

# A prospective study on the mucocutaneous manifestations in HIV/AIDS patients in relation to CD4 count

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## Abstract

**Aim:** To study the mucocutaneous manifestations of HIV infection and its relation to CD4 count. **Materials and Methods:** This is a prospective and observational study, carried out in the out-patient department of DVL. One hundred (100) patients having mucocutaneous manifestations and who tested HIV Antibodies positive at ICTC according to NACO guidelines were taken up for the study. Detailed history was taken and each case was thoroughly examined with regard to involvement of skin, scalp, hair, nail, oral and genital mucosa, lymph glands and other symptoms. All routine investigations were done for all the cases. In cases with doubtful clinical diagnosis of skin disorder, Skin biopsies were taken for histopathological examination and also relevant laboratory test like KOH, Tzanck test, ANA, Anti ds DNA, Anti histone antibodies were performed. The CD4 counts were estimated in all cases by flow cytometry. **Results:** The common age affected in the present study was 19-29 years. 64% were males and 36% were females, with a male to female ratio of 1.8:1. Heterosexual route (90%) was the commonest mode of acquisition of HIV infection. 49% patients had CD4 counts below 200 cells/ $\mu$ I. 41% had CD4 counts between 200-499 cells/ $\mu$ I. 10% had CD4 counts above 500 cells/ $\mu$ I. Mean CD4 count was 280 cells/ $\mu$ I. The infectious diseases were the commonest mucocutaneous manifestations among HIV patients. The majority of the patients had viral infections (26%), with the mean CD4 count 276 cells/ $\mu$ I. The second commonest infection was the fungal infection (23%), with the mean CD4 count 268 cells/ $\mu$ I. Pruritic papular eruptions (8%) were the commonest among non-infectious disease with mean CD4 count 234 cells/ $\mu$ I. The second commonest was drug reaction (7%) with mean CD4 count 113 cells/ $\mu$ I. Out of 100 patients, 19% patients were with CD4 counts below 50 cells/ $\mu$ I. Out of these patients, 13% patients developed infectious mucocutaneous manifestations which include oral candidiasis, genital herpes and other manifestations. The remaining 6% patients developed non-infectious mucocutaneous manifestations. Among these patients 3% had drug reactions, 2% had PPE and 1% of patients had psoriasis. **Conclusion:** The skin disorders are common and diverse in HIV patients and patients with advanced stages of skin problems have relatively low CD4 counts, an inverse relationship. A low CD4 counts was associated with higher number of skin disorders and increased incidence of viral, fungal infections, PPE, adverse drug reactions. Cutaneous manifestations can serve as dependable markers of HIV disease. Cutaneous manifestations of HIV can be considered as good clinical indicators to predict and assess the underlying immune status and also prognostic markers in resource-poor countries. The results of this study indicated that all HIV positive patients should be examined for skin disorders because early diagnosis and management of such problems will improve the quality of life in these patients.

**Key Word:** HIV infection, CD4 counts, mucocutaneous manifestations, clinical indicators

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## INTRODUCTION

AIDS was first recognized in the United States in 1981. In 1983, HIV was isolated and by 1984 it was demonstrated clearly to be the causative agent of AIDS. HIV/AIDS occurrence is a major health problem facing all countries in the world. Dermatological involvement in AIDS has been appreciated since the disease was first recognized as a cryptic acquired immune deficiency illness in homosexual men and before the causative virus was identified. HIV has been demonstrated in the

dermis of infected individuals and may be present in Langerhans cells<sup>1</sup>. It is estimated that more than 90% of HIV-infected patients developed skin or mucous membrane disorders at some time during their phase of infection<sup>2</sup>. The knowledge of skin manifestations such as bacillary angiomatosis, Kaposi's sarcoma, oral candidiasis and hairy leukoplakia, may provide a clue for diagnosing a previously undetected HIV positive status. Not unlike certain oral manifestations in HIV-infected patients, some skin manifestations, including skin infections are frequently used as indicators for patients immunological status, especially in the setting where testing for CD4+ cell count and HIV-1 RNA viral load cannot be performed regularly. The spectrum of skin cancers, as seen in the general population in certain settings are expected to increase in HIV positive long-term survivors, though melanoma is rare in Asian countries. All HIV positive patients should be examined for skin disorders because early diagnosis and management of such problems will improve the quality of life in these patients. Therefore this study was done to understand spectrum of mucocutaneous manifestations of HIV infection and its relation to CD4 count.

## MATERIALS AND METHODS

This is a prospective and observational study, carried out in the out-patient department of Dermatology, Venereology and Leprosy, Gandhi Hospital and Medical College, Hyderabad during the period November 2015 to October 2017.

### Inclusion Criteria

1. Patients whose HIV status has been proved as per NACO guidelines
2. HIV/AIDS patients with symptoms and signs suggested of dermatological diseases.

### Exclusion Criteria

1. Pregnant women with HIV/AIDS
2. Children

One hundred (100) patients having mucocutaneous manifestations and who tested HIV Antibodies positive at ICTC according to NACO guidelines were taken up for the study. A detailed history was taken in each case. An attempt was made to know the possible modes of transmission of HIV infection in each patient and/ or a history of any risk factor(s) in the spouse. History of fever, cough, breathlessness, diarrhoea, and weight loss, sexually transmitted diseases (past or present), skin lesions, mucosal lesions, pulmonary and extra-pulmonary tuberculosis was elicited in every case. Cases were thoroughly examined with regard to involvement of skin, scalp, hair, nail, oral and genital mucosa, lymph glands and other symptoms. All routine investigations like haemoglobin, total count, differential count, ESR, urine albumin, sugar and micro study, baseline weight, X-ray chest PA view VDRL, HBsAg, Montoux test, Ultrasonography of abdomen were done in all cases. In cases with doubtful clinical diagnosis of skin disorder, skin biopsies were taken for histopathological examination and also relevant laboratory test like KOH, Tzanck test, ANA, Anti ds DNA, Anti histone antibodies were performed. The CD4 counts were estimated in all cases by flow cytometry (gold standard for CD4 T lymphocytes measurements).

## RESULTS

**Table 1:** Infectious Mucocutaneous manifestations and mean CD4 cell count, CD4 count range and Immune categories

	Diagnosis	Total No. of patients (73)	% of patients	Mean CD4 counts (cells/ µl)	CD4 cells count range (cells/µl)	No.of Patients with CD4 cell count> 500 (cells/µl)	No.of Patients with CD4 cell count 499-200(cells/µl)	No.of Patients with CD4 cell count< 200 (cells/µl)
	<b>Viral infections</b>	26	26	276.75	14-821	4	10	12
1	Herpes zoster	10	10	196.45	24-381	-	4	6
2	Herpes simplex	7	7	284.37	14-650	1	2	4
3	Warts	5	5	334.5	38-701	1	2	2
4	<b>Molluscumcontagiosum</b>	4	4	493.75	177-821	1	2	1
	<b>Fungal and Yeast</b>	23	23	268.11	05-992	1	12	10
1	Oral candidiasis	10	10	261.58	05-488	-	4	6
2	T.corporis	7	7	263.87	52-721	1	2	4
3	T.Curis	4	4	292.45	52-392	-	3	1
4	T.FACIEI	1	1	198.5	21-254	-	1	-
5	T.Versicolor	1	1	147.33	37-299	-	1	-
	<b>Bacterial Infection</b>	17			19-843	2	4	11
1	Furunculosis	7	7	222.7	40-843	1	2	4
2	Folliculitis	5	5	255.57	19-702	1	-	4

3	Leprosy	1	1	87.5	12-154	-	-	1
4	Impetigo	1	1	102	52-164	-	-	1
5	Ecthyma	1	1	212	18-287	-	1	-
6	Cellulitis	1	1	115	24-179	-	-	1
7	Cutaneous Tuberculosis	1	1	367	44-367	-	1	-
	<b>Other infections</b>							
1	Scabies	4	4	316	33-473	-	2	2
2	Syphilis	2	2	385	176-600	-	1	1
3	Lymphogranuloma venereum	1	1	278	24-278	-	1	-

**Table 2:** Non-infectious mucocutaneous manifestations and mean CD4 cell count, CD4 count range and Immune categories

	Diagnosis	Total no of patients (27)	%	Mean CD4 count (cells/ $\mu$ l)	CD4 count range (cells/ $\mu$ l)	No. of Patients with CD4 cell count > 500 (cells/ $\mu$ l) C1	No. of Patients with CD4 cell count 499-200 (cells/ $\mu$ l) C2	No. of Patients with CD4 cell count < 200 (cells/ $\mu$ l) C3
1	PRD	8	8	234.33	31-571	1	2	5
2	<b>Drug Reactions</b>	7	7	113	26-259	0	2	5
	MPR	2	2	74.5	35-114	0	0	2
	SJS	3	3	148	37-259	0	1	1
	TEN	1	1	98	14-225	0	0	1
	EMF	1	1	26	12-116	0	0	1
	FDE	1	1	186.5	28-222	0	1	0
3	Eczema	3	3	232.33	114-310	0	2	1
4	Psoriasis	2	2	222.53	46-401	0	1	1
5	Seborrhoeic Dermatitis	2	2	328.5	284-373	0	2	0
6	Photosensitive Dermatitis	1	1	106.37	22-223	0	1	0
7	LSC	1	1	160.5	19-355	0	0	1
8	SLE	1	1	88.33	42-150	0	0	1
9	Acne	1	1	268	38-388	0	1	0
10	LPP	1	1	392	12-418	0	1	0

**Table 3:** Skin Manifestations below 50 cells/ $\mu$ l

INFECTIOUS CONDITIONS	NO OF PATIENTS
OC	3
Herpes Zoster	2
Herpes Simplex	1
Warts	1
T.Cruris	1
Folliculitis	3
Furunculosis	1
Scabies	1
NON-INFECTIOUS CONDITIONS	NO OF PATIENTS
Drug reactions	3
PPE	2
Psoriasis	1

## DISCUSSION

### Mucocutaneous manifestations and CD4 cell count

#### Infectious mucocutaneous manifestations and CD4 count:

The dermatological diseases were classified into infections and non-infectious. The infectious diseases were the largest category of cutaneous disorders associated with HIV infection. In the present study, the most common infectious cutaneous disease was viral infection. Out of 100 patients, 26% patients had viral infections. Among the viral infections, herpes zoster was the commonest infection 10%. However Shobhana *et al* reported herpes zoster only in 6% HIV patients in their study<sup>3</sup>. Whereas Naburi AE *et al* reported herpes zoster in as high as 25% HIV patients<sup>4</sup>. In the present study, CD4 range among herpes zoster patients between 24-381 cells/ $\mu$ l which is comparable with the study by Shobhana *et al* who have reported CD4 range between 20-659 cells/ $\mu$ l among herpes zoster Patients<sup>3</sup>. In the present study among herpes zoster patients, 6% had below 200 cells/ $\mu$ l while 2% had CD4 counts above 200 cells/ $\mu$ l. This is comparable with study by Goh *et al* who have reported CD4 counts below 200 cells/ $\mu$ l in 9.6% of patients and above 200 cells/ $\mu$ l in 4.1% of patients<sup>5</sup>. However Zanacanarao *et al* reported 1.8% with CD4 Counts below 200 cells/ $\mu$ l and 0.4% with CD4 counts above 200 cells/ $\mu$ l<sup>6</sup>. In the present study, 8% patients had Herpes simplex which is consistent with the study by Shobhana *et al* who have reported herpes simplex in 5% HIV patients<sup>3</sup>. CD4 range among herpes simplex patients recorded on the present study range between 14-650 cells/ $\mu$ l which is comparable with the CD4 range reported by Shobhana *et al* (33-672 cells/ $\mu$ l).<sup>3</sup> In the present study 4% of herpes simplex patient had CD4 counts below 200 cells/ $\mu$ l and 4% had CD4 counts above 200 cells/ $\mu$ l which is comparable with study by Zanacanarao *et al* who reported 5.4% with CD4 counts below 200 cells/ $\mu$ l and 2.2% with CD4 counts above 200 cells/ $\mu$ l<sup>6</sup>. Goh *et al* reported more number of patients (12.5%) with CD4 counts below 200 cells/ $\mu$ l and less number of patients (5.2%) above 200 cells/ $\mu$ l<sup>5</sup>. In the present study, 4% patients had molluscum contagiosum which is consistent with the study by Shobhana *et al* who have reported molluscum contagiosum in 4% patients<sup>3</sup>. CD4 range with molluscum contagiosum was between 177-821 which is higher than the CD4 range reported by Shobhana *et al* (100-409 cells/ $\mu$ l)<sup>3</sup>. In the present study 1% patients had CD4 count below 200 cells/ $\mu$ l and 3% had CD4 counts above 200 cells/ $\mu$ l while Zanacanarao *et al* reported more number of patients (7.29%) with CD4 counts below 200 cells/ $\mu$ l and less number of patients (1.7%) with CD4 counts above 200 cells/ $\mu$ l<sup>6</sup>. In the present study, warts were noted on 5% patients with CD4 range

between 38-701 cells/ $\mu$ l which is comparable with the study by Shobhana *et al* who found range between 59-958 cells/ $\mu$ l in HIV patients<sup>3</sup>. Fungal infections are an early manifestation of immunosuppression and they are more frequent when the CD4 cell count approaches 450 cells/ $\mu$ l. The second commonest dermatological disease among infections in the present study was fungal infections (23%). Out of the 100 patients, 13% patients had dermatophytosis. This finding is comparable with the studies of Shobhana *et al* and Kumaraswamy *et al* who reported 13% and 8% patients with dermatophytosis respectively<sup>3, 7</sup>. However Kaviarasan *et al* found higher number of patients with fungal infections (22.2%) in his studies<sup>8</sup>. Tinea corporis was the commonest dermatophytosis and was seen in 7% patients. However Kaviarasan *et al* who reported higher percentage of Tinea corporis patients 58.79% in their studies. Other dermatophyte infections observed in this study were Tinea cruris 4%, and Tinea faciei 1%. These findings are in contrast with that of Kaviarasan *et al* where Tinea cruris was seen in 49.9% and Tinea faciei in 14.6%. The higher percentage of dermatophyte infections in Kaviarasan *et al* study could be attributable to hot and humid climate in that area (Pondicherry)<sup>8</sup>. Dermatophytic infections like Tinea faciei (1%) and T. Versicolor (1%) were less commonly noted in our present study. In the present study, oral candidiasis was observed in 10% patients. However Shobhana *et al* and Farrokh *et al* reported oral candidiasis in 36% and 31.4% among HIV patients in their studies respectively<sup>3, 9</sup>. This low proportion of oral candidiasis in the present study could be partially explained by the fact that HIV positive patients only with oral candidiasis were referred to gastroenterology OPD directly. CD4 count among oral candidiasis patients range between 5-488 cells/ $\mu$ l which is comparable with CD4 range in study by Shobhana *et al* (17-551 cells/ $\mu$ l)<sup>3</sup>. In the present study 6% HIV positive patients with oral candidiasis had CD4 count below 200 cells/ $\mu$ l and 4% had CD4 counts above 200 cells/ $\mu$ l<sup>3</sup>. Goh *et al* in his study reported CD4 count below 200 cells/ $\mu$ l in 12.5% of patients and CD4 counts above 200 cells/ $\mu$ l in 4.1% of the patients<sup>5</sup>. In the present study bacterial infections accounted for 17% of patients. Bacterial infections like Furunculosis (7%), Folliculitis (5%), leprosy (1%), Impetigo (1%), Ecthyma (1%), Cellulitis (1%) and Cutaneous Tuberculosis (1%) were less commonly noted. This is contrast with study of Farrokh *et al* who have reported bacterial infections in 45% of patients<sup>9</sup>. Therapy with Septran in all HIV positive patients to prevent opportunistic infections could be responsible for the less number of cases of bacterial infections in the present study. In the present study, 4% patients

presented with scabies which is comparable with the study by Shobhana *et al* who reported scabies in 5% patients<sup>3</sup>. In the present study 2% scabies patients had CD4 counts below 200 cells/ $\mu$ l and 2% patients had CD4 count above 200 cells/ $\mu$ l. Farrokh *et al* reported 4.1% patients with CD4 counts below 200 cells/ $\mu$ l<sup>9</sup>.

#### **Non-infectious mucocutaneous manifestations and CD4 cell count**

In the present study, the most common non-infectious mucocutaneous manifestation was pruritic papular eruption, observed in 8% patients. This is similar to the studies by Kumaraswamy *et al* (7.7%) and Maniar *et al* (4.8%)<sup>7,10</sup>. However Sharma *et al* (35.8%) and Goh *et al* (32.29%) reported pruritic papular eruptions respectively<sup>11,5</sup>. In the present study, CD4 range among pruritic papular eruption patients between 31-571 cells/ $\mu$ l. In the present study, 5% of pruritic papular eruption patients had CD4 counts below 200 CD4 cells/ $\mu$ l and 3% of patients had CD4 counts above 200 cells/ $\mu$ l. However Goh *et al* reported higher patients (25%) with CD4 counts below 200 cells/ $\mu$ l and 7.29% of patients had CD4 counts above 200 cells/ $\mu$ l. In the present study, drug reacts on 7%, was the next common dermatological manifestation among non-infectious group which is similar to studies by Goh *et al* (17.1%) and Sharma *et al* (12.5%)<sup>5,11</sup>. However Kumaraswamy *et al* reported drug reaction in only in 1.32% of patients<sup>7</sup>. In the present study 5% of patients with drug reaction had CD4 counts below 200 cells/ $\mu$ l and 2% of patients had CD4 counts above 200 cells/ $\mu$ l which is almost similar to the study by Goh *et al* who have reported 15.6% of patients with CD4 counts below 200 cells/ $\mu$ l and 2.8% of patients with CD4 counts above 200 cells/ $\mu$ l<sup>5</sup>. In the present study, out of 7% of patients with drug reactions, 2% of the patients had maculopapular drug rash which is similar to the study of Sharma *et al* who have reported 4.25% of patients with maculopapular rash in their study<sup>11</sup>. Other drug reaction like SJS (3%), TEN (1%), EMF (1%), FDE (1%) were less commonly noted. Other non-infectious disease included eczema (3%), psoriasis (2%), seborrheic dermatitis (2%), photosensitive dermatitis (1%), LSC (1%), LPP (1%), SLE (1%), and acne (1%) were less common.

**Mean Cd4 Count:** In this study mean CD4 count was 280 cells/ $\mu$ l which is consistent with the reports of Zanacanarao *et al* (269 cells/ $\mu$ l) and Kumaraswamy *et al* at<sup>6,7</sup>. However higher mean CD4 count was reported by Farrokh *et al* (640 cells/ $\mu$ l)<sup>9</sup>.

**Immune Categories:** Various skin disorders in HIV patients were grouped into C1, C2 and C3 under the CDC classification system based on the CD4 count. In the present study 49% patients were in C3 category

which is consistent with the study by Zanacanarao *et al* who have reported 48.52% patients in C3 category<sup>6</sup>. In the present study 41% were in C2 category and 10% were in C1 category.

**MANIFESTATIONS BELOW 50 (Cells/ $\mu$ l):** In the present study, out of 100 patients, 19% had CD4 counts below 50 cells / $\mu$ l. However Goh *et al* who have found 38.5% of patients with CD4 counts below 50cells/ $\mu$ l which is slightly higher<sup>5</sup>. In the present study out of 19% patients having CD4 counts below 50cells/ $\mu$ l, 13% patients had infectious mucocutaneous manifestations including oral candidiasis (3%), Folliculitis (3%), herpes zoster (2%), herpes simplex (1%), Furunculosis (1%),scabies (1%), tinea cruris (1%), Warts (1%). Remaining 6% of patients had non-infectious mucocutaneous manifestations. Among them 3% patients had drug reactions, 2% patients had PPE, and 1% of patients had psoriasis.

#### **CONCLUSION**

100 patients were studied over a period of 2 years with a mean age of 29.25 years (range 19 years to 60 years.) The common age affected in the present study was 19-29 years. 64% were males and 36% were females, with a male to female ratio of 1.8:1. Heterosexual route (90%) was the commonest mode of acquisition of HIV infection. 71% were married, 17% here unmarried, 12% were widowed. Most of the patients were workers (29%). Most of the patients were illiterate (61%). 49% patients had CD4 counts below 200 cells/ $\mu$ l. 41% had CD4 counts between 200-499 cells/ $\mu$ l. 10% had CD4 counts above 500 cells/ $\mu$ l. Mean CD4 count was 280 cells/ $\mu$ l. The infectious diseases were the commonest mucocutaneous manifestations among HIV patients. The majority of the patients were viral infections (26%), with the mean CD4 count 276 cells/ $\mu$ l. The second commonest infection was the fungal infection (23%), with the mean CD4 count 268 cells/ $\mu$ l. Pruritic papular eruptions (8%) was the commonest among non-infectious disease with mean CD4 count 234 cells/ $\mu$ l. The second commonest was drug reaction (7%) with mean CD4 count 113 cells/ $\mu$ l. Out of 100 patients, 19% patients with CD4 counts below 50 cells/ $\mu$ l, 13% patients developed infectious mucocutaneous manifestations which include oral candidiasis, genital herpes and other manifestations. Among 6% patients with non-infectious mucocutaneous manifestations, 3% had drug reactions, 2% had PPE and 1% of patients had psoriasis.

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