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Original Research Article

Study of cutaneous manifestation of HIV disease in correlation with CD4 lymphocyte count

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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 considered among key clinical indicators for prediction of underlying immune status and disease progression. To study occurrence of various cutaneous manifestations and its correlation with CD4 cell counts in HIV infected Patients.
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 (Uttarakhand, India) were studied from December 2013 to January 2016.
Results: Among 120 HIV positive patients in our cross-sectional study, 50.83% of patients belonged to 31-40 years age group. Male to female ratio was 1.9:1 and heterosexual route was most common route of transmission. 69.17% of our study population had CD4 cell counts below 200 cells/mm^3 and 23.33% of patients had CD4 cell counts <50 cells/mm^3. Among these, commonest cutaneous manifestations were pruritic papular eruption, cutaneous drug reactions, molluscum contagiosum, seborrheic dermatitis. 17 patients (14.17%) had more than one cutaneous disorder with mean CD4 cell count of 121.5 cells/mm^3 indicating advanced stage.
Conclusions: At the end of study we concluded that cutaneous manifestations can be considered as a good clinical indicators for the progression of disease and underlying immune status in resource poor setting.

Keywords: HIV, Cutaneous manifestations, CD4 cell counts

INTRODUCTION

Recognized as an emerging disease only in early1980s, AIDS has rapidly established itself throughout the world and is likely to endure and persist well in 21st century. India has the world's third largest population suffering from HIV/AIDS. As per the recently released, India HIV Estimation 2015 report, National adult (15–49 years) HIV prevalence in India is estimated at 0.26% (0.22–0.32%) in 2015. In 2015, adult HIV prevalence is estimated at 0.30% among males and at 0.22% among females. In early 1980s, Kaposi's sarcoma was recognised 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] Eosinophilic folliculitis is associated with CD4 cell count of <250-300 cells/mm^3 and it 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, 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] So far there has been no major study conducted on cutaneous manifestations correlated with their CD4 and CD8 cell counts in HIV infection in our local setting.

Keeping in mind the large number of patients suffering from HIV infection reporting at our hospital, this study is undertaken with a view to understand the correlation of various cutaneous manifestations with CD4 and CD8 cell counts in HIV patients.

METHODS

This is a cross-sectional observational study, which was conducted in a tertiary care centre Dehradun (Uttarakhand, India) from December 2013 to January 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 cross ectional 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+ and CD8+T 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. Correlation of cutaneous manifestations related with HIV infection was made with CD4+ and CD8+ T cell counts at the end of study.

RESULTS

120 HIV positive patients with various cutaneous manifestations attending dermatology OPD were studied. All patients received CD4 cell count and CD8 cell count tests, which were correlated with their skin conditions. The various observations are given in (Tables 1-4).

The patients' age in our study ranged from 14-70 years. The most common age group was 31-40 years and 61 patients (50.8%) belonged to this age group. 78 patients were male and 42 were females and male to female ratio was 1.9:1. Out of 78 males, 73 were married and 5 unmarried. All 42 females were married. 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: Demographic parameters of HIV infected patients (n=120).

Variables	No. of patients (%)
Age (years)	
14-20	0 (0)
21-30	39 (32.5)
31-40	61 (50.83)
41-50	16 (13.33)
>50	04 (3.33)
Sex wise distribution	
Male	78 (65)
Female	42 (35)
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)
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)
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 (n=120).

Stage	No. of patients	Percentage (%)
Stage I	00	00
Stage II	23	19.17
Stage III	83	69.17
Stage IV	14	11.66

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	CD4 cell count (cell/mm^3)		
		>500	200-500	<200
Pruritic papular eruptions	27	0	9	18
Herpes zoster	18	2	7	9
Cutaneous drug reactions	17	0	1	16
Molluscum contagiosum	13	0	1	12
Psoriasis	13	2	4	7
Seborrheic dermatitis	8	0	1	7
Eosinophilic folliculitis	4	0	1	3
Sacbies	1	0	0	1
Cutaneous cryptococcosis	1	0	0	1
Interface dermatitis	2	0	0	2
Staphylococcal infection	6	0	3	3
Demodecidiosis	5	0	1	4
Leprosy	5	1	1	3
Dermatophyte infection	13	1	2	4
Erythema multiforme	3	0	0	3
Xerosis	3	0	0	3
Herpes simplex	2	0	0	2
Verruca vulgaris	4	0	1	3
Cutaneous tuberculosis	4	0	1	1
Vasculitis	1	0	1	0
Dermatitis herpetiformis	1	0	0	1
Contact dermatitis	2	0	0	2
Scabies	13	3	3	7
Erythroderma	10	0	3	7

Maximum no. of patients in our study was that of pruritic popular eruption.

Table 4: Various cutaneous manifestations on presentation in study.

Type of manifestation	No. of cases	Percentage (%)	Mean CD4 cell count (cells/mm^3)
Pruritic papular eruptions	27	22.5	151.3
Herpes zoster	18	15	249
Cutaneous drug reaction	17	14.17	111.6
Molluscum contagiosum	13	10.8	86.1
Psoriasis	13	10.8	176.5
Seborrheic dermatitis	8	6.67	122.7
Dermatophytic infection	13	10.83	182
Staphylococcal infection	6	5	236.3
Leprosy	5	4.17	229
Eosinophilic folliculitis	4	3.33	201.7
Erythema multiforme	3	2.5	152.3
Demodecidiosis	5	4.17	140.57
Xerosis	3	2.5	125.3
Herpes simplex	2	1.67	112
Verruca vulgaris	4	3.33	81.5
Cutaneous tuberculosis	2	1.67	158.5
Scabies	13	11	184
Interface dermatitis	1	1.67	51
Cutaneous cryptococcosis	1	0.8	40
Vasculitis	1	0.8	253
Dermatitis herpetiformis	1	0.8	32
Irritant contact dermatitis	2	1.67	40
Erythroderma	10	8.33	151

Maximum patients in our study presented with CD4 count <200 (67.5%). 27.5% of the patient had CD4 count in between 200-500. The 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. 67.5% (81) patients of our crossectional study population had CD4 cell count <200 cells/mm^3. Among these patients common cutaneous manifestation were pruritic papular eruption, drug reaction, seborrheic dermatitis, molluscum contagiosum. 17 patients (14.17%) had more than one cutaneous manifestation with mean CD4 cell count of 121.5%. Among varied cutaneous manifestations, pruritic papular eruption was the most common disorder encountered in our study (22.5%) with mean CD4 cell count of 151.3 cells/mm^3. Herpes zoster was second most common condition and was seen in 18 patients (15%) with mean CD4 cell count was 249 cells/mm^3. Molluscum was seen in 13 (10.8%) patients. Seborrheic dermatitis was noted in 8 patients (6.67%) with mean CD4 cell count of 122.7 cells/mm^3. Dermatophytic infection was seen in 13 patients (10.83%) with mean CD4 cell count in our study was 182cells/mm^3. Staphylococcal infections were seen in 6 patients (5%) with mean CD4 cell count in our study was 236.3 cells/mm^3.

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 78 patients were male and 42 were females. All the females were married while out of 78 males,73 were married. Male to female ratio was 1.9:1. This distribution differed from a study carried out in United States by Smith et al who reported a male to female ratio of 9:1 as homosexual behaviour is a common mode of transmission in USA.[7] However, studies carried out by Raju et al and Kumarswamy et al reported male to female ratio of 2:1 & 2.4:1 respectively which was similar to our study and correlates well with the fact that heterosexual route of transmission accounts for majority of cases of HIV infection in India.[5,8] 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 who reported high prevalence among skilled labourers (56.25%).[9] 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 and Singh et al where they reported heterosexual route as most common route of transmission i.e., 85% and 96% respectively. [5,10] 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 reported most common symptom of weight loss (62%) followed by fever (56%).[11] 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 themselves to medicine department for constitutional symptoms.

67.5% (81) patients of our cross sectional study population had CD4 cell count <200 cells/mm^3. Among these patients common cutaneous manifestation were pruritic popular eruption, drug reaction, molluscum contagiosum, psoriasis, seborrheic dermatitis.17 patients (14.17%) had more than one cutaneous manifestation with mean CD4 cell count of 121.5% and this probably suggest that coexistence of more than one cutaneous disorder could be a marker of a greater degree of immunosuppression. Among varied cutaneous manifestations, pruritic popular eruption was the most common disorder encountered in our study (22.5%). Liataud et al and Goldstein et al reported PPE as the most common cutaneous disorder with prevalence of 46% and 11.4% respectively.[12,13] The mean CD4 cell count of 151.3 cells/mm^3 which was compatible with the study conducted by Kumarswamy et al where they reported mean CD4 cell count of 149.24 cells/mm^3.[5] Herpes zoster was second most common condition seen in 18 patients (15%). Similarly Raju et al reported Herpes zoster as most common condition in their study with prevalence of 16%.[8] In our study mean CD4 cell count in patients with hepes zoster was 249cells/mm^3. Kumarswamy et al, Raju et al, Goldstein et al reported variable mean CD4 cell count of 176.33, 347.18 and 411 cells/mm^3 respectively.[5,8,13] Molluscum was seen in 13 (10.8%) patients, which is correlating with the prevalence of 8.1% and 12% as reported by Goldstein et al and Raju et al.[8,13] We observed psoriasis in 13 patients (10.8%). This prevalence is higher than prevalence of 2.3% and 1.8% as reported by Goldstein et al and Spira et al repectively.[13,14] Mean CD4 cell count in our study was 176.5 cells/mm^3. Similar finding was also reported by Spira et al.[14] Seborrheic dermatitis was noted in 8 patients (6.67%). Coldiron et al reported seborrheic dermatitis as the most common condition with prevalence of 49%.[1] However prevalence in our study is similar to that of 7.4% as seen in Goldstein et al.[13] Mean CD4 cell count in our study was 122.7 cells/mm^3, higher as compared to mean CD4 cell count of 37 cells/mm^3 as reported by Goldstein et al[13] but it was lower than that of 530 cells/mm^3 as reported by

Raju et al.[8] We found 13 patients (10.83%) of dermatophytic infection. The prevalence is higher as compared to that of 7% and 3.6% reported by Raju et al and Spira et al respectively, as the overall incidence of dermatophytic infections in common population is rising now a days.[8,14] Mean CD4 cell count in our study was 182 cells/mm^3 which is compatible with that 176 cells/mm^3 as reported by Kumarswamy et al.[5] Staphylococcal infections were seen in 6 patients (5%). This prevalence was higher than prevalence of 2.8% as reported by Goldstein et al and was lower than that of 7% reported by Raju et al.[8,13] Mean CD4 cell count in our study was 236.3 cells/mm^3 which was lower as compared to mean CD4 cell count of 410 and 465 cells/mm^3 as reported by Kumarswamy et al and Raju et alrespectively.[5,8] We observed 5 cases (4.17%) of leprosy in our study. Out of five cases, one presented with relapse of borderline tuberculoid leprosy with type1 reaction with CD4 cell count of 149 cells/mm^3. 2 patients were of borderline lepromatous and two were of lepromatous leprosy with one patients having type2 reactions which may be related to IRIS. Mean CD4 cell count in our study was 229 cells/mm^3. Pereira et al reported 22 cases of leprosy with HIV infection with mean CD4 cell count of 181.4 cells/mm^3 which is compatible with our findings.[15] 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 reported increased frequency of relapse of leprosy in HIV patients as observed in one of our patients.[16] In the present study, four cases of cutaneous tuberculosis were seen. Similarly, Spira et al reported prevalence of 3.83%. One patient had scrofuloderma secondry to tuberculosis inguinal lymphadenopathy with CD4 cell count of 101 cells/mm^3.[14] Two patients presented with lupus vulgaris and one patient had tuberculous verrucosa cutis with CD4 cell count of 216 cells/mm^3. The mean CD4 cell count in our study was 182 cells/mm^3 which is comparable with the finding of Kumarswamy et al having mean CD4 cell count of 178.41 cells/mm^3.[5] However, Raju et at and Spira et al reported higher mean CD4 cell counts of 496.14 cells/mm^3 and 316 cells/mm^3 respectively.[8,14] Thus, extensive and widerspread involvement of dermatophyte infection is more common in HIV infection, although severity did not correlate with degree of immunosusppression in our patient. Cutaneous drug reactions were encountered as the third most common disorder in our study. They 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). Mitsuyasu et al reported prevalence of cutaneous drug reactions (69%) associated with sulfamethoxazole-trimethoprim combination.[17] Mean CD4 cell count in our study was 111.6 cells/mm^3 (35-411). This finding was lower as compared to mean CD4 cell count of 203 cells/mm^3 as reported by Spira et al.[14] However, Spira et al did not mention severity of drug reaction so, probably most of their patients were presenting with milder type of drug rash with higher CD4 cell count.[14]

CONCLUSION

We conclude that cutaneous manifestation of HIV infection can be considered as good clinical indicators for the prediction of underlying immune status. The dermatological manifestations have high prevalence among HIV positive subjects. Pruritic popular eruption, severe cutaneous drug reactions like SJS and TEN, extensive and giant mollusci, eosinophilic folliculitis were seen with advanced stage and could be considered as clinical markers of advanced immunosuppression. The frequency and severity of episodes of skin disorders such as herpes zoster, seborrheic dermatitis increased as CD4 cell count decreased <200 cells/mm^3.

Thus, the presence of these conditions in HIV seropositive patients makes CD4 count testing mandatory and initiation of antiretroviral therapy, if necessary. This assumes great significance in resource poor settings where laboratory markers of immune suppression like CD4 count are not easily accessible due to cost and infrastructural factors, at a time when efforts are ongoing to provide large access to antiretroviral therapy.

A patient with unknown serostatus presenting with conditions like pruritic popular eruption, molluscum contagiosum etc can be considered for HIV pre test counseling 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.

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