



CORRELATION OF MUCOCUTANEOUS MANIFESTATIONS, CD4+ T CELL COUNTS AND WHO CLINICAL STAGING IN HIV/ AIDS IN A TERTIARY CARE CENTRE

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ABSTRACT

Introduction: Human Immunodeficiency Virus (HIV) infected individuals develop variety of skin manifestations. They may not only point towards the diagnosis of HIV infection but tend to appear at specific stage in the progression of HIV and act as an indicator of the development of AIDS (Acquired Immunodeficiency Syndrome).

Objectives: To identify and correlate mucocutaneous disorders to CD4⁺ T cell count and to study the correlation between CD4⁺ T cell counts and WHO clinical staging in HIV/AIDS patients.

Materials and Methods: Data were collected from 110 consecutive HIV positive adult patients with skin manifestations, on a pre-designed proforma followed by detailed clinical examination and relevant diagnostic tests.

Results: Majority of patients were young and the predominant mode of transmission was heterosexual contact. Most common dermatological manifestations were herpes zoster, seborrheic dermatitis, scabies, longitudinal melanonychia, maculopapular drug rash and molluscum contagiosum. Significant correlation was observed between the CD4⁺ T cell counts and WHO clinical staging.

Conclusions: WHO clinical staging has an important role in the management of HIV/AIDS especially in our part of the world. Skin is an important clinical organ for assessment, prediction of immune status, and management of HIV/AIDS, particularly for hard to reach and resource limited health settings.

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INTRODUCTION

Skin is the most commonly affected organ in patients with HIV infection. A wide range of infectious and noninfectious skin lesions develop during the course of the disease and in many, these may be the earliest and the only sign of HIV/AIDS. Skin manifestations occur in upto 90% of HIV infected individuals. The diagnosis of HIV/AIDS can often be suspected based on the combination of skin lesions[1]. They tend to appear at a specific stage in the progression of HIV and also act as an indicator of the development of AIDS. As the disease progresses they become more severe and varied, causing significant morbidity and psychological distress.

CD4⁺ T cell count is one of the essential tools in the clinical evaluation and the management of an HIV infected patient. It is a key marker for determining disease progression and risk for opportunistic infection in HIV infected patients[2]. However, expenses and requirement of sophisticated laboratory facilities make its availability limited, especially in the resource poor settings. WHO clinical staging can be used in place of CD4⁺ T cell count to assess the progression to AIDS and as a guide to start antiretroviral therapy[3]. So the

present study was conducted to identify and correlate mucocutaneous manifestations in patients with HIV/AIDS with CD4⁺ T cell count and WHO clinical staging.

MATERIAL AND METHODS

Study design: It was a cross-sectional study, conducted in the outpatient department of Dermatology, Venereology and Leprosy and Regional STD Teaching, Training and Research Centre, VMMC and Safdarjung Hospital, New Delhi from October 2013 to September 2015. The study included 110 HIV positive male and female patients of (18 years or more) presenting to the skin outpatient department. Patients were informed about the purpose of the study and their detailed history, presenting complaints and physical examination were recorded.

Diagnostic tests for mucocutaneous manifestations: Relevant tests like potassium hydroxide mount of skin scrapings for dermatophytosis and candidiasis, Tzanck smear for herpes infection, dark field microscopic examination for syphilitic lesions and skin biopsy were performed wherever required.

CD4⁺ T cell estimation: The estimation of CD4, CD3 lymphocytes and CD4/CD3 was done by FACS (Fluorescent Activated Cell Sorter) count system (Becton Dickenson Flowcytometry system, San Jose, CA 95131 -1807) at the Regional STD Centre

Staging: Clinical staging according to WHO criteria was done[4].

Data analysis The data were analyzed using Microsoft excel and SPSS version 16. chi-squared test for correlation, p< 0.05 was considered as statistically significant.

RESULTS

A total of 110 patients with HIV/AIDS were enrolled and examined for mucocutaneous manifestations. Out of 110 patients, 48 (43.60%) were females and 62 (56.40%) were males. Male: female ratio in this study was 1.29. Number of manifestations seen in females was 114 (58.76%) and in males were 80 (41.24%). Majority of patients belonged to the age group of 18-30 years (40%), followed by 31-40 year (38.2%), 41-50 years (15.5%), 51-60 years (4.5%) and 61-70 years (1.8%). Majority of patients were married (84.55%) followed by unmarried (8.18%), divorced (2.73%) and widowed (4.55%) (Table1).

Table 1 Demographic data of the study population

| Category | No. of cases |
|-------------------------------------|--------------|
| 1. Sexwise distribution | |
| Male | 62 (56.40%) |
| Female | 48 (43.60%) |
| 2. Age wise distribution (in years) | |
| 18-30 | 44(40.00%) |
| 31-40 | 42(38.20%) |
| 41-50 | 17(15.50%) |
| 51-60 | 5(4.50%) |
| 61-70 | 2 (1.80%) |
| 3. Marital status | |
| Married | 93(84.55%) |
| Unmarried | 9(8.18%) |
| Divorced | 3(2.73%) |
| Widow | 5 (4.55%) |
| 4. Educational status | |
| Primary | 18(16.40%) |
| Secondary | 31(28.20%) |
| High school | 21(19.10%) |
| Bachelor,s degree | 10(9.10) |
| Master's degree | 1(0.90%) |
| Illiterate | 29(26.40%) |
| 5. Occupation | |
| Skilled | 18 (16.40%) |
| Semiskilled | 29(26.40%) |
| Manual labour | 17(15.50%) |
| Unemployed | 10(9.10%) |
| Housewife | 33(30.00%) |
| Student | 3(2.70%) |

The most common mode of transmission was heterosexual route (92, 83.60%), followed by needle stick injury (10, 9.10%), blood transfusion (5, 4.50%) and homosexual route (1, 0.90%). In 2 cases, mode of transmission was unknown. Out of 110 patients, 37 patients (33.63%) had CD4⁺ T cell count <200 cells/mm³, 60 patients (54.54%) had CD4⁺ T cell count between 200-499 cells/mm³ and 13 (11.81%) had CD4⁺ T cell count >=500 cells/mm³. Total of 66 patients (60%) were on HAART while 44 patients (40%) were not receiving HAART (Table 2). Majority of the patients were in WHO Stage II (42, 38.20%) followed by Stage I (34.50%), Stage III (20, 18.20%) and Stage IV (10, 9.10%). The most common manifestation in our study was Herpes zoster (17, 8.76%), followed by seborrheic dermatitis (13, 6.7%), scabies (10, 5.15%),

longitudinal melanonychia (10, 5.15%), molluscum contagiosum (9, 4.64), maculopapular drug rash (9, 4.64) and genital warts (8, 4.12). In our study, it was seen that there was significantly high occurrence of herpes zoster (p<0.001), dermatophytosis (p<0.0004) and scabies (p<0.001) with high CD4⁺T cell counts (200-499 cells/mm³). A statistically significant negative correlation was also found between stage of infection and CD4⁺ T cell count (Table 3).

Table 2 Distribution of patients according to Highly Active Antiretroviral therapy

| Type of HAART | No. of patients |
|--------------------------------------|-----------------|
| Nevirapine + Lamivudine + Zidovudine | 49(44.50%) |
| Nevirapine + Lamivudine + Stavudine | 5(4.50%) |
| Lamivudine + Zidovudine + Efavirenz | 12(10.90%) |
| No HAART | 44(40.00%) |
| Total | 110(100.00%) |

Table 3 Distribution of patients according to WHO clinical staging

| Stage | No. of patients | Mean CD4+ T cell count (cells/mm ³) |
|-------|-----------------|---|
| I | 38(34.50%) | 344.66 |
| II | 42(38.20%) | 324.74 |
| III | 20(18.20%) | 180.85 |
| IV | 10(9.10%) | 129.20 |
| Total | 110(100.00%) | 287.681 |

Table 4 Cutaneous disorders and its correlation with CD4 counts

| Skin manifestation | Mean CD4+ T cell count (cells/mm ³) | | p-value |
|---------------------------|---|-------|---------|
| | <200 | >=200 | |
| Herpes zoster | 4 | 13 | <0.001 |
| Seborrheic dermatitis | 5 | 4 | 0.176 |
| Dermatophytosis | 4 | 6 | 0.0004 |
| Scabies | 2 | 8 | <0.001 |
| Longitudinal melanonychia | 3 | 7 | 0.549 |
| Molluscumcontagiosum | 3 | 7 | 0.549 |
| Maculopapular drug rash | 1 | 8 | N.A. |
| Genital warts | 2 | 4 | 0.187 |

Significant value calculated by chi-squared test. p<0.05 was considered significant.

DISCUSSION

More than 90% of patients develop skin or mucous membrane lesions at some time during their disease and often skin is the first organ to be affected[5]. The minimally impaired skin immune system; early in the course of HIV infection is believed to be responsible for frequent occurrence of both infectious and non infectious skin disease even before the development of gross immunodeficiency[6]. Moreover, several skin diseases have proven to be sensitive and useful measures by which progression of HIV infection can be monitored[7].

We studied 110 HIV positive patients and it was observed that male to female ratio was 1.29. The results were consistent with the studies of Srikanth *et al* (2010)[8], Singh *et al* (2009)[9], X-Huang *et al* (2011)[10]. This could be explained by the fact that more number of male patients attended the hospital compare to females and also by greater involvement of males in "high risk" activities[11]. A detailed history about occupation of the study group revealed increased occurrence of HIV among house wives, unskilled workers and manual laborers. This is because the main route of transmission in females is sexual contact with their spouse and free services

provided by government hospitals are utilized more by people of middle and low socioeconomic groups. Most of the patients belonged to rural areas with poor educational background. Hence, their awareness regarding the disease and its routes of spread was poor. The most common mode of transmission was unprotected heterosexual exposure (83.6%), which was consistent with the studies by Singh, et al. (2009)[9] and Srikanth, et al. (2010)[8] who reported 94.16 % and 72% respectively.

The most common mucocutaneous manifestation was Herpes zoster which was present in 17 patients (8.76%). This was consistent with the study of Huang et al [10] where it was seen in 9.37% patients. There are reports of herpes zoster occurring in 6% to 25% of HIV patients [12]. In our study, 2 patients presented with disseminated Herpes zoster and 4 patients presented with ulceration which healed with prominent scars. The mean CD4⁺ T cell count was 385.058 cells/mm³. Seborrheic dermatitis was the second most common disease and was seen in 13 patients (6.7%) which is similar to 7% cases reported by Atilli et al [13]. The mean CD4⁺ T cell count is 245.769 cells/mm³ which was comparable with the value of 240 cells/mm³ observed by Shobhana et al and Kore et al [12, 14]. The other common manifestations were scabies (10, 5.15%) with mean CD4⁺ T cell count of 245.769 cells/mm³, longitudinal melanonychia (10, 5.15%) with mean CD4⁺ T cell count of 351.3 cell/mm³, molluscum contagiosum (9, 4.64%) with the mean CD4⁺ T cell count of 113.6 cells/mm³, maculopapular drug rash (9, 4.64%) with mean CD4⁺ T cell count of 252.44 cells/mm³ and genital warts (8, 4.12%) with mean CD4⁺ T cell count of 304.375 cells/mm³.

Majority (54.54%) of patients in our study had CD4⁺ T cell count between 200-499 cells/mm³. The probable reason may be because 60% of the patients were on highly active anti retroviral therapy and also because some patients who were not on treatment had CD4⁺ T cell count above 350 cells/mm³ which is cut off level below which antiretroviral therapy is started in our institution. In our study majority of patients presented to us in Stage II (42, 38.20%) followed by Stage I (34.50%). This finding was consistent with the fact that majority of patients had CD4 counts between 200-499 cells/mm³. Significant negative correlation was found between WHO stage and CD4⁺ T cell counts in our study which suggests that patients with advanced stages of HIV infection had significantly lower CD4⁺ T cell counts. This can be explained by the fact that with decreasing CD4⁺ T cell counts, there is development of various opportunistic infections and neoplasms with consequent change in the stage of the disease. It was seen that there was significantly high occurrence of herpes zoster (p<0.001), dermatophytosis (p<0.0004) and scabies (p<0.001) with high CD4⁺ counts (200-499 cells/mm³) (Table 4). Reasons may be that herpes zoster and scabies can occur in any stage of HIV infection and in our study, the highest number of patients had CD4⁺ T cell count between 200 and 499 cell/mm³.

CONCLUSION

It can be concluded from our study that heterosexual transmission is still the major mode of transmission. The factors like low socioeconomic status and low literacy levels play a major role in spread of the disease. Dermatological manifestations are common at every stage of HIV infection and some of them can serve as predictors of infection and its progression. In our study it was clearly apparent that the stage

of the disease progressed with the fall in the CD4⁺ T cell count. In settings where facilities for sophisticated lab tests are not available, clinical staging can serve as a useful tool in the management of the disease.

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Reference

1. James WD B TaED. Andrews' Diseases of the Skin, 10th Edition. Clinical Dermatology 2006(10th ed):367-420.
2. Nnoruka EN, Chukwuka JC, Anisui B. Correlation of mucocutaneous manifestations of HIV/AIDS infection with CD4 counts and disease progression. *Int J Dermatol* 2007 Oct;46 Suppl 2:14-8.
3. Oninla OA. Mucocutaneous Manifestations of HIV and the Correlation with WHO Clinical Staging in a Tertiary Hospital in Nigeria. *AIDS Res Treat* 2014;2014:360970.
4. WHO. Antiretroviral therapy in HIV infection in adults and adolescence in resource limited setting : towards universal access. 2006.
5. Coldiron BM BR. Prevalence and clinical spectrum of skin disease in patients infected with HIV. *Arch Dermatol* 1989;125:357-61.
6. Tschachler E, Bergstresser PR, Stingl G. HIV-related skin diseases. *Lancet* 1996 Sep 7;348(9028):659-63.
7. Prabhakaran N, Jaisankar TJ, Hamide A, Malathi M, Kumari R, Thappa DM. Effect of antiretroviral therapy on mucocutaneous manifestations among Human Immunodeficiency Virus-infected patients in a tertiary care centre in South India. *Indian J Sex Transm Dis* 2015 Jul-Dec;36(2):166-73.
8. Srikanth KP VS, Aparna. A hospital based cross sectional study of mucocutaneous manifestations in the HIV infected. *Int J CRIMPH* 2010;2:50-78.
9. Singh H, Singh P, Tiwari P, Dey V, Dulhani N, Singh A. Dermatological manifestations in HIV-infected patients at a tertiary care hospital in a tribal (Bastar) region of Chhattisgarh, India. *Indian J Dermatol* 2009;54(4):338-41.
10. Huang XJ, Li HY, Chen DX, et al. Clinical analysis of skin lesions in 796 Chinese HIV- positive patients. *Acta Derm Venereol* 2011 Sep;91(5):552-6.
11. Sharma S, Puri KJ, Gambhir ML. Male preponderance in HIV seropositive patients with mucocutaneous complaints in a tertiary care hospital in North India. *Asian Pac J Trop Biomed* 2014 May;4(Suppl 1):S186-8.
12. Shobhana A, Guha SK, Neogi DK. Mucocutaneous manifestations of HIV infection. *Indian J Dermatol Venereol Leprol* 2004 Mar-Apr;70(2):82-6.
13. Attili VSS SV, Sundar S. Relationship Between Skin Diseases and CD4 Cell Counts in a Hospital-based Cohort of HIV-infected Adults in North India. *JACM* 2008;9:20-5.
14. Kore SD, Kanwar AJ, Vinay K, Wanchu A. Pattern of mucocutaneous manifestations in human immunodeficiency virus-positive patients in North India. *Indian J Sex Transm Dis* 2013 Jan;34(1):19-24.