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A RELATIONSHIP BETWEEN CD4 COUNT AND ORAL LESIONS IN HIV PATIENTS ON ANTIRETROVIRAL THERAPY

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ABSTRACT

Background: Human immunodeficiency virus (HIV) infection causes a quantitative and qualitative depletion of CD4 lymphocyte count which gradually destroys the body's immune system and increases the risk of opportunistic infections. **Aim:** To check correlation between oral lesions with CD4 count in HIV patients on antiretroviral treatment. **Material and Methods:** Total 90 HIV infected patients on antiretroviral treatment were selected by simple random sampling and their oral cavity screened for any oral lesions and their latest CD4 count noted. **Results:** HIV infection destroys the immune system by depletion of CD4 counts making the patient susceptible to various infections. With the advent of antiretroviral therapy, the scenario has changed drastically. Still many patients show different oral manifestations related to disease or drug therapy. **Conclusions:** According to the results, it seems that CD4 counts and oral lesions are related to the degree of immunosuppression and such lesions can be considered as indicators of the progression of the HIV infection.

KEYWORDS: Antiretroviral treatment, ART, CD4 count, Candidiasis, HIV, Oral lesions.

INTRODUCTION

Human immunodeficiency virus is a retrovirus which has specific affinity for CD4 cells (T helper cells).[1] On entry into the host's body, the HIV attacks and disturbs immune system, thereby making the host susceptible to oral lesions and life-threatening opportunistic infections, neurological disorders, unusual malignancies.[2] It also affects central nervous system, cardiovascular system and hematolymphoid organs.[3] It represents a great multifaceted challenge not only at an individual level but also in the public health domain, which leads to a gradual decrease of immunity and subsequent development of acquired immune deficiency syndrome (AIDS).[1]

In people infected with HIV, antibodies are developed but are not protective. The virus may remain silent and causes CD4 cell depletion resulting in a subsequent decrease in T‑helper cell number, with a resultant loss in immune function which hampers the body's ability to fight infections.[3]

Generalized lymphadenopathy, sore throat, fever, dysphagia, night sweat, maculopapular rash, headache, myalgia, diarrhea and peripheral neuropathies are common signs and symptoms seen with HIV/AIDS. The earliest and most important indicators of HIV infection are oral manifestationsand are seen in 50% of HIV‑infected patients and up to 80% of them will be due to acquired immunodeficiency.[4-6] The most common oral manifestations of HIVare candidiasis, herpes simplex infection, linear gingival erythema, parotid enlargement and recurrent aphthous stomatitis. Periodontal infections are less commonly seen, while hairy leukoplakia and Kaposi's sarcoma are very rare.[7-9] These oral disorders may be implicated in the diagnosis and prognosis of HIV-infected patients.[2]

HIV infection leads to depletion of CD4 lymphocyte count quantitative and qualitatively leads to increase risk of opportunistic infections.CD4+ cell count of <200/µL is key factor that predispose to HIV‑related oral lesions determining both the urgency of HAART initiation and the need for prophylaxis for opportunistic infections.[10-12] Oral manifestations may suggest possible HIV infection in person with unknown HIV status, although they are not diagnostic of infection.[3] However, documentation of relation of CD4 count and oral manifestation in Saurashtra region of Gujarat, India have been sparse. The aim of the study to check correlation

between oral lesions with CD4 count in HIV patients on ART.

MATERIALS AND METHOD

Present study was performedon patients at OPD of ART center of General Hospital, Amreli, Gujarat for 2 years. Before conducting study, research proposal was submitted to institutional ethics committee and permission to conduct the study was obtained. Total 90 patients taken for the study who were agreed to participate and met the criteria. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and later versions.

Sample size estimation was done using formula n = n = (z2* σ2)/ME2 (where n = sample size, ME = margin of error, σ=1 − confidence interval, Z = critical standard score). Sampling was done using simple random sampling. According sample size formula final sample size calculated was 90.

Inclusion Criteria: Patients having HIV and on ART.

Exclusion Criteria

1. Patients who are not willing to participate in the study.
2. Patients below 18 years and/or mentally compromised.

Data Collection

After written informed consent was taken from participant, thorough history was taken and all patients were examined by using mouth mirror and probe under artificial light taking universal precaution. Data were collected in a specially designed proforma.

A cross‑sectional study was conducted on ninety randomly chosen patients who were diagnosed as HIV positive and were on ART therapy independent of age and sex. The patients who were in the window period and not on ART therapy were excluded from the study. All the patients were examined for their oral manifestations, current CD4 counts and duration of the ART therapy.

The subjects were groupedaccording to the status of CD4 count and duration of ARTreceived as follows:
The CD4 counts which were recorded were divided into underthree ranges:
1. CD4 count <200
2. CD4 count between 200 and 400
3. CD4 count >400

The duration of the ART was also divided intothree ranges:
1. ART duration<4 years
2. ART duration between 4 and 8 years
3. ART duration>8 years.
All the ranges were expressed in percentages.

A structured self-administered questionnaire was developed to determine individual characteristics (age, sex), environmental characteristics (ART status and duration), biological function (CD4+ T-lymphocyte count and presence of co-infection), and oral manifestation(any soft or hard tissue lesion etc).

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively. Data were comparing using chi-square test.

RESULTS

Total of 90 patients participated in the study with age range from 21 to 65 years with ean age of 41 years. Out of 90, 57 were male and 33 were female. They were groupedaccording to latest CD4 count into three categories; CD4 count less than 200, between 200 and 400 andmore than 400. Among them 40 patients (24 male, 16 female) have less than 200 CD4 count, 26 patients (16 male, 10 female) have CD4 count between 200 to 400 and 24 patients (17 male, 7 female) have more than 400 CD4 count. [Table 1]

In the same three categories of CD4 count, patients were divided according to their age i.e. 21-30, 31-40, 41-50, 51-60 and more than 60 years. Most patients were in third decade of life. [Table 2] Mean CD4 count were highest among 41-50 age range group. [Table 3]

There are many different oral lesions were seen in patients' mouth. Most common manifestation seen was oral candidiasis. Other lesions seen were gingivitis, periodontitis, linear gingival erythema, herpetic ulcers, apthous ulcers, glossitis, melanotic hyperpigmentation. In one patient, benign gingival growth was seen. Few patients had xerostomia. Out of 90, there were 66 patients have oral manifestations. Highest lesions seen in patients with less than 200 CD4 counts i.e. 39 out of 40 patients have different oral manifestations. 16 out of 26 patients have oral manifestations who have CD4 count between 200 to 400 and 11 out of 24 patients have oral manifestation in patients have more than 400 CD4 counts. [Table 4]

The duration of the ART was also divided intothree ranges:<4 years, between 4 and 8 years and >8 years. There were total 41 patients with less than 4 years duration of ART out of which 32 patients have oral manifestations. 33 patients were between 4 to 8 years on ART out of which 23 patients and 10 out of 6 patients have oral lesions who were on ART for more than 8 years. [Table 5]

DISCUSSION

Since more than two decades in history of HIV epidemic, medical complications expected in a greater number of patients at advance stage of disease and it is a challenge for the health-care delivery system.[2]

The magnitude of this modern disease is really difficult to believe. India is the third largest country in the world in HIV‑infected patients and the HIV epidemic is growing so rapidly.[13,14] HIV is a critical disorder which severely damages the body's normal defenseto infections by reducing immunity thereby making the host vulnerable to life threatening infections and conditions including malignancies.[2] People are living longer and are suffering fewer opportunistic infections with the advent of highly active antiretroviral therapy (HAART).[3]

In patients with HIV infection, often an early frequent finding are oral lesions which affect the quality of life of the patients and are useful markers of disease progression and immunosuppression.[1] In some cases, oral manifestations are the first features of HIV/AIDS or they may be the indication in determination of general health; even some of oral lesions are considered as poor prognosis.[1] Themost important laboratory parameters to evaluate the progression of the diseases arethe cluster of differentiation (CD)4+ T-lymphocyte count and viral load.[15] The laboratory test is generally accepted as the best indicator of the immediate immunological status of the HIV infection[16] and it is an important determinate of the diseases stage and prognosis in seropositive individuals.[17]

HIV causes progressive impairment of the body's cellular immune system, leading to increased susceptibility to tumours, and the fatal condition's known as AIDS.[18] AIDS patient having reduced or compromised immunity due to inadvertent destruction of circulating CD4 T-cells. This often leads to increase in the opportunisticinfections(OIs) in oral cavity caused by commensal oral microbes. With the degree of immunosuppression with disease progression, overall incidence of opportunistic diseases increases.[19] In this way, AIDS-related mortality and morbidity, which is significantly higher in number as compared to other diseases, is actually due to OIs rather than HIV itself.[20] Oral candidiasis is a commonly described OI globally and has been reported as a marker of immunosuppression. The high incidence of oral candidiasis, especially at low CD4 counts, necessitates the introduction of appropriate intervention for the same.[21] The fact is that oral lesions can be readily detected by a trained oral clinician in a standardized, objective fashion without any complicated or expensive diagnostic technique.[2]

In our study prevalence of oral lesions was seen around 73% which was almost similar agreed with the studies done by Bodhade A et. al, Bravo IM et al. and Gaurav S et al.[10,15,22] We observed that the peak age of occurrence of HIV infection was the third and fourth decades of life and that there was slight male predilection which is similar to other Indian studies.[2,10]

A wide range of oral lesions were seen in our study. The most frequently foundoral lesion was oral candidiasis, which was consistent with many studies.[1,2,10,15,23] Among oral candidiasis, the cases of pseudomembranous candidiasis outnumbered those of erythematous candidiasis. This finding wasin accordance with Ranganathan et al.[24] whereas Bodhade A et.[10] alhad reportedpseudomembranous candidiasis as the predominant lesion. Erythematous candidiasis may developin patients taking broad-spectrum antimicrobials. It iscommon in HIV patients who take antibiotics and anti-microbial agents. Moreover, smoking is one of the prevalent habits in India which mayresponsible for an increased incidence of erythematous candidiasis.

We observed periodontal disease more frequently next to candidiasis on our patients which is similar findings with many studies.[25-27] Periodontal disease manifestations in HIV infected individuals include linear gingival erythema, necrotizing ulcerative gingivitis and necrotizing ulcerative periodontitis.

Lower CD4 count, age and gender are considered as predisposing factors for the increasing incidence rate. WHO clinical staging, poor drug adherence, no regular medication and follow ups, co-morbidity, immunological and clinical conditions of the patients were considered as the determinants for occurrence of opportunistic infections like oral candidiasis.[28] It has been showed that thelow circulating CD 4+ cell count is associated withthe progression of HIV infection to AIDS and is usedas a marker for the staging of the disease.[3]

Presence of oral hairy leukoplakia is a fairly reliable indicator of HIV seropositive and is a predictor of declining immunocompetence. As our patients were on ART, immunocompetence was good, hence less no of oral hairy leukoplakia cases were seen as compared to other findings from previous studies investigating HIV associated orallesion.[10,22,25] Less no. of cases of xerostomia, atypical ulceration, herpetic lesions in our HIV infected subjectsare suggestive of good immunocompetence. Occurrence rate of melanin pigmentation was quite high as it could be due to chronic use of antiretroviral drugs by most of our subjects.[25]

Response to ART is affected by the immune stage at which it is started with individuals commencing ART with advanced immunodeficiency to have better virological outcomes than those who commence with more severe immunodeficiency. Adults starting ART with much lower CD4 cell counts have a much greaterrisk of death.[29]

Table 1: Gender wise distribution of study group according to CD4 count categories.

CD4 COUNTS	MALES N (%)	FEMALES N (%)	P value
Less than 200	24 (60%)	16 (40%)	0.56
200 to 400	16 (61.5%)	10 (38.5%)	
More than 400	17 (70.8%)	7 (29.2%)	
Total	57 (63.3%)	33 (36.7%)	

Statistically significance at p≤0.05, test applied chi-square test

Table 2: Age wise distribution of study group according to CD4 count categories.

CD4 COUNTS	Age (Years)					P value
	21-30	31-40	41-50	51-60	More than 60	
Less than 200	2 (5%)	18 (45%)	13 (32.5%)	5 (12.5%)	2(5%)	0.66
200 to 400	4 (15.4%)	11 (42.3%)	7 (26.9%)	4 (15.4%)	0	
More than 400	4 (16.7%)	8 (33.3%)	10 (41.7%)	2 (8.3%)	0	
Total	10 (11.1%)	37 (41.1%)	39 (33.3%)	11 (12.2%)	2(2.3%)	

Statistically significance at p≤0.05, test applied chi-square test

Table 3: Age wise Distribution of cases.

Age Group (Year)	No of Patients	Mean CD4 Count
21-30	10	10.00±6.28
31-40	37	11.52±7.47
41-50	30	14.03±8.9
51-60	11	7.7±6.6
More than 60	2	10±1.41

Table 4: Lesion wise distribution of study group according to CD4 count categories.

CD4 COUNTS	Lesions		P value
	Yes N (%)	No N (%)	
Less than 200	39 (97.5%)	1 (2.5%)	0.001*
200 to 400	16 (61.5%)	10 (38.5%)	
More than 400	11 (45.8%)	13 (54.2%)	
Total	66 (73.3%)	24 (26.7%)	

* indicates statistically significance at p≤0.05, test applied chi-square test

Table 5: Percentage distribution of oral lesions in patients with different duration of antiretroviral therapy.

Lesion	Duration			P value
	Less than 4	4-8	More than 8	
Yes	32 (48.5%)	24 (36.4%)	10 (15.2%)	0.48
No	9 (37.5%)	9 (37.5%)	6 (25%)	
Total	41 (45.6%)	33 (36.7%)	16 (17.8%)	

Statistically significance at p≤0.05, test applied chi-square test

CONCLUSION

The prevalence of oral candidiasis is inversely related to the CD4 counts. Some oral lesions are associated with degree of immunosuppression and can be considered as indicators for prognosis of the HIV infection. The prevalence of oral manifestations depends upon variables like race, socioeconomic status, sex, drug therapy, genetics, oral habits, degree of immune suppression, and variation in diagnostic criteria. Thus, further studies across the country with correlation analyses needed for valid conclusions. There is need for aggressive strategies for the prevention, early diagnosis and treatment of HIV/AIDS and related co-morbidities.

Study limitations and Prospects

All of our participants attended follow-up care at the hospital, and were therefore mostly in relatively good physical condition. Thus, our results cannot be applied to all HIV patients, such as those who are inpatients, those at home and unable to come to the ART center. Further large research studies with larger sample size and a long-term assessment in the form of a longitudinal study are needed involving government and private hospitals to know the actual estimate the relation of oral lesions with CD4 counts. Considering these factors and the fact that this was a preliminary study done on a small scale, we cannot generalize these results to other communities.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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