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Original Article

A clinical study of mucocutaneous manifestation of HIV/AIDs and its correlation with CD4 count

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Abstract

Background Acquired immune-deficiency syndrome (AIDS) is a fatal illness caused by a retrovirus known as Human Immunodeficiency Virus (HIV) which breaks down the immune system of the body, leaving the victim vulnerable to a host of life-threatening opportunistic infections, neurological disorders, or unusual malignancies. Dermatological disorders are health problems among HIV positive patients which present with a variety of manifestations. Skin diseases cause significant morbidity and may be initial signs of immunosuppression. They affect between 80 and 95% of HIV-infected patients, occurring at any time in the course of infection.

Objective 1- To study the pattern of mucocutaneous manifestation of HIV infected patients attending Dermatology Outpatient Department (OPD) of Karnataka Institute Of Medical Sciences (KIMS) Hubballi. 2- To assess the relation of mucocutaneous manifestations of HIV infected patients with CD4 count.

Methods All HIV positive patients with mucocutaneous manifestation attending Dermatology OPD, KIMS, Hubballi from December 2017 to May 2019 were enrolled.

Results In this study, the most common dermatosis was pruritic papular eruption (21%) with a mean CD_4 count of 499.81±319.31 cells/mm^3. Among viral infections, the most common infection was herpes genitalis (32.4%) with a mean CD_4 count of 291.25±194.22 cells/mm^3. The most common fungal infection was dermatophytosis (59.1%) with a mean CD_4 count of 489.69±260.13 cells/mm^3. The most common bacterial infection was pyoderma (73.7%) and the mean CD_4 count was 485.21±308.30 cells/mm^3. The most common parasitic infestation was scabies with a mean CD_4 count of 375.60±117.59 cells/mm^3. Among malignancies, only two cases of basal cell carcinoma was seen in this study and the mean CD_4 count was 89.50±57.28 cells/mm^3.

Conclusion The skin manifestations in HIV can serve as an important marker for underlying immunodeficiency state. The CD_4 count of a patient can be used to know the level of immunosuppression as different dermatosis are seen at various stages of HIV infection.

Key words
AIDs; HIV; CD4 count; mucocutaneous.

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Introduction

Human immunodeficiency virus (HIV) infection is acquired sexually, from blood or blood products, or vertically from an infected mother during pregnancy, birth or breastfeeding. The

virus infects immunocompetent cells including CD4+ T. cells and macrophages.[1] Since the beginning of the epidemic, 75 million people have been infected with the HIV virus and about 32 million people have died of HIV. Globally, 37.9 million [32.7–44.0 million] people were living with HIV at the end of 2018.[2] In India, there was an estimated adult (15-49 years) prevalence of 0.22% [0.16-0.30] in 2017. Around 21.40 lakh people living with HIV (PLHIV) were living in the country. Almost 97% of the total PLHIV belonged to the 15+ years of age group. Females constituted 42% of estimated PLHIV (15+ years). 87.58 thousand people were newly infected with HIV in 2017, while 69.11 thousand PLHIV died from AIDS-related causes in the same year.[3] Cutaneous disease occurs in nearly every patient during the course of HIV disease due to the acquired immunodeficiency or effect of the treatment.[4] Skin diseases cause significant morbidity and may be initial signs of immunosuppression. Cutaneous disorders are numerous in HIV infection. Some cutaneous disorders reflect the progression of HIV disease.[5] Unusual manifestations of a common dermatosis and presentation of a previously uncommon disorder is the hallmark of cutaneous manifestation of HIV/AIDS patients. Atypical presentation leads to diagnostic difficulties even in the hands of most experienced dermatologists. Skin findings are regarded by WHO as useful in assessing the severity of HIV infection in resource limited environment.

Objectives of the study

1. To study the pattern of mucocutaneous manifestation of HIV infected patients attending Dermatology Outpatient Department (OPD) of Karnataka Institute of Medical Sciences (KIMS) Hubballi.
2. To assess the relation of mucocutaneous manifestations of HIV infected patients with CD4 count.

Materials and Methods

After informed consent, all HIV positive patients with mucocutaneous manifestations attending dermatology OPD of Karnataka institute of medical sciences Hubballi, over a period of 18 months from December 2017 to May 2019 were enrolled in the study. Sample size was calculated by using the following formula $n=Z^2 p (1-p)/ d^2$. where Z=Table value for 90% confidence, p= Proportion of candidiasis and d=allowable error.

Observations and Results

There were 130 HIV patients with mucocutaneous manifestation in our study. Majority of the patients belonged to the age group between 31-40 years (42%), followed by 41- 50 years (23. 8%) **(Figure 1)**. In this study, there were almost equal number of males and females (1:1.06). Most of the patients were married (66%) and number of patients belonging to working (56.2%) class were more than nonworking class (43.8%). Approximately half of the patients were educated (51.5%) with 42.3% and 9.2% having primary and secondary level of education respectively and rest (49%) of them were illiterate.

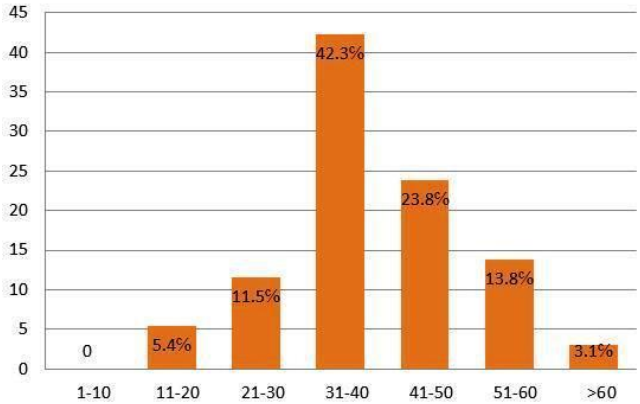

Figure 1 Distribution of cases according to age (yrs).

Table 1 Distribution of cases according to CD4 count (n=130).

CD_4 count	*No. of cases (n)*	*Percentage (%)*
<200	15	11.5
200- 349	36	27.7
350-499	34	26.2
≥500	45	34.6
Total	130	100.0

Table 2 Distribution of cases according to muco-cutaneous manifestation (n=130).

Skin manifestations	*No. of cases (n)*	*Percentage (%)*
Basal cell carcinoma	1	0.8
Candidial Balanoposthitis	1	0.8
Candidial Vulvovaginitis	3	2.3
Dermatophytosis	13	10.0
Ecthyma	1	0.8
Eosiophillic Folliculitis	2	1.5
Hansens	1	0.8
Herpes Genitalis	12	9.2
Herpes labialis	5	3.8
Herpes Zoster	8	6.2
Insect bite reactions	2	1.5
Molluscum contagiosum	5	3.8
Onychomycosis	2	1.5
Oral Candidiasis	1	0.8
Pediculosis	1	0.8
Pityriasis Versicolor	3	2.3
Pruritic popular eruption	21	16.2
Pyoderma	14	10.8
Scabies	10	7.7
Seborrhoeic dermatitis	10	7.7
Syphilis	3	2.3
Urticaria	1	0.8
Wart	7	5.4
Xerosis	3	2.3
Total	130	100.0

In this study, 68.5% of the patients belonged to urban population and 31.5% belonged to rural area. All patients (130) were on ART, most being on it for less than a year (33.8%) and most commonly followed regimen was tenofovir, lamivudine and efavirez (86%). The most common route of transmission of HIV infection was heterosexual (97%) and vertical transmission was seen in 3.1% of the patients. In this study, majority of the patient had CD4 count of >500 cell/mm^3 (35%), followed by 200-349 cells/mm^3 (28%), 350-499 cells/mm^3 (26%) and

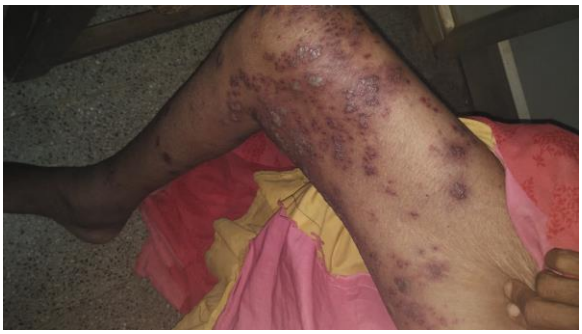

Figure 2 Haemorrhagic herpes zoster.

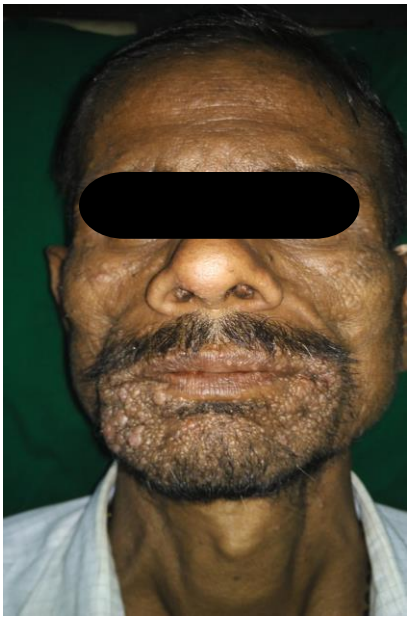

Figure 3 Extensive facial molloscum contagiosum.

<200 cells/mm^3 (11%) **(Table 1)**. The most common dermatosis encountered in this study was pruritic papular eruption (21%) **(Table 2)**. Among bacterial infections, the most common infection was pyoderma (10.8%). Other bacterial infections were syphilis (2.3%), Hansens (0.8%) and ecthyma (0.8%). The most common viral infection was herpes genitalis (9.2%). This was followed by herpes zoster (6.2%) **(Figure 2)**, viral wart (5.4%), herpeslabialis (3.8%) and molluscumcontagiosum (3.8%) **(Figure 3)**. Most common fungal infection was dermatophytosis (10%) which was followed by candidialvulvovaginitis/ balanophostitis (3.1%), pityriasis versicolor (2.3%) and onychomycosis (1.5%). Among the parasitic infections, scabies was diagnosed in 7.7% of the cases and

pediculosis in 9.1% cases. Among inflammatory dermatosis, the most common dermatosis was pruritic papular eruption (16.2%). The other inflammatory dermatosis were seborrheic dermatitis (7.7%), urticaria/ Insect bite hypersensitivity (2.3%), xerosis (2.3%) and eosiophillic folliculitis (1.5%). Apart from two cases of basal cell carcinoma, no other malignancies were reported in this study. Nail changes were seen in only 15 % of the cases and most common change was longitudinal melanonychia (7%). Other nail changes were pitting, dystrophy, discoloration and paronychia. In this study oral involvement was seen in 34.6% of the patients and most common was oral candidiasis which was seen in 20% of the cases. Other manifestations were pigmentation, angular stomatitis and erosions/ulcers. In this study, majority of the patients did not show any hair disorder except for telogen effluvium which was seen in 18% of the patients.

Discussion

HIV/AIDS has become highly prevalent in recent times and around 90% of HIV infected patients develops at least one type of dermatoses during the course of their HIV infection. Skin manifestations are diverse and show atypical presentations. These mucocutaneous manifestation helps in diagnosing the disease as well as predicting the degree of immunosuppression. In this present study, 130 HIV positive patients were examined for various cutaneous manifestations along with the CD4 count. The most common age group affected was 31- 40 years (42.3%). This was followed by the age group of 41- 50 years (23.8%). A study conducted by Singh *et al*.[5] also showed higher prevalence among age group of 30-39 years (54%). There were 67 (51.5%) females and 63 (48.5%) male patients. The distribution was almost equal among male and female patients with a ratio of 1:1.06. A higher female preponderance was reported by Kiran Raju *et al*.[6] with male to female ratio of 1:1.5. While another study conducted by Kore SD, *et al*.[7] showed a higher prevalence among male with a male to female ratio of 2:1. Majority of the patients in our study were married comprising a total of 86 (66%) patients. This was followed by widow/widower (15.4%), unmarried (13.1%) and divorced (5.4%) respectively. In a study conducted by Swamiappan M *et al*.[8] majority of the patient were also married (87.5%) which correlates well with this study. Occupationally, 73 (56.2%) of the patients were working and 57(43.8%) were not working. Dash *et al*.[9] reported a higher prevalence among working population accounting for 64% among the study population. Regarding educational status, majority of the patients were educated (51.5%) with 42.3% and 9.2% having primary and secondary level of education respectively. The rest 48.5% patients were illiterate. This result was similar to the study conducted by Neerja *et al*.[10] in which majority of the patients (52.6%) were educated. This finding signifies that there is a lack of awareness about HIV/AIDS not only among the illiterate people but also among the educated group. Most of the patients belonged to urban population (68.5%) and rest were from rural area (31.5%). This study included patients who were already diagnosed with HIV and who presented to us with skin manifestations. So all the patients enrolled in this study were taking one of the regimens of ART. The most common regimen which the patients were taking was tenofovir, lamivudine and efavirez (86%). This drug regimen is recommended by NACO as the first line treatment for all adults except those with known renal disease or HIV-2 or HIV- 1 & 2 infections or women with single dose of Nevirapine exposure in past pregnancy. The other regimens were zidovudine + lamivudine + efavirenz (10%), zidovudine + lamivudine + nevirapine (3.1%), Abacavir + lamivudine + efavirenz (0.8%). Majority of the patients

presenting with cutaneous disease in this study were on ART for less than one year (33.8%).

Mode of transmission The most common route of transmission in this study was heterosexual (97%). The other route of transmission was through vertical transmission (3%). No case of homosexual or transmission through blood transfusion/ IV drugs was reported in this study. This is in accordance with the study conducted by Shobhana A *et al*.[11] where the predominant mode of transmission was also heterosexual (88%). In fact, heterosexual route continues to be the most common route of transmission reported worldwide.

Mucocutaneous manifestation Overall the most common dermatosis encountered in this study was pruritic papular eruption (21%). A similar high prevalence of purpritic papular eruption (35.8%) was reported in a study conducted by Sharma A *et al*.[12] Among infections, the most common presentation was pyoderma (10.8%). With the advent of HAART, the prevalence of infectious dermatosis compared to inflammatory dermatosis has come down drastically due to the restored immunity.

Inflammatory dermatosis Pruritic papular eruption (PPE) comprised majority of the cases in inflammatory dermatosis as well as among all the dermatosis. PPE may appear as an initial cutaneous disease with high CD4 count and is described as a stage II disease by WHO. In our study, PPE manifested at a mean CD4 count of 499.81 cells/mm^3. The other inflammatory dermatosis were seborrhoeic dermatitis (7.7%), urticaria/ insect bite reactions (IBR) (2.3%), xerosis (2.3%) and eosiophillic folliculitis (1.5%). Among the inflammatory conditions, statistically significant association with the CD4 count was seen in seborrhoeic dermatitis (p < .00), PPE (p < .00) and urticaria/ IBR (p < .012).

Viral infections Herpes genitalis was among the most common viral infection encountered in this study (9.2%). This was followed by herpes zoster (6.2%), viral wart (5.4%), herpes labialis (3.8%) and molluscum contagiosum (3.8%). A study conducted by Davarpanah *et al.*[13] also showed herpes genitalis as the most common viral infection in HIV patients. Herpes genitalis showed a mean CD4 count of 291.25 cells/mm^3. Four patients with a CD4 count of < 200 cells/mm^3 presented with giant ulcerative lesion which responded on treatment with acyclovir. Evidence indicates that HSV-HIV-1 interactions can affect the outcome of HIV-1 infection and AIDS progression in HIV-infected patients, and control of HSV infection may decelerate HIV infection.[14] Herpes genitalis is reported to be the most common cause of genital ulcers among both immunocompetent and immunosuppressed individuals. HIV and HSV acts as a co-transmitter of each other. Multidermatomal herpes zoster was reported in 2 patients with hemorrhagic bullae and crusting. Extensive molluscum contagiosum over the face and genital area was seen in another two patients. Among viral infections, statistically significant association with the CD4 count was seen in herpes genitalis (p < .00), herpes zoster (p<.00), wart (p<.002), molluscum contagiosum (p<.011) and herpes labialis (p<.012).

Fungal infections Dermatophytosis was among the most common fungal infection (10%), followed by candidial vulvovaginitis/ balanophostitis (3.1%), pityriasis versicolor (2.3%) and onychomycosis (1.5%). The mean CD4 count in dermatophytosis was 489.69 cells/mm^3. Though, the presentation of dermatophytosis was very much similar to non-HIV patients, there were 4 patients out of 13 patients who presented with extensive, atypical, anergic form of dermatophytosis. In most of the studies, candidiasis was the most common fungal infections to be reported. The high

prevalence of dermatophyte infection in this study can be attributed to the rising trend of dermatophytosis among the general population who are not immunosuppressed. Among fungal infections, statistically significant association with the CD4 count was seen in dermatophytosis (p<.00) and pityriasis versicolor (p<.048).

Bacterial infections The most common bacterial infection in this study was pyoderma (10.8%). Other bacterial infections were syphilis (2.3%), Hansens (0.8%) and ecthyma (0.8%). The mean CD4 count in pyoderma was 485.21cells/mm^3. Furuncle was the most common type of pyoderma seen. A study done by Dash M *et al.*[9] reported an incidence of 11% bacterial infection among HIV infected individuals. With regard to bacterial STD's, 3 cases of syphilis were reported in this study. All the cases presented as secondary syphilis. Moreover, the incidence of syphilis seems to be increasing among HIV patients compared to other STDs. No other bacterial STDs were seen. This low incidence can be attributed to the indigenous use of antibiotics among the general population as a whole. There was one case of borderline tuberculoid Hansens who presented with partial claw hand derformity. Among bacterial infections, statistically significant association with the CD4 count was seen in pyoderma (p<.00).

Parasitic infestations The parasitic infections seen were scabies (7.7%) and pediculosis (0.8%). The mean CD4 count in scabies was 375.60 cells/mm^3. Similar incidence of scabies (6%) was reported in a study done by Prerna *et al*.[15] The incidence of pediculosis were not reported in most of the studies. Among parasitic infestations, statistically significant association with the CD4 count was seen in scabies (p<.00).

Malignancy Among malignancies, two cases of BCC were reported in this study. The mean CD4 count in BCC was 89.50 cells/mm^3. BCC was also the most common cutaneous malignancy reported in a retrospective study done by Nancy Crum-Cianflone *et al*.[16] In fact, the incidence rates of cutaneous non–AIDS-defining cancers (NADCs), in particular BCC, have exceeded the rates of cutaneous AIDS-defining cancers such as Kaposi sarcoma (ADCs) with the advent of HAART and increased life expectancy.

Nail changes Nail changes were seen in 14.6% of the cases. The most common nail changes was longitudinal melanonychia (6.9%). This was followed by diffuse hyperpigmentation (3.1%), nail dystrophy (2.3%), nail discoloration (1.5%) and paronychia (0.8%). Zidovudine may produce longitudinal, transverse, or diffuse pigmentation of the nails but nail pigmentation has also been observed in patients with HIV who have never received the drug.[17]

Oral manifestation Oral lesions were seen in 34.6% of the patients enrolled in this study. The most common oral lesion encountered was oral candidiasis (20%). This was followed by hyperpigmentation (9.2%), angular stomatitis (3.1%) and oral erosions/ulcers (2.3%). Oral candidiasis was seen at a mean CD4 count of 312.91 cells/mm^3. The most common presentation of oral candidiasis was pseudomembranous type. This is in accordance with the findings of the studies conducted by Abhinandan *et al*.[18] who observed oral candidiasis in 14% of the HIV-infected patients, and Rao *et al*.[19] who noted oral candidiasis in 16.4% of the HIV-infected patients.

Hair changes In this study, telogen effluvium was seen in 17.7% of the patients. No other significant hair change was encountered. Chronic diffuse hair loss in HIV infected individuals has been attributed to infection with HIV itself, nutritional deficiencies, drugs, endocrine and immunologic dysregulation.[20]

Elongation of the eyelashes and straightening of the scalp hair has been reported in patients with HIV infection in a study done by Shobhana *et al*.[11]

Conclusion

Mucocutaneous manifestations in HIV patients can be used as a marker for underlying immunosuppression and can also guide in monitoring the progression of the disease. Awareness of varied pattern of manifestations would help in diagnosis and treatment which in turn would decrease the morbidity and improve the quality of life.

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