A systematic review of four decades of prevalence of oral soft tissue infections and conditions among adult HIV patients in India

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ABSTRACT

Oral lesions are a cue for decreased immunity among Human Immunodeficiency Virus (HIV) positive patients. There is no cumulative data available related to the prevalence of oral soft tissue lesions among the HIV positive patients. Hence, the present review was carried out to assess the various oral lesions reported among adult HIV patients across India. Two search engines were used—Google Scholar and PubMed, with key words of HIV/Acquired Immune Deficiency Syndrome(AIDS), soft tissue, oral cavity, India, and adults for searching the articles from January 1990 to December 2020. After initial review, 21 articles that fulfilled the criteria were included in the review. We used 9 parameters to access the quality of the reports. Most common lesion reported was that of oral candidiasis. Not all articles reported about sample size determination or of sampling design and technique. Other lesions like hyperpigmentation, gingivitis, and periodontitis were also found to be highly prevalent. Most reports were from South India. Further epidemiological data are required from different regions for using it to develop planning and execution related to oral health care for the HIV positive patients in India.

Keywords: HIV, India, infections, oral cavity, oral mucosa, periodontitis

Introduction

Oral lesions are a frequent finding and present early stages of decreased immunity in HIV positive individuals. This serves as a cue for further evaluation needed to underline the depleting immunity. The mouth not only serves as an indicator but also reflects the response to the treatment being provided. Most of the lesions associated with HIV are found even in individuals with compromised immunity due to other reasons (like on steroids or in diabetes mellitus) but certain lesions are characteristic hallmarks of HIV/AIDS.[1–4] There is still uncertainty with regard to the exact mechanism of how HIV infection may affect the oral cavity at large. HIV is majorly spread due to the mucosal surface response of the host, which when compromised assists in acquisition and rapid spread of the virus. A breakdown of the same barrier can serve dual purposes of facilitating the spread as well as translocating the microbial products for further infection and inflammation. Although it is suggested that, as a response to the infection, the immunological changes alters the physical barriers in the oral cavity and also assists in further destruction.[5] It facilitates as a reservoir for further spread in the form of bacteremia and septicemia. The European Community (EC) Clearinghouse classification provided the common manifestation of oral lesions in HIV affected individuals.[6] Multiple studies in literature have reported the oral side effects of HIV as well as that of Anti Retro Viral Therapy (ART) drugs which includes...
erythema multiforme, hyperpigmentation, xerostomia, parotid lipomatosis, cheilitis, perioral parathesis, taste alterations, facial oedema, and ulcers. Gallant et al. suggested that the best way to manage HIV cases is through a multidisciplinary team of HIV specialists including family care physicians and family nurse practitioners. Family physicians have a larger role to play and can be the workforce to bank upon in the coming decades for HIV. Unlike the west, India does not have specialist HIV practice or training. Hence, providing family physicians a greater role can bring in quality as well as cost effectiveness to the treatment plan. A team of nurses, oral experts, as well as physicians can act as providers for family care and help improve the present treatment approach.

Oral lesions are a hallmark for disease severity in HIV positive patients. These are affected by the CD4 count as well as the dietary patterns. There is no data reported till now on the epidemiology of oral lesions and HIV across India. This paper brings forward a systematic view of the papers reported in dental literature regarding the prevalence of various lesions across Indian HIV population.

**Materials and Method**

The study was registered in PROSPERO (CRD42021268581). A literature search was carried out using PubMed and Google scholar to access articles from January 1990 to December 2020. All freely available full text articles were selected. The key words used for searching the articles were—India, HIV, AIDS, Soft tissue, and oral cavity. The inclusion criteria were:

1. All Indian-based studies, reporting epidemiological data related to HIV and oral soft tissues diseases or conditions
2. All participants on ART

The initial review was carried out based on the title and the abstract. Later, a full text review was done for the entire article text. The search overall revealed 21 articles that were found eligible. The data extraction was done by the first author based on the following 09 criteria for qualitative assessment of the articles.

1. Study setting-College, hospital, Non Governmental Organization (NGO), home, or any other place
2. Aim and objectives clearly mentioned
3. Sample size Formula and estimation process clearly stated
4. Sample design mentioned which type of sampling design was followed
5. Criteria/index used for recording
6. Calibration of the examiners with the Kappa statistics for reliability and validity
7. Clearly stated if generalizability is possible or not. If not, stated reasons for the same.
8. Clearly mentioned if the participants were on ART/HAART Highly Active Anti retro Viral Therapy or just positive.
9. Clearly stated the inclusion and exclusion criteria

After data extraction, all the 21 articles were independently reviewed by the rest of the authors and any discrepancy was solved by discussion and by generating a common consensus. The PRISMA guidelines was followed for reporting [Figure 1]. The entire process of review and report generation was done in 1 month (January 2020).
Results

Of the 21 articles found eligible for study, majority were from the South part of the country. All the studies focussed on the presence of oral candidiasis except for the study by Krishna et al. For the ease of reporting, we have not classified the candidiasis, but presented the overall percentage. We also classified any form of gingivitis (either bleeding on probing, desquamative gingivitis, or liner erythema gingivitis) as one category of gingivitis. Any such form of periodontitis was also considered under periodontitis. Most of the studies were reported by dental specialists only. Two studies reported oral manifestations as a part of the general physical examination. They were not exclusively concentrating on the oral lesions only. Kumar et al. focussed only on oral candidiasis and no other oral lesions. The same study also reported that soft tissue lesions have no correlation with CD4 count or with ART therapy duration. Rest of the studies reported an inverse relationship

| Author | Year | Place | Samples | Major findings | Outcome/Conclusion |
|--------|------|-------|---------|----------------|-------------------|
| Panda et al. | 1992 | Manipur | 131 | 20.61% Herpes, 5.34% Oral thrush, 10.68% pruritic papular eruptions | “Oral thrush, Herpes zoster and pruritic papular eruptions showed a high specificity and positive predictive value for HIV among intravenous drug users”. |
| Chakraborty et al. | 2008 | Kolkata | 125 (not specified as to ART) | 88% Oral candidiasis | “Opportunistic infections showed an inverse relationship to the CD4 counts” |
| Gnanasundaram et al. | 2010 | Chennai, Tamil Nadu | 686 (not specified as to ART) | 51.5% oral candidiasis, 10.5% Gingivitis, 8.8% Hairy leukoplakia, 5.4% Oral ulcers | “Careful examination of the oral cavity will help to detect these oral manifestations so as a clinician can identify aids in the body through oral manifestation” |
| Shrimali L. | 2010 | Not mentioned | 50 (not specified as to ART) | 100% periodontal disease, 72% oral candidiasis, 32% xerostomia, 42% lymphadenopathy, 36% angular chelitis, 22% persistent oral ulceration, 2% oral hairy leukoplakia, 8% herpes zoster, 10% parotomegaly, 8% facial palsy | “For reducing morbidity from HIV, early detection is necessary, therefore physicians must look for oral manifestation in suspected cases of HIV which aid in early diagnosis and treatment” |
| Saha et al. | 2011 | Kolkata | 204 (not specified as under ART) | 53.4% Oral candidiasis | “Patients who presented HIV associated oral candidiasis without any type of Anti-Retroviral Therapy (ART) had a median CD4+ count lower than 200 cells/mm³, an associated inverse relationship between CD4+ count and the prevalence of OC could be inferred” |
| Bodhade et al. | 2011 | Nagpur, Maharashtra | 399 (not on ART) | 39.3% Oral candidiasis, 19.5% hyperpigmentation, 11.5% Oral hairy leukoplakia, 8.5% Necrotizing gingivitis, 5.3% Necrotizing periodontitis | “Oral manifestations may be used as an alternative to CD4 count at field-based settings to diagnose the immune compromised status of HIV-infected individuals.” |
| Hegde et al. | 2012 | Mangalore, Karnataka | 125 (not specified as to ART) | 52% periodontitis, 32.8% Hyperpigmentation, 15.2% Oral hairy leukoplakia, 16.8% linear gingival erythema, 12.8% Angular chelitis | “Oral lesions have been found to be associated with the early manifestation of HIV and a measure of disease severity” |
| Krishna et al. | 2012 | Chennai, South India | 3729 (71% males and 29% females) | 18.8% males and 10.3% in females- oral candidiasis, 1.2% males and 0.4% females- oral hairy leukoplakia | “Males had a higher risk of oral lesions, especially OC and OHL, than females. This different immunological status of the females compared to males should be taken into consideration in the evaluation and management of HIV positive patients in our country.” |
| Annapurna et al. | 2012 | Tamil Nadu | 50 on ART | 54% Candidiasis, 28% melanotic pigmentation, 6% Oral ulcers, 4% herpes Zoster, 2% Oral hairy leukoplakia, 2% Squamous Cell carcinoma | “Clinical stage C and lower CD4 count may be useful predictors for HIV, with greater prevalence of oral manifestations” |
| Jindwani et al. | 2013 | Central India, MP | 514 patients on ART | 41.5% Oral candidiasis, 23.15% Linear gingival erythema, 14% Oral hairy leukoplakia, 4.8% necrotising ulcerative gingivitis and periodontitis, Ulceration (atypical)- 4.47% | “Usefulness of orofacial examination of the patients by collaborative effort of dental surgeons and physicians and increases their index of suspicion of the infection with the appearance of these HIV associated oral lesions” |

Contd...
### Table 1: Cond...

| Author            | Year | Place                  | Samples                | Major findings                                      | Outcome/Conclusion                                                                 |
|-------------------|------|------------------------|------------------------|-----------------------------------------------------|-------------------------------------------------------------------------------------|
| Kumar et al.[27]  | 2013 | Karnataka              | 1063 patients (on HAART) | 23.5% Oral candidiasis                              | “CD4 count is likely to prove and expressed the opportunistic infections and Oral candidiasis. Early inception of HAART, Good ARV drug adherence can reduce the incidence rate.” |
| Kumar et al.[28]  | 2014 | Ujjain, North India    | 126 on ART             | Candidiasis- 36.5%                                  | “The study shows that HIV positive patients have poor oral health status compared to the HIV negative individuals. Majority of the people living with HIV belong to lower socioeconomic status and also have less awareness about oral health. The use of antiretroviral drugs further depletes their oral health and is responsible for development of oro mucosal lesions” |
| Sanadhya et al.[29] | 2014 | Rajasthan              | 232 (not specified as under ART) | 26.3% Oral candidiasis                              | “The results indicated that among the patients being infected with HIV, there exists a relationship between the occurrence of oral lesions and oral lesions. So, diagnosis of oral lesions is of utmost importance to help identify the underlying or predisposing diseases” |
| Ravi et al.[27]   | 2015 | Karnataka              | 72                     | 46% oral candidiasis                                | “In HIV/AIDS patients as the condition progresses, virus further weakens the immune system leading to multiple oral manifestations and an increase in susceptibility to severe infections and diseases causing failure of organ function leading to comorbid conditions.” |
| Krishna et al.[30] | 2015 | Hyderabad              | 200 (not specified as to ART) | More cases of depapillation and hyperpigmentation | “Subjects with and without ART did not show any difference in the prevalence of periodontal status. Hyperpigmentation was the common condition found among subjects with ART” |
| Patil et al.[25]  | 2015 | North Karnataka        | 50 on HAART and 50 not on HAART | 14% oral pigmentation                              | “Number and severity of oral lesions decreased due to HAART” |
| Hegde et al.[31]  | 2016 | Mangalore, Karnataka   | 112 patients on ART    | 12.5% hyperpigmentation 3.6% herpes simplex and lichen planus 1.8% candidiasis and leukopla 27.8% Candidiasis 42.6% Hyperpigmentation Linear gingival erythema: 2.7% Kaposi Sarcoma: 1.9% | “Oral lesions are considered to be markers of progression of HIV into the final stage of AIDS. Advent of HAART has shown a significant reduction in the oral lesions and a better quality of life in patients with HIV” |
| Denny et al.[32]  | 2016 | Mangalore, Karnataka   | 108 on ART             | 5.3% oral candidiasis, 1.8% Leukoplakia              | “Oral manifestations of HIV infection might serve as good markers for monitoring, not only restoration of immune function, but also HAART failure” |
| Usha et al.[34]   | 2017 | Bangalore, Karnataka   | 600 on HAART and 600 not on HAART but positive | 64% Oral candidiasis 44.5% oral pigmentation, 43% gingival or periodontal infection, 33% reduced salivary Secretion 35% dental caries. | “It was concluded that high incidence of candidiasis may be due to the habits or history of tuberculosis, pigmentation, and xerostomia due to the medication.” |
| Dongade et al.[35] | 2017 | Karnataka              | 373 on ART             | 0.58% oral candidiasis, 1.76 Leukoplakia, 25.29 Hyperpigmentation, 45.29 Periodontitis 1.76 Ulceration | “There was no association between the oral mucosal conditions and the age and the adverse habits, such as tobacco and alcohol, CD4 count, and the time duration of HIV and ART among these patients” |
| Muralidharan et al.[36] | 2018 | Raichur, Karnataka      | 170 on ART             |                                                     |                                                                                      |

between the CD4 count and the oral manifestations. Hence, considering local factors like plaque and oral hygiene practices along with medications apart from ART/HAART should be taken into consideration while diagnosing the cases [Table 1]. The clinical assumption that lower CD4 count means more chances of infection may not hold true for all cases.
Quality assessment of the articles

The above-mentioned 09 parameters were used for quality assessment of the articles as shown in Table 2. Extrapolation of the data was mentioned by only 2 studies.[12,13] The most common classification scale used was the EC clearinghouse for soft tissue manifestation of HIV/AIDS and that by the World Health Organization Oral health Assessment 1997. Studies by Annapurna,[23] Krishna,[13] Muralidharan,[33] and Dongade[31] reported of sample size estimation and the way the samples were calculated; which was missing with the other articles. Even though there was no development of any form of scoring or a rating scale for the studies, overall quality development suggests poor pattern of reporting or at times selective reporting of the data. Not all studies reported of periodontitis and gingivitis while reporting the other oral lesions. Hence, a major part of the information that can be useful for treatment planning and execution is missing with the studies.

Discussion

Unlike the west, we do not have a fixed pattern of assessment and reporting of data for HIV in India. All authors have used different standardized criteria for examination and classification. There is no common consensus or direction in Indian scenario for reporting data in such special groups. Also there is no equitable reporting. Most of the people covered are from the south of India. No stringent sampling technique is followed. The reviewed studies have reported of the participants being on first line ART/HAART. Unfortunately, no studies have been performed on those on second line ART. This is a big lacuna that needs to be addressed. As stated in before, even the ART drugs have ill effects on the oral mucosa, which may manifest in a number of ways. There is no corelation mentioned across the studies related to etiological factors for the conditions. The data presented does not actually represent the current status across the whole of India. It is always possible that some of the participants may be from risky professions like truck drivers, professional sex workers, or intra venous drug abuse users. But no report of such profession risk with oral health has been mentioned in any of the articles. No study mentions about oral sex. It is necessary to record such data also because this may be one risk factor for infection transmission. A special training module can be developed in accordance with family care physicians to focus on data gathering and reporting apart from health advocacy in such cases. Surprisingly, the north east zone hardly finds mention in the oral diseases reporting. The South of India has a multitude of medical and dental institutions that boasts of post-graduation and further studies in dental and allied streams. Hence, it is quite possible that this may lead to number of studies from this particular region of India. The data overall does not serve the purpose of assisting in planning any comprehensive treatment procedures. The arena of managing HIV/AIDS has seen a tremendous change in the last decade. Early diagnosis and prompt treatment is the key for a sustainable institution and continuation of ART. With an improvement in the life and awareness upsurge, as health care workers, there is always a big challenge to the rising risks related to oral health among the...
patients. These highly significant and characteristic features are not just to be recorded but also to be tackled. A national data center for collection of the oral lesions and also a plan to tackle the same is essential. The execution of such complex plans can be carried out easily through the speciality of family care physicians. While oral lesions may not be deadly, unlike Tuberculosis or Hepatitis infections in HIV, they still alter the health slowly and gradually. As the patients undergo regular physical evaluation and drug regime revisions for systemic illness, a similar policy for an oral check-up and preceding treatment is essential. Training and sensitization for health care workers like nursing staff and multipurpose health workers and counselors is required for a greater out reach. India is a diverse country with a number of factors that affect health seeking behavior patterns of the people. In a sensitive case like HIV which is already stigmatized in the society, family care physicians can play a pivotal role for providing health care as well as basic counseling. This expands their role as well as opens up new avenues for their expertise to explore.

What we observed from the review:
1. There is a need to standardize the methods and reporting criteria for HIV and oral health related lesions and conditions in India
2. More intensive training is required to all the clinicians for assessment and also for referral procedures
3. Oral lesions may not always be the hallmark of CD4 count of the cases
4. Team of health care workers need to be working toward the improvement of oral health standards of the sero positive patients
5. No association of these lesions with parameters like comorbidities or quality of life.

The review has certain limitations.
1. Unreported data/grey literature related to conference proceedings or from NACO (National AIDS Control Organization) was not considered for search and review.
2. Possibility of having missed a few articles with richer data that did not appear across indexed journals
3. No risk of bias assessment.

Conclusion
There is a high prevalence of oral candidiasis even among HIV positive patients on ART. More data to compile is available only from South India. Rest regional data is sparse. A range of soft tissue lesions are prevalent and in higher proportions. This can serve as a step to analyze the need to have a nation-wide data and intervention strategies for tackling HIV/AIDS associated opportunistic infections.

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Conflicts of interest
There are no conflicts of interest.
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