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Prevalence of hypomineralised second primary molars (HSPM): A systematic review and meta-analysis

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Abstract

Aim: To evaluate the prevalence of HSPM worldwide on a child and a tooth level and investigate the influence of diagnostic criteria on the prevalence of HSPM. **Design:** A comprehensive literature search was performed through MEDLINE/ PubMed, Scopus, and Web of Science databases. The grey literature was also screened as were the reference lists of included studies. An adaptation of the Newcastle-Ottawa Scale was used to evaluate the quality of the studies. A metaanalysis was performed to determine the pooled prevalence of HSPM.

Results: The search strategy identified 1,988 articles, 487 were retrieved for fulltext evaluation, and 37 studies were included in the meta-analysis (32 for child and 23 for tooth level prevalence), providing data from 26,805 individuals and 81,107 molars. The prevalence of HSPM was 6.8% (95% CI 4.98%-8.86%) on a child level and 4.08% on a tooth level (95% CI = 2.80%-5.59%). The diagnostic criteria used did not seem to influence the prevalence results (P > .05). The majority of the papers (75%) showed a low-to-moderate risk of bias.

Conclusion: There was a broad variation in the prevalence reported that may be attributed to differences in the study population. The present meta-analysis showed a HSPM prevalence worldwide of 6.8% on a child level and 4.1% on a tooth level.

KEYWORDS

children, hypomineralised second primary molars, meta-analysis, prevalence, systematic review

1 INTRODUCTION

Enamel hypomineralisation is a qualitative defect of the enamel resulting from a disturbance during initial calcification and/or maturation.^{1,2} This condition in first

permanent molars/incisors is known as molar incisor hypomineralisation (MIH).² In the primary dentition, a similar presentation has been observed in the second primary molar, which is now termed hypomineralised second primary molars (HSPM).²⁻⁴ HSPM is currently defined as

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hypomineralisation of one to four second primary molars including the presence of demarcated opacities, posteruptive breakdown (PEB), atypical caries/restorations, and extractions due to HSPM.^{3,5}

The detection of demarcated opacities in both the primary and permanent dentitions has been reported in the literature using different indices, such as the developmental defects of enamel (DDE), modified DDE (mDDE), and self-devised indices.⁶ More recently, a new diagnostic criterion, the MIH/HSPM index, has been developed combining elements of the European Academy of Paediatric Dentistry (EAPD) and mDDE indices.⁷ This index focuses specifically on hypomineralised defects, whereas the DDE indices included a broader range of enamel defects such as diffuse opacities, hypoplasia, and other defects. In addition, the MIH/HSPM index records the presence of PEB, atypical caries lesions, atypical restorations, and extractions due to MIH/HSPM.

The prevalence of HSPM has varied widely in the literature.⁶ Despite the development of the 2003 EAPD criteria, comparability between studies remains challenging because of the use of different diagnostic criteria, examination variability, and different age groups. To date, no systematic review on HSPM prevalence has been conducted. The aim of this systematic review was to evaluate the prevalence of HSPM in the population worldwide on a child and tooth level and investigate the influence of the diagnostic criteria on the prevalence of HSPM.

2 | METHODS

This systematic review and meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement checklist recommendations and was registered on PROSPERO (International Prospective Register of Systematic Reviews) (protocol number CRD42020220498).

2.1 | Search strategy

A comprehensive literature search was performed through MEDLINE/PubMed and then adapted for the others based on the following PICO question: 'What is the prevalence of hypomineralised second primary molars (HSPM)?'

MEDLINE/PubMed, Scopus, and Web of Science databases were used to identify all relevant papers published up to and including March 2021. The grey literature search was done at Opengrey.eu. The reference lists of the included studies were manually searched to retrieve all eligible papers that could not have been identified during

Key points

- The present systematic review is the first to explore HSPM prevalence on a global level with a pooled child prevalence of 6.80%
- The use of a HSPM-specific criterion allows the recording of demarcated opacities, PEB, and atypical caries/restorations/extractions.
- There is a need for more high-quality prevalence studies worldwide with standardised criteria.

the main search. A language restriction existed with only English publications included.

2.1.1 | MEDLINE/PubMed/OpenGrey search strategy

("primary tooth" OR "primary teeth" OR "deciduous tooth" OR "deciduous teeth" OR "primary molar*" OR "deciduous molar*" OR child* OR pre-schooler*) AND ("hypomineralized second primary molar*" OR "hypomineralised second primary molar*" OR HSPM OR "deciduous molar hypomineralization" OR "deciduous molar hypomineralisation" OR hypomineralisation OR hypomineralization OR "demarcated opacities" OR opacity OR "deciduous molar hypoplasia" OR "hypoplastic primary teeth" OR "hypoplastic primary tooth" OR "primary molar hypoplasia" OR "hypoplasia of primary molars") AND (Prevalence (MeSH) OR prevalence (all) OR incidence OR epidemiolog*)

2.1.2 | Scopus search strategy

TITLE-ABS-KEY (prevalence OR incidence OR epidemiolog*) AND ("primary tooth" OR "primary teeth" OR "deciduous tooth" OR "deciduous teeth" OR "primary molar*" OR "deciduous molar*" OR child* OR pre-schooler*) AND ("hypomineralized second primary molar*" OR "hypomineralised second primary molar*" OR "HSPM" OR "deciduous molar hypomineralization" OR "deciduous molar hypomineralisation" OR "hypomineralisation" OR "hypomineralization" OR "hypomineralisation" OR "hypomineralization" OR "demarcated opacities" OR "deciduous molar hypoplasia" OR "hypoplastic primary teeth" OR "hypoplastic primary tooth" OR "primary molar hypoplasia" OR "hypoplasia of primary molars").

2.1.3 | Web of Science search strategy (combined searches)

TS = ("primary tooth" OR "primary teeth" OR "deciduous tooth" OR "deciduous teeth" OR "primary molar*" OR "deciduous molar*" OR child* OR pre-schooler*)

TS=("hypomineralized second primary molar*" OR "hypomineralised second primary molar*" OR "HSPM" OR "deciduous molar hypomineralization" OR "deciduous molar hypomineralisation" OR "hypomineralisation" OR "hypomineralization" OR "demarcated opacities" OR "deciduous molar hypoplasia" OR "hypoplastic primary teeth" OR "hypoplastic primary tooth" OR "primary molar hypoplasia" OR "hypoplasia of primary molars") TS=(prevalence OR incidence OR epidemiolog*)

2.2 Inclusion criteria

Potentially eligible references were imported into an Excel file. Databases were merged into one spreadsheet file and organised in an alphabetical order with duplicates removed manually. Two independent reviewers (CMC and IO) were involved in the screening of articles by title and abstract according to predetermined inclusion criteria described below:

Criteria 1—DDE/enamel defect description: This was related to the presence of any developmental defect of enamel including both quantitative and qualitative enamel defects such as enamel hypoplasia, enamel hypomineralisation, diffuse opacities (fluorosis), and Amelogenesis imperfecta (AI).

Criteria 2—Child population: It was required that the study population include children. Studies involving adult participants (defined as an individual aged 18 years and older) were not included.

Criteria 3—Epidemiological study design: This study design was a requirement for inclusion, which included cohort, case-control, and cross-sectional studies. Systematic reviews, literature reviews, case reports, and case series were not included.

Criteria 4—English language: Only articles published in the English language were accepted.

In the case of disagreement regarding inclusion, a third reviewer (RL) was involved in reaching a consensus. If there was a lack of clarity in any of the criteria evaluated, the study was included for full-text evaluation.

2.3 | Exclusion criteria

The full texts of articles were read by the same two examiners involved in the inclusion process (CMC and IO), and

articles were excluded based on predetermined criteria. When a disagreement arose, a third examiner (RL) was involved in reaching a consensus. Articles were excluded when any one of five exclusion criteria described below were not met:

Criteria 1—Was the defect described HSPM? HSPM was defined as enamel hypomineralisation affecting one to four second primary molars characterised by demarcated opacities, PEB, atypical caries, atypical restorations, and atypical extractions. Criteria that have been designed specifically for HSPM diagnosis include the EAPD judgement criteria and MIH/HSPM diagnostic criteria, and articles using these criteria were retained.^{7,8} Description of demarcated opacity was required to be classified as a HSPM diagnosis. Therefore, other diagnostic criteria, such as mDDE and other self-devised indices, were included as long a clear description of the above was provided.

Criteria 2—Prevalence data: The authors needed to provide sufficient data in order to calculate the prevalence of HSPM. It was a requirement of the meta-analysis to include child- and tooth-level prevalence, and therefore, the total sample size (children/SPM) and the total number (children/SPM) affected by HSPM needed to be available for calculation.

Criteria 3—Full text: Articles were excluded when the full text was unavailable.

Criteria 4—Missing data: Incomplete data included missing the total sample size or missing the total number of participants affected by HSPM. In the case of missing data, authors were contacted and given a period of six weeks to provide required information after which articles were excluded if not provided.

Criteria 5—No repeated data: When more than one study was conducted using the same sample, only the original or the most complete article was included.

2.4 Data extraction

Information on the included studies was collected by two teams of reviewers (CMC/RL and IO/AOC). Should disagreement exist, a consensus was reached by all authors. A data collection proforma was developed (Supplemental material S1) and the following data were systematically collected from each included study: publication details (authors, country, year, and study type), population details (location, population type—general or specific—age range, and gender), evaluation (examination conditions), diagnostic criteria (standardised and self-devised options given), outcomes (child and tooth level prevalence), and defect characteristics.

3

TABLE 1 Characteristics of the selected studies

			Examination details	;	
Study	Country	Study Design	Setting	Criteria	Wet/Dry
da Silva et al, 2017 ²³	Brazil	Cross-sectional	School	EAPD	Wet
Mittal et al, 2016 ²⁴	India	Cross-sectional	School	EAPD	NR
Norrisgaard et al, 2019 ²⁵	Denmark	RCT	Dental clinic	EAPD	NR
Gambetta-Tessini et al, 2018 ²⁶	Australia	Cross-sectional	School	Ghanim et al, 2015	Dry (cotton rolls/gauze)
Murray & Shaw, 1979 ²⁷	England	Cross-sectional	Portable chair	Young, 1973; Al- Alousi, 1977	Dry (air)
Elfrink et al, 2012 ⁴	The Netherlands	Cohort	Medical Centre	EAPD	Wet
Reyes et al, 2019 ¹³	Brazil	Cross-sectional	School	mDDE	Wet
Wagner, 2017 ²⁸	Germany	Cohort	Dental clinic	mDDE	Dry (cotton rolls/gauze)
Corrêa-Faria et al, 2013 ²⁹	Brazil	Cross-sectional	Healthcare unit	DDE	NR
Farsi, 2010 ³⁰	Saudi Arabia	Cross-sectional	School	mDDE	Wet
Temilola et al, 2015 ³¹	Nigeria	Cross-sectional	Household	EAPD	Wet
Chaves et al, 2007 ³²	Brazil	Cohort	Household	DDE	Dry (Cotton rolls/gauze)
De Lima et al, 2015 ¹⁴	Brazil	Cross-sectional	School	EAPD	NR
Silva et al, 2019 ³³	Australia	Cohort	Research facility/ Household	Ghanim et al, 2015/ DDE	Wet
Mittal & Sharma, 2015 ³⁴	India	Cross-sectional	School	EAPD	Wet
Oyedele et al, 2016 ¹⁵	Nigeria	Cross-sectional	School	EAPD	Wet
Negre-Barber et al, 2016 ¹⁶	Spain	Cross-sectional	Dental Clinic	Ghanim et al, 2015	Wet
Elfrink et al, 2008 ³	The Netherlands	Cross-sectional	Portable chair	EAPD	NR
Costa-Silva et al, 2013 ³⁵	Brazil	Cohort	School	EAPD	Wet
Schüttfort et al, 2020 ³⁶	Germany	Cross-sectional	Hospital	DDE	Dry (Gauze)
Folayan et al, 2020 ³⁷	Nigeria	Cross-sectional	Suburban area	EAPD	NR

		Sample			
Light	Clean	Child (Total/ HSPM)	Teeth (Total/ HSPM)	HSPM defect characteristics	Age (range in years)
Artificial	Toothbrush	1590/103	6360/139	By tooth Demarcated opacities $n = 80 (57.6\%)$ PEB enamel only, $n = 17 (12.2\%)$ PEB dentine/ atypical restoration/extraction, n = 42 (30.2%)	6-11
Natural	NR	223/10	-	By child Demarcated opacities =8 (80%) PEB =2 (20%)	3-5
Artificial	No	496/61	-	NR	6
Artificial	Toothbrush	327/26	-	NR	6-12
Artificial	NR	-	1140/58	NR	6
Photographs	Toothbrush	5561/499	23722/955	By child Demarcated opacities, n = 382 (76.6%) PEB, n = 159 (31.9%) Atypical restoration, n = 97 (19.4%) Atypical caries, n = 73 (14.6%) Atypical extraction, n = 56 (11.2%)	5-6
Artificial	Gauze	731/69	-	NR	8
Artificial	Gauze	377/6	-	NR	3
Natural	Gauze	-	1509/16	NR	3-5
Artificial	Clean (not specified)	-	2003/62	NR	4-5
Natural	Gauze	1169/15	-	NR	1-19
Natural	Gauze	-	816/31	NR	1-3
Artificial	Toothbrush	-	583/7	NR	11-14
Artificial	Cotton rolls	344/68	1382/141	By child Demarcated opacities, n = 36 (52.9%) PEB/atypical caries/restorations/extractions, n = 32 (47.1%)	6
Artificial	Clean (not specified)	978/55	3912/136	By surface Demarcated opacities, n = 177 (69.4%) PEB =77 (30.2%)	6-8
Natural	Gauze	469/27	1876/73	By child Demarcated opacities, n = 13 (48.14%) PEB/atypical caries/restorations/extractions, n = 14 (51.8%)	8-10
Artificial	Gauze	414/60	-	By child Demarcated opacities, $n = 55 (91.7\%)$ PEB/atypical caries/restorations/extractions, n = 5 (8.3%)	8-9
NR	NR	386/19	1517/55	By tooth Demarcated opacities, $n = 48 (87\%)$ PEB =22 (40%) Atypical restorations, $n = 8 (15\%)$	5
Natural	Toothbrush	134/27	864/64	Demarcated opacities, $n = 134 (100\%)$	4-6
Artificial	Gauze	31/0	124/0	NR	2
NR	NR	1173/25	-	NR	3-5

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TABLE 1 (Continued)

			The sector of the sector		
			Examination details	•	
Study	Country	Study Design	Setting	Criteria	Wet/Dry
Fernandes et al, 2020 ³⁸	Brazil	Cross-sectional	School	EAPD	Dry (air)
Lima et al, 2020 ³⁹	Brazil	Cross-sectional	School	EAPD	Dry (Gauze)
Sidhu et al, 2019 ⁴⁰	Canada	Cross-sectional	Hospital	Ghanim et al, 2015	Wet
Slayton et al, 2001 ⁴¹	USA	Cross-sectional	Portable chair	DDE (Clarkson 1992)	Wet
Halal & Raslan, 2020 ⁴²	Syria	Cross-sectional	School	Ghanim et al, 2015	Wet
Zakirulla et al, 2020 ⁴³	Saudi Arabia	Cross-sectional	Dental chair	EAPD	Wet
Ng et al, 2015 ⁴⁴	Singapore	Cross-sectional	School on-site dental clinic	EAPD	NR
Ahmed et al, 2020 ¹⁷	USA	Cross-sectional	School on portable unit	Ghanim et al, 2015	Wet
Goyal et al, 2019 ⁴⁵	India	Cross-sectional	School	EAPD	Dry (Cotton rolls)
Kühnisch et al, 2014 ¹⁸	Germany	Cohort	Hospital	EAPD	Wet
Elger et al, 2020 ⁴⁶	Germany	Cohort	Research centre	EAPD	NR
Gambetta-Tessini et al, 2019 ⁴⁷	Chile	Cross-sectional	School	Ghanim et al, 2015	Dry (cotton roll)
Temilola et al, 2015 ⁴⁸	Nigeria	Cross-sectional	Field (chair)	Kemoli et al, 2008	Wet
Owen et al, 2018 ⁴⁹	Australia	Cross-sectional	Early childhood centre	EAPD/M-DDE	Dry (cotton roll)
Ghanim et al, 2013 ⁵	Iraq	Cross-sectional	School	EAPD	Dry (cotton roll)
Kar et al, 2014 ⁵⁰	India	Cross-sectional	Dental Science and Research Institute	mDDE	Dry (gauze)

Abbreviations: NR, not reported; PEB, post-eruptive breakdown.

		Sample			
Light	Clean	Child (Total/ HSPM)	Teeth (Total/ HSPM)	HSPM defect characteristics	Age (range in years)
Natural	Toothbrush	610/7	1804/10	By tooth Demarcated opacities, $n = 9 (90\%)$ PEB =1 (10%)	6-12
Artificial	Toothbrush	811/121	3244/238	By tooth White/cream demarcated opacities, n = 170 (71.4%) Yellow/brown demarcated opacities, n = 68 (28.6%) PEB, n = 27 (11.34%) Atypical restorations, n = 4 (1.7%) Atypical caries, n = 27 (11.34%)	5
Artificial	Prophylaxis	365/19	-	By tooth White/cream demarcated opacities, n = 170 (71.4%) Yellow/brown demarcated opacities, n = 68 (28.6%) PEB, n = 27 (11.34%) Atypical restorations, n = 4 (1.7%) Atypical caries, n = 27 (11.34%)	
Artificial	NR	694/99	2743/155	By surface White demarcated opacities, 67% Brown demarcated opacities, 9% PEB, 24%	4-5
Photographs	Toothbrush	600/246	2400/715	NR	4-5
Artificial	Toothbrush	596/32	2292/110	NR	7-10
NR	NR	1083/31	4277/52	By tooth White/cream demarcated opacities, n = 15 (28.8%) Yellow/brown demarcated opacities, n = 37 (71.2%)	7-8
Artificial	Toothbrush	337/8	-	NR	8-10
Artificial	Toothbrush	3013/249	12029/479	By tooth Creamish demarcated opacities, $n = 176 (36.7\%)$ Yellow demarcated opacities, $n = 138 (28.8\%)$ Brown demarcated opacities, $n = 165 (34.4\%)$ PEB, $n = 101 (21.1\%)$ Atypical restoration, $n = 20 (4.1\%)$ Atypical extraction, $n = 33 (6.9\%)$	3-6
Artificial	Toothbrush	693/28	2722/49	NR	10
NR	NR	958/38	-	NR	1-6
Artificial	Toothbrush	577/29	-	NR	6-12
Natural	Gauze	327/15	1305/45	NR	3-5
Artificial	Toothbrush	623/88	2483/144	NR	3-5
Artificial	Toothbrush	809/53	-	NR	7-9
Natural	Prophylaxis	306/0	-	NR	3-5

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2.5 | Training and calibration

Reviewers were trained and calibrated in paper selection. The calibration exercise involved a randomised selection of papers (10% of included articles; n = 147), which were screened for eligibility. Kappa analysis was carried out to determine inter-examiner reliability for inclusion of selected papers (yes/no) (K = 0.954), and for the reasons why the article was not included (criteria 1–4; K = 0.899).

2.6 | Risk-of-bias evaluation

Following data extraction, the same two reviewer teams independently assessed possible risk of bias among eligible studies using a bias assessment tool (Modified Newcastle-Ottawa Quality Assessment Scale-adapted for cross-sectional studies).9,10 This tool was adapted further with minor modifications made to the starring system. Reviewers scored the articles that sufficiently fulfilled each methodological criterion and provided a score with a maximum of 13 stars. The tool consisted of three sections, which included selection, comparability, and outcome. Section 1 included selection criteria, which comprised sample representativeness, sample size, and non-respondents (maximum of 6 stars). Section 2 described comparability referring only to studies that included different groups (maximum of 2 stars). The final section described outcome criteria including diagnostic criteria, training, and calibration (maximum of 5 stars).

Studies that received ≥ 9 stars were considered to be of high quality or to have a low risk of bias. Those with 7-8 stars were considered to be of medium quality or to have a moderate risk of bias. Those with ≤ 6 stars had low methodological quality or a high risk of bias. In the case that a certain area was not described in the study, an entry of 'not reported' (NR)was made.

2.7 | Data analysis

MedCalc 20 (MedCalc Software Ltd.) statistical software was used to determine inter-examiner reliability for inclusion of selected articles using kappa calculation.

All searches' results were exported and managed in an Excel file (Microsoft Inc, USA). Data collection for the meta-analysis included the number of children evaluated in the study and the respective number of children with HSPM. In relation to tooth prevalence, the total number of second primary molars evaluated and how many presented with HSPM were calculated. A forest plot was generated using Stata 17.0 statistical software (StataCorp LLC, Texas, USA) using a randomeffects model including the subgroup prevalence data and the overall pooled effects. Jamovi software (The Jamovi Project, 2021; version 1.6) was used for meta-regression

analysis using criteria as a moderator. The Paul-Mandel mixed-effects model was used for estimating overall pooled prevalence and between-study variability in the meta-regression.

3 | RESULTS

One thousand, nine hundred and eighty-eight (1988) potentially relevant articles were identified in the systematic literature search; 519 were considered duplicate and were therefore removed. After screening of titles and abstracts, 983 were considered as non-eligible. The principal reason for non-inclusion was that studies did not describe a DDE (n = 756), followed by non-clinical studies (n = 123), studies not involving children (n = 68), and non-English studies (n = 36).

A total of 487 studies were revised with full-text evaluation carried out, from which 450 articles were excluded. The main reason for exclusion was that the article did not describe HSPM (n = 374). Other reasons included no prevalence data (n = 44), missing data (n = 17), duplicated data (n = 11), and no full text (n = 4). A manual search of references from the included 36 papers was performed with one additional paper retrieved. Finally, 37 papers were included in the systematic review (32 papers showed appropriate data for child prevalence and 23 papers for tooth prevalence meta-analysis). Figure 1 displays the study selection process.

The included studies provided data from 26,805 individuals (ranging from 31 to 5561 children) and 81,107 primary second molars (ranging from 124 to 23,722 teeth). Articles were published between 1979 and 2020 in countries including Europe, Australia, Asia, Africa, and South/ North America. The main characteristics of the included studies are presented in Table 1.

A forest plot depicting child prevalence is shown in Figure 2. A total of 32 studies were included in the metaanalysis. Great variation existed between studies with a range of between 0% and 41% prevalence reported. The overall pooled child prevalence of HSPM was 6.80% (95% CI 4.98%-8.86%; $I^2 = 97.35\%$).

For tooth prevalence, a total of 23 studies were included in the meta-analysis. A broad variation existed between studies with a reported prevalence ranging from 0% to 29.79%. The overall pooled prevalence of HSPM was 4.08% (95% CI 2.80%-5.59%; $I^2 = 98.92\%$).



In the studies in which the EAPD or MIH/HSPM index was used (Figure 2), we observed a child level pooled prevalence of 7.54% (95% CI 5.48%-9.89%), whereas in those that used other indices, the pooled prevalence was 3.65% (95% CI 0.43%-9.33%). Figure 3 depicts the pooled prevalence at tooth level as 4.65% (95% CI 2.96%-6.70%; weight =70.34%) for studies that used EAPD or MIH/HSPM index, which represented the majority of the studies included in the meta-analysis. When other indices were used, the prevalence was 2.98% (95% CI 1.73%-4.55%; weight =29.66%). The diagnostic criteria, however, did not influence the pooled prevalence on a child level (estimate -0.034; CI -0.104 to 0.037; P = .347) or a tooth level (estimate -0.024; CI -0.077 to 0.028; P = .359).

Figure 4 illustrates the geographical distribution of studies reporting on HSPM prevalence worldwide with the numer in each yellow zone reflecting the number of studies published in that country. Table 2 illustrates the quality assessment of the included studies in relation to selection, comparability, and outcome-related biases. Bias scores ranged from 3 to 11 stars, and the majority of the papers (75%) showed a low-to-moderate risk of bias. Only nine studies had a high risk of bias (≤ 6 stars). An equal number of studies (14 each) presented with a low (≥ 9 stars) and moderate (7-8 stars) risk of bias.

Fifteen studies provided information on HSPM defect characteristics. Demarcated opacities represented the most common HSPM presentation on both a child and tooth level in the majority of studies. PEB prevalence varied between 11.34% and 21.1%, whereas atypical caries/restorations/extractions were less commonly reported, with a prevalence varying between 13.34% and 45.2%. The majority of the papers that used EAPD or MIH/HSPM criteria did not report the data separately by each category, and data were often incomplete (Table 1).



FIGURE 2 Forest plot using the mixed-effects model for determining child prevalence according to the diagnostic criteria used

DISCUSSION 4

The present systematic review is the first to explore HSPM prevalence on a global level. Great variation existed between studies with a range in child prevalence of between 0% and 41% reported. The overall pooled prevalence of HSPM was 6.80% (95% CI 4.98%-8.86%).

In the subgroup analysis, we observed a pooled prevalence of 7.54% (95% CI 5.48%-9.89%) in the studies in which the EAPD or MIH/HSPM index was used (n = 26). Alternatively, a lower pooled prevalence of 3.65% (95% CI 0.43%-9.33%) was found in those studies that used other indices (n = 6). Although we initially hypothesised that

the diagnostic criteria may influence the prevalence results, following meta-regression, we found no differences in the prevalence regardless of the criteria used. This can be explained by the fact that demarcated opacities were the most common presentation reported, which is captured by all indices as reported in Table 1. Although 26 studies used the EAPD/MIH/HSPM criteria, only 14 studies used the index in its entirety (including PEB, atypical caries/restorations, and extractions related to HSPM).

 I^2 statistic identifies what proportion of the observed variance reflects differences in the true effect sizes rather than sampling error (proportion of observed dispersion that is real, rather than spurious). The I^2 statistic revealed



FIGURE 3 Forest plot using the mixed-effects model for determining tooth prevalence according to the diagnostic criteria used

that 99.75% of the observed variance reflected differences in true effect sizes rather than sampling error. This variance could be explained by the characteristics of the population (age group, environmental factors, socio-economic characteristics, etc) and study methodology (training/calibration of the examiners, examination conditions).

A tooth prevalence range of 0% and 29.8% was reported, with a pooled HSPM tooth prevalence of 4.08% (95% CI = 2.80%-5.59%). As expected, the tooth prevalence was lower than the child prevalence, since not all second primary molars may be affected by HSPM. This result is comparable to MIH prevalence studies where not all first permanent molars are involved.^{11,12}

Although the age at examination varied among the studies, the optimal age for HSPM diagnosis has been

suggested to be 5 years.⁶ Examining this age group is advantageous as gross destruction masking the original defect is less likely to occur in earlier years.⁶ Several studies have used older age groups, which could influence the reporting of true defect prevalence.^{5,13-18} As age increases, so too does potential for PEB, atypical caries lesions and restorations, which can mask any underlying hypomineralisation defect.^{5,15}

Seven of the studies used the DDE or mDDE criteria, which presents major drawbacks. This index does not allow for scoring of PEB or is mistakenly classified as hypoplasia. Furthermore, caries, restorations, and extractions that are atypical in nature are not accounted for.⁶ Demarcated opacities were often the only aspect of HSPM which was scored in included studies resulting in a limited



FIGURE 4 Geographical distribution of HSPM worldwide-yellow zones reflect countries that have reported on HSPM prevalence (child or tooth level)

picture of HSPM prevalence. Adherence to a standardised specific HSPM diagnostic criterion is recommended to decrease the variation between studies. Criteria that include all aspects of HSPM presentation may be helpful in determining the true spectrum of HSPM defects. Moreover, this may also improve the quality of studies recording defect progression over time.

Although the majority of the papers (75%) showed low-to-moderate risk of bias, flaws were identified in the methodology of included studies. Few studies followed the STROBE guidelines for reporting observational data. Regarding sampling procedure, 19 of the studies did not report on sample size, lowering the study quality. A total of 13 studies did not describe the training provided for their examiners in applying the diagnostic criteria. Although data quality depends critically on the examiners' ability to apply the diagnostic criteria consistently over time, not all studies described the examiners' training and calibration data.

As a limitation of the present study, only articles published in the English language were retrieved. Although a comprehensive literature search would ideally not have language restrictions, the majority of papers within medical and health science are published in the English language. Moreover, non-English papers usually represent a small proportion of included articles and rarely impact the results and conclusion of a systematic review.¹⁹ Another limitation of the present study is that only articles indexed on MEDLINE/PubMed, Scopus, Web of Science, and OpenGrey databases were included.²⁰ This may have

resulted in relevant articles being excluded and therefore increase the likelihood of selection bias.

Demarcated opacities represented the most common clinical presentation of HSPM, which is favourable considering that this is the mildest form of the detection that usually requires preventive care alone and monitoring. Those affected by PEB and atypical caries, however, may present with an increased treatment burden including restorative care (atypical restorations) and loss of the second primary molar affected by HSPM. The clinical significance of a child presenting with demarcated opacities also relates to the predictive nature of HSPM for MIH development.²¹ This awareness may aid dentists in increasing surveillance of erupting first permanent molars and enabling an earlier MIH diagnosis. The prevalence of HSPM in the present study is lower than the global reported prevalence for MIH (13.1%).²² This could be explained by the fact that the mineralisation period for the first permanent molar is considerably longer than that for the second primary molar. Therefore, the window of opportunity for aetiological insults is greater for the first permanent molar.

In conclusion, there was a broad variation in the prevalence reported that may be attributed to differences in the study population. The present meta-analysis showed a HSPM prevalence worldwide of 6.8% on a child level and 4.1% on a tooth level. There is a need for more standardised information to be provided on the type of HSPM defect, presence of sensitivity, and respective treatment needs. Further research is also required in certain

CARF	A ET AL.																			ERN/		NAL J	OUR	NAL	OF	W	'IL	E	$r \perp$	13
	k ≤6 = high 7-8 = derate ≥9 = low	lerate	lerate		~	Ч	lerate	~	lerate	~	lerate	lerate	~	~	ч	~	lerate	lerate	lerate	<u>-</u> G	_G	<u>ч</u>	ENI	131	× Y	4	lerate	lerate	Ч	(Continues)
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BIAS	Stars	7	7	10	10	5	7	10	7	6	8	7	6	10	9	10	8	8	8	4	3	2	10	11	10	5	8	7	4	
	Calibration Max 3*	*	* **	* **	* *	***	**	* **	***	***	* **	* **	* **	* **	*	* **	* **	* **	* **	*	*	NR	* **	* **	* **	**	* **	***	NR	
ome	t Training Max 1*	*	*	*	×	NR	NR	*	*	*	*	NR	NR	NR	NR	*	NR	×	*	NR	*	NR	*	*	*	*	NR	NR	NR	
3. Outco	Criteria Max 1*	*	*	*	*	No	*	No	No	No	No	*	*	*	*	*	*	*	*	*	No	*	*	*	*	No	*	*	*	
2. Comparability	Specific groups Max 2*	NA	NA	*	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	Non respondents Max 2*	**	NR	**	*	NR	**	**	*	**	NR	NR	**	**	*	**	NR	NR	*	NR	NR	NR	**	**	**	NR	NR	NR	NR	
	Sample Size Max 1 *	NR	NR	*	*	NR	NR	*	NR	*	*	*	*	*	NR	NR	*	*	NR	NR	NR	*	NA	*	*	NR	*	NR	NR	
L. Selection	Representativeness Max 3*	×	×		**	×	*	**	×	*	**:	×	×	**:		**:	**:	*	×	×		**:	**	**	×	×	**	**	**:	
-	- I Country I	Brazil *	India *	» benmark	Australia *	England *	The Netherlands *	Brazil *	Germany *	Brazil *	Saudi Arabia *	Nigeria *	Brazil *	Brazil *	Australia *	India *	Nigeria *	Spain *	The Netherlands *	Brazil *	Germany *	Nigeria *	Brazil *	Brazil *	Canada *	* NSA	syria *	Saudi Arabia *	Singapore *	
	Study	da Silva et al, 2017 ²³	Mittal et al, 2016 ²⁴	Norrisgaard et al, 2019 ²⁵	Gambetta-Tessini et al, 2018 ²⁶	Murray & Shaw, 1979 ²⁷	Elfrink et al, 2012 ⁴	Reyes et al, 2019 ¹³	Wagner, 2017 ²⁸	Corrêa-Faria et al, 2013 ²⁹	Farsi, 2010 ³⁰	Temilola et al, 2015 ³¹	Chaves et al, 2007 ³²	De Lima et al, 2015 ¹⁴	Silva et al, 2019 ³³	Mittal & Sharma, 2015^{34}	Oyedele et al, 2016 ¹⁵	Negre-Barber et al, 2016 ¹⁶	Elfrink et al, 2008 ³	Costa-Silva et al, 2013 ³⁵	Schüttfort et al, 2020 ³⁶	Folayan et al, 2020 ³⁷	Fernandes et al, 2020^{38}	Lima et al, 2020 ³⁹	Sidhu et al, 2019 ⁴⁰	Slayton et al, 2001 ⁴¹	Halal & Raslan, 2020 ⁴²	Zakirulla et al, 2020 ⁴³	Ng et al, 2015 ⁴⁴	

TABLE 2 Quality assessment of the primary studies

TABLE 2 (Continued)

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		1. Selection			2. Comparability	3. Outcon	le		BIAS		v
Study	Country	Representativeness Max 3*	Sample Size Max 1 *	Non respondents Max 2*	Specific groups Max 2*	Criteria Max 1*	Training Max 1*	Calibration Max 3*	Stars	Risk ≤6 = high 7-8 = moderate ≥9 = low	VILEI
Ahmed et al, 2020 ¹⁷	USA	**	NR	*	NA	*	*	***	∞	Moderate	PA
Goyal et al, 2019 ⁴⁵	India	***	*	**	NA	*	*	***	11	Low	EDI
Kühnisch et al, 2014 ¹⁸	Germany	**	NR	*	NA	*	*	***	8	Moderate	ATR
Elger et al, 2020 ⁴⁶	Germany	NR	NR	NR	NA	*	*	***	5	High	IC D
Gambetta-Tessini et al, 2019 ⁴⁷	Chile	***	×	*	NA	*	*	* **	10	Low	ENTIST
Temilola et al, 2015 ⁴⁸	Nigeria	**	*	NR	NA	No	*	***	7	Moderate	FRY
Owen et al, 2018 ⁴⁹	Australia	***	*	*	NA	*	*	***	10	Low	
Ghanim et al, 2013 ⁵	Iraq	***	NR	**	NA	*	*	***	10	Low	
Kar et al, 2014 ⁵⁰	India	**	NR	NR	**	No	*	NR	5	High	
Abbreviations: NR, not repor	ted; NA, not applicab	ole.									

countries where no prevalence data exist. Determining the prevalence of HSPM will inform early detection and management strategies according to the defect severity.

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AUTHOR CONTRIBUTIONS

Charlotte McCarra conceived the ideas, collected the data, analysed the data, and led the writing. Isabel Cristina Olegário conceived the ideas, collected the data, analysed the data, and reviewed the manuscript. Anne C. O'Connell collected the data and reviewed the manuscript. Rona Leith conceived the ideas, collected the data, and reviewed the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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