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## Predictive value of group I oral lesions for HIV infection

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**Objectives.** Attendees presenting for treatment of acute illness at primary health care facilities in South Africa were assessed to determine the prevalence of human immunodeficiency virus (HIV) infection and the predictability of group I oral lesions (GOLs) for HIV infection.

**Methods.** This was a cross-sectional analytical study. Patients >18 years of age were recruited and underwent an oral examination and a HIV test.

**Results.** A total of 522 attendees were examined and the HIV prevalence was 40%. None of them were taking antiretroviral drugs. GOLs were diagnosed in 53% of HIV patients, with pseudomembranous and erythematous candidiasis being the most common (38% and 24%, respectively). The average odds and likelihood ratios for multiple lesions were high (32 and 30, respectively) and showed a strong correlation between GOLs and a positive HIV status.

**Conclusion.** The prevalence of HIV (40%) and GOLs (53%) was high. GOLs were useful markers of HIV infection, with multiple lesions being highly predictive of HIV infection. (*Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;109:720-723)

The prevalence rate of human immunodeficiency virus (HIV) infection in South Africa has been increasing annually,<sup>1</sup> and despite numerous awareness campaigns the uptake of voluntary counseling and testing has remained fairly low.<sup>2,3</sup> Therefore, many patients remain unaware of their HIV status.

Oral manifestations of HIV/acquired immune deficiency syndrome (AIDS) occur in >60% of HIV-positive patients and are often the first sign of underlying immune suppression.<sup>4</sup> A classification system based on the prevalence of these oral manifestations has been developed by the World Health Organization (WHO) and the European Community (EC) Clearinghouse.<sup>5</sup> Group I oral lesions (GOLs) have been the most prevalent oral lesions diagnosed in patients who are infected with HIV.<sup>4,6-8</sup> For the purpose of the present study, GOLs have been identified according to the EC Clearinghouse as follows<sup>5</sup>: pseudomembranous candida (PC), erythematous candida (EC), oral hairy leukoplakia (OHL), angular cheilitis (AC), Kaposi sarcoma, necrotizing ulcerative gingivitis (NUG), and necrotizing ulcerative periodontitis.

Many studies<sup>9-14</sup> have reported that GOLs, either singly or in combination, could be used as markers for screening

diagnosis of suspected HIV-positive patients. These studies have suggested that oral lesions associated with HIV could be used to predict HIV in settings where resources are limited and where patients are reluctant to test their HIV status or where their status is unknown.<sup>6,9-14</sup> Health care workers could use GOLs as markers to alert them to patients who may be infected with HIV. A study done to predict HIV amongst dental patients, who were unaware of their HIV status, reported that if a patient presented with NUG, the likelihood of them testing positive for HIV was 40 times greater compared with a patient without NUG.<sup>12</sup> However, very few studies<sup>9,10,14</sup> have shown the correlation of GOLs with a positive HIV status among a general population attending medical facilities. There has been no study which has predicted the HIV status among outpatients attending for acute illnesses at a medical primary health care (PHC) facility using the GOLs as predictors.

The present study sought to determine the prevalence of HIV and GOLs among adult patients attending for acute illnesses at primary health care facilities in Gauteng, South Africa, and the predictive value of GOLs for HIV infection using epidemiologic tools. Unique in its design is that GOLs were used as a screening tool to determine the HIV status in participants who were unaware of their status, and the study was performed in medical facilities, not in dental clinics or specialized HIV clinics.

### METHODS

This was a cross-sectional analytic study. All patients >18 years old who had attended the Khutsong and Heidelberg PHC facilities in Johannesburg, South Africa, were included in the study population. These 2 PHC facilities, located within the Gauteng province of South

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Africa, were randomly selected for the study. The study period consisted of 1 week at each facility extending from Monday to Saturday during April 2005.

Only outpatients who presented with acute illnesses (i.e., presenting with signs and/or symptoms of ill-health) were included. Patients who were classified as inpatients (staying overnight) and those who presented for chronic treatment, such as for hypertension, diabetes, and antenatal care, were excluded, because this study sought to determine the HIV prevalence among patients who routinely attended for acute and current illnesses only. In this way, the burden (and prevalence) that HIV was placing on the PHC facilities could also be established. Each participant received counseling regarding the purpose of the study, and both written and verbal consent was obtained. All patients were unaware of their HIV status and had never been tested before. Although none of the patients were currently taking any antiretroviral (ARV) or highly active antiretroviral (HAART) treatment, they were still questioned about their use of ARVs/HAART.

Data were collected in 2 stages on the same visit. The first stage comprised a comprehensive clinical oral examination, which was followed by the second stage consisting of an oral fluid test to determine the patient's HIV status. Oral examinations were performed by 2 calibrated dentists who were trained at an international calibration workshop titled, "Calibration of Oral Lesions in HIV Disease," hosted by the University of the Witwatersrand in Johannesburg, South Africa.

The diagnosis of the GOLs was made based on the EC Clearinghouse criteria<sup>5</sup> and confirmed by consensus. Every tenth patient on each day was reexamined to ensure inter- and intraexaminer reliability. Kappa scores of 0.85 and 0.9 were achieved for inter- and intraexaminer reliability, respectively. The clinicians were blinded to the patients' HIV status at the time of the oral examination. After completing the oral examination, a qualified PHC nurse, blinded to the results of the oral examination, took an oral fluid sample using the OraQuick Rapid HIV 1/2 Antibody Test kit according to the manufacturer's instructions. Results of the tests were confirmed 20 minutes after each oral examination was complete, per the manufacturer's instructions. All data were recorded onto data-capturing forms and coded to ensure anonymity. Data were entered and analyzed using the Epi Info 2002 software package.<sup>15</sup> The presence of GOLs were regressed against the HIV status using logistic regression analysis. *P* values of <.05 were statistically significant, and the confidence interval (CI) was set at 95%. GOLs that were significantly associated with a positive HIV status were identified, and further epidemiologic tests, such as positive predictive value (PPV), negative predictive value (NPV); odds ratio (OR), and likelihood ratio (LR), were calculated to determine the degree of association between the GOLs and a

**Table I.** Prevalence of group I oral lesions among HIV-positive patients (n = 210)

Oral lesions	No. of patients (%)
Pseudomembranous candidiasis (PC)	80 (38)
Erythematous candidiasis (EC)	50 (24)
Oral hairy leukoplakia (OHL)	41 (20)
Angular cheilitis (AC)	12 (6)
Kaposi sarcoma (KS)	1 (0.5)
Necrotizing ulcerative gingivitis (NUG)	1 (0.5)

positive HIV status. The LRs were used because they have proven to be both robust and accurate<sup>14-16</sup> for predicting diseases using clinical signs and symptoms, especially when the LR is >10.

**RESULTS**

A total of 522 patients attended the 2 PHC facilities, and all of them agreed to participate in the study. There were no statistical differences among the attendees at the 2 facilities in terms of age, gender, and HIV status, and, therefore, they were pooled for ease of description and analysis.

There were significantly more women (73%) than men (*P* < .005; CI 95%), and the combined mean age was 41.95 years (range 18-94 years). A total of 210 patients (40%) tested positive for HIV, with the majority (58%) of them being female. More than one-half of these patients (64%) were between 25 and 44 years old. There were no significant differences between the HIV status and variables such as race, age, and gender.

Of those patients who tested negative for HIV, 19% presented with GOLs. The most common GOLs were pseudomembranous (86%) and erythematous (25%) candidiasis. In contrast, more than half (53%) of the patients who tested positive for HIV presented with ≥1 GOL (Table I). Four of these lesions, PC, EC, AC, and OHL, were significantly associated (*P* < .05) with a positive HIV status.

Table II describes the number of patients and correlations between the most prevalent GOLs and positive HIV status. The PPVs ranged from 57% (95% CI 48%-65%) to 95% (95% CI 84%-99%) for single and from 74% (95% CI 59%-86%) to 98% (95% CI 83%-100%) for multiple oral lesions. The NPVs were between 60% (95% CI 60%-61%) and 66% (95% CI 60%-70%). The OR varied from 3 (95% CI 2.3-4.7) for PC to 38 (95% CI 9.9-142.4) for OHL to a maximum of 78 (95% CI 8.0-765.9) for the combination of PC and OHL. Almost all LR values for multiple lesions and 2 for single lesions (AC and OHL) were >10. Some combinations of GOLs, such as EC + OHL and PC + OHL, yielded LR values >60, which indicated that the presence of these lesions were strongly associated with a positive HIV status.

**Table II.** Association between group I oral lesions and the presence of HIV using various epidemiologic tools

No. of patients	Lesion	PPV, % (95% CI)	NPV, % (95% CI)	OR (95% CI)	LR (95% CI)
140	PC	57.1 (48-65)	66.0 (60-70)	3.2 (2.3-4.7)	2.4 (1.8-3.1)
72	EC	69.4 (57-79)	64.4 (59-68)	4.1 (2.4-7.0)	3.4 (2.1-5.4)
13	AC	92.3 (63-99)	61.1 (56-65)	18.8 (3.1-113.6)	17.8 (3.0-106.8)
43	OHL	95.3 (84-99)	64.7 (60-69)	37.6 (9.9-142.4)	30.5 (8.4-113.8)
Average—single lesion		78.5	64.1	15.9	13.5
35	EC + PC	74.3 (58.5-85.7)	62.2 (61.1-63.0)	4.8 (2.2-10.2)	4.3 (2.1-8.9)
20	EC + OHL	97.6 (81.1-99.8)	62.1 (61.4-62.2)	67.3 (6.8-659.2)	60.8 (6.4-593.9)
3	AC + OHL	87.5 (39.7-98.7)	60.1 (59.7-60.2)	10.5 (0.98-113.0)	10.4 (0.98-110.9)
9	AC + PC	88.9 (56.8-98.0)	60.6 (60.1-60.8)	12.3 (1.8-76.3)	11.9 (1.96-73.1)
8	AC + EC	94.4 (63.2-99.4)	60.7 (60.1-60.8)	26.2 (2.6-264.1)	25.2 (2.5-252.9)
23	PC + OHL	97.9 (83.2-99.8)	62.5 (61.8-62.6)	78.3 (8.0-765.9)	69.7 (7.3-679.1)
6	EC + PC + AC	92.9 (56.4-99.2)	60.4 (60.0-60.5)	19.9 (1.9-202.8)	19.3 (1.9-196.2)
11	EC + PC + OHL	95.8 (70.2-99.6)	61.0 (60.461.1)	36.0 (3.6-358.4)	34.1 (3.5-338.2)
2	EC + PC + AC + OHL	95.8 (70.2-99.6)	61.0 (60.4-61.1)	36.0 (3.6-358.4)	34.1 (3.5-338.2)
Average—multiple lesions		91.7	61.2	32.4	30.0

PPV, Positive predictive value; CI, confidence interval; NPV, negative predictive value; OR, odds ratio; LR, likelihood ratio; other abbreviations as in Table I.

## DISCUSSION

In this study, the HIV prevalence was 40% which is considerably higher than the latest South African National HIV and Syphilis Antenatal Seroprevalence survey finding of 18%.<sup>1</sup> The higher prevalence observed here could be attributed to the fact that: 1) the national figures are an estimate of the general population, whereas the present study was comprised of ill patients attending PHC facilities; 2) the national figures are obtained from attendees of antenatal facilities (pregnant woman only) throughout the country and extrapolated for the entire population, whereas the present study was based on results from 2 PHC facilities in 1 province (Gauteng); and 3) both PHC facilities were located in close proximity to gold mines and serve a large portion of the mining community. This migrant community has been known to have higher HIV prevalence rates, which could be one of the reasons for the high rate that was recorded.<sup>17</sup>

In agreement with other South African studies,<sup>18,19</sup> most of the HIV-positive patients were female (58%) and between 25 and 44 years old (64%). It must be noted that none of these patients were taking ARVs. The high prevalence rate among this age group is indicative of the sexually active and mobile work force that exists within South Africa as described by previous HIV prevalence studies.<sup>1,2,19</sup>

Testing for HIV is routinely done using blood samples. However, more recently, oral fluid (saliva) has been used as a medium to confirm HIV status. The oral fluid kits currently being used to test HIV have been shown to be acceptable, regarding both sensitivity and specificity.<sup>20-23</sup> Studies that have used these HIV kits have reported a specificity between 99% and 99.87% and a sensitivity between 96% and 100%. The kit which was used in this study (Ora-

Quick Rapid HIV 1/2 Antibody Test kit) was evaluated by Major et al.<sup>22</sup> and Bhore et al.<sup>23</sup> and showed an average specificity and sensitivity of 100% and 98.3%, respectively. It has also been used in other similar types of screening studies throughout the world.<sup>12,24,25</sup>

Although the prevalence of GOLs in the present study cannot be directly compared with other studies because of differences in training and calibration of study diagnosticians, differences in health care settings used for recruitment, and differences in the population comprising the study sample, some generalizations nevertheless can be made. First, HIV-positive patients in this setting continued to present with GOLs, and oral candidiasis was still the most common lesion diagnosed. Second, multiple lesions were more common in the HIV positive cohorts; and third, candida and OHL were highly predictive of HIV.

Studies have been performed that have predicted HIV using GOLs but most of these have been done at dental facilities,<sup>12,13</sup> specialized HIV clinics,<sup>7</sup> or special medical units treating high-risk HIV patients.<sup>9,14</sup> All of those studies concluded that specific GOLs are predictive of HIV and that the strength of the association varies according to the prevalence of the condition. Unlike others,<sup>12,14</sup> we also used LR analyses, which demonstrated that several combinations of GOLs were highly associated with HIV. The ORs were also high, with that for OHL being 38 (95% CI 9.9-142.4) and for multiple lesions of PC and OHL being 78 (95% CI 8.0-765.9). Similarly to other studies,<sup>12,14</sup> the PPVs were relatively high, with the average PPV for multiple GOLs generally exceeding (88%) for patients testing positive for HIV. Our data also demonstrated that patients with OHL were almost certain (95%) to test positive for HIV. In contrast, the average NPV for single (64%) and multiple lesions (61%) confirmed that on av-

erage, 6 out of every 10 patients who did not present with GOLs tested negative for HIV. Therefore, a clinician gains valuable diagnostic information from the presence or absence of these lesions.

Together, these data indicate that GOLs both in single (average LR 14) and in multiple combinations (average LR 26) can confidently be used as screening tools for HIV, especially in resource-poor settings where laboratory tests are often nonexistent and/or expensive. Patients who present with GOLs should raise strong suspicion and should be sent for confirmatory investigations. The usefulness of GOLs is limited by the ability of clinicians to correctly recognize and diagnose these lesions. Thus the importance of training clinicians in the diagnosis of these lesions may increase the number of patients being referred for HIV testing and subsequently being placed onto ARVs.

## CONCLUSION

The HIV prevalence in these PHC facilities was high (40%) and more than half (53%) of all HIV-positive patients presented with  $\geq 1$  GOL. Some combinations of GOLs (AC and OHL, AC and PC, and PC and OHL) can be considered to be significant predictors of a patient's HIV status. Multiple oral lesions were shown to be excellent predictors of HIV in this study. Single oral lesions, such as OHL and AC, demonstrated high LR values and also are useful predictors of HIV. The presumptive clinical diagnosis of certain HIV-associated oral lesions could be used in resource-poor settings to suggest possible undiagnosed HIV infection warranting further laboratory-based diagnostic testing.

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