Original Article

Association of dermatological manifestations with CD4 count among people living with HIV attending tertiary care hospital of South Gujarat

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Abstract

Introduction: Dermatological manifestations are common manifestations of human immunodeficiency virus (HIV) disease, seen in 80% to 95% of HIV-infected patients. Dermatological manifestations are considered clinical indicators to predict and assess the underlying immune status. **Aim:** This study aims to document the dermatological manifestations in relation to CD4 count in people living with HIV (PLHIV). **Materials and Methods:** Cross-sectional study in 250 PLHIV fulfilling inclusion–exclusion criteria was conducted. Variables including sociodemographic profile, recent CD4 count (data from antiretroviral therapy center), and dermatological manifestation (physical examination) were collected. Clinical diagnosis was established, and patients were grouped according to the World Health Organization immunological staging **Results:** Majority of PLHIV (39.6%) were in the age group of 31–40 years. Males were affected more than females (1.6:1). A total of 364 dermatoses were observed; dermatological manifestation per patient ranged from 1 to 4. 32.80%. PLHIV had CD4 count >500 cells/mm^3, 15.60% had CD4 count between 200–349 cells/mm^3. Majority of dermatosis had infectious etiology (77.6%), out of which dermatophytosis (27.2%) was the most common infectious condition, whereas pruritic papular eruption was the most common (11.6%) noninfectious condition. A statistically significant association of CD4 count was found with dermatophytosis ($P \leq 0.001$) and candidiasis ($P = 0.001$). **Conclusion:** The study showed a significant association between the number of dermatological manifestation and CD4 count as majority of study participants (67.2%) had CD4 <500 cells/mm^3 at the time of episode of dermatosis.

Key words: CD4 count, dermatological manifestations, people living with HIV

Introduction

Generalized immunosuppression is observed in human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) as well as localized mucocutaneous immune dysregulation is also noticed which is responsible for the development of skin and mucosal infections. Dermatological manifestations can occur in all stages of HIV infection. Dermatological manifestations may be the initial signs of immunosuppression which may be seen in 80%–95% of HIV-infected patients.[1] Few selected dermatoses serve as sensitive and useful clinical indicators of HIV infection and disease progression. Dermatological manifestations may be reflective of the CD4 count in an individual which indicates the degree of immune status.[2] Hence, the present study will help to predict patterns of dermatological manifestations in people living with HIV (PLHIV) and also to predict association with CD4 count.

As per estimation released by the UNAIDS on the eve of World AIDS Day 2021, a total of 37.7 million (30.2–45.1 million) people globally were living with HIV and 1.5 million (1.0–2.0 million) people became newly infected with HIV in 2020. India has the third-largest HIV epidemic in the world.[3] The current study concentrates and aims to document on the burden of dermatological manifestation reported among the PLHIV availing services from a tertiary care center of South Gujarat with respect to the change in

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CD4 count over time leading to an episode of dermatosis. South Gujarat specifically Surat was named as the "Driving Engine"[4] of HIV epidemic in the early 1990s, but since the inception of the National AIDS Control Programme, a control over the episodes of HIV associated co-infection has been achieved.

Materials and Methods

The antiretroviral therapy (ART) center attached to New Civil Hospital Surat caters 6000 PLHIVs (alive and on ART) and has a strong referral network with the department of dermatology, venereology, and leprosy for any mucocutaneous complaints among HIV-positive patients. Desk review of the dermatology outpatient department (OPD) fulfilling inclusion criteria was done from May 2019 to July 2019 to ascertain an average number of participants expected to visit the OPD. By desk review, we found that average 5–7 participants visit every week. During the data collection period of 1 year, 288 participants were expected. Considering 10% loss of miss out, incomplete information and denial of consent, the total sample size was 258. However, we were able to recruit 250 participants with the difference of 8 participants.

This cross-sectional study was carried out for 1-year duration (September 2019–August 2020) in the Department of Dermatology, Venereology and Leprosy at New Civil hospital, Surat, after receiving approval from Institutional Human Research and Ethics Committee as well as Gujarat State AIDS Control Society.

Inclusion criteria

PLHIV on ART having dermatological manifestations and those who were willing to give informed valid consent and are above 18 years of age.

Exclusion criteria

PLHIV not taking ART was excluded from the study. The study participants were enrolled based on inclusion–exclusion criteria. A pre-structured pro forma containing the following variables was used: socio-demographic profile such as age, sex, occupation, education and migration. Outcome variables collected were clinical features (dermatological manifestations) and investigations. Clinical diagnosis of dermatological manifestations was done by the first author (dermatologist with more than 15 years of experience in diagnosing and treating PLHIV). CD4 count was advised and recorded from ART center of the hospital. Complete blood count, random blood sugar, liver function tests, renal function tests, urine examination, potassium hydroxide KOH mount, gram stain, rapid plasma regain test, skin biopsy, electrocardiogram, X-ray chest, ultrasonography of abdomen were done as required. The participants were classified into four groups according to the WHO immunological staging.[1] The data were collected and analyzed using Microsoft Office Excel 2013. The association between CD4 count and dermatological manifestation was established using Chi-square test. A $P < 0.05$ was considered statistically significant.

Results

A total of 250 study participants were recruited in the study, out of which 61.60% were male and 38.40% were female (1.6:1). Maximum PLHIV (39.6%) were in the age group of 31–40 years [Table 1].

According to the WHO immunological staging,[1] out of 250 PLHIV, nearly one-third (32.80%) had no significant immunosuppression (CD4 count >500 cells/mm) followed by 31.20% had mild immunosuppression (CD4 count 350–499 cells/mm) [Chart 1].

Among 250 cases, a total of 364 dermatoses were observed. Dermatological manifestation per patient ranged from 1 to 4 in numbers [Table 2]. 62% (155) of study participants had one dermatological manifestation, 31.2% (78) had two manifestations, 6% (15) had three, and only 0.8% (2) had four dermatological manifestations.

On statistical analysis, significantly higher proportion (77.6%) of dermatological manifestation were due to infectious etiology ($P = 0.001$) [Table 3]. Fungal infection was the most common cause of infectious dermatoses [Figure 1a and b]. Among fungal infection, dermatophytosis were of 27.2%, of which predominantly tinea corporis (15.6%) followed by tinea cruris (11.2%) and onychomycosis (7.6%). PLHIV with severe and advanced immunosuppression group had extensive and atypical lesions for a prolonged duration. The most common type of candidiasis was oral (5.6%), followed by vulvovaginal (3.2%), and candidal balanoposthitis (2.4%). 9 cases (3.6%) had pityrosporum infection, out of which six had pityrosporum folliculitis and 3 had pityriasis versicolor.

Herpes simplex virus (HSV) infection (12.8%) was the most common viral infection [Figure 2a and b] [Table 4]. Among these, 21 (8.4%) had herpes genitalis and 11 (4.4%) had herpes labialis. PLHIV with severe immunosuppression group had atypical and extensive ulcerative lesions.

Among the noninfectious dermatological manifestation pruritic papular eruption (PPE) [Figure 3] was the most

Table 1: Sociodemographic profile of study participants (*n*=250)

	Number of patients (%)
Age group (years)	
18-20	1 (0.4)
21-30	37 (14.8)
31-40	99 (39.6)
41-50	89 (35.6)
51-60	22 (8.8)
>60	2 (0.8)
Gender	
Males	154 (61.60)
Females	96 (38.40)
Total	250

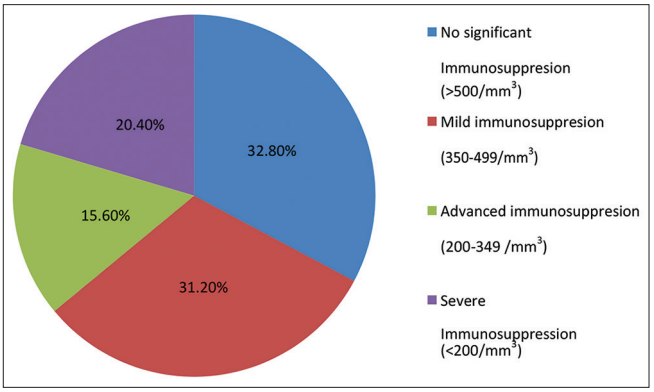

Chart 1: Classification of study participant as per WHO immunological staging (*n* = 250)

common condition seen in 11.6% cases. The mean CD4 count among PPE participants was 448.69/mm^3.

Statistically significant association of CD4 count among various dermatoses was found with dermatophytosis ($P \leq 0.001$) and candidiasis ($P = 0.001$). However, the association between CD4 count and bacterial, viral, or parasitic infection was found to be clinically relevant [Table 4]. Statistically no significant relation was found between noninfectious dermatoses and CD4 count.

15.2% (38) of study participants were having sexually transmitted infection, of which herpes genitalis was the most common 21 (55%) followed by syphilis in 9 (23.7%), anogenital wart 6 (15.8%), and chancroid 2 (5.5%). Among 12.8% cases of HSV infection, 21 (8.4%) had herpes genitalis, and 11 (4.4%) had herpes labialis. There were six (2.4%) cases of anogenital warts and three (1.2%) patients with verruca vulgaris. One case presented with primary syphilis, three patients had secondary syphilis while 5 patients were in the early latent stage. All cases had RPR titer >1:8.

Adverse cutaneous drug reaction (ADR) were identified as the cause of developing dermatological manifestation in 25 study participants, predominant being maculopapular rash (76%) [Figure 4], followed by urticaria (12%), fixed drug eruption (8%), and erythema multiforme (4%). Nevirapine was the major drug responsible for developing maculopapular rash (11 cases) followed by antituberculosis drugs (5 cases).

Scabies was the only parasitic infestation observed in 7.2% of participants. Among miscellaneous, there was one case of leprosy (released from treatment), vitiligo and melasma.

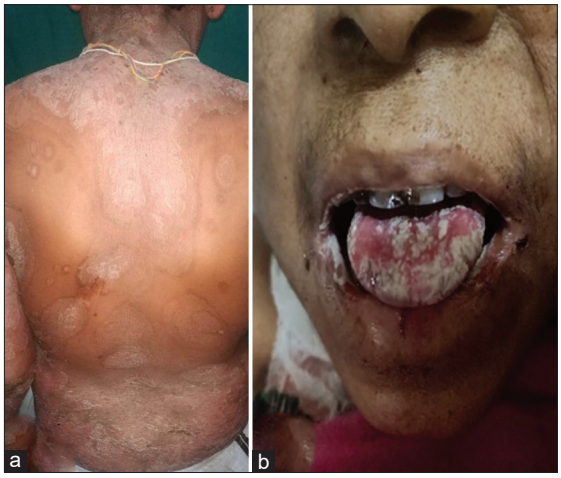

Figure 1: (a) Extensive tinea corporis. (b) Oral candidiasis

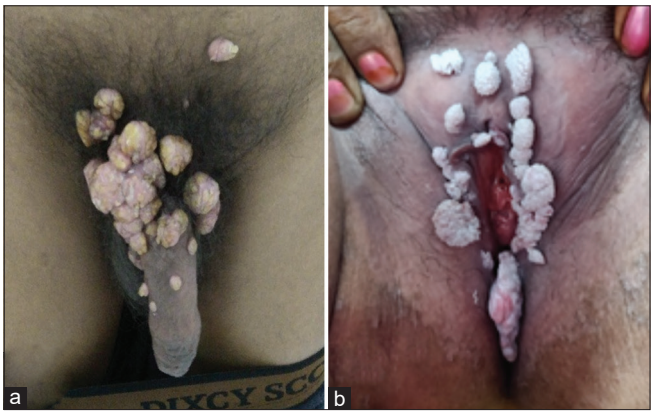

Figure 2: (a) Giant genital molluscum contagiosum. (b) Genital warts

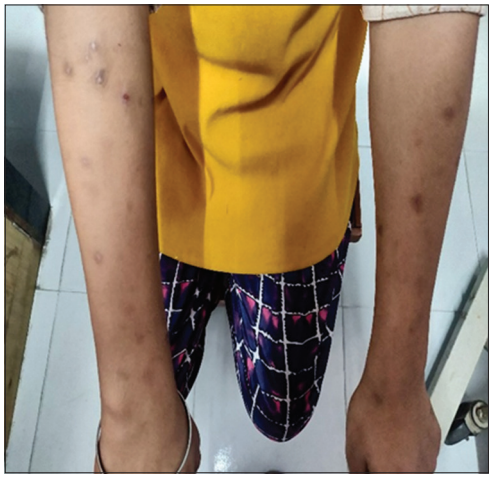

Figure 3: Pruritic papular eruption

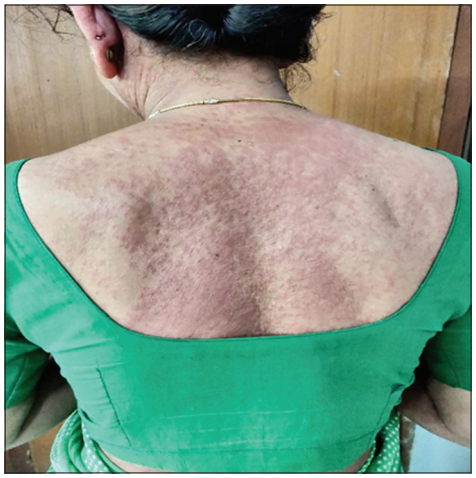

Figure 4: Maculopapular rash

Table 2: Number of dermatological manifestations per patient CD4 count (*n*=250)

Number of dermatological manifestations	>500 (cells/mm^3), *n* (%)	350-499 (cells/mm^3), *n* (%)	200-349 (cells/mm^3), *n* (%)	<200 (cells/mm^3), *n* (%)	Total, *n* (%)
1	61 (74.39)	54 (69.23)	28 (71.79)	12 (23.53)	155 (62)
2	17 (20.73)	21 (26.92)	9 (23.08)	31 (60.78)	78 (31.2)
3	3 (3.66)	3 (3.85)	2 (5.13)	7 (13.73)	15 (6)
4	1 (1.22)	0	0	1 (1.96)	2 (0.8)
Total	82 (32.8)	78 (31.2)	39 (15.6)	51 (20.4)	250 (100)

Table 3: Type of dermatosis with CD4 count (*n*=250)

Dermatological conditions	>500 (cells/mm³), *n* (%)	350-499 (cells/mm³), *n* (%)	200-349 (cells/mm³), *n* (%)	<200 (cells/mm³), *n* (%)	Total, *n* (%)	*P*	χ^2
Infectious conditions	57 (22.8)	58 (23.2)	29 (11.6)	50 (20)	194 (77.6)	0.001	17.709
PPE	12 (4.8)	10 (4)	2 (0.8)	5 (2)	29 (11.6)	0.457	2.603
Adverse drug reaction	10 (4)	9 (3.6)	2 (0.8)	4 (1.6)	25 (10)	0.586	1.936
Seborrheic dermatitis	4 (1.6)	5 (2)	4 (1.6)	5 (2)	18 (7.2)	0.616	1.797
Xerosis	2 (0.8)	3 (1.2)	1 (0.4)	1 (0.4)	7 (2.8)	0.920	0.493
Eczema	2 (0.8)	3 (1.2)	0	1 (0.4)	6 (2.4)	0.637	1.698
Pellagra	2 (0.8)	2 (0.8)	0	2 (0.8)	6 (2.4)	0.689	1.473
Acne	2 (0.8)	0	1 (0.4)	1 (0.4)	4 (1.6)	0.592	1.907
Nail discoloration	0	2 (0.8)	1 (0.4)	0	3 (1.2)	0.660	1.595
Psoriasis	1 (0.4)	0	0	1 (0.4)	2 (0.8)	0.574	1.991
Diffuse hair loss	0	1 (0.4)	1 (0.4)	0	2 (0.8)	0.419	2.830
Photodermatitis	1 (0.4)	0	0	1 (0.4)	2 (0.8)	0.574	1.991
Lichenoid dermatitis	2 (0.8)	0	0	0	2 (0.8)	0.248	4.131
Miscellaneous	2 (0.8)	0	1 (0.4)	0	3 (1.2)	0.198	4.660
Total	97	93	42	71	303		

PPE=Pruritic papular eruption

Table 4: Infectious dermatosis with CD4 count (*n*=250)

Infectious dermatosis	>500 (cells/mm³), *n* (%)	350-499 (cells/mm³), *n* (%)	200-349 (cells/mm³), *n* (%)	<200 (cells/mm³), *n* (%)	Total, *n* (%)	*P*	χ^2
Fungal							
Dermatophytosis	15 (6)	9 (3.6)	15 (6)	29 (11.6)	68 (27.2)	<0.001	38.107
Candidiasis	4 (1.6)	7 (2.8)	3 (1.2)	14 (5.6)	28 (11.2)	0.001	17.709
Pityrosporum infection	1 (0.4)	4 (1.6)	2 (0.8)	2 (0.8)	9 (3.6)	0.544	2.142
Viral							
HSV infection	12 (4.8)	9 (3.6)	5 (2)	6 (2.4)	32 (12.8)	0.939	0.407
Herpes zoster	6 (2.4)	9 (3.6)	3 (1.2)	7 (2.8)	25 (10)	0.598	1.878
Molluscum contagiosum	5 (2)	7 (2.8)	1 (0.4)	4 (1.6)	17 (6.8)	0.607	1.837
HPV infection	4 (1.6)	2 (0.8)	1 (0.4)	2 (0.8)	9 (3.6)	0.858	0.763
Bacterial							
Pyoderma	9 (3.6)	14 (5.6)	3 (1.2)	9 (3.6)	35 (14)	0.323	3.485
Syphilis	4 (1.6)	2 (0.8)	1 (0.4)	2 (0.8)	9 (3.6)	0.858	0.763
Mycobacterial infection	1 (0.4)	1 (0.4)	1 (0.4)	0	3 (1.2)	0.744	1.236
Chancroid	0	1 (0.4)	0	1 (0.4)	2 (0.8)	0.558	2.070
Parasitic infestation	7 (2.8)	5 (2)	4 (1.6)	2 (0.8)	18 (7.2)	0.646	1.658
Total	68	70	39	78	255		

HSV=Herpes simplex virus; HPV=Human papillomavirus

Discussion

Majority of the PLHIV (39.6%) were in the age group of 31–40 years. The youngest patient was 19-year-old and the oldest was 62 years old. The mean age was 39.74 years which is comparable to the study done by C. Chandrakala *et al.*[5] having 36% of the study population belong to 31–40 years with mean age 38.6 years. Kore SD *et al.*[6] reported 49.7% of cases in the age group of 31–40 years.

In the present study, males were affected more than females with male to female ratio of 1.6:1. Singh *et al.*[7] reported 60.58% males and 39.41% females having male to female ratio of 1.54:1. C. Chandrakala *et al.*[5] observed 53% male and 47% female with 1.13:1 male to female ratio.

Based on the WHO immunological staging in the current study, 32.80% PLHIV had no significant immunosuppression (CD4 count >500 mm³), 31.2% of patients had mild immunosuppression (CD4 count between 350 and 499 mm³), 15.60% had advanced immunosuppression (CD4 count between 200 and 349/mm³) and 20.40% patients had severe immunosuppression (CD4 count <200 mm³). In a study by Chawhan *et al.*[8] 10% had CD4 count >500/mm³, 31% patients had CD4 count 200-500/mm³ and 59% patients had CD4 count <200/mm³.

The average dermatological manifestations per patient in the current study were 1.46. In this study, single dermatological manifestation (74.39%) was highest in group of PLHIV having no significant immunosuppression. There was increase in number of dermatological manifestations with decrease in immunity as reflected by decrease of CD4 count. More than one dermatosis (76.47%) were highest in severe immunosuppression group (CD4 count <200/mm³).

In the present study, infectious conditions (77.6%) were most common among all dermatosis. In a study done by Kore SD *et al.*[6] 74.1% cases and C. Chandrakala *et al.*[5] had 91% cases of infection origin. Among all dermatological manifestations of current study statistically significant association of CD4 count was found only with infectious condition (P = 0.001).

PPE was the most common noninfectious condition seen in 11.6% of cases while Mohammed *et al.*[9] had 11.35% of cases. Statistically no significant association was found

between noninfectious dermatoses and CD4 count, which is similar to study by Kore *et al.*[6] PPEs may appear as an initial cutaneous disease with high CD4 count and can be manifest in advanced immunosuppressive stage.[10]

ADR was seen in 10% of patients while by Kore *et al.*[6] 6.3% had adverse drug reaction.

Seborrheic dermatitis was seen in 7.2% of patients. In study by Kore SD *et al.*[6] 8.2% had seborrheic dermatitis. Generalized xerosis was seen in 2.8% of patients. In a study by Singh *et al.*[7] 5.5% of patients had xerosis.

Among various etiologies, fungal infection (38.8%) was the most common infectious cause responsible for dermatological manifestations in PLHIV followed by viral infection (32.4%). In a study by Kore SD *et al.*[6] fungal infection (30.1%) was also most common infectious condition followed by viral infection (29.7%). Fungal infection was reported as the most common mucocutaneous manifestations among HIV-infected individuals in different studies.[5,6,11]

The most common type of fungal infection in the present study was dermatophytosis (27.2%) and seen across all four CD4 count group. In study by Kore SD *et al.*[6] dermatophytosis was seen in 11.9% of patients and candidiasis in 16.2%. Shobhana *et al.*[12,13] reported 13% of cases of dermatophytosis. The current study reported dermatopytosis as more common type of fungal infection than candidiasis in PLHIV. Studies report 10%–22% incidence of dermatophytes in general populations.[13] There has been overall an increase in the incidence of dermatophytosis across the country in the past decade and especially over the past 5–6 years, according to recent studies. It would prove to be a difficult task to choose between the terms "epidemic" and "hyperendemic" to describe the current alarming situation of increased incidence as well as the prevalence of superficial dermatophytosis in India.[12]

The second number of fungal infection was candidiasis with 11.2% of patients. In a study done by Singh *et al.*[7] 17.5% cases and C. Chandrakala *et al.*[5] 31% had candidiasis. Statistically significant association of CD4 count was found with dermatophytosis ($P \leq 0.001$) and candidiasis ($P = 0.001$). Kore SD *et al.*[6] were also found statistically significant association between CD4 count and dermatophytosis ($P = 0.008$).

HSV infection was the most common viral infection in the present study (12.8% cases). In a study by C. Chandrakala *et al.* 11.9% and by Kore SD *et al.*[6] 10.2% of cases had HSV infection.

The most common bacterial infection was pyoderma (14%). In a study by C. Chandrakala *et al.*[5] 4.3% had pyoderma and in Kore *et al.*[6] 8% had pyoderma. In study done by Shobhana *et al.*[12] 5% of cases had scabies.

Conclusion

The present study describes various dermatological manifestations in relation to CD4 count among PLHIV on anti-retroviral therapy representing south Gujarat populations. The study showed a significant association between the number of dermatological manifestation and CD4 count as majority of study participants (67.2%) had CD4 <500 cells/mm^3 at the time of episode of dermatosis. Thus, a lower CD4 count marks the higher chances of developing dermatological manifestations and other HIV-associated sexually transmitted infection/reproductive tract infections.

Strengths

- All cutaneous manifestations of HIV were assessed in the present study
- Cutaneous manifestations were studied in association with CD4 count.

Limitations

- Patients of <18 years were not included in the study
- Association between dermatophytosis and CD4 count is required for further assessment.

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Conflicts of interest

There are no conflicts of interest.

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