Oral manifestations and related factors of HIV positive patients in south-east of Iran

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Abstract

Introduction: Oral manifestations can be the first signs of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and a useful marker for the progression of this disease. The present study aimed to determine the prevalence of oral manifestations and examine their relationship with socio-demographic factors in HIV-positive patients in the health centers affiliated to Zahedan University of Medical Sciences (Southeast Iran). **Methods:** In this cross-sectional study in addition to determining oral manifestations based on the classification of EC-clearing house (European Commission clearing house), information such as age, gender, marital status, residence, education, occupation, habits, oral hygiene, loss of weight in the last six months. Body Mass Index (BMI), mode of HIV transmission, stage of disease, anti-retroviral therapy (ART), and duration of HIV were gathered through direct question from the patients or the information contained in their records. Then the relationship between various factors and oral manifestations was analyzed using Chi-square, Fisher's Exact Test, Student T Test, Mann- Whitney tests and logistic regression. **Results:** Oral examination was performed on 119 HIV-positive patients who were 69.7% male and 30.3% female and had a mean age of 35.4±12.7 years. Oral manifestations were found in 57.1% of the patients. Pseudomembranous candidiasis (34.1%) and linear gingival erythema (33%) were the most common lesions in these patients. The probability of oral manifestations occurrence increased with age and duration of smoking in smokers with HIV (P=0.036 and P=0.012, respectively). **Conclusion:** Most oral manifestations were those strongly associated with HIV infection (91%). Timely diagnosis and treatment of oral manifestations in HIV patients should be considered in conjunction with other treatments.

Key words: Human immunodeficiency virus, Acquired immunodeficiency syndrome, Oral manifestation, Oral lesions, Risk factor

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Introduction

Human immunodeficiency virus (HIV) infection has affected residents of all countries, while the majority of affected people live in developing countries(1). According to the facts, 24651 people are infected with the virus since the beginning of report of HIV cases in Iran until 2011(2). Oral manifestations can be the first signs of HIV infection that commonly (30-80%) occur in these patients. These lesions can predict decrease in CD4 T cell, increase in viral load, and disease progression toward acquired immunodeficiency syndrome (AIDS)(3, 4). The oral lesions associated with HIV lead to patients' discomfort, function disorder, inability and adversely affect the quality of life.(5).

Linear gingival erythema, oral candidiasis, lymphadenopathy, melanotic hyperpigmentation, necrotizing ulcerative gingivitis (NUG), and oral hairy leukoplakia (OHL) are the most common oral manifestations that occur in patients with HIV(6). Various factors affect the prevalence of oral lesions in people with HIV, such as smoking, alcohol consumption, and oral health status (6). Today, anti-retroviral therapies (ARTs) are used to treat HIV patients and different results have been reported about their effects on the prevalence of oral manifestations (6,7).

Early detection of oral manifestations can enhance the quality of health care(8). Few studies have examined prevalence of oral lesions in patients with HIV in Iran (6,9,10) and revealed differences with each other. Since the prevalence of oral manifestations among HIV-positive patients in the health centers affiliated to Zahedan University of Medical Sciences have not been evaluated so far, this study aimed to investigate these lesions and their relation to some demographic, social, and medical factors in this area.

Materials and Methods

In a cross-sectional study in September 2013, patients with HIV diagnosed via ELISA and western blot tests, having active medical records were identified from the health centers of Zahedan Medical Sciences University. Prior to participate in the research, patients signed an informed consent. The study was approved by the Ethics Committee of Research Deputy of Zahedan Medical Sciences University with the code of 2527. Information such as age, gender, marital status, residence, education, occupation, and habits such as smoking, pan and smokeless tobacco use, oral hygiene, loss of weight in the last six months, mode of HIV transmission, stage of the disease, anti-retroviral therapy (ART) status, and duration of HIV were gathered through questioning from the patients or the information contained in their records. Height and weight of patients were also measured. It should be noted that since it was not possible to check the CD4 count in all health centers, the stage of the disease was identified according to the information contained in the past 3 months records of the patients. The oral examination is conducted only by a final-year dental student that exclusively was trained by supervisors (an oral diseases specialist and an oral pathologist) regarding oral manifestations in patients with HIV. The intra-oral examination was then performed on a dental unit in the vertical position using dental disposable mirror, periodontal probe and sterile pads under proper lighting of the unit; the results of the examinations were then recorded. If clinical diagnoses need to confirm, patients were referred to the oral medicine department of Zahedan dental School to perform other laboratory tests. Oral lesions were classified into three categories according to European Commission Clearinghouse (EC-Clearing house EC-clearing house): 1. Lesions strongly associated with HIV infection; 2. Lesions less commonly associated with HIV infection; and 3. Lesions seen in patients with HIV infection (11). All extracted data were analyzed using SPSS 21(SPSS Inc., Chicago, IL). Data normality was initially examined by Kolmogorov-Simonov test. Then the relationship between various factors and oral lesions was analyzed using Chi-square, Fisher's Exact Test, Student T Test, Mann- Whitney test and logistic regression. *P*-values less than 0.05 were considered statistically significant.

Results

Among 119 HIV-patients whose mouths were examined, 68 (57.1%) had oral manifestations, of them 62 (91%) cases had lesions strongly associated with HIV, 2 (3%) cases had lesions less commonly associated with HIV, and 4 (6.1%) cases had both lesions strongly associated with HIV and lesions less commonly associated with HIV. No third category lesions were observed in patients with HIV in this study. As can be seen in Table 1, oral pseudomembranous candidiasis (34.1%) was the most common oral manifestation observed in patients, while hyperpigmentation (3.4%) and necrotizing ulcerative periodontitis (3.4%) had the lowest prevalence. In addition, one case of lichen planus, two cases of hyperkeratosis, and two cases of coated tongue was also observed in examinations. Furthermore, chronic and acute periodontitis are seen in 43 and 12 patients with HIV, respectively. These manifestations are not classified as lesions associated with HIV. The lesions were located in the gingiva (39.8%), tongue (37.5%), palate (9.1%), buccal mucosa (6.8%), labial commissure (4.5%), and the parotid salivary glands

(2.3%). 26.5% with oral manifestations had more than one lesion and even a patient had four different oral lesions. Overall, the average number of oral manifestation was 1.3±0.6 and there were no significant differences in the number of oral lesions in different stages of disease (HIV or AIDS) (P=0.15 Mann- Whitney test).

Statistical analysis showed no relationship between the factors of gender, marital status, residence, education, occupation, habits such as smoking, pan and smokeless tobacco use, oral hygiene, mode of HIV transmission, and weight loss in the last six months and stage of disease and the presence of oral lesions. (Table2)

The mean age of patients and duration of smoking in smokers were 35.4±12.7 (1-66) and 9.4±6 (2-25) years, respectively. With increasing age and duration of smoking in smokers with HIV, the probability of presence of oral lesions increased; this association was statistically significant.(p=0.036 and p=0.012, respectively) (Table 3) Also, the mean duration of HIV infection and BMI was 5.8±4.2 (1-20) years and 20.8±6.5 (0.8-35.9) (kg/m^2), respectively. As can be seen in Table 3, no significant association was observed between duration of HIV infection and BMI and the presence of oral lesions. (p=0.07 and p=0.44, respectively).

According to the logistic regression model in the presence of independent variables only age have significant effect on the incidence of oral lesions (P=0.007). This means that the risk of oral lesions increased by 7%with age.

Table 1. Distribution of oral lesions according to the type in HIV-positive patients

	Type of lesion	**Stage of disease**		**Total (%)**
		HIV (%)	**AIDS (%)**	
Lesions strongly associated with HIV infection	Pseudomembranous candidiasis	24(36.9)	6(26)	30 (34.1)
	Erythematous candidiasis	8(12.3)	2(8.7)	10 (11.4)
	Oral hairy leukoplakia	8(12.3)	1(4.4)	9 (10.2)
	Linear gingival erythema	20(30.8)	9(39.1)	29 (33)
	Necrotizing ulcerative periodontitis	2(3.1)	1(4.4)	3 (3.4)
Lesions Less associated with HIV infection	Hyperpigmentation	1(1.5)	2(8.7)	3 (3.4)
	HIV-related salivary gland disease	2(3.1)	2(8.7)	4 (4.5)
Total		65(100)	23(100)	88 (100)

Table 2. The prevalence of oral lesions according to related factors in HIV-positive patients

	Oral lesions						
	Yes		No		Total		
Related factors	**N**	**%**	**N**	**%**	**N**	**%**	**P value**
Gender							
Male	46	55.4	37	44.6	83	100	0.69*
Female	22	61.1	14	38.9	36	100	
Marital status							
Single	40	55.6	32	44.4	72	100	0.71*
married	28	59.6	19	40.4	47	100	
Residence							
City	37	62.7	22	37.3	59	100	0.27*
Village	31	51.7	29	48.3	60	100	
Education							
Uneducated	24	55.8	19	44.2	43	100	
Primary school degree	41	59.4	28	40.6	69	100	0.68**
Diploma and academic degree	3	42.9	4	57.1	7	100	
Occupation							
Employee	10	66.7	5	33.3	15	100	0.58*
Jobless	58	55.8	46	44.2	104	100	
Smoking							
Smoker	26	59.1	18	40.9	44	100	0.85*
Non smoker	42	56	33	44	75	100	
Pan and smokeless tobacco use							
User	23	53.5	20	46.5	43	100	0.57*
Non user	45	59.2	31	40.8	76	100	
Tools of oral hygiene							
Tooth brush and paste	21	50	21	50	42	100	
Chewing sticks	36	62.1	22	37.9	58	100	0.48**
Rinsing with water after meals	11	57.9	8	42.1	19	100	
Frequency of oral hygiene							
More than once in a day	12	66.7	6	33.3	18	100	
Once in a day	41	55.4	33	44.6	74	100	0.68**
Once in a Week	15	55.6	12	44.4	27	100	
Transmission path							
Blood	35	57.4	26	42.6	61	100	
Sexual contact	31	59.6	21	40.4	52	100	0.47**
Vertical transmission	2	33.3	4	66.7	6	100	
Weight loss in last 6 months							
Yes	13	65	7	35	20	100	0.47*
No	55	55.6	44	44.4	99	100	
Stage of disease							
AIDS	21	46.7	24	53.3	45	100	0.09*
HIV	47	63.5	27	36.5	74	100	
ART							
Yes	21	46.7	24	53.3	45	100	0.09*
No	47	63.5	27	36.5	74	100	

*Fisher's Exact Test

**chi-square test

Table 3: The prevalence of oral lesions according to age, duration of disease and smoking, and BMI in HIV-positive patients

Oral lesion		Age (years)	HIV duration (years)	BMI (kg/m^2)	Smoking duration (years)
with oral lesion	Number	68	68	68	26
	Mean	37.5	6.4	20.7	11.2
	Median	35	4.5	21.3	10
	Std. Deviation	12.8	4.5	5. 9	6.5
	Interquartile range	21.5	7	4.9	10
without oral lesion	Number	51	51	51	18
	Mean	32.6	4.9	20.8	6.79
	Median	33	4	21. 8	5
	Std. Deviation	12.3	3.6	7.3	3.94
	Interquartile range	10	6	6	7
	P Value	0.036*	0.07**	0. 44*	0.012**

*Student T Test

** Mann-Whitney Test

Discussion

The prevalence of oral lesions in different parts of the world varies between 23.5% and 86.6%. (12, 13) In the present study, the prevalence of oral manifestations in HIV patients was 57.1% which was lower than the prevalence reported by Khatibi et al. (74.5%) in Tehran, Iran (6). The main reasons for diversities in the prevalence of oral manifestations in HIV patients in different countries may arise from difference in sample size, stage of disease, degree of immunodeficiency, regional patterns of various diseases, high-risk behaviors, geographic location, race, economic, cultural, and biological diversities, different daily lives and public health care conditions, as well as various tools used such as lesions classification system and diagnostic criteria and methods (9, 14-17).

Candidiasis was the most common manifestation in the present study (40%); this rate was almost similar to that of studies conducted by Bodhade et al. (39.3%) and Sen et al.(38.3%)(18, 19). The highest prevalence of candidiasis was reported by Tami-Maury in Mali (95%). (8) CD4 less than 350 cells/mm^3, alcohol consumption, and female gender are identified as predisposing factor of oral candidiasis in patients with HIV(20). In the study by Ranganathan et al., periodontal diseases (gingivitis: 72.3%, periodontitis: 33.2%) were the most common oral manifestations in HIV-positive individuals(13), while they were the second prevalent oral manifestations (34.1%) in the present study. Periodontal disease is another oral lesion in HIV-positive patients with low CD4 levels which may arise from poor oral hygiene, smoking, and use of alcohol and drugs (3, 9). The reason for its different prevalence in various studies relies on factors such as disease stage and criteria used to diagnosis of periodontal disease (18).

Same as the studies carried on by Alexio et al., Taiwo and Hassan and Pedreira et al., most patients had single lesion in the present study (21-23); It was also identified that the occurrence of four or more oral lesions in HIV-positive patients is significantly associated with the levels of CD4 less than 200 cells/mm^3, and the occurrence of four or more oral lesions in these patients is a good predictor for severe immune suppression (24).

There was a significant association between the mean age of patients and the prevalence of oral manifestations in patients with HIV. So, the mean age of patients with oral lesions was approximately five years more than patients without oral lesions. This finding is similar to the results reported by Yengopal and Naidoo (5). Ermias et al. reported a higher incidence of oral manifestations in people older than 40 years (25). In contrast to these results, Kerdpon et al. attributed younger age to the occurrence of oral lesions in southern Thailand (26).

Different studies reported prevalence diversities of oral manifestations in males and females; so some studies attributed the occurrence of oral lesions in patients with HIV to male gender (27-29) and explained it by more effective cell-mediated immunity and higher control of HIV function in the early stages of the disease in women than in men (27). However, Taiwo and Obuekwe and their cooperators reported significantly higher occurrence of oral manifestations in women with HIV (22, 30). Similar to the present research, no correlation was seen in many studies between the occurrence of oral manifestations in HIV-positive people and gender (12,16,31).

In the study performed by Taiwo and Hassan, about 52% of HIV-positive patients were married (22), while in the present study, 40% of the patients were married; also the patients were almost equally rural and urban. There were also no specified correlation between marital status and residential location and the presence of oral manifestations; this relationship was not investigated in other studies so far.

Education was proposed as a factor associated with oral manifestations by Khatibi et al. So, people with more education have fewer oral manifestations due to more attention to their oral health (6). Only about 6% of patients in the present study had high school and university education. Because of low number of high educated people in this study, evaluation of the relationship between education and oral lesions in people with HIV isn't provided. Also, more than 87.4% of people were unemployed and no relationship was found between the prevalence of oral manifestations and occupation status; this finding is consistent with the study of Ermias et al., Khatibi et al., Yengopal and Naidoo (5, 6, 25). Unemployment and social isolation were suggested as social effects of HIV in Iran(32); so that on one hand, the patient's income is not sufficient to use dental services and on other hand, an isolated person is depressed and doesn't pay attention to his physical health.

Srousi et al. showed that smoking is associated with the presence of oral lesions in HIV-positive patients independent of CD4 (33). In another study, Ermias et al. revealed that smoking triples the risk of oral lesions in such patients(25). In contrast to these results, the present study found no association between smoking and the presence of oral lesions. It is also necessary to mention that Alexio et al. and Gaurav et al. similarly have reported no relationship between these two variables (21, 31). The present study also showed that the long duration of smoking is due to the high possibility of oral manifestations occurrence. In the research done by Yengopal and Naidoo, the mean years of smoking in HIV-positive patients with oral lesions was higher than those without oral lesions (5); but this association, unlike our study, was not significant. Smoking can change innate immune responses with different mechanisms and Facilitate microbial colonization and infectious disease development in oral cavity. Also abnormal inflammation due to smoking can lead to the development of bone loss and periodontal disease(34). So, it appears when duration of smoking is long, high complications due to smoking on oral cavity and evolution of oral disease are also seen. Due to the adverse effects of smoking on oral health, smoking cessation should be emphasized in people with HIV.

There was not significant correlation between smokeless tobacco and pan use and oral manifestations in HIV-positive individuals; this finding is consistent with the study by Tami–Maury et al (28).

The present study found no significant association between the frequency of cleaning the mouth and the mode of oral hygiene and oral lesions occurrences. In contrast to this result, Ermias et al. recognized with complete similar items that people who frequently clean their mouth had significantly less oral manifestations(25). However, people with HIV should always be encouraged to oral hygiene, because it is obvious that oral hygiene is necessary for having a healthy mouth.

Most HIV positive patients with oral lesions were infected via blood. In addition, the proportion of people who were infected through sexual relations and had oral lesions was high compared to those without oral lesions; although this increase was not statistically significant; this finding is consistent with the study of Tami –Maury(28). High-risk sexual behavior and transmission of certain viral and fungal infections through genital area to the mouth are suggested as possible causes of oral lesions increase (6).

Sixty-nine percent of patients with oral manifestations were in HIV positive stage. The mean duration of HIV infection in people with oral lesions was 1.5 years longer than those without oral lesions; although, the association between disease stage and the duration of HIV infection and the presence of oral lesions were not statistically significant. In the study by Khatibi et al., people who were entered into AIDS stage and more time passed from their affection had significantly more oral-mucosal lesions (6). When HIV infection progresses into the AIDS, CD4+ T-cells reduce(4). Several studies have been shown of the relationship between decrease of CD4+ T-cells and increase of oral lesions (9, 18, 20). This means reduced level of immunity provides opportunities for development of various oral diseases.

Many studies have shown that the use of ART can result in lower incidence of oral manifestations in HIV-positive people (6, 35). Unlike these studies, ART have little effect on the prevalence of oral lesions in the present study. This finding may be due to improper time for beginning ART, irregular use of medications by patients or their impact on only some oral diseases.

The results of Ermias et al. showed that a significant association exists between oral lesions and weight loss in the last 6 months and BMI (25). However, in our study, although the number of people who had lost weight in the last 6 months and had oral lesions was more than people without oral lesions, this relationship was not significant. It must be acknowledged that oral lesions in HIV-positive people

result in weight loss in the one hand, and not receiving food causes damage to oral epithelial tissue in the other hand.

It must inserted that recommendation and prescriptions of oral treatment was initiated for all patients with oral manifestations and these patients was referred to oral medicine department of Zahedan dental faculty for other treatments and follow up.

Conclusion

More than half of patients with HIV had oral manifestations in the health centers in Zahedan University of Medical Sciences and the majority of these lesions are those associated with HIV. The strength points of this study were the assessment of numerous demographic factors in people with HIV and the presence of oral lesions was associated with some demographic factors such as age; hence, we suggest investigating the impact of demographic factors in larger populations. Also, it was better to various laboratory tests is performed simultaneously with oral examination but these tests were rather expensive and we have financial limitation. In the end, the need for dental care, dental examinations and timely diagnosis and treatment of oral lesions in order to prevent malnutrition and morbidity in patients with HIV must be emphasized alongside other therapies.

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