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Original Article

Morphological spectrum of cutaneous manifestations with CD4 correlation in patients with AIDS

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Abstract

Objective To determine the frequency and spectrum of cutaneous manifestations in patients with AIDS and their relationship to CD4 counts.

Methods 300 HIV seropositive patients who visited the Dermatology outpatient department and HIV clinic of Services Hospital, Lahore over a period of 1year (June 2017- May 2018) were included in this cross sectional study. Out of 300 patients, 290 were on ART. Thorough cutaneous examination was performed after informed consent. CD4 counts (cells/mm^3) of the patients noted from medical record. All the mucocutaneous conditions of the patients were noted and categorized as infectious, noninfectious dermatoses and drug reactions. Clinical and immunological staging method developed by World Health Organization (WHO) was used to classify patients into different stages. Data analysis was carried out using SPSS V.22.

Results Among the 300 HIV-positive individuals, a gender ratio of 3:1 was observed with 228 (76.0%) men and 72 (24%) women. Patients' average age was 33.67±10.84 years. Heterosexual route of transmission was the commonest route 96 (32%), followed by blood transfusion 84 (28%), surgical procedure 72 (24%), intravenous drug abuse 44 (14.7%) and sharing of common needle or injection 20 (6.7%).The mean duration of HIV was 1.49±0.77 years. There were more dermatoses per subject as the CD4 count dropped. Immunological deterioration lead to increase in the number of patients having dermatoses; 8% patients with CD4 count of >500 compared to 77.3% patients with CD4 count of 200-350. Dermatophytosis was the most common infection, 60 patients with a mean CD4 count of 165.6±10.2 followed by candidiasis, 40 patients with CD4 count of 220 ±179.1. Xerosis was the most common non-infectious disorder.

Conclusion Mucocutaneous manifestations develop during the course of HIV infection. Dermatophytosis and candidiasis exhibit a significant reciprocal relationship with CD4 cell count, and because of this they can be utilised as an indirect evidence of severe immunosuppression to initiate highly active anti-retroviral therapy in the absence of access to resources for CD4 cell count.

Key words
Antiretroviral therapy; CD4 cell count; Human Immunodeficiency Virus infection: Mucocutaneous manifestations.

Introduction

A single stranded RNA retrovirus called the human immunodeficiency virus (HIV) is the cause of a chronic, potentially fatal illness known as acquired immune deficiency syndrome (AIDS). Pakistan is among the four countries in the WHO Eastern Mediterranean Region where the incidence of HIV infections is rising alarmingly since 1987. New cases of HIV increased from 14000 in 2010 to 22000 in 2018, with a 369% rise in HIV-related deaths during this period. The recent epidemic of HIV in Pakistan is described as a concentrated

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epidemic. The most recent estimation of people living with HIV (PLHIV) in 2017 was 150,000 despite the fact that the general adult prevalence is below 1%.[1]

Skin is among the different tissues and organs that the human immunodeficiency virus (HIV) can affect. Skin lesions appear in more than 90% patients and oral lesions in 30-80% patients during the course of the disease.[2,3] Skin disorders are divided into primary and secondary skin lesions. Secondary skin lesions are caused by the decrease in CD4 count (including opportunistic infections and malignant skin cancers), while the etiopathogenesis of the primary cutaneous disorders is still under consideration. Majority of cutaneous inflammatory illnesses linked to AIDS are still common, despite a dramatic decline in the prevalence of opportunistic infections and Kaposi sarcoma since the introduction of highly active antiretroviral therapy. Seborrheic dermatitis, xerosis, psoriasis, pruritic papular eruption, eosinophilic folliculitis and photodermatitis are the main primary skin conditions linked to AIDS.[4]

HAART has significantly altered the pattern of mucocutaneous manifestations. Despite the decline in the number of infectious and inflammatory dermatoses, there is an increase in the incidence of adverse cutaneous drug reactions.[5] In addition to being the most frequent AIDS manifestation, mucocutaneous lesions serve as sensitive and effective markers of the patients' immunological health. Compared to healthy people, these lesions are typically more severe, unusual, extensive, and resistant in HIV-infected patients.[6]

In developed regions, AIDS is evaluated using the CD4 lymphocyte count, viral load, and viral culture. The dearth of these facilities in underdeveloped regions emphasized the significance of clinical markers. In order to diagnose HIV infection and gauge the patient's immunological health, cutaneous assessment can be helpful. There is paucity of data on correlation between mucocutaneous lesions and CD4 levels. By determining the pattern of mucocutaneous manifestations in relation to CD4 counts, we will be able to use these manifestations as clinical markers to anticipate the immunological health of patients. Even in the ART era, there is a significant burden of skin diseases experienced by PLHIV. AIDS-related skin disorders can have high morbidity and mortality rates, therefore deep understanding of HIV-specific conditions, as well as those that change course or management of HIV, is critical for the practicing dermatologist.[7]

Methods

This cross sectional study included 300 HIV seropositive patients who visited the Dermatology outpatient department and HIV clinic of Services Hospital, Lahore over a period of 1year (June 2017- May 2018). Out of 300 patients, 290 were on ART. Following informed consent demographic details were recorded on predesigned proforma. A thorough clinical examination of skin and mucosae was carried out. Patients' most recent CD4 count (cells/mm^3) retrieved from medical record. Mostly the diagnosis was made clinically. KOH smear, Tzanck smear or skin biopsy was performed when necessary. All the mucocutaneous conditions of the patients were noted and categorized as infectious, noninfectious dermatoses including malignancies and drug reactions. Clinical and immunological staging method devised by WHO used to classify patients into different stages.

Results

Among 300 HIV- positive individuals a gender ratio of 3:1 was observed with 228 (76.0%) men

Table 1 Prevalence of mucocutaneous manifestations according to the WHO immunological stage of HIV infection

CD4 count	*<200*	*200-350*	*350-500*	*>500*	*Total*
Infectious	23(71.8%)	212(91.3%)	19(67.8%)	3(37.5%)	257
Non infectious	6(18.7%)	14(6.03%)	9(32.1%)	5 (62.5%)	34
Mixed	3(9.3%)	6(2.58%)	0%	0%	9
Total	32	232	28	8	300

and 72 (24%) women. Patients' average age was 33.67±10.84 years. 236 (78.7%) patients were of age 20-40 years and 64 (21.3%) were of age 41-65 years. There were 175 (58.7%) patients from low socioeconomic status, 120 (40%) from middle and 5 (1.3%) from high socioeconomic status class. Heterosexual route of transmission was the commonest route [96 (32%)], followed by blood transfusion [84 (28%)], surgical procedure [72 (24%)], intravenous drug abuse [44 (14.7%)] and sharing of common needle or injection [20 (6.7%)]. The mean duration of HIV was 1.49±0.77 years. 72% of cases were illiterate and 28% were literate. 85% cases were married, 10% were unmarried and 5% were separated or widow.

CD4 counts <200, 200 to 350, 350 to 500, and >500 were seen in 32 patients, 232 patients, 28, and 8 patients, correspondingly. Dermatoses per subject on average was 1.2. As the CD4 count dropped, the average number of dermatoses per patient increased. Immunological deterioration lead to increase in the proportion of patients with dermatoses; 8% of patients with CD4 counts >500 compared to 77.3% of patients with CD4 counts 200-350 **(Table1)**.

Dermatophytosis was the most common infection, seen in 60 patients with a mean CD4 count of 165.6±10.2 followed by candidiasis, 40 patients with CD4 count of 220±179.1. Other infective dermatoses were herpes zoster, herpes simplex, pyoderma, HPV infection, molluscum contagiosum (MC) and scabies. Dermatophytosis and MC with low CD4 count demonstrated a significant relationship when patients were grouped according to CD4 count **(Table 2)**.

Table 2 Prevalence of infectious manifestations with mean CD4 count.

Infections	*No. of patients*	*Mean CD4 count*
Dermatophytosis	60	165.6±10.2
Candidiasis	40	220±179.1
Herpes zoster	32	245±164.1
Herpes simplex	30	260.4±166.8
HPV infections	29	194±138.2
Pyoderma (Furunculosis)	26	178.2±110.5
Molluscum contagiosum	20	137.2±75.1
Scabies	8	198±137.2
Pityriasis Versicolor	5	420.1±370.2
Mycobacterial infection	2	346±0.00
Deep Mycosis	1	279±0.00
Syphilis	1	475.5±295.3

Table 3 Prevalence of noninfectious manifestations.

Non Infectious manifestations	*Number of patients*
Xerosis	30
Seborrheic dermatitis	9
Photodermatitis	4
Pruritic papular eruption	3
Pruritis	3
Pigmentary disorders	2
Kaposi Sarcoma	2
Adverse drug reactions	2
Psoriasis	1
Nail discoloration	1

Thirty patients had xerosis, which was the most prevalent non-infectious condition. The frequency of non-infectious manifestations showed no discernible variation with respect to the immunological stage of HIV infection **(Table 3)**.

Discussion

The CD4 cell population is the principal target of HIV. One of the most notable and persistent immunological characteristics of HIV-related disorders is a persistent decline in the number and function of CD4 cells. The CD4 count

decreases progressively as the HIV illness worsens.[8] With declining immune function, skin problems become more common and severe.[9]

Sohan Lahoti's study found that 169 of 200 patients had multiple mucocutaneous manifestations, with an average of 2.045 dermatoses per patient.[9] According to Vijaya Kumari *et al*; each patient had an average of 1.9 dermatoses.[10] In our study, dermatoses per patient on average was 1.2. There were more dermatoses per subject as the CD4 count dropped. Immunological decline was accompanied by an increase in the number of patients with dermatoses; 8% with CD4 counts greater than 500 compared to 77.3% with CD4 counts between 200 and 350.

300 patients were seen during the course of the 12-month study period. The gender split was 3:1 between men and women. This could be attributed to societal reasons, as females are more hesitant when it comes to examination and testing on volunteer basis. Most common infectious dermatoses was dermatophytosis (Tinea corporis and cruris). This result agreed with earlier research by Ashraf *et al*. and H. Tito *et al*.[11,12] Patients with severe immunosuppression had considerably higher rates of dermatophytosis, which had an inverse relationship with CD4 counts.[13] Oral candidiasis was the next most frequent infection. This result is in line with the results of the earlier research by Swamiapan *et al*.[14]

Herpes zoster was the most prevalent viral infection in patients, followed by herpes simplex, HPV infection, and molluscum contagiosum. Patients had herpes zoster that affected several dermatomes. Similar results were also shown in earlier studies by Ashraf and Santosh.[11,15] As majority of our patients were on ART, the increased prevalence of herpes zoster could be attributed to immune reconstitution. Recurrent, persistent, and resistant to treatment furunculosis that required high doses of antibiotics for extended periods of time was common. In comparison to earlier research by Fernandes MS and Karishna, our study found a reduced incidence of pyoderma.[15,16]

Dermatophytosis, MC, and pyoderma patients' mean CD4 counts were statistically lower than those of patients without these dermatoses. When patients were divided into those with a CD4 count of 200 or higher, only the prevalence of dermatophytosis and MC showed a significant association.[16-18]

The most common noninfectious dermatoses were found to be xerosis, followed by pruritic papular eruption. This is consistent with the findings of studies conducted by Fernandes MS and Davarpanah MA.[3,16] Kore described seborrheic dermatitis as a common manifestation in another study.[13]

Many of the HIV-associated dermatoses have decreased during the ART era, but cutaneous adverse drug reactions (CADRs) and inflammatory skin conditions have increased. Patients receiving nevirapine have experienced severe and potentially fatal skin reactions such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), hypersensitivity reactions, and hepatotoxicity, including fatal cases of fulminant hepatitis.[19] In our study one patient had Steven Johnson syndrome due to Nevirapine (NVP). NVP is the anti-retroviral drug most frequently linked to CADRs according to a number of prior studies.[20] Our study reported 2 cases of Kaposi sarcoma. The study further revealed its association with low CD4 cell count (≤200 cells/µl). A study by Semango GP revealed the same result.[21]

Conclusion

The outcomes of our study indicate that

mucocutaneous manifestations develop during the progression of HIV infection. Dermatophytosis and candidiasis exhibit a significant reciprocal relationship with CD4 cell count, and because of this they can be utilised as an indirect evidence of severe immunosuppression to initiate highly active anti-retroviral therapy in the absence of access to resources for CD4 cell count.

In otherwise healthy persons, mucocutaneous symptoms can raise suspicions of HIV infection. They are capable of acting as a reliable clinical indicator of HIV infection. Understanding the different patterns of these manifestations will aid in the early diagnosis and management of HIV infection, reducing morbidity and enhancing the quality of life for those who suffer from it.

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