Assessment of the Oral Health Status of Healthcare-seeking Adults Living with HIV in Kathmandu Valley, Nepal

Gaunt F[1], Rai A[2], Kinkel HT[3]

[1]BMS World Mission, PO BOX 49, 129 Broadway Didcot, Oxfordshire, UK. [2]SPARSHA Nepal, Latitpur, Nepal. [3]Gesellschaft fuer Internationale Zusammenarbeit (GIZ), HRP, Kathmandu/Nepal.

Abstract

Aims: This study looks to assess the oral health status in the study subjects and to quantify the prevalence of WHO defined HIV-related oral stage 3 and 4 lesions (HIV-OL) as those conditions are indicating need for treatment independently of CD4 count.

Methods: This quantitative screening study used both structured questionnaire and clinical examination to determine the prevalence of HIV-OL in 83 adults living with HIV randomly selected from a list of service users at a community based HIV organization.

Results: The screening revealed a 40 % (95%-CI: 30-51%) prevalence of HIV-OL in this population where 71 are under Antiretroviral Therapy (ART). Most frequent HIV-OL found were persistent oral candidiasis (19% prevalence), and acute necrotizing gingivitis/stomatitis (18% prevalence) Prevalence of HIV-OL was correlating with CD4 count. Patients with multiple HIV-OL have a mean of 133 CD4 cells/µl, patients with a single HIV-OL have 327 CD4 cells/µl and patients without HIV-OL do have a mean of 457CD4 cells/µl (ANOVA-p=0.002). 6 of 12 patients not taking ART yet were found to have stage 3 or 4 HIV-OL. 46 (55%) of the study population had poor or very poor oral hygiene and 29 (35%) had never had an oral examination, 36 (43%) had attended only for extraction. Only 4 of 54 patients who had previously accessed oral health care have revealed their HIV status to the dentist at that time.

Conclusions: Wider access to oral healthcare is required for people living with HIV in Kathmandu Valley/Nepal. In this setting HIV-OL are still an important consideration in assessing patients living with HIV, which can have decisive therapeutic implications. Stage 3 and 4 conditions are, independently of CD4 count, indication to start ART without delay in people living with HIV.

Introduction

According to the Government of Nepal in 2011 the estimate "based on global proxies due to a lack of Nepal specific data, which may not best fit…" was that 50,288 people were living with HIV in Nepal. In 2011 the number of HIV-related deaths in Nepal among people living with HIV was 4,722, which was 9.4% of the number of people living with HIV: one of the highest proportions of all countries in the world [1,2]. According to the most recent national guidelines for Antiretroviral Therapy (ART) in Nepal, people living with HIV and a CD4 count < 350 cells/µl or HIV-related clinical stage 3 or 4 conditions are eligible for ART which consists as first line therapy of two nucleotide/nucleoside analog reverse-transcriptase inhibitors (lamivudine (3TC) with either tenofovir (TDF) or zidovudine (AZT)) in combination with a non-nucleoside analog reverse-transcriptase inhibitor (Efavirenz (EFV) or Nevirapine (NPV)). Second-line therapies are relying on a combination with the ritonavir-boosted protease-inhibitor lopinavir (LPV/r) [3]. In 2012 reported 7,719 people were receiving ART in Nepal, which means that 2 out of 3 people in need of ART have still not received ART [2]. Health care for people living with HIV in Nepal is provided in many locations, mainly in the Kathmandu Valley. Community based services such as SPARSHA are an important part of care for people living with HIV in Kathmandu. Here people get voluntary counseling and testing for HIV, have general medical treatment and have their ART dispensed.

Oral Lesions have been described since the beginning of the global HIV epidemic. Several oral lesions associated with HIV (HIV-OL, *Table 1*) are included in the WHO staging of HIV/AIDS [4].

Dental care is an important part of a holistic treatment for people living with HIV. HIV-OL is debilitating, disfiguring, painful and progressive. In people living with HIV adherent to an effective Antiretroviral Treatment (ART) dental health is an important factor in self-esteem, employment and general health [5-7]. 40-50% of people living with HIV develop oral fungal, bacterial or viral infections early in the course of the disease and oral lesions – especially oropharyngeal candidiasis - are still among the most frequent opportunistic infections in the region and Nepal [8-12].

This study looks to assess the oral health status in the population studied and to quantify the prevalence of WHO defined stage 3 and 4 HIV-OL as those conditions are indicating need for treatment independently of CD4 count.

Methods

This quantitative study utilized both a structured questionnaire and clinical examination to form an assessment of the oral health of the participants. Ethical approval for this screening study was received from the Nepal Health Research Council 29/8/13 registration number 98/2013/.

Inclusion criteria for the survey were: living with HIV, being

Table 1. *HIV related Oral Lesions (HIV-OL) included in WHO clinical staging of HIV/AIDS [5]*

Clinical Stage	Adults / Adolescents aged 15 or older: Oral manifestation of HIV
1	-
2	Angular Cheilitis Recurrent oral ulceration
3	Persistent oral candidiasis Oral Hairy Leukoplakia Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
4	Chronic (>1 month) Orolabial herpes simplex Kaposi's Sarcoma

Corresponding author: Francesca Gaunt, BMS World Mission, PO BOX 49, 129 Broadway Didcot, Oxfordshire, UK; Tel: +9779803405665; e-mail: Francescagaunt@gmail.com

registered with "SPARSHA Nepal" and currently living in Kathmandu Valley/Nepal. From a list of 210 service users registered in 2013 with "SPARSHA Nepal" 84 participants were randomly selected and offered dental screening at "SPARSHA Nepal".

All 84 service users gave written or – in case of illiteracy – oral consent and underwent questionnaire-based interview and clinical examination. 1 participant was excluded from data-analysis due to his age < 15 years due to the different clinical staging manifestations for adolescents < 15.

One qualified and UK/Nepal registered dentist screened all participants in a methodical manner. The questionnaire consisted of basic demographic questions and data (age, gender, marital status, area of habitation) and questions relating to HIV status (time since diagnosis or infection if known, last known CD4 Count, assumed route of transmission, medication history). Medical history was assessed by patient questionnaire and patient notes. Social history questions were asked (cigarette and tobacco use (frequency, duration) alcohol use (duration, frequency) and current drug use and time since last drug use if relevant.

A dental history was taken (previous attendance, experience of procedures and local anaesthetic and whether patient disclosed HIV status to dentist). Detailed history of any oral or dental complaint, pain or swelling was taken. Full inspection of the head, neck and oral cavity was undertaken; teeth were charted and assessed for caries using good illumination and mirrors. Mucosal abnormalities were examined with illumination and mirrors. Photographs were taken with patient consent. Periodontal treatment need was assessed using the "Basic Periodontal Examination" of the British Society of Periodontology [13]. Diagnosis was based on the clinical criteria outlined in 'WHO's Guide for Epidemiological studies of Oral Manifestations of HIV infection.'[14].

In the case of any acute oral problem such as abscess, acute necrotising ulcerative gingivits and symptomatic candidiasis appropriate treatment was provided. Treatment need was explained to the patient and information was made available for access to further treatment facilities. Help in attendance was offered from SPARSHA staff.

Statistical Analysis was performed using SPSS (version 22) and Microsoft Excel (version 2013); Graphs were created with Microsoft Excel (version 2013).

Results

In total 83 adult participants were included in the analysis (*Table 2*). This comprised of 9 females and 74 males. The average age was 37 years with a range of 16-53years. For 47 (56%) patients assumed route of HIV-transmission is injecting use of opioids often in combination with pharmaceutical drugs.

Body mass Index was in average 21.7 kg/m^2 (range 14.7-30.6) with 1 patient with severe thinness (BMI < 16) and 15 (18%) patients with underweight (BMI < 18.5). There was no significant correlation found in this study between BMI and CD4 count or HIV-OL.

Forty (48%) report that they are co-infected with Hepatitis C and 8 (9.6%) were currently in treatment for active tuberculosis.

Table 2. *Number and prevalence of diagnosed HIV-related oral pathologies, stratified by gender and antiretroviral therapy.*
Other HIV-related oral pathologies, e.g. chronic herpes simplex infection, cervical B-cell lymphoma or Kaposi sarcoma have not been diagnosed.
[a]95% Confidence Interval of the percentage
[b]Fisher's Exact Test
[c]comparison "no HIV-related oral pathology" vs. "one or multiple HIV-related oral pathologies".

HIV-related oral pathology	Total (n=83) (%) 95%-CI[a]	Sex		P[b]	Antiretroviral Therapy		P[b]
		Male (n=74)	Female (=9)		ART (n=71)	No ART (n=12)	
No HIV-related oral pathology	50 (60%) (49-70%)	42	8	0.05[c]	44	6	n.s.[c]
One HIV-related oral pathology	26 (31%) (22-42%)	25	1		21	5	
Multiple HIV-related oral pathologies	7 (8.4%) (4-16%)	7	0		6	1	
Angular Cheleitis	4 (4.8%) (2-12%)	4	0	n.s.	4	0	n.s.
Recurrent oral ulceration	3 (3.6%) (1-10%)	3	0	n.s.	3	0	n.s.
Persistent oral candidiasis	16 (19%) (12-29%)	16	0	n.s.	12	4	n.s.
Acute necrotizing stomatitis/gingivitis	15 (18%) (11-28%)	14	1	n.s.	13	2	n.s.
Oral Hairy Leukoplakia	4 (4.8%) (2-12%)	4	0	n.s.	3	1	n.s.

Home oral care, risk factors and oral health care

Forty six (55%) patients had poor or very poor oral hygiene with visible hard and removable soft deposits of plaque and calculus on the teeth. Eighty two (100% of those with teeth) had at least some need for periodontal treatment with visible supra- or subgingival calculus. Fifty two (63%) currently smoke cigarettes with 19 (23%) reporting smoking more than 20 cigarettes a day. Chewing tobacco use was more difficult to quantify, but 44 (53%) of patients were chewing tobacco daily.

Fifteen (18%) patients never use or have never used alcohol and 56 (67%) were now abstinent for varying lengths of time after a period of alcohol use disorder, 12 (14%) reported current alcohol use.

For 29 (35%) patients this was the first ever occasion of visiting any dental/medical service to inspect their teeth or oral cavity. At least one oral pathology which is *not* qualified as HIV-related (dental caries, gingivitis, periodontal disease, dentine sensitivity, pericoronitis, tooth impaction, abscess and tobacco pouch keratosis) was observed in all participants and no significant correlation was found between these non-HIV-related oral pathologies and immune status (CD4 count).

Prevalence-rates of HIV-OL have not been found to differ significantly between gender and ART (*Table 2*). ART consisted in AZT+3TC+EFV (27 patients), AZT+3TC+NVP (19 pat.), TDF+3TC+EFV (15 pat.), TDF+3TC+NVP (5 pat.), AZT+3TC+LPV/r (3 pat.), or TDF+3TC+LPV/r (2 pat.). HIV-related oral pathologies other than the ones listed in *Table 2*, e.g. chronic herpes simplex infection, cervical B-cell lymphoma or Kaposi sarcoma have not been found in any patient.

There was a clear and statistically significant correlation between CD-count and prevalence of HIV-OL (*Table 3*): In the lowest CD4-stratum (<200 cell/µl) 14 HIV-OL have been found in 16 patients, while in the highest CD4-stratum (>500 cell/µl) only 3 HIV-OL have been found in 22 patients (Fisher's exact t-test: $p<0.001$).

When analysed from a more clinical perspective, prevalence of one or multiple HIV-OL was significantly correlating with CD4 count (*Figure 1*). Patients with no HIV-OL (n=45) have an average CD4 count of 457 cells/µl (95%-CI 385-529), patients with a single HIV-OL (n=24) have an average CD4 count of 327 cells/µl (95%-CI 250-404), patients with a multiple HIV-OL (n=5) have an average CD4 count of 132 cells/µl (95%-CI 3-261). (ANOVA-p=0.002, post-hoc-t-test multiple HIV-OL vs. single HIV-OL p=0.03, single HIV-OL vs. no pathology p=0.02).

Six patients (50% of all patients not on ART and 7.2% of all examined patients) had stage 3 or 4 clinical conditions but no ART. These 6 patients have been diagnosed with persistent oral candidiasis (n=3), persistent oral candidiasis plus necrotizing gingivitis (n=1), necrotizing gingivitis (n=1) and oral hairy leukoplakia (n=1). 2 of these 6 patients had a CD4 count of 500 cells/µl and 667 cells/µl respectively and 1 had an unknown CD4 count. Those three patients qualify for ART exclusively by clinical criteria. The remaining 3 of the 6 patients would have qualified for ART by clinical and immunological criteria (*Figure 2*).

Discussion

The assessment of oral health in this random sample of 83 people living with HIV who are seeking health care with an NGO in Kathmandu Valley/Nepal revealed a 40 % (95%-CI: 30-51%) of people living with HIV who are already under care suffer at least one oral HIV-related clinical stage 3 condition. This is in line with previous findings of Patton et al, who reported a prevalence of HIV-related oral lesions of 37.5% in the ART era and a recently published study of 81 people living with HIV in the Eastern Terai region of Nepal which found the prevalence of HIV-OL to be 60.5% [15,16]. However the 53% of their study population were not taking ART and this study also included 'melanosis' as a clinical diagnosis. Oral pigmentation was noted in our study, and had various etiology: ethnic (present before HIV infection), related to ART (appeared following AZT use) and potentially related to immune deficiency. This was not studied in depth in this group.

Our study is also in line with international findings and the before mentioned study from Eastern Nepal insofar that oropharyngeal candidiasis has been found as the most prevalent oral stage 3 or 4 condition: in our study 19% and in the study from Eastern Nepal 21%. Other studies report 32% and 15.5% prevalence of oral candidiasis in people living with HIV who access health services in Nepal [8,17].

Compared with overall low estimates of HIV prevalence in Nepal, the number of AIDS-related deaths in Nepal is high [1]. One study from Far West region in Nepal recently reported a mortality rate per 100 patient years at risk for the first year after ART initiation of 11.9%, with much higher rates during the first 3 months and among male patients. This study concludes that delayed diagnosis and delayed ART-initiation are the main causes of this high fatality rate [18].

A study from Nepal investigating the factors responsible for delayed enrolment for antiretroviral treatment concluded, that "majority (47%) of the delays were due to the physician's failure to suspect and refer them for HIV testing at the earliest opportunity" [19].

Table 3. *HIV-related oral pathologies stratified by CD4 count in cells/µl. Included are patients with known CD 4 count within the 6 months before examination (n=75).*

HIV-related oral pathology		CD 4 count (cells/µl)			
	Total (n=75)	< 200 (n=16)	200-349 (n=22)	350-500 (n=15)	>500 (n=22)
Angular Cheleitis	3	0	1	1	1
Recurrent oral ulceration	2	1	0	1	0
Persistent oral candidiasis	13	7	5	1	0
Acute necrotizing stomatitis/gingivitis	11	2	3	4	2
Oral Hairy Leukoplakia	4	4	0	0	0
Σ	33	14	9	7	3

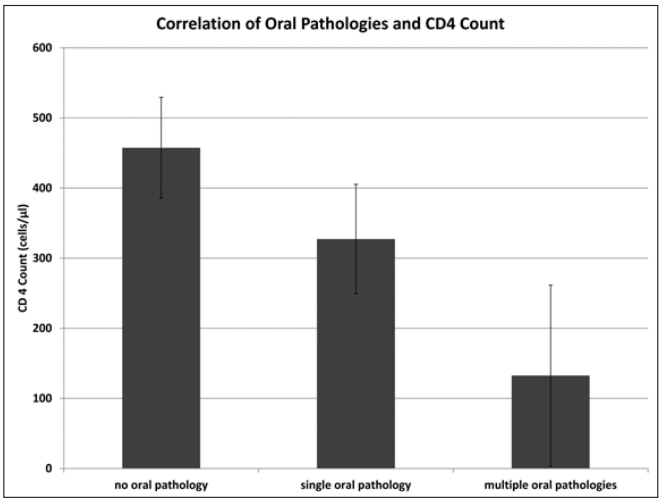

Figure 1. *High correlation of oral HIV-related pathologies and CD 4 count.*
Oral HIV-related pathologies as defined in the text.
Included in this analysis are only patients with known CD 4 count within 6 months before assessment of oral health (n=74).
Patients with no HIV-related oral pathology (n=45) have an average CD4 count of 457 cells/µl (95%-confidence interval 385-529), patients with a single HIV-related oral pathology (n=24) have an average CD4 count of 327 cells/µl (95% confidence interval 250-404), patients with a multiple HIV-related oral pathologies (n=5) have an average CD4 count of 132 cells/µl (95% confidence interval 3-261).
ANNOVA-p=0.002, post-hoc-t-test multiple vs. single p=0.03, single vs. no pathology p=0.02.

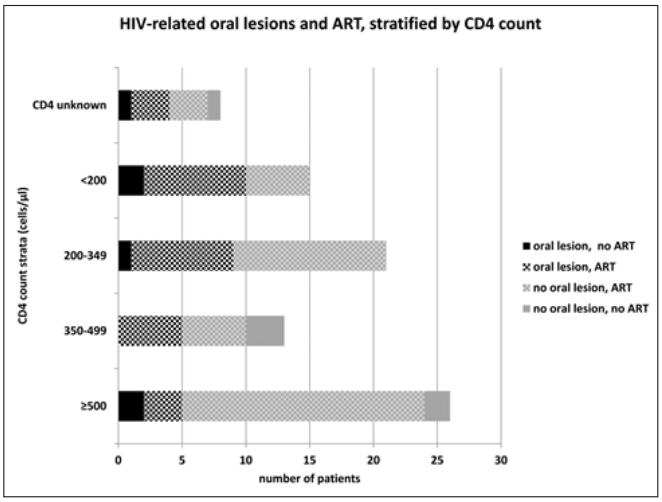

Figure 2. *HIV-related oral lesions and ART, stratified by CD4 count. With pattern fill: patients treated with ART. With solid fill: patients not receiving ART.*
In black: patients with HIV-related oral conditions. In grey: patients with no HIV-related conditions.
6 (7.2% of all examined patients) have stage 3 or 4 clinical conditions but no ART. The 6 patients have been diagnosed with persistent oral candidiasis (n=3), persistent oral candidiasis plus necrotizing gingivitis (n=1), necrotizing gingivitis (n=1) and oral hairy leukoplakia (n=1).
3 of these 6 patients had a CD 4 count of 500 cells/µl and 667 cells/µl respectively and qualify for ART exclusively by clinical criteria. The remaining 3 of the 6 patients would have qualified for ART by clinical and immunological criteria.

Another study reported that in 2009 still people living with HIV in Nepal "perceived health professionals lacking knowledge and sensitivity in providing health care to often marginalize … patients. Doctors and other health professionals appear suspicious, even unaware, of contemporary biomedical knowledge as it relates to HIV", however "the beginning of positive changes in the knowledge base and attitude of health providers seemed to be apparent to some participants of this study" [20].

Identifying clinical oral manifestations suggestive of HIV infection is relatively easy and does not require laboratory, radiologic or otherwise expensive examinations. Better performance of medical and dental health care providers in terms of screening and diagnosing of oral lesions suggestive of HIV-infection seems important, as stage 3 and 4 conditions are, independently of CD4 count, indication to start ART without delay in people living with HIV. New or recurrent incidents of stage 3 and 4 conditions in patients on ART are important in clinically assessing treatment efficacy. Our results show that HIV-related oral manifestations are frequent and - as expected - more prevalent in patients with low CD4 count. This finding is in line with the literature [21]. In 6 of the 12 patients (50%) who were not taking ART, stage 3 or 4 clinical conditions were seen (7.2% of all participants). These patients should be offered ART without delay.

Tobacco use in this group was very high, and as a risk factor for oral cancer, the most common form of cancer in men in Nepal [22]. Other risk factors for oral cancer such as alcohol use were also looked at in this study, although in this group alcohol use was historical with only 14 % currently drinking alcohol at all.

In the "Nepal National Pathfinder Survey 2004" which was screening otherwise healthy adolescents, the prevalence of periodontal disorders, mainly gingivitis and calculus, was > 60% [23]. Oral health for people living with HIV seems even more important due to additional risks – such as immunodeficiency, but also co-existing risk factors for impaired dental health, such as opioid use disorder. All patients with teeth that were screened in our study had some need for professional supra and/or sub gingival calculus or plaque removal. As an etiological factor for periodontal disease this is important especially when combined with chewing (53%) and smoking (63%) tobacco use and potentially poor diet inferred from the 18 % patients with underweight (BMI <18.5). Loss of teeth through caries, periodontal disease or accident negatively impacts on self-esteem, employability and general health; all important issues for people living with HIV.

54 of the participants had attended for dental treatment before, but on further inspection only 8 patients had had any experience of restorations, 36 attended for tooth extraction. On unstructured discussion unanimously previous attendance was only on pain presentation. An interesting finding was that only 4 of the 54 (7.4%) that had attended for dental treatment disclosed their HIV status. For 2 of these patients the revealing of their HIV status became such a bad experience of confidentiality breeches and discrimination that they stated they would not disclose in the future. The other 2 patients who revealed their HIV status to the dentist reported good experiences with doing so. Disclosure of HIV to the dentist is essential to enable effective and tailored treatment of dental disease, but more importantly for prevention of oral disease for those most at risk [24].

There are limitations to applying this data to all people living with HIV in Nepal. The patients that attended were already known to be receiving services from the NGO "SPARSHA Nepal" and so it is probable that they are more motivated than an average population of people living with HIV in Nepal. Medical and dental care in Nepal is far from homogenous. Outside of the Kathmandu valley access to dental care and access to HIV-care are very limited quite apart from for patients living with what is still a heavily stigmatised disease [20,24]. Taking into consideration that ART coverage in 2012 was still only 32% meaning that approximately 15,000 people living with HIV in Nepal who are in need of ART but do not have access yet, the importance of clinical assessment of people who do not have access to routine HIV testing and ART services is a matter of course. There is a need to increase oral health awareness not only among health care providers but also specifically for people living with HIV to support access to oral/dental health services not just in acute situations. Issues of substance use disorder (opioids, alcohol, and tobacco) must be raised as risk factors for dental and oral diseases including cancer. But most importantly a non-stigmatizing, non-discriminatory approach to people living with HIV is a key to achieve better oral health in a substantial proportion of people [25].

Conclusion

This study found the oral health status of people living with HIV in Kathmandu/Nepal was generally poor, 55% of the studied population had poor or very poor oral hygiene, 100% had at least one non-HIV-related oral disease and 40 % of the studied population was exhibiting at least one HIV-related oral pathology; despite the majority of participants already receiving ART. The most frequent HIV-related oral lesion was oral candidiasis (19 % or participants). 6 of 12 patients, who did not yet receive ART, were suffering one or more oral, HIV-related, clinical stage 3 of 4 conditions and would therefore be eligible for ART.

Medical and dental health care providers should be competent and committed to screening and diagnosing oral lesions which is relatively easy and low-cost but has often important therapeutic consequences. Discriminatory attitudes of dentists towards patients who were revealing their HIV status have been reported.

Health care providers should increase efforts to raise awareness among patients for risk factors (e.g. substance use, general oral hygiene and prevention among their patients living with HIV), and the importance of general oral health.

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