



ORAL MANIFESTATIONS IN INDIVIDUALS WITH SEXUALLY TRANSMITTED INFECTIONS: INTEGRATIVE REVIEW

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ABSTRACT

Identify, in scientific production, the main oral manifestations associated with sexually transmitted infections. This is an integrative literature review, with timeframe from 2009 to 2018, using the descriptors “Oral Manifestations” and “Sexually Transmitted Diseases” in PubMed, Scopus, Web of Science, LILACS and SciELO databases. Of the 12 articles selected, 25% were conducted in Brazil, 58.33% were published in dental journals and 66.66% aimed to evaluate the prevalence of oral manifestations associated with the human immunodeficiency virus. The most frequent oral manifestations were oral candidiasis, periodontal disease, oral hairy leukoplakia, melanotic hyperpigmentation, herpes simplex, dental caries, nonspecific ulcer, Kaposi's sarcoma and xerostomia. It is concluded that, despite the limitations of the included studies, it was possible to notice that the changes promoted in the oral cavity by STI ranged from the most common conditions, such as caries and periodontal diseases, to specific conditions such as Kaposi's sarcoma.

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INTRODUCTION

Sexually Transmitted Infections (STI) are conditions caused by different microorganisms transmitted primarily by condomless sexual contact with an infected person. Difficult to control dissemination, STI are a major public health problem worldwide, being linked to the most prevalent pathologies and a higher number of deaths. Its repercussion goes beyond the physical state of the individual, extending to economic, social and psychological aspects (World Health Organization, 2017). As for its incidence, STI have been progressively growing, with over one million cases occurring every day. In 2012, *Chlamydia trachomatis*, *Human Papillomavirus* (HPV), *N. gonorrhoeae*, *Trichomonas vaginalis* and *Treponema pallidum*, considered the most common etiological agents of STI, contributed 357 million new cases (Newman *et al.*, 2015). For the human immunodeficiency virus (HIV) / AIDS, considered to be the most serious because there is no cure, the data show that approximately 36.7 million people worldwide are affected (Unaiads, 2017).

In Brazil, it is estimated that 10 to 12 million new cases occur annually (Araújo *et al.*, 2015). In addition to this high quantity, STI stand out for their diversity and severity, compromising not only sexual, reproductive and maternal-fetal health, but also the life of the infected individual. In fact, STI can result in emotional disorders, pelvic inflammatory disease, infertility, ectopic pregnancy, cervical and anogenital cancer, and facilitate the spread and acquisition of HIV (Azevedo *et al.*, 2014; Tsevat *et al.*, 2017). In addition to these impacts, some STI may affect the oral cavity and cause various manifestations (Antunez, Mathias, 2013). In the context of the influence of STI on oral health, the literature mentions that infections such as HIV/AIDS (Motta *et al.*, 2014; Silva *et al.*, 2015), syphilis (Bunn *et al.*, 2014), gonorrhea and condyloma acuminata (Tristao *et al.*, 2012), may promote various manifestations in the oral cavity, corresponding to the first clinical signs of the disease. This was observed by Motta *et al.* (2014), who pointed to oral candidiasis, necrotizing ulcerative periodontitis, oral hairy leukoplakia and angular cheilitis as oral manifestations more associated with HIV infection. Although the pathogenesis of these manifestations is not

completely understood, immune system depletion, resulting in increased susceptibility to opportunistic infections, viral overload, poor oral hygiene and xerostomia have been reported as the main risk factors (Antunez, Mathias, 2013). As supporting factors in this process, alcohol and tobacco have been mentioned (Petruzzi *et al.*, 2013). Also as part of these events, it is known that the oral amendments caused by STIs can negatively impact an individual's life, hindering chewing and swallowing, and promote physical and psychosocial changes and increase the risk of oral cancer. Thus, based on this impact, it is necessary to know oral manifestations promoted by STI for proper diagnosis, early treatment and better prognosis. However, this knowledge should not be limited to the dental surgeon, but should involve the different health professionals, since many of them have easy access and establish links with the population affected by these infections. Given the above, the present study aimed to identify, in scientific production, the main oral manifestations associated with STI.

MATERIALS AND METHODS

This is an integrative literature review about oral manifestations associated with sexually transmitted infections. The elaboration of the review was based on the following guiding question: What are the oral manifestations associated with STI? The search for articles was made in June 2018, through the Descriptors in Health Sciences (DeCS), “*Oral Manifestations e Sexually Transmitted Diseases*”, in the following databases: US National Library of Medicine (PubMed), Scopus, *Web of Science*, *Literatura Latino-Americana em Ciências de Saúde (LILACS)* e *Scientific Electronic Library Online (SciELO)*. The PubMed, Scopus, *Web of Science* and LILACS databases were used as search “*Oral Manifestations*” AND “*Sexually Transmitted Diseases*”. At SciELO, we used “*Oral*” AND “*Manifestations*” AND “*Sexually Transmitted Diseases*”. The inclusion criteria for the selection of articles were: articles published from 2009 to 2018, in English, Spanish and Portuguese, and available in their entirety and free of charge by electronic means. The exclusion criteria were articles that were not related to the theme, literature reviews and clinical cases. For data collection and analysis, a validated instrument was used and adapted to meet the study objective (Ursi, Galvão, 2006). Topics of interest addressed in the instrument were: study identification, database, year of publication, country where study was published, type of study, journal / area, level of evidence, title of study, objective, oral manifestations and pathology associated. For the level of evidence, the classification suggested by Melnyk and Fineout-Overholt (2011) was used.

RESULTS

From the selected descriptors, 74 articles were found, among which 02 were excluded because they were not available electronically and for free in the Pubmed and Web of Science databases, resulting in 72 articles. After reading the titles, abstracts and full texts, carefully directed to the guiding question, 40 articles that did not address the research theme, 11 literature reviews and 09 case reports were removed from the study. Thus, 12 articles remained that constituted the study sample. Among the 12 articles selected, 11 (91.66%) were in the Pubmed database and 01 (8.33%) in SciELO. Regarding

the year of publication, 03 (25%) articles were published in 2011, 03 (25%) in 2012, 03 (25%) in 2015, 01 (8.33%) in 2008, 01 (8.33%) in 2014 and 01 (8.33%) in 2018. Of the total studies, 03 (25%) were performed in Brazil and 02 (16, 66%) in India. For the others, an equal amount (8.33%) was conducted in Venezuela, Australia, Germany, Czech Republic, Mozambique and Mali.

When analyzing the journals in which the articles were published, 02 (16.66%) were published in *Indian Journal of Dental Research*. Each of the following magazines presented only 01 (8.33%) published article: *Journal of Applied Oral Science*, *Rev. Salud Pública*, *Journal of Oral Science*, *The Official Journal of the Australian Dental Association*, *Pan African Medical Journal*, *Ciência & Saúde Coletiva*, *Oral Surg Oral Med Oral Pathol Oral Radiol*, *Revista da Sociedade Brasileira de Medicina Tropical*, *Acta Médica (Hradec Králové)* e *Universidad y Salud*. As for the study area, 07 (58.33%) articles were from the dental area, 03 (25%) from the medical area, 01 (8.33%) from public health and 01 (8.33%) from public health. Regarding the type of study, all articles were descriptive and classified as level of evidence VI. Among them, 05 (41.66%) were descriptive only, 03 (25%) were descriptive and cross-sectional, 03 (25%) were descriptive and retrospective and 01 (8.33%) were descriptive and analytical. When analyzing the objectives, 08 articles (66.66%) aimed to evaluate the prevalence of oral manifestations associated with the human immunodeficiency virus (HIV), 01 (8.33%) article involved the study on syphilis and human papillomavirus (HPV).) as associated pathologies and 03 (25%) evaluated the association between oral manifestations and CD4 + T lymphocyte count. The most commonly observed oral manifestations were: oral candidiasis (pseudomembranous, erythematous and angular cheilitis), periodontal diseases (gingivitis and periodontitis), oral hairy leukoplakia, melanotic hyperpigmentation, caries, nonspecific ulcer, Kaposi's sarcoma and xerostomia. Although less frequently, the articles also mentioned lymphadenopathy, non-Hodgkin's lymphoma and others (Table 1).

DISCUSSION

Considering the articles analyzed, although they were conducted in different countries and continents, oral alterations were mainly related to the presence of HIV / AIDS. This fact, in addition to highlighting the importance of AIDS on the world stage, as it is the sixth cause of death, shows the repercussion of this pathology in different systems, especially the oral cavity (Holmes *et al.*, 2017). Indeed, AIDS is usually associated with conditions such as malignant neoplasms, cardiovascular disease, diabetes, liver damage and renal dysfunction (Casper *et al.*, 2017), not mentioning oral involvement. Although this review only addressed studies on AIDS, syphilis, and HPV, other STI are able to promote changes in the oral cavity, such as gonorrhea, chlamydia (Tristan *et al.*, 2012), genital herpes (Passariello *et al.*, 2017), and cytomegalovirus infection (Mainville *et al.*, 2015). Indeed, the literature points to the association of these pathologies with the development and progression of periodontitis (Fernandes *et al.*, 2018), oropharyngeal infection (Peters *et al.*, 2014), oral mucosal ulceration (Mainville *et al.*, 2015), gingivitis and periodontal abscess (Ambili *et al.*, 2014). Regarding the oral manifestations most commonly found in this review, they included: oral candidiasis, periodontal disease, oral hairy leukoplakia, melanin hyperpigmentation, herpes simplex,

Table 1. Distribution of studies according to numbering, title, purpose, oral manifestations and associated pathology. Redenção, CE, 2019

N°	Title	Objective Oral Manifestations Associated Pathology	Objective Oral Manifestations Associated Pathology	Objective Oral Manifestations Associated Pathology
A1	Epidemiological and oral manifestations of HIV-positive patients in a specialized service in Brazil	To evaluate the prevalence of oral lesions in HIV-positive patients treated at the Department of Infectious Diseases and Parasites of the Department of Health of the State of Pará (URE-DIPE / SESPA), in Belém, PA, Brazil.	Candidiasis, Periodontal Disease, Cervical-facial Lymphadenopathy, Hairy Leukoplakia, Melanin Hyperpigmentation, Ulcerative Stomatitis, Herpes Simplex, Frictional Keratosis and Granuloma.	HIV
A2	Manifestaciones orales y caries dental em niños expuestos al virus de inmunodeficiencia humana	To determine oral manifestations and caries in children exposed to Human Immunodeficiency Virus (HIV)	Caries, Oral Candidiasis, Linear Gingival Erythema, Angular Cheilitis and Periodontitis.	HIV
A3	Comparison of oral manifestations with CD4 count in HIV-infected patients	Correlate oral and general changes in HIV-infected patients with CD4 + lymphocyte count	Oral Candidiasis, Oral Hair Leukoplakia, Periodontal Disease, Xerostomia and Melanin Pigmentation.	HIV
A4	Comparison of oral manifestations with CD4 count in HIV-infected patients	Identify oral manifestations in HIV-infected individuals and their association with reduced TCD4 + lymphocyte count	Erythematous Candidiasis, Pseudomembranous Candidiasis, Angular Cheilitis, Melanin Hyperpigmentation, Nonspecific Ulcers, Oral Gingival Erythema, Necrotizing Gingivitis, Necrotizing Periodontitis, Molluscum Contagiosum, Herpes Simplex, Lymphoma Herpes Simplex, Lymphoma, Non-Specific Ulcers Facial paralysis and erythema multiforme.	HIV
A5	Oral health in Australian HIV patients since the advent of combination antiretroviral therapy	Describe the prevalence of various oral manifestations in HIV-infected individuals in an Australian population.	Oral Candidiasis, Ulcerative Gingivitis, Periodontitis, Oral Hairy Leukoplakia, Herpes Simplex Virus Ulcer, HPV Papilloma, Foot-and-Mouth Ulceration, Parotid Queer, Kaposi's Sarcoma, EBV Ulcer, Facial Lipodystrophy, Ulcerative Pigmentation, Zidovudine Pigmentation, Traumatic Pigmentation Manifestations of Tongue (Middle Rhomboid Glossite and Fissured Tongue) and Fibro-Epithelial Polyp.	HIV
A6	First report of HIV-related oral manifestations in Mali	To determine the prevalence of HIV-related oral manifestations during the first month of ART therapy at a Mali health center.	Oral Candidiasis	HIV
A7	Oral manifestations in HIV+ children in Mozambique	To identify the prevalence of oral manifestations in patients with HIV + / AIDS of the Maputo Day Pediatric Hospital	Angular Cheilitis, Gingivitis, Herpetic Stomatitis, Pseudomembranous Candidiasis, Fistula and Cold Sores	HIV/AIDS
A8	Associations of periodontitis and oral manifestations with CD4 counts in HIV-pregnant women in Thailand	To investigate the associations between TCD4 + lymphocyte count and chronic periodontitis and HIV-related oral lesions in HIV-infected pregnant women in Thailand.	Candidiasis, Oral Hairy Leukoplakia, Herpes, Foot-and-Mouth Ulcer, Necrotizing Periodontitis and Necrotizing Gingivitis	HIV
A9	Effect of highly active antiretroviral therapy use on oral manifestations in pediatric patients infected with HIV	To evaluate the prevalence of oral lesions in HIV-infected children undergoing highly active antiretroviral therapy (HAART) and the association between duration of HAART use and oral lesions.	Gingivitis, Linear Gingival Erythema and Parotid Hypertrophy	HIV
A10	Oral and systemic manifestations in HIV-1 patients	To estimate the prevalence of the most frequent oral and systemic manifestations in patients with Human Immunodeficiency Virus 1 (HIV-1) positive.	Periodontal Disease, Candidiasis and Carious Injuries	HIV
A11	Dental and oral lesions in HIV-positive individuals in East Bohemia – Czech Republic, Single Centre Experience	Document oral conditions of HIV-positive patients and the pattern and frequency of oral and dental lesions.	Caries, Chronic Gingivitis, Pulp Necrosis, Pulpitis, Apical Periodontitis, Oral Candidiasis, Intraoral Herpes Simplex, Non-Specific Ulcerations, Erosive Form of Oral Lichen Planus, Hemangioma, Kaposi's Sarcoma and Sialadenitis.	HIV
A12	Manifestaciones bucales de enfermedades de transmisión sexual identificadas en tres servicios de estomatología en Sur América	To determine the characteristic lesions in the oral cavity of sexually transmitted diseases.	Ulcer, Papule, Keratosis, Warts, Vegetation Injury, Spots and Plates	Syphilis and HPV

Source: Authors.

caries, nonspecific ulcer, Kaposi's sarcoma and xerostomia (Tami-Mauri *et al.*, 2012; Freman *et al.*, 2012; Pedreira *et al.*, 2008; Dávila, Gil, 2011; Sontakke *et al.*, 2011; Bodhade *et al.*, 2011; Sales-Peres *et al.*, 2012; Pattrapornnan, Derouent, 2013; Oliscovicz *et al.*, 2015; Menezes *et al.*, 2015; Sembera *et al.*, 2015; Carmona-Louduy *et al.*, 2018; Meira *et al.*, 2017). Also, in these studies, several factors that contribute to these manifestations were found, highlighting: the patient's immune status; change in salivary flow and salivary glands caused by medication use; inefficient oral hygiene and lack of information due to poor oral health promotion practices (Dávila, Gil, 2011; Sontakke *et al.*, 2011; Sales-Peres *et al.*, 2012). Alcohol use and smoking were also cited as factors responsible for these changes (Pedreira *et al.*, 2008). Regarding the above mentioned manifestations, oral candidiasis stands out as one of the most common oral fungal pathologies. Triggered by the genus *Candida* spp., Particularly the species *Candida albicans* (Meira *et al.*, 2017), oral candidiasis is an opportunistic infection promoted by factors such as immunodeficiency, hyposalivation, systemic diseases, use of dental prosthesis, and consumption of certain medications. of tobacco (Chu, 2017). Susceptibility to immune system deficiency was evident in the studies by Dávila *et al.* (2011), Sontakke *et al.* (2011) and Sales-Peres (2012), included in this research. In the first, 73% of immunosuppressed children had oral candidiasis, and in the second, 32.25% of immunosuppressed patients had pseudomembranous or erythematous candidiasis.

In the third study, candidiasis was the most common oral manifestation in children with HIV / AIDS, in addition to parotid gland hypertrophy and an increase in the Decayed, Extracted and Obtained Deciduous Teeth Index (Sales-Peres *et al.*, 2012). For Sontakke *et al.* (2011) and the authors of other research included here (Bodhade *et al.*, 2011; Tami-Mauri *et al.*, 2012; Pattrapornnan, Derouent, 2013; Menezes *et al.*, 2015), the occurrence of oral candidiasis is associated with low levels of TCD4 + lymphocytes. As a consequence, its manifestation can be used as a marker of advanced or severe immunodeficiency, especially when TCD4 + cell counting is not possible. As for its clinical presentation, oral candidiasis involves white (pseudomembranous and hyperplastic candidiasis) and erythematous (acute atrophic candidiasis, denture stomatitis, median rhomboid glossitis, angular cheilitis, and linear gingival erythema) forms (Meira *et al.*, 2017). For these authors, there are also other clinical forms not included in this classification, represented by chronic mucocutaneous candidiasis, cheilocandidiasis and chronic multifocal candidiasis. Currently, oral candidiasis is accepted as primary (when the infection is limited to oral and perioral tissues) and secondary (when the disease results from a systematic and widespread *Candida* infection) (Terai *et al.*, 2018), grouping the white and erythematous forms as primary. Regardless of classification, in the present review, pseudomembranous and erythematous forms, including angular cheilitis, were reported in most studies.

Regarding its signs and symptoms, oral candidiasis may manifest in different ways depending on the type of infection. It is able to promote loss of taste, pain and aversion to food (Manik, Bahl, 2017), as well as dry mouth, burning sensation and easy bleeding (Zhou *et al.*, 2017; Telles *et al.*, 2017). In severe infections, it can affect life-threatening visceral organs (Zhou *et al.*, 2017). Its diagnosis may involve a test with topical antifungal application (in the case of superficial forms),

incisional biopsy, exfoliative cytology or culture (Telles *et al.*, 2017). Its treatment involves the prescription of topical or systemic agents, preferably the first ones. As for periodontal disease, which has been reported in several studies of this review, it corresponds to inflammation that affects the supporting tissues of the teeth, which can be chronic if there is not due attention (Menezes *et al.*, 2015). Its relationship with the individual's immunological status was evidenced in a study included here (Pattrapornnan, Derouent, 2013), which showed a similar prevalence between this pathology and oral candidiasis, a condition that affects about 50% to 95% of individuals infected with the disease. HIV (Fidel, 2011). For the authors, periodontal disease may be caused by reduced salivary ability to control microbiota and plaque, worsening in patients with compromised immune status. This possible association was observed in the study with HIV-positive pregnant women (Pattrapornnan, Derouent, 2013), in which the occurrence of mild or severe periodontal disease was related to low TCD4 + cell count.

Although the literature indicates periodontal disease as one of the main and most frequent oral lesions in HIV positive subjects, which may be due to the immunosuppression promoted by this virus and the potentialization of periodontal destruction by resident and opportunistic microorganisms, research conducted by Barros *et al.* (2017), with different databases, stated that there seems to be a relationship between periodontal disease and HIV infection. However, the authors were clear in mentioning the need for further studies to clarify the mechanisms involved in this association. With regard to oral hairy leukoplakia, this is an asymptomatic oral manifestation caused by the *Epstein-Barr* virus, characterized by the presence of a flat, wavy or hairy non-removable whitish plaque on the lateral edge of the tongue (unilaterally or bilaterally) or in other regions of the tongue. oral cavity (Shanahan *et al.*, 2018). Initially associated with AIDS and later immunosuppression for malignant haematological diseases and use of organ transplant immunosuppressants, currently oral hairy leukoplakia is related to the use of inhaled or topical steroids and age (Shanahan *et al.*, 2018). Its occurrence in immunocompetent individuals is rare (Cade *et al.*, 2017). Although it should not be considered as a pathognomonic manifestation of AIDS, its correlation with HIV infection was observed in the study by Pattrapornnan and Derouent (2013), in which hairy leukoplakia was the most common oral manifestation in people with HIV. In the research by Pedreira and collaborators (Pedreira *et al.*, 2008), leukoplakia, besides being associated with the presence of HIV, was related to alcohol and smoking in patients with this type of infection.

As for its complications, oral hairy leukoplakia may be associated with *Candida* superinfection, in addition to compromising the individual's quality of life due to the impact on their mental and physical health. Its treatment may be based on the symptoms related to the lesion, the desire for elimination for aesthetic reasons, the use of topical and systemic antivirals, and the possibility of spontaneous resolution (Cade *et al.*, 2017). About HIV-associated oral melanin hyperpigmentation, it presents as one or more dark or light brown macules of varying size and shape, well or poorly defined and usually asymptomatic. As for its location, it can affect any area of the oral mucosa. Their onset is associated with the use of antiretrovirals and antifungals, as well as stimulation of the melanin pathway as a consequence of HIV

cytokine dysregulation (Abe *et al.*, 2017), and adrenocortical dysfunction (Jayachandran, 2017). This latter mechanism was observed in the study by Sontakke *et al.* (2011), in which the authors cite oral melanin hyperpigmentation as a manifestation of HIV-depressed patients, promoted by adrenal infection by various parasites. As for its frequency, in the article by Bodhade *et al.* (2011), oral melanin hyperpigmentation was the most common oral condition, affecting 19.5% of patients with HIV. Regarding herpes, this is a condition caused by the Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2), which affect the orofacial and genital region, respectively. However, according to the literature, HSV-1 has been identified in genital lesions, as has HSV-2 in oral conditions (Looker *et al.*, 2015). Its primary infection is followed by the displacement of HSV from sensory neurons to neuronal ganglia, a phenomenon that enables the reactivation of the disease. The latter may be due to the deficiency of the immune system, which justifies the presence of herpes in the articles by Freeman *et al.* (2012), Pedreira *et al.* (2008) and Pattrapornnan and Derouent (2013). In addition to herpes, caries was also mentioned in the articles of this review, particularly in the study by Dávila and Gil (2011), in which 45.9% of children with HIV had carious lesions. In Menezes *et al.* (2015), the carious process was identified as the most frequent oral manifestation, followed by oral candidiasis and periodontal disease.

The presence of this pathology among patients with HIV may be due to hyposalivation promoted by the use of medications such as antiretrovirals, antihypertensives, antidepressants, anxiolytics or analgesics (Sales-Peres *et al.*, 2012). Like caries, xerostomia, defined as the sensation of dry mouth (Silva *et al.*, 2016), reported in studies (Freman *et al.*, 2012; Sales-Peres *et al.*, 2012) may result from this use. As for Kaposi's sarcoma, it, along with non-Hodgkin's lymphoma, is one of the most common cancers in HIV-positive patients (Ministry of Health, 2015). Associated with human herpes virus type 8 infection, Kaposi's sarcoma is a malignant neoplasm characterized by proliferation of endothelial cells capable of affecting the skin, mucous membranes and viscera. In addition to the epidemic (AIDS-related) form, it can be either classic (present in Jewish and Mediterranean men), endemic (present in equatorial and sub-Saharan Africa prior to the advent of AIDS) or associated with solid organ transplantation (Ferreira *et al.*, 2016). In the present research, Pedreira *et al.* (2008) reported that Kaposi's sarcoma is the most frequent malignant neoplasm in HIV patients, along with oral hairy leucoplakia, both of which are considered as pathognomonic signs of this disease. However, in his article, there was no evidence of such cases. Such result differs from Freeman *et al.* (2012), who stated that Kaposi's sarcoma is a rare manifestation, with a reduction in its frequency among immunosuppressed patients.

Conclusion

This review showed a reduced scientific production portraying the oral manifestations associated with STI, being concentrated in countries such as Brazil and India. This production was advertised especially in dental journals, limiting the access of other health professionals. The studies were limited to the description of oral manifestations, little explaining the cause-effect relationship, besides portraying predominantly oral alterations associated with HIV. Despite these limitations, it was possible to notice that the changes promoted in the oral cavity by STI ranged from general conditions, such as caries

and periodontal diseases, to specific conditions such as Kaposi's sarcoma. Still, oral manifestations occurred from the patient's immune status and the use of medications to inefficient oral hygiene practice, lack of information and inadequate lifestyle.

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