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Prevalence of oral manifestations in HIV-infected children: a literature review

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• Conflicts of interest: none declared.

Abstract

Objective: to review the literature on the most common oral lesions in HIV-infected children. **Material and Methods:** a literature review was performed in Medical Literature (PubMed/Medline) and Health Virtual Library (HVL) databases from 2000 to 2015. **Results:** there were 163 papers and 11 were selected according with inclusion and exclusion criteria. Oral candidiasis was the most prevalent oral lesion followed by aphthous ulcerations, linear gingival erythema and oral hairy leukoplakia. **Conclusion:** despite advances in the disease treatment with the introduction of potent antiretroviral therapy, oral manifestations remain frequent in HIV-infected patients, with candidiasis being the most common finding. The review showed the importance of the dentist in the identification and early treatment of these lesions.

Keywords: Children; HIV; Oral manifestations.

Introduction

Acquired immunodeficiency syndrome (AIDS) is a disease caused by the human immunodeficiency virus (HIV) where the main cells affected are $CD4^+$ T lymphocytes and macrophages.[1,2] As a consequence, there is a reduction in the host's immune response, making him more susceptible to opportunistic infections and neoplasias.[1,3-5] The oral manifestations of HIV infection have been correlated with immunosuppression and can be considered as markers of disease progression.

The transmission of HIV to children occurs mostly through vertical (mother-to-child) transmission during pregnancy, labor, delivery or breastfeeding.[6-16] Its diagnosis is difficult due to the presence of the maternal anti-HIV antibody that crosses the placental barrier and may be detectable in children up to 18 months of age.[6,17] After virus infection, patients can spend several years without manifesting the disease. The immunological markers that define disease progression are the decline of $CD4^+$ T lymphocyte count and the inversion of $CD4^+/CD8^+$ ratio.[3,17,18] In children, the progression of HIV infection is evaluated by monitoring changes in $CD4^+$ T lymphocyte percentage, which are more stable parameters than the absolute count of these cells, especially in children under 5 years.[19]

The introduction of the antiretroviral therapy (ART) increased the survival and improved the life quality of HIV-infected children,[16,19-21] also resulting in a considerable decrease in the frequency of oral manifestations.[6,7,9,14,15,22-24]

Some challenges such as diet care, drug administration, emotional factors and prejudice are still part of the daily life of these families, making it necessary to develop strategies that allow these children to grow and develop with quality of life.[16,19,20]

Due to children's immature immune system, HIV infection symptoms are different from adults, manifesting with faster progression of the disease, higher frequency of bacterial infections and a lower prevalence of oral neoplasias.[7,8,17,19,25]

HIV-infected children have a higher prevalence of oral soft tissue lesions, salivary gland dysfunction and dental caries compared with the general pediatric population.[8,10,26] Oral manifestations commonly associated with HIV in children differ according to the stage of the disease and include candidiasis, herpes simplex, linear gingival erythema, parotid enlargement, and aphthous stomatitis.[27] Lesions such as Kaposi's sarcoma, non-Hodgkin's lymphoma, and oral hairy leukoplakia (OHL) are strongly associated with HIV but they are not common in children.[27]

The aim of this literature review was to identify the most frequent oral manifestations in HIV-infected children.

Material and Methods

Searches in PubMed/Medline and Virtual Health Library (VHL) databases were performed using the descriptors *HIV*, *children* and *oral manifestations*. As inclusion criteria were considered papers with complete observational clinical studies with HIV-positive children published between 2000 and 2017, and only those assessing intraoral lesions were selected for the present review. Case reports and papers not written in English or Portuguese were excluded. A descriptive analysis of the results was performed.

Results

From a total of 163 papers found in the database searches, 11 were selected according to the inclusion and exclusion criteria. Although the search criteria included papers in English and Portuguese, the majority (10 papers) was written in English. The studies were conducted in different countries, 4 in Brazil, 1 in the USA, 1 in Mexico, 2 in India and 3 in the African continent (Table 1). The intraoral lesions

found in the studies are described in Table 2 and the most frequent were candidiasis, angular cheilitis, aphthous ulcer and linear gingival erythema.

Table 1. Results of the review of papers published between 2000 and 2015 assessing oral manifestations in HIV-positive pediatric patients

Authors	Sample (N)	Age (years)	Under HAART (Yes/No)	Country
Kozinetz *et al.* 2000	73	6 - 9	Y- 73	USA
Gaitán-Cepeda *et al.* 2002	48	8m - 12	N- 48	Mexico
Miziara e Weber 2008	459	0 - 12	Y- 459	Brazil
Ribeiro *et al.* 2008	57	3m - 14	Y- 57	Brazil
Dornelas *et al.* 2008	21	2 - 12	Y- 21	Brazil
Ranganathan *et al.* 2010	212	6m - 14	N- 212	India
Rwenyonyi *et al.* 2011	237	1 - 12	Y- 118 N- 119	Uganda
Adebola *et al.* 2012	105	2m - 13	Y- 65 N- 40	Nigeria
Ponnam *et al. 2012*	190	5 - 15	Y- 95 N- 95	India
Nabbanja *et al. 2013*	368	1,5 - 17	Y- 248 N- 120	Uganda
Oliscovicz *et al.* 2015	111	2 - 16	Y- 97 N- 14	Brazil

Y-number of patients under highly active antiretroviral therapy (HAART).
N- number de patients not using antiretroviral drugs.

Discussion

Some diseases are frequently observed in HIV-infected patients and may be indicators of AIDS, namely oral candidiasis, herpes simplex, angular cheilitis, OHL, and parotid hypertrophy.[27]

Oral candidiasis is frequent among the first signs of immunosuppression.[1,9] Consistently, it was the most common oral lesion found in this literature review, being reported in all 11 papers (Table 2). In a study with children not under antiretroviral therapy, its prevalence reached 56.1%.[8]

Aphthous ulcer and angular cheilitis were also reported in most of the selected studies, being identified in 8 of the 11 papers (Table 2). Aphthous ulcers are common in HIV-infected children and often present with larger sizes. These oral lesions deserve special attention because they are accompanied by considerable pain and interfere in normal feeding.[13,21]

Among the periodontal alterations, linear gingival erythema is quite frequent in HIV-positive adults and children. It was reported in 4 out of the 11 selected studies and was the third most common oral lesion in the present literature review.

Although they are more frequent in adult patients, OHL and Kaposi's sarcoma can affect children and were identified in 4 and 3 studies, respectively (Table 2). The diagnosis of these lesions is very important because they are strongly associated with HIV and can be indicators of seropositivity in individuals who do not know their serological status.[17,27] Cytopathological analysis is an important tool in OHL diagnosis, especially in HIV-positive children because it is fast,

Table 2. Prevalence of intraoral lesions found in the literature search between 2000 and 2015

Authors	Candidiasis	Angular cheilitis	Ulcer	Stomatitis	Oral hairy leukoplakia	Kaposi's Sarcoma	Necrotizing gingivitis	Linear gingival erythema
Kozinetz *et al.* 2000	32.87%	-	16.43%	-	1.36%	-	-	-
Gaitán-Cepeda *et al.* 2002	20.83%	2.08%	-	-	-	-	-	2.08%
Miziara e Weber 2008	11.54%	4.13%	5.44%	3.92%	0.43%	0.21%	-	-
Ribeiro *et al.* 2008	7.01%	8.77%	7.01%	-	-	-	-	7.01%
Dornelas *et al.* 2008	19.04%	19.04%	-	-	-	-	-	4.76%
Ranganathan *et al.* 2010	56.1%	20.28%	4.24%	-	1.41%	-	-	-
Rwenyonyi *et al.* 2011	Y- 16.10% N- 25.21%	Y- 3.38% N- 10.08%	Y- 0.84 N- 1.68	-	-	Y- N- 0.84%	Y- N- 0.84%	Y- N- 1.68%
Adebola *et al.* 2012	35.23%	43.80%	12.38%	-	-	-	-	-
Ponnam *et al. 2012*	Y- 16.84% N- 28.43%	-	-	Y- 12.63% N- 25.26%	-	-	-	-
Nabbanja *et al. 2013*	50.54%	10.32%	4.07%	-	4.34%	3.26%	4.07%	-
Oliscovicz *et al.* 2015	Y- 2% N-	-	Y-2% N-	-	-	-	-	Y- 9.8% N-

Y-number of patients under highly active antiretroviral therapy (HAART).
N- number de patients not using antiretroviral drugs.

painless, non-invasive, inexpensive and material collection is quite simple. It also has the advantage of allowing the diagnosis subclinical OHL when clinical aspects are not evident.[28]

The least common intraoral lesions found in the literature were necrotizing gingivitis and aphthous stomatitis. Necrotizing gingivitis was reported in two African studies.[9,13] One of them[9] was conducted with children not exposed to antiretroviral therapy and only one child had necrotizing gingivitis. In the other study,[13] with children exposed and not to antiretroviral therapy, 15 (4.1%) out 368 children had necrotizing gingivitis.

A single case of mucocele was observed in one study conducted in India.[6] This oral manifestation is caused by a local trauma and is commonly observed in children with or without HIV seropositivity. Therefore, it was not presented in Table 2.

The findings of this review show the importance of a thorough oral clinical examination for the early diagnosis of the lesions most commonly found in seropositive children in order to start the appropriate treatment. The presence of oral manifestations suggestive of immunodeficiency should alert to the possibility of HIV infection as well as to a possible therapeutic failure, since the adherence of the child and parents/caregivers is still a challenge.[16,20]

Conclusion

Despite the advent of antiretroviral therapy for HIV control, oral manifestations are still common in HIV-infected children. Candidiasis remains the most common oral condition in these individuals. It is worth mentioning that oral manifestations may be suggestive of HIV seropositivity or may warn to a possible failure in treatment adherence or even in the therapeutic approach. The studies demonstrate the importance of integrating oral health care into the clinical management of HIV-infected children in a way to have multidisciplinary approach that provide oral health and contribute to improve their quality of life.

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Mini Curriculum and Author's Contribution

1. Marcela Carraro Bina Fonyat de Lima - dentist. Contribution: data collection, data interpretation, study conception and design, writing of manuscript
2. Arley Silva Junior - dentist, PhD. Contribution: critical review and final approval.
3. Sandra Regina Torres - dentist, PhD. Contribution: critical review and final approval.

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