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Original Research Article

A Retrospective Comparative Assessment of the Changing Profile of Cutaneous Manifestations of HIV after the Advent of Antiretroviral Therapy

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Abstract

Aim: The primary objective of this study is to evaluate cutaneous manifestations of HIV in patients on antiretroviral therapy, as compared to patients who are not on antiretroviral therapy.

Methods: This was a retrospective study conducted in the department of Skin and VD, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India.100 records were included in the analysis. These were classified as antiretroviral naïve (50 medical records) and antiretroviral experienced (50 medical records).

Results: Of the 100 patients included in the analysis, 40 (40%) were on antiretroviral therapy while 60 (60%) were antiretroviral naive. 48 patients (48%) were male while 52 (52%) were female. For patients on antiretroviral therapy, the majority (45%) were in the age group 36 to 45 years. The majority of antiretroviral naive patients (36.67%) were in the age group 36 to 45 years.

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

Keywords: Antiretroviral therapy, Mucocutaneous conditions, Antiretroviral naïve, Clinical stage of HIV, Infectious dermatoses

Introduction

Human immunodeficiency virus (HIV) infection is an acquired condition that represents a secondary immunodeficiency disorder. Cutaneous manifestations can often herald findings of immunodeficiency disorders, and various dermatoses are associated with HIV infection. Skin disease can be uniquely associated with HIV infection or acquired immunodeficiency syndrome (AIDS) but is more often due to common disorders that are more severe in HIV patients.

The burden of skin disease in developing countries has a serious impact on the quality of life resulting in loss of productivity at work and school and disfigurement. [1,2] Infectious dermatoses, particularly superficial fungal infections, scabies, and impetigo, are the most common skin problems due to overcrowding with a hot and humid

environment, poor sanitary conditions, sharing of personal effects or fomites, and poor access to medical supplies and treatment. [3]

The skin problems here are further compounded by the high prevalence of human immunodeficiency virus (HIV) which commonly causes skin lesions. [4] It was reported that approximately 90% of people living with HIV have skin changes and symptoms during the course of their disease. [5] Skin diseases are significantly higher among HIV-positive than HIV-negative individuals. [6]

Differences in skin pigmentation, climate, hygiene, and genetic, environmental, demographic, and behavioral factors cause different clinical presentations and epidemiologic patterns of HIV-associated skin disease in different countries. [7] Skin findings are regarded by the WHO as useful in assessing severity of HIV infection in patients in resource-limited environment. [8]

Skin disease can be uniquely associated with HIV disease, but more often represents common disorders, which may be more severe and recalcitrant to treatment. The spectrum of skin conditions includes skin findings associated with primary HIV infection and a broad range of skin problems related to the immune deficiency of advanced AIDS. [9] Knowledge of the skin and mucosal signs of HIV/AIDS is important, as mucocutaneous lesions are usually the first manifestation of HIV, ensures early diagnosis and prompt treatment, and reveals complications as HIV causes atypical and severe presentations of these conditions. [10]

A phenomenon that is increasingly seen in patients on antiretroviral therapy is immune reconstitution inflammatory syndrome (IRIS). IRIS may present with new cutaneous manifestations, or worsening of pre-existing skin disease. [11] In addition, trichodysplasiaspinulosa (TS); a rare disease of immunosuppressed patients caused by trichodysplasia-associated polyomavirus (TSPyV) where dermatological features are of folliculocentric papules and keratin spicules; may get unmasked after antiretroviral therapy. [12,13] HIV-pruritus may increase due to drug reactions because of ART. [14]

The primary objective of this study is to evaluate cutaneous manifestations of HIV in patients on antiretroviral therapy, as compared to patients who are not on antiretroviral therapy.

Methods

This was a retrospective study conducted in the department of Skin and VD, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India. At enrolment, each patient was given a unique patient identifying number.

Inclusion criteria

Only medical records belonging to patients aged 18 and above, who had a dermatological diagnosis, were considered for inclusion in the analysis. All medical records were required to have results of CD 4 count at baseline, and at the time of dermatological diagnosis, in order to be included.

Exclusion criteria

Medical records of patients who had dermatological disorder prior to the diagnosis of HIV and/or had undergone dermatological treatments in the 6-12 weeks prior to commencement of antiretroviral therapy were excluded. Patients with co-existent diabetes or kidney disease were not included in the study. Patients having co-existent peripheral vascular disease, connective tissue disease or internal malignancy were excluded.

Methodology

HIV testing was done by using Determine Rapid HIV test kits, followed by

confirmation with Standard Diagnostics (SD) Bioline HIV 1/2 test kit. CD-4 count was measured by flow-cytometry using the PD-FACS count machine. Testing for syphilis was done using Bioline 3.0 syphilis Rapid test. We tested for the Hepatitis B surface antigen (HBsAg) using Standard Diagnostics Bioline HBsAg 3.0 Elisa test kits. Biochemistry tests were done using the Pentra 2000 machine. Hematological tests were done using Sysmex-XT-1800i machine. Data was collected during the period for 2 years.

Sample size and data extraction

100 records were included in the analysis. These were classified as antiretroviral naïve (50 medical records) and antiretroviral experienced (50 medical records). Data was extracted from the medical records using a structured data collection tool.

Statistical analysis

Data was analyzed using SPSS version 23. The primary outcome variable was the difference in the frequency and type of cutaneous diseases between patients on antiretroviral therapy, and patients not on antiretroviral therapy. The secondary outcome variable was the relationship between dermatological conditions and the CD4 cell count, and the relationship between dermatological conditions and the clinical stage of the disease. Descriptive statistics were use to describe the demographic and baseline laboratory parameters of the study population. Chi-square test was used to determine association between categorical variables. A P-value less than 0.05 were considered as statistically significant. Fischer's exact p value was used where at least one of the cells had expected frequencies less than 5. For bivariate analysis, cutaneous lesions were classified as either infectious or non-infectious. Eosinophillic folliculitis, popular pruritic eruption, allergic dermatitis, alopecia and hyper pigmentation were classified as noninfectious. The rest of the cutaneous conditions were classified as infectious.

Results

Table 1: Demographic characteristics of study participants

Parameters		Not on ART		On ART		Total
		N	%	N	%	
Age groups	15-25	3	5	2	5	5
	26-35	20	33.33	10	25	30
	36-45	22	36.67	18	45	40
	46-55	9	15	6	15	15
	>55	6	10	4	10	10
Sex	Male	28	46.66	20	50	48
	Female	32	53.34	20	50	52
Marital Status	Single	16	26.66	14	35	30
	Married	30	50	20	50	50
	Divorced	6	10	4	10	10
	Widowed	8	13.14	2	5	10
Education level	College/University	30	50	20	50	50
	Never been to the school	3	5	2	5	5
	Primary	12	20	18	45	20
	Secondary	15	25	10	25	25

Of the 100 patients included in the analysis, 40 (40%) were on antiretroviral therapy while 60 (60%) were antiretroviral naive. 48 patients (48%) were male while 52 (52%) were female. For patients on antiretroviral therapy, the majority (45%)

were in the age group 36 to 45 years. The majority of antiretroviral naive patients (36.67%) were in the age group 36 to 45 years. Demographic characteristics of the study population likemarital status, occupation, income, education level are described in (Table 1).

Table 2: Baseline parameters of study participants

Parameters		Not on ART		On ART		Total
		N	%	N	%	
Baseline RPR	Negative	32	58.34	10	25	42
	Not tested	18	30	20	50	48
	Positive	10	16.66	10	25	35
	Total	60		40		100
Baseline HBSAg	Negative	25	41.67	8	20	33
	Not tested	30	50	22	55	52
	Positive	5	8.33	10	25	15
	Total	60		40		100

35% of the study population tested positive for Syphilis. 15 % had positive HbsAg tests, as shown in (Table 2).

Table 3: CD4 count of study population having dermatological conditions in both groups

CD4 cell count	Not on ART N (%)	On ART N (%)	P value
<200	32 (53.33)	20 (50)	0.350
200-350	8 (13.34)	10 (25)	0.220
>350	20(33.33)	10 (25)	0.920
Total	60	40	

There was no significant difference in the CD 4 categories between patients on antiretroviral therapy and antiretroviral naive patients. Among anti-retroviral naive patients 53.33% (32) had dermatological conditions at CD4 count below 200. 13.34% (8) of antiretroviral naïve patients had dermatological conditions at CD4 count between 200 and 350; while 33.33% (20) had dermatological conditions at CD4 count above 350. Among patients on antiretroviral therapy, 50% (20) had CD4 count below 200, 25% (10) had CD4 count between 200 and 350, while 25% (10) had CD4 count above 350. The association between CD4 count and antiretroviral status is shown in (Table 3).

Table 4: Type of cutaneous manifestation

Type of cutaneous lesions	n (%)	95% CI
Oral	55 (55)	48.50-60.25
Mucosal	60 (60)	55.40-65.70
Cutaneous	58 (58)	52.28-64.84
STI	25 (25)	21.98-31.41
Immunologic	30 (30)	22.8-32.10
Tumoral	8 (8)	5.35-12.22
Reaction	1 (1)	0.08-2.07
Viral	40 (40)	32.44-42.76
Bacterial	15 (15)	13.15-21.21
Mucotic/parasitic	60 (60)	50.40-62.89

Table 4 shows the type of dermatologic manifestations. Our findings were classified into infectious and noninfectiouscauses based on their etiologies. Viral infections were observed in 40% of cases and bacterial infections in 15% of cases.

Most frequent infections were oropharyngeal candidosis (52%), herpes zoster (17%), seborrheic dermatitis (16%), syphilis (14%), anal condyloma (5%) and leukoplakia (4%). Coinfection with hepatitis B virus was observed in 15% of patients, with hepatitis C virus in 2%, with syphilis in 20%, and with tuberculosis in 6% of patients.

Discussion

As this long period had witnessed changes in ART guidelines, new recommendations for HIV related diagnosis and practices, as well as in epidemiology of HIV/AIDS related/unrelated dermatological conditions, findings of this study may give better insights for future dermatology practice. [15-17] Turning point of HIV pandemic was highly active antiretroviral therapy (HAART), which not only changed the mortality statistics but also the profile of the disease. [18] In olden times, in pre-ART era, skin manifestations were considered to be important “tell-tale” signs, to suspect HIV infection and more than 90% would present with skin manifestations. [19] These manifestations were present as presenting feature and could forecast the immune status of a patient.23 Since the advent of antiretroviral therapy, these classic skin manifestations, severity and incidence of such manifestations have decreased. [20]

Various other parameters like demographic profile, stages of illness and CD4 count of patients were analyzed in lieu of dermatological features in both groups. HIV infection typically affects young and middle age men and women in the reproductive age group was also finding of this study like other studies. [21,22] More than 50% of the study population can be classified as having AIDS, as they had a CD4 count less than 200. The study showed that patients on antiretroviral therapy had lower baseline median CD4 count as compared to those on antiretroviral therapy. This may have been due to previous guidelines which recommended antiretroviral therapy only for patients with CD4 count below 200. [23]

Dermatologic manifestations can be considered as good clinical indices to predict the status of immunity in HIV-positive patients in less developed countries. [24] At present, there are ample amount of evidence about the relationship between dermatologic manifestations and weakened immune system in adults and children. CD4 cell count is a proper criterion for the diagnosis of a weakened immune system or disease progression. KS can be transmitted through sexual contact which is more common in homosexuals than heterosexuals. Anal sex is a major risk factor. The skin infections in people with HIV/AIDS which exacerbate and become resistant to treatment could be a sign of disease progression. [25] Those involved in health care of HIV patients must therefore know the type, pattern, and prevalence of skin diseases in their locality.

Mucocutaneous diseases have been correlated with CD4 counts in many studies, while few studies documented the clinical correlation of these diseases to the WHO clinical stages. Cutaneous manifestations of HIV disease may result from HIV infection itself or from opportunistic disorders secondary to the decline in immunocompetence from the disease. [26,27]

Cutaneous disorders may be the initial signs of HIV-related immunosuppression. Recognizing HIV-related skin changes may lead to the diagnosis of HIV infection in the early stages, allowing initiation of appropriate antiretroviral therapy. Many

associated skin diseases are more severe in this group. HIV-associated dermatoses are very common. Recognition of characteristic eruptions can facilitate early diagnosis of HIV. A broad variety of neoplastic, infectious, and noninfectious diseases can manifest in the skin and may alert the clinician to decline of the immune system. [28,29] Diagnosis of cutaneous disease can be challenging. While some conditions reliably present with stereotyped lesions, other diseases may have highly variable manifestations, leading to diagnostic uncertainty that may necessitate specialist consultation and skin biopsy. [30,31]

Conclusion

Dermatological complications of HIV/AIDS arise from a variety of conditions with various etiologies. Therefore, careful considerations should be given to timely diagnosis and prompt treatment of dermatological complications among HIV patients. Besides the clinical difficulty in preventing and treating skin diseases, the skin also affects the patient's general appearance and their quality of life. The high prevalence of skin diseases, severity of complications, and overall influence on the patient's quality of life highlight the need for further investigation of therole of the immune system in dermatologic manifestations among HIV patients.

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