ORAL AND CONSTITUTIONAL MANIFESTATIONS OF HIV-INFECTED HOSPITAL PATIENTS IN NORTHERN VIETNAM

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Abstract. This study reports clinical features, with emphasis on oral lesions and constitutional signs, of 170 patients in a regional hospital in northern Vietnam, of whom 56 were HIV positive. The purpose of the study was to investigate the relationship of oral hairy leukoplakia (OHL) and oropharyngeal candidiasis (OPC) with HIV infection and late stage HIV disease. Late stage HIV disease was defined as WHO stage III or IV and/or a total lymphocyte count below 1,200 cells/mm^3. The 56 HIV positive patients included all patients with a positive HIV test between July 7th and September 9th 2002. A total of 114 HIV negative controls were included as well. All patients had a detailed medical history and examination as well as a thorough oral examination, which were all done without prior knowledge of the patient's HIV serostatus. HIV positive patients were then grouped according to WHO clinical stage and total lymphocyte count. Thirty-six patients (64.3%) out of 56 HIV positives were in WHO stage III+IV and 28 patients (50.0%) had a total lymphocyte count below 1,200 cells/mm^3. The presence of OPC, weight loss of more than 10% of body weight and/or chronic fever of more than one month's duration showed a significant association and high positive prediction with HIV infection, especially late stage HIV disease [all with odds ratio (OR) and 95% confidence interval (CI>1)]. The presence of OHL only showed a significant association with positive HIV serostatus and WHO stage III+IV. It can be concluded that in North Vietnam, HIV positive patients and patients suspected of having HIV infection would benefit from initial and repeat oral examinations. OPC, together with other signs of progressive infection (constitutional signs, such as weight loss and chronic fever) may serve as indicators for institution of prophylactic drugs against opportunistic infections and even antiretroviral (ARV) therapy, when available. However, further research is needed to demonstrate the role of OHL in HIV patients in North Vietnam.

INTRODUCTION

The first case of HIV-infection in Vietnam was reported in 1990 in Ho Chi Minh City. Since then the epidemic has grown rapidly to include all 61 provinces of the country. By the end of 2003 the estimated number of people living with HIV/AIDS was 220,000 out of a total population of 79 million. The highest prevalence of HIV-infection is found among intravenous drug-users and female sex workers. The northern provinces of Quang Ninh and Hai Phong have some of the highest reported prevalences in the country, with 0.5% and 0.3%, respectively (UNAIDS, 2004).

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In developed countries, the CD4+ count plus HIV RNA viral load are standard markers used as prognostic tools for progression of the disease. These investigations are expensive and demand sophisticated laboratory equipment, and in developing countries, where these diagnostic facilities are not readily available, there is a need for reliable surrogate markers. The relationship between oral lesions and HIV-infection is well established and has been classified in the EC Clearinghouse classification and diagnostic criteria for oral lesions in HIV infection (EC-Clearinghouse 1993). Both oropharyngeal candidiasis (OPC) and oral hairy leukoplakia (OHL) are included in the two globally accepted clinical case-definitions from the World Health Organization (WHO, 1990) and the Center for Disease Control and Prevention (CDC, 1992) in the US. The diagnosis of these two conditions is easy and

inexpensive due to their characteristic clinical appearance. Both OPC and OHL have been shown to be useful markers for the CD4+ count as well as for the viral load (Katz *et al*, 1992; Glick *et al*, 1994; Begg *et al*, 1997; Baqui *et al,* 1999; Ramirez-Amador *et al*, 2001; Birnbaum *et al*, 2002; Campo *et al*, 2002), and thus potential markers for both the diagnosis and monitoring of HIV-infection. Diagnosing OPC is also important in order to avoid the discomfort that follows, which might lead to further weight loss, dehydration and malnutrition (Heslin, 2001). Furthermore, OPC and OHL provide clues to the presence of other opportunistic infections, such as tuberculosis (TB), *Pneumocystis carinii* pneumonia (PCP) and cryptococcosis (Nittayananta *et al*, 2002).

Few results have been published regarding the relationship between oral lesions and HIV-infection in Southeast Asia, mostly from Thailand (Khongkunthian *et al*, 2001; Nittayananta *et al*, 2002; Kerdpon *et al*, 2004), Malaysia (Jing and Ismail, 1999), Hong Kong (Tsang and Samaranayake, 1999), Cambodia (Pichith *et al*, 2001; Bendick *et al*, 2002) and Singapore (Lim *et al*, 2001). In Vietnam, one study showed a 58% prevalence of OPC in IVDU's in Ho Chi Minh City in southern Vietnam but no cases of OHL (Follezou *et al*, 1999) and so far nothing has been published on this issue in northern Vietnam. The high prevalence provinces of Quang Ninh and Hai Phong, and other parts of northern Vietnam have a different geographical origin of the HIV epidemic when compared to the southern part of the country (Kato *et al*, 1999; Beyrer *et al*, 2000).

The purpose of this study was to investigate the relationship between oral lesions (oropharyngeal candidiasis and oral hairy leukoplakia) and HIV-infection in northern Vietnam, and to determine the value of these two conditions as markers of clinical and paraclinical disease progression. Different constitutional manifestations (weight loss, chronic diarrhea, chronic fever, nutritional status and subjective health perception) were included for similar analysis.

MATERIALS AND METHODS

Uong Bi Hospital is a regional hospital in the northern province of Quang Ninh in Vietnam that serves the provinces of Quang Ninh, Hai Phong and Hai Duong with an estimated population of over two million. The capacity of the hospital is 540 beds.

Between July 7th and September 9th, 2002, 56 HIV seropositive patients were examined, which included all patients that tested positive at the hospital in this period. The patients were recruited from the departments of internal medicine, infectious diseases and surgery as well as the outpatient department, and consisted of 52 men and 4 women. One hundred fourteen HIV seronegative controls were selected within the age-range of 15-40 years based on an estimated average age of 25-30 years for the HIV positive patients. The control group was selected to have the same relative distribution on the four different departments as the group of HIV positive patients. In this group there were 58 men and 56 women. Informed consent was obtained from each of the patients. Before the study was started, the Director of Uong Bi Hospital as well as the local Peoples Committee in Uong Bi district approved the protocol.

All patients were evaluated by the same clinician, who performed the HIV testing and, in the case of positive results, a full blood count (FBC) and differential count. The total lymphocyte count was used as a surrogate for the CD4+ count, since this test was not available. The total lymphocyte count has previously been shown to have significant correlation with the CD4+ count and to be a useful substitute in resource-limited settings (Blatt *et al*, 1993; Hosp *et al*, 2000; Kumarasamy *et al*, 2002; Mahajan *et al*, 2004). All patients were serologically HIV tested using a particle-agglutination assay for HIV-antibodies (Serodia, Fuji-Rebio, Tokyo, Japan) and two ELISA tests (Genescreen, NEN Research Products, Boston MA, USA; HIV-Uniform II Plus, Organon Teknika, Oss, The Netherlands).

Each patient was then assigned a number before being passed on to one of 3 examining clinicians who did not know the HIV serostatus of the patient. The examining clinicians did a full medical history and physical examination, including a thorough oral examination, following a specially designed form. Since oral health is influ-

enced by alcohol consumption, smoking and the use of antibiotics (Maier *et al*, 1994; Palacio *et al*, 1997; Shiboski *et al*, 1999), a history of these factors was also explored. Based on the oral examination, a diagnosis of OPC or OHL was made in accordance with the EC-Clearinghouse guidelines (EC-Clearinghouse, 1993).

A presumptive diagnosis of OPC was made from the characteristic appearance of the lesions (Leigh *et al*, 2004). Pseudomembranous OPC is characterized by the presence of white or yellow spots or plaques where the surface can be removed leaving a red bleeding surface. The erythematous form of OPC presents as red areas with a high rate of occurrence on the palate and dorsum of the tongue, which are occasionally mixed with white spots. Microscopy of a wet smear for the presence of *Candida* hyphae was done in cases of a presumptive clinical diagnosis of either of the two types of OPC; a positive result on this test was used as definitive diagnosis.

The diagnosis of OHL was made on clinical grounds only, based on the characteristic non-painful and non-removable white lesions on the lateral borders of the tongue (Leigh *et al*, 2004). This can be confirmed by biopsy with microscopy and demonstration of Epstein-Barr virus, but this was not technically possible. In most hospitals in developing as well as developed countries this is not common practice and OHL remains a clinical diagnosis.

Thus, all examinations were done in a way that could easily be implemented later under the existing technical and financial conditions of the public health system of most provinces in Vietnam.

Based on the medical history and physical examination, the HIV positive patients were categorized as being in either stage I, stage II or stage III+IV in accordance with the WHO clinical staging criteria (WHO, 1990), as shown in Table 1. As the diagnosis of many of the conditions listed in stage IV were not technically possible, patients in stage III and stage IV were pooled into stage III+IV. The total lymphocyte count was used to group patients as lymphocytopenic (total lymphocyte count <1,200 cells/mm^3) or non-lymphocytopenic (total lymphocyte count ≥1,200 cells/mm^3). The body mass index [BMI = Weight in kg / (height in m)^2] was calculated as an indicator of the nutritional status of each patient. The normal cut-off value for underweight was modified from 20 to 18 in order to fit with the normal constitution of the Vietnamese population.

The statistical significance of the investigated oral and constitutional manifestations was then calculated as the odds ratio (OR) with 95% confidence interval (CI). In a few cases this was not possible due to the distribution of the numbers, and the Fisher's exact test was then used to calculate a p-value.

RESULTS

Of the 56 HIV positive patients, 52 were male and 4 were female. The mean age in this group was 27.8 years (range 16-39 years). In the HIV negative group, 58 patients were women and 56 were men, with an overall mean age of 26.2 years (range 14-42 years).

None of the HIV positive patients received any antiretroviral treatment. The distribution of oral lesions according to HIV serostatus is shown in Table 2. The association between the results and late WHO stages (stage III+IV) as well as lymphocytopenia is shown within the group of HIV positive patients in Tables 3 and 4. Also listed are constitutional signs (weight loss, chronic diarrhea and chronic fever), nutritional status, subjective health perception and the different factors that might influence the oral health of the patients. In 10 patients, of whom 5 were HIV positive, it was not possible to measure the BMI due to the condition of the patients.

In the patients studied, oral lesions were only present in HIV infected patients in WHO stage III+IV and only one patient presented with two oral lesions. In the groups of patients with oropharyngeal candidiasis (N=21), oral hairy leukoplakia (N=9), and constitutional signs (N=85), the majority were HIV positive and had progressed to late stage disease (WHO stage III+IV or a total lymphocyte count below 1,200 cells/mm^3).

Patients with OPC (N=21), OHL (N=9), weight loss more than 10% of body weight

Table 1
WHO staging system for HIV infection.

Stage 1: - Persistent generalized lymphadenopathy And/or performance scale 1: Asymptomatic, normal activity Stage 2: - Weight loss between 5% and 10% of body weight - Minor mucocutaneous lesions (seborrhoic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular stomatitis) - Herpes zoster within the past 5 years - Recurrent upper airway infections (*eg* Bacterial sinusitis) And/or performance scale 2: Symptomatic, normal activity Stage 3: - Weight loss of more than 10% of body weight - Oral candidiasis - Oral hairy leukoplakia - Unexplained chronic diarrhea for more than 1 month - Unexplained prolonged fever (intermittent or constant) for more than 1month - Pulmonary tuberculosis within the past year - Severe bacterial infections (*eg* Pneumonia, pyomyositis) And/or performance scale 3: Bedridden for less than 50% of the day during the last month	Stage 4[a]: - HIV wasting syndrome[b] - *Pneumocystis carinii* pneumonia - (Toxoplasmosis of the brain) - (Cryptosporidiosis with diarrhea for more than 1 month) - (Cryptococcosis, extrapulmonary) - (Cytomegalovirus infection of an organ other than liver, spleen, or lymph nodes) - (Herpes simplex virus infection, - mucocutaneous for more than 1 month or visceral of any duration) - (Progressive multifocal leucoencephalopathy) - (Any disseminated endemic mycosis) - (Candidiasis of the esophagus, trachea, bronchi, or lungs) - (Atypical mycobacteriosis, disseminated) - (Non-typhoidal *Salmonella* septicemia) - (Extrapulmonary tuberculosis) - Lymphoma - Kaposi sarcoma - HIV encephalopathy[c] And/or performance scale 4: Bedridden for more than 50% of the day during the last month

[a]Brackets indicate that the diagnosis was not technically or practically possible.
[b]Defined by the CDC as weight loss of greater than 10% of body weight, plus either unexplained prolonged fever (for more than 1 month) or chronic weakness and unexplained prolonged fever (for more than 1 month).
[c]Defined by the CDC as clinical findings of disabling cognitive dysfunction and/or motor dysfunction, interfering with activities of daily living, progressing over weeks to months in the absence of concurrent illness or condition other than infection with HIV that could explain the findings.

(N=41), chronic fever of more than one month duration (N=17), low BMI (N=72) and poor subjective health perception (N=45) all showed a significant association with positive HIV serostatus. Specificity and positive predictive values were generally high (>70%) except for low BMI. Sensitivity was lower, ranging from 16% (OHL) to 59% (low BMI).

OPC (N=21), weight loss of more than 10% of the body weight (N=29), chronic fever of more than one month duration (N=13), a low BMI (N=33) and poor subjective health perception (N=29) all showed a significant association with progression to late-stage disease within the group of HIV positive patients. This was true both when progression was measured as WHO stage III+IV and a total lymphocyte count below 1,200 cells/mm^3. The diagnosis of OHL (N=9) was only significantly higher with late WHO stages and for patients without lymphocyte counts. Again specificity and positive predictive value were higher than sensitivity. Generally, the diagnostic value of the different manifestations were higher when HIV progression was measured as WHO stage III+IV than when measured as lymphocytopenia.

The difference in the prevalence of smoking and alcohol abuse was only significant be-

Table 2
Prevalence of oral lesions, constitutional signs and subjective health perceptions in the investigated cohort according to HIV serostatus.

	Total		HIV serostatus						
			Negative		Positive				
	No.	%	No.	%	No.	%	OR	95% CI	p
Total	114	170	100	67.1	56	32.9			
Oral lesions									
OPC	21	12.4	0	0	21	37.5	-	-	<0.01
OHL	9	5.3	0	0	9	16.1	-	-	<0.01
Constitutional signs									
Weight loss	41	24.1	12	10.5	29	51.8	9.1	4.1-20.2	-
Chronic diarrhea	5	2.9	2	1.8	3	5.4	3.2	0.5-19.5	-
Chronic fever	17	10	4	3.5	13	23.2	8.3	2.6-26.9	-
BMI ≤18[a]	72	42.4	39	34.2	33	58.9	2.8	1.4-5.3	-
Health perception[b]									
Good	24	14.1	19	16.7	5	8.9	0.5	0.2-1.4	-
Fair	101	59.4	79	69.3	22	39.3	0.3	0.2-0.6	-
Poor	45	26.5	16	14	29	51.8	6.6	3.1-13.9	-
Oral risk factors									
Smoking	92	54.1	41	36	51	91.1	18.2	6.7-49.1	-
Alcohol abuse	52	30.6	28	24.6	24	42.9	2.3	1.2-4.6	-
IV drug use	48	28.2	9	7.9	39	69.6	26.8	11.0-65.0	-
Antibiotic use	45	26.5	28	24.6	17	30.4	1.3	0.7-2.7	-

[a]BMI = Weight in kg / (height in m)^2.
[b]Health perception indicates the patient's subjective statement on perceived health status.
OR = Odds Ratio (with 95% confidence interval included).
p = p-value calculated using Fisher's exact test.

tween the group of HIV positive patients and the group of HIV negative patients. Within the group of HIV positive patients, the prevalence of smoking and alcohol abuse did not show significant variation between the different sub-groups. There was no significant difference in the use of antibiotics between any of the groups.

The conditions that showed a significant association with HIV infection and late stage HIV disease have been summarized in Table 5 according to their diagnostic importance.

DISCUSSION

This study demonstrated the clinical usefulness of 6 clinical markers in the diagnosis of HIV infection as well as late stage HIV disease in northern Vietnam. These 6 markers were OPC of any type (pseudomembranous or erythematous), OHL, recent weight loss of more than 10% of the body weight, chronic fever of more than one month's duration, BMI below 18 and subjective health perception stated as poor.

The oral manifestations both had very high specificities and positive predictive values (PPV) for HIV infection and progression to WHO stage III+IV in HIV infected patients. However, only OPC showed a significant relationship to lymphocytopenia, and in this case specificity (79%) and PPV (67%) were both lower. The sensitivity was medium or low in all cases. The lack of association between OHL and lymphocytopenia is in contrast to most other studies where this condition has been shown to be almost patognomic of HIV infection and disease progression. As mentioned above, this lack of association was also found in Ho Chi Minh City in a previous study (Pichith *et al*, 2001).

Table 3
Prevalence of oral lesions, constitutional signs and subjective health perceptions among HIV positive patients according to WHO stage.

	WHO stage						
	I+II[c]		III+IV[c]				
	N	%	N	%	OR	95% CI	p
Total	20	35.7	36	64.3			
Oral manifestations							
OPC	0	0	21	58.3	-	-	<0.01
OHL	0	0	9	25	-	-	0.012
Constitutional manifestations							
Weight loss	0	0	29	80.6	-	-	<0.01
Chronic diarrhea	0	0	3	8.3	-	-	0.258
Chronic fever	0	0	13	36.1	-	-	<0.01
BMI ≤18[a]	5	25	28	77.8	10.5	2.9 -37.8	-
Health perception[b]							
Good	3	15	2	5.6	0.3	0.1 -2.2	-
Fair	15	75	7	19.4	0.1	0.0 -0.3	-
Poor	2	10	27	75	27	5.2 -139.8	-
Oral risk factors							
Smoking	18	90	33	91.7	1.2	0.2 -8.0	-
Alcohol abuse	9	45	15	41.7	0.9	0.3 -2.6	-
IV drug use	11	55	28	77.8	2.9	0.9 -9.3	-
Antibiotic use	4	20	13	36.1	2.3	0.6 -8.2	-

[a]BMI = Weight in kg / (height in m)^2.
[b]Health perception indicates the patient's subjective statement on perceived health status.
[c]The WHO stages I to IV have been pooled in Stages I+II and III+IV.
OR = Odds Ratio (with 95% confidence interval included).
p = p-value calculated using Fisher's exact test.

Of the different constitutional signs, weight loss and chronic fever were the most useful in the diagnosis of HIV infection and late stage HIV disease. The findings of a BMI ≤18 and subjective health perception both had generally lower diagnostic validity, but showed the highest values in predicting late WHO stages.

Thus the most useful result were the demonstration of the diagnostic value of oropharyngeal candidiasis, weight loss and chronic fever, especially in predicting late stage HIV disease.

HIV testing facilities are, in general, available in all major hospitals in Vietnam. Finding the conditions mentioned above should therefore guide the attention of the involved healthworkers to the possibility of HIV infection and further testing. Furthermore, in a known HIV positive patient, the conditions could serve as an easy tool in directing initiation of antiretroviral therapy (ARV) as well as prophylaxis/treatment of emerging/concurrent opportunistic infections. Finally, it is important to recognize the oral lesion in order to relieve the discomfort and general deterioration that follows.

In neighboring Thailand, one study showed that oral lesions could serve as specific clinical markers for tuberculosis (TB) and *Pneumocystis carinii* pneumonia (PCP) (Nittayananta *et al*, 2002). The prevalence of TB in Vietnam ranks as number 13 in the world, and the national DOTS program is the only one on the list of "WHO TB high burden countries" that meets the WHO standards for case detection and DOTS-treatment (WHO, 2004). Both a need and the capacity for detection and treatment of TB in HIV positive patients is thus clearly present, and oral

Table 4
Prevalence of oral lesions, constitutional signs and subjective health perceptions among HIV positive patients according to total lymphocyte count.

	Total lymphocyte count						
	≥1,200 cells/mm^3		<1,200 cells/mm^3				
	N	%	N	%	OR	95% CI	p
Total	33	58.9	23	41.1			
Oral manifestations							
OPC	7	21.2	14	60.9	5.8	1.8-18.9	-
OHL	3	9.1	6	26.1	3.5	0.8-16.0	-
Constitutional manifestations							
Weight loss	13	39.4	16	69.6	3.5	1.1-10.9	-
Chronic diarrhea	0	0	3	13	-	-	0.064
Chronic fever	2	6.1	11	47.8	14.2	2.7-73.8	-
BMI ≤18[a]	14	42.4	19	82.6	6.4	1.8-23.2	-
Health perception[b]							
Good	4	12.1	1	4.3	0.3	0.0-3.2	-
Fair	16	48.5	6	26.1	0.4	0.1-1.2	-
Poor	13	39.4	16	69.6	3.5	1.1-10.9	-
Oral risk factors							
Smoking	31	93.9	20	87	0.4	0.1-2.8	-
Alcohol abuse	17	51.5	7	30.4	0.4	0.1-1.3	-
IV drug use	24	72.7	15	65.2	0.7	0.2-2.2	-
Antibiotic use	7	21.2	10	43.5	2.9	0.9-9.2	-

[a]BMI = Weight in kg / (height in m)^2.
[b]Health perception indicates the patient's subjective statement on perceived health status.
OR = Odds Ratio (with 95% confidence interval included).
p = p-value calculated using Fisher's exact test.

Table 5
Validity of oral and constitutional manifestations for the diagnosis of HIV infection and progression of HIV disease measured as WHO stage and lymphocytopenia.

	HIV infection			WHO stage III+IV			Lymphocytopenia[c]		
	SPE	SEN	PPV	SPE	SEN	PPV	SPE	SEN	PPV
OPC	100	37.5	100	100	58.3	100	78.8	60.9	66.7
OHL	100	16.1	100	100	25	100	NS	NS	NS
Weight loss	89.5	51.8	70.7	100	80.6	100	60.6	69.6	55.2
Chronic fever	96.5	23.2	76.5	100	36.1	100	93.9	47.8	84.6
BMI ≤18[a]	65.8	58.9	45.8	75	77.8	84.9	57.6	82.6	57.6
Health perception poor[b]	90	51.8	64.4	90	75	93.1	60.6	69.6	55.2

[a]BMI = Weight in kg / (height in m)^2.
[b]Health perception indicates the patient's subjective statement on perceived health status.
[c]Total lymphocyte count <1,200 cells/mm^3.
SEN = Sensitivity; SPE = Specificity; PPV = Positive predictive value.

lesions can serve as useful markers for further diagnostic investigations as well as prescription of prophylactic antibiotic therapy. This study only demonstrated three cases of active pulmonary TB, and further investigations will be needed to cast light on this issue.

Co-trimoxazole is a cheap and widely available drug. Besides its effect on PCP, it is also effective in the treatment of toxoplasmosis, another opportunistic infection seen in HIV positive patients. The diagnosis of OPC or OHL can be used as a clinical indicator for the initiation of prophylactic therapy.

Treatment of oropharyngeal candidiasis is usually done with azoles, such as clotrimazole topically and fluconazole or itraconazole systemically. Amphotericin B is an option for fluconazole-resistant cases (Vazquez, 2000; Patton *et al*, 2001). In fluconazole-resistant cases, replacement of *Candida albicans* with *Candida dubliniensis* should be kept in mind as a reason for antimycotic resistance (Jabra-Rizk *et al*, 2001; Gutierrez *et al*, 2002; Martinez *et al*, 2002). A cheap and widely available treatment of OPC is topical use of a sodium benzoate solution (Moshi *et al*, 1998). OHL is usually asymptomatic, and no specific treatment is necessary. If symptoms become bothersome, symptoms can often be temporarily relieved with topical podophyllin or systemic acyclovir (Greenspan and Greenspan, 1989).

With the possible future introduction of ARV therapy in Vietnam, it is important to have guidelines for the selection of patients who should receive treatment. In countries where the CD4+ count is generally available, WHO has recommended a cut-off point of 200 cells/mm^3 irrespective of the clinical status of the patient. When CD4+ count monitoring is unavailable, it has been recommended in the same guidelines that patients in WHO stage IV or patients in WHO stage II-III with a total lymphocyte count below 1,200 cells/mm^3 should receive ARV treatment (WHO, 2002). The diagnosis of OPC, and the presence of weight loss and chronic fever would thus be simple tools for the selection of candidates for ARV treatment.

A potential problem with the use of oral conditions in diagnosis is the fact that both clinicians (Cruz *et al*, 1996; Hilton *et al*, 2001) and patients (Patton, 2001) have been shown to under-diagnose these conditions to some extent. Therefore, it would be appropriate to educate patients in self-reporting as well as to emphasize the importance of oral lesions in official guidelines for the management of HIV infection. The large difference between the male:female ratios (M:F) in the HIV positive patients (M:F = 13:1) and the HIV negative patients (M:F = 1:1) may indicate selection bias. This would only affect the comparison between HIV positive and HIV negative patients though. A large proportion of the patients were recruited in the outpatient department. For most of these patients it was not feasible to arrange an appointment for further questioning or examination. Therefore, it was not generally possible to obtain more information regarding medications other than ARV treatment and/or general antibiotic therapy, even though specific information regarding antifungal drugs and acyclovir would have been relevant.

This study found a significant positive predictive value for OPC and major constitutional signs with HIV infection and late stage HIV disease. It can be concluded that all HIV patients should have a thorough oral examination and be educated to report any changes in oral health to their physician, in order to time the institution of relevant prophylactic therapy and ARV therapy if this is an option.

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