

Original Research Article


Study of cutaneous manifestations in HIV infection

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Abstract

Background: HIV infection is associated with numerous cutaneous changes even before the onset of immunologic dysfunction and AIDS. We all know that as search for reliable clinical indicators for management of human immunodeficiency syndrome in resource poor settings continues, cutaneous disorder can be a good clinical marker of HIV infection, underlying immune status and the disease progression.

Aim and objectives: To study occurrence of various cutaneous manifestations in a patients infected with HIV.

Materials and methods: 120 HIV positive patients above 14 year old with definite cutaneous manifestations attending dermatology OPD in Department of Skin, STD and Leprosy, in a tertiary care centre Dehradun were studied from December 2013 to January 2016.

Results: Among 120 HIV positive patients in our cross-sectional study highest number of patients belonged to 31-40 years age group. Male to female ratio was 1.9: 1 and heterosexual route was the most common route of transmission. Among all cutaneous manifestations pruritic papular eruption, cutaneous drug reactions, molluscum contagiosum, seborrheic dermatitis were common. 14.17% had more than one cutaneous disorder and they had advanced stage of the disease.

Conclusion: Early recognition of the cutaneous manifestation can help in better management of HIV infection in resource poor setting as it can indicate progression of the disease and underlying immune status.

Key words

HIV, Cutaneous manifestations, AIDS, Pruritic papular eruptions, Seborrheic dermatitis.

Introduction

Recognized as an emerging disease only in early 1980s, AIDS has rapidly established itself throughout the world and is likely to endure and persist well in 21st century. The total number of people living with HIV in India is established at 21.17 lakh in 2015. As per the recent India HIV Estimation 2015 report, National adult (15–49 years) HIV prevalence in India was estimated at 0.26% (0.22% – 0.32%). Adult HIV prevalence is estimated at 0.30% among males and at 0.22% among females. In early 1980s, Kaposi's sarcoma was recognized as the first cutaneous marker of HIV infection. Today, at least 56 disorders have been associated with HIV infection. Pruritic papular eruption (PPE) has been reported to be the most common of all. In a study, seborrheic dermatitis was most prevalent (49% of all patients) [1]. With CD4 cell count of <250-300 cells/mm³ eosinophilic folliculitis appear to be an important marker of HIV infection, particularly in patient at increased risk of developing opportunistic infections. Infection with Herpes simplex virus is also extremely common and the incidence rises inversely with decreasing cell counts [2].

Cutaneous disorders occur with increasing frequency as HIV infection clinically advances and immune function deteriorates. Monitoring of HIV infection includes routine clinical assessment and measurement of CD4 cell count and plasma viral load. Absolute CD4 count has been the most widely used predictor of progression to AIDS [3]. Keeping in mind the large number of patients suffering from HIV infection reporting at our hospital, this study is undertaken with a view to establish a correlation of various cutaneous manifestations and HIV infection.

Materials and methods

This was a cross-sectional observational study, which was conducted in a tertiary care centre

Dehradun from December 2013 to December 2016. HIV infected patients more than 14 years presenting to the Dermatology OPD and patients referred from various departments with cutaneous manifestations were included in the study whereas the patients with no definite cutaneous manifestations, with only mucosal manifestations and those not willing or unable to give informed consent were excluded from the study. All participants were administered an informed consent. Routine investigations, complete clinical history, systemic and dermatological examination were done. CD4+ cell count was done by flow cytometry. Tzanck smear, KOH mount, punch/ incisional/ excisional biopsy of the lesion was done depending upon the need. Histopathological study was done in pathology department.

Results

120 HIV positive patients with various cutaneous manifestations attending dermatology OPD were studied. A brief account of demographic profile of the study population is given in **Table - 1**. The mean age in our study was 35.7 years. The patients' age in our study ranged from 14-70 years. The most common age group was 31-40 years, out of 120 patients 61 (50.8%) patients belonged to 31-40 year age group. Out of 120 patients 78 were males and 43 were females. The male to female ratio was 1.9: 1. Out of 78 males, 73 were married and 5 unmarried. All 42 females were married. As shown in **Table - 3** unskilled labourers formed the major group in our study (26.67%) followed by drivers (17.5%), skilled workers (14.17%), housewives (11.67%), farmers (8.33%), hotel workers (5%), student (>0.8%) and unemployed (0.8%). Heterosexual route was the most common mode of transmission (85.82%), followed by blood transmission (4.17%), homosexual behaviour (1.67%) and multiple risk factors (**Table - 1**). The commonest presenting symptoms in our study was malaise (60.83%) followed by fever

(40%), weight loss (33.3%), cough (25%), mental changes (7.5%) and diarrhoea (4.17%).

Table - 1: Demographic parameters of HIV infected patients.

Age in years	No. of patients (%)
14-20	0 (0)
21-30	39 (32.5)
31-40	61 (50.83)
41-50	16 (13.33)
>50	04 (3.33)
Total	120
Sex wise distribution	
Male	78 (65)
Female	42 (35)
Total	120
Marital status	
Male (married)	73(93.59)
Female (married)	42(100)
Occupations	
Unskilled labour	32 (26.67)
Driver	21 (17.5)
Skilled labour	17 (14.17)
Housewife	14 (11.67)
Hotel worker	10 (8.33)
Farmer	6 (5)
Student	1 (0.8)
Unemployed	1 (0.8)
Other	18 (15)
Total	120
Route of transmission	
Heterosexual	103 (85.82)
Blood transfusion	5 (4.17)
Homosexual	2 (1.67)
Multiple risk factors	2 (1.67)
Occupational	0 (0)
IV Drug users	0 (0)
Unknown	8 (6.67)
Total	120
Symptoms	
Malaise	73 (60.83)
Fever	48 (40)
Weight loss	40 (33.33)
Cough	30 (25)
Mental changes	9 (7.5)
Diarrhoea	5 (4.17)

Table – 2: WHO staging of the patient at the time of study.

Stage	No. of patients	Percentage
Stage I	00	00
Stage II	23	19.17
Stage III	83	69.17
Stage IV	14	11.66
	120	100

Majority of the (69.17%) patients in our study were in stage III.

Table - 3: Correlation of some cutaneous manifestation with CD4 cell count.

Cutaneous manifestation	No. of cases	%
Pruritic papular eruptions	27	22.5
Herpes zoster	18	15
Cutaneous drug reactions	17	14.16
Molluscum contagiosum	13	10.83
Psoriasis	13	10.83
Seborrheic dermatitis	20	16.67
Eosinophilic folliculitis	4	3.33
Scabies	13	10.83
Cutaneous cryptococcosis	1	0.08
Interface dermatitis	2	0.16
Staphylococcal infection	6	5
Demodecidiosis	5	4.16
Leprosy	5	4.16
Dermatophyte infection	17	14.16
Erythema multiforme	3	2.5
Xerosis	10	8.33
Herpes simplex	2	0.16
Verruca vulgaris	4	3.33
Cutaneous tuberculosis	4	3.33
Vasculitis	1	0.08
Dermatitis herpetiformis	1	0.08
Contact dermatitis	2	0.16
Scabies	13	10.83
Erythroderma	10	8.33

Table - 2 shows that maximum patient in our stage were in stage III (69.17%), then 19.17 in stage II (19.17%). 11.66% were in stage IV. Among these patients the most common cutaneous manifestation was pruritic papular eruption (22.5%), second was seborrheic

dermatitis (16.67%) followed by herpes zoster (15%), cutaneous drug reaction (14.16%), dermatophytosis (14.16%), molluscum contagiosum (10.83%), psoriasis (10.83%), scabies (10.83%), erythroderma (8.33%) and others. Staphylococcal infections were seen in 6 patients (5%). 27 patients (22.5%) had more than one cutaneous manifestation. We observed higher prevalence of leprosy (4.17%). Also there was high prevalence of reaction (80%) and relapse (20%) among our leprosy patients. In the present study, four cases (3.33%) of cutaneous tuberculosis were seen. Xerosis was observed in 10 (2.5%) patients.

Discussion

The cutaneous manifestations in HIV patients, including many opportunistic infections, are quite common [4, 5]. This study was mainly focused on the dermatological manifestations of HIV positive patients attending a tertiary care centre, Dehradun (Uttarakhand) for treatment.

The patient's age in our study ranged from 14-70 years and the most common age group was 31-40 years (50.8%). The mean age in our study was 35.7 years which was compatible with the studies done by Sharma, et al. [6] (35.1 years) and Coldiron, et al. (33 years) [1]. In our study male to female ratio was 1.9:1. This distribution differed from a study carried out in United States by Smith, et al. [7] who reported a male to female ratio of 9:1 as homosexual behaviour is a common mode of transmission in USA. However, studies carried out by Raju, et al. [8] and Kumarswamy, et al. [5] reported male to female ratio of 2:1 and 2.4:1 respectively which was slightly higher than our study. This ratio correlates well with the fact that heterosexual route of transmission accounts for majority of cases of HIV infection in India. Unskilled labourers formed the major group in our study (26.67%) followed by drivers (17.5%), skilled workers (14.17%), housewives (11.67%), farmers (8.33%), hotel workers (5%), student (>0.8%) and unemployed (0.8%). Our findings was in contrast to findings of study carried out in

Manglore by Bhandary, et al. [9] who reported high prevalence among skilled labourers (56.25%). Unskilled labourers and drivers who lived away from home for work were more prevalent in our study. Heterosexual route was the most common mode of transmission (85.82%), followed by blood transmission (4.17%), homosexual behaviour (1.67%) and multiple risk factors which was compatible with the studies done by Kumarswamy, et al. [5] and Singh, et al. [10] where they reported heterosexual route as most common route of transmission i.e. 85% and 96% respectively. Commonest presenting symptoms in our study was malaise (60.83%) followed by fever (40%), weight loss (33.3%), cough (25%), mental changes (7.5%) and diarrhoea (4.17%) whereas study conducted by Chacko, et al. [11] reported most common symptom of weight loss (62%) followed by fever (56%). The findings in our study were less as compared to the above study because our study was carried out in dermatology department and many of our patients were self-referred to medicine department for constitutional symptoms.

Among these patients 27 patients (22.5%) had more than one cutaneous manifestation and this probably suggest that coexistence of more than one cutaneous disorder could be a marker of a greater degree of immunosuppression. Pruritic papular eruption was the most common disorder encountered in our study (22.5%). Liataud, et al. [12] and Goldstein, et al. [13] reported PPE as the most common cutaneous disorder with prevalence of 46% and 11.4% respectively. Pruritic papular eruption is a unique dermatosis associated with HIV infection. Such patients were generally profoundly immunocompromised with CD4 cell count of 100-200 cell/mm³. Though the cause is not clear, it may be a reaction pattern to an internal focus of infection and allergy. Thus it can be considered as an important clinical marker of advanced HIV infection and patients with this unique disorder are in danger of developing other opportunistic infections / AIDS defining conditions.

Seborrheic dermatitis was the second most common manifestation in our study seen in 20 patients (16.67%). Coldiron, et al. [1] reported seborrheic dermatitis as the most common condition with prevalence of 49%, which is markedly higher than our study. However prevalence in our study is higher than that of 7.4% and 11% as seen in Goldstein, et al. [13] and Sharma, et al. [6] respectively. The prevalence of 16.67% is quite higher than 1-3% as seen in general population. Three patients presented with recurrence, widespread involvement and treatment resistance. Widespread, severe involvement, recurrence, generalized erythroderma found in our study may be related to advanced immunosuppression.

Herpes zoster was 3rd most common condition seen in 18 patients (15%). Similarly Raju, et al. [8] reported herpes zoster as most common condition in their study with prevalence of 16%. We reported 17(14.17%) of dermatophytosis. The prevalence is higher as compared to that of 7% and 3.6% reported by Raju, et al. [8] and Spira, et al. [14] respectively, as the overall incidence of dermatophytic infections in common population is rising nowadays. We also found combination of tinea at more than two sites in many affected patients (85%). This can owe to the fact that generalized tinea is becoming very common in local population and also it can be due to immunosuppression in HIV infection.

Cutaneous drug reactions were seen in 17 patients (14.17%). Antituberculous therapy (AKT) was most common implicated during in 6 cases followed by sulfamethoxazole-tremethoprim combination (4 cases), NSAID (3 cases) and in remaining cases, other drugs like ciprofloxacin, ampicillin etc. were implicated for drug rash. Mitsuyasu R, et al. [17] reported prevalence of cutaneous drug reactions (69%) associated with sulfamethoxazole-trimethoprim combination. We found erythematous maculopapular rash as commonest clinical presentation and it was seen in 7 patients (41.2%) followed by TEN (4 patients,) SJS (3 patients), erythroderma (2 cases) and erythema multiforme (1 case). It is a well-known fact that cutaneous

drug reactions are more common in HIV infection and more severe type of drug reactions like SJS and TEN are observed with advanced immunosuppression. Molluscum contagiosum was seen in 13 (10.8%) patients, which was correlating with the prevalence of 8.1% and 12% as reported by Goldstein, et al. [13] and Raju, et al. [8].

Verruca vulgaris was seen in 4 patients (3.33%) in our study. 2 patients had genital lesions and 2 patients had multiple, large lesions over forearms and hands. One patient had concomitant cryptococcal meningitis. Herpes simplex was the presenting condition in two patients (1.67%). One patient had herpes genitalis. The other patients had long standing chronic ulceration (1 month) over vermilion border of lip fulfilling the AIDS defining criterion.

We observed psoriasis in 13 patients (10.8%). This prevalence is higher than prevalence of 3.1%, 2.3% and 1.8% as reported by Bhandary, et al. [9], Goldstein, et al. [14] and Spira, et al. [14] respectively. As our institute is a tertiary referral centre and many of the cases were referred from periphery, this may be the reason for higher prevalence. 4 patients presented with erythroderma. All these patients had history of long duration of disease and development of erythroderma in these patients may be related to immunosuppression. One patient had widespread extensive lesions with concomitant molluscum contagiosum. 5 patients presented with pustular out of which 4 had generalized pustular psoriasis. Psoriasis may present in HIV patients in all stages (asymptomatic stage, symptomatic stage or in full blown AIDS stage). With advanced stage, it may present with pustular lesions and erythroderma.

Staphylococcal infections were seen in 6 patients (5%). This prevalence was higher than prevalence of 2.8% as reported by Goldstein, et al. [13] and was lower than that of 7% reported by Raju, et al. [8].

We found 4 cases (3.33%) of eosinophilic folliculitis characterized clinically by intensely pruritic, erythematous follicular papules and few pustules over face, neck, upper trunk and arms. Our findings were comparable with the findings of Rosenthal, et al. [22]. One patient had concomitant oral candidiasis. Out of 4 patients, 3 (75%) had past history of opportunistic infections. Thus eosinophilic folliculitis can be a marker for advanced HIV infection.

Being a tertiary referral center for skin and leprosy, we observed higher prevalence of leprosy (4.17%). Also there was high prevalence of reaction (80%) and relapse (20%) among our leprosy patients. We observed 5 cases (4.17%) of leprosy in our study. Out of five cases, one presented with relapse of borderline tuberculoid leprosy. 2 patients were of borderline lepromatous and two were of lepromatous leprosy with one patient having type 2 reactions which may be related to IRIS. We observed increased frequency of reaction (4 out of 5 patients), and unusual presentation (noduloulcerative lesions in the absence of reaction) in one patient. Lienhardt, et al. [16] reported increased frequency of relapse of leprosy in HIV patients as observed in one of our patients.

In the present study, four cases (3.33%) of cutaneous tuberculosis were seen. Similarly, Spira, et al. [14] reported prevalence of 3.83%. One patient had scrofuloderma secondary to tuberculosis inguinal lymphadenopathy. Two patients presented with lupus vulgaris and one patient had tuberculous verrucosa cutis.

We observed 3 cases (2.5%) of erythema multiforme in our study of which one was drug induced (Anti-tuberculous therapy). We included erythema multiforme as a separate group because 2 out of 3 patients had recurrent episodes of erythema multiforme secondary to herpes labialis. In both of these patients, lesions were self limited, recurrent and responded to oral acyclovir therapy. Previous Indian and western studies (e.g. Raju, et al. [8], Kumarswamy, et al.

[5], Spira, et al. [14]) did not report cases of erythema multiforme. Viral infections are known triggers of these skin disorders (Choy AC, et al. [18]). In more than 70% of patients with recurrent erythema multiforme, an episode of herpes infection precedes.

Generalized dry skin or xerosis is a common problem in HIV patients. Xerosis was observed in 10 (8.33%) patients, similar as compared to prevalence of 9.8% in Spira, et al. [14] study. Xerosis or acquired ichthyosis is reported to occur in 20-30% of HIV patients (Osborne GEN, et al. [19]).

We observed 10 (8.33%) cases of erythroderma in whom cause was different than psoriasis and drug reaction. In 5 patients out of 10 no specific disease can be diagnosed. In 3 patients atopic dermatitis was the cause and these patients also had increased serum IgE level. Two patients had erythroderma secondary to seborrheic dermatitis.

We saw 13 (10.8%) cases of scabies. 4 patients out of 13 had crusted scabies, which is well known to be associated with advanced immunosuppression.

We observed one (0.8%) patient of dermatitis herpetiformis in our study. Along with classic lesions like pruritic papules, vesicles and crusted lesion, he also had atypical lesions like grouped bullae over chest and pubic region. Skin biopsy and direct immunofluorescence were suggestive of dermatitis herpetiformis. He had concomitant oral candidiasis and seborrheic dermatitis. Very few case reports regarding association of dermatitis herpetiformis in HIV infection are reported (e.g. by Hasson, et al. [20], Mitsuhahsi, et al. [21]). The association of dermatitis herpetiformis in HIV/AIDS infection can be simple coincidence and further studies are needed to rule out any association. We observed two cases of contact dermatitis. We also saw one case of interface dermatitis, one of vasculitis and one of cryptococcosis.

Conclusion

We conclude that cutaneous manifestation of HIV infection can be considered as good clinical indicators of the infection itself and also for the prediction of underlying immune status. Recognition of the protean cutaneous diseases in HIV/AIDS helps earlier diagnosis of HIV as well as a measure of the immune status of individual. The dermatological manifestations had high prevalence among HIV positive subjects. Pruritic popular eruption, severe cutaneous drug reactions like SJS and TEN, extensive and giant mollusci, eosinophilic folliculitis, crusted scabies were seen with advanced stage and could be considered as clinical markers of advanced immunosuppression. A patient with unknown serostatus presenting with conditions like pruritic popular eruption, molluscum contagiosum etc. can be considered for HIV pre-test counselling and sero-testing as these manifestations are probable markers of HIV infection. Thus, patients with such skin complaints may be motivated to report for voluntary counselling and treatment.

References

1. Coldiron BM, Bergstresser PR. Prevalence and clinical spectrum of skin disease in patients with HIV. *Arch Dermatol.*, 1998 Mar; 125: 357-61.
2. Srikanth Tripathy. Classification and staging of HIV disease. In: HIV/AIDS: diagnosis and management. Eds Vinay Kulkarni, Prayas, 1st edition, 1999, p. 85-96.
3. Schwartzman W, Lambertus MW, Kennedy CA, et al. Staphylococcal pyomyositis in patients infected by HIC. *Am J Med.*, 1991 May; 90: 595-600.
4. Wiwanitkit V. Prevalence of dermatological disorders in Thai HIV-infected patients correlated with different CD4 lymphocyte count statuses: A note on 120 cases. *Int J Dermatol.*, 2004; 43: 265-8.
5. Kumarswamy N, Solomon S, Madhivanan P, et al. Dermatologic manifestations among HIV patients in South India. *Int J Dermatol.*, 2000; 39: 192-95.
6. Sharma YK, Sawhney MPS, Bhakuni DS, et al. Orocutaneous manifestations as markers of disease progression in HIV infection in Indian setting. *MJAFI*, 2004; 60: 239-43.
7. Smith KJ, Skelton HG, Yeager J, et al. Cutaneous findings in HIV-1 positive patients: a 42 month prospective study. *J Am Acad Dermatol.*, 1994; 31: 746
8. PV Krishnam Raju, Rao GR, Ramani TV, et al. Skin disease: Clinical indicator of immune status in HIV infection. *Int J Dermatol.*, 2005; 44: 646-49.
9. Bhandary PG, Kamath NK, Pai GS, Rao G. Cutaneous manifestations of HIV infection. *Indian J Dermatol Venereol Leprol.*, 1997; 63: 35-7.
10. Singh A, Thappa MD, Hamide A. The spectrum of mucocutaneous manifestations during the evolutionary phases of HIV disease: an emerging Indian scenario. *J Dermatol.*, 1999; 26(5): 294-304.
11. Chacko S, John TJ, Babu PG, et al. Clinical profile of AIDS in India. *JAPI*, 1995; 43(8): 535-38.
12. Liataud B, Pape JW, DeHovitz JA, et al. Pruritic skin lesions; A common initial presentation of AIDS. *Arch Dermatol.*, 1989 May; 125: 629-32.
13. Goldstein B, Berman B, Sukenik E, et al. Correlation of skin disorders with CD4 lymphocyte counts in patient with HIV/AIDS. *J Am Acad Dermatol.*, 1997 Feb; 36(2): 262-64.
14. Spira R, Mignard M, Doutre MS, et al. Prevalence of cutaneous disorders in a population of HIV- infected patients. *Arch Dermatol.*, 1998 Oct; 134: 1208-12.
15. Pereira GA, Stefani MMA, Filho JAA, et al. HIV-I and Mycobacterium leprae co-infection: HIV – I subtypes and clinical, immunologic and histopathologic

- profiles in a Brazilian cohort. *Am J Trop Med Hyg.*, 2004; 71(5): 679-84.
16. Lienhardt C, Kamate B, Jamet P, et al. Effect of HIV infection on leprosy: a three year survey in Bamako Mali. *Int J Lepr other Mycobact Dis.*, 1996 Dec; 64 (4): 383-91.
 17. Mitsuyasu R, Groopman J, Volberding P. Cutaneous reaction to trimethoprim-sulfamethoxazole in patients with AIDS and Kaposi's sarcoma. *N Eng J Med.*, 1983; 308: 1535-36.
 18. Choy AC, Yarnold PR, Brown JE, et al. Virus induced erythema multiforme and Stevens- Johnson syndrome. *Allergy Proc.*, 1995 July-Aug; 16(4): 157-61.
 19. Osborne GEN, Taylor C, Fuller LC. The management of HIV-related skin disease. Part I: Infections. *Int J STD & AIDS*, 2003; 14: 78-88.
 20. Hasson A, Gutierrez MC, Martin L, et al. Dermatitis herpetiformis and AIDS-related complex. *J Am Acad Dermatol.*, 1990 June; 22 (6): 1117-19.
 21. Mitsuhashi Y, Hohi D. dermatitis herpetiformis in a patient with AIDS-related complex. *J Am Acad Dermatol.*, 1987; 16: 1129-44.
 22. Rosenthal D, Leboit PE, Klumpp L, et al. Human Immunodeficiency Virus-associated eosinophilic folliculitis. *Arch Dermatol.*, 1991 Feb; 127: 206-209.