

Prevalence and Early-Life Factors Associated with Molar–Incisor Hypomineralization in Children in Northwest China: A Population- Based Cross-Sectional Study

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Abstract

Objective: To estimate the prevalence of molar–incisor hypomineralization (MIH) among primary school children in Shaanxi Province, China, and to explore associated prenatal, perinatal, and early-life factors.

Method: A population-based cross-sectional study was conducted using a stratified cluster random sampling design. Children aged 7–10 years were recruited from three cities (Yan'an, Xianyang, and Hanzhong). Standardized oral examinations were performed by calibrated examiners according to the European Academy of Paediatric Dentistry (EAPD) criteria. Structured questionnaires were administered to caregivers to collect information on prenatal, perinatal, and early childhood exposures. Associations were evaluated using chi-square tests and multivariate logistic regression, with odds ratios (ORs) and 95% confidence intervals (CIs) reported.

Results: A total of 2,694 children were included. The overall prevalence of MIH was 22.16%, with no significant sex difference. Significant regional variation was observed, with higher prevalence in Yan'an and Xianyang compared with Hanzhong. In multivariate analysis, amoxicillin exposure (OR=18.88, 95%CI:14.10–25.28) and maternal diarrhea during the third trimester (OR=9.72, 95%CI:4.15–22.74) were strongly associated with MIH. In contrast, preterm birth (OR=0.60, 95%CI: 0.45–0.79) and low birth weight (OR=0.35, 95%CI: 0.23–0.54) showed inverse associations after adjustment.

Conclusion: MIH is highly prevalent among schoolchildren in Shaanxi Province and shows significant geographic variation. Several prenatal and early-life factors were associated with MIH; however, causal relationships remain uncertain. These findings provide important epidemiological evidence to support early identification of high-risk groups and inform future longitudinal research.

Introduction

Molar–incisor hypomineralization (MIH) is a developmental enamel defect first defined by Weerheijm in 2001, affecting one or more first permanent molars, with or without involvement of permanent incisors [1]. It is characterized by qualitative hypomineralization of enamel, resulting in increased porosity and structural weakness [1]. Clinically, MIH presents as demarcated opacities ranging from white to yellow or brown discoloration and may progress to post-eruptive enamel breakdown when affected enamel fails under masticatory stress [1, 2].

MIH has become an important pediatric oral health concern due to its high clinical burden. Affected teeth are at increased risk of dental caries [3–5], and patients frequently experience tooth hypersensitivity that compromises oral function and hygiene behaviors [6]. In addition, MIH complicates behavioral management during dental treatment in children and adolescents, increasing treatment difficulty and resource utilization [7, 8]. Beyond clinical consequences, MIH negatively affects oral health–related quality of life, imposing psychosocial and functional burdens on affected children and their families [9].

Epidemiological studies have reported substantial global variation in MIH prevalence, ranging from 0.48% to 58.5% [10–12], largely due to differences in diagnostic criteria, study design, and population characteristics. In China, available data remain limited and geographically inconsistent, with reported prevalence ranging from 2.8% in Hong Kong [13], 25.5% in Wenzhou [14], 4.45% in Suzhou [15], and 5.04% in Wuhan [16]. However, these studies are predominantly concentrated in southern and central China, and robust population-based data from Northwest China remain lacking.

The etiology of MIH is considered multifactorial, involving both environmental exposures and genetic susceptibility. Systemic insults during enamel development–occurring in prenatal, perinatal, and postnatal periods–have been widely implicated. Reported prenatal factors include maternal illness, infection, stress, and smoking [17], while perinatal factors include prematurity, cesarean delivery, and neonatal hypoxia [18]. Postnatal exposures such as early childhood illness, fever episodes, antibiotic use, prolonged breastfeeding, and environmental toxins have also been associated with MIH occurrence [18]. In parallel, genetic susceptibility has been proposed, with evidence suggesting that variants in enamel formation-related genes may influence individual vulnerability [19]. Despite growing evidence on MIH globally, there is a persistent lack of population-based data from Northwest China, and no study to date has comprehensively evaluated MIH prevalence together with a

multidimensional risk factor profile incorporating prenatal, perinatal, postnatal, and genetic-related exposures in this region [20].

Therefore, this population-based cross-sectional study was designed to estimate the prevalence of MIH among children in Shaanxi Province, Northwest China, and to identify associated prenatal, perinatal, postnatal, and genetic-related risk factors, thereby providing evidence for targeted prevention strategies and early-life intervention policies

Methods

Questionnaire survey

A structured questionnaire was developed based on previously validated instruments. A pilot study including 240 mother–child pairs demonstrated good internal consistency (Cronbach’s $\alpha = 0.817$).

The final questionnaire was administered to mothers or primary caregivers via face-to-face or telephone interviews by a trained investigator (Gao Yuyang).

The questionnaire comprised three sections:

- (1) sociodemographic characteristics (age, sex, residential location);
- (2) prenatal exposures during the third trimester, including maternal vomiting, diarrhea, common cold, fever, hypertension, diabetes, alcohol consumption, and antibiotic use;
- (3) perinatal and early childhood factors, including gestational age, delivery mode, birth weight, and systemic conditions occurring before 3 years of age (e.g., jaundice, asthma, diarrhea, pneumonia, tonsillitis, otitis media, and antibiotic exposure).

Questionnaires and informed consent forms were distributed through participating primary schools. Study procedures were explained to caregivers in detail, and only children with signed informed consent were included.

Clinical examination

Two dentists underwent standardized training and calibration prior to the survey. Calibration was conducted on 15 children with MIH who were not included in the final sample.

Intra- and inter-examiner reliability were assessed using Cohen’s kappa statistics, yielding values of 0.97 and 0.95 for intra-examiner agreement, and 0.94 for inter-examiner agreement, respectively.

Clinical examinations were performed under standardized conditions. Teeth were cleaned using cotton rolls to remove debris. Children were seated in an upright position under adequate natural illumination. First permanent molars and incisors were examined after the child was instructed to occlude and reopen the mouth. Tooth surfaces were evaluated in a slightly moist environment.

Photographs taken during the study showing MIH diagnosis as based on the EAPD diagnostic criteria: a Demarcated enamel opacities in first permanent molar, b Demarcated enamel opacities in incisor.

Statistical Analysis

Data were entered and managed using EpiData 3.0 (EpiData Association, Odense, Denmark). To ensure data quality, double data entry was independently performed for a random sample of 100 participants, yielding an inter-entry consistency rate of 99.98%, indicating high data reliability.

All statistical analyses were conducted using SPSS version 18.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize participant characteristics and study variables. Categorical variables were presented as frequencies and percentages.

Group comparisons between children with and without MIH were performed using the chi-square test. Variables with a *p*-value < 0.10 in univariate analyses were considered candidates for multivariate analysis.

Multivariate logistic regression models were constructed to identify independent risk factors associated with MIH. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Statistical significance was defined as a two-sided *p*-value < 0.05.

Results

Prevalence of MIH and general characteristics

MIH diagnosis was based on the criteria of the European Academy of Paediatric Dentistry (EAPD) [20, 21], and standardized epidemiological diagnostic guidelines proposed by Ghanim et al. [22, 23]. Representative clinical manifestations of MIH are shown in Fig. 1.

A total of 2,694 children aged 7–10 years were included in this study. The sample consisted of 1,397 boys (51.86%) and 1,297 girls (48.14%). Regarding geographic distribution, 991 participants (36.78%) were from Yan’an, 865 (32.11%) from Xianyang, and 838 (31.11%) from Hanzhong.

The overall prevalence of MIH was 22.16%. Stratified analysis showed a slightly higher prevalence in boys (22.40%) than in girls (21.90%). Regional differences were observed, with the lowest prevalence in Hanzhong (8.80%), compared with higher rates in Yan’an (29.50%) and Xianyang (26.70%) (Table 1).

		Table 1 MIH distribution according to sex and regional location						
		MIH+ (597)		MIH- (2097)		Total(2694)		<i>p</i> -Value
		n	%	n	%	n	%	
sex	Male	313	22.40	1084	77.60	1397	51.86	0.393
	Female	284	21.90	1013	78.10	1297	48.14	
Regional location	Yan’an	292	29.50	699	70.50	991	36.78	0.001*
	Xianyang	231	26.70	634	73.30	865	32.11	
	Hanzhong	74	8.80	764	91.20	838	31.11	

MIH+ affected with MIH, MIH- not affected with MIH

* Statistically significant *p*-value < 0.05

Maternal prenatal factors and MIH

Maternal conditions during the third trimester were significantly associated with MIH. Maternal diarrhea, common cold, fever, and antibiotic use were significantly correlated with MIH occurrence (all *p* < 0.05). In contrast, maternal vomiting, alcohol consumption, hypertension, and diabetes mellitus showed no significant associations (Table 2).

Table 2
Associations between MIH and maternal third-trimester factors

		MIH+(597)		MIH-(2097)		Total (2694)		χ^2	p-Value
		n	%	n	%	n	%		
Vomiting	Yes	210	23.9	668	76.1	878	32.59	2.333	0.127
	No	387	21.3	1429	78.7	1816	67.41		
Diarrhea	Yes	33	78.6	9	21.4	42	1.56	78.709	0.000*
	No	564	21.3	2088	78.7	2652	98.44		
Common cold	Yes	109	29.9	256	70.1	365	13.55	14.522	0.000*
	No	488	21.0	1841	79.0	2329	86.45		
Fever	Yes	15	39.5	23	60.5	38	1.41	6.698	0.010*
	No	582	21.9	2074	78.1	2656	98.59		
Alcohol consumption	Yes	2	25.0	6	75.0	8	0.30	0.038	0.846
	No	595	22.2	2091	77.8	2686	99.70		
Hypertension	Yes	6	15.4	33	84.6	39	1.45	1.053	0.305
	No	591	22.3	2064	77.7	2655	98.55		
Diabetes mellitus	Yes	1	16.7	5	83.3	6	0.22	0.105	0.746
	No	596	22.2	2092	77.8	2688	99.78		
Antibiotic use	Yes	8	47.1	9	52.9	17	0.63	6.148	0.013*
	No	589	22.0	2088	78.0	2677	99.37		

MIH+ affected with MIH, MIH- not affected with MIH

* Statistically significant p -value < 0.05

Perinatal and early childhood factors (univariate analysis)

Univariate chi-square analyses identified several perinatal factors significantly associated with MIH. Preterm birth was associated with increased MIH prevalence (27.9%; $\chi^2 = 10.007$, $p = 0.002$). Delivery mode was also significant ($\chi^2 = 4.789$, $p = 0.029$), with a slightly lower prevalence observed in vaginal delivery (20.7%) compared with cesarean section (24.3%). Low birth weight showed the strongest association (41.5% vs. 21.2%; $\chi^2 = 29.735$, $p < 0.001$) (Table 3).

Table 3
Association between MIH and child-related factors.

Etiological Factors		MIH+(597)		MIH-(2097)		Total (2694)		χ^2	p-Value
		n	%	n	%	n	%		
Gestational age	Yes	121	27.9	312	72.1	433	16.07	10.007	0.002*
	No	476	21.1	1785	78.9	2261	83.93		
Delivery mode	Yes	335	20.7	1281	79.3	1616	59.99	4.789	0.029*
	No	262	24.3	816	75.7	1078	40.01		
Birth weight	Yes	54	41.5	76	58.5	130	4.83	29.735	0.000*
	No	543	21.2	2021	78.8	2564	95.17		
Neonatal jaundice	Yes	122	23.8	391	76.2	513	19.04	0.966	0.326
	No	475	21.8	1706	78.2	2181	80.96		
Asthma	Yes	13	16	68	84	81	3.01	1.808	0.179
	No	584	22.3	2029	77.7	2613	96.99		
Pneumonia	Yes	104	30.4	238	69.6	342	12.69	15.453	0.000*
	No	493	21	1859	79	2352	87.31		
Tonsillitis	Yes	289	24.3	901	75.7	1190	44.17	5.582	0.018*
	No	308	20.5	1196	79.5	1504	55.83		
Febrile episodes	Yes	346	24.8	1048	75.2	1394	51.74	11.852	0.001*
	No	251	19.3	1049	80.7	1300	48.26		
Otitis media	Yes	15	27.8	39	72.2	54	2.00	1.008	0.315
	No	582	22	2058	78	2640	98.00		
Chickenpox	Yes	25	23.1	83	76.9	108	4.01	0.064	0.801
	No	572	22.1	2014	77.9	2586	95.99		
Diarrhea	Yes	332	23.9	1056	76.1	1388	51.52	5.135	0.023*
	No	265	20.3	1041	79.7	1306	48.48		
Mumps	Yes	11	31.4	24	68.6	35	1.30	1.766	0.184
	No	586	22	2073	78	2659	98.70		
Eczema	Yes	116	26.6	320	73.4	436	16.18	5.959	0.015*
	No	481	21.3	1777	78.7	2258	83.82		
Antibiotic use	Yes	250	37.5	417	62.5	667	24.76	120.632	0.000*
	No	347	17.1	1680	82.9	2027	75.24		
Amoxicillin	Yes	290	73.8	103	26.2	393	14.59	711.077	0.000*
	No	307	13.3	1994	86.7	2301	85.41		

Note: MIH + and MIH- denote children affected and not affected with MIH, respectively. For gestational age, delivery mode, and birth weight, "Yes" indicates preterm birth, vaginal delivery, and low birth weight, respectively, whereas "No" indicates full-term, cesarean section, and normal birth weight. *Statistically significant ($p < 0.05$)

Early childhood exposures

Several early childhood factors within the first 3 years of life were significantly associated with MIH, including pneumonia, tonsillitis, hyperpyrexia, diarrhea, eczema, and antibiotic exposure (particularly amoxicillin). In contrast, neonatal jaundice, asthma, otitis media, and chickenpox were not significantly associated with MIH (Table 3).

Multivariate logistic regression analysis

Variables with $p < 0.10$ in univariate analysis were entered into the multivariate logistic regression model. After adjustment for potential confounders, several independent associations with MIH were identified (Table 4).

Among child-related exposures, amoxicillin use showed the strongest association with MIH (OR = 18.88, 95% CI: 14.10–25.28; $p < 0.001$), followed by overall antibiotic exposure in early childhood (OR = 1.35, 95% CI: 1.03–1.77; $p = 0.032$). Maternal diarrhea during the third trimester was also independently associated with MIH (OR = 9.72, 95% CI: 4.15–22.74; $p < 0.001$).

Interestingly, some variables that were significant in univariate analysis showed inverse associations after adjustment. Preterm birth (OR = 0.60, 95% CI: 0.45–0.79; $p < 0.001$), low birth weight (OR = 0.35, 95% CI: 0.23–0.54; $p < 0.001$), and a history of tonsillitis (OR = 0.73, 95% CI: 0.57–0.92; $p = 0.009$) were negatively associated with MIH after adjustment for covariates.

Table 4
Multivariate logistic regression of independent risk etiological factors for MIH

Multivariate Binary Logistic Regression Analysis (Full Model)							Goodness of Fit of the Model		
		B	SE	p-Value	OR	95%CI	Tests of Model Coefficients	Hosmer and Lemeshow Test	Percentage Correct Classification
Maternal third-trimester factors	Diarrhea	2.274	0.434	0.000*	9.718	4.153–22.740	0.000	0.226	85%
	Common cold	0.288	0.159	0.070	1.333	0.977–1.820			
	Fever	0.356	0.450	0.429	1.428	0.591–3.451			
	Antibiotic use	-0.544	0.681	0.424	0.581	0.153–2.204			
Child-related factors	Premature birth	-0.512	0.142	0.000*	0.599	0.454–0.791			
	Vaginal delivery	-0.150	0.113	0.183	0.861	0.691–1.073			
	low birth weight	-1.040	0.219	0.000*	0.353	0.230–0.543			
	Pneumonia	-0.171	0.170	0.317	0.843	0.604–1.178			
	Tonsillitis	-0.322	0.124	0.009*	0.725	0.569–0.923			
	hyperpyrexia	-0.129	0.124	0.298	0.879	0.690–1.120			
	Diarrhea	-0.027	0.118	0.820	0.974	0.772–1.227			
	Eczema	-0.022	0.154	0.885	0.978	0.723–1.322			
	Antibiotic use	0.299	0.139	0.032*	1.348	1.027–1.771			
	Amoxicillin	2.938	0.149	0.000*	18.880	14.103–25.276			
Constant		-7.717	1.680	0.000	0.000				
* Statistically significant p -value < 0.05; regression coefficients (B), standard errors (SE), odds ratios (OR), 95% confidence intervals (95%CI)									

Discussion

1.1 Prevalence and comparison with previous studies

In the present study, the prevalence of MIH in Shaanxi Province was 22.16%, indicating that MIH represents a considerable pediatric oral health burden in Northwest China. However, prevalence estimates vary widely across populations worldwide. For example, Subramaniam et al. reported a prevalence of 0.48% in Bangalore, India, whereas Samha et al. observed a markedly higher prevalence of 58.5% in children from Ajman [10,11]. The prevalence observed in the present study (22.16%) falls within the mid-to-high range of global estimates and is higher than those reported in several Chinese cities, including Suzhou and

Wuhan [15,16]. This wide variability likely reflects differences in diagnostic criteria, examiner calibration, age ranges, tooth selection, and study design, as well as underlying socioeconomic and environmental heterogeneity across populations.

In agreement with most previous studies, no significant sex-related difference was observed in the present study [10,11,24,25]. This finding suggests that sex is unlikely to play a major role in MIH susceptibility, although subtle interactions between sex-related biological factors and environmental exposures cannot be fully excluded and warrant further investigation. MIH is widely recognized as a multifactorial condition with a complex and incompletely understood etiology. Enamel formation of first permanent molars and incisors occurs from late gestation through the first three years of life, representing a critical window during which systemic disturbances may disrupt ameloblast function. Interactions between genetic susceptibility and environmental exposures during this period are considered central to MIH pathogenesis [23].

1.2 Geographic variation and potential explanations

A significant geographic variation in MIH prevalence was observed across the three surveyed regions in Shaanxi Province ($p = 0.001$). The highest prevalence was identified in Yan'an (29.50%), followed by Xianyang (26.70%), while Hanzhong showed a markedly lower prevalence (8.80%).

This north–south gradient may reflect regional differences in environmental exposures, dietary patterns, healthcare accessibility, and socioeconomic conditions. Shaanxi Province spans diverse ecological and geographic zones, including northern Shaanxi, the Guanzhong plain, and southern Shaanxi, with notable differences in altitude, climate, and lifestyle factors. These contextual differences may contribute to variations in early-life exposures during critical periods of enamel development.

1.3 Risk factors identified in this study

In the present study, several prenatal and early-life factors were significantly associated with MIH. Maternal diarrhea, fever, common cold, and antibiotic use during the third trimester of pregnancy were associated with increased MIH occurrence. Similarly, perinatal factors such as mode of delivery, gestational age, and birth weight, as well as early childhood factors including pneumonia, tonsillitis, eczema, diarrhea, high fever, and antibiotic exposure (including amoxicillin), showed significant associations in univariate analyses.

These findings are broadly consistent with previous studies reporting associations between early-life systemic disturbances and MIH [24–26]. Many of these conditions are associated with systemic inflammation, fever, hypoxia, or metabolic stress, which may interfere with ameloblast activity during enamel maturation.

1.4 Biological plausibility and gene–environment interactions

Genetic susceptibility has also been implicated in MIH development. Variants in enamel-related genes such as ENAM and AMELX have been suggested to influence enamel mineralization and structural integrity [26]. Furthermore, gene–environment interactions may play an important role, as suggested by Bussanelli et al., who reported that interactions between TGFBR1 polymorphisms and childhood pneumonia may increase MIH risk [27].

Systemic conditions such as pneumonia, asthma, and upper respiratory infections may induce hypoxia, fever, and disturbances in acid–base balance, potentially affecting ameloblast function. These physiological disruptions may alter enamel matrix protein processing and hydroxyapatite crystal formation, ultimately leading to hypomineralization [28,29].

In the present study, pneumonia and febrile illnesses were significantly associated with MIH, whereas asthma was not, suggesting that not all respiratory conditions exert equal effects on enamel development.

1.5 Interpretation of inconsistent findings

Koruyucu et al. previously reported multiple perinatal and postnatal risk factors for MIH, including prematurity, maternal complications, and various childhood illnesses [24]. In the present study, maternal diarrhea and fever during pregnancy and preterm birth were confirmed as significant factors in univariate analysis. However, other reported associations such as otitis media, chickenpox, and mumps were not significant, highlighting population-specific differences in exposure profiles and susceptibility.

Importantly, while preterm birth and low birth weight were positively associated with MIH in univariate analyses, both factors showed inverse associations in the multivariable model. This inconsistency may be explained by residual confounding, collinearity among early-life variables, or over-adjustment in the regression model. Similar inconsistencies have also been reported in previous epidemiological studies [21,30], suggesting that perinatal factors may act as proxies for broader systemic vulnerability rather than independent causal determinants.

1.6 Key risk factors and interpretation of antibiotic association

Multivariable logistic regression identified amoxicillin exposure and maternal diarrhea during pregnancy as the strongest associated factors for MIH. However, the observed association between amoxicillin use and MIH should be interpreted with caution.

Although some studies have suggested a potential link between early antibiotic exposure and enamel defects, others have found no significant association [27,30]. Amoxicillin is commonly prescribed for respiratory infections, making it difficult to distinguish the effect of the medication itself from the underlying infectious disease. Therefore, the association observed in this study may reflect confounding by indication rather than a direct causal effect. Laisi et al. proposed that early amoxicillin exposure may be a risk indicator rather than a direct etiological factor [31].

Taken together, these findings suggest that early-life systemic illness and related treatments may jointly contribute to MIH risk, but causal pathways remain uncertain.

1.7 Strengths and limitations (integrated narrative style)

This study has several strengths, including its population-based stratified cluster sampling design, large sample size, standardized diagnostic criteria based on EAPD guidelines, and excellent examiner reliability. Additionally, the comprehensive assessment of prenatal, perinatal, and early childhood exposures provides a multidimensional perspective on MIH risk factors.

Nevertheless, several limitations should be acknowledged. The cross-sectional design precludes causal inference, and retrospective parental recall may introduce recall bias. In addition, unmeasured confounders such as nutritional status and environmental fluoride exposure were not fully captured. Finally, the observed associations may be influenced by residual confounding inherent in observational epidemiological studies.

1.8 Implications and future directions

The findings of this study highlight MIH as a significant public health concern in Northwest China. Early-life systemic conditions appear to play an important role in MIH development, although causal relationships remain unclear. Future prospective cohort studies incorporating genetic, environmental, and microbiological data are needed to clarify etiological pathways and support the development of targeted preventive strategies.

Conclusion

MIH is highly prevalent among children in Shaanxi Province, Northwest China, and is associated with multiple prenatal and early-life systemic exposures. Although causality cannot be established, these findings provide important epidemiological evidence supporting the multifactorial nature of MIH and highlight the need for longitudinal studies to clarify etiological pathways and inform prevention strategies.

Abbreviations

MIH
Molar-Incisor Hypomineralization
EAPD
European Academy of Pediatric Dentistry
OR
Odds Ratios
95%CI
95% Confidence Intervals
SE
Standard Errors

Declarations

Ethics approval and consent to participate

This study involving human participants was approved by the Ethics Committee of the School of Stomatology, Xi'an Jiaotong University (Approval No. XJKQ-2019-007). All procedures were performed in compliance with local laws and institutional regulations. Written informed consent was secured from the legal guardians of all participating individuals.

Consent for publication

Not Applicable.

Availability of data and materials

The raw data supporting the conclusions of this article will be made available by the authors upon reasonable request, without undue reservation, subject to the applicable licenses and restrictions.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

All authors have read and approved the manuscript. P.Z. and R.H contributed to the design of the study and the writing of the protocol and review. S.Z. and Y.G. led the study conduct. J.T. provided resources and contributed to the design of the study. P.H. and L.Z. led the study organization and supervision. P.Z. and S.Z. contributed to original draft. J.Z. contributed to reviewing the statistical analysis plans and reports and post-hoc analyses. B.Z. reviewed, edited and commented on manuscript drafts.

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Figures

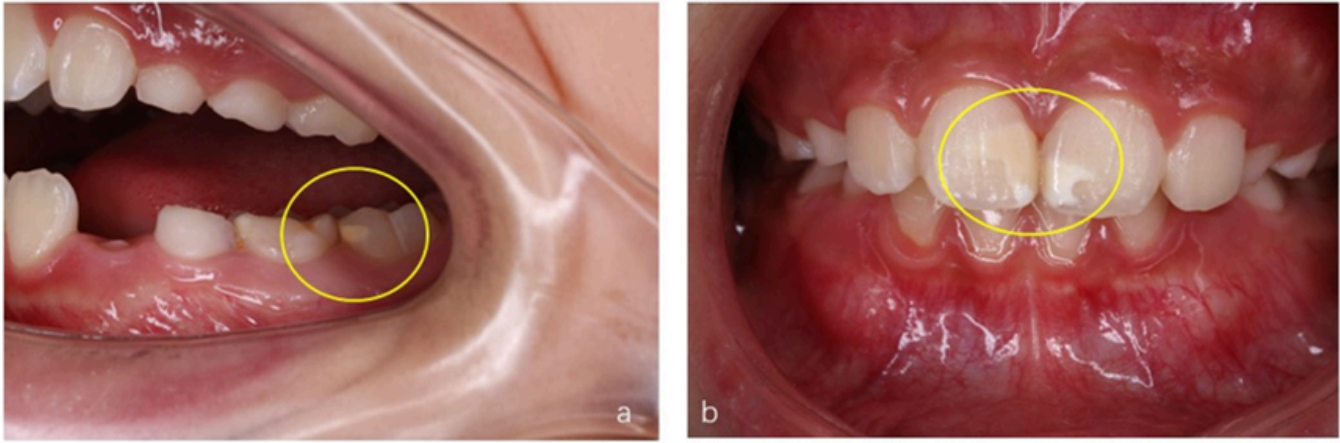


Figure 1

Intraoral photographs of typical MIH symptoms.

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