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Research Article

CORRELATION OF MUCOCUTANEOUS MANIFESTATIONS WITH CD4 COUNT IN HIV INFECTED PATIENTS IN TERTIARY CARE HOSPITAL

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ABSTRACT

While there are other parameters for prediction of progression of HIV, mucocutaneous manifestations of HIV are considered among key clinical indicators for prediction of underlying degree of immunosuppression. 175 HIV infected patients were included in this study. Demographic parameters such as age, gender, occupation, educational status, family history were recorded. Laboratory parameter (CD4 counts) and treatment regimen were noted. Patients were examined for mucocutaneous manifestations by a dermatologist. Data was analyzed using chi-square test for categorical variables. Mean CD4 cell count of asymptomatic HIV patients was 499.85 cells/mm³, compared to 480.62 cells/mm³ in symptomatic HIV patients. This was correlated using student t-test and was statistically significant (P=3.88). Maximum number of cases were observed in CD4 count range of (200-500) cells/mm³. CD4 count was significantly less in Symptomatic cases than in asymptomatic cases. Thus mucocutaneous manifestations can give clue to suspect the diagnosis of HIV infection in an otherwise healthy patient.

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INTRODUCTION

HIV infection constitutes a major health problem worldwide¹⁻³. Mucocutaneous lesions are usually the first manifestations of HIV which help in early diagnosis and prompt treatment.⁴ More than 90% of patients develop skin lesions and 30%–80% of patients develop oral manifestations during the course of disease. Mucocutaneous lesions in HIV patients have been correlated with CD4 counts in many studies. The dermatological manifestations increase both in frequency and severity with the progression of HIV and decline in CD4+ cell counts and can serve as important markers of disease progression especially in countries with poor resources.⁵ This study is an attempt to correlate mucocutaneous manifestations of HIV infection with CD4 cell counts.

MATERIAL AND METHODS

Total of 175 HIV positive patients attending ART centre of a tertiary care hospital were included in our study. All patients were undergoing antiretroviral therapy (ART). Informed consent was taken from the patients. Demographic details like age, gender, educational status, occupation, family history were recorded on a structured proforma. A thorough clinical examination of the skin, oral cavity, nails, genitalia was done. Diagnosis was mainly based on clinical examination. Duration

of mucocutaneous manifestations and duration of ART were noted. The most recent CD4 counts (cells/mm³) of the patients were obtained from the medical records. ART regimens were noted for individual patients. Data was statistically analyzed using Chi-square test and student's t test.

RESULTS

Out of total 175 patients included in this study, 97 were females and 78 were males. Among 175, lowest age of patient was 1 year and highest was 69 years. Majority of the patients belonged to average socioeconomic strata. Majority that is 66 of 175 were illiterate and only 19 were educated above college level. The main risk factor for HIV transmission was heterosexual contact. Out of 175 HIV positive patients, 100 patients had mucocutaneous lesions while 75 patients were asymptomatic and had no mucocutaneous involvement. 20 of 175 patients had tuberculosis and were on anti Koch's treatment (AKT). 89 patients had family h/o of HIV. Duration of mucocutaneous lesions varied from lowest 1 day to highest 5 years. While duration of ART varied from lowest 3 days to highest 14 years. Maximum number of patients of 175 that is 110 were on tenofovir, lamivudine, efavirenz (TLE) regimen, while few were on zidovudine, nevirapine, lamivudine (ZLN). The major mucocutaneous findings reported by HIV positive patients attending the ART centre were, xerosis, fungal

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infections, cutaneous pigmentation, bacterial infections, viral infections, drug rash, parasitic infestations while Other conditions such as nail changes, pruritic popular eruptions (PPEs),ichthyosis, hair loss, stomatitis, angular cheilitis, oral white lesion were also occasionally present. Various mucocutaneous manifestations in correlation with CD4 counts are summarized in Table no.1.

Table no 1 Distribution of cases according to Diagnosis of skin disorder and CD4 count

Diagnosis of skin disorder	No. of cases	CD4 count			
		<200	200-500	500-1000	≥1000
Angular cheilitis	1	0	0	1	0
Bacterial infection	11	0	9	1	1
Cutaneous pigmentation	12	0	3	7	2
Cutaneous pigmentation and fungal infection	1	0	0	1	0
Drug rash	6	1	4	1	0
Fungal infection	13	2	5	5	1
Fungal infection and parasitic infestation	1	0	1	0	0
Hair loss	1	0	1	0	0
Ichthyosis	1	0	1	0	0
Nail changes	3	0	3	0	0
Nail changes and cutaneous pigmentation	1	0	0	0	1
Nail changes and drug rash	1	0	1	0	0
Oral pigmentation	1	0	0	1	0
Oral white lesion	1	0	0	0	1
Others	11	1	5	4	1
Parasitic infestation	6	1	1	4	0
Pruritic papular eruptions	2	1	1	0	0
Pruritic papular eruptions and bacterial infection	1	0	1	0	0
Stomatitis and cutaneous pigmentation	1	0	1	0	0
Viral infection	9	2	4	3	0
Xerosis	16	4	10	2	0
Total	100	12	51	30	7

Table no 2 Distribution of patients according to CD4 count

CD4 count	No. of cases	Percentage
<200	12	12%
200-500	51	51%
500-1000	30	30%
≥ 1000	07	07%
Total	100	100

According to table no. 2, maximum mucocutaneous lesions were seen in CD4 count range of 200-500 cells/mm³.

Table no 3 Correlation of mucocutaneous manifestations with mean CD4 cells and standard deviation

Diagnosis of skin disorder	No. of cases	Mean	SD
Angular cheilitis	1	645.00	0.00
Bacterial infection	11	427.64	243.73
Cutaneous pigmentation	12	666.42	258.46
Cutaneous pigmentation and fungal infection	1	903.00	0.00
Drug rash	6	353.33	266.93
Fungal infection	13	510.46	300.61
Fungal infection and parasitic infestation	1	456.00	0.00
Hair loss	1	340.00	0.00
Ichthyosis	1	244.00	0.00
Nail changes	3	441.33	75.74
Nail changes and cutaneous pigmentation	1	1165.00	0.00
Nail changes and drug rash	1	307.00	0.00
Oral pigmentation	1	722.00	0.00
Oral white lesion	1	1020.00	0.00

Others	11	593.36	429.09
Parasitic infestation	6	562.83	353.96
Pruritic papular eruptions	2	282.00	237.59
Pruritic papular eruptions and bacterial infection	1	207.00	0.00
Stomatitis and cutaneous pigmentation	1	473.00	0.00
Viral infection	9	331.22	215.23
Xerosis	16	334.38	221.95
Total	100		

Mean CD4 Count of asymptomatic and symptomatic HIV patients in various groups was computed and Chi-square test was applied. It was statistically highly significant. Mean CD4 count and SD values of asymptomatic and symptomatic HIV patients were computed and Student’s t-test was applied as shown in Table no.4.

Table no 4 Comparison of CD4 count in asymptomatic and symptomatic patients

CD4 count	Asymptomatic	Symptomatic
Average	499.85	480.62
SD	267.89	301.17
Test statistic	t = 3.88 ,P<0.01	

Statistically CD4 count in Symptomatic patients is significantly less than in Asymptomatic cases (P<0.01).

DISCUSSION

HIV targets a subset of T cells that is, CD4 T cells. A progressive reduction in number and function of CD4 T cells is one of the most consistent and important feature of HIV related disorders.⁶The CD4 count progressively decreases as HIV disease advances.⁷ The incidence and severity of skin disorders increase as immune function deteriorates.⁸ In our study out of 175,100 patients had mucocutaneous manifestations and their CD4 count was less compared to those not having mucocutaneous manifestations. Similar findings were found in study done by Lahoti *et al*, where 169 of 200 patients had mucocutaneous manifestations.⁹

Cutaneous lesions can be grouped as: infectious, autoimmune, drug induced, HIV related, and cutaneous malignancies. Often these lesions present atypically, in more severe form and need prolonged treatment in HIV infected individuals as compared to general population.¹⁰ Various cutaneous manifestations can be classified as, 1.Infections- fungal, bacterial, viral, parasitic. 2. Autoimmune- pemphigus, bullous pemphigoid, cutaneous lupus erythematosus. 3.Drug induced- lesions secondary to ART or other drugs. 4. HIV related- eosinophilic folliculitis, pruritic papular eruptions. 5. Cutaneous malignancies- kaposi’s sarcoma.

Table no 5 Categories of infectious lesions

Category	Infectious lesion	No. of cases %
Bacterial	Leprosy	3
	Tuberculosis	1
Fungal	others	8
	Dermatophytosis	14
Viral	Oral candidiasis	1
	Herpes zoster	8
parasitic	HPV	1
	Scabies	7
Total		43

In our study we encountered patients with all types of infections, 15 with fungal, 12 with bacterial, 9 with viral and 7

with parasitic. Maximum number being affected with cutaneous fungal infections. Thus 43% patients had infectious lesions. In study done by Chawhan *et al*, 57 out of 110 (52%) patients had infectious lesions¹¹. Patients with CD4 count less than 200 had severe and multiple lesions. Patients with viral infections had lowest mean CD4 count that is 331.22, and most common viral infection encountered was herpes zoster. Muñoz-Pérez (1998) stated that various dermatoses such as genital herpes, tinea, Kaposi's sarcoma, xerosis, HSV, drug eruptions, candidial folliculitis, *M. contagiosum*, psoriasis, abscess, verruca vulgaris, PPE, oral hairy leukoplakia and seborrheic dermatitis could be used as clinical markers of disease progression due to their strong association with CD4 counts.¹²

In our study, amongst non-infectious lesions, xerosis (16%) followed by cutaneous pigmentation (14%) were the most common. While Chawhan *et al* reported PPE as most common non-infectious skin manifestation.¹¹ The most common noninfectious skin manifestation found in study done by Lahoti *et al* was nail changes.⁹ Xerosis is usually associated with a late stage disease. Nutritional factors may lead to xerosis because these patients suffer considerable weight loss and cachexia.¹² 16 cases showed xerosis with a mean of CD4 cell count of 334.38. Cutaneous pigmentation was mostly seen on face, followed by neck and hands. There were total of 14 cases of cutaneous pigmentation with mean CD4 count as 666.42.



Lupus vulgaris



Erythema nodosum



Melanonychia with cutaneous pigmentation



Oral candidiasis



Onychomycosis with Drug rash



Herpes zoster

Figure no. 1 Photographs of HIV patients

Drug induced cutaneous eruption was next common finding in study. Among 6 cases of drug rash, in 3 cases culprit drug was efavirenz, in 2 cases was cotrimoxazole and one due to anti-tubercular drug. Morphologically rash was erythema multiforme type in 2 cases and maculopapular in 4 cases. Drug rash was seen with interval of 1 to maximum 10 days. Anti-TB drug induced acneiform eruption was seen after 5 months of starting treatment. Out of 6, 4 patients had CD4 count between 200-500, with mean CD4 count of 353.33.

PPE is a dermatosis associated with advanced HIV infection, characterized by sterile papules, nodules, or pustules with a hyperpigmented, urticarial appearance, and pruritus. When patients present with intractable, unexplained itching, one must consider a diagnosis of PPE and investigate for HIV infection.¹⁰ Our study showed total 3 cases with mean CD4 count of 207.

All 20 nails were examined and we found 5 patients with nail changes. Nail changes were, melanonychia, onychomycosis, onychodystrophy. Lahoti *et al* found maximum number of patients with nail changes with longitudinal melanonychia.⁹ In our study both patients with melanonychia were on Zidovudine. Melanonychia is attributed to use of zidovudine.⁹ According to Cribier B *et al* melanonychia can be due to increased levels of α melanocyte-stimulating hormone.¹³

Other cutaneous manifestations found in study were eczema, vitiligo, lichen planus, urticaria, angioedema, post herpetic neuralgia. Oral pigmentation was found in only one patient with CD4 count of 722. Patchy brown to brownish black asymmetrical lesion of > 1cm was found on dorsal aspect of tongue.

We did not find any case of neoplastic lesion, i.e., Kaposi's sarcoma, lymphoma, or any other cutaneous malignancies. Chawhan *et al*,¹¹ Wiwanitkit,¹⁴ Lanjewar¹⁵ also found striking low prevalence of cutaneous malignancies in their studies.

CONCLUSION

There is a strong negative association between CD counts and the prevalence and severity of mucocutaneous lesions in HIV/AIDS patients. HIV infection should be suspected when a cutaneous lesion tends to be chronic, severe and involves more than one dermatome. This small cross sectional study emphasizes variety of mucocutaneous manifestations in HIV/AIDS with low CD4 counts. Still fluctuations in CD4 counts need to be studied in detail. Studies with larger sample size will help to interpret results in better manner and provide guidelines.

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