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Differences in methodologies of measuring the prevalence of oral mucosal lesions in children and adolescents

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Summary. *Aim.* This review offers a brief summary of three of the more commonly surveyed and reported oral mucosal conditions found in children, and an appraisal of the variation between selected elements of prevalence study methodologies.

Design. Searches of electronic databases (i.e. MEDLINE, CINAHL, EMBASE and EBM Reviews) were conducted to find publications related to oral mucosal conditions in children. Studies were included and reviewed if they contained data on the prevalence of any of the following oral mucosal conditions: geographical tongue, oral ulceration and herpes labialis in children or adolescents (up to the age of 19 years).

Results. A total of 29 articles out of 333 met the inclusion criteria and were reviewed. Of these 29 reports, 18 considered geographical tongue, 12 herpes labialis and 10 oral ulceration, although a number of the surveys reported on more than one condition. The approaches used in these studies varied on a number of the potentially important areas associated with validity, comparability, and whether or not the findings may be extrapolated beyond the study population, such as the sampling frame, diagnostic criteria, training and calibration, and examination features.

Conclusion. Although there were a number of surveys relating to the prevalence of geographical tongue, herpes labialis and oral ulcers in children and adolescents, reported prevalences varied and few studies were directly comparable in terms of the methodology applied. In particular, there was substantial variation between surveys in terms of the diagnostic criteria and method of detection employed although, in many instances, there was inadequate detail to allow full appraisal of the methodology. There is a need for more good-quality epidemiological studies in this area.

Introduction

Understanding the distribution, aetiology, natural history and epidemiology of oral mucosal pathologies is essential to promote primary prevention, early diagnosis, prompt treatment and the provision of appropriate health services [1]. Despite World Health Organization (WHO) recommendations [2] to encourage more epidemiological assessment of oral mucosal lesions, the volume of literature in this area is much more limited than that on other oral conditions such as dental caries and periodontal diseases [3].

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The epidemiological literature relating to oral mucosal lesions in children and adolescents is mostly related to oral mucosal lesions such as oral ulceration, herpes labialis and other mucosal alterations which are of interest because of the absence of a clear understanding of their aetiology and relationship to other conditions.

Assessing the validity of observational studies and comparing findings is not an easy task since no standard measure of study quality exists for them. However, examination settings (e.g. lighting conditions and the position of the subject), sample selection and calibration among examiners are important elements in improving the validity, representativeness and reproducibility of findings in any epidemiological study, and also to allow comparisons on the prevalence rates among different studies. Almost as important as designing a study well is how it is reported in order that readers may appraise the evidence presented.

This review offers a brief summary of three of the more commonly surveyed and reported oral mucosal conditions found in children, and an appraisal of the variation between selected elements of prevalence study methodologies.

Materials and methods

The following databases were searched for studies of the prevalence of oral mucosal lesions in children and adolescents: MEDLINE, CINAHL, EMBASE and EBM Reviews (from the inception of the databases to January 2004).

The following keywords and their combinations were used to carry out the search: prevalence; oral mucosal lesions; soft tissue lesions; geographical tongue; oral ulcers; aphthae; mucosal swellings; oral lichen planus; mucocele; oral pigmented lesions; herpes labialis; herpes simplex; children; adolescents; teenagers; toddlers; infants; child. Neither the publication year nor languages were limited. Using the titles and abstracts (where available), all potentially relevant publications were retrieved. The search was complemented by reviewing the reference lists of these papers for further relevant studies. Studies were included and reviewed if they contained data on the prevalence of any of the following oral mucosal conditions: geographical tongue, oral ulceration and herpes labialis in children or adolescents (up to the age of 19 years).

The following features were extracted from each of the papers which met the inclusion criteria: sample size; age range (years); population features (e.g. schoolchildren or clinic attendees); reported sampling frame; the diagnostic criteria used; whether or not training and calibration was conducted; examination features (e.g. the instruments used, lighting conditions and adjuncts/alternatives to a clinical examination); and prevalence.

Results and discussion

A total of 29 of 333 articles met the inclusion criteria and were reviewed. Of these 29 reports, 18 considered geographical tongue, 12 herpes labialis and 10 oral ulceration, although a number of the surveys reported on more than one condition. Before drawing out some of the common points of interest between these 29 studies, a summary of each condition and the reported prevalences are discussed after each of the following subheadings. Tables 1–3 highlight some of the important areas of variation between studies.

Geographical tongue

Employing the search strategy described earlier, this was the most commonly reported oral mucosal condition in the epidemiological literature concerning children and adolescents (18 of 29 publications). The condition is also known as benign migratory glossitis or erythema migrans, and it occurs on the dorsum of the tongue, where it presents as red patches surrounded by white margins. This benign condition is intermittent and is normally symptomless, and other than reassurance, no treatment is required. However, the aetiology and age of onset of geographical tongue remains unclear. Therefore, information on prevalence in different populations could be important in deriving hypotheses about which factors may be associated with this condition.

In the 18 papers reviewed, there was a great variation in prevalence, which ranged from 0·2% [5] to 14·3% [6]. However, the average prevalence in most studies was low, which could indicate that this lesion is not seen very often in children. The highest prevalence of geographical tongue was reported in a study by Rahamimoff and Musham [6], where children were examined several times over the study period, which may have optimized the opportunity to detect this condition since it can undergo periods of remission.

Comparing the findings of these studies is difficult; however, given the wide variations in age cohorts, population features and diagnostic criteria, at least seven different sets of diagnostic criteria were described, although a number of articles did not provide these details and others modified existing criteria systems. Table 1 details the data extracted from these studies measuring the prevalence of geographical tongue and highlights some of the variations between approaches.

Herpes labialis

This was the second most commonly reported oral mucosal condition in the epidemiological literature reviewed (12 of 29 publications). Herpes labialis is a common disease caused by infection with herpes simplex virus, most often type 1. Primary infection with herpes simplex is asymptomatic in the majority of children (88–99%), but when symptomatic, it commonly presents as acute gingivostomatitis [21]. Herpes labialis is the reactivation of the primary infection, often following a prodromal period, and lesions present early on as clusters of vesicles on the lip which soon burst and scab over. The lesions

Table 1. Studies reporting on the prevalence of geographical tongue: (WHO) World Health Organization.

Author [ref]	Sample size	Age range (years)	Population features	Reported sampling frame	Diagnostic criteria	Examiners' training and calibration	Examination	Prevalence of geographical tongue (%)
Rahamimoff & Musham [6]	5 425	0–2	Israeli children	Clinic attendees	–*	–	–	14·29
Redman [7]	3 611	5–18	American Caucasian students	Public schools	By Redman *et al*. [38]	–	Portable high-intensity light/gauze/mouth mirror	1·41
Chosack *et al*. [8]	70 359	6–18	Israeli schoolchildren	Receiving dental care	By Witkop & Barros [39]	Yes	Mouth mirrors/natural light	1·14
Sedano [9]	6 180	6–15	Argentinian children	Selected schools	Described (no source)	–	Natural and/or artificial light/tongue depressors	1·5
Camargo [4]	1 060	7–15	Brazilian schoolchildren	Public schools	–	–	Mouth mirror/gauze/ wooden spatula/artificial light	6·1
Kullaa Mikkonen *et al*. [10]	381	3–8	Finnish children	Clinic attendees	Described (no source)	–	–	2·1
Ghose & Baghadady [11]	6 090	6–12	Iraqi schoolchildren	Randomly selected	By Witkop & Barros [39]	Yes	Mouth mirrors/natural light/gauze	4·3
Sawyer *et al*. [12]	2 203	10–19	Nigerian schoolchildren	Selected schools	Described (no source)	–	Mouth mirrors/natural and/or artificial light/explorers	0·3
Salem *et al*. [5]	1 932	6–12	Saudi Arabian schoolchildren	Selected schools	By Shafer [40]	Yes	Two mouth mirrors	0·2
Crivelli *et al*. [13]	846	4–13	Argentinian schoolchildren	Selected schools	By WHO [35]	–	Dental mirrors/wooden spatulas/artificial light	2·9
Sedano *et al*. [14]	32 022	5–14	Mexican schoolchildren	Selected schools	Agreed by examiners and project director	Yes	Tongue depressors/natural and/or artificial light	1·9
Crivelli *et al*. [15]	660	3–13	Argentinian children	Clinic attendees	By WHO [35]	–	Tongue depressors/artificial light/gauze	3·63
Kleinman *et al*. [3]	39 206	5–17	American schoolchildren	NIH [44]	By Axell [41]/ Pindborg [42]	Yes	Two mouth mirrors/two gauzes/fibre-optic light	0·6
Arendorf & van der Ross [16]	1 051	–	South African preschool children	Random sample	By WHO [2]	Yes	Artificial light/mirrors	1·6
Baldani *et al*. [17]	200	0–2	Brazilian children	Clinic attendees	Described (no source)	–	Tongue depressors/natural light/gauze	5·0
Voros-Balog [18]	1 017	1–14	Hungarian children	Clinic attendees	By Lascaris [43]	–	Dental surgery/plain mouth mirrors/artificial light	5·7
Bessa *et al*. [19]	1 211	0–12	Brazilian children	Clinic attendees	By WHO [2]/ Axell [41]	Yes	Artificial light/disposable retractors	9·0
Santos *et al*. [20]	331	0–12	Amazonian Indians	Random sample	By Axell [41]/ WHO [2]/ Witkop & Barros [39]	Yes	Artificial light/glass slide/ mirrors/gauze/disposable saliva extractors	7·6

*Not reported.

Table 2. Articles reporting on the prevalence of herpes labialis: (WHO) World Health Organization; and (NIH) National Institutes of Health.

Author (year)	Sample size	Age range (years)	Population features	Reported sampling frame	Diagnostic criteria	Examiners' training and calibration	Examination	Prevalence of *herpes labialis* (%)
Crivelli *et al*. [13]	846	4–13	Argentinian schoolchildren	Selected schools	By WHO [35]	–*	Dental mirrors/wooden spatulas/artificial light	5·20
Becker *et al*. [22]	197	1–15	Navajo children	Clinic attendees	Serologic assays	–	–	73
Katz *et al*. [24]	99	–	HIV-infected children	Clinic attendees	Described (no source)	Yes	–	24
Kleinman *et al*. [3]	39 206	5–17	American schoolchildren	NIH [44]	By Axell [41]/ Pindborg [42]	Yes	Two mouth mirrors/two gauzes/fibre-optic light	0·78/32·7
Arendorf & van der Ross [16]	1 051	Pre-school	South African preschool children	Random sample	By WHO [2]	Yes	Artificial light/mirrors	0·8
Wanankul & Thisyakorn [25]	91	0–13	HIV-infected Thai children	Clinic attendees	–	–	–	2·2
Magalhaes *et al*. [45]	38	2–13	HIV patients	Selected clinic attendees	Biopsies, cytology, culture, X-rays	–	–	5·2
Spicher *et al*. [23]	2 048	1–17	Swiss schoolchildren	Selected schools	Saliva assay	–	–	23·9
Santos *et al*. [26]	80	2–12	HIV-infected Brazilian children	Clinic attendees	By WHO collaborating centre [36]	Yes	Mouth mirror/gauze/ flashlight	1·3
Gaitan-Cepeda *et al*. [27]	48	0–12	HIV-infected Mexican children	Clinic attendees	By WHO collaborating centre [46]	Yes	Artificial light (dental lamp)	2·1
Bessa *et al*. [19]	1 211	0–12	Brazilian children	Clinic attendees	By WHO [2]/ Axell [41]	Yes	Artificial light/ disposable retractors	0·82
Santos *et al*. [20]	331	0–12	Amazonian Indians	Random sample	By Axell [41]/ WHO [2]/Witkop & Barros [39]	Yes	Artificial light/glass slide/ mirrors/gauze/disposable saliva extractors	0·3

*Not reported.

Table 3. Articles reporting on the prevalence of oral ulceration: (RAS) recurrent aphthous stomatitis; (WHO) World Health Organization; (NIH) National Institutes of Health; and (FOTI) fibre-optic transillumination.

Author (year)	Sample size	Age range (years)	Population features	Reported sampling frame	Diagnostic criteria	Examiners' training and calibration	Examination	Prevalence of oral ulceration (%)
Miller *et al*. [32]	1 303	< 5–15+	Children of parents with a history of RAS	Selected	History of RAS/ identification by photograph	–*	Interview	39·2
Crivelli *et al*. [13]	846	4–13	Argentinian schoolchildren	Selected schools	By WHO [35]	–	Dental mirrors/wooden spatulas/artificial light	10·87
Addy [33]	720	15–16	Southern Welsh schoolchildren	Stratified sample	History of recurrent aphthous ulceration	–	Interview	34·9
Fayle & Curzon [34]	43	2–15	Oncology patients	Inpatients	Described (no source)	–	–	
Kleinman & Pindborg [42]	39 206	5–17	American schoolchildren	NIH [44]	By Axell [41]/ Pindborg [42]	Yes	Two mouth mirrors/two gauzes/FOTI†	1·23/36·5
Arendorf & van der Ross [16]	1 051	Pre-school	South African preschool children	Random sample	By WHO [2]	Yes	Artificial light/mirrors	0·5
Magalhaes *et al*. [45]	38	2–13	HIV patients	Selected clinic attendees	Biopsies, cytology, culture, X-rays	–	–	2·6
Garcia-Pola *et al*. [31]	624	6	Spanish children	Systematic sampling	By WHO [2]	–	Two dental mirrors/probes/ gloves/swabs	2·24
Bessa *et al*. [19]	1 211	0–12	Brazilian children	Clinic attendees	By WHO [2]/ Axell [41]	Yes	Artificial light/disposable retractors	1·57
Santos *et al*. [20]	331	0–12	Amazonian Indians	Random sample	By Axell [41]/ WHO [2]/Witkop & Barros [39]	Yes	Artificial light/glass slide/mirrors/gauze/ disposable saliva extractors	1·2

*Not reported.
†Plus interview.

usually last for 7–10 days before resolving. Like geographical tongue, the condition is intermittent, and its precipitating factors are said to include trauma, immunosuppression, exposure to sunlight, stress or other illness.

In the 12 papers reviewed, the reported prevalence was between 0·3% and 73%, and five of these studies surveyed only HIV children, in whom the prevalence ranged between 1·3% and 24%. The methods of determining whether or not an individual suffered from herpes labialis which were reported included, in addition to or instead of a clinical examination, the use of self-report to ascertain a history of the condition [3], serology [22] and saliva sampling [23].

As might be expected, the highest prevalence was reported by a study using serological assays [22] and the second highest prevalence (24%) was found using saliva samples [23]. A survey of HIV-infected children [24] reported a similar high prevalence of 24%, but this paper did not report on the method of determination that the authors employed.

Again, with the small number of studies published in this area as well as the variation in methods employed, it is difficult to compare findings. Although there were similarities in the diagnostic criteria employed in some papers, no two studies reported identical approaches. Data extracted from these studies which highlight some of the variations between approaches are detailed in Table 2.

Oral ulceration

Oral ulceration was the least reported of the three conditions reviewed (10 of 29 publications) despite being a relatively common oral mucosal lesion in children and adolescents. The most common types of oral ulceration in children include aphthous and traumatic ulcers, although there are many less-common causes, such as: acute gingivostomatitis; herpangina; hand, foot and mouth disease; and those secondary to cancer treatment.

Recurrent aphthous stomatitis (RAS) is characterized by mucosal ulcers less than 1 cm in size, with a short duration, recurring after periods of remission [28]. One or more small ulcers may occur at frequent intervals and the majority of aphthous ulcers in children are of a minor variety, usually healing within 2 weeks [29]. The major type is rarer, affecting one in 10 patients with RAS. It normally has its onset after puberty and it is chronic, with ulceration lasting several weeks [30].

Ten articles which met the inclusion criteria were reviewed, and the prevalences reported were very varied, ranging from 0·5% to 39·2%. Again, the intermittent nature of these lesions makes it more difficult to compare prevalence rates; three different approaches, and combinations of these, were reported within the studies reviewed: clinical examination, self-reported history of oral ulceration and other tests (e.g. biopsy and cytology).

In the surveys which based their findings on the day of examination, when only current lesions were detected [3,15,16,19,20,31], prevalence rates varied between 0·5% and 10·8%. Two of these studies [16,31] used the same diagnostic criteria as described by the WHO [2], and their prevalence rates were 0·5% and 2·24%.

The three studies which took into consideration the history obtained from the patient through interviews or questionnaires [3,32,33] reported comparable and substantially higher prevalence rates between 34% and 39%.

Table 3 highlights some of the variations between the approaches taken in these studies measuring the prevalence of oral ulceration.

Common points of interest between studies of the prevalence of oral mucosal lesions

This review aimed to examine what epidemiological information on oral mucosal lesions in children and adolescents was available from the literature. Assessing the quality and validity of observational studies is difficult not only because of the lack of a standard method of measuring this, but also because of the variation in the approaches employed and the limited nature of the information included in publications.

Tables 1–3 illustrate how studies varied in a number of the potentially important areas associated with validity, comparability, and whether or not the findings may be extrapolated beyond the study population, such as the sampling frame, diagnostic criteria, training and calibration, and examination features.

Sampling frame

In order to produce findings which can be extrapolated beyond those studied, an effort should be made to ensure that the sample is random and representative of the population of interest. The sampling

frames in the studies described in this review were very variable and were often difficult to determine. Only five studies [3,11,16,20,33] reported randomly generated samples; most of the other papers reported the use of selected groups such as hospital or clinic attendees. Because of limitations in the information reported in many cases, it was not possible to ascertain whether these studies took reasonable efforts to avoid the possible bias of studying selected groups, which may differ from the population of interest.

Diagnostic criteria

A variation in the diagnostic criteria applied was one of the main reasons why comparisons of prevalence among studies in this review were difficult. Although there are standardized WHO criteria [2,35] which are applicable to each of the conditions reviewed, few studies used these – less variation in prevalence was observed among most of those who did use identical WHO criteria. Again, in many cases, limitations in what was reported made it difficult to determine the exact nature of the criteria which had been used, and thus, whether they were comparable with other systems.

Training and calibration

In the context of epidemiology, calibration of examiners is another important procedure in order to ensure high levels of agreement. The calibration training is also an opportunity to identify problems, and discuss protocols and diagnostic criteria, which should ensure that valid and reproducible data are collected. Less than half of the articles in this review referred to the training and calibration of examiners. Among those who reported this, only a few described the process in more detail [3,8,19,20] and the majority only mentioned the procedure, but gave no further details. It is not possible to determine whether this is an example of a failure to include important procedures related to the process of obtaining prevalence data or merely a reflection of the limitation in the length of the publications.

Examination features

The WHO highlighted the importance of the consistency of illumination throughout surveys, i.e. whether it is natural or artificial [37], and most of the studies reviewed reported on this and used a consistent light source, although two studies used a mixture [9,12]. Differences in lighting conditions between studies may influence the amount of disease detected, and this should be borne in mind when comparing prevalence rates among studies employing different light sources. Artificial light is probably more reproducible during surveys than natural light and was the choice reported in most surveys reviewed in this study which described the lighting system applied [3,4,7,13,15,16,18–20,25,26]. Although the examination position employed in a survey may be influential in determining the visibility of the oral mucosa (i.e. seated, standing, reclined or supine), this was not widely reported.

The intermittent nature of each the conditions included in this review would also contribute to the variation in prevalence, and a number of researchers adopted adjuncts or alternatives to the clinical examination to determine more information about whether individuals had previously been affected. However, whilst the use of blood or saliva sampling and biopsy may add useful information, these methods might not be appropriate for epidemiological surveys because of the costs and invasive nature of some of the tests. A number of studies used interviews to establish the history of lesions such as herpes and ulcers, but this approach is not without limitations since self-report may be unreliable, especially from younger children, and also open to recollection bias.

It should also be highlighted that epidemiological data collected from any selected samples, such as HIV and oncology patients, need to be evaluated with caution since they are not comparable with randomly selected samples and their results cannot be extrapolated.

What this paper adds

- This paper reviews the literature reporting on the prevalence of three of the most commonly reported oral mucosal conditions in children and adolescents: geographical tongue, oral ulceration and herpes labialis.
- It also draws attention to issues relating to the difficulty in surveying and reporting such conditions.
- This review indicates that there is a need for further high quality research in this area.

Why this paper is important for paediatric dentists

- This article gives an overview of three of the most common oral mucosal conditions seen in day-to-day practice.
- It highlights particular methodological issues in prevalence studies which should be taken into consideration by those planning epidemiological studies in an area where little substantial information is available.

Conclusions

This review found few studies relating to the prevalence of geographical tongue, herpes labialis and oral ulcers in children and adolescents. Although there were a number of studies on each condition, few were directly comparable in terms of the methodology applied. There was substantial variation between reports in a number of elements important to an epidemiological study, such as the diagnostic criteria and method of detection employed, although, in many instances, there was inadequate detail to allow full appraisal of the methodology. There is a need for more good-quality epidemiological studies in this area. The methodological issues highlighted in this paper are some of the challenges which ought to be addressed in order to make available more valid, reliable and comparable studies.

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