

## Original Research Article

# Mucocutaneous manifestations in newly diagnosed cases of HIV, correlation with CD4 counts and WHO staging at a tertiary care center

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### ABSTRACT

**Background:** Mucocutaneous infections have played an important role in initial diagnosis of HIV infection and in clinical staging of the disease. Mucocutaneous manifestations in HIV infected individuals are myriad and can serve as a main indicator of other problems. Health care personnel involved in HIV health care must therefore have a clear idea of type, pattern, and prevalence of skin diseases in their locality. The objective of the study was to determine the various mucocutaneous manifestations in newly diagnosed cases of HIV and to correlate them with CD4 cell counts. The manifestations and CD4 cell counts are correlated with WHO staging of the disease.

**Methods:** Data was collected from all the newly diagnosed cases of HIV presenting to the Department of Dermatology. Thorough clinical examination was done and findings were noted. CD4 cell counts were performed by FACS counter and supportive laboratory tests were done for diagnosis of other skin manifestations.

**Results:** 250 cases were enrolled with males 148 and 102 females. Most common age group was middle age group and hetero sexual route was the most common route of transmission. Bacterial skin infections were more common and candidiasis was most common among fungal infections. Herpes zoster was most common in viral infections. Significant correlation was observed between CD4 cell counts and WHO clinical staging of disease. Majority of infections were more common at advanced stage of HIV.

**Conclusions:** To conclude, HIV-related mucocutaneous manifestations are a good clinical clue in diagnosis of advanced stages of HIV. Most of these manifestations can serve as diagnostic and prognostic markers in HIV infection. Management of HIV related mucocutaneous manifestations should always be precluded with a screening of CD4 cell counts. A lowered CD4 cell counts will prolong the duration of treatment and may significantly alter the outcome of the disease.

**Keywords:** Mucocutaneous manifestations, Human Immunodeficiency Virus, CD4 counts, Candidiasis, *Herpes zoster*

### INTRODUCTION

Ever since its recognition in 1981, HIV/AIDS still continues as one of the main diseases that threatens the mankind. At the end of 2014, an estimated 36.9 million people are infected globally with 2 million new cases added annually. According to United Nations report,

India is considered to have the third highest number of living people with 2.1 million cases by the end of 2013.<sup>1</sup> Mucocutaneous infections have played an important role in initial diagnosis of HIV infection and in clinical staging of the disease. Mucocutaneous manifestations in HIV infected individuals are myriad and can serve as a main indicator of other problems. These manifestations

are seen in any stage of HIV stage, but are more common in the advanced stages of HIV infection. Hence dermatologic examinations can serve as a guide in terms of staging and severity of disease.<sup>2</sup> Approximately 90% of HIV patients develop cutaneous disease and provide a suspicion for diagnosis of HIV and systemic complications.<sup>3</sup> However differences in skin pigmentation, racial factors, climate, environmental, demographic and behavioral factors cause different clinical presentations and epidemiological patterns of HIV –associated skin conditions. Health care personnel involved in HIV health care must therefore have a clear idea of type, pattern, and prevalence of skin diseases in their locality. Mucocutaneous conditions have been correlated with CD4 counts in many studies. But correlation of CD4 counts, clinical manifestations with WHO staging's are only few and limited.<sup>4</sup>

The aim of the present study was to determine the various mucocutaneous manifestations in newly diagnosed cases of HIV and to correlate them with CD4 cell counts. The manifestations and CD4 cell counts are correlated with WHO staging of the disease.

## METHODS

A Prospective cross sectional study was conducted at Narayana Medical College and General hospital, a tertiary care hospital by Department of Dermatology for a period of one year from January 2015 to December 2015. The study included all the newly diagnosed cases of HIV and presented to the skin clinic. The study group was 250 cases with 148 males and 102 females.

### Inclusion criteria

Patients between the age group 18 to 65 years. Patients presented with mucocutaneous condition.

### Exclusion criteria

Known HIV cases already on HAART. Patients on primary or secondary prophylaxis for opportunistic infections. Patients on any other medication for systemic diseases. Patients who didn't consent for the study.

Informed consent was obtained from all the cases who participated in the study. A detailed history including the demographic parameters (age, sex, marital status etc.) were noted, and a thorough clinical examination was done and the findings were recorded in separate pre-designed proforma. Patients were staged as per the WHO guidelines and CD4 counts were done for every patient at the time of presentation. To confirm the clinical diagnosis supportive laboratory investigations Eg: Tzanck smear, KOH preparations, Culture etc. were done.<sup>5</sup>

### HIV diagnosis

HIV was confirmed as per the Guidelines of NACO.<sup>6</sup>

### CD4 estimation

CD3+ and CD4+ cell counts were done by FACS (Fluorescent Activated Cell sorter) counter system (Beckton-Dickinson, USA).

### Statistical analysis

All the data was entered in Microsoft excel spread sheet and analyzed.

## RESULTS

A total of 250 newly diagnosed cases of HIV were enrolled in the study with 148 males (59.2%) and 102 females (40.8%) and male to female ratio of 1:0.7. The age range was 18 to 64 years with a mean of 38 years. The most common age group in the study was 20-29 years (35.20%) followed by 30-39 years (28%). Heterosexual route of transmission was the commonest route (85.6%), 2.4% of cases by blood transfusion, 12% of the cases the route was not known. None of the cases in our study documented homosexual route of transmission. 71.20% of cases were illiterate in our study and 28.8% were literate (Could complete 5th class of Basic education). 80.80% of cases were married, 12% unmarried and 7.20% were separated/ widow (Table 1).

All the mucocutaneous conditions of the patients were noted and categorized as infectious conditions and non-infectious conditions. Some of the Patients in the study presented with both infectious and non-infectious conditions simultaneously. The total infectious conditions were 426 among 250 cases in the study. Majority were bacterial infections with 95.6% followed in order by fungal infections 41.2%, viral infections 30.8% and 2.8% of infestations. The type of infections with regard to their number, sex wise distribution and CD4+ cell counts are summarized in Table 2. The CD4+ cell counts of all the patients were estimated at diagnosis and classified as with CD4+ cell counts  $\geq 500/\text{mm}^3$ , 499-350 cells/ $\text{mm}^3$ , 349-200 cells/ $\text{mm}^3$  and  $<200$  cells/ $\text{mm}^3$ . Among the fungal infections, Candidiasis was the commonest (62.14%) followed by Onychomycosis (19.42%). Staphylococcal skin infections were commonest in bacterial infections (51.88%) followed by folliculitis (26.36%). *Herpes zoster* was the commonest viral infection noticed (59.74%) followed by *Herpes simplex* lesions (23.38%). All the above lesions were more common in cases with CD4+ cell counts  $<200$  cells/ $\text{mm}^3$  (Table 2).

Overall 51 non-infectious conditions were noted among 250 cases in the study. The type of infections their sex wise distribution and CD4+ cell counts are presented in Table 3. Xerosis was the commonest non-infectious condition (31.37%) followed in order by Seborrheic dermatitis (23.53%), Generalized Hyper pigmentation of skin (19.61%). Less common conditions were Psoriasis, Diffuse alopecia and Lichen planus. No cases of Molluscum contagiosum, genital warts and Kaposi's sarcoma were noted in the study.

**Table 1: Demographic parameters of cases in the study.**

Parameter	Sex distribution		Total (no) (%)	
	Male (no) (%)	Female (no) (%)		
Age in years	<19 years	12 (8.11)	6 (5.88)	18 (7.20)
	20-29 years	54 (36.49)	34 (33.33)	88 (35.20)
	30-39 years	44 (29.73)	26 (25.49)	70 (28)
	40-49 years	24 (16.22)	14 (13.73)	38 (15.20)
	50-59 Years	8 (5.41)	4 (3.92)	12 (4.80)
	>60 years	6 (4.05)	18 (17.65)	24 (9.60)
<b>Total</b>	148 (59.2)	102 (40.8)	250 (100)	
Educational status	Illiterate	102 (68.92)	76 (74.51)	178 (71.20)
	Literate	46 (31.08)	26 (25.49)	72 (28.80)
Marital status	Married	120 (81.08)	82 (80.39)	202 (80.80)
	Unmarried	22 (14.86)	8 (7.84)	30 (12)
	Widow/divorcee	6 (4.05)	12 (11.76)	18 (7.20)
Mode of transmission	Homosexual	0	0	0
	Heterosexual	126 (85.14)	88 (86.27)	214 (85.6)
	Blood transfusion	4 (2.70)	2 (1.96)	6 (2.4)
	Unknown	18 (12.16)	12 (11.76)	30 (12)

**Table 2: Prevalence of infectious mucocutaneous manifestations and their relation to CD4 counts.**

Dermatologic manifestations	No of patients (n=250)		CD4 counts (/mm <sup>3</sup> )				Total (no) (%)
	Male (no)	Female (no)	≥500 (n=30)	499-350 (n=44)	349-200 (n=50)	<200 (n=126)	
<b>Fungal infections</b>							103 (41.2)
Oral candidiasis	38	26	4	8	12	40	64 (62.14)
Onychomycosis	8	12	1	0	3	6	20 (19.42)
Tinea pedis	4	6	2	1	3	4	10 (9.71)
Tinea corporis	1	8	0	2	3	4	9 (8.74)
<b>Bacterial infections</b>							239 (95.6)
Staphylococcal skin infections	68	56	4	10	24	86	124(51.88)
Acne vulgaris	28	24	0	2	6	44	52 (21.76)
Folliculitis	38	25	0	2	7	54	63 (26.36)
<b>Viral infections</b>							77 (30.8)
Herpes zoster	24	22	1	3	5	38	46 (59.74)
Condyloma acuminata	6	3			2	7	9 (11.69)
Herpes simplex	8	10	3		4	11	18 (23.38)
Molluscum contagiosum	2	2			2	2	4 (5.19)
<b>Infestations</b>							7 (2.8)
Scabies	2	2	1	1		2	4 (57.14)
Pediculosis		3				3	3 (42.86)

**Table 3: Prevalence of non-infectious mucocutaneous manifestations and their relation to CD4 counts.**

Dermatologic manifestations	No of patients (no) (%)		CD4 Counts (/mm <sup>3</sup> )				Total (no) (%)
	Male (no)	Female (no)	≥500 (n=30)	499-350 (n=44)	349-200 (n=50)	<200 (n=12)	
<b>Generalized hyperpigmentation of skin</b>	4	6			2	8	10 (19.61)
<b>Xerosis</b>	8	8		1	6	9	16 (31.37)
<b>Seborrheic dermatitis</b>	7	5	1		3	8	12 (23.53)
<b>Psoriasis</b>	2	4	2	1		1	6 (11.76)
<b>Lichen planus</b>	1	3	2	1	1		4 (7.84)
<b>Diffuse alopecia</b>	1	2	1			2	3 (5.88)
<b>Total</b>							51 (20.4)

**Table 4: Distribution of patients according to WHO.**

Stage	No of patients	Mean CD4+cell counts (cells/mm <sup>3</sup> )
<b>I</b>	33	378.44
<b>II</b>	72	321.63
<b>III</b>	96	242.66
<b>IV</b>	49	166.24
<b>Total</b>	250	277.24

There were 33 cases in WHO Clinical stage 1, 72 in Stage 2, 96 in stage 3 and 49 in stage 4. The mean CD4+ cell counts in each stage are summarized in Table 4. The mean CD4+ cell counts in the total study was 277.24 cells/mm<sup>3</sup> (Range: 12-1294 cells/mm<sup>3</sup>). A statistically significant correlation of low CD4+ cell counts was found with candidiasis, herpes zoster, staphylococcal infections and folliculitis.

## DISCUSSION

In the present study, 250 cases were enrolled with HIV diagnosis and having mucocutaneous manifestations. Males were more predominant in our study with 59.2% as mentioned in many other studies universally and in India. This may be explained by more number of males attending the outpatient clinic and more involved in high risk exposure.<sup>7,8</sup> In the present study, the most common age group was 20-29 years followed by 30-39 years which is a sexually active middle age group, findings of our study correlates with the findings of many studies globally. Unprotected heterosexual route was the most common route of transmission with a rate of 85.6% in our study which is on par with findings of Singh et al and Srikanth et al, who reported 94% and 77%.<sup>9,10</sup> No cases of homosexual transmission were observed in our study. 71.2% were illiterate group with >50% unaware of HIV and routes of HIV transmission as explained, HIV is most commonly observed in illiterate persons and truck drivers. Most of them were from rural and tribal areas, few of them were wanderers.

Findings from the study of Shobana et al reported the prevalence of Mucocutaneous manifestations in India in range of 40-87.6%.<sup>11</sup> In our study the overall prevalence of both infectious and non-infectious manifestations were 64.2%, but this is in contrast to findings of Mawenzi et al who reported the prevalence as 42.1% in his study.<sup>12</sup> Infectious manifestations accounted for 55.21% overall while non-infectious manifestations are 22.12%. Findings of our study were compatible with findings of Salami et al who reported the Infectious manifestations as 58.2% and non-infectious 24%.<sup>13</sup> Most common infections were bacterial with staphylococcal infections, more common, followed by folliculitis. Similar findings were reported by Spira et al and Garbe et al in their study with bacterial infections as most common.<sup>14,15</sup> Oral candidiasis was the most common fungal infection in the study and was found more associated with CD4 count <200 and in

WHO Stage 4. Similar findings were reported by Chopra et al and many more studies.<sup>16</sup> Other less commonly seen fungal infections were Onychomycosis, Tinea pedis and Tinea corporis. No cases of Dermatophytosis have been reported in our study. Herpes zoster was the most common viral infection in our study with a prevalence of 59.74% among other viral infections and overall prevalence of 8%. This is similar to the findings of Azfar et al who reported the similar prevalence rate of Herpes zoster in his study.<sup>17</sup> There are reports of Herpes zoster occurring in 6% to 255 of HIV patients. In our study Condylomata acuminata was reported at 11.69% which is on par with findings of Huang et al and Kim who reported the similar prevalence in their studies.<sup>18,19</sup> Other less common viral infections were herpes simplex and Molluscum contagiosum. In our study Molluscum contagiosum was reported as 5.19% which coincides with the findings of Kore et al.<sup>20</sup>

Among non-infectious manifestations, Xerosis was the most common and reported with prevalence of 31.37%, these findings were on contrary with findings of Raju who reported the prevalence as 22.17% in his study, but similar to Kumaraswamy et al who reported as 37% in his study.<sup>21,22</sup> Followed in next order, generalized pigmentation was observed with 19.61% prevalence and Seborrhoeic dermatitis in 23.53%. The prevalence of pigmentation and seborrhoeic dermatitis was considerably less than in other studies. Scabies and Pediculosis were less commonly observed infestations in our study. In our study Lichenplanus, Psoriasis and diffuse alopecia were less commonly observed. As reported in some of the studies, these manifestations are more common in western countries than in Asian countries.<sup>23</sup>

In present study, majority of patients presented to the OP in stage-3 (38.4%) and minority in stage-1 (13.2%). Mucocutaneous manifestations correlate well with the WHO clinical stages. However some of the lesions were nonspecific. There was a positive correlation between CD4 cell counts and mucocutaneous manifestations in our study which were similar to findings of Han et al.<sup>24</sup> The mean CD4 cell count in the study group was 277.24 cells/mm<sup>3</sup> which is similar to reports of many studies in India.<sup>25</sup> Most of the mucocutaneous manifestations were noticed in stag-3 and stage 4. Most of the studies in their findings reported a significant association between low CD4 counts and immunosuppression which is associated with more manifestations.

To conclude, HIV-related mucocutaneous manifestations are a good clinical clue in diagnosis of advanced stages of HIV. Oropharyngeal candidiasis, herpes zoster, xerosis of skin, staphylococcal infestations was found to have a significant relation with WHO staging in the disease. Most of these manifestations can serve as diagnostic and prognostic markers in HIV infection. Management of HIV related mucocutaneous manifestations should always be precluded with a screening of CD4 cell counts.

A lowered CD4 cell counts will prolong the duration of treatment and may significantly alter the outcome of the disease.

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