Original Article

Oral Lesions and Conditions Associated with Human Immunodeficiency Virus Infection in 1000 South Indian Patients

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Abstract

Introduction: Human immunodeficiency virus (HIV) infection is a major health problem in India. The importance of oral lesions as clinical features of HIV infection and their gender specificity have been reported worldwide. However, there are very few reports on this aspect from the Indian subcontinent. Materials and Methods: The study population comprised 1000 consecutive HIV seropositive patients presenting to YRG CARE, a non-governmental organisation in Chennai, South India. The oral lesions were diagnosed based on clinical appearance using international criteria. Data were entered into a database and analysed using the SPSS package. Results: The male-to-female ratio was 3.4:1, and 95% of the patients had acquired infection via heterosexual contact. Majority of the patients (84%) were in the 21- to 40-year-old age groups. Pulmonary tuberculosis (12%) was the most common systemic finding. Oral lesions were seen in 86.6% of the patients. Gingivitis (72.3%) and periodontitis (33.2%) were the most common lesions followed by oral pigmentation (26.3%), oral candidiasis (23.8%), angular cheilitis (7.9%), oral ulcers (3.3%), oral hairy leukoplakia (2.1%), oral submucous fibrosis (0.9%) and leukoplakia (1.5%). The prevalence of oral candidiasis, periodontitis and oral hairy leukoplakia was higher in males than in females. Conclusions: Oral lesions occur commonly in HIV infection. A comprehensive oral examination plays an important role not only in the management of the patients, but also in assessing the immune status and in their follow-up.

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Key words: Candidiasis, Gender, HIV, India, Oral pigmentation

Introduction

Human immunodeficiency virus (HIV) infection is a major global health problem. It is estimated that the number of people living with HIV infection in India, by the end of 2002, is 4 to 5 million.[1] Systemic and oral lesions in HIV infection reflect the immune status of the patients. These lesions are not only important for the morbidity they cause but also for their diagnostic value in monitoring the immune status of the patient.

HIV-related oral lesions are frequent and often an early finding in HIV infection.[2-8] Many studies, from different parts of the world, have also documented the increasing number of women affected by HIV infection and the gender differences in HIV-related oral lesions.[9-13] However, there are very few reports of oral manifestations of HIV infection from India. In this context, we had earlier reported the clinical presentation and prevalence of oral lesions in 300 HIV sero-positive patients in Chennai, which to our knowledge was the single largest report so far published from this part of the Indian sub-continent.[14] The present study reports the oral lesions and the gender differences in a cohort of 1000 HIV seropositive patients.

Material and Methods

One thousand consecutive HIV/AIDS patients attending the YRG CARE (Centre for AIDS Research and Education)

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over a period of 3 years (from February 2000 till February 2003) constituted the study group. All attended, or were referred, because of known or suspected HIV disease. A trained counsellor confirmed sources of infection. Confirmation of HIV sero-status for all patients was by ELISA (Merind Diagnostics, Belgium) and Western blot (Biotechnology kit, Singapore). CD4 cell counts were performed for only 450 patients, who could either afford the expense or were funded by projects requiring specific criteria. A diagnosis of AIDS was made on the basis of criteria set by the Centers for Disease Control, USA.[15]

A thorough history was taken. Trained dental surgeons and physicians performed clinical oral examination and systemic examination, respectively, and the findings recorded in the same format. The oral lesions were diagnosed according to the criteria established by the EC Clearinghouse and WHO,[16] and as described in detail in our earlier report.[14]

All statistical analyses were performed using the SPSS v10.05 software. Means, standard deviations and percentages of various variables were calculated. A chi-square test of association was used to find out the association between variables. A t-test was done to compare the mean differences in normally distributed data. Mann-Whitney U test was applied to assess the statistical differences between groups of patients when data were not normal. The ANOVA test was used when a comparison was made between a continuous variable and a nominal variable with more than 2 categories. Odds ratio (OR) and 95% confidence interval (CI) were calculated for all oral lesions. A *P* value of <0.05 was considered statistically significant.

Results

Table 1 shows the demographics of 1000 HIV seropositive patients. Seven hundred and seventy-four (77.4%) were males and 226 were females (22.6%), giving a male-to-female ratio of 3.4:1. The age of the youngest patient was 7 months and the age of the oldest patient was 72 years. The maximum number of cases in females was in the 21 to 30 years age group, while for males it was in the 31 to 40 years age group (56.2% and 52.2%, respectively). There were no significant differences in the educational status between the sexes. Majority (75.7%) of the women were not employed and were housewives/homemakers.

Table 2 shows the source of infection. The main source of infection for both males and females (96.4% and 90.3%, respectively) was through the heterosexual route. This was followed by infection via blood transfusion (2.0%)

Of the 1000 patients, 107 (89 males, 18 females) were on anti-retroviral therapy (ART). CD4 counts were available for 450 patients. Of these, 196 patients (169 males, 27 females) had CD4 count of ≤200; 254 patients (187 males, 67 females) had CD4 count of >200.

Table 3 shows the prevalence of HIV-related oral lesions by gender. Of the 1000 patients, 134 (93 males, 41 females) had no oral lesions. The types of oral lesions and conditions observed included candidiasis, gingivitis pigmentation, periodontitis, ulcers, oral hairy leukoplakia (OHL), oral submucous fibrosis (OSMF) and leukoplakia. More males (88%) than females (82%) had oral lesions and this was statistically significant (*P* <0.05)

A total of 723 patients (562 males, 161 females) had gingivitis. Periodontitis was present in 332 patients (281 males, 51 females). Two hundred and sixty-three patients (208 males, 55 females) had brown to black oral pigmentation. Pigmented areas were unique and were different from racial pigmentation. Common sites of pigmentation were the palate and buccal mucosa. The pigmented areas were dark brown to brownish-black in colour and presented as diffuse or irregular patches.

Oral candidiasis (OC) was present in 238 patients (202 males, 36 females). One hundred and sixty-one (137 males, 24 females) patients had pseudomembranous candidiasis (PC), 31 (27 males, 4 females) had erythematous candidiasis (EC) and 12 (9 males, 3 females) had hyperplastic candidiasis. There were more male (26%) than female patients (16%) with OC. This difference was statistically significant (*P* <0.05). There was a positive correlation between smoking and candidiasis (*P* <0.05) in males.

Table 1. Demographics of 1000 HIV Seropositive Patients

Variable	Male (n = 774) No. (%)	Female (n = 226) No. (%)
Age group (y)		
<20	6 (0.8)	15 (6.6)
21-30	252 (32.6)	127 (56.2)
31-40	404 (52.2)	61 (27.0)
41-50	97 (12.5)	22 (9.7)
>50	15 (1.9)	1 (0.4)
Education status		
No formal education	69 (11.4)	34 (21.8)
Primary school	244 (40.4)	66 (42.3)
Secondary school	175 (29.0)	31 (19.9)
College	116 (19.2)	25 (16.0)
Occupation		
Business	198 (25.5)	4 (1.8)
Skilled person	111 (14.3)	10 (4.4)
Commercial sex worker	1 (0.1)	7 (3.1)
Truck driver	175 (22.6)	-
Healthcare worker	4 (0.5)	1 (0.4)
Housewife	-	171 (75.7)
Labourer	94 (12.2)	10 (1.4)
Farmer	130 (16.8)	8 (3.5)
Unemployed	14 (1.8)	5 (2.2)
Unknown	39 (5.0)	9 (4.0)
Student	5 (0.6)	1 (0.4)
Others	3 (0.4)	-

Table 2. Distribution of HIV-positive Patients by Source of Infection

Source of infection	Total (n = 1000)		Male (n = 774)		Female (n = 226)	
	No.	(%)	No.	(%)	No.	(%)
Heterosexual	950	95.0	746	96.4	204	90.3
Homosexual	1	0.1	1	0.1	0	0
IVDU	2	0.2	2	0.3	0	0
Blood transfusion	20	2.0	8	1.0	12	5.3
Vertical transmission	5	0.5	2	0.3	3	1.3
Unknown	19	1.9	14	1.8	5	2.2
Needle prick injuries	3	0.3	1	0.1	2	0.9

IVDU: intravenous drug use

Table 3. Prevalence of HIV-related Oral Lesions by Gender

Oral lesions	Male (n = 774)		Female (n = 226)		Odds ratio*	95% CI	*P* value
	No.	(%)	No.	(%)			
Candidiasis	202	(26.1)	36	(15.9)	1.86	1.26-2.76	0.001†
Pseudomembranous	137	(17.7)	24	(10.6)	1.81	1.14-2.87	0.010‡
Erythematous	27	(3.5)	4	(1.8)	2.0	0.70-5.79	0.27
Hyperplastic	9	(1.2)	3	(1.3)	0.88	0.24-3.26	0.74
Angular cheilitis	68	(8.8)	11	(4.9)	1.88	0.98-3.62	0.07
Gingivitis	562	(72.6)	161	(71.2)	1.07	0.77-1.49	0.67
Pigmentation	208	(26.9)	55	(24.3)	1.14	0.81-1.61	0.49
Periodontitis	281	(36.3)	51	(22.6)	1.96	1.39-2.76	0.00†
Ulcers	25	(3.2)	8	(3.5)	0.91	0.40-2.05	0.833
Oral hairy leukoplakia§	21	(2.7)	0		12.93	0.78-214.23	0.007†
Oral submucous fibrosis	8	(1.0)	1	(0.4)	2.35	0.29-18.88	0.69
Leukoplakia	13	(1.7)	2	(0.9)	1.913	0.43-8.54	0.54
Others	45	(5.8)	4	(1.8)	3.426	1.22-9.63	0.01‡
Any oral lesion	681	(88.0)	185	(81.9)	1.623	1.09-2.43	0.02‡
Number of lesions‖							
0	93	(12.0)	41	(18.1)	1	-	-
1-2	505	(65.2)	153	(67.7)	1.455	0.97-2.19	0.07
3-4	164	(21.2)	32	(14.2)	2.259	1.33-3.83	0.002†
>4	12	(1.6)	0		217.17	0.01-6.4+E07	0.402

OR: odds ratio

* OR was calculated with reference to female

† Significant at 1% level of significance

‡ Significant at 5% level of significance

§ 0.5 added to each cell frequency to calculate OR

‖ ORs were calculated only for males, 0 as the reference category

Oral ulcers were present in 33 patients (25 males, 8 females), 22 of which were non-specific, 5 due to herpetic infection and 6 were aphthous ulcers. Twenty-one patients (2.1%) presented with OHL. All were males. Nine patients (8 males, 1 female) had OSMF and 15 patients (13 males, 2 females) had leukoplakia, all 24 patients were habituated betel nut and/or tobacco users.

Table 4 shows the systemic features of 1000 patients with HIV disease. Pulmonary tuberculosis (TB) (11.8%) was the most common systemic disease, followed by genital ulcers (8.9%), pharyngeal candidiasis (8.6%), gastroenteropathy (3.6%), herpes zoster (3.3%), extrapulmonary TB (1.5%) and eosinophilic folliculitis (1.3%). The systemic features between males and females were not statistically significant.

Discussion

Progression of HIV infection is associated with a range of oral manifestations. Oral lesions have been widely studied and some were found to have both diagnostic and prognostic values.[3,17-19]

In our previous report of 300 cases, we had suggested that comprehensive oral examination might not only detect HIV disease but also useful in monitoring disease progression.[14] In the present study, we described the occurrence of oral lesions in 1000 HIV-positive patients. We have also attempted to assess if gender specificity exists with respect to oral lesions, as there are differences between males and females with respect to the occurrence of HIV infection related oral lesions.[11,20] Gender differences

Table 4. Systemic Features of 1000 HIV/AIDS Patients

Systemic feature*	Total (1000)	Male		Female	
		Patient without oral lesion (93)	Patient with oral lesions (681)	Patient without oral lesion (41)	Patient with oral lesions (185)
Asymptomatic	156 (15.6)	9 (9.7)	80 (11.7)	13 (31.7)	54 (29.2)
Pulmonary tuberculosis	118 (11.8)	16 (17.2)	89 (13.1)	5 (12.2)	8 (4.3)
Genital ulcers	89 (8.9)	10 (10.8)	55 (8.1)	2 (4.9)	22 (11.9)
Others	66 (6.6)	3 (3.2)	53 (7.8)	1 (2.4)	9 (4.9)
Pharyngeal candidiasis	86 (8.63)	11 (11.8)	64 (9.4)	2 (4.9)	9 (4.9)
Gastroenteropathy	36 (3.6)	2 (2.2)	28 (4.1)	-	6 (3.2)
Herpes zoster	33 (3.3)	5 (5.4)	23 (3.4)	1 (2.4)	4 (2.2)
Eosinophilic folliculitis	13 (1.3)	3 (3.2)	8 (1.2)	1 (2.4)	1 (0.5)
Tinea infections	12 (1.2)	2 (2.2)	8 (1.2)	-	2 (1.1)
Extra pulmonary tuberculosis	15 (1.5)	3 (3.2)	10 (1.5)	-	2 (1.1)
Herpes simplex	9 (0.9)	1 (1.1)	8 (1.2)	-	-
Bacterial skin infection	11 (1.1)	1 (1.1)	8 (1.2)	1 (2.4)	1 (0.5)
P. pneumoniae	10 (1.0)	1 (1.1)	8 (1.2)	-	1 (0.5)
Leukorrhoea	5 (0.5)	-	-	1 (2.4)	4 (2.1)
Venereal warts	6 (0.6)	1 (1.1)	5 (0.7)	-	-
Hepatosplenomegaly	4 (0.4)	-	4 (0.6)	-	-
Cryptococcal meningitis	4 (0.4)	-	4 (0.6)	-	-
Lower respiratory infections	1 (0.1)	-	1 (0.1)	-	-
Cytomegalovirus retinitis	2 (0.2)	-	1 (0.1)	-	1 (0.5)
Toxoplasmosis	2 (0.2)	-	2 (0.3)	-	-
Scabies	1 (0.1)	-	1 (0.1)	-	-

* Some patients had more than one systemic finding.

in CD4 cell counts can influence the prevalence and management of opportunistic infections and clinical outcome.[21]

The mean age of males and females in our study was 33 years and 29 years, respectively; this difference was statistically significant (P <0.05). The main source of infection was the heterosexual route for both males and females and 84.8% of these women had acquired the HIV infection from their spouses. These figures are similar to the findings of our earlier study and other reports from India.[22,23] There was a significant difference in the mean CD4 counts between males and females (295.28 ± 270.53 and 453.77 ± 376.98, respectively; P <0.05) and the prevalence of oral lesions was higher in males than in females (P <0.05). This was unlike that reported by Campisi et al[10] where the prevalence of HIV infection-related oral lesions was significantly higher in HIV-positive women than men.

Pulmonary TB (11.8%) was the most common systemic disease. This was significantly less than the 32% reported in our previous study.[14] Interestingly, we found significant association between the occurrence of the oral lesions and systemic TB. Patients who presented with oral candidiasis had 1.73 times higher risk of having TB compared to those without candidiasis. This is similar to the report from Nittayananta et al,[24] where a significant association between the occurrence of oral candidiasis and TB was observed. The occurrence of pharyngeal candidiasis (8.63%) had come down from our previously reported figure of 22%.[14] This has been mainly due to early diagnosis and prophylactic management with anti-fungal medications.

The overall prevalence of OC showed a reduction in occurrence compared to our previous study.[14] Reported prevalence of OC in HIV-positive patients ranges from 12% to 84.2%.[2,14,25-29] 60.4% of the patients with candidiasis were smokers and all of them were males. OC was highly associated with smoking, being 1.7 times more frequent in persons who smoke than in non-smokers (P <0.05). There was a significant difference between male and female patients in the overall prevalence of OC (26.1% in males and 15.9% in females; P <0.05). Males had a 1.86 times (95% CI, 1.26-2.76) higher risk of acquiring OC than females. This is consistent with the report of Shiboski et al,[20] where the prevalence of OC was 24% in men and 13% in women. In our study, the most frequently encountered variant of candidiasis was the pseudomembranous type, contrary to prevalence studies of oral lesions, where EC has been reported to be the most common type of OC in HIV-infected individuals.[30-33] However, this is consistent with the findings reported by other investigators.[29,34] We also observed a higher prevalence of PC in males than in females (17.7% and 10.6%, respectively; P <0.05). Patients with OC had 1.96 times higher chance of having their CD4

counts ≤200 than patients without OC. Patient with PC had 2.67 times higher chance of having their CD4 counts ≤200 than patients without PC.

OHL was seen in 2.1% of our patients and all were males. The overall low prevalence of this lesion and the absence of this lesion in female patients is similar to other reports from India.[14,35] The odds of presenting with periodontitis were 1.96 (95% CI, 1.39-2.76) times more in males than in females (P <0.05). Fifty per cent of male patients were smokers and none of the female patients had the habit of smoking. This may be one of the reasons for the higher prevalence of conventional periodontitis in males. The high prevalence of gingivitis and periodontitis in our normal population limits the significance of occurrence of these oral lesions in our HIV population. There is a necessity for other analytical studies with matched normal controls to understand and evaluate the prevalence of gingivitis and periodontitis as related to immune suppression in the Indian context.

An interesting observation in our cohort was the occurrence of intra-oral pigmentation (26.3%), which was unique and distinct from racial pigmentation. There were no differences in the prevalence of intra-oral pigmentation between males and females. Increased melanin pigmentation in skin and oral mucosa have been reported by Langford et al,[36] Smith et al[37] and Ceballos-Salobrena et al.[38] Some of the reasons that have been put forward to explain the intra-oral pigmentation are increased release of α-melanocyte-stimulating hormone (α-MSH) due to deregulated release of cytokines in HIV disease; use of melanocyte stimulating drugs: certain antiretrovirals, antifungals; and Addison's disease. When the prevalence of pigmentation was compared between gender and within the gender between CD4 counts ≤200 and CD4 counts >200, we did not observe any significant difference.

We had 10 cases of OSMF in our cohort. OSMF is not uncommon in the Indian subcontinent where 2.5 million people are affected by this condition due to the habit of chewing areca nut. These patients are being followed up to understand if there is any difference in the progression of OSMF in HIV-positive patients and non-HIV patients. Fifteen patients in our cohort had leukoplakia and all had habits related to either chewing tobacco or smoking tobacco.

In conclusion, oral lesions are a feature of HIV-positive patients. There was a significant difference in the occurrence of oral lesions between genders. Presence of oral lesions, particularly extensive oropharyngeal candidiasis, was associated with HIV infection. The drop in the prevalence rate of OC from our previous study reflects the earlier detection of HIV-infected patients and increased use of prophylactic drugs. Though OC was observed in both males and females, it was more prevalent in males. Further studies are needed to highlight the gender differences and similarities. This knowledge will enable us to understand the nature of these lesions, assist in their management and monitor the progression of HIV infection and to establish protocol for management. The present study emphasises the usefulness of oral examination and their role in screening the population at risk.

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