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ORIGINAL ARTICLE

Oral lesions in HIV-positive dental patients – one more argument for tobacco smoking cessation

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OBJECTIVE: To determine the prevalence of oral lesions associated with human immunodeficiency virus (HIV) in a population of dental patients and analyze its association with psycho-social variables and biological markers.
STUDY DESIGN: The dental charts of 415 dental patients consecutively treated between May and July 2005 in a dedicated HIV dental clinic were reviewed. Oral soft tissue examinations, psycho-social and medical variables were extracted and recorded for each patient. Ethnicity, gender, HIV treatment, peripheral CD_4 counts and tobacco usage were analyzed in correlation with oral lesions associated with HIV.
RESULTS: Fifty-five percent of all subjects had at least one oral lesion associated with HIV, with oral candidiasis, salivary gland enlargement and oral hairy leukoplakia being the most commonly observed conditions. Gender and ethnicity did not correlate with a higher prevalence in lesions. However, tobacco smoking correlated significantly with a higher prevalence of oral lesions, independent of CD_4 counts.
CONCLUSIONS: These findings suggest that oral lesions remain commonly observed morbidities among HIV-infected dental patients independent of gender and ethnicity and that tobacco usage is a major and often underestimated risk factor for those lesions.
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Keywords: oral manifestation of HIV; tobacco; prevalence; ethnicity; gender

Introduction

The human immunodeficiency virus (HIV) is a retrovirus carried by more than 40 million people worldwide (Zarocostas, 2005) and for which there is no cure and no preventative vaccine. HIV represents an enormous and multifaceted challenge at the individual and at the public health levels. HIV infection leads to a gradual deterioration of the immune system and to the eventual development of the acquired immune deficiency syndrome (AIDS). With disease progression, the deleterious effect of HIV on the immune system results in an escalating incidence of widely recognized and described opportunistic infections and diseases; among which are the oral manifestations of HIV (OMHs) (Greenspan and Greenspan, 1987; Patton *et al*, 2002; Reznik, 2005).

OMHs have been well documented since the onset of the HIV pandemic as early markers of HIV infection and progression (Melnick *et al*, 1989; Greenspan *et al*, 1991; Begg *et al*, 1997). Oral candidiasis (OC) and oral hairy leukoplakia (OHL), two lesions associated with fungal and viral pathogens, respectively, are the most frequently occurring OMHs. Other OMHs such as human papilloma virus-related warts, aphthous-like ulcers and Kaposi's sarcoma have also been extensively reported. The risk of developing an OMH correlates significantly with a decreasing peripheral CD_4 count, a marker of HIV disease progression (Adurogbangba *et al*, 2004) and with HIV viral load (Greenspan *et al*, 2000; Bravo *et al*, 2006).

While it has been repeatedly shown that lower CD_4 counts and a lack of anti-viral HIV medications are important risk factors for OMHs, other factors have also been investigated for their association with OMHs. For example, a decrease in the prevalence of OHL was noted in women (Shiboski *et al*, 1996; Chattopadhyay *et al*, 2005a) and an increased risk for OC and OHL has been linked to sexual practices and tobacco smoking (Shiboski *et al*, 1999; Chattopadhyay *et al*, 2005a).

The introduction of HAART into common clinical practice resulted in a significant decrease in the prevalence of opportunistic diseases including that of OMHs. For instance, a significant decrease in the prevalence of OC and OHL coupled with an increased CD_4 count has been shown to be associated with HAART (Nicolatou-Galitis *et al*, 2004). Seemingly in contradiction to those findings, in spite of a marked improvement in CD_4-cell

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count, an increased prevalence in oral warts and salivary gland enlargement has been noted by some investigators (Patton *et al*, 2000; Greenspan *et al*, 2001; King *et al*, 2002). Taken together, the epidemiology of OMHs in the HAART era seems to indicate that OMHs are, as a whole, less frequent and that new and poorly understood paradoxes are emerging.

Accordingly, the purpose of the present investigation was to examine the prevalence of OMHs in dental patients with chronic HIV infection and analyze its association with psycho-social and medical variables such as gender, ethnicity and reported tobacco smoking. The aims of this study were to determine the distribution of different OMHs in an ethnically and sexually diverse population and establish independent risk factors associated with OMHs.

Methods

The target population for our study was the Ryan White Dental clinic at the University of Illinois at Chicago, which is a dedicated HIV dental clinic to which HIV-infected patients are referred for routine dental care from the greater Chicago area. The study was conducted with the approval of the institutional review board (IRB) at the University of Illinois at Chicago (UIC) by retrospective review of patients' charts. The charts of all patients treated between March and July 2005 were examined. In this clinic, patients present with a referral which includes laboratory data confirming HIV status and indicating CD_4 lymphocyte counts as well as recommended precautions and limitations associated with the anticipated dental care. As part of the routine care, soft tissue examination lesions were conducted by trained and calibrated examiners. The presumptive oral lesions were diagnosed according to the criteria described by Greenspan and Greenspan (1997). For this study, OC includes the erythematous and pseudomembranous candidiasis variants as well as angular cheilitis. Normal examination was defined as an examination for which no oral manifestation of HIV was diagnosed intra-orally and no major salivary gland enlargement was noted.

Patients also completed a self-report questionnaire which included demographic variables such as age and ethnicity as well as psycho-social variables. Other parameters such as tobacco usage, time since HIV infection and whether the subjects were on HAART were recorded. These variables were examined, using zero-order and partial correlations, for their association with the prevalence of OMHs.

Table 1 Social and medical demographic information

Gender (male:female)	3.28 (318:97)
Age, years [mean ± s.d. (range)]	45.2 ± 10.02 (11–79)
Ethnicity, *n* (%)	
AA	190 (45.8)
C	123 (29.6)
H	74 (17.8)
O	11 (2.7)
M	17 (4.1)
CD_4 (mean ± s.d.)	410.0 ± 232.8
$CD_4 \leq 200$ cells μl^{-1} (%)	19.7
$CD_4 > 200$ cells μl^{-1} (%)	80.3
% smokers	42.2
% on HAART	81.0
Months since suspected HIV infection [mean ± s.d. (range)]	125.5 ± 70.3 (0–300)
Annual individual income per year (%)	
< $10 000	65.6
$10 000–25 000	24.0
> $25 000	10.4

s.d., standard deviation; AA, African-American; C, Caucasian; H, Hispanic; O, Other; M, missing data/refused to state.

Results

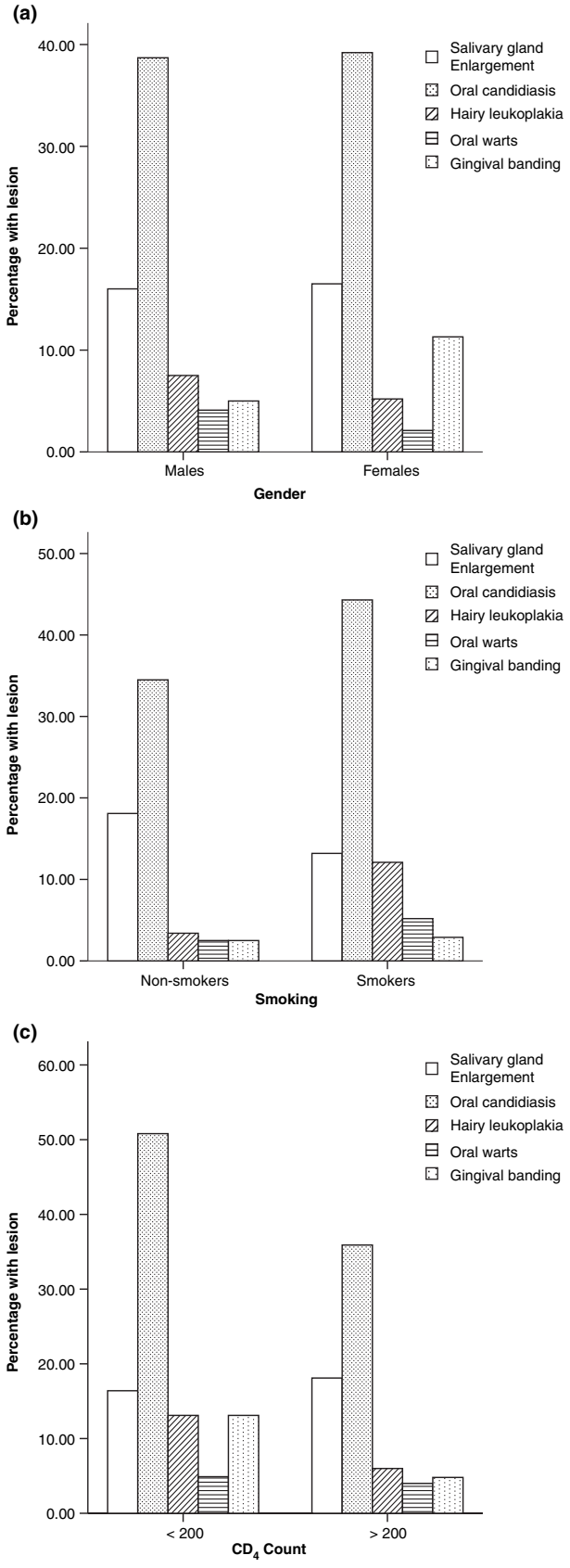
The study sample included 415 patients (318 men and 97 women). The mean age was 45.2 years (ranged 11–79). A summary of social and medical demographic information is presented in Table 1.

In this sample, 55% of the subjects (Table 2) did not have a normal examination. The three most common lesions were OC, salivary gland disease, and hairy leukoplakia (38%, 16.1%, and 7%, respectively). Figure 1 displays the percentage of subjects who had a particular lesion by gender (a), smoking (b) and CD_4 count (c). Overall, OC was the most common lesion for males, females, smokers, and non-smokers, with its prevalence slightly higher in men than in women (39.2% and 38.7%, respectively) and in smokers than in non-smokers (44.3% and 34.5%, respectively). Salivary gland enlargement was similar in both men and in women (16%), but was more common for non-smokers (18.1%) than for smokers (13.2%). While men had only slightly more hairy leukoplakia than women (8% and 5%, respectively), almost four times more smokers had hairy leukoplakia than non-smokers (12.1% and 3.4%, respectively).

Table 2 Prevalence of OMHs

	Total sample	*Male*	*Female*	*Smokers*	*Non-smokers*
Subject with at least one oral manifestation of HIV (%)	55	61	51	56	44
Average number of lesion (for the subjects with lesion), mean (s.d.)	1.48 (0.07)	1.50 (0.06)	1.41 (0.08)	1.52 (0.07)	1.45 (0.06)
Percentage with oral candidiasis	39	39	39	44	47

OMH, oral manifestations of HIV; HIV, human immunodeficiency virus; s.d., standard deviation.



Correlations were performed to further explore the relationship between OMHs and gender, smoking, and ethnicity. Partial correlations were used to control for CD_4 due to the significant correlation between CD_4 and OMHs previously reported[8]. For example, previous analysis with this sample found that CD_4 counts correlated with OMHs for patients with a history of HIV infection shorter than 10 years but not for patients with a history of HIV infection longer than 10 years (Sroussi *et al*, 2006). For each expression, zero-order correlations between the two test variables and partial correlations are reported (Table 3).

Tobacco use and the number of cigarettes smoked per day was negatively correlated with normal examination with non-smokers being more likely to have a normal examination (zero-order $r = -0.106$, $P = 0.03$; zero-order $r = -0.111$, $P = 0.024$, respectively). The magnitude of this relationship increased when controlling for CD_4 (partial $r = -0.117$, $P = 0.04$; partial $r = -0.129$, $P = 0.024$, respectively). Overall, smoking behaviors were associated with increased risk of having an OMH regardless of CD_4 count levels. All zero-order and partial correlations were nonsignificant for normal examination and gender, normal examination and ethnicity, as well as for normal examination and HAART (Table 3).

Discussion

This study has highlighted the prevalence of oral soft tissue lesions associated with HIV infection in a diverse population of dental patients attending a dedicated HIV dental clinic. The data indicate that oral lesions remain a common morbidity in this population. While our data, which are not longitudinal, do not allow testing whether OMHs are less frequent since the introduction of HAART, they clearly indicate that OMHs remain a common problem in HIV-infected patients in the post-HAART era. In our study population, over 50% of the subjects had at least one OMH and more than a third of the subjects were diagnosed with OC, a marker of poor HIV/AIDS prognosis (Dodd *et al*, 1991).

The data indicate that the prevalence of OMHs is independent of ethnicity, gender, and use of anti-viral HIV medication. This finding suggests that the changing demographics of new HIV infections in this country with a larger representation of minorities and women are unlikely to influence the epidemiology of the oral diseases associated with HIV infection.

The predominant OMHs diagnosed in this study were OC followed by salivary gland disease and OHL. While

Figure 1 Distribution of the most commonly diagnosed oral lesions associated with human immunodeficiency virus by gender and tobacco smoking. The percentage of patients who were diagnosed with each lesion is presented for each gender (**a**), for tobacco and non-tobacco users (**b**), and for CD_4 counts below and above 200 (**c**). Oral candidiasis represents erythematous candidiasis, pseudomembranous candidiasis, and angular cheilitis. Other lesions such as AZT pigmentation, recurrent herpetic stomatitis, aphthous-like ulcers and Kaposi's sarcoma are not illustrated and were diagnosed in 2.9%, 1.2%, 0.5%, 0.2% of the patient population, respectively

Table 3 Partial correlations (controls for variable 1) and Pearson's correlations (variables 2 and 3)

Variable 1	*Variable 2*	*Variable 3*	*Partial R (sig)*	*Correlation (sig)*
CD4	Normal examination	Smokers	−0.117 (0.040)	−0.106 (0.030)
CD4	Normal examination	Cigarettes per day	−0.129 (0.024)	−0.111 (0.024)
CD4	Normal examination	Ethnicity	n.s.	n.s.
CD4	Normal examination	Gender	n.s.	n.s.
CD4	Normal examination	HAART	n.s.	n.s.

HAART, highly active antiretroviral therapy; n.s., not significant.

this confirms that OC and OHL represent a large portion of all OMHs, it also indicates that the prevalence of salivary gland disease may be increasing, a finding previously documented by others (Patton *et al*, 2000; Greenspan *et al*, 2001). Our study cannot refute or confirm an increased prevalence of oral warts, although the results clearly indicate that oral warts remain a much less common disease than OC, OHL, and the emerging salivary gland disease.

Other than an intuitive and previously documented relationship between the risk of developing an OMH and a lower CD_4 count (Margiotta *et al*, 1999; Ramirez-Amador *et al*, 2005), smoking emerged as a major risk factor associated with a higher prevalence of OMHs in accordance with previous reports (Palacio *et al*, 1997; Chattopadhyay *et al*, 2005b). Whether smoking itself or smoking-associated factors such as poor oral hygiene and/or diet explain this association should be studied further. Nonetheless, our study shows that an increased risk for OMHs may be an additional reason for including tobacco cessation in routine oral health care for HIV-infected patients.

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