

Full Length Research Paper

# Oral lesions and systemic diseases in HIV-infected subjects

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The aim of this study was to determine the prevalence of oral lesions and systemic diseases in HIV-infected subjects and to assess possible relationship between them. This was a cross-sectional analytical study. Oral examination was performed in HIV-infected adult individuals. CD4+ count and viral load were recorded and systemic diseases classified. The most common oral lesions were oral candidiasis (26.8%), oral hairy leukoplakia (7.3%) and salivary gland enlargement (6.1%), and systemic diseases were diarrhea (36.6%), HPV infection (24.4%), genital herpes (18.3%), gonorrhea (14.6%), herpes zoster virus infection (13.4%), toxoplasmosis (13.4%) and syphilis (12.2%). A significant association was found between oral lesions and systemic diseases ( $p = 0.005$ ) and particularly with diarrhea ( $p = 0.010$ ). There was a significant association between oral candidiasis and systemic diseases ( $p = 0.030$ ), STDs ( $p = 0.039$ ), diarrhea ( $p = 0.023$ ), *Pneumocystis jiroveci* pneumonia ( $p=0.014$ ) and furunculosis ( $p = 0.014$ ). The results indicate high prevalence of oral lesions in conjunction with similar prevalence of systemic diseases; oral candidiasis and systemic infections were noted especially.

**Key words:** AIDS, oral candidiasis, systemic disease.

## INTRODUCTION

Opportunistic infections are very prevalent in HIV-infected individuals and one of the most frequent causes of death and comorbidity in such patients (Awadh and Anazi, 2009; Chakraborty et al., 2010). Among other highlights Oral candidiasis (OC) is considered an important clinical marker of immunosuppression (Bhayat et al., 2010; Noce et al., 2009), the presence of OC suggests HIV infection in undiagnosed patients and may be one of the first signs of evolution to the acquired immune deficiency syndrome (AIDS) (Gasparin et al., 2009) During early treatment with highly active anti-retroviral therapy (HAART), some individuals develop immune reconstitution syndrome IRS), (in which there is an exacerbation of opportunistic infections such as pulmonary tuberculosis (TB), pneumonia, toxoplasmosis, herpes simplex virus (HSV) and human papillomavirus

(HPV) infections, as well as oral candidiasis has been suggested in some studies (Awadh and Anazi, 2009; Chakraborty et al., 2010; Tangsinmankong et al., 2004; Gaitán-Cepeda et al., 2005) as part of the clinical manifestations of IRS.

Thus, even with the advent of antiretroviral medication, the prevalence of oral and systemic opportunistic infections may be high. Studies have shown an association between oral lesions and systemic diseases in HIV infected individuals and indicate oral candidiasis as a possible predictor of systemic opportunistic infections (Nittayananta et al., 2002; Ranganathan et al., 2004) attracting the interest of researchers to confirm this relationship. Thus, the purpose of this study was to evaluate the relationship and association between the occurrence of oral lesions and systemic diseases among HIV-infected subjects.

## METHODS

This study was approved by the Ethics Committee on Human

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**Table 1.** Demographic characteristic of 82 HIV seropositive patients.

Variables	Category	No.(%)
Sex	Male	54(65.9)
	Female	28(34.1%)
Age	20-30	30(19.5)
	31-40	36(44)
	41-50	23(28)
	51-60	6(7.3)
	61-62	1(1.2)
Marital status	Single	54(65.9)
	Married	15(18.3)
	Divorced	6(7.3)
	Widowed	7(8.5)
Education status	No schooling	2(2.4)
	Primary school	43(52.2)
	Secondary school	22(26.8)
	University	15(18.3)
Absolute CD4+ counts	<200 cells mm <sup>-3</sup>	11(13.4)
	200-500 cell mm <sup>-3</sup>	40(48.7)
	>500 cellmm <sup>-3</sup>	31(37.8)
Viral load counts	Undetectable at <10.000	54(65.9)
	≥10.000	13(15.9)

Research of the Center for Health Sciences, Federal University of Paraíba, Brazil, under protocol 524/06. The sample consisted of 82 HIV-infected adults of both genders, treated at the Dental Service of Clementino Fraga Hospital Complex, Joao Pessoa, Brazil, from October 2006 to May 2007. This is a referral center specialized in the diagnosis and management of infectious diseases. Only HIV-infected adults who signed the informed consent form were included in the study. Patients who refused to participate, had an illness that prevented oral examination or who had incomplete medical records were excluded. Oral examination of each patient was conducted by a dentist and oral lesions were diagnosed according to the presumptive criteria of the EC-Clearinghouse classification (EC-Clearinghouse, 1993). Medical history and the systemic diseases referred to by the patients at the time of consultation were registered, the systemic diseases were listed and the STD's (HPV infection, genital herpes, gonorrhea and syphilis) were grouped.

With respect to immune status, individuals were classified as severely immunosuppressed, moderately immunosuppressed and not immunosuppressed when their CD4 counts were < 200, 200 to 500, and >500 cells/mm<sup>3</sup>, respectively. With regard to viral load, grade 1 was considered for levels between undetectable and <10,000 copies/ml and grade 2 for levels ≥10,000 copies/ml (Gaitán-Cepeda et al., 2005; Taiwo and Hassan, 2010). Data entry, database management and analysis was performed using SPSS® 13.0 software. Chi-square and Spearman's correlation tests were applied and a P value of <0.05 was considered statistically significant.

## RESULTS

A total of 82 HIV-infected subjects were evaluated. The age range was 22 to 62 years. A total of 65.9% were male and 34.1% female. The mean age was 38.3±8.7; a majority (65.9%) of the patients were unmarried and 52.2% had only elementary schooling. The majority 96.3% reported that they did not consume drugs. A total of 90.2% of the patients acquired the infection through sexual contact and 64.6% were heterosexual. With respect to immune status, 13.4% of patients were severely immunosuppressed, 48.7% moderately immune-suppressed and 37.8% were not immunosuppressed. With regard to viral load, 65.9% of patients were undetectable. Of the 84.1% of patients with a detectable viral load, 15.9% of them were considered a viral load level 2 (above 10.000 copies/mm<sup>3</sup>). Demographic data are given in Table 1. Of the individuals studied, 41.5% and 46.3% had at least one oral lesion and systemic disease, respectively. Table 2 shows the oral lesions and systemic diseases in this cohort study. The most frequent oral lesions were oral candidiasis 26.8%, oral hairy leukoplakia 7.3% and salivary gland enlargement 6.1%. With respect to systemic diseases, a total of 42.7% had some type of STD (24.4% HPV infection, 18.3% genital herpes, 14.6% gonorrhea and 12.2%, syphilis), 36.6% had diarrhea, 13.4% herpes zoster virus infection, 13.4% toxoplasmosis, 9.8% pulmonary tuberculosis and 9.8% hypertension. A statistically significant association between oral lesions and systemic diseases ( $p = 0.005$ ) and was diarrhea, the only one of a subset analysis of systemic diseases in general that showed statistical significance ( $p = 0.010$ ). Among the oral lesions, oral candidiasis showed a statistically significant association with systemic diseases ( $p = 0.030$ ), STDs ( $p = 0.039$ ), diarrhea ( $p = 0.023$ ), Pneumocystis jiroveci pneumonia ( $p = 0.014$ ) and furunculosis ( $p = 0.014$ ). A statistically significant correlation was found between oral candidiasis, lower CD4+ counts ( $p = 0.024$ ) and higher viral loads ( $p = 0.007$ ).

## DISCUSSION

Most of the study subjects were male with a mean age of 38.1 ± 8.6 years, a finding similar to that observed by other authors (Santos et al., 2010; Bravo et al., 2006). The vast majority of patients acquired the disease through sexual intercourse and was heterosexual, corroborating other results (Noce et al., 2009; Bravo et al., 2006; Ramírez-Amador et al., 2003). Several studies show a high prevalence of oral lesions in HIV-infected individuals (Awadh and Anazi, 2009; Noce et al., 2009; Bhayat et al., 2010; Gaitán-Cepeda et al., 2005; Nittayananta et al., 2002) and that oral candidiasis and oral hairy leukoplakia were the most frequent, which is consistent with the findings of this study. However, our results differed from those observed in studies on HIV +

**Table 2.** Oral lesions and systemic diseases in HIV seropositive patients.

Lesions/diseases	Number of patients (n=82) (%)
<b>Oral lesions</b>	34 (41.5)
Oral candidiasis	22 (26.8)
Oral hairy leukoplakia	6 (7.3)
Salivary gland enlargement	5 (6.1)
Oral ulcers	2 (2.4)
Linear gingival erythema	1 (1.2)
<b>Systemic diseases</b>	38(46.3)
Diarrhea	30 (36.6)
Human papillomavirus infection	20 (24.4)
Genital herpes	15 (18.3)
Gonorrhoea	12 (14.6)
Herpes zoster virus infection	11 (13.4)
Toxoplasmosis	11 (13.4)
Syphilis	10 (12.2)
Pulmonary tuberculosis	8 (9.8)
Hypertension	8 (9.8)
Rheumatic fever	4 (4.9)
Seborrheic dermatitis	4 (4.9)
Diabetes	4 (4.9)
<i>Pneumocystis jiroveci</i> pneumonia	2 (2.4)
Meningitis	2 (2.4)
Furunculosis	2 (2.4)
Hansen's disease	2 (2.4)
Hepatitis	2 (2.4)

individuals conducted in India, where only 3.7% of subjects exhibited oral hairy leukoplakia (Ranganathan et al., 2004). This difference may be due to the non-availability of antiretroviral agents in certain regions. The occurrence of opportunistic infections with herpes zoster virus, toxoplasmosis and pulmonary tuberculosis was similar to that observed in some studies (Tangsinmankong et al., 2004; Ranganathan et al., 2004; Stoner et al., 2010) however, it was very different from others (Ranganathan et al., 2004; This may be due to HIV-related immunosuppression, favoring these clinical manifestations (Tangsinmankong et al., 2004; Dames et al., 2009) or causing IRS in patients on Highly Active Antiretroviral Therapy (HAART) (Awadh and Anazi, 2009; Chakraborty et al., 2010; Tangsinmankong et al., 2004; Gaitán- Cepeda et al., 2005). However, this cannot be confirmed because the duration of antiretroviral medication use was not determined, representing a limitation of this study.

With regard to systemic diseases, STDs showed the highest rate in the study sample. It is believed that the coexistence of HIV / STDs is due to the similar form of contagion under all conditions. Syphilis is also thought to

increase the risk of HIV transmission and acquisition, owing to the formation of cancers and syphilitic ulcers (Stoner et al., 2010; Farhi and Dupin, 2010). An important systemic disease observed in the present study was diarrhea, which is consistent with the findings reported by other studies, where diarrhea and abdominal pain were the most common gastrointestinal symptoms in HIV/AIDS (Awadh and Anazi, 2009). The present study showed a significant association between oral lesions and systemic diseases, confirming results previously reported in Thailand (Nittayananta et al., 2002) and India (Ranganathan et al., 2004). In these studies, an association between oral candidiasis and pulmonary tuberculosis was observed; in our study, the association was found between oral candidiasis and *P. jiroveci* pneumonia. In other studies, oral hairy leukoplakia was reported more frequently in patients with HIV-associated tuberculosis (Sharma et al., 2006). These authors suggest the need for increased monitoring using laboratory tests and prophylaxis against pulmonary tuberculosis pneumonia in patients with oral candidiasis, underscoring the importance of the correlation between systemic and oral lesions in HIV<sup>+</sup> patients (Nittayananta et al., 2002; Ranganathan et al., 2004). In the present study, statistically significant associations were observed between candidiasis and STDs, diarrhea and furunculosis. New studies are needed to confirm these results. Another limitation of our study is that we cannot determine the sequence of occurrence of oral lesions and systemic diseases in HIV-infected subjects. In addition, the relationship between these two conditions may not be direct and is certainly influenced by the immune-suppression status of the HIV patient. We suggest that further studies be conducted to clarify these issues.

## Conclusion

The results indicate high prevalence of oral lesions in conjunction with similar prevalence of systemic diseases; oral candidiasis and systemic infections were especially noted.

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