

Study of mucocutaneous manifestations of HIV and its relation to total lymphocyte count

P. K. Ashwini, Jayadev Betkerur, Veeranna Shastry
Department of Dermatology, JSS Hospital, Mysore, Karnataka, India

Address for correspondence:

Dr. P. K. Ashwini, Department of Dermatology, JSS Hospital, MG Road, Mysore - 570 004, Karnataka, India.
E-mail: drashwinipk@gmail.com

Abstract

Introduction: HIV is associated with various mucocutaneous manifestations which may be the first pointers toward HIV and can also be prognostic markers for disease progression. This study was done to note the different mucocutaneous lesions present in HIV and their relation to total lymphocyte count (TLC). **Methodology:** Three hundred and seventy-nine HIV patients attending the Department of Dermatology, Venereology, and Leprosy were included in the study. They were screened for the presence of any mucocutaneous lesions. TLC in patients presenting with mucocutaneous lesions was done and also CD4 count was done wherever possible. **Results:** Among 379 patients, 53.8% developed mucocutaneous manifestations. Male: female ratio was 2.2:1. Majority of patients belonged to 20–39 years age group. Among mucocutaneous manifestations, oral candidiasis was the most common, followed by herpes zoster and dermatophytoses. Adverse drug reactions were noted in few. The majority of patients had TLC $<1500/\text{mm}^3$ and CD4 <200 . **Conclusion:** Mucocutaneous manifestations are common and have varied presentation in HIV/AIDS. Patients with mucocutaneous manifestations were clustered at lower TLC and CD4 count. Like CD4 count, TLC can be considered as a marker for disease progression.

Key words: Cutaneous manifestations, HIV, total lymphocyte count

INTRODUCTION

Dermatological manifestations are seen at every stage of HIV/AIDS and are often the presenting features. These manifestations may act as marker of disease progression.^[1]

CD4 cell count and CD4 percentage are key markers for determining disease progression in HIV-infected patients. Many studies had demonstrated a reasonable correlation between total lymphocyte count (TLC) and CD4 count. It was recommended that TLC can be used as a laboratory marker to initiate antiretroviral therapy in resource-poor settings, where CD4 is not available.^[2]

Aims and objectives

1. To study the prevalence of various mucocutaneous

manifestations in patients with HIV/AIDS
2. To determine the correlation between TLC and mucocutaneous manifestations in patients with HIV/AIDS.

METHODOLOGY

Study population

The study population included all HIV-positive patients, who attended Department of Dermatology, Venereology, and Leprosy of JSS Hospital, Mysore. The patients were screened for mucocutaneous manifestations, over a period of 2 years. After an informed consent, a detailed history and complete examination was done according to preformed pro- forma.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Ashwini PK, Betkerur J, Shastry V. Study of mucocutaneous manifestations of HIV and its relation to total lymphocyte count. Indian J Sex Transm Dis 2020;41:47-52.

Submitted: 24-Jun-2016

Accepted: 14-Nov-2017

Published: 11-Apr-2018

Access this article online

Quick Response Code:



Website:

www.ijstd.org

DOI:

10.4103/ijstd.IJSTD_58_16

Investigations

Hemoglobin percentage, complete blood count, peripheral blood smear, urine analysis, and TLC was estimated. Investigations pertaining to opportunistic infection were done whenever necessary. CD4 count was done in patients who were willing.

Follow-up

Patients were followed up regularly and complete cutaneous and systemic examination was performed. In patients, presenting with mucocutaneous manifestations, the TLC was done. CD4 cell count was done whenever possible.

Statistical analysis

The prevalence rate of mucocutaneous manifestations was estimated. The statistical significance was evaluated using Chi-square test. The significance level used was at 95% level.

The mucocutaneous manifestations were classified into major six groups. The distribution of the mucocutaneous manifestations according to CD4 count and the total lymphocyte was prepared. The mean and standard deviation of CD4 count and TLC were estimated for disease categories, and ANOVA was applied to test the significant difference between manifestation category. The Pearson correlation coefficient was estimated for CD4 count and TLC. The statistical significance was evaluated using Z-test.

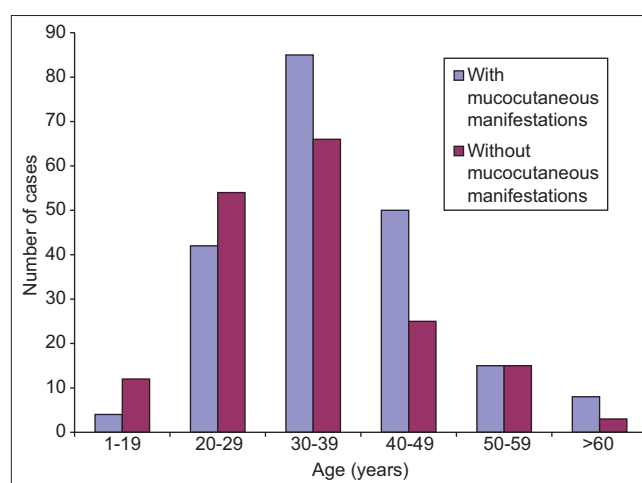
RESULTS

A total of 379 patients with HIV/AIDS were examined and screened for mucocutaneous manifestations. A total of 261 (68.8%) were males and 118 (31.13%) were females. The age group of patients ranged from 2 to 70 years with 247 (65.17%) patients belonging to the age group 20–39 years [Graph 1]. There were seven children in the study group aged between 2 and 12 years, who were diagnosed after their parents were found to be seropositive.

Two hundred and four (53.8%) patients presented with 330 episodes of mucocutaneous manifestations. Among 204, there were 48 patients who presented with multiple mucocutaneous manifestations. A total of 74 patients in the study group were on highly active antiretroviral therapies (HAART). Out of them, 62 patients presented with mucocutaneous manifestations during the study period. The manifestations occurred before or during the therapy.

The patients who presented with mucocutaneous manifestations were categorized into seven groups as follows:

1. Bacterial infections



Graph 1: Age wise distribution of HIV patients with and without mucocutaneous manifestations

2. Fungal infections
3. Viral infections
4. Infestations such as scabies
5. Adverse drug reactions
6. Noninfectious conditions including xerosis, generalized pruritus, and pruritic papules of HIV.

Sexually transmitted diseases such as herpes genitalis, nonherpetic genital ulcer disease, candidal vulvovaginitis, and candidal balanoposthitis were grouped as per their etiological agents under bacterial, fungal, and viral groups.

Among 330 mucocutaneous episodes presenting in 204 patients, TLC was done in 324 episodes. As six of them lost for follow-up, they were excluded from the study. One hundred and ninety-nine (61.41%) presented with fungal and viral infection which forms the most common manifestations observed.

One hundred and twenty (37.3%) of patients had TLC <1200, but we noted that 198 (61.1%) patients had TLC <1500 [Tables 1 and 2].

There were 56% patients with mucocutaneous manifestations who had CD4 count <200/ μ L and 44% patients with mucocutaneous manifestation had CD4 count >200/ μ L [Table 3].

Among patients who presented with mucocutaneous manifestations, 45 different mucocutaneous manifestations were noted [Figures 1–4]. Oral candidiasis is the most common followed by herpes zoster and dermatophytosis. Among dermatophytosis, tinea cruris was more commonly seen. The manifestations occurred at different TLC values [Graph 2].

Oral candidiasis occurred at lower average TLC of 1270 compared to dermatophytoses, xerosis, insect bite reaction (IBR), pruritus, and eczema which occurred at around

Table 1: Distribution of total lymphocyte counts according to disease category

TLC (/mm ³)	Bacterial	Fungal	Viral	Infestation	Drug reaction	Noninfectious	Total
100-499	1	2	2	-	2	4	11
500-999	9	19	11	1	6	14	60
1000-1499	6	54	35	1	4	28	127
1500-1999	2	19	12	2	1	10	46
2000-2499	3	12	9	1	2	12	39
2500-2999	1	3	9	1	3	2	19
3000-3499	-	5	-	-	1	2	8
3500-3999	-	1	1	-	2	1	5
4000-4499	-	-	-	-	-	2	2
>4500	1	3	2	-	-	1	7
Total	22	118	81	6	21	76	324

TLC=Total lymphocyte count

Table 2: Distribution of total lymphocyte counts according to disease category

Mucocutaneous manifestation	TLC		Total
	<1200/mm ³	>1200/mm ³	
Bacterial	13	9	22
Fungal	39	79	118
Viral	27	54	81
Infestation	1	5	6
Drug reaction	10	11	21
Noninfectious	30	46	76
Total	120	204	324

TLC=Total lymphocyte count

Table 3: Distribution of CD4 count according to disease category

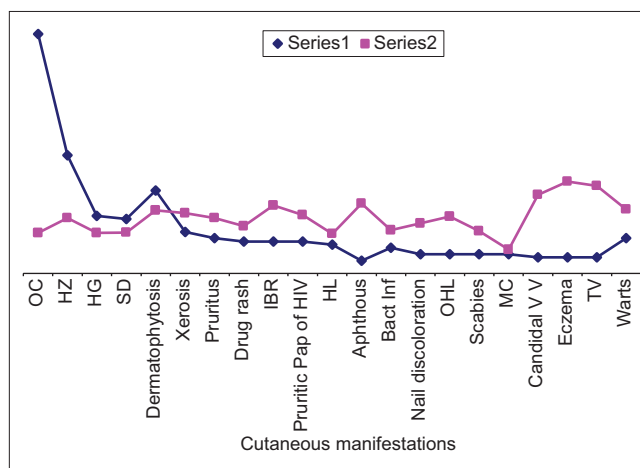
Mucocutaneous manifestation	CD4		Total
	<200	>200	
Bacterial	1	8	9
Fungal	41	26	67
Viral	22	20	42
Infestation	2	1	3
Drug reaction	6	5	11
Noninfectious	25	16	41
Total	97	76	173

1700–2800 TLC. Molluscum contagiosum was noted to occur at average TLC of 741 whereas oral hairy leukoplakia (OHL) occurred at average TLC of 1783.

DISCUSSION

HIV infection is associated with several dermatological manifestations, which can be the initial presenting feature. Cutaneous manifestations can occur in up to 90% of HIV-infected individuals. Often these conditions present atypically, are much more severe, and need prolonged treatment in HIV-infected patients than in the non-HIV group. With the advent of HAART, the mucocutaneous manifestations have become less frequent and less severe.^[3,4]

In our study, male preponderance was noted which could be explained by the fact that more number of male patients



Graph 2: Common cutaneous manifestations and average total lymphocyte count. Series 1 = Frequency of mucocutaneous manifestations; Series 2 = Corresponding total lymphocyte count. TV = Tinea Versicolor; VV = Vulvovaginitis; OC = Oral candidiasis; HZ = Herpes zoster; HG = Herpes genitalis; MC = Molluscum contagiosum; OHL = Oral hairy leukoplakia; HL = Herpes labialis; SD = Seborrheic dermatitis; Others = Psoriasis, LSC = Lichen Simplex Chronicus, sweets syndrome, eosinophilic folliculitis

attend the outpatient department. About 65.17% patients belonged to the age group of 20–39 years. This is similar to other worldwide studies. Out of 379 patients, 53.8% patients developed mucocutaneous manifestations during the study period. The prevalence of mucocutaneous manifestations in various other studies ranges from 40% to 90%.

The most common manifestation observed was oral candidiasis seen in 22.7% patients. In various Indian reports, the prevalence of oral candidiasis in HIV ranges from 16% to 70%.^[5-7] The pseudomembranous “white patches” variant is associated with more severe immunosuppression. CD4 ranged between 107 and 189 cells/ μ L in various studies. In our study, the average TLC for oral candidiasis LSC was 1270 which supports the fact that it occurs with immunosuppression.

Herpes zoster was the second most common cutaneous manifestation occurring in 11.1% of our patients. There are reports of herpes zoster occurring in 6%–25% of HIV



Figure 1: Oral Hairy Leucoplakia



Figure 2: Herpes zoster with secondary infection



Figure 3: Genital Wart



Figure 4: Nevirapine rash

patients.^[5,7] Herpes zoster can occur early in the course of HIV.^[8,9] About 80% of HIV patients had herpes zoster at a CD4 of 250 cells/ μ L.^[3] The average TLC noted was 1731. In patients with HIV, it presents with necrotizing ulcers in a multidermatomal pattern, can last longer than usual 2–3 weeks and heal leaving prominent scars.

Among the 8.7% patients who presented with dermatophytoses in our study, the most common was tinea cruris, followed by tinea corporis. Studies report 10%–22% incidence of dermatophytes.^[10,11] We noted that this manifestation occurred at an average TLC of 1972 which is slightly higher than the values associated with oral candidiasis and herpes zoster.

Herpes genitalis and herpes labialis occurred with an average TLC of 1273 and 1236, respectively. Goldstein *et al.* reported herpes genitalis occurred in 10.8% of his study group of HIV patients.^[12]

Verruca plana, verruca vulgaris, and condyloma acuminata were seen. With an average TLC of 2071. It is reported

that HIV-infected men are at increased risk for anal human papillomavirus (HPV) infection and HIV-infected women are at an increased risk for cervical HPV infection. Studies have shown an higher risk of oral warts in HIV-infected individuals despite treatment with HAART.^[13]

Among our patients who presented with molluscum contagiosum, no atypical forms were noted. Giant molluscum contagiosum and disseminated molluscum contagiosum have been reported in AIDS.^[3,14]

Onychomycosis involving fingernails was noted in few. A prevalence of 20%–25% was noted in various studies.^[10,15,16] Proximal white subungual onychomycosis known to be pathognomonic of HIV was not seen in our study.

OHL presented in six of our patients. Worldwide, the prevalence ranges from 0% to 26%. One study in South India reported OHL in 4% of 594 HIV patients where CD4 was 129 cell/ μ L.^[15] In our study, the average TLC in these patients was 1783. In HIV patients, OHL serves as an indicator of disease severity and rapid progression to AIDS.

Twenty-two of our patients presented with various bacterial infections including staphylococcal infections such as furuncles and folliculitis. Staphylococcal skin infection is the most common cutaneous bacterial infection in HIV patients. It was reported in 1.3% of HIV patients and occurred at CD4 of 410 cell/ μ L.^[17] We observed that these infections occurred at TLC of 1353.

Xerosis, generalized pruritus, exaggerated IBR, and pruritic papules of HIV manifested in few patients in our study. Xerosis and generalized pruritus were most common manifestations in few studies.^[18,19] In western countries, pruritic papules of HIV are the most common cutaneous manifestation.^[20] Exaggerated IBR may be an indication of impending immune suppression.^[21] The prevalence of xerosis in various other studies ranges from 5.3% to 73%.^[3,22]

Adverse drug reactions such as nevirapine rash, Stevens–Johnson syndrome, toxic epidermal necrolysis, fixed drug eruptions, and lipodystrophy were observed. In a study, it was reported that nevirapine rash was the most common.^[3] A partially inherited increased susceptibility to the toxic effects of oxidative drug metabolites is noted in HIV. An interaction between drugs and viral infections such as HIV has been implicated.^[23]

Lipodystrophy syndrome includes apparent abnormal fat redistribution and metabolic disturbances seen in HIV patients receiving combination protease inhibitors and nucleoside analogues. The prevalence of lipodystrophy has been estimated to be between 30% and 50%. The nucleoside analogue linked most strongly is stavudine. Hyperpigmented bands on fingernails are reported to be seen in HIV patients on zidovudine.

Seborrheic dermatitis, pityriasis versicolor, and psoriasis were seen in few patients in our study. There are reports of the above occurring in 7.4%–56% of HIV patients.^[7,12,24] It is one of the earliest clinical marker of HIV. Psoriasis can present with severe and atypical lesions in HIV.^[25,26]

CD4 count is considered as a marker of disease progression. CD4 count should be monitored every 3–6 months to identify this. In resource-poor set up, it may not be possible to get the CD4 count done at regular intervals.

Other surrogate markers such as TLC and HB% have been recommended by initiation of ART.

Many studies conducted in developed and developing countries have demonstrated a reasonable correlation between TLC and CD4 counts in symptomatic patients. It means that even if CD4 cell count testing is unavailable, simple test like TLC can be used as laboratory markers to initiate HAART in resource-poor settings.^[2]

However, it is said that the sensitivity and specificity of TLC are not sufficiently high to replace CD4 counts. In addition, the use of TLC in monitoring response to treatment is unproven. Hence, TLC is not recommended as a marker for decision about initiation of ART till now.^[27] Studies regarding the occurrence of mucocutaneous manifestations and the corresponding TLC are lacking. In our study, among the patients who presented with cutaneous manifestation, 37% had TLC <1200 and 63% had TLC >1200; we also noted that 40% of the patients had TLC between 1200 and 1500 among the 61% patients who had TLC <1500. It means that the majority of patients clustered in between TLC 1200 and 1500. Among patients who presented with mucocutaneous manifestation, 56.1% had a CD4 <200 and 43.9% had a CD4 >200/ μ L.

The mean TLC and mean CD4 among the patients with mucocutaneous manifestations was 1570 and 229, respectively. The mean TLC and CD4 of different disease categories was not statistically significant. In our study, the correlation between CD4 count and TLC was not found to be significant.

CONCLUSION

Mucocutaneous manifestations are common in patients with HIV/AIDS. In our study, the prevalence was 53.8%. The most common manifestation in our study was oral candidiasis, followed by herpes zoster and dermatophytoses. Adverse drug reaction to HAART was less commonly seen.

Majority of patients had a TLC <1500 and CD4 <200/ μ L. There was a cluster of patients between TLC 1200 and 1500. This is slightly higher than the TLC which was recommended as a criteria to start ART, that is 1200. In our study, the correlation between TLC and CD4 count was statistically not significant. However, due to the clustering of cases between 1200 and 1500, we recommend that the cut off could be altered so that TLC can still be considered as a surrogate marker when CD4 is unavailable. Since CD4 is not easily available in most of centers, TLC at this level can also be considered as a marker for disease progression.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Coldiron BM, Bergstresser PR. Prevalence and clinical spectrum of skin disease in patients infected with human immunodeficiency virus. *Arch Dermatol* 1989;125:357-61.
2. WHO. Scaling up Antiretroviral Therapy in Resource Limited Settings – 2003 Revision. Geneva: WHO; 2003. p. 18-27.
3. Kumarasamy N, Vallabhaneni S, Flanigan TP, Mayer KH, Solomon S. Clinical profile of HIV in India. *Indian J Med Res* 2005;121:377-94.
4. Narain JP, Raviglione MC, Kochi A. HIV-associated tuberculosis in developing countries: Epidemiology and strategies for prevention. *Tuber Lung Dis* 1992;73:311-21.
5. Shobhana A, Guha SK, Neogi DK. Mucocutaneous manifestations of HIV infection. *Indian J Dermatol Venereol Leprol* 2004;70:82-6.
6. Nair SP, Moorthy KP, Suprakasan S. Clinico-epidemiological study of HIV patients in Trivandrum. *Indian J Dermatol Venereol Leprol* 2003;69:100-3.
7. Kar HK, Narayan R, Gautam RK, Jain RK, Doda V, Sengupta D, *et al.* Mucocutaneous disorders in HIV positive patients. *Indian J Dermatol Venereol Leprol* 1996;62:283-5.
8. Williamson BC. Disseminated herpes zoster in HIV positive homosexual men without complications. *Cutis* 1987;40:485-91.
9. Mandal BK. Herpes zoster and the immunocompromised. *J Infect* 1987;14:1-5.
10. Kaviarasan PK, Jaisankar TJ, Thappa DM, Sujatha S. Clinical variations in dermatophytosis in HIV infected patients. *Indian J Dermatol Venereol Leprol* 2002;68:213-6.
11. Muñoz-Pérez MA, Rodríguez-Pichardo A, Camacho F, Colmenero MA. Dermatological findings correlated with CD4 lymphocyte counts in a prospective 3 year study of 1161 patients with human immunodeficiency virus disease predominantly acquired through intravenous drug abuse. *Br J Dermatol* 1998;139:33-9.
12. Goldstein B, Berman B, Sukenik E, Frankel SJ. Correlation of skin disorders with CD4 lymphocyte counts in patients with HIV/AIDS. *J Am Acad Dermatol* 1997;36:262-4.
13. Hagensee ME, Cameron JE, Leigh JE, Clark RA. Human papillomavirus infection and disease in HIV-infected individuals. *Am J Med Sci* 2004;328:57-63.
14. Dhar S, Jain S, Verma G, Tanwar RK. Disseminated and atypical molluscum contagiosum in an AIDS patient. *Indian J Dermatol Venereol Leprol* 1996;62:331-2.
15. Kumarasamy N, Solomon S, Flanigan TP, Hemalatha R, Thyagarajan SP, Mayer KH, *et al.* Natural history of human immunodeficiency virus disease in Southern India. *Clin Infect Dis* 2003;36:79-85.
16. Gupta AK, Taborda P, Taborda V, Gilmour J, Rachlis A, Salit I, *et al.* Epidemiology and prevalence of onychomycosis in HIV-positive individuals. *Int J Dermatol* 2000;39:746-53.
17. Kumarasamy N, Solomon S, Madhivanan P, Ravikumar B, Thyagarajan SP, Yesudian P, *et al.* Dermatologic manifestations among human immunodeficiency virus patients in South India. *Int J Dermatol* 2000;39:192-5.
18. Bhandary PG, Kamath NK, Pai GS, Rao G. Cutaneous manifestations of HIV infection. *Indian J Dermatol Venereol Leprol* 1997;63:35-7.
19. Josephine M, Issac E, George A, Ngole M, Albert SE. Patterns of skin manifestations and their relationships with CD4 counts among HIV/AIDS patients in Cameroon. *Int J Dermatol* 2006;45:280-4.
20. Hevia O, Jimenez-Acosta E, Ceballos PI, Gould EW, Penneys NS. Pruritic papular eruption of the acquired immunodeficiency syndrome: A clinicopathologic study. *J Am Acad Dermatol* 1991;24:231-5.
21. Ajithkumar K, George S, Babu PG. Abnormal insect bite reactions: A manifestation of immunosuppression of HIV infection? *Indian J Dermatol Venereol Leprol* 2001;67:72-4.
22. Raju PV, Rao GR, Ramani TV, Vandana S. Skin disease: Clinical indicator of immune status in human immunodeficiency virus (HIV) infection. *Int J Dermatol* 2005;44:646-9.
23. Shastri V, Betkerur J, Kushalappa PA, Savita TG, Parthasarathi G. Severe cutaneous adverse drug reaction to leflunomide: A report of five cases. *Indian J Dermatol Venereol Leprol* 2006;72:286-9.
24. Kavirasan PK, Jaisankar TJ, Thappa DM, Sujatha S. Pityrosporum infection in HIV infected patients. *Indian J Dermatol* 1990;35:215-7.
25. Alexander E, Pinto J, Pal GS, Kamath N, Kuruvilla M. Disease concomitance in psoriasis: A clinical study of 61 cases. *Indian J Dermatol Venereol Leprol* 2001;67:66-8.
26. Singh A, Thappa DM, Hamide A. HIV associated psoriasis: A clinical study. *Indian J Dermatol* 2001;46:15-9.
27. Gupta SB, Pujari SN, Joshi SR, Patel AK. AIDS Society of India Guidelines Development Committee. API consensus guidelines or use of antiretroviral therapy in adults (API-ART guidelines). Endorsed by the AIDS Society of India *J Assoc Physicians India* 2006;54:57-74.