Oral Diseases (2004) 10, 138–144

http://www.blackwellmunksgaard.com

HIV Disease/Oral Medicine

Oral manifestations of HIV infection in relation to clinical and CD4 immunological status in northern and southern Thai patients

D Kerdpon[1], S Pongsiriwet[2], K Pangsomboon[1], A Iamaroon[2], K Kampoo[1], S Sretrirutchai[3], A Geater[4], V Robison[5]

[1]*Stomatology Department, Faculty of Dentistry, Prince of Songkla University, Haadyai, Songkhla, Thailand;* [2]*Department of Odontology and Oral Pathology, Faculty of Dentistry, Chiang Mai University, Chiang mai, Thailand;* [3]*Department of Pathology, Faculty of Medicine, Prince of Songkla University, Songkla, Thailand;* [4]*Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkla, Thailand;* [5]*Johns Hopkins School of Hygiene and Public Health, Department of Epidemiology, Baltimore, Maryland, USA*

OBJECTIVES: To assess prevalence and variations in the oral manifestations of HIV in HIV-infected subjects in southern Thailand (a new HIV epidemic) and northern Thailand (a mature epidemic), and the association with age, sex, risk behaviours, CD4 count and medication used.

SUBJECTS AND METHODS: A total of 102 and 135 HIV-infected individuals were enrolled in northern and southern hospitals, respectively. Oral and haematological examination was performed after sociodemographic interview of the patients. Clinical history was retrieved from patients' medical records.

RESULTS: Oral candidiasis (OC, 55%), oral hairy leucoplakia (OHL, 21%) and HIV-associated-periodontal disease (14%) were among the most common oral lesions in southern Thailand. OHL (38%), OC (25%), HIV-associated-periodontal disease (15%) were the three most common lesions in the north. A significant association was found between any oral lesion, OC, particularly the pseudomembranous type (PC), and CD4 < 200 cells mm^{-3} at both sites. A negative relationship was found between systemic antifungal treatment and OC including PC and erythematous candidiasis (EC) in the southern data. OHL showed a positive relationship with male sex and a negative relationship with antiretroviral treatment in the northern site. Younger age and being a current smoker were positively associated with oral lesions in the southern group.

CONCLUSION: OC, particularly PC, could be useful as a marker for immunosuppression, particularly where CD4 count cannot be determined routinely. Antifungal treatment is of benefit in the subjects who cannot afford highly active antiretroviral therapy (HAART).
Oral Diseases (2004) **10**, 138–144

Keywords: HIV; AIDS; CD4; oral manifestations; Thailand

Correspondence: Duangporn Kerdpon, Stomatology Department, Faculty of Dentistry, Prince of Songkla University, Haadyai, Songkhla 90112, Thailand. Tel.: 66 74 429878, Fax: 66 74 212922, E-mail: kduangpo@ratree.psu.ac.th
Received 13 June 2003; revised 5 November 2003; accepted 17 November 2003

Introduction

Human immunodeficiency virus (HIV) infection is a devastating disease which produces serious socioeconomic effects and changes in population structures worldwide. In Thailand, the rate of HIV transmission increased following the first national serosurveillance study in 1989, then steadied and began to decline in 1993–95. The HIV epidemic in Thailand varies according to region of the country. There is evidence that the HIV epidemic has matured and declined in northern Thailand, yet trends are less clear in other parts of the country, where the epidemic appears to be growing among some groups. An increased prevalence in pregnant women (1.7%) and in donated blood (0.44%) in 1999 may be a sign of a re-emergence of HIV transmission among the general population (Division of Epidemiology, Ministry of Public Health, 2000).

The epidemiology and oral manifestations of HIV infection are comprehensively documented in the literature from the west (Palmer *et al*, 1996; Patton *et al*, 1998; Margiotta *et al*, 1999). The Asian countries, which show a somewhat higher HIV prevalence and different patterns of transmission compared with the west, have fewer reports (Nittayananta and Chungpanich, 1997; Ranganathan *et al*, 2000; Khongkunthian *et al*, 2001; Bendick, Scheifele and Reichart, 2002). Some reports

from Thailand (Nittayananta and Chungpanich, 1997; Khongkunthian *et al*, 2001; Nittayananta *et al*, 2001) have documented the prevalence of oral lesions in HIV/AIDS with varying results. Specific common oral lesions have been documented to be related with immune suppression as indicated by CD4 depletion, medication used, oral habits and risk behaviour. This finding has implications for diagnosis, prognosis, therapy and transmission during the course of HIV infection (Glick *et al*, 1994; Margiotta *et al*, 1999; Patton, 2000). None of the Thai or southeast Asian studies have reported the relationship of oral lesions and immune status as indicated by CD4 count that has prognostic and therapeutic implications in these patients. The aims of the present study, therefore, were to describe oral manifestations in HIV-infected individuals and to examine their relationship to important markers such as CD4 count, medications used, age, sex, oral habits and risk behaviours. The present study was designed to investigate HIV patients in two regions: northern Thailand, which has a mature epidemic and a high prevalence of HIV infection, and southern Thailand, which has a newer epidemic and a much lower prevalence in the general population (Division of Epidemiology, Ministry of Public Health, 2000).

Subjects and methods

This cross-sectional study was a collaboration between the two dental faculties of Prince of Songkla University and Chiang Mai University, the only dental faculties in southern and northern Thailand, respectively. The stage of HIV infection was classified according to established criteria (Centers for Disease Control and Prevention (CDC), 1992). The EC-Clearinghouse's classification and diagnostic criteria for oral lesions in HIV infection (EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Human Immunodeficiency Virus, 1993), were used in the study. Calibration of the oral examiners and the interviewers was performed at the beginning and after a pilot study. Patients in the northern study were examined by two of the authors (SP and AI) whereas patients in the southern study were examined by DK. All three examiners are oral medicine and oral pathologist specialists who are familiar with oral lesions associated with HIV infection. The oral examiners also provided complementary oral medicine treatment or further investigation according to the oral lesions/condition of the patient. Thus the diagnosis was confirmed by a relevant investigation and a response of the patient to specific treatment. The study was conducted between April and November 1999 under the approval of the Ethics Committee of each hospital. All HIV-infected clinic attendees were offered participation and provided written informed consent before enrolment in this study. They were privately interviewed to obtain sociodemographic information using a structured questionnaire prior to oral examination. Absolute CD4 count was obtained on the date of the oral examination. Clinical history was obtained from patients' medical records. The northern study was carried out on a total of 102 HIV-infected cases. Of these, there were 58 patients from the Maharaj Nakorn Chiang Mai University Hospital and 44 patients from Sansai Community Hospital, Chiang Mai Province. The southern study was conducted on 135 HIV-seropositive subjects who attended the HIV Clinic, Hatyai Regional Hospital (123 cases), Songkla Province and Satun General Hospital, Satun Province (12 cases). All patients were diagnosed to have HIV infection by positive enzyme-linked immunosorbent assay (ELISA) and western blot confirmation test.

Epi Info Version 6.04 b (CDC, Atlanta, GA, USA) was used for double data entry. Statistical analysis was performed using STATA software (Stata Corp 2001 Statistical Software, Release 7.0, Stata Corporation, College Station, TX, USA). Associations between subject variables and each type of oral lesion were analysed using logistic regression.

Results

The distributions of demographic and clinical characteristics of HIV-seropositive patients at both research sites are shown in Table 1. The ratios of male to female in the north and south were opposite, with females being a majority in the north (74%), and males a majority in the south (70%). In the north, 54 of the 75 (72%) females were widows and five of the 27 males (19%) were widowers. The age ranges in the north and south were 21–58 and 20–64 years, respectively, with a similar peak of age distribution (31–40 years). A median age in the north and south study groups was 32 years. Sexual transmission was the most common route of transmission at both sites. Generally, the northern group had samples with higher absolute CD4 counts than the southern group.

Patients from the northern site included a lower proportion of those with a history of smoking [23 (23%) *vs* 62 (46%)] or alcohol drinking [15 (15%) *vs* 68 (50%)] than those in the southern site. There were 22 (16%) and seven (7%) current smokers, and 10 (7%) and one (1%) current alcohol drinkers in the southern and the northern group, respectively. Antiretroviral medication, included zidovudine (AZT), didanosine (ddl), lamivudine (3TC) or stavudine (d4T) in combination or as monotherapy, was taken by 40 (30%) of the southern patients and 34 (33%) of the northern patients. Systemic antifungal treatment such as ketoconazole, itraconazole or fluconazole was prescribed in 20 (15%) and seven (7%) of the southern and northern patients, respectively.

Oral lesions were present in 104 (77%) patients of the southern group and in 71 (70%) of the northern group. The three most common oral lesions in the southern study were oral candidiasis (OC, 55%), oral hairy leucoplakia (OHL, 21%) and HIV-associated-periodontal disease (14%), whereas OHL was the most common in the northern study (38%), followed by OC (25%), and HIV-associated-periodontal disease (15%) (Table 2).

Table 1 Distribution of demographic, clinical and immunological characteristics, by study site

Variables	*Category*	*South (%)*	*North (%)*
Sex	Male	94 (70)	27 (26)
	Female	41 (30)	75 (74)
Age	20–30 years	50 (37)	39 (38)
	31–40 years	63 (47)	53 (52)
	41–50 years	18 (13)	7 (7)
	51–64 years	4 (3)	3 (3)
Marital status	Single	40 (30)	13 (13)
	Married	78 (58)	26 (25)
	Divorced	10 (7)	4 (4)
	Widowed	7 (5)	59 (58)
Level of education	No school	2 (1)	1 (1)
	Primary school	50 (37)	61 (60)
	Secondary school	53 (39)	21 (21)
	Vocational school	13 (10)	11 (11)
	University	17 (13)	8 (8)
Occupation	General worker	39 (29)	66 (65)
	Unemployed	25 (19)	12 (12)
	Civil service	20 (15)	4 (4)
	Farmer-gardener	15 (11)	12 (12)
	Business	11 (8)	6 (6)
	Housewife	10 (7)	0
	Fisherman	6 (4)	0
	Other	9 (7)	2 (2)
Risk behaviour	Sexual contact only	106 (79)	99 (97)
	Sexual & IV	4 (3)	0
	IV only	4 (3)	1 (1)
	Unidentified	21 (16)	2 (2)
Absolute CD4 count	<200 cells mm^{-3}	90 (67)	45 (44)
	200–499 cells mm^{-3}	26 (19)	40 (39)
	≥ 500 cells mm^{-3}	14 (10)	17 (17)
	Not determined	5 (4)	0

Percentages may not add to 100 because of rounding.

Table 2 Distribution of oral lesions, by study site

Oral lesions	*South (%)*	*North (%)*
Candidiasis[a]	74 (55)	25 (25)
Pseudomembranous	57 (42)	15 (15)
Erythematous	34 (25)	18 (18)
Angular cheilitis	5 (4)	3 (3)
Hairy leucoplakia	29 (21)	39 (38)
HIV-associated-periodontal disease[a]	19 (14)	15 (15)
Linear gingival erythema	16 (12)	15 (15)
Necrotizing (ulcerative) gingivitis	1 (1)	2 (2)
Necrotizing (ulcerative) periodontitis	2 (1)	0
Salivary gland enlargement	1 (1)	1 (1)
Herpes labialis	1 (1)	1 (1)
Recurrent aphthous stomatitis	4 (3)	7 (7)
Ulceration (not otherwise specified)	4 (3)	0
Histoplasmosis	1 (1)	0

[a]Some cases had more than one sub-type of lesion.

Table 3 shows those factors (age, sex, CD4 count, medications used and oral habits) which were independently associated with specific oral lesions according to study site. Smoking and younger age were found to be positively associated with the presence of oral lesion in the southern group. OC, including pseudomembranous candidiasis (PC) and erythematous candidiasis (EC), had a negative relationship with systemic antifungal treatment in the southern data. CD4 count of less than 200 cells mm^{-3} showed a strong association with the presence of any oral lesion and OC but not with HIV-associated-periodontal disease in both study sites. The evidence for association between lower CD4 count and EC is weaker than that for PC in the southern data. No EC was present in subjects with CD4 count more than 500 cells mm^{-3} in the northern study. There is weak evidence of an association between decreased CD4 count and oral hairy leucoplakia (OHL) in the northern study (trend OR = 2.08, 95% CI 1.03–4.19, P for trend = 0.053). No OHL was present in those who had CD4 count of more than 500 cells mm^{-3} in the south. In the northern study, males were more likely than females to have OHL and there was an inverse relationship between antiretroviral treatment and OHL.

Table 4 shows factors associated with the number of oral lesions. Decreased CD4 count was associated with an increased number of oral lesions in the southern but not in the northern site. Those who received antiretroviral treatment had progressively lower relative risk of having one or more lesions in the northern study, while a similarly reduced relative risk was associated with antifungal treatment among the southern study subjects.

Discussion

The sex difference between our two populations was striking and reflects different stages in Thailand's HIV epidemic. The predominance in the northern study of female subjects and widows results from a regional variation in HIV epidemiology in which the wave of infection began earlier in northern Thailand. In Thailand's heterosexually transmitted epidemic, men first acquire HIV from commercial sex workers and then pass the virus on to their wives. The age distribution was similar between the two groups and comparable with other Thai and Asian studies (Nittayananta and Chungpanich, 1997; Bendick *et al*, 2002). The group from the south seems to have a higher level of education than the north – 38% of the southern group had no school or only primary school compared with 61% in the northern group. The level of education may affect their occupation. The northern group had a high percentage of general workers (65%) compared with less than 30% in the south. Irrespective of age, sex and level of education, sexual contact, especially heterosexual was still the major route of transmission. The peak distribution (31–40 years) and the predominance of sexual transmission are important characteristics of our two study populations and are relevant to the status of Thailand's HIV epidemic and its prevention. A high prevalence of HIV-infection in the working age group could lead to a decrease in the workforce and have an adverse affect on the socioeconomic status of the country. This finding indicates that sustained efforts of the national programme for HIV control, the '100% Condom Program', to promote condom use among patrons of commercial sex workers are still needed, even though the programme has resulted in an overall decline in HIV transmission

Table 3 Variables associated with oral lesions in HIV-infected patients, by study site

		South			*North*		
Lesions	*Variable*	*aOR*	*95% CI*	*P-value*[a]	*aOR*	*95% CI*	*P-value*[a]
Any oral lesion	Age group[b]	0.24	0.08–0.78	0.0405			
	Current smoking	3.58	1.31–9.77	0.0115			
	CD4 200–499 cells mm^{-3}	3.88	0.87–17.37	0.0208	1.52	0.49–4.76	0.0004
	CD4 < 200 cells mm^{-3}	6.56	1.75–24.60		9.00	2.38–34.1	
Oral candidiasis	Systemic antifungal treatment	0.13	0.04–0.40	0.0001			
	CD4 200–499 cells mm^{-3}	2.84	0.63–12.71	0.0003	3.39	0.38–30.0	0.0090
	CD4 < 200 cells mm^{-3}	9.54	2.42–37.70		9.71	1.18–80.0	
Pseudomembranous	Systemic antifungal treatment	0.18	0.06–0.60	0.0021			
	CD4 200–499 cells mm^{-3}	1.87	0.32–10.80	0.0002	0.84	0.07–9.96	0.0086
	CD4 < 200 cells mm^{-3}	8.80	1.84–42.20		5.82	0.69–48.70	
Erythematous	Systemic antifungal treatment	0.10	0.01–0.79	0.0034			
	CD4 200–499 cells mm^{-3}[c]	5.02	0.55–45.90	0.1098			
	CD4 < 200 cells mm^{-3}	6.09	0.75–49.30		3.09	1.06–9.04	0.0337
HIV-associated-periodontitis	Antiretroviral treatment	0.28	0.06–1.31	0.0664			
	CD4 200–499 cells mm^{-3}	1.45	0.13–15.9	0.7975	0.19	0.04–0.94	0.1121
	CD4 < 200 cells mm^{-3}	1.86	0.22–15.9		0.44	0.12–1.65	
Hairy leucoplakia	Female				0.25	0.09–0.75	0.0103
	Antiretroviral treatment				0.16	0.05–0.55	0.0019
	CD4 200–499 cells mm^{-3}[d]				3.22	0.57–18.1	0.0930
	CD4 < 200 cells mm^{-3}	2.26	0.79–6.49	0.1081	5.45	1.00–29.8	

aOR, Adjusted odds ratio; CI, Confidence interval.
[a]*P*-value from likelihood ratio on removal of the variable from the model.
[b]Age group filled as a trend variable across age groups shown in Table 1.
[c]No erythematous candidiasis present in those with CD4 count more than 500 cells mm^{-3} in the north study.
[d]No patient with CD4 ≥ 500 cells mm^{-3} had hairy leucoplakia from southern data.

Table 4 Variables associated with number of oral lesions in HIV-infected patients, by study site

	No lesion vs one lesion		*Two or more lesions vs one lesion*		
Variable	*RRR*	*95% CI*	*RRR*	*95% CI*	*P-value*
South					
Antifungal treatment	3.00	0.97–9.27	0.15	0.02–1.32	0.0031
CD4 200–499 cells mm^{-3}	0.39	0.09–1.66	1.86	0.16–21.2	0.0013
CD4 < 200 cells mm^{-3}	0.11	0.03–0.43	2.18	0.23–20.7	
North					
Antiretroviral treatment	2.77	0.88–8.72	0.54	0.14–2.13	0.0521
CD4 200–499 cells mm^{-3}	0.64	0.16–2.58	0.69	0.12–4.08	0.1236
CD4 < 200 cells mm^{-3}	0.24	0.06–1.02	0.91	0.17–4.92	

RRR, Relative risk ratio; CI, Confidence interval.
P-value from likelihood ratio on removal of the variable from the model.

(Celentano *et al*, 1998). This promotion should be applied to those who are not spouses.

Oral lesions were highly prevalent in both northern and southern Thailand. OC, OHL and HIV-associated-periodontal disease were among the most common oral lesions found in this study. It should be noted that some oral lesions such as Kaposi's sarcoma (KS), non-Hodgkin's lymphoma and penicilliosis are not prevalent in this study or other Asian studies (Anil and Challacombe, 1997; Ranganathan *et al*, 2000; Khongkunthian *et al*, 2001) which all together have included a total of 808 patients with at least 36% AIDS cases. Another two Asian studies, of 133 HIV and AIDS patients, did not report these oral lesions (Tsang and Samaranayake, 1999; Bendick *et al*, 2002). Only one study, of 124 Thai AIDS patients, reported oral lesions of non-Hodgkin's lymphoma in five (4%) and penicilliosis in two (2%) (Nittayananta and Chungpanich, 1997). Further large sample size studies on oral penicilliosis in AIDS patients and in those with disseminated infection in endemic areas will provide more insight into the prevalence and risk factors for the oral lesions. Data from major centres in each region of Thailand and other southeast Asian countries will provide more reliable prevalence estimates of rare oral diseases including deep fungal infection and non-Hodgkin's lymphoma in HIV-infected patients.

The result of the present study is consistent with the finding that oral KS has not been reported from Asian studies where heterosexual intercourse is the major route of HIV transmission (Anil and Challacombe, 1997; Nittayananta and Chungpanich, 1997; Tsang and Samaranayake, 1999; Ranganathan *et al*, 2000).

The northern study had a lower percentage of patients who presented with oral lesions than the southern study, most likely caused by a generally higher CD4 count in the northern group. A higher proportion of patients with a smoking and drinking history was found in the southern site, possibly because of the predominance of females in the northern study population.

The literature on HIV-associated oral lesions has reported widely different prevalence estimates for specific lesions. These differences may be a result of variations in study populations such as race, socioeconomic status, sex, route of transmission, stage of HIV infection and access to drug therapy, and also to variations in study design and diagnostic criteria. Likewise, in our study, the differences in oral lesions in the southern and northern study groups are likely a result of some of the factors mentioned above, rather than to geographical site.

A relationship between age and the presence of oral lesions in HIV-infected patients has been reported (McCarthy *et al*, 1991; Hilton *et al*, 1997; Nittayananta *et al*, 2001; Campo *et al*, 2002). Hilton *et al*, 1997 observed higher odds of OHL before age 40 whereas Campo *et al*, 2002 found a significant association between OC and age under 35 years. However, McCarthy *et al*, 1991 reported OC was twice as likely to develop in patients over 35 years compared with those younger. Our study found a reduced odds of any oral lesion as the age increased which is inconsistent with another Thai study (Nittayananta *et al*, 2001) that reported a lower risk of oral lesions in patients older than 30 years.

Nittayananta *et al*, 2001 found no relationship between current smoking and the presence of any oral disease, and postulated that a difference in tobacco product and/or host factor from those of western countries may be responsible for their finding. The result of our study is in contrast with their postulate as the southern data shows a similar result to that of Palmer *et al*, 1996, who reported a significant association between current smoking and the presence of any oral lesion. The northern subjects had too small a number of smokers to provide statistically significant results. Other studies have reported the relationship of current cigarette smoking with OC (Conley *et al*, 1996; Palacio *et al*, 1997; Patton *et al*, 1998; Campo *et al*, 2002), OHL (Conley *et al*, 1996; Patton *et al*, 1998) and warts (Palacio *et al*, 1997).

Accumulated epidemiological data reveal a marked increase in the prevalence of OC as CD4 declines during the progress of HIV infection (Glick *et al*, 1994; Palmer *et al*, 1996; Patton *et al*, 1998; Patton, 2000; Ranganathan *et al*, 2000), and our findings are consistent with this. Pseudomembranous candidiasis (PC) has a clear correlation with the progression of HIV infection (Palmer *et al*, 1996; Robinson *et al*, 1997). However, the association of erythematous candidiasis (EC) with poor prognosis is still controversial. Two studies (Dodd *et al*, 1991; Nielsen *et al*, 1994) suggested similar rates of progression towards AIDS in patients with the two forms of OC. However, some studies (Palmer *et al*, 1996; MacPhail *et al*, 2002) found a relationship only for PC but not for EC. CD4 <200 cells mm^{-3} and late stage of the disease were reported to have a significant association with OC and PC but not EC (Ramirez-Amador *et al*, 1998). Our study result supports the correlation of OC and PC with advanced HIV infection because OC and PC were more strongly associated with lowered immune status than was EC.

Similar to other studies, our data show an association between OHL and poor immune status (CD4 <200 cells mm^{-3}) (Glick *et al*, 1994; Palmer *et al*, 1996; Patton, 2000) and between OHL and male sex (Shiboski *et al*, 1996; Patton *et al*, 1998; Nittayananta *et al*, 2001). The association of OHL and male sex, particularly in men who have sex with men (MSM), has been documented in a previous study (Shiboski *et al*, 1996). The increased prevalence of OHL in men, and specifically in MSM, may relate to a higher exposure to the Epstein-Barr virus (EBV), the causative agent of OHL, or to sex differences in the way EBV is expressed in the oral epithelium (Greenspan *et al*, 1985; Rahman *et al*, 1989).

There was a relatively higher prevalence of OHL (38%) compared with OC (25%) in the northern data. This may result from the differences of the study subjects; the clinical, immunological and viraemic status of the patients including unidentified independent variables. To gain more insight about OHL, further studies still need to be undertaken to detail the route of HIV transmission such as oro-genital or oro-anal practices, homosexual, heterosexual or bisexual transmission, and the nature of EBV infection.

The effect of medications such as antifungals or antivirals on the prevalence of oral diseases has been documented (Patton, 2000; Tappuni and Fleming, 2001). Patton (2000), reported that the prevalence and sensitivity to detect CD4 <200 cells mm^{-3} of OC and OHL were greatest in HIV patients who were on no antiretroviral therapy (ART) and were lowest among patients on combination ART including one or more protease inhibitor. Tappuni and Fleming, 2001 found that subjects on dual and triple highly active antiretroviral therapy (HAART) therapy had significantly fewer oral lesions than did those on AZT monotherapy ($P < 0.05$) and those on no ART regimen ($P = 0.014$). The present study found that ART reduced the risk of having OHL and a trend of reduced numbers of oral lesions among northern subjects. This relationship was not shown in the southern data. Most ART prescribed for our subjects was AZT monotherapy, thus the result of reducing oral lesions was not marked. The effect of antifungals on the presence of oral disease is complex. Palmer *et al*, 1996 reported that candidiasis was more common among patients taking antifungals than those who were not. The present study revealed a strong negative relationship between systemic antifungal treatment and the presence of OC including PC and EC. Nittayananta *et al*, 2001 also reported a reverse relationship between the use of antifungal drugs and the presence of OC. Our groups and the latter's findings indicate that antifungal treatment could be beneficial in those Thai patients who cannot afford HAART.

A limitation of our study is that the multivariate analyses present data for only the most common oral

lesions. We cannot describe the relationship of less common lesions to risk factors because of our small sample size. Furthermore, our subjects were a 'convenience' sample of people seeking HIV treatment at hospital clinics and, therefore, they were not fully representative of persons with HIV infection in northern and southern Thailand. However, findings from our study may be generalized to populations of persons who know they are seropositive and who are seeking care at government hospitals.

HIV-associated oral lesions were highly prevalent in our study. Risk factors that influenced the prevalence of oral lesions in northern and southern Thai populations, such as sex, CD4 count, oral habits and medications, are consistent with studies from non-Asian countries. OC, particularly PC, may be useful as a prognostic indicator of advancing HIV infection, particularly in those who cannot afford expensive laboratory assays to monitor their disease progression. Antifungal treatment is useful in these subjects without access to HAART.

Acknowledgements

The authors are grateful to the staff of the HIV Clinic, Hatyai Regional Hospital, Songkla Province, Satun General Hospital, Satun Province, the Maharaj Nakorn Chiang Mai University Hospital and Sansai Community Hospital, Chiang Mai Province, for their assistance with patient access. This study was supported by the Danish International Development Agency.

References

Anil S, Challacombe SJ (1997). Oral lesions of HIV and AIDS in Asia: an overview. *Oral Dis* **3** (Suppl 1)**:** S36–S40.

Bendick C, Scheifele C, Reichart PA (2002). Oral manifestations in 101 Cambodian patients with HIV infection and AIDS. *J Oral Pathol Med* **31:** 1–4.

Campo J, Del Romero J, Castilla J, Garcia S, Rodriguez C, Bascones A (2002). Oral candidiasis as a clinical marker related to viral load, CD4 lymphocyte count and CD4 lymphocyte percentage in HIV-infected patients. *J Oral Pathol Med* **31:** 5–10.

Celentano DD, Nelson KE, Lyles CM *et al* (1998). Decreasing incidence of HIV and sexually transmitted diseases in young Thai men: evidence for success of the HIV/AIDS control and prevention program. *AIDS* **12:** 29–36.

Centers for Disease Control and Prevention (CDC) (1992). 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR* **41:** 1–19.

Conley LJ, Bush TJ, Buchbinder SP, Penley KA, Judson FN, Holmberg SD (1996). The association between cigarette smoking and selected HIV-related medical conditions. *AIDS* **10:** 1121–1126.

Division of Epidemiology, Ministry of Public Health (2000). HIV serosurveillance in Thailand: Result of 17th round, June 1999. *Mthly Epidemiol Surv Rep (Thailand)* **31** (Suppl 1)**:** S1–S14.

Dodd CL, Greenspan D, Katz MH, Westenhouse JL, Feigal DW, Greenspan JS (1991). Oral candidiasis in HIV infection: pseudomembranous and erythematous candidiasis show similar rates of progression to AIDS. *AIDS* **5:** 1339–1343.

EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Human Immunodeficiency Virus (1993). Classification and diagnostic criteria for oral lesions in HIV infection. *J Oral Pathol Med* **22:** 289–291.

Glick M, Muzyka BC, Lurie D, Salkin LM (1994). Oral manifestations associated with HIV-related disease as markers for immune suppression and AIDS. *Oral Surg Oral Med Oral Pathol* **77:** 344–349.

Greenspan JS, Greenspan D, Lennette ET *et al* (1985). Replication of Epstein-Barr virus within the epithelial cells of oral 'hairy' leukoplakia, an AIDS-associated lesion. *N Engl J Med* **313:** 1564–1571.

Hilton JF, Donegan E, Katz MH *et al* (1997). Development of oral lesions in human immunodeficiency virus-infected transfusion recipients and hemophilics. *Am J Epidemiol* **145:** 164–174.

Khongkunthian P, Grote M, Isaratanan W, Piyaworawong S, Reichart PA (2001). Oral manifestations in HIV-positive adults from northern Thailand. *J Oral Pathol Med* **30:** 220–223.

McCarthy GM, Mackie ID, Koval J, Sandhu HS, Deley TD (1991). Factors associated with increased frequency of HIV-related oral candidiasis. *J Oral Pathol Med* **20:** 332–336.

MacPhail LA, Komaroff E, Alves MEAF, Navazesh M, Phelan JA, Redford M (2002). Differences in risk factors among clinical types of oral candidiasis in the Women's Interagency HIV Study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **93:** 45–55.

Margiotta V, Campisi G, Mancuso S, Accurso V, Abbadessa V (1999). HIV infection: oral lesions, $CD4^+$ cell count and viral load in an Italian study population. *J Oral Pathol Med* **28:** 173–177.

Nielsen H, Bentsen KD, Hojtved L *et al* (1994). Oral candidiasis and immune status of HIV-infected patients. *J Oral Pathol Med* **23:** 140–143.

Nittayananta W, Chungpanich S (1997). Oral lesions in a group of Thai people with AIDS. *Oral Dis* **3** (Suppl 1)**:** S41–S45.

Nittayananta W, Chanowanna N, Sripatanakul S, Winn T (2001). Risk factors associated with oral lesions in HIV-infected heterosexual people and intravenous drug users in Thailand. *J Oral Pathol Med* **30:** 224–230.

Palacio H, Hilton JF, Canchola AJ, Greenspan D (1997). Effect of cigarette smoking on HIV-related oral lesions. *J Acquir Immune Defic Syndr Hum Retrovirol* **14:** 338–342.

Palmer GD, Robinson PG, Challacombe SJ *et al*. (1996). Aetiological factors for oral manifestations of HIV. *Oral Dis* **2:** 193–197.

Patton LL (2000). Sensitivity, specificity, and positive predictive value of oral opportunistic infections in adults with HIV/AIDS as markers of immune suppression and viral burden. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **90:** 182–188.

Patton LL, McKaig RG, Strauss RP, Eron, Jr, JJ (1998). Oral manifestations of HIV in a southeast USA population. *Oral Dis* **4:** 164–169.

Rahman MA, Kingsley LA, Breinig MK *et al* (1989). Enhanced antibody responses to Epstein-Barr virus in HIV-infected homosexual men. *J Infect Dis* **159:** 472–479.

Ramirez-Amador V, Esquivel-Pedraza L, Sierra-Madero J, Ponce-de-Leon Sa, Ponce-de-Leon Se (1998). Oral manifestations of HIV infection by gender and transmission category in Mexico City. *J Oral Pathol Med* **27:** 135–140.

Ranganathan K, Reddy BVR, Kumarasamy N, Solomon S, Viswanathan R, Johnson NW (2000). Oral lesions and conditions associated with human immunodeficiency virus infection in 300 south Indian patients. *Oral Dis* **6:** 152–157.

Robinson PG, Challacombe SJ, Sheiham A, Zakrzewska JM (1997). Is erythematous candidiasis associated with advanced HIV disease? *Oral Dis* **3** (Suppl 1)**:** S116–S118.

Shiboski CH, Hilton JF, Neuhaus JM, Canchola A, Greenspan D (1996). Human immunodeficiency virus-related oral manifestations and gender. A longitudinal analysis. *Arch Intern Med* **156:** 2249–2254.

Tappuni AR, Fleming GJP (2001). The effect of antiretroviral therapy on the prevalence of oral manifestations in HIV-infected patients: A UK study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **92:** 623–628.

Tsang PCS, Samaranayake LP (1999). Oral manifestations of HIV infection in a group of predominantly ethnic Chinese. *J Oral Pathol Med* **28:** 122–127.