ORIGINAL ARTICLE

Route of transmission might influence the clinical expression of periodontal lesions in "Human immunodeficiency virus" positive patients

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Abstract

Background: Various routes have been reported with respect to the transmission of human immunodeficiency virus (HIV) from one individual to another. But it is not clear whether they alter the clinical expression of the disease. This study was conducted to know whether there exists any difference in the occurrence of periodontal lesions among untreated HIV subjects who acquired the disease either through intravenous drug abuse or sexual contact and to correlate those lesions with immune suppression as indicated by CD 4 T lymphocyte counts.

Materials and Methods: In this cross-sectional study 213 HIV-positive subjects who had not started on Highly Active Anti Retroviral Therapy (HAART) were selected and divided into two groups intravenous drug users (IVDU) and non-IVDU (NIVDU). CD 4 T lymphocyte counts were evaluated and clinical examination was done to detect the presence of pathologic periodontal lesions.

Results: Mean probing depth (PD) and clinical attachment level (CAL) are significantly higher in drug users than nondrug users. When periodontal lesions are compared with CD 4 cell counts, it is found that significant inverse relation exists between linear gingival erythema, necrotizing ulcerative periodontitis, and CD 4 counts, but only in nondrug users.

Conclusion: An inverse correlation between linear gingival erythema, necrotizing ulcerative periodontitis, and CD 4 counts in NIVDU indicating their reliability as a marker for immune suppression. Periodontitis is more prevalent among drug users indicating some difference in disease expression among the groups.

Key words: Cd4 counts, Highly Active Anti Retroviral Therapy, human immunodeficiency virus, intravenous drug abuse, periodontitis

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Introduction

Periodontitis is an infectious disease resulting in inflammation within the supporting structures of the teeth, progressive attachment loss and bone loss.[1] It is a known fact that oral lesions can be a part of HIV infection and lesions involving periodontal structures are of no exception. Winkler and Murray[2] first reported the relationship between HIV infection and periodontal pathology associated with that. This was a breakthrough as after this report periodontal lesion was given utmost importance in diagnosing HIV-positive patients. But there exist controversies regarding the relationship between periodontal lesions and HIV disease progression, as evaluated by CD 4 T lymphocyte counts.[2,3] It is a well-known fact that HIV has four main routes of transmission and the most common being intravenous drug abuse and promiscuous sexual contact. Reports in the medical literature, although with conflicting results, have shown that the systemic presentation of this illness might vary according to the route of transmission.[4-6] Whereas studies by Palenicek *et al.*[4] and Margolick *et al.*[5] showed

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increased occurrence of oral candidiasis in drug users and homosexuals respectively, study by Routy *et al.*[6] proved that no such predilection exists between these two groups with respect to disease expression. But these kinds of reports are lacking in periodontal literature, in spite of such reports existing with respect to oral lesions seen in HIV infection.[7-9] Thus, the aims and objectives of this study were not only to know whether there exists a relationship between the periodontal lesions and immune suppression as indicated by CD 4 T lymphocyte counts but also to find whether there exists any difference in the occurrence of periodontal lesions among the above-mentioned two groups in individuals who were not under Highly Active Anti Retro-viral Therapy (HAART) as HAART is found to improve the overall immune status of HIV-positive individuals.[10,11]

Materials and Methods

This study was conducted at Anti Retroviral Therapy Centre, Government General Hospital, Chennai from June 2007 to August 2008. All the patients who were diagnosed to have HIV illness (positive for HIV-1 or 2 antibody, confirmed by at least two diagnostic tests, one being confirmatory test), reporting to this centre, were screened, of which subjects who met the inclusion criteria were allowed to participate in this study. The inclusion criteria to participate in this study were gender of either sex, patients who acquired this illness either through intravenous drug abuse or sexual contact and patients who have either good or fair oral hygiene (as determined by simplified oral hygiene index).[12] Exclusion criteria include smokers, pregnant females, patients who had oral prophylaxis within a period of 6 months, history of any systemic illness other than HIV, subjects who acquired the disease through both the routes and people who have started on HAART. Individuals who acquired the illness through other established routes or whose route of acquisition was unclear were also excluded from the study. All the details regarding the route of acquisition and socio demographic data were asked individually, by interviewing them in a private room by a single examiner (A.T.R.) in their regional language. All the patients were asked to give their consent after being informed about the study. This study got the approval from the Institutional ethical Committee, Madras Medical College, Chennai. A total of 213 individuals who met the above said inclusion criteria were divided into two groups [intra venous drug users (IVDU) and those acquired through sexual contact (NIVDU)] and subjected to clinical examination, which included measurement of probing pocket depth (PD), clinical attachment level (CAL) and examination to detect the presence of periodontal lesions related to HIV infection namely linear gingival erythema (LGE), necrotizing ulcerative gingivitis (NUG), and necrotizing ulcerative periodontitis (NUP) by a single examiner (A.T.R). Other oral lesions that were present were also recorded. Probing depth was measured using a probe with William's marking. Three measurements on the buccal surface and three on the palatal/lingual surface were made for each tooth. CAL was calculated using probing depth keeping cemento enamel junction as a reference point.[13] LGE, NUG, and NUP were diagnosed according to the standardized criteria given by Axell *et al.*[14] Briefly, LGE was diagnosed when there is a distinct, complete erythematous band present from one papilla to adjacent papilla and extending to at least 2 mm from the gingival margin. NUG was diagnosed when at least one papilla appears ulcerated or had a crater like appearance and the patient had moderate to severe pain or history of pain in the area within the last 6 months. NUP was diagnosed by same criteria except, in addition to the above-said features, necrotic alveolar bone was exposed or there was evidence of at least 3 mm of probing attachment loss in the interproximal area. CD 4 T cell counts were estimated by Flow Cytometry (BD FACSAria, Beckton Dickinson Pvt. Ltd., India) for all these patients,1-2 days prior, or on the day of examination. Data thus collected were analyzed statistically using SPSS. A Student t-test was used to compare PD and CAL between the groups and a chi-square test was employed to compare the periodontal lesions between the two groups. Kendall's τ correlation coefficient was used to know the correlation between the lesions and declining CD 4 T cell counts. Results were considered to be significant at a P value < 0.05.

Results

Our study comprised 213 untreated HIV-positive individuals divided into two groups, IVDU (n=40) and NIVDU (n=173). NIVDU included both males and females between the age group of 25-60 years with mean age of 34.08 + 9.08 years, including homosexuals, bisexuals, and heterosexuals, whereas IVDU consisted of only males within the age group of 2448 years with mean age of 37.1 + 7.07 years. Lack of females in the drug user group is due to the reduced number of female drug users, especially in our part of the country.

When the prevalence of periodontal lesions was considered in the entire cohort under study, LGE was seen in 45.5%, NUG in 1.4%, and NUP in 1.9% of the individuals. The prevalence of these lesions in each group is shown in Table 1. Oral lesions seen in our study group were oral candidiasis, oral hairy leukoplakia, and median rhomboid glossitis.

Table 1: Comparison of periodontal lesions between IVDU and NIVDU

Lesion	IVDU (n=40) (%)	NIVDU (n=173) (%)	P value
LGE	21 (52.5)	76 (43.9)	0.32
NUG	01 (2.5)	02 (1.2)	0.51
NUP	01 (2.5)	03(1.7)	0.74

IVDU = Intra venous drug users; NIVDU = Non intravenous drug users ; LGE = Linear gingival erythema; NUG = Necrotizing ulcerative gingivitis; NUP = Necrotizing ulcerative periodontitis

When periodontal parameters were compared between both the groups, PD ranged from minimum of 2.31 mm to maximum of 5 mm in the group IVDU, whereas it ranged from 2.1 mm to 4.52 mm in the case of NIVDU. CAL ranged from 2.3 to 6.85 mm in the group IVDU and 2.4 to 6.2 mm in NIVDU. When the periodontal parameters, namely PD and CAL, were compared between both the groups, CAL was seen more in IVDU than in NIVDU as shown in Table 2.

No periodontal lesion showed significant prediction toward IVDU or NIVDU.

CD 4 T cell was classified into three groups, counts above than 500, between 200 and 500, and counts less than 199 cells/mm^3. The number of individuals displaying periodontal lesions and their stratification according to the CD 4 counts were shown in Table 3. When the decrease in CD 4 T cell counts was correlated with CAL or pocket depth, no statistically significant correlation was found to exist in both the groups as shown in Table 4, but there existed a significant inverse correlation between LGE and NUP and CD 4 counts, but only in the group NIVDU as shown in Table 5.

Discussion

Acquired immunodeficiency syndrome is a universal epidemic affecting all the domains of population. It is a well-established fact that oral manifestations might be the initial presentation of this illness. Among the various oral lesions, periodontal manifestations have important implications as they are supposed to be strongly associated with this infection. Some of the periodontal lesions like NUP tend to occur more as the CD 4 count decreases, indicating the reliability of these lesions in indicating immune suppression.[15]

Patients not under HAART tend to have more lesions than patients under HAART and hence we decided to study those people in whom the clear clinical manifestation of HIV infection can be studied.[10] We aimed correlating these lesions with CD 4 counts in an attempt to know the effect of immune suppression on periodontal tissues, as CD 4 counts show the true immune status of these individuals. When CD 4 counts were correlated with all the lesions identified, we found no correlation between declining CD 4 counts and pocket depth or CAL in both the groups, similar to the findings of Goncalves *et al*.[16]

But in IVDU, we found an inverse relationship between LGE, NUP and depleting CD 4 counts. Even though Ceballos-salobrena *et al*.[17] and Margiotta *et al*.[18] showed similar results, the above-mentioned studies do no differentiate the study group into intravenous and nonintravenous drug users, whereas we have attempted to differentiate the study group into drug users and nondrug users.

With respect to NUP, Glick *et al*[15] mentioned that NUP should be considered for inclusion in AIDS surveillance definition. In our study, though NUP does not correlate with declining CD 4 counts in the drug users, the patients who showed NUP had CD 4 value less than 200 cells/ mm^3. Thus this study depicts the occurrence of periodontal lesions in HIV patients unmasked by HAART therapy. The reason for this difference between our study and the study by Glick *et al*.[15] might be that the study group in ours comprised patients not under HAART, whereas the ART status of the latter was not mentioned. But this proves the validity of the statement given by Glick *et al*.[15] that NUP can be considered as a marker of immune suppression and further studies with increased sample size are required to confirm this.

Table 2: Comparison of PD and CAL between IVDU and NIVDU

Periodontal parameters	IVDU Mean+SD (mm)	NIVDU Mean+SD (mm)	*P* value
PD	2.59 ± 0.46	2.44 ± 0.37	0.03*
CAL	3.22 ± 0.80	2.85 ± 0.70	0.004*

*Statistically significant.

Table 3: Stratification of lesions according to CD 4 counts in two groups

Lesion	IVDU *n*=40 (%)	NIVDU *n*=173 (%)
LGE NUG	>500 cells/mm^3 - 06 (15)	>500 cells/mm^3 - 23 (13.2)
NUP	200-499 cells/mm^3 - 09 (70)	200-499 cells/mm^3 - 32 (18.4)
	<199 cells/mm^3 - 06 (15)	<199 cells/mm^3 - 21 (12.1)
	>500 cells/mm^3 - 0	>500 cells/mm^3 - 0
	200-499 cells/mm^3 - 01 (2.5)	200-499 cells/mm^3 - 02 (1.15)
	<199 cells/mm^3 - 0	<199 cells/mm^3 - 01 (2.5)
	>500 cells/mm^3 - 0	>500 cells/mm^3 - 0
	200-499 cells/mm^3 - 0	200-499 cells/mm^3 - 0
	<199 cells/mm^3 - 01 (2.5)	<199 cells/mm^3 - 03 (1.73)

LGE = Linear gingival erythema; NUG = Necrotizing ulcerative gingivitis; NUP = Necrotizing ulcerative periodontitis

Table 4: Correlation between periodontal parameters and CD 4 counts in IVDU and NIVDU

Lesion	IVDU		NIVDU	
	Correlation coefficient	*P* value	Correlation coefficient	*P* value
PD	-0.14	0.9	-0.06	0.2
CAL	-0.16	0.19	-0.07	0.2

PD = Pocket depth; CAL = Clinical attachment level

Table 5: Correlation between Periodontal lesions and CD 4 counts in IVDU and NIVDU

Lesion	IVDU		NIVDU	
	Correlation coefficient	*P* value	Correlation coefficient	*P* value
LGE	0.06	0.6	-0.14	0.04*
NUG	-0.19	0.19	-0.09	0.2
NUP	-0.19	0.19	-0.19	0.009*

*Statistically significant.

This also denotes that even though the organism might be the same, the route by which this organism enters the tissue might play a role in disease expression. There are studies in the literature which associated oral and periodontal lesions in HIV infected individuals,[17-19] but very few studies have been attempted to find difference in disease expression in periodontal tissues among the above said groups.[20,21] In the medical literature, there are many studies related to this issue.[4,5,6,22] But there are scanty studies focusing at this issue with respect to periodontal lesions and to the best of our knowledge, no studies have been done in our population. Study by Pehrson *et al.*[22] showed the rate of progression of AIDS indicating illness from HIV-positive state is more with homosexuals than in drug users. With respect to periodontal tissues, study by Friedman *et al.*[20] showed no difference in disease expression among the groups, but we found attachment loss is seen more with IVDU compared to NIVDU, indicating not only severe periodontal destruction in drug users, but also denotes route of transmission might play an important role in the initiation of immune response.[22] One important factor to be considered while interpreting these results is that the number of drug users in our study is very less owing to their reduced prevalence in our part of the country. In addition females are not included in the drug users group restricting us to find the influence of gender in interpretation of the results. This is the major limitation of this study, and further studies will be done in this aspect. But the results obtained through this preliminary study cannot be under estimated as this shows there is difference in disease expression between the two groups. This difference can be due to the transmission route determining the immune response, as immune response might differ according to the route of disease acquisition.[23] This occurs as the body mounts immune response to disparate viral strains operating in drug users.[22] This denotes the importance of route of acquisition but further studies must be done in this aspect to support this hypothesis.

When we compare other oral lesions among the groups, none of the lesions showed predilection towards any of the group, showing similar disease expression among the groups which is similar to the study by Routy *et al.*[5] where they showed the disease expression is same in both drug users and non drug users.

Before making a final conclusion, it becomes essential to discuss about the microbial flora, as, the presence of syncytium inducing HIV serotype can lead to accelerated CD4 count depletion, immune suppression and hence more periodontal destruction.[23] This study thus opens the view stating that route of disease acquisition might play a role in the disease expression and future studies are required in this direction to identify the actual mechanism underlying this.

Conclusion

It can be inferred from our study that LGE and NUP are the two lesions which are inversely correlated with CD4 counts, but only in NIVDU. This and the increased prevalence of periodontal destruction in IVDU as indicated by increased CAL show evidence route of transmission might play a role in clinical expression of the disease.

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References

1. Flemmig TF. Periodontitis. Ann periodontal 1999;4:32-8.
2. Winkler JR, Murray PA. A potential intra oral expression of AIDS may be a rapidly progressive periodontitis. Calif Dent Assoc J 1987;15:20-4.
3. Cross DL, Smith GL. Comparison of periodontal disease in HIV seropositive subjects and controls (II): Microbiology, immunology and predictors of disease progression. J Clin Periodontol 1995;22:569-77.
4. Palenicek J, Nelson KE, Vlahov D, Galai N, Cohn S, Saah AJ. Comparison of clinical symptoms of human immunodeficiency virus disease between intravenous drug users and homosexual men. Arch Intern Med 1993;153:1806- 12.
5. Margolick JB, Muñoz A, Vlahov D, Astemborski J, Solomon L, He XY, *et al*. Direct comparison of the relationship between clinical outcome and change in CD4+ lymphocytes in human immunodeficiency virus-positive homosexual men and injecting drug users. Arch Intern Med 1994;154:869-75.
6. Routy JP, Vanhems P, Rouleau D, Tsoukas C, Lefèbvre E, Côté P, *et al*. Comparison of clinical features of acute HIV-1 infection in patients infected sexually or through injection drug use. The Investigators of the Quebec Primary HIV Infection Study. J Acquir Immune Defic Syndr 2000;24:425-32.
7. Lamster IB, Begg MD, Mitchell-Lewis D, Fine JB, Grbic JT, Todak GG, *et al*. Oral manifestations of HIV infection in homosexual men and intravenous drug users. Study design and relationship of epidemiologic, clinical, and immunologic parameters to oral lesions. Oral Surg Oral Med Oral Pathol 1994;78:163-74.
8. Begg MD, Panageas KS, Mitchell-Lewis D, Bucklan RS, Phelan JA, Lamster IB. Oral lesions as markers of severe immunosuppression in HIV-infected homosexual men and injection drug users. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;82:276-83.
9. Phelan JA, Begg MD, Lamster IB, Gorman J, Mitchell-Lewis D, Bucklan RD, *et al*. Oral candidiasis in HIV infection: predictive value and comparison of findings in injecting drug users and homosexual men. J Oral Pathol Med 1997;26:237-43.
10. Patton LL, McKaig R, Strauss R, Rogers D, Eron JJ Jr, Chapel Hill NC. Changing prevalence of oral manifestations of HIV in the era of protease inhibitor therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;89:299-304.
11. Tappuni AR, Fleming GJ. The effect of ART on the prevalence of oral manifestations in HIV infected patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;92:623-8.
12. Greene JC, Vermillion JR. The simplified oral hygiene index. J Am Dent Assoc 1964;68:7-13.
13. Grant DA, Stern IB, Listgarten MA: Periodontics. St. Louis: The CV Mosby Company; 1988 p.545-7.
14. Axell T, Azul AM, Challacombe SJ, Ficcara G, Flint S, Greenspan D, *et al*. 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 Immunodeficiency Virus. J Oral Pathol Med 1993;22:289-91.
15. Glick M, Muzyka BC, Salkin KM, Curie D. Necrotizing ulcerative peiodontitis: a marker for immune deterioration and predictor of diagnosis of AIDS J Periodontol 1994;65:393-7.
16. Goncalves LS, Ferreira SM, Silva A Jr, Villoria GE, Costinha LH, Colombo AP. Association of T CD4 lymphocyte levels and chronic periodontitis in HIV-infected brazilian patients undergoing highly active anti-retroviral therapy: clinical results. J Periodontol 2005;76:915-22.
17. Ceballos-salobrena A, Aguirre-urizar JM, Bagan-sebastian JV. Oral manifestations associated with HIV infection in a Spanish population. J Oral Pathol Med 1996;25:525-7.

18. Margiotta V, Campisi G, Mancuso S, Accurso V, Abbaessa V. HIV infection: Oral lesions, CD4+ cell count and viral load in an Italian study population. J Oral Pathol Med 1999;28:173-7.
19. Martinez-Canut P, Guarinos J, Bagan JV. Periodontal disease in HIV seropositive patients and its relation to lymphocyte subsets. J Periodontol 1996;67:33-6.
20. Friedman RB, Gunsolley J, Gentry A, Dinius A, Kaplowitz L, Settle J. Periodontal status of HIV seropositive and AIDS patients. J Periodontol 1991;62:623-7.
21. Grbic JT, Mitchell-Lewis DA, Fine JB, Phelan JA, Bucklan RS, Zambon JJ, *et al*. The relationship of candidiasis to linear gingival erythema in HIV-infected homosexual men and parenteral drug users. J Periodontol 1995;66:30-7.
22. Pehrson P, Lindbäck S, Lidman C, Gaines H, Giesecke J. Longer survival after HIV infection for injecting drug users than for homosexual men: implications for immunology. AIDS 1997;11;1007-12.
23. Spijkerman IJ, Koot M, Prins M, Keet IP, van den Hoek AJ, Miedema F, *et al*. Lower prevalence and incidence of HIV-I syncytiuminducing phenotype among injecting drug users compared with homosexual men. AIDS 1995;9: 1085-92.

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