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Diagnóstico histopatológico em estomatologia pediátrica: estudo retrospectivo de 43 anos de 1.480 casos de uma instituição brasileira.

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Diagnóstico histopatológico em estomatologia pediátrica: estudo retrospectivo de 43 anos de 1.480 casos de uma instituição brasileira.

Trabalho de conclusão de curso apresentado a Faculdade de Odontologia da UFU, como requisito parcial para obtenção do título de Graduado em Odontologia

Orientador: Prof. Dr. Adriano Mota Loyola

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Sumário

The Journal of Pediatrics

Histopathological diagnosis in pediatric stomatology: a 43-year retrospective study of 1,480 cases from a Brazilian institution

Abstract:	Objective to analyze the prevalence of histopathological diagnoses for oral biopsied tissues obtained from Brazilian children. Study design an analytical, cross-sectional retrospective study was performed with biopsy files of patients ≤ 14 years of age from a Brazilian oral pathology laboratory over a 43-year period. Data included sex, age, location, and diagnoses. The prevalence was calculated by means of relative frequency. Associations between sex, age groups and diagnoses were verified with Pearson's chi-square test. Results from 19,456 oral biopsies, 1,480 (7.6%) were obtained from patients aged ≤ 14 years. Most children were 10-14 years of age (60.1%) and females (55.1%), with an overall M:F of 1:1.2. Children aged 0-9 years and males had a higher frequency of lesions of the oral mucosa, whilst the 10-14 year age group showed a higher frequency of cysts, odontogenic tumors, and salivary gland lesions. The latter was also significantly higher in females. Samples consisted mostly of soft tissue lesions (53%) obtained from the lower lip (30.7%). Intraosseous lesions showed a slight predilection for the mandible (21.2%). Salivary gland lesions (28.8%) was the most common diagnostic category, followed by reactive lesions (18.8%), and cysts (16.1%). Mucocele (33.5%), dentigerous cyst (6.7%), and fibrous hyperplasia (5.9%) were the top three histopathological diagnoses. Malignant lesions affected only 0.9% of this population. Conclusion our results were similar to other retrospective studies. Due to the low frequency of oral biopsies in children, data on the prevalence of oral pathology in this population might aid in the clinical and histopathologic diagnoses.

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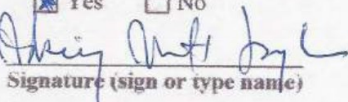*An additional sheet can be used if there are more than 9 authors*

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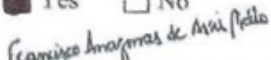**Author:** Francisco Amazonas de Assis Mellor

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Histopathological diagnosis in pediatric stomatology: a 43-year retrospective study of 1,480 cases from a Brazilian institution.

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RESUMO

Objetivo: analisar a prevalência de diagnósticos histopatológicos para tecidos orais biopsiados obtidos de crianças brasileiras. **Desenho do estudo:** foi realizado um estudo retrospectivo analítico, transversal, com arquivos de biópsia de pacientes de 0 a 14 anos de um laboratório brasileiro de patologia bucal durante um período de 43 anos. Os dados incluíram sexo, idade, localização e diagnósticos. A prevalência foi calculada por meio de frequência relativa. As associações entre sexo, faixas etárias e diagnósticos foram verificadas com o teste do qui-quadrado de Pearson. **Resultados:** das 19.456 biópsias orais, 1.480 (7,6%) foram obtidas de pacientes com idade até 14 anos. A maioria das crianças tinham entre 10-14 anos de idade (60,1%) e eram do sexo feminino (55,1%), com um M:F geral de 1:1,2. Crianças de 0 a 9 anos e do sexo masculino apresentaram maior frequência de lesões da mucosa oral, enquanto a faixa de 10 a 14 anos apresentou maior frequência de cistos, tumores odontogênicos e lesões de glândulas salivares. Este último também foi significativamente maior no sexo feminino. As amostras consistiram principalmente de lesões de partes moles (53%) obtidas do lábio inferior (30,7%). As lesões intraósseas mostraram discreta predileção pela mandíbula (21,2%). Lesões de glândulas salivares (28,8%) foi a categoria diagnóstica mais comum, seguida por lesões reativas (18,8%) e cistos (16,1%). Mucocele (33,5%), cisto dentígero (6,7%) e hiperplasia fibrosa (5,9%) foram os três principais diagnósticos histopatológicos. As lesões malignas afetaram apenas 0,9% dessa população. **Conclusão:** nossos resultados foram semelhantes a outros estudos retrospectivos. Devido à baixa frequência de biópsias orais em crianças, dados sobre a prevalência de patologia oral nesta população podem auxiliar no diagnóstico clínico e histopatológico.

ABSTRACT

Objective: to analyze the prevalence of histopathological diagnoses for oral biopsied tissues obtained from Brazilian children. **Study design:** an analytical, cross-sectional retrospective study was performed with biopsy files of patients ≤ 14 years of age from a Brazilian oral pathology laboratory over a 43-year period. Data included sex, age, location, and diagnoses. The prevalence was calculated by means of relative frequency. Associations between sex, age groups and diagnoses were verified with Pearson's chi-square test. **Results:** from 19,456 oral biopsies, 1,480 (7.6%) were obtained from patients aged ≤ 14 years. Most children were 10-14 years of age (60.1%) and females (55.1%), with an overall M:F of 1:1.2. Children aged 0-9 years and males had a higher frequency of lesions of the oral mucosa, whilst the 10-14 year age group showed a higher frequency of cysts, odontogenic tumors, and salivary gland lesions. The latter was also significantly higher in females. Samples consisted mostly of soft tissue lesions (53%) obtained from the lower lip (30.7%). Intraosseous lesions showed a slight predilection for the mandible (21.2%). Salivary gland lesions (28.8%) was the most common diagnostic category, followed by reactive lesions (18.8%), and cysts (16.1%). Mucocele (33.5%), dentigerous cyst (6.7%), and fibrous hyperplasia (5.9%) were the top three histopathological diagnoses. Malignant lesions affected only 0.9% of this population. **Conclusion:** our results were similar to other retrospective studies. Due to the low frequency of oral biopsies in children, data on the prevalence of oral pathology in this population might aid in the clinical and histopathologic diagnoses.

INTRODUCTION

The pediatric population is subject to a wide range of oral lesions, some of which are specific to childhood and adolescence, and whose clinical features differ from the conditions affecting adult patients. Data on the prevalence of oral diseases in children is limited due to unstandardized study designs[1], especially in terms of age range and diagnostic criteria. In general, oral candidiasis, traumatic lesions and recurrent oral ulcers are common occurrences in pediatric stomatology[1]. Some of these conditions, however, will not demand oral biopsy prior to clinical management, whilst others might require histopathological analysis to confirm the clinical diagnosis. In this context, retrospective studies with biopsy files are conducted to identify the most common diagnoses in pediatric pathology, aiding both clinicians and pathologists to better diagnose and manage such lesions.

Pediatric oral diseases account from 2.6% to 20.6% of all histopathological diagnoses provided by oral health institutions worldwide[2-27]. In Brazil, the averaged prevalence is 9%[2-11]. Differences in the relative frequency result in part from the age ranges used in epidemiological surveys, which have investigated patients with 0-12[10], 0-14[2,3,16,26], 0-15[13,20,27], 0-16[7,8,11,14,15,18,19,22,25], 0-17[23], 0-18[4,5,17,21,24], 0-19[6,9], and 0-20 years[12]. It also varies according to geographic location, and the literature is currently provided with retrospective studies from Brazil[2-11], United States[12,22], Turkey[13], United Kingdom[14], Thailand[15,25], Taiwan[16], Saudi Arabia[17], Chile[18], Australia[19], India[20,26], Iran[17,21], and New Zeeland[27]. Since there are few long-term researches with patients ≤14 years of age in Brazil, the purpose of this study was to analyze the prevalence of histopathological diagnoses for oral

biopsied tissues obtained from children ≤14 years, which were requested by professionals so a diagnostic conclusion in the clinical setting could be achieved.

MATERIALS AND METHODS

Study design and ethical issues

This analytical, cross-sectional retrospective study was conducted on patient records retrieved from the archives of the Department of Oral and Maxillofacial Pathology, School of Dentistry, Federal University of Uberlandia, Minas Gerais, Brazil, after approval of the local Ethics Committee on Human Research (No. 185/2007). Data collection was carried out in accordance with the World Medical Association's Declaration of Helsinki and results were reported as proposed by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist [28].

Sample selection

A total of 19,456 patient records were included in this survey by convenience sampling of all biopsy entries at the Department of Oral Pathology within the period of 1978 and 2021. Patients with 0 to 14 years of age submitted to oral biopsy surgery were considered eligible, in accordance to the statistically oriented definition of children proposed by the United Nations. Study variables included age, sex, anatomical location, and histopathological diagnoses. Extraoral lesions and records with insufficient patient information (age and/or sex) were excluded from this research. Hematoxylin and eosin-stained slides were reviewed on light microscopy by an experienced pathologist and, whenever diagnoses were inconclusive or

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outdated, new conclusive diagnoses were made according to the latest World Health Organization criteria [29]

For description purposes, patients were grouped according to age (0-3, 4-9, and 10-14 years). Histopathological diagnoses were further distributed into ten categories proposed by Happonen *et al*. (1982) [30]: hyperplastic and reactive lesions, benign soft tissue tumors, lesions of the oral mucosa, cystic lesions, periapical inflammation and pulpal diseases, odontogenic tumors, bone pathology, salivary gland lesions, malignant tumors, and healthy soft tissues and teeth. Lesions were allocated according to site of involvement, as follows: upper lip, lower lip, buccal mucosa, floor of mouth, tongue, gingiva, palate, maxilla, mandible, and alveolar ridge.

Data analysis

Quantitative data were described as means ± standard deviation and relative frequency. Considering the study hypothesis that there are no significant differences in the frequencies of oral lesions with respect to gender and age group (0-9 and 10-14 years) in the pediatric population, associations between categorical variables were verified with Pearson's chi-square test followed by post hoc Z-test with Bonferroni adjustment. Significance level was set at 5% and 80% of power. Both descriptive and inferential statistics were performed with IBM® SPSS Statistics software, version 28.0.0. (SPSS Inc., Chicago, Illinois, USA).

RESULTS

From 19,456 lesions diagnosed between 1978 and 2021, 1,490 occurred in patients with 0 to 14 years of age. From this cohort, 1,480 (7.6%) met the eligible criteria. Out of the ten excluded cases, four had lesions affecting extraoral sites, four consisted of duplicates, one lacked patient age and another patient sex description. In addition, the anatomical location was not appropriately informed in 61 (4.1%) biopsy files.

Mean age of the participants was 9.7 ± 3.4 years, with the youngest child being six days old. Most patients were in the 10-14 years age range (60%). Children aged ≥ 3 years, on the other hand, represented less than 5% of our cohort. Biopsied oral lesions were slightly more frequent in females (55.1%) than in males (44.9%), with an overall male to female ratio (M:F) of 1:1.2. Salivary gland lesions accounted for 35.7% of all histopathological diagnoses, followed by hyperplastic and reactive lesions (18.8%), cysts (16.2%), and odontogenic tumors (8%). Malignant lesions (0.9%) were rare in children ≤ 14 years of age.

The distribution of diagnostic categories according to age and sex are described in Table 1. Patients aged 10-14 years showed a significant higher relative frequency of cysts, odontogenic tumors, salivary gland lesions and healthy tissues when compared to children with 0-9 years of age, whist the latter had a higher frequency of lesions of the oral mucosa (Pearson's chi-square test with Bonferroni adjustment, *p*<.001).

Female participants had a higher relative frequency of histopathological diagnoses in the category of salivary gland lesions, with a M:F of 1:1.6; the opposite was observed for lesions of the oral mucosa, with a M:F of 1.7:1. Contingency

analysis showed that these differences were statistically significant (Pearson's chi-square test with Bonferroni adjustment, $p<.001$).

Soft tissue lesions composed most of our samples (n=787, 53%) in comparison to intraosseous diseases (n=637, 42.9%). Solitary lesions (99.5%) were more prevalent than multifocal diseases, which were observed in five odontogenic tumors and two lesions of the oral mucosa.

Table 2 shows the distribution of oral biopsied lesions according to anatomical location. With regard to extraosseous sites, specimens were more frequently biopsied from the lower lip (30.7%), tongue (8.8%) and buccal mucosa (3.7%). The mandible (21.1%) was slightly more affected than the maxilla (17.1%).

From the 1,480 biopsy files included in this study, we identified 108 different histopathological diagnoses in children aged 0-14 years. The twelve most prevalent of them are described in Table.

They accounted for 77% of all diseases affecting this population. Mucocele was the most frequent histopathological diagnosis in children aged 0 to 14 years (33.5%), followed by dentigerous cyst (6.9%) and fibrous hyperplasia (5.8%). Within each of the ten categories proposed by Happonen *et al.* (1982), the following lesions were the most common in pediatric patients, respectively: fibrous hyperplasia (31.7%), squamous papilloma (60.6%), verruca vulgaris (18.2%), dentigerous cyst (42.1%), periapical granuloma (80%), odontoma (58%), fibrous dysplasia (16.7%), mucocele (93.8%), Langerhans cell histiocytosis (23.1%), and dental follicle (81.7%).

When analyzing patient sex separately, 81 histopathological diagnoses were identified in male children, including: mucocele (28%), dentigerous cyst (7.7%),

dental follicle (7.1%), fibrous hyperplasia (5.6%), pyogenic granuloma (5.4%), odontoma (4.5%), and papilloma (4.2%). Females, in turn, were diagnosed with 79 distinct lesions, among which were mucocele (38%), fibrous hyperplasia (6.3%), dentigerous cyst (6.1%), odontoma (4.8%), dental follicle (4.7%), pyogenic granuloma (4.4%), and papilloma (3.6%).

Regarding patent age, thirty types of lesions were observed in children aged ≤ 3 years, including mucocele (23.6%), fibrous hyperplasia (11.1%), giant cell fibroma (5.6%), hemangioma (5.6%), gingival hyperplasia (5.6%), and papilloma (4.2%). Interestingly, this was the only patient group affected by oral hamartomas and heterotopies, such as gastrointestinal heterotopy, and lipoblastomatous and leiomyomatous hamartomas. Children aged 4-9 years were diagnosed with 64 different lesions, mainly mucocele (44.4%), dentigerous cyst (8.5%), fibrous hyperplasia (6.2%), papilloma (4.6%), peripheral giant cell lesion (3.5%), pyogenic granuloma (3.5%), and odontoma (3.3%). In the 10-14 year age group, 86 different lesions were identified, the most frequent of which were mucocele (27.9%), dental follicle (8.1%), dentigerous cyst (6.2%), pyogenic granuloma (5.9%), odontoma (5.6%), fibrous hyperplasia (5.4%), radicular cyst (4.2%), odontogenic keratocyst (3.4%), and papilloma (3.4%). A rare case of chondroid choristoma was also observed in this patient group.

DISCUSSION

The percentage of biopsied oral lesions in the pediatric population ranges from 2.6 to 20.6% of all histopathological diagnoses[2-27]. In the 43-year experience of this single institution, oral lesions in children aged 0-14 years accounted for 7.6% of all biopsy records, which was similar to other studies investigating the same age range[2,3,5,26]. The frequency of oral biopsies increased with age, as most of our patients belonged to the 10-14 years age group. Other studies also reported a higher prevalence of oral biopsied lesions early in the second decade of life[2,7,8,14,16-18,20,25,27]. Our results demonstrate that females were subject to oral biopsy and histopathological diagnosis more frequently than male children, in accordance with most authors[4-6,8,10,13,20,21,25].

Our samples consisted mostly of oral soft tissue pathology[5,6,21], but other authors reported a predominance of intraosseous lesions[3,8,20,23] with a slight predilection for the mandible[3,8,10,20,23,25]. Oral soft tissue lesions in children usually affect the lower lip, tongue and buccal mucosa[10,25], as our results have shown. In other studies, the gingiva was the top anatomical site[12,13,21], especially in infectious diseases and physical trauma[22].

There is no consensus in the literature regarding the method for classification of diagnoses in pediatric oral pathology. Recent studies have applied the original or modified classification of Jones and Franklin[7-9,14,19,23,27], others have used the classification of Neville's textbook[21,23], but most used different sets of categories[2-6,10,11,13,15-18,20,22,25,26]. The classification used in this survey, proposed by Happonen et al.[30], was also used in another Brazilian study[11]. Whenever considered as a category apart, salivary gland lesions accounted for most

of diagnoses 9,22,27], as observed in the present study. Otherwise, most common lesions in children belonged to the reactive/inflammatory category[10,11,16,22,25].

Mucocele was the most frequent lesion in children submitted to oral biopsy, representing from up to 37% of all histopathological diagnosis in this population[2,4-10,16,22,23,25,27]. In other studies, the dentigerous cyst[15,19], radicular cyst[26], fibrous hyperplasia[11], peripheral giant cell granuloma[13,21], and hemangioma[17] were the most prevalent histopathological diagnoses in the pediatric population.

We identified that certain diagnostic categories had significant predilection for specific patient groups. The higher prevalence of cysts, odontogenic tumors in patients with 10-14 years of age might be associated to the mixed dentition period[15,20], as some developmental lesions are associated to unerupted teeth. Periapical inflammation and healthy tissues and teeth were also more frequent in this age group due to the higher prevalence of dental caries[14,19]. In turn, lesions of the oral mucosa might affect children aged up to 9 years due to their relatively immature immune system, making them susceptible to viral or fungal infections, especially when there are other systemic conditions involved[1].

Salivary gland lesions were more frequent in female patients. Nearly 94% of the biopsied lesions in this category were mucoceles, which affected mainly female children from 4-14 years of age and the lower lip, as demonstrated by other authors[31,32]. Most cases might occur due to chronic trauma caused by parafunctional oral habits. Their prevalence in children with mixed dentition varies from 33% to 93%[33,34], with lip or cheek biting affecting up to 16%[34] of this population. Females also show a higher prevalence of oral habits[33]. The frequency

of parafunctional habits in female children in the mixed dentition period is therefore a possible explanation to the prevalence of mucocele in this population.

Lesions of the oral mucosa, on the other hand, showed a significant predilection for males. Two of the most frequent lesions in this category were HPV-related papillary lesions, verruca vulgaris and focal epithelial hyperplasia. In spite of the large documentation of cutaneous and genital warts, the literature lacks the information on the prevalence and sex distribution of HPV-related papillary lesions in the oral mucosa of healthy children[35].

Although salivary gland lesions were the most common diagnosis in pediatric patients due to the high prevalence of mucocele, benign and malignant neoplasms in this category are rare [36]. There were five cases (0.9%) of pleomorphic adenoma, one in the 0-3 year patient group and the others in children aged 10-14 years. No malignant tumors were found in our cohort, however. Pleomorphic adenoma is the benign tumor of salivary gland most commonly reported in children[2,4-6,9,10,13-16,18,20,22,23,25,27]. Sialadenoma papiliferum[2,27] and myoepithelioma[2,6] have also been identified. Malignant tumors in this category include mucoepidermoid carcinoma[2,5,9,10,13-16,21,23,25], acinic cell carcinoma[2,14,22], epithelial-myoepithelial carcinoma[14], adenoid cystic carcinoma[21], adenocarcinoma NOS[9,10], and carcinoma ex-pleomorphic adenoma[9]. Since the proportion of benign and malignant tumors of salivary gland in children is nearly 1:1, every suspicious lesion must be submitted to histopathology analysis[14].

Hyperplastic and reactive lesions (18.8%) ranked as the second most frequent category in pediatric pathology. Studies that did not include mucocele and/or

ranula [2,3,5,9,11,14,21,24] reported a prevalence ranging from 10.2%[14] to 45.5%[21]. Fibrous hyperplasia (31.7%), pyogenic granuloma (25.9%) and peripheral giant cell lesion (12.2%) were the most frequent histopathological diagnoses[3,11,14,24]. These lesions develop in the oral cavity in the presence of biofilm, dental calculus, poorly-adapted restorations, orthodontic brackets, and others, which triggers an exuberant tissue repair[37]. A higher number of reactive lesions was observed in the 10-14 years age group. Agarwal et al.[38] have shown an age-related difference in gingival inflammatory reaction to biofilm accumulation in children and adolescents, with the highest response observed in the 12-14 years age group, showing that gingival reactivity increases gradually from early childhood to adult age.

Cysts were the third most frequent category in our cohort (16.2%), but their prevalence in other studies ranged from 3% to 38.7%[2,3,11-13,16,25,26]. Most cysts in children are of odontogenic origin, with a reported prevalence between 4% and 33%[4,5,7,9,14,19,23,24,27]. On the other hand, non-odontogenic cysts accounts for less than 2%[4,5,7,9,14,15,23,24,27]. Developmental cysts (68.2%) were more prevalent when compared to inflammatory cystic lesions (31.8%), which is corroborated by several other studies[5,9,10,15,25,27]. Dentigerous cyst (42.1%), radicular cyst (20.8%), and odontogenic keratocyst (14.2%) were the most common cystic lesions in children, as other studies have shown[15,17,20,24,26,27]. There were other surveys, however, in which inflammatory cysts, mainly radicular cyst, were the most frequently biopsied cyst of the jaw in the pediatric population[14,15,18,20,26].

Odontogenic tumors were the fourth most common diagnostic category (8%). Other studies reported a relative frequency varying from 4% to 14%, with odontoma and ameloblastoma as the most frequent lesions of the group[2-4,7-9,11,14,19,24,26,27]. In this survey, central giant cell granuloma followed odontoma, but other studies have regarded this lesion as bone pathology. Both odontoma[7,8,13,14,22,27] and central giant cell granuloma[7,8] were ranked among the overall most prevalent oral biopsied diseases in the pediatric population. Central giant cell granuloma affected females more than males, with a M:F of 1:4. Such a marked gender predilection was not found in other studies[17,23].

Malignant tumors were the least frequent type of oral disease in this cohort (0.9%) and others[2-27]. Taweevisit et al.[25] reported the highest frequency (5%) of pediatric oral malignancies in the current literature. Most of our cases consisted of Langerhans cell histiocytosis, followed by unspecified lymphoma. A multicenter retrospective study identified a prevalence of pediatric oral malignant neoplasms of 0.06% in Brazil, where mucoepidermoide carcinoma, osteosarcoma, squamous cell carcinoma and Burkitt's lymphoma were the most frequent lesions[39]. Recent meta-analysis, on the other hand, showed that the prevalence is nearly 2%, the most common lesions of which are unspecified lymphomas and rhabdomyosarcoma[40].

In conclusion, our results were similar to other retrospective studies. Oral lesions in children submitted to biopsy and histopathological analysis were mostly non-neoplastic and reactive in nature. Oral mucosal lesions were more frequent than bone pathology, and most diseases were solitary. Malignancies were very rare. Due to the low frequency of oral biopsies in children when compared to adult patients,

data on the prevalence of oral pathology in this population might aid in the clinical practice of pediatric dentistry.

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ATTACHMENTS

Table 1. Distribution of biopsied oral lesions in children according to patient age and sex.

Category[1]	Total n.[2] (%)	Age n.[2] (%)				p	Sex n.[2]. (%)		p	M:F[3]
		0 - 3	4 - 9	0 - 9	10 - 14		Male	Female		
Salivary gland lesions	529 (35.7)	18 (25.0)	234 (19.2)	252 (42.6)	277 (31.2)	<.01*	202 (30.3)	323 (40.1)	<.01*	1:1.6
Hyperplastic/reactive lesions	278 (18.8)	23 (31.9)	95 (18.3)	118 (19.9)	160 (18)	ns	136 (20.5)	142 (17.4)	ns	1:1.0
Cystic lesions	240 (16.2)	3 (4.2)	77 (14.8)	80 (13.5)	160 (18)	<.01*	112 (16.9)	128 (15.7)	ns	1:1.1
Odontogenic tumors	119 (8.0)	3 (4.2)	29 (5.6)	32 (5.4)	87 (9.8)	<.01*	51 (7.7)	68 (8.3)	ns	1:1.3
Healthy soft tissues and teeth	104 (7.0)	3 (4.2)	15 (2.9)	18 (3.0)	86 (9.7)	<.01*	56 (8.4)	48 (5.9)	ns	1:1.1
Benign tumors	94 (6.4)	13 (18.1)	30 (5.8)	43 (7.3)	51 (5.7)	ns	45 (6.8)	49 (6.0)	ns	1:1.1
Periapical inflammation	40 (2.7)	1 (1.4)	8 (19.2)	9 (1.5)	31 (3.5)	<.01*	19 (2.9)	21 (2.6)	ns	1:1.1
Lesions of the oral mucosa	33 (2.2)	4 (5.6)	16 (3.1)	20 (3.4)	13 (1.5)	<.01*	21 (3.2)	12 (1.5)	<.01*	1.7:1
Bone pathology	30 (2.0)	1 (1.4)	11 (2.1)	12 (2.0)	18 (2.0)	ns	17 (2.6)	13 (1.6)	ns	1.3:1
Malignant tumors	13 (0.9)	3 (4.2)	5 (1.0)	8 (1.3)	5 (0.6)	ns	5 (0.8)	8 (1.0)	ns	1:1.6
Total	1480 (100)	72 (4.9)	520 (35.1)	592 (40)	888 (60)	ns	664 (44.9)	816 (55.1)	ns	1:1.2

[1]Categories according to Happonen *et al.* (1982); [2]n.=number; [3]M:F= male to fe

*Statistically significant differences with Pearson's chi-square and Z-test v

distribution analysis was performed with two age groups (0-9 yrs and 10-14 yrs

Table 2. Distribution of biopsied oral lesions in children according to location.

Anatomical location	n.[1] (%)
Lower lip	455 (30.7)
Upper lip	36 (2.4)
Buccal mucosa	55 (3.7)
Floor of mouth	42 (2.8)
Tongue	130 (8.8)
Gingiva	36 (2.4)
Palate	33 (2.4)
Alveolar ridge	70 (4.7)
Maxilla	254 (17.1)
Mandible	313 (21.1)
NI	61 (4.1)
Total[2]	1845 (100)

1. Number; 2. Total of lesions considering multifocal diseases.

Table 3. Sex distribution of the twelve most prevalent biopsied oral lesions in children.

Rank	Oral lesion	Total n.[1] (%)	Age n.[1] (%)			Sex n.[1] (%)		M:F[2]
			0 - 3	4 - 9	10 - 14	Male	Female	
1	Mucocele	496 (33.5)	17 (3.4)	231 (46.6)	248 (50)	186 (37.5)	310 (62.5)	1:1.8
2	Dentigerous cyst	101 (6.8)	2 (2.0)	44 (43.6)	55 (54.5)	51 (50.5)	50 (49.5)	1:1.0
3	Fibrous hyperplasia	88 (5.9)	8 (9.1)	32 (36.4)	48 (54.5)	37 (42.0)	51 (58.0)	1;1.4
4	Pericoronal dental follicle	85 (5.7)	1 (1.2)	12 (14.1)	72 (84.7)	47 (55.3)	38 (44.7)	1.2:1
5	Pyogenic granuloma	72 (4.9)	2 (2.8)	18 (25.0)	52 (72.2)	36 (50.0)	36 (50)	1:1
6	Odontoma	69 (4.7)	2 (2.9)	17 (24.6)	50 (72.5)	30 (43.5)	39 (56.5)	1:1.3
7	Squamous cell papilloma	57 (3.9)	3 (5.3)	24 (42.1)	30 (52.6)	28 (49.1)	29 (50.9)	1:1
8	Radicular cyst	50 (3.4)	0 (0.0)	13 (26.0)	37 (74.0)	22 (44.0)	28 (56.0)	1:1.3
9	Peripheral giant cell lesion	34 (2.3)	1 (2.9)	18 (52.9)	15 (44.1)	18 (53.0)	16 (47.0)	1.1:1
10	Odontogenic keratocyst	34 (2.3)	0 (0.0)	4 (11.8)	30 (88.2)	13 (38.2)	21 (61.8)	1:1.6
11	Periapical granuloma	32 (2.2)	0 (0.0)	6 (18.8)	26 (81.3)	18 (56.3)	14 (43.7)	1.3:1
12	Central giant cell lesion	20 (1.4)	1 (5.0)	4 (20.0)	15 (75.0)	4 (20.0)	16 (80.0)	1:4
Total		1.138 (77)	37 (3.3)	423 (37.2)	678 (59.6)	490 (43.1)	648 (56.9)	1:1.3

[1]n=number of lesions. [2]M:F= male to female ratio.

Table 4. Distribution of biopsied oral lesions in children according to histopathological diagnosis.

Rank	Oral lesion	Total n.[1] (%)	Age n.[1] (%)			Sex n.[1] (%)		M:F[2]
			0 - 3	4 - 9	10 - 14	Male	Female	
Hyperplastic and reactive lesions of the oral mucosa								
1	Fibrous hyperplasia	88 (31.6)	8 (34.7)	32 (33.6)	48 (30)	37 (27.2)	51 (35.9)	1:1.4
2	Pyogenic granuloma	72 (25.8)	2 (8.7)	18 (18.9)	52 (32.5)	36 (26.4)	36 (25.3)	1:1
3	Peripheral giant cell granuloma	34 (12.2)	1 (4.3)	18 (18.9)	15 (9.4)	18 (13.2)	16 (11.2)	1.1:1
4	Peripheral ossifying fibroma	16 (5.7)	0 (0.0)	2 (2.1)	3 (1.9)	3 (2.2)	6 (4.2)	1:2
5	Giant cell fibroma	13 (4.7)	4 (17.3)	3 (3.1)	6 (3.7)	8 (5.8)	5 (3.5)	1.6:1
6	Gingival hyperplasia	9 (3.2)	4 (17.3)	2 (2.1)	3 (1.9)	3 (2.2)	6 (4.2)	1:2
7	Chronic inflammation	9 (3.2)	2 (8.7)	6 (3.1)	1 (0.6)	7 (5.1)	2 (1.4)	3.5:1
8	Neuroma	8 (2.8)	0 (0.0)	2 (2.1)	6 (3.7)	5 (3.7)	3 (2.1)	1.6:1
9	Epithelial hyperplasia	7 (2.5)	2 (8.7)	1 (1.0)	4 (2.5)	4 (2.9)	3 (2.1)	1.3:1
10	Scar tissue	6 (2.1)	0 (0.0)	2 (2.1)	4 (2.5)	2 (1.5)	4 (2.8)	1:2
11	Papillomatous hyperplasia	4 (1.4)	0 (0.0)	2 (2.1)	2 (1.2)	1 (0.7)	2 (1.4)	1:2

12	Oral fistula	4 (1.4)	0 (0.0)	3 (3.1)	1 (0.6)	1 (0.7)	3 (2.1)	1:3
13	Pericoronaritis	3 (1.1)	0 (0.0)	2 (2.1)	2 (1.2)	1 (0.7)	1 (0.7)	1:1
14	Chronic gingivitis	2 (0.7)	0 (0.0)	2 (2.1)	0 (0.0)	2 (1.5)	0 (0.0)	-
15	Foreign body mucositis	2 (0.7)	0 (0.0)	0 (0.0)	2 (1.2)	2 (1.5)	0 (0.0)	-
16	Lymphoid reactive hyperplasia	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	-
Benign soft tissue tumors								
1	Squamous papilloma	57 (60.6)	3 (23.1)	24 (80)	30 (58.8)	28 (62.2)	29 (59.1)	1:1
2	Hemangioma	15 (15.9)	4 (30.7)	4 (13.3)	7 (13.7)	6 (13.3)	9 (18.3)	1:1.5
3	Lymphangioma	8 (8.5)	0 (0.0)	1 (3.3)	7 (13.7)	3 (6.6)	5 (10.2)	1:1.6
4	Neurilemoma/Schwannoma	4 (4.25)	0 (0.0)	0 (0.0)	4 (7.8)	3 (6.6)	1 (2.0)	3:1
5	Congenital epulis	4 (4.25)	2 (15.3)	0 (0.0)	2 (3.9)	1 (2.2)	0 (0.0)	-
6	Lipofibroma	1 (1.1)	1 (1.7)	0 (0.0)	0 (0.0)	1 (2.2)	0 (0.0)	-
7	Gastrointestinal heterotopy	1 (1.1)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	-
8	Lipoblastomatous hamartoma	1 (1.1)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	-
9	Leiomyomatous hamartoma	1 (1.1)	1 (1.7)	0 (0.0)	0 (0.0)	1 (2.2)	0 (0.0)	-
10	Nodular fasciitis	1 (1.1)	0 (0.0)	1 (3.3)	0 (0.0)	1 (2.2)	0 (0.0)	-
11	Chondroid choristoma	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.9)	1 (2.2)	0 (0.0)	-
Lesions of the oral mucosa								
1	Focal epithelial hyperplasia	6 (18.2)	1 (25)	4 (25)	1 (7.6)	2 (9.5)	4 (33.3)	1:2
2	Mucositis	6 (18.2)	1 (25)	3 (18.7)	2 (15.4)	5 (23.8)	1 (8.3)	5:1
3	Verruca vulgaris	6 (18.2)	0 (0.0)	4 (25)	2 (15.4)	3 (14.2)	2 (16.6)	1.5:1
4	Paracoccidioidomycosis	3 (9.1)	0 (0.0)	1 (6.2)	1 (7.6)	2 (9.5)	1 (8.3)	2:1
5	Acanthosis	2 (6.1)	0 (0.0)	1 (6.2)	1 (7.6)	2 (9.5)	0 (0.0)	-
6	Candidosis	2 (6.1)	1 (25)	1 (6.2)	0 (0.0)	2 (9.5)	1 (8.3)	-
7	White Sponge Nevus	2 (6.1)	0 (0.0)	1 (6.2)	1 (7.6)	1 (4.8)	0 (0.0)	-
8	Hyperkeratosis	1 (3.0)	0 (0.0)	0 (0.0)	1 (7.6)	0 (0.0)	1 (8.3)	-
9	Oral leukoplakia	1 (3.0)	0 (0.0)	1 (6.2)	0 (0.0)	1 (4.8)	0 (0.0)	-
10	Melanotic macule	1 (3.0)	0 (0.0)	0 (0.0)	1 (7.6)	0 (0.0)	1 (8.3)	-
11	Oral pemphigus	1 (3.0)	0 (0.0)	0 (0.0)	1 (7.6)	1 (4.8)	0 (0.0)	-
12	Oral pemphigoid	1 (3.0)	0 (0.0)	0 (0.0)	1 (7.6)	1 (4.8)	0 (0.0)	-

#		Total						Ratio
13	Riga-Fede disease	1 (3.0)	1 (25)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	
14	Traumatic ulcer	1 (3.0)	0 (0.0)	0 (0.0)	1 (7.6)	1 (4.8)	0 (0.0)	-

Cystic lesions

#		Total						Ratio
1	Dentigerous cyst	101 (42)	2 (66.6)	44 (57.1)	55 (34.3)	51 (45.5)	50 (39)	1:1
2	Radicular cyst	50 (20.8)	0 (0.0)	13 (16.8)	37 (23.1)	22 (19.6)	28 (21.8)	1:1.2
3	Odontogenic keratocyst	34 (14.2)	0 (0.0)	4 (5.2)	30 (18.7)	13 (11.6)	21 (16.4)	1:1.6
4	Unspecified odontogenic cyst	19 (7.9)	0 (0.0)	6 (7.7)	13 (8.1)	13 (11.6)	6 (4.7)	2.1:1
5	Traumatic bone cyst	13 (5.4)	0 (0.0)	2 (2.5)	11 (6.8)	3 (2.7)	10 (7.8)	1:3.3
6	Inconclusive	6 (2.5)	0 (0.0)	3 (3.9)	3 (1.8)	2 (1.8)	4 (3.1)	1:2
7	Eruption cyst	4 (1.6)	0 (0.0)	1 (1.3)	3 (1.8)	4 (3.6)	0 (0.0)	-
8	Epidermoid cyst	3 (1.2)	1 (33.3)	0 (0.0)	2 (1.2)	0 (0.0)	3 (2.3)	-
9	Unspecified inflammatory cyst	2 (0.8)	0 (0.0)	2 (2.5)	0 (0.0)	1 (0.8)	1 (0.8)	1:1
10	CEOC	2 (0.8)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.8)	1 (0.8)	1:1
11	Paradental cyst	2 (0.8)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	2 (1.5)	-
12	Aneurysmal bone cyst	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.8)	-
13	Teratoid cyst	1 (0.4)	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (0.8)	-
14	Lymphoepithelial cyst	1 (0.4)	0 (0.0)	1 (1.3)	0 (0.0)	1 (0.8)	0 (0.0)	-
15	Nasopalatine duct cyst	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.8)	1 (0.8)	1:1

Periapical inflammation and pulpal diseases

#		Total						Ratio
1	Granuloma	32 (80)	0 (0.0)	6 (75)	26 (83.8)	18 (94.7)	14 (66.6)	1.2:1
2	Acute pulpitis	3 (7.5)	0 (0.0)	1 (12.5)	2 96.4)	1 (5.3)	2 (9.5)	1:2
3	Pulp fibrosis	2 (5)	0 (0.0)	0 (0.0)	2 (6.4)	0 (0.0)	2 (9.5)	-
4	Dental abscess	2 (5)	1 (100)	1 (12.5)	0 (0.0)	0 (0.0)	2 (9.5)	-
5	Chronic pulpitis	1 (2.5)	0 (0.0)	0 (0.0)	1 (3.2)	0 (0.0)	1 (4.7)	-

Odontogenic tumors

#		Total						Ratio
1	Odontoma	69 (57.9)	2 (66.6)	17 (58.6)	50 (57.4)	30 (58.8)	39 (57.3)	1:1.3
2	Central giant cell granuloma	20 (16.8)	1 (33.3)	4 (13.7)	15 (17.2)	4 (7.8)	16 (23.5)	1:4
3	Ameloblastoma	12 (10)	0 (0.0)	4 (13.7)	8 (9.2)	6 (11.7)	6 (8.8)	1:1
4	Adenomatoid odontogenic tumor	5 (4.2)	0 (0.0)	0 (0.0)	5 (5.7)	5 (9.8)	0 (0.0)	-
5	Unicystic ameloblastoma	5 (4.2)	0 (0.0)	1 (3.4)	4 (4.6)	5 (9.8)	0 (0.0)	-

#	Lesion						
6	Odontogenic myxoma	3 (2.5)	0 (0.0)	1 (3.4)	2 (2.3)	0 (0.0)	2 (2.9)	-
7	Ameloblastic fibroma	2 (1.7)	0 (0.0)	0 (0.0)	2 (2.3)	0 (0.0)	2 (2.9)	-
8	Odontogenic fibroma	2 (1.7)	0 (0.0)	0 (0.0)	2 (2.3)	0 (0.0)	2 (2.9)	-
9	Odontogenic ghost cell tumor	1 (0.8)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.5)	-

Bone pathology

#	Lesion						
1	Fibrous dysplasia	5 (16.7)	0 (0.0)	3 (27.3)	2 (11.1)	4 (23.5)	2 (15.4)	2:1
2	Chronic osteomyelitis	4 (13.3)	0 (0.0)	2 (18.2)	2 (11.1)	2 (11.8)	2 (15.4)	1:1
3	Proliferative periostitis	4 (13.3)	1 (100)	2 (18.2)	1 (5.6)	3 (17.6)	1 (7.7)	3:1
4	Benign fibro-osseous lesion	3 (10)	0 (0.0)	1 (9.1)	2 (11.1)	1 (5.9)	2 (15.4)	1:2
5	Osteoma	3 (10)	0 (0.0)	0 (0.0)	3 (16.6)	1 (5.9)	2 (15.3)	1:2
6	Acute osteomyelitis	2 (6.7)	0 (0.0)	1 (9.1)	1 (5.6)	1 (5.9)	1 (7.7)	1:1
7	Juvenile ossifying fibroma	2 (6.7)	0 (0.0)	1 (9.1)	1 (5.6)	2 (11.8)	0 (0.0)	-
8	Exostosis	2 (6.7)	0 (0.0)	1 (9.1)	1 (5.6)	2 (11.8)	0 (0.0)	-
9	Bone sclerosis	2 (6.7)	0 (0.0)	0 (0.0)	2 (11.1)	2 (11.8)	0 (0.0)	-
10	Temporomandibular ankylosis	1 (3.3)	0 (0.0)	0 (0.0)	1 (5.6)	0 (0.0)	1 (7.7)	-
11	Reactive bone and fibrosis	1 (3.3)	0 (0.0)	0 (0.0)	1 (5.6)	1 (5.9	0 (0.0)	-
12	Bone hyperplasia	1 (3.3)	0 (0.0)	0 (0.0)	1 (5.6)	0 (0.0)	1 (7.7)	-

Salivary gland lesions

#	Lesion						
1	Mucocele	496 (93.8)	17 (94.4)	231 (98.7)	248 (89.5)	186 (92.1)	310 (94.8)	1:1.6
2	Ranula	19 (3.6)	0 (0.0)	2 (0.9)	17 (6.1)	10 (5.0)	9 (2.7)	1.1:1
3	Chronic unspecified sialadenitis	6 (1.1)	0 (0.0)	1 (0.4)	5 (1.8)	2 (1.0)	4 (1.2)	1:2
4	Pleomorphic adenoma	5 (0.9)	1 (5.6)	0 (0.0)	4 (1.4)	2 (1.0)	3 (0.9)	1:1.5
5	Sialectasia	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.7)	1 (0.5)	1 (0.3)	1:1
6	Sialolitiasis	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.5)	0 (0.0)	-

Malignant tumors

#	Lesion						
1	Langerhans cell histiocytosis	3 (23.1)	2 (66.7)	0 (0.0)	1 (20)	2 (40.0)	1 (12.5)	2:1
2	Unspecified lymphoma	2 (15.4)	1 (33.3)	0 (0.0)	1 (20)	0 (0.0)	2 (25.0)	-
3	Carcinoma	1 (7.7)	0 (0.0)	0 (0.0)	1 (20)	0 (0.0)	1 (12.5)	-
4	Fibrosarcoma	1 (7.7)	0 (0.0)	1 (20)	0 (0.0)	0 (0.0)	1 (12.5)	-
5	Myeloblastic leukemia	1 (7.7)	0 (0.0)	1 (20)	0 (0.0)	0 (0.0)	1 (12.5)	-

[1]n=number of lesions. [2]M:F= male to female ratio.

#								
6	Soft parts sarcoma	1 (7.7)	0 (0.0)	0 (0.0)	1 (20.0)	0 (0.0)	1 (12.5)	-
7	Ewing's sarcoma	1 (7.7)	0 (0.0)	1 (20)	0 (0.0)	0 (0.0)	1 (12.5)	-
8	Neurosarcoma	1 (7.7)	0 (0.0)	1 (20)	0 (0.0)	1 (20.0)	0 (0.0)	-
9	Rhabdomyosarcoma	1 (7.7)	0 (0.0)	1 (20)	0 (0.0)	1 (20.0)	0 (0.0)	-
10	Osteosarcoma	1 (7.7)	0 (0.0)	0 (0.0)	1 (20.0)	1 (20.0)	0 (0.0)	-
Healthy soft tissues and teeth								
1	Pericoronal cap	85 (81.7)	1 (33.3)	12 (80)	72 (83.7)	47 (83.9)	38 (79.2)	1.2:1
2	Normal dental tissues	5 (4.8)	0 (0.0)	1 (6.7)	4 (4.7)	3 (5.4)	2 (4.2)	1.5:1
3	Supernumerary teeth	4 (3.8)	0 (0.0)	0 (0.0)	4 (4.7)	1 (1.8)	3 (6.3)	1:3
4	Other normal tissues	3 (2.9)	0 (0.0)	0 (0.0)	3 (3.5)	1 (1.8)	2 (4.2)	1:2
5	Decalcified teeth	2 (1.9)	0 (0.0)	1 (6.7)	1 (1.2)	1 (1.8)	3 (6.3)	1:3
6	Neonatal teeth	2 (1.9)	2 (66.7)	0 (0.0)	0 (0.0)	2 (3.6)	0 (0.0)	-
7	Blood clot	1 (1.0)	0 (0.0)	1 (6.7)	0 (0.0)	0 (0.0)	1 (2.1)	-
8	Dysplastic dentin	1 (1.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.8)	0 (0.0)	-
9	External tooth resorption	1 (1.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	1 (2.1)	-

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For Articles in Press (online)

Hellems MA, Gurka KK, Hayden GF. A review of *The Journal of Pediatrics*: The first 75 years. J Pediatr (2008). doi:10.1016/j.jpeds.2008.08.049.

For books

Rosenstein BJ, Fosarelli PD. Pediatric pearls: the handbook of practical pediatrics. 3rd ed. St Louis: Mosby; 1997.

Virginia Law Foundation. The medical and legal implications of AIDS. Charlottesville (VA): The Foundation; 1987.

For chapters in books

Neufeld EF, Muenzer J. The mucopolysaccharidoses. In: Scriver CR, Beaudet AL, Sly WS, et al, eds. The metabolic and molecular bases of inherited diseases. New York: McGraw-Hill; 2001. p. 3421-52.

For websites

American Medical Association [homepage on the Internet]. Chicago: The

Association; c1995-2002 [updated 2001 Aug 23; cited 2002 Aug 12]. AMA Office of Group Practice Liaison; [about 2 screens]. Available from: http://www.ama-assn.org/ama/pub/category/1736.html

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