH worldwide, likely reflecting differences in geographical region, ethnicity, and environmental exposures [5, 6]. Meta-analytical estimates suggest a global prevalence of approximately 12–13% [7, 8]. Given the high prevalence and potential long-term impact of MIH on oral health, early identification, standardized diagnostic protocols, and timely intervention are considered essential in the pediatric dental management of affected children.

The etiology of MIH is not yet fully understood, although this condition is generally considered to be multifactorial, involving interactions between genetic susceptibility and environmental exposures that may disrupt enamel formation during critical periods of amelogenesis [9–12]. Several studies have reported associations between MIH and early-life systemic conditions, including illness, fever, respiratory disease, and perinatal complications, as well as exposure to medications or environmental stressors [11, 13–15]. Similarly, developmental dental anomalies (DDAs), including abnormalities in

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the number, size, morphology, and structure of teeth, are also thought to arise from disturbances during tooth development influenced by genetic and environmental factors [16, 17]. The etiology of DDAs is considered to be multifactorial, involving both genetic factors, such as variants in Msh homeobox 1 (*MSX1*), Paired box 9 (*PAX9*), and Runt-related transcription factor 2 (*RUNX2*), which are associated with hypodontia and other dental anomalies [18–20], and non-genetic factors, including adverse perinatal events, systemic diseases, and environmental exposures that may affect tooth development and amelogenesis [21–23].

With increasing understanding of the pathogenesis of MIH, some studies have begun to investigate its potential co-occurrence with DDAs [24–27]. From a biological perspective, both MIH and DDAs are associated with disturbances occurring during tooth development, and the potential overlap in genetic susceptibility, ameloblast dysfunction, and early-life environmental exposures provides a plausible basis for their association [18, 28, 29]. However, the available evidence remains inconsistent. One study reported a significant association between MIH and DDAs [24], whereas other studies did not identify a significant increase in the overall prevalence of DDAs among MIH patients [26, 27]. These discrepancies may reflect differences in study populations, sample sizes, and the types of DDAs assessed. In particular, variations in the types of anomalies included when defining overall DDAs may have contributed to inconsistent findings.

Most existing studies are observational and have relatively small sample sizes, and differences in the classification and reporting of DDAs may further limit the comparability of findings. Therefore, whether MIH is associated with DDAs overall or only with specific anomaly subtypes remains unclear. To date, no systematic review and meta-analysis has specifically evaluated this association. Therefore, this systematic review and meta-analysis aimed to synthesize the available evidence on the relationship between MIH and DDAs in children and adolescents and to investigate potential differences among various anomaly subtypes.

2. Materials and methods

2.1 Protocol and registration

This systematic review and meta-analysis was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [30]. The PRISMA checklist is provided as **Supplementary material 1**. The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD420261294642).

2.2 Focused question and study selection

A systematic literature search was conducted using four electronic databases: PubMed, Web of Science, Scopus, and Embase, from inception to 18 February 2026 (the date of the last search), with no restrictions on language. In addition, manual searches of the reference lists of the included studies were performed to identify potentially relevant articles. The detailed search strategies for each database are provided in **Supplementary Table 1**.

The focused question was formulated according to the PECOS framework: population (P): children and adolescents (aged less than 18 year) without syndromic conditions, craniofacial anomalies, or severe systemic diseases; exposure (E): diagnosis of MIH in children or adolescents; comparison (C): children and adolescents without MIH; outcomes (O): DDAs, including number anomalies (*e.g.*, hypodontia, hyperdontia), shape anomalies (*e.g.*, peg-shaped lateral incisors, fusion, gemination, taurodontism, dilaceration), size anomalies (*e.g.*, microdontia), and position anomalies (*e.g.*, ectopic eruption of maxillary permanent first molars, palatally displaced canines, and infraocclusion of primary molars); and study design (S): observational studies, including cross-sectional, case–control, and cohort studies.

Studies were excluded if they met any of the following criteria: (1) case reports, case series, literature reviews, expert opinions, or animal studies; (2) studies without a control group, or studies for which outcome data for the non-MIH comparison group could not be extracted separately; (3) participants with syndromic conditions, severe systemic diseases, congenital malformations, or craniofacial anomalies; and (4) studies that did not report data on DDAs (number, size, shape, or position), or relevant outcome data were unavailable for analysis.

The literature search, initial screening, and full-text assessment were independently performed by two reviewers (YL and XH). Following the removal of duplicate records, the titles and abstracts were screened for eligibility. The full texts of potentially eligible studies were then reviewed to determine eligibility for inclusion in the final analysis. The reference lists of the included studies were also manually screened to identify additional relevant publications, and forward citation tracking was performed using Web of Science to identify studies citing the included articles. Any disagreements between the two reviewers were resolved by discussion; if necessary, a third reviewer (LD) was consulted to reach a consensus.

2.3 Data extraction

Data were independently extracted by two reviewers (YL and XH) using a standardized data extraction form. The extracted information included the author and year of publication, country, sample size, and age range of participants, diagnostic criteria for MIH and DDAs, types of DDAs assessed, and key study findings. Any discrepancies were resolved by discussion and consensus with a third reviewer (LD).

2.4 Quality assessment

The methodological quality of the included studies was assessed using the modified Newcastle-Ottawa Scale (NOS) [31]. Methodological quality was evaluated across three dimensions, including the selection of study populations (up to 5 points), comparability of the exposed and control groups (up to 2 points), and the assessment of study outcomes (up to 3 points). Based on the total NOS score, studies were categorized as very high (9–10), high (7–8), moderate (5–6), or low quality (1–4) [32]. Quality assessment was independently conducted by two reviewers (YL and XH),

and disagreements were resolved through discussion and consensus with a third reviewer (LD).

2.5 Data synthesis and meta-analysis

For dichotomous outcomes, pooled odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were calculated using a random-effects model. Statistical heterogeneity among studies was assessed using the Q test and I^2 statistic. A p-value < 0.05 for the Q test or an I^2 value $> 50\%$ was considered indicative of substantial heterogeneity. Sensitivity analyses were performed by sequentially excluding individual studies to evaluate the robustness of the pooled estimates. When at least two studies reported the same DDA subtype with sufficient clinical and methodological comparability, quantitative synthesis was performed. When meta-analysis was considered inappropriate due to substantial clinical or methodological heterogeneity, findings were synthesized narratively. For narrative synthesis, studies were grouped according to the specific DDA subtypes evaluated. Findings were compared by describing the direction and consistency of associations reported across studies, while considering differences in study characteristics and outcome definitions. Publication bias was not assessed due to the limited number of included studies (<10). All statistical analyses were performed using Review Manager (RevMan) software (version 5.4, developed by the Cochrane Collaboration, London, UK).

2.6 GRADE

The certainty of the evidence was assessed according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework [33, 34]. Because the included studies were cross-sectional in design, the evidence was initially rated as low certainty. Five domains were considered for potential downgrading: risk of bias, inconsistency of findings, indirectness of the evidence, imprecision of effect estimates, and publication bias. In addition, three factors that may justify upgrading the certainty were evaluated, including a large magnitude of effect, the presence of a dose–response gradient, and evidence that residual confounding was unlikely to explain the observed associations. Based on this comprehensive assessment, the overall certainty of the evidence was categorized as high, moderate, low, or very low. The GRADE certainty assessments were independently performed by two reviewers (YL and XH). Any disagreements were resolved through discussion and consensus with a third reviewer (LD). The Summary of Findings table was produced using the GRADEpro GDT (Guideline Development Tool) (https://www.gradepro.org, McMaster University and Evidence Prime, Hamilton, ON, Canada).

3. Results

3.1 Literature search and study selection

A total of 2343 relevant records were identified through the literature search, including 160 from PubMed, 507 from Web of Science, 1554 from Scopus, and 122 from Embase. After removing 643 duplicates, 1700 records remained for screening. Following screening of the title and abstract of these 1700 records, 11 studies were assessed by full-text review. Ultimately, 6 studies met the pre-defined inclusion criteria and were included in this systematic review and meta-analysis [24–27, 35, 36]. The reasons for exclusion are presented in Fig. 1.

3.2 Study characteristics

The main characteristics of the six studies included in our meta-analysis are summarized in **Supplementary Table 2**. Of these, two were conducted in Turkey [26, 35], two in Brazil [24, 25], one was a multicentre study conducted in 14 countries [36], and one was conducted in Spain [27]. With regard to DDAs, two studies reported outcomes on number, position, size, and shape anomalies [26, 36]; one reported on number, position, and size anomalies [24]; one on number, position, and shape anomalies [35]; one on number and position anomalies [27]; and one reported only on number anomalies [25]. Allincluded studies diagnosed MIH according to the criteria established and modified by the European Academy of Paediatric Dentistry [1, 37].

3.3 Quality assessment

Overall, the methodological quality of the included studies ranged from moderate to very high, with detailed scores presented in Table 1. With regard to study selection, several studies were limited by their single-center designs and restricted sample representativeness, with only one study receiving full credit for this domain due to its multicenter design and broader sample coverage [36]. With regard to the assessment of exposure, most studies were downgraded because MIH diagnosis was primarily based on clinical case records, although two studies used intra-oral photographic assessment with standardized scoring systems, which may have enhanced objectivity and reproducibility [24, 25]. In terms of comparability, most studies were assigned lower score due to insufficient adjustment for key confounders, including sex, age, and geographical region. For outcome assessment, the majority of studies were assigned low score bacauseblinded assessment was not reported, with only one study reporting the handling of anonymized data, which may have reduced measurement bias, at least in part [36].

3.4 Results

3.4.1 Number anomalies

Regarding numerical anomalies, six studies were included to analyze hypodontia [24–27, 35, 36]. Meta-analysis suggested a possible association between MIH and hypodontia, with individuals with MIH exhibiting higher odds of hypodontia than those without MIH (OR = 1.63, 95% CI: 1.03–2.59, p = 0.04, I^2 = 67%) (Fig. 2A). However, the relatively wide confidence interval, withits lower bound being close to unity, indicates considerable imprecision in the effect estimate. Sensitivity analyses using the leave-one-out approach showed that heterogeneity was not substantially reduced after excluding individual studies, suggesting that the observed heterogeneity may be attributable to differences in multiple study characteristics rather than being driven by a single study. In contrast,

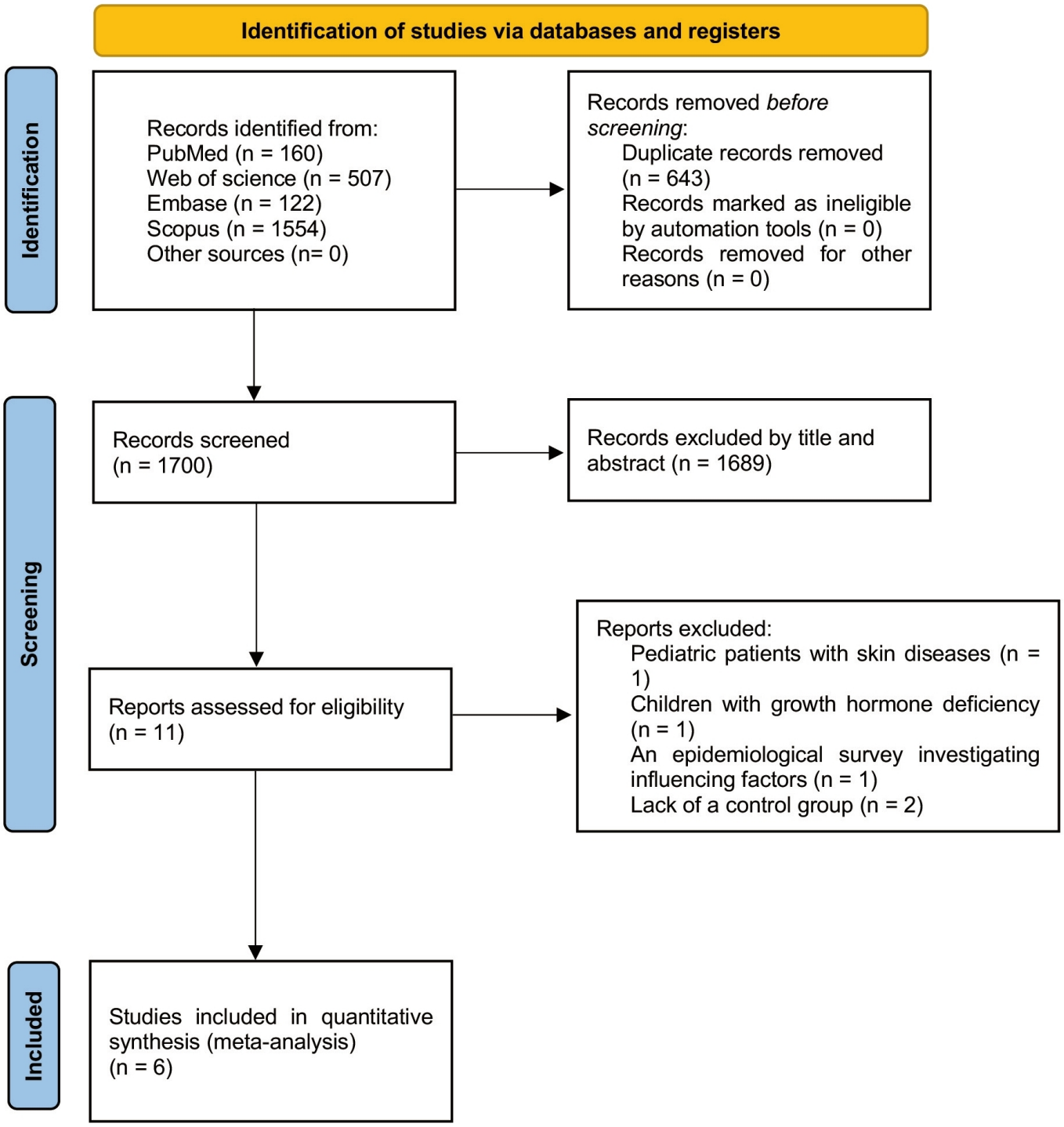


FIGURE 1. PRISMA flow diagram of the literature screening process and reasons for study exclusion.

four studies evaluated hyperdontia [24, 26, 35, 36]. The pooled results showed no statistically significant difference between the MIH and non-MIH groups (OR = 0.79, 95% CI: 0.47–1.33, $p = 0.37$, $I^2 = 0\%$) (Fig. 2B).

3.4.2 Size anomalies

Three studies assessed microdontia [24, 26, 36]. Pooled analysis indicated a higher odds of microdontia in the MIH group than in the control group (OR = 1.79, 95% CI: 0.96–3.36, $I^2 = 18\%$); however, this difference was not statistically significant ($p = 0.07$) (Fig. 3A).

3.4.3 Shape anomalies

Three studies reported on taurodontism; meta-analysis did not reveal a statistically significant association between MIH and taurodontism (OR = 1.80, 95% CI: 0.51–6.38, $p = 0.36$, $I^2 = 56\%$) (Fig. 3B) [26, 35, 36]. After exclusion of one study, heterogeneity was reduced, suggesting that the pooled findings may not be fully robust [36]. No statistically significant differences were observed between the MIH and control groups in the prevalence of root dilaceration and peg-shaped maxillary lateral incisors (**Supplementary Fig. 1**).

TABLE 1. Methodological quality assessment of the included studies using the modified Newcastle-Ottawa Scale (NOS).

Author, year	Selection				Comparability	Assessment of Outcome		Total NOS score
	Representativeness of the sample (*)	Sample Size (*)	Nonrespondents (*)	Ascertainment of the exposure (**)	Based on design and analysis (**)	Assessment of the outcome (**)	Statistical test (*)	
Betül Şen Yavuz 2023		*	*	*	*	*	*	6*
Eloisa Cesario Fernandes 2025 (dental anomalies)		*	*	**	*	*	*	7*
Hani Nazzal 2025	*	*	*	*	**	**	*	9*
Eloisa Cesario Fernandes 2024 (tooth agenesis)		*	*	**	*	*	*	7*
Maria Marcianes 2024		*	*	**	*	*	*	7*
Gokcen Deniz Bayrak 2025		*	*	*	*	*	*	6*

** indicates 1 point, and ** indicates 2 points. Quality categories were classified based on the total NOS scores: low quality (1–4 points), medium quality (5–6 points), high quality (7–8 points), and very high quality (9–10 points).*

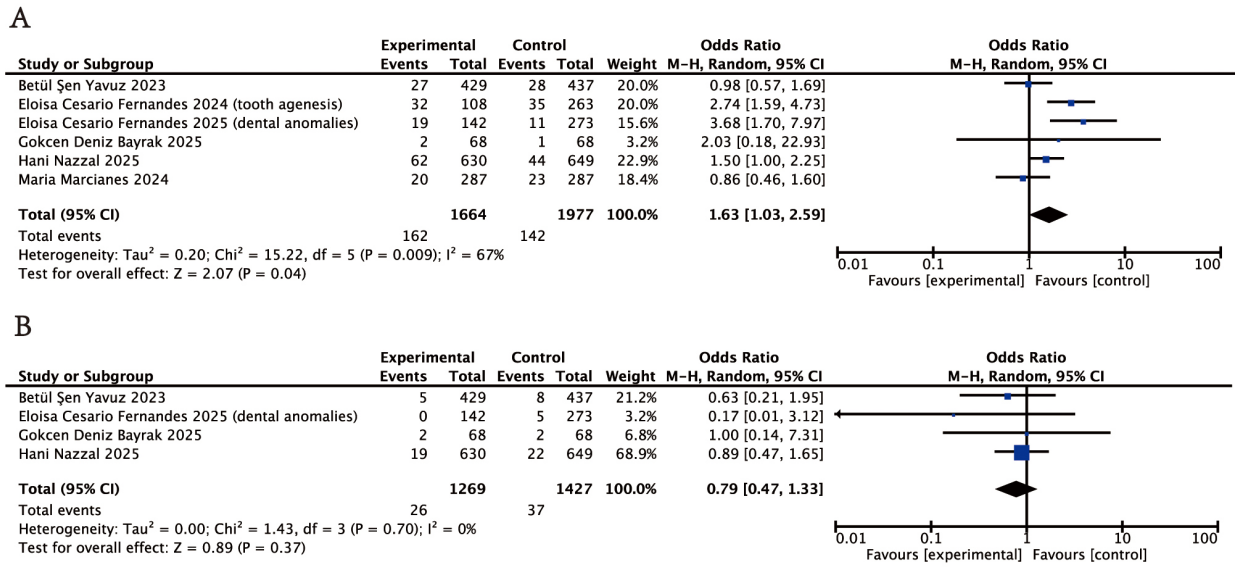


FIGURE 2. Forest plots evaluating the association between molar-incisor hypomineralization and developmental dental anomalies. (A) Hypodontia, (B) Hyperdontia. CI: confidence interval; M–H: Mantel–Haenszel.

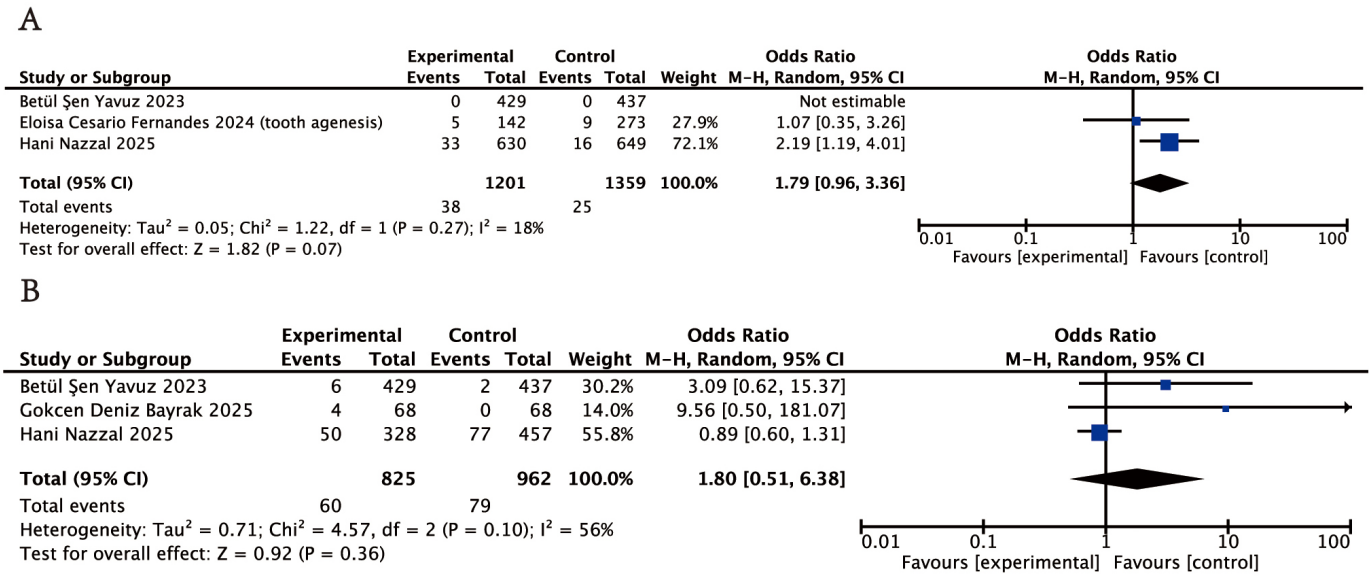


FIGURE 3. Forest plots evaluating the association between molar-incisor hypomineralization and developmental dental anomalies. (A) Microdontia, (B) Taurodontism. CI: confidence interval; M–H: Mantel–Haenszel.

3.4.4 Position anomalies

For positional anomalies, pooled analyses were conducted for ectopic eruption of the first permanent molars, palatally displaced canines, and infraocclusion of primary molars. No significant differences were detected between the MIH and control groups, as follows: ectopic eruption of the first permanent molars (OR = 0.95, 95% CI: 0.63–1.44, $p = 0.80$, $I^2 = 0\%$), palatally displaced canines (OR = 1.15, 95% CI: 0.59–2.25, $p = 0.68$, $I^2 = 39\%$), and infraocclusion of primary molars (OR = 1.42, 95% CI: 0.82–2.47, $p = 0.21$, $I^2 = 5\%$) (Fig. 4).

3.4.5 Overall DDAs

Three studies were included to assess the overall occurrence of DDAs [24, 26, 35]. One study reported a slightly higher occurrence of DDAs in children with MIH compared with controls [24], whereas the other two studies did not identify a statistically significant difference between the MIH and control groups [26, 35]. Given the heterogeneous nature of DDAs and the differences in the types of DDAs evaluated across the included studies, the association between MIH and overall DDAs was described as an exploratory analysis rather than a primary pooled outcome. Nevertheless, an exploratory meta-analysis was performed using the available data. The pooled analysis showed no statistically significant difference between the MIH and control groups (OR = 1.71, 95% CI: 0.96–3.07, $p = 0.07$, $I^2 = 71\%$) (Fig. 5).

Overall, compared with controls, individuals with MIH showed a higher prevalence of hypodontia, whereas no apparent differences were observed for morphological or positional anomalies.

3.5 GRADE

According to the GRADE approach, evidence derived from observational studies was initially rated as low certainty and was ultimately downgraded to very low certainty. This downgrading was predominantly attributable to heterogeneity between studies and the imprecision of the effect estimates. A detailed account of the assessment process is provided in **Supplementary Table 3**, and a summary of findings is presented in **Supplementary Table 4**.

4. Discussion

This meta-analysis systematically evaluated the association between MIH and different types of DDAs. Meta-analysis of specific anomaly types revealed that individuals with MIH had higher odds of hypodontia than those with controls; however, this association was of weak-to-moderate magnitude, with a relatively wide CI and a lower boundary close to unity. Therefore, this result should be interpreted with caution. In contrast, other types of DDAs, including hyperdontia, taurodontism, microdontia, and various positional anomalies, were not significantly associated with MIH. An exploratory meta-analysis combining overall DDAs showed no statistically significant association between MIH and the overall occurrence of DDAs. These findings may suggest that the association between MIH and DDAs could vary according to the specific type of anomaly. However, given the limited number of available studies and the observational nature of the included studies, causal relationships between MIH and specific types of DDAs cannot be established; therefore, these findings shoulde be interpreted with caution.

With regard to numerical anomalies, this meta-analysis showed higher odds of hypodontia in individuals with MIH, whereas no significant difference was observed for hyperdontia. Hypodontia arises during the initiation and early morphogenesis of tooth development and has been linked to the genetic, epigenetic, and environmental factors involved in odontogenesis [38–41]. Previous studies have also suggested that MIH may involve developmental disturbances occurring during the early stages of tooth formation [28, 29, 42]. Therefore, the observed association between MIH and hypodontia may reflect certain shared developmental

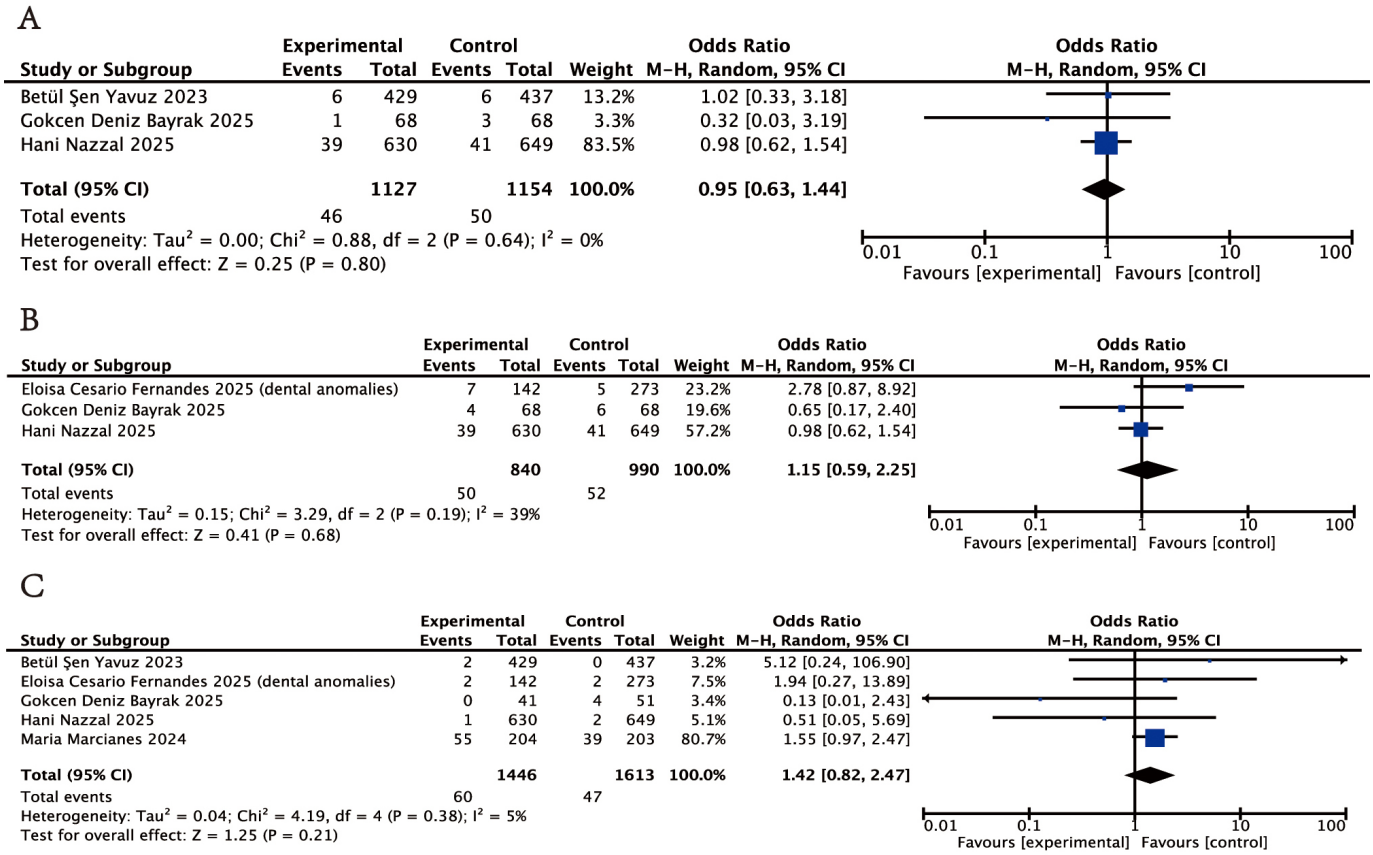


FIGURE 4. Forest plots evaluating the association between molar incisor hypomineralization and developmental dental anomalies: (A) Ectopic eruption of the first permanent molars, (B) Palatally displaced canines, (C) Infraocclusion of primary molars. CI: confidence interval; M–H: Mantel–Haenszel.

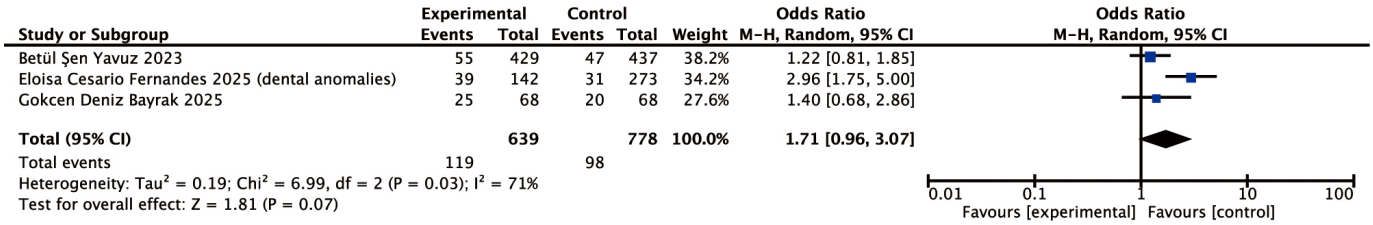


FIGURE 5. Forest plot evaluating the association between molar-incisor hypomineralization and overall developmental dental anomalies. CI: confidence interval; M–H: Mantel–Haenszel.

influences, although the specific mechanisms underlying such as association remain unclear. However, substantial heterogeneity was observed among the included studies. Sensitivity analyses performed by sequentially excluding individual studies showed that heterogeneity remained substantial, suggesting that the observed variability was not driven by a single study alone. Moreover, the CI around the pooled estimate was relatively wide and approached the null value, indicating some degree of uncertainty; therefore, the findings should be interpreted cautiously. In contrast, hyperdontia is generally considered to arise through different developmental processes, such as tooth germ dichotomy or localized hyperactivity of the dental lamina [43, 44]. No significant association was observed for hyperdontia; however, their relatively low prevalence and the limited sample sizes of the included studies may have reduced the statistical power to detect potential associations.

No statistically significant associations were detected between MIH and microdontia, morphological anomalies, or positional anomalies. The absence of significant associations for positional anomalies may reflect their multifactorial etiology. Previous studies have suggested that local factors, such as maxillary hypoplasia, retrognathism, the premature loss of primary molars, and certain iatrogenic factors, may contribute to the development of positional anomalies [45, 46]. For example, the inadequate marginal adaptation of stainless-steel crowns placed on primary second molars has been reported to interfere with the normal eruption of the first permanent molars [47]. In addition, the limited number of available studies and their relatively small sample sizes

may have reduced the statistical power to detect potential associations. Therefore, these findings should be interpreted with caution. Further well-designed studies with larger sample sizes and standardized diagnostic criteria are needed to clarify the relationship between MIH and specific DDAs.

This meta-analysis did not identify a statistically significant difference in the overall risk of DDAs between individuals with and without MIH. This null finding should not be interpreted as evidence that no biological association exists; rather, it may reflect the marked etiological and developmental heterogeneity of DDAs. These anomalies encompass a wide range of conditions affecting the number, size, morphology, and position of teeth, arising at different stages of odontogenesis and influenced by genetic, epigenetic, and environmental factors [48–50]. Furthermore, the types of DDAs included in the assessment of overall DDAs varied across the original studies, with different studies evaluating different combinations of anomaly subtypes. Given the substantial heterogeneity of DDAs, the overall DDA analysis should be interpreted as an exploratory analysis, as the pooled estimate may be influenced by differences in anomaly classification and outcome definitions. Therefore, the biological interpretation of this pooled estimate should be approached with caution.

From a clinical perspective, these findings may provide limited evidence to increase awareness among pediatric dentists of the potential co-occurrence of MIH and hypodontia and to support more attentive screening during routine clinical examinations. However, this systematic review has several limitations. First, most of the included studies were cross-sectional, which limits causal inference. Second, potential residual confounding factors, including genetic susceptibility and differences in clinical characteristics of MIH, could not be fully accounted for due to the observational nature of the included studies. Third, although multiple electronic databases were searched, the Cochrane Library was not included, and grey literature was not systematically searched. Therefore, the possibility that some relevant studies may not have been identified cannot be completely excluded. Fourth, the small sample sizes for certain anomaly subtypes may have reduced statistical power, potentially influencing the stability and reliability of the results. In addition, the limited number of included studies precluded a formal assessment of publication bias, and the potential impact of publication bias on the overall confidence in the conclusions cannot be ruled out. Consequently, confidence in the current evidence remains limited.

Future research should further investigate the associations between MIH and specific DDA subtypes. Given the limited number of available studies, larger and well-designed studies with more comprehensive reporting are needed to improve the reliability and comparability of the evidence. Furthermore, considering the possible weak association between MIH and hypodontia, future studies may explore whether this relationship varies according to the location or pattern of hypodontia.

5. Conclusions

Within the limitations of this systematic review and the available evidence, our findings suggest a weak association between MIH and hypodontia, while no statistically significant associations were identified for other types of DDAs. However, the certainty of evidence was very low, and several analyses were based on a limited number of studies with relatively small sample sizes. Therefore, these findings should be interpreted with caution. Further high-quality, well-designed studies with larger sample sizes and standardized methodologies are required to verify these associations and clarify their clinical relevance.

AVAILABILITY OF DATA AND MATERIALS

All data and materials are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

YSL—designed the research study, performed the research, and wrote the manuscript. XXH and JXL—performed the research and analyzed the data. LSD—analyzed the data and wrote the manuscript. All authors contributed to the editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

ACKNOWLEDGMENT

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.jocpd.com/files/article/2117504093985357824/attachment/Supplementary%20material.zip.

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