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World Workshop on Oral Medicine VII: Relative frequency of oral mucosal lesions in children, a scoping review

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Abstract

Objective: To detail a scoping review on the global and regional relative frequencies of oral mucosal disorders in the children based on both clinical studies and those reported from biopsy records.

Materials and Methods: A literature search was completed from 1 January 1990 to 31 December 2018 using PubMed and EMBASE.

Results: Twenty clinical studies (sample size: 85,976) and 34 studies from biopsy services (40,522 biopsies) were included. Clinically, the most frequent conditions were aphthous ulcerations (1.82%), trauma-associated lesions (1.33%) and herpes simplex virus (HSV)-associated lesions (1.33%). Overall, the most commonly biopsied lesions were mucoceles (17.12%), fibrous lesions (9.06%) and pyogenic granuloma (4.87%). By WHO geographic region, the pooled relative frequencies of the most common oral lesions were similar between regions in both clinical and biopsy studies. Across regions, geographic tongue (migratory glossitis), HSV lesions, fissured tongue and trauma-associated ulcers were the most commonly reported paediatric oral mucosal lesions in clinical studies, while mucoceles, fibrous lesions and pyogenic granuloma were the most commonly biopsied lesions.

Conclusions: The scoping review suggests data from the clinical studies and biopsy records shared similarities in the most commonly observed mucosal lesions in children across regions. In addition, the majority of lesions were benign in nature.

KEYWORDS

child, frequency, mouth diseases, oral manifestations, oral pathology

1 | INTRODUCTION

Paediatric Dentistry is an age-defined specialty providing comprehensive preventive and therapeutic oral health care for infants and children through adolescence, including those with special healthcare needs (Commission on Dental Accreditation, 2018; Dental Board of Australia, 2016; Specialty Advisory Committee for Paediatric Dentistry, 2009). Paediatric dentists possess breadth of

knowledge across various dental disciplines adapted to the unique requirements of children and adolescents. In childhood, dental caries is the most common chronic childhood disease (Chen, Gao, Duangthip, Lo, & Chu, 2018; Duangthip, Gao, Lo, & Chu, 2017; Dye, Hsu, & Afful, 2015); however, the literature suggests oral mucosal lesions are not uncommon (Colaci & Sfasciotti, 2013; Furlanetto, Crighton, & Topping, 2006; Rioboo-Crespo Mdel, Planells-del Pozo, & Rioboo-Garcia, 2005). Fortunately, most lesions are benign or transient, with either an infectious or traumatic aetiology. Rarely, mucosal lesions represent an oral manifestation of systemic diseases (for example human immunodeficiency virus (HIV) infection), or adverse effects and toxicity from medical therapies (for example oral mucositis following anti-neoplastic chemotherapy).

The majority of papers are largely narrative in nature with the exception of two studies which attempt to quantify the prevalence of oral mucosal disorders in children (Colaci & Sfasciotti, 2013; Furlanetto et al., 2006). Colaci and Sfasciotti (2013) included 12 studies published between 1988 and 2013 in their review and found wide variations in the reported prevalence of oral mucosal lesions ranging from 4.1% to 69.5%. Despite the variance in overall prevalence, aphthous stomatitis, herpes labialis, geographic, coated and fissured tongue, candidiasis and traumatic lesions were found to be the most frequently observed lesions in children (Colaci & Sfasciotti, 2013). Their findings were supported by Furlanetto et al. (2006) who had similar conclusions. Unfortunately, the reviews either had unclear methodology (unclear inclusion and exclusion criteria) or focused on specific lesion types making it difficult to ascertain the true prevalence of oral lesions in children compared to adults. It is therefore difficult to define the true prevalence of paediatric mucosal lesions because of methodology issues in both the original studies and reviews.

This publication details a scoping review on the global and regional relative frequencies of oral mucosal disorders in the children based on clinical studies and those reported from biopsy services. Although rare, the early detection, diagnosis and treatment of malignant oral lesions will significantly enhance survival rates. Therefore, a secondary aim was to conduct a scoping review on potentially malignant and malignant oral lesions reported in children.

2 | MATERIALS AND METHODS

A literature search was completed from 1 January 1990 to 31 December 2018 using PubMed and EMBASE. Manuscripts selected for review were limited to the English language and based on the following inclusion and exclusion criteria. Clinical studies and biopsy reports on oral mucosal lesions and focussed studies on potentially malignant and malignant lesions in children and adolescents aged 20 or below were included. Systematic or narrative reviews, opinion papers, case reports, abstracts, animal model, in vitro studies, studies whereby data of sample of interest could not be extracted and papers without access (even after authors were contacted by email) were excluded. In addition, HIV-related oral manifestations, medical therapy-induced oral manifestations and periodontitis as a manifestation of systemic diseases were excluded. The plain text or MESH (if applicable) terms used for the PubMed search were as follows: "Candidiasis, Oral", "Leukoedema, Oral", "Lichen Planus, Oral", "Lip Diseases", "Mouth Diseases", "Mouth Mucosa", "Mouth Neoplasms", "Mucositis", "Oral Manifestations", "Oral Ulcer", "Periodontal Diseases", "Salivary Gland Disorders", "Stomatitis", "Tongue Diseases", "Pathology, Oral", "Pediatric Dentistry", "Surgery, Oral" were crossed with ("AND") "Biopsy", "Prevalence", "Incidence" and "Epidemiology." The search strategy was adapted for the EMBASE search using the expertise of a health sciences librarian. All references were managed by reference manager software (Endnote), and duplicate papers were removed. Data were extracted using a standard electronic form. Only data on soft tissue lesions are detailed in this manuscript.

The titles and abstracts of all identified studies from the electronic search were independently assessed by the reviewers (CH, CN, DD, KH, SG) for eligibility. Full text of studies that appeared to meet the inclusion criteria was evaluated using a piloted data collection form. Disagreements concerning the eligibility of studies were resolved by discussion with group consultants.

2.1 | Statistical analysis

Quantitative analysis was carried out only for clinical and biopsy studies on oral mucosal lesions. These studies were categorized into data either from clinical studies or from biopsy records. The outcome measures used were pooled and overall relative frequency or percentage of oral lesions for clinical and biopsy studies, respectively.

Relevant data were extracted from included studies for analysis of pooled relative frequency/percentage estimates. Statistical heterogeneity was assessed using I^2 statistics and chi-square test. Considering variation in true differences across sample (clinical heterogeneity and statistical heterogeneity), DerSimonian and Laird's random effects model was applied for the analysis at a 95% confidence level.

However, some lesions were reported only in studies from certain regions, which resulted in an overestimation of that particular lesion when using pooled estimates. To overcome this potential bias, the overall relative frequency/percentage of oral lesions was also computed. The overall relative frequency/percentage of oral lesions was computed using the total frequency count of each oral lesion. The sample sizes of each included studies were summed up as denominator in computation of overall relative frequency or percentage of oral lesions.

3 | RESULTS

3.1 | Studies on oral mucosal lesions

The PubMed and EMBASE searches identified over 10,000 articles (Figure 1). Of the 214 full-text papers assessed for eligibility,

FIGURE 1 PRISMA diagram

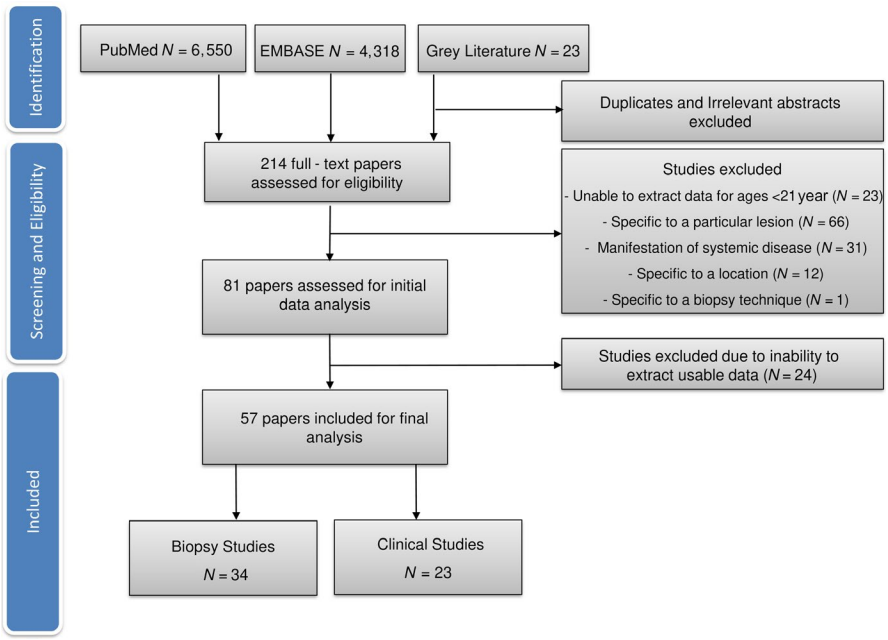

TABLE 1 Top 20 most frequent (overall and pooled) oral conditions based on clinical studies

Condition	Total cases (out of 85,976)	Overall relative frequency (%)	Number of studies	Pooled relative frequency (%)	95% CI (%)
Aphthous ulcer	1,569	1.82	15	1.75	1.05–2.61
HSV[a] lesions	1,145	1.33	13	1.38	0.79–2.13
Trauma-associated lesions	1,145	1.33	10	3.55	1.99–5.55
Migratory glossitis	1,106	1.29	17	2.08	1.33–2.97
Candidiasis	1,029	1.20	13	1.34	0.13–3.68
Ulcer	410	0.48	8	2.45	0.50–5.76
Cheilitis	381	0.44	14	1.37	0.49–2.64
Hyperkeratosis	292	0.34	7	1.38	0.53–2.59
Tobacco-induced	274	0.32	4	0.21	0.03–0.54
Melanotic macule	273	0.32	8	2.92	0.52–7.10
Hairy tongue	237	0.28	4	0.70	0.09–1.79
Fordyce granule	212	0.25	8	1.91	0.70–3.67
HPV[b] lesions	185	0.22	13	0.59	0.24–1.06
Mucocele	174	0.20	12	0.89	0.35–1.65
Fissured tongue	168	0.20	13	0.90	0.36–1.66
Nevi	158	0.18	2	1.44	1.22–1.68
Coated tongue	129	0.15	1	23.84	20.31–27.67
Commissural lip pits	115	0.13	3	2.46	0.00–9.32
Other (NOS[c])	108	0.13	1	0.25	0.20–0.30
Tumours (NOS[c])	84	0.10	2	0.15	0.12–0.19

[a]Herpes simplex virus.
[b]Human papillomavirus.
[c]Not otherwise specified.

the majority were excluded due to the inability to extract data on the age group of interest. Eighty-one papers were included in the initial data analysis; however, a further 24 papers had to be excluded due to the inability to extract raw data (data presented in graphs) or the failure of the papers to report a total sample size (Figure 1).

3.1.1 | Data from clinical studies

There were 20 studies included in the data analysis for a total sample size of 85,976 (Amadori, Bardellini, Conti, & Majorana, 2017; Arendorf & van der Ross, 1996; Basalamah & Baroudi, 2016; Bessa, Santos, Aguiar, & do Carmo, 2004; Garcia-Pola, Garcia-Martin, & Gonzalez-Garcia, 2002; Kleinman, Swango, & Pindborg, 1994; Kose, Guven, Ozmen, Akgun, & Altun, 2013; Majorana et al., 2010; Mathew, Pai, Sholapurkar, & Vengal, 2008; Mumcu, Cimilli, Sur, Hayran, & Atalay, 2005; Parlak et al., 2006; Pessoa et al., 2015; dos Santos, Bessa, Aguiar, & do Carmo, 2004; Shulman, 2005; Unur, Bektas Kayhan, Altop, Boy Metin, & Keskin, 2015; Vieira-Andrade et al., 2015, 2013; Vučićević Boras et al., 2013; Yáñez et al., 2016; Yilmaz et al., 2011). Overall, the most prevalent conditions were aphthous ulcerations (1.82%), trauma-associated lesions (1.33%) and herpes simplex virus (HSV)-associated lesions (1.33%). Table 1 illustrates the top 20 conditions (overall and pooled percentages) identified in these studies.

The most prevalent potentially malignant lesions were tobacco-induced lesions (0.33%), leukoplakia (0.01%) and oral lichen planus (0.003%).

Stratifying by World Health Organization (WHO) geographic regions, nine studies were from the European region, eight from the Region of the Americas and one each from the African, South-East Asia and the Eastern Mediterranean regions, respectively. The pooled relative frequency (random effect) of oral conditions by WHO region is presented in Table 2. Pooled relative frequency of the most common oral lesion varied between WHO regions; however, several conditions consistently appeared in the top ten: ulcers (four regions), geographic tongue (migratory glossitis) (four regions), HSV-associated lesions (three regions), fissured tongue (three regions) and trauma-associated lesions (three regions).

Three studies (Cetinkaya et al., 2011; Flinck, Paludan, Matsson, Holm, & Axelsson, 1994; George, Bhat, & Hegde, 2008) were separately analysed as they examined conditions only in newborns ranging from 0 to 1 week old. Of a total sample of 4,080, the three most prevalent conditions were mucosal cysts (36.57%) followed by Bohn's nodules (12.06%) and Epstein pearls (8.95%).

3.1.2 | Data from biopsy records

The review analysed data from 34 studies for a total of 40,522 biopsies performed (Abdullah, Qader, & OA and Mussedi OS, 2016; Ataide et al., 2016; Bataineh & Al-Dwairi, 2005; Cavalcante, Turatti, Daniel, Alencar, & Chen, 2016; Chen, Lin, Huang, Lin, & Yan, 1998; Chidzonga, Lopez, & Portilla Alvarez, 1996; Colaci & Sfasciotti, 2013; Das & Das, 1993; Dhanuthai, Banrai, & Limpanaputtajak, 2007; Gultelkin, Tokman, & Turkseven, 2003; Ha, Kelloway, Dost, & Farah, 2014; Jaafari Ashkavandi, Ahmadi Sheshdeh, & Kamali, 2014; Jones & Franklin, 2006; Keszler, Guglielmotti, & Dominguez, 1990; Krishnan, Ramesh, & Paul, 2014; Kwok, Dovigi, Eversole, & Dovigi, 2015; Lapthanasupkul, Juengsomjit, Klanrit, Taweechaisupapong, & Poomsawat, 2015; Lawoyin, 2000; Lei et al., 2014; Lima Gda et al., 2008; Maaita, 2000; Maia, Merly, Castro, & Gomez, 2000; Martins-Filho et al., 2015; Melo, 2011; Mieko, 2007; Munsamy, Mahomed, & Rikhotso, 2011; Seyedmajidi, Hamzehpoor, & Bagherimoghaddam, 2011; Shah, Le, & Carpenter, 2009; Sixto-Requeijo, Diniz-Freitas, Torreira-Lorenzo, Garcia-Garcia, & Gandara-Rey, 2012; Sklavounou-Andrikopoulou, Piperi, Papanikolaou, & Karakoulakis, 2005; Sousa, Etges, Correa, Mesquita, & Araujo, 2002; Taweevisit, Tantidolthanes, Keelawat, & Thorner, 2018; Wang, Chang, Chang, Huang, & Guo, 2009; Zuniga, Mendez, Kauterich, & Paniagua, 2013). Overall, the most common biopsied lesions were mucoceles (17.12%), fibrous lesions (9.06%) and pyogenic granulomas (4.87%). The top 20 oral conditions (overall and pooled percentages) are presented in Table 3.

Burkitt's lymphoma (0.26%), non-Hodgkin's lymphoma (0.12%), adenoid cystic carcinoma (0.10%) and rhabdomyosarcoma (0.10%) were the most prevalent malignancies in children based on biopsy studies.

Stratifying by WHO geographic regions, 13 studies were from the Region of the Americas, five each from the Western Pacific and Eastern Mediterranean regions, four each from the European and South-East Asia regions, and three from the African region. The pooled percentages (random effect) of oral conditions from each WHO region are presented in Table 4. As with the data from the clinical studies, the most common biopsied lesion varied between WHO regions. The most common lesions consistently reported were mucoceles (all regions), fibrous lesions all regions) and pyogenic granulomas (five regions).

3.2 | Focused studies on malignant lesions

Sixty-two papers, reporting exclusively on malignant lesions in children and adolescents, were identified. Forty-eight papers were excluded. The main reasons for exclusion were the inability to extract data (N = 23) or that the age range was outside of the interest group (N = 13). Other reasons included non-oral or unclear cancer diagnosis terminology (N = 9) or the full text was unavailable or not retrievable (N = 3). Fourteen studies were retained, and all were based on biopsy data (Abiose, Ogunniyi, & Oyejide, 1991; Adebayo, Ajike, & Adekeye, 2001; Al-Khateeb, Al-Hadi Hamasha, & Almasri, 2003; Aregbesola, Ugboko, Akinwande, Arole, & Fagade, 2005; Arotiba, 1996; de Arruda et al., 2017; Budhy, Soenarto, Yaacob, & Ngeow, 2001; Creath, Cutter, Bradley, & Wright, 1991; Effiom et al., 2008; Iatrou, Theologie-Lygidakis, Tzerbos, & Schoinohoriti, 2013; Mohtasham, Saghravanian, Goli, & Kadeh, 2015; Piloni, Molina, & Keszler, 2009; Sato, Tanaka, Sato, & Amagasa, 1997; Trobs, Mader, Friedrich, & Bennek, 2003). Stratifying by WHO geographic regions, five studies were from the African region (Abiose et al., 1991; Adebayo et al., 2001; Aregbesola et al., 2005; Arotiba, 1996; Effiom et al., 2008), three from the Americas (de Arruda et al., 2017; Creath et al., 1991; Piloni et al., 2009), two each from the Eastern Mediterranean (Al-Khateeb et al., 2003; Mohtasham et al., 2015) European (Iatrou et al., 2013; Trobs et al., 2003) and South-East Asia/Western Pacific regions (Budhy et al., 2001; Sato et al., 1997).

TABLE 2 Top 10 most frequent (pooled) oral conditions by WHO regions based on clinical studies

African region (Arendorf & van der Ross, 1996)			Eastern Mediterranean region (Basalamah & Baroudi, 2016)			European region (Amadori et al., 2017; Garcia-Pola et al., 2002; Kose et al., 2013; Majorana et al., 2010; Mumcu et al., 2005; Parlak et al., 2006; Unur et al., 2015; Vučićević Boras et al., 2013; Yilmaz et al., 2011)		
Condition	**Pooled relative frequency (%)**	**95% CI (%)**	**Condition**	**Pooled relative frequency (%)**	**95% CI (%)**	**Condition**	**Pooled relative frequency (%)**	**95% CI (%)**
Cheilitis	15.13	13.01–17.44	Fissured tongue	4.00	2.87–5.41	Trauma-associated lesions	3.48	1.21–6.58
Commissural lip pits	9.61	7.90–11.55	Ankyloglossia	1.80	1.07–2.83	Fistula	3.21	1.97–4.91
Trauma-associated lesions	2.47	1.62–3.60	Migratory glossitis	0.90	0.41–1.70	Ulcers	3.20	2.79–3.64
Migratory glossitis	1.62	0.95–2.58	Macroglossia	0.40	0.11–1.02	Candidiasis	2.87	0.55–6.85
HSV[a] lesions	0.95	0.46–1.75	Hairy tongue	0.30	0.06–0.87	Hyperkeratosis	2.78	2.42–3.17
Pigmented lesions	0.76	0.33–1.49				Epstein pearls	2.68	1.16–5.20
Fissured tongue	0.57	0.21–1.24				Migratory glossitis	2.15	1.20–3.35
Ulcers	0.48	0.15–1.11				Aphthous ulcer	2.09	0.95–3.63
HPV[b] lesions	0.48	0.15–1.11				HSV[a] lesions	1.91	1.04–3.03
Necrotizing ulcerative gingivitis	0.19	0.02–0.69				Cheilitis	1.08	0.37–2.13

Region of the Americas (Bessa et al., 2004; Kleinman et al., 1994; Pessoa et al., 2015; dos Santos et al., 2004; Shulman, 2005; Vieira-Andrade et al., 2015, 2013; Yáñez et al., 2016)			South-East Asia region (Mathew et al., 2008)			Western Pacific region (no studies)		
Condition	**Pooled relative frequency (%)**	**95% CI (%)**	**Condition**	**Pooled relative frequency (%)**	**95% CI (%)**	**Condition**	**Pooled relative frequency (%)**	**95% CI (%)**
Coated tongue	23.84	20.31–27.67	Fordyce granule	0.50	0.19–1.09			
Other inflammatory lesions (NOS[c])	8.61	5.93–12.00	Hyperkeratosis	0.42	0.14–0.98			
Melanotic macule	7.35	1.34–17.53	Ulcers	0.34	0.09–0.86			
Pyogenic granuloma	5.28	3.21–8.12	Aphthous ulcer	0.34	0.09–0.86			
Ulcers	4.76	0.00–16.78	Fissured tongue	0.34	0.09–0.86			
Fordyce granule	4.74	0.16–14.71	Migratory glossitis	0.08	0.00–0.47			
Trauma-associated lesions	4.12	1.17–8.72	Mucocele	0.08	0.00–0.47			
Migratory glossitis	2.79	1.32–4.77	HSV[a] lesions	0.08	0.00–0.47			
Peripheral ossifying fibroma	2.50	1.15–4.69	Candidiasis	0.08	0.00–0.47			
Dermatologic disorders	2.50	1.15–4.69	Tobacco-induced	0.08	0.00–0.47			

[a]Herpes simplex virus.
[b]Human papilloma virus.
[c]Not otherwise specified.

TABLE 3 Top 20 most frequent (overall and pooled) oral conditions based on biopsy reviews

Condition	Total cases (out of 40,522)	Overall percentage (%)	Number of studies	Pooled relative frequency (%)	95% CI (%)
Mucocele	6,938	17.12	27	16.70	13.27–20.43
Fibrous lesions	3,671	9.06	30	7.36	5.33–9.67
Pyogenic granuloma	1,975	4.87	31	6.38	4.87–8.08
Dental follicle	1,462	3.61	19	4.93	3.39–6.72
Human papillomavirus lesions	1,136	2.80	27	2.38	1.76–3.08
Chronic inflammation	998	2.46	19	4.55	3.13–6.21
Giant cell lesions (soft tissue)	971	2.40	21	3.75	2.36–5.43
Hyperkeratosis	842	2.08	9	3.26	1.06–6.57
Peripheral ossifying fibroma	509	1.26	16	1.89	1.31–2.58
Gingivitis	487	1.20	10	1.33	0.62–2.28
Gingival hyperplasia	409	1.01	10	2.06	0.76–3.94
Haemangioma	393	0.97	24	2.09	1.43–2.86
Ulcer	148	0.37	11	1.25	0.71–1.92
Lymphangioma	135	0.33	13	1.06	0.61–1.62
Sialadenitis	119	0.29	8	0.75	0.29–1.40
Burkitt's lymphoma	107	0.26	9	1.12	0.21–2.63
Melanotic macule	90	0.22	4	0.64	0.22–1.26
Pleomorphic adenoma	90	0.22	14	0.70	0.27–1.29
Naevus	89	0.22	9	0.53	0.26–0.89
Neurofibroma	80	0.20	12	0.48	0.27–0.75

In the African region, the most consistently reported oral soft tissue malignancy in children and adolescents appeared to be rhabdomyosarcoma from four studies (Abiose et al., 1991; Adebayo et al., 2001; Aregbesola et al., 2005; Arotiba, 1996). The last study was a Nigerian study that specifically evaluated 233 cases of oral squamous cell carcinoma (SCC) over a 15-year period to characterize its behaviour. They found 19 cases of oral SCCs in children aged 0–19 years of age (Effiom et al., 2008). In this subset, oral SCCs were more common in males (*N* = 15) and majority of the SCCs were poorly differentiated (*N* = 9) (Effiom et al., 2008).

In the Americas region, Piloni et al. (2009) reported 24 malignant lesions of 2,434 biopsied lesions in Argentinian children and adolescents between 1990 and 2005. Of these, nine were located in soft tissue; leiomyosarcoma (*N* = 2, location: cheek), rhabdomyosarcoma (*N* = 1, location: lip), malignant fibrous histiocytoma: (*N* = 1; location: cheek); non-Hodgkin lymphoma (*N* = 2, location: sulcus) and SCC (*N* = 1, location: tongue) (Piloni et al., 2009). The other study by de Arruda et al. (2017) found 58 malignant conditions out of 9,411 histopathological records in individuals aged 0–19 years old (de Arruda et al., 2017). Excluding hard tissue malignancies, six were SCC (location: tongue), three were mucoepidermoid carcinoma (location: jugal mucosa), two were leiomyosarcoma (location: cheek) and one each of rhabdomyosarcoma (location: jugal mucosa) and adenocarcinoma (location: lip) (de Arruda et al., 2017). The study by Creath et al. (1991) was not comparable to the above studies as this study focused exclusively on oral leukoplakia in a sample where smokeless tobacco use was high.

In the Eastern Mediterranean study by Mohtasham et al. (2015), the authors described the characteristics of non-SCC malignant oral neoplasms over a 43-year period. Lymphomas (*N* = 13) were the most prevalent malignant condition in children aged 0–19 years of age (Mohtasham et al., 2015). Unfortunately, the study did not detail the location of the lymphomas; thus, it was unclear whether these were hard or soft tissue lesions. However, the study did clearly stipulate the occurrence of other malignant oral lesions presenting on soft tissue. There was a single case of undifferentiated sarcoma, fibrosarcoma, leiomyosarcoma and rhabdomyosarcoma each (Mohtasham et al., 2015). In the other Eastern Mediterranean study by Al-Khateeb et al. (2003), the authors found 26 malignant lesions (out of 258) in North Jordanian children over a 10-year period. The most common malignant lesions were extra-nodal non-Hodgkin's lymphoma (*N* = 6) and rhabdomyosarcoma (*N* = 6). Although the location was specified in the study, the description given was vague and thus making it difficult to definitively ascertain whether the lesions occurred intraorally or extraorally (Al-Khateeb et al., 2003).

In Europe, a German study found 12 (13%) malignant oral lesions in children and adolescents aged 0–16 years of age presenting to their institution between 1970 and 1999. Of these, 5 (rhabdomyosarcoma:

TABLE 4 Top 10 most frequent (pooled) oral conditions by WHO regions based on biopsy reviews

African region (Chidzonga et al., 1996; Lawoyin, 2000; Munsamy et al., 2011)			Eastern Mediterranean region (Abdullah et al., 2016; Bataineh & Al-Dwairi, 2005; Jaafari Ashkavandi et al., 2014; Maaita, 2000; Seyedmajidi et al., 2011)			European region (Gultelkin et al., 2003; Jones & Franklin, 2006; Sixto-Requeijo et al., 2012; Sklavounou-Andrikopoulou et al., 2005)		
Condition	**Pooled relative frequency (%)**	**95% CI (%)**	**Condition**	**Pooled relative frequency (%)**	**95% CI (%)**	**Condition**	**Pooled relative frequency (%)**	**95% CI (%)**
Pyogenic granuloma	11.54	6.28–18.13	Pyogenic granuloma	20.27	10.75–31.73	Fibrous lesions	16.41	1.09–44.29
Mucocele	9.11	7.81–10.50	Fibrous lesions	20.18	2.78–46.43	Mucocele	15.73	9.24–23.43
Fibrous lesions	5.38	4.37–6.48	Giant cell lesions (Soft tissue)	14.59	8.94–21.25	Pyogenic granuloma	8.82	2.46–18.54
Epidermoid carcinoma	4.26	2.69–6.38	Lymphangioma	10.47	6.32–16.03	Giant cell lesions (Soft tissue)	7.22	0.89–18.77
Burkitt's lymphoma	4.01	0.21–11.98	Peripheral ossifying fibroma	7.12	5.16–9.53	Chronic inflammation	6.18	1.96–12.51
Peripheral ossifying fibroma	3.97	2.96–5.21	Hyperkeratosis	6.33	5.27–7.49	HPV[b] lesions	3.17	0.39–8.37
Gingival cyst	3.88	2.38–5.92	Mucocele	5.78	4.76–6.89	Peripheral ossifying fibroma	1.77	0.03–5.74
Benign soft tissue neoplasm NOS[a]	3.58	2.62–4.76	Non-specific lesions	5.68	4.48–7.08	Hyperkeratosis	1.66	1.30–2.08
Pleomorphic adenoma	2.81	2.08–3.63	Haemangioma	4.29	0.86–10.01	Sialadenitis	1.63	1.28–2.05
Haemangioma	2.41	1.56–3.43	Neurilemmoma	4.07	1.65–8.21	Gingivitis	1.48	1.14–1.88
Region of the Americas (Ataide et al., 2016; Cavalcante et al., 2016; Das & Das, 1993; Keszler et al., 1990; Kwok et al., 2015; Lima Gda et al., 2008; Maia et al., 2000; Martins-Filho et al., 2015; Melo, 2011; Shah et al., 2009; Sousa et al., 2002; Vale et al., 2013; Zuniga et al., 2013)			**South-East Asia region (Dhanuthai et al., 2007; Krishnan et al., 2014; Lapthanasupkul et al., 2015; Taweevisit et al., 2018)**			**Western Pacific region (Lei et al., 2014; Wang et al., 2009; Chen et al., 1998; Ha et al., 2014; Mieko, 2007)**		
Condition	**Pooled relative frequency (%)**	**95% CI (%)**	**Condition**	**Pooled relative frequency (%)**	**95% CI (%)**	**Condition**	**Pooled relative frequency (%)**	**95% CI (%)**
Mucocele	19.23	13.69–25.47	Mucocele	20.02	12.62–28.61	Mucocele	18.62	7.91–32.54
Remaining lesions in the inflammatory group	11.43	10.18–12.78	Pyogenic granuloma	7.25	4.07–11.23	Chronic inflammation	10.23	5.29–16.54
Fibrous lesions	7.15	5.22–9.35	Nevi	5.65	3.04–9.47	Epstein pearls	5.13	2.68–8.79
Hyperkeratosis	4.68	0.06–15.51	Fibrous lesions	5.08	3.71–6.65	Fibrous lesions	4.23	1.27–8.76
Non-diagnostic	4.53	3.75–5.41	Hyperkeratosis	2.61	0.96–5.59	Normal tissue	3.14	0.24–8.91
Chronic inflammation	3.90	2.15–6.14	Adenoid cystic carcinoma	2.52	1.76–3.49	Laceration	2.99	1.21–6.07
Pyogenic granuloma	3.35	2.66–4.12	Haemangioma	2.09	0.29–5.33	Ulcer	2.52	1.54–3.72
Gingival hyperplasia	3.25	1.21–6.16	Chronic inflammation	1.99	1.49–2.56	Pyogenic granuloma	2.42	1.94–2.95
HPV[b] lesions	2.66	1.96–3.45	Rhabdomyosarcoma/Incisive Canal Cyst/Ewing's Sarcoma/Plasmacytoma/Round Cell Tumour	1.03	0.03–5.61	Haemangioma	2.05	1.00–3.45
Giant cell lesions (Soft tissue)	2.54	1.66–3.58				Candidiasis	1.96	1.20–3.00

[a]Not otherwise specified.
[b]Human papilloma virus.

N = 2, fibrosarcoma: *N* = 2, metastasis of neuroblastoma: *N* = 1) presented either in the cheek or lips (Trobs et al., 2003). Iatrou et al. (2013) reported on orofacial tumours and tumour-like lesions in 211 Greek children aged between <1 and 15 years of age over an 11-year period and found rhabdomyosarcoma (*N* = 6) to be the most common malignant lesion. Majority of these were in hard tissue, and only one presented in soft tissue (i.e. cheek).

In the South-East Asia/Western Pacific regions, a study from Indonesia found SCC to be the most common malignancy in children aged 0–19 years of age (Budhy et al., 2001). The study did not specify the anatomic location of the lesions. This contrasted with the other Asian study in Japan which reported that sarcoma was the most common (*n* = 14 out of 18) malignant oral tumours in their population (Sato et al., 1997). Majority of these lesions occurred in hard tissue, and only three were in soft tissue (i.e. buccal mucosa) (Sato et al., 1997).

4 | DISCUSSION

In many countries, paediatric dentists or general dentists are children's initial point of contact for oral symptoms and therefore will frequently be the first to notice an oral mucosal lesion. However, the broad scope and fast pace of Paediatric Dentistry may limit the provider's experience with rarer oral mucosal disorders. To our knowledge, this review represents the first attempt to quantify the global and region-specific relative frequency of oral mucosal disorders in the paediatric sample. This study also systematically examined both clinical and histopathological studies allowing for a more complete description of the spectrum of mucosal disorders in children than previously reported. Information on the relative lesion frequency from this review may serve as a guide for deriving differential diagnosis for oral lesions encountered in children.

In general, data from the clinical studies revealed similarities in the most commonly observed mucosal lesions in children across regions. They were trauma-associated lesions (2.5%–4.1%), fissured tongue (0.3%–4.0%), oral ulcers (0.3%–4.8%) and migratory glossitis (0.1%–2.8%). An exception was the study by Arendorf and van der Ross (1996), who found that angular cheilitis (15.1%) and commissural lip pits (9.6%) were the two most common oral mucosal lesions in South African preschool children (15.1%) which differed from other regions. Authors attributed the high frequency of angular cheilitis and commissural lip pits to be secondary to nutritional deficiencies and ethnicity predilection (Arendorf & van der Ross, 1996). Another possibility is the exclusion of commissural lip pits in the reporting of oral pathology in other studies.

In newborns, mucosal cysts, Bohn's nodules and Epstein pearls were the top three most common lesions (Cetinkaya et al., 2011; Flinck et al., 1994; George et al., 2008). This finding is aligned with current knowledge from textbooks and reports from the literature (Neville, Allen, & Chi, 2015). Although there were other studies that included newborns in their sample, the specific data for this age group could not be extracted.

As with the data from the clinical studies, most of the lesions reported from biopsy samples were similar across regions, with pyogenic granuloma (2.4%–20.3%), fibrous lesions (4.2%–20.2%) and mucocele (5.8%–20.0%) being the most common.

The qualitative review on malignant lesions found that variations in study design made the comparison of the results between studies difficult or impossible even in those originating from the same geographic region. However, it was clear that overall oral soft tissue malignancies were rare in children. Rhabdomyosarcomas appeared to be the most common oral soft tissue malignancy in majority of the geographic regions. Of note, the study by Budhy et al. (2001) deviated from this trend and oral SCCs were reported to be most common malignancy in children. The authors proposed that the low social economic status and poor nutritional status of the East Javan population may have contributed to this finding but this was not specific to children. The finding that rhabdomyosarcoma being the most common oral soft tissue malignancy was also not align with the quantitative data from the biopsy review. This is likely due to the exclusion of malignant conditions presenting in hard tissue during the qualitative review on oral soft tissue malignancies.

A significant limitation of undertaking this review was the varying definitions across reports of what was considered "paediatric." For this review, age 20 years was chosen as the upper limit of what was considered "paediatric" as the blanket exclusion of all groups with older age thresholds would have inappropriately eliminated data addressing our research objective. Given the physiologic, developmental and social differences between early childhood and adolescence, it would have been worthwhile to analyse the data by ages. However, varying maximum age of what was considered "paediatric," the arbitrary classification of lesions by age (e.g. 0–10 years old vs. 11–20 years old) and the inability to extract raw data by age made this impossible.

Similar to other groups, our review noted several inherent limitations when combining and interpreting data from studies with different study designs. We found significant differences in the studies relative to study samples, diagnostic criteria, lesion nomenclature and sampling time frame. Although majority of clinical studies used the WHO guide to epidemiology and diagnosis of oral mucosal diseases (Kramer, Pindborg, Bezroukov, & Infirri, 1980), wide variations in lesion nomenclature across studies were still present. The general observation was the failure of the studies to use the exact terminology stipulated by the guide. As such, there was a need to make some assumptions regarding lesion terminology. Initial data abstraction recorded the exact terminology from each included study. These terms were then reviewed by two of the authors and combined for data analysis. In the majority of the cases, the decision to combine terms was straightforward (recurrent aphthous stomatitis and aphthous ulcerations). In instances where it was unclear, the term was left unchanged or grouped based on aetiology (e.g. HSV-associated lesion rather than primary or recurrent HSV) to avoid misinterpretation of the data presented in the primary source.

Despite the limitations, a scoping review on the relative frequencies of oral lesions in children is the first step towards

defining Paediatric Oral Medicine. The management of all oral mucosal lesions does not clearly fall within the scope of Paediatric Dentistry, and patients may be referred to either Oral Medicine or other (e.g. Oral Pathology, Oral Surgery, Periodontology) specialties for evaluation and treatment. Oral medicine specialists are dentists that are concerned with the diagnosis and management of oral and medical conditions that affect the oral and maxillofacial region, but often lack experience working with children. The question then lies as to whom and how should these two specialties collaborate to manage oral lesions affecting the children. To address this, collaboration between Oral Medicine and Paediatric Dentistry is essential to ensure that children affected with common oral conditions are promptly diagnosed and managed within Paediatric Dentistry, while those afflicted with rarer and potentially more severe disorders are quickly referred to the appropriate specialists for management. Joint Paediatric Dentistry/Oral Medicine clinics specific for the diagnosis and management of oral mucosal lesions in children, while ideal, are uncommon and only available in select institutions. Thus, a good starting point may be to utilize information from this report to refine the curricula in Paediatric Dentistry and Oral Medicine specialty training programmes to reflect lesion epidemiology and the global burden of disease. Emphasis can be placed on the identification, diagnosis and management of lesions most commonly encountered in practice and also on rare life-threatening diseases with significant potential impact on a patient's quality of life. Our next steps are to elicit input from educators of Paediatric Dentistry specialty programmes on current oral medicine curricula and the considerations made when determining the scope of oral medicine content in their paediatric programmes. Additionally, a focused survey of paediatric dentists and oral medicine specialists who deliver "joint" clinics aims to elicit whether conditions managed in this clinical setting mirror the results reported here. We hope information from both initiatives will provide another element to better define Paediatric Oral Medicine and direct delineation of practice of oral medicine in children across paediatric dentists and oral medicine specialists.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

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