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Original Research Article

# A Retrospective Assessment of the Change in Profile of Cutaneous Manifestations of HIV after the Advent of Antiretroviral Therapy

**Rajeev Jain[1], Rudra Pratap Singh Kaurav[2], Rajesh Kumar[3]**

[1]Assistant Professor, Department of Skin and VD, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India

[2]Assistant Professor, Department of Skin and VD, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India

[3]Assistant Professor, Department of Skin and VD, Shree Narayan Medical Institute and Hospital, Saharsa, Bihar, India

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**Corresponding Author: Dr. Rudra Pratap Singh kaurav**
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**Abstract**

**Aim:** The aim of the present study was to determine the prevalence of mucocutaneous conditions among HIV positive patients on antiretroviral therapy.

**Material & Methods:** A retrospective medical record review of patients attending an out-patient antiretroviral clinic at department of skin and VD were reviewed. 150 records were included in the analysis. These were classified as antiretroviral naïve (100 medical records) and antiretroviral experienced (50 medical records).

**Results:** Of the 150 patients included in the analysis, 50 (33.34%) were on antiretroviral therapy while 100 (66.66%) were antiretroviral naive. 74 patients were male while 76 were female. For patients on antiretroviral therapy, the majority were in the age group 45 to 55 years. The majority of antiretroviral naive patients were in the age group 35 to 44 years. The mean duration on ART was 66.94 weeks (95% CI 42.86 to 95.85; standard deviation 102.18) for patients on antiretroviral therapy. The median baseline CD4 count was 154 for antiretroviral naive patients and 122 for patients on antiretroviral therapy. 15 patients tested positive for Syphilis and 5 had positive HbsAg tests. There was no significant difference in the CD 4 categories between patients on antiretroviral therapy and antiretroviral naive patients. Our findings were classified into infectious and non-infectious causes based on their etiologies. Viral infections were observed in 60 cases and bacterial infections in 20 cases.

**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.

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



## Introduction

Human immunodeficiency virus (HIV) infection is an acquired condition that represents a secondary immunodeficiency disorder. With development of antiretroviral drugs, human immunodeficiency virus (HIV) infected individuals live longer and better, both in developed and developing countries. [1] In 2010, 7.7 million HIV-infected population of the world were on antiretroviral therapy which rose to 24.5 million at the end of June, 2019. 62% of HIV infected adult population accessed antiretroviral therapy. [2]

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. [3,4] 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.

[5] Antiretroviral therapy has changed the profile of mucocutaneous manifestations of HIV. Incidence, prevalence and severity of some of the dermatological conditions have changed. [6]

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 preexisting skin disease. [7] IRIS represents a paradoxical worsening of patients' clinical condition weeks to months after commencing antiretroviral therapy. IRIS is most frequently seen in HIV patients who are co-infected with Mycobacterium tuberculosis (TB), Mycobacterium avium complex (MAC), Cryptococcus neoformans and Cytomegalovirus infection (CMV). [8] About 52-78% of the cases of IRIS involve the skin. [8]

In addition, trichodysplasiaspinulosa (TS); a rare disease of immunosuppressed patients caused by trichodysplasia associated polyomavirus (TSPyV) where dermatological features are of folliculo-centric papules and keratin spicules; may get unmasked after antiretroviral therapy. [9,10] HIV pruritus may increase due to drug reactions because of ART. [11]

Hence the objective of this study was to determine the prevalence of mucocutaneous conditions among HIV positive patients on antiretroviral therapy.

## Material & Methods

A retrospective medical record review of patients attending an out-patient antiretroviral clinic at Department of Skin and VD, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India were reviewed. At enrolment, each patient was given a unique patient identifying number. 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 within the duration of 6 months.

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.

### Sample Size and Data Extraction

150 records were included in the analysis. These were classified as antiretroviral naïve (100 medical records) and antiretroviral experienced (50 medical records). Data was extracted from the medical records using a structured data collection tool. A copy of this is included in the appendix. Data was collected within the duration of 6 months.

### 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 non-infectious. 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 | % | |
| | 15-24 | 6 | 6 | 4 | 2 | 10 |
| | 25-34 | 24 | 24 | 8 | 16 | 32 |
| **Age groups (years)** | 35-44 | 40 | 40 | 15 | 30 | 55 |
| | 45-55 | 22 | 22 | 16 | 32 | 38 |
| | 56+ | 8 | 8 | 7 | 14 | 15 |
| **Sex** | Female | 48 | 48 | 28 | 56 | 76 |
| | Male | 52 | 52 | 22 | 44 | 74 |
| | Divorced | 18 | 18 | 4 | 8 | 22 |
| | Married | 40 | 40 | 24 | 48 | 64 |
| **Marital status** | Single | 26 | 26 | 10 | 20 | 36 |
| | Widowed | 9 | 9 | 4 | 8 | 13 |
| | Unknown | 7 | 7 | 8 | 16 | 15 |
| | Formal Govt | 14 | 14 | 7 | 14 | 21 |
| | Formal Private Sector | 15 | 15 | 8 | 16 | 23 |
| **Occupation** | Self Employed | 42 | 42 | 19 | 38 | 61 |
| | Student | 6 | 6 | 10 | 5 | 16 |
| | Unemployed | 11 | 11 | 4 | 8 | 15 |
| | Unknown | 12 | 12 | 2 | 4 | 14 |
| | College/University | 38 | 38 | 19 | 38 | 57 |
| | Never been to school | 3 | 3 | 2 | 2 | 5 |
| **Education Level** | Primary | 10 | 10 | 4 | 8 | 14 |
| | Secondary | 39 | 39 | 14 | 28 | 53 |
| | Unknown | 10 | 10 | 11 | 22 | 21 |

Of the 150 patients included in the analysis, 50 (33.34%) were on antiretroviral therapy while 100 (66.66%) were antiretroviral naive. 74 patients were male while 76 were female. For patients on antiretroviral therapy, the majority were in the age group 45 to 55 years. The majority of antiretroviral naive patients were in the age group 35 to 44 years.

**Table 2: Baseline parameters of study participants**

| Parameter | On ART | Mean | SE | 95 % CI for mean | | Me-dian | SD | Skewness | Kurtosis |
|---|---|---|---|---|---|---|---|---|---|
| **Weeks on ART** | Yes | 66.94 | 12.48 | 42.86 | 95.85 | 34 | 102.18 | 1.901 | 4.936 |
| **Baseline** | No | 12.38 | 0.266 | 11.82 | 12.88 | 12.5 | 2.48 | -0.154 | 0.644 |
| **Hb** | Yes | 12.38 | 0.286 | 10.72 | 12.96 | 10.5 | 2.22 | -0.922 | 2.708 |
| **Baseline** | No | 33.04 | 3.27 | 24.56 | 36.44 | 25.5 | 28.32 | 3.716 | 18.2 |
| **ALT** | Yes | 27.43 | 1.88 | 23.67 | 31.25 | 22.2 | 14.02 | 1.324 | 1.402 |
| | No | 96.74 | 8.52 | 83.7 | 114.76 | 88.62 | 62.64 | 6.694 | 51.155 |
| **Creatinine** | Yes | 86.54 | 4.976 | 76.54 | 96.44 | 82.28 | 36.44 | 3.397 | 16.504 |
| **Baseline** | No | 43.72 | 3.603 | 36.54 | 50.90 | 33.70 | 31.21 | 2.452 | 6.982 |
| **AST** | Yes | 42.79 | 4.051 | 34.62 | 50.96 | 34.75 | 26.87 | 1.697 | 2.857 |
| **Baseline** | No | 216.44 | 22.598 | 172.48 | 258.32 | 154 | 198.2 | 1.194 | 1.806 |
| **CD4 count** | Yes | 165.3 | 20.393 | 124.44 | 206.11 | 122 | 155.31 | 1.430 | 1.782 |

The mean duration on ART was 66.94 weeks (95% CI 42.86 to 95.85; standard deviation 102.18) for patients on antiretroviral therapy. The median baseline CD4 count was 154 for antiretroviral naive patients and 122 for patients on antiretroviral therapy.

**Table 3: Baseline parameters of study participants**

| Parameters | | Not on ART N (%) | On ART N (%) | Total |
|---|---|---|---|---|
| | Negative | 48 (48) | 19 (38) | 67 |
| | Not tested | 40 (40) | 28 (56) | 68 |
| **Baseline RPR** | Positive | 12 (12) | 3 (6) | 15 |
| | Total | 100 (100) | 50 (100) | 143 (100) |
| | Negative | 45 (45) | 16 (32) | 61 |
| | Not tested | 52 (52) | 32 (64) | 84 |
| **Baseline HBsAg** | Positive | 3 (3) | 2 (4) | 5 |
| | Total | 100 (100) | 50 (100) | 143 (100) |

15 patients tested positive for Syphilis and 5 had positive HbsAg tests.

**Table 4: CD4 count of study population having dermatological conditions in both groups**

| CD4 cell count | Not on ART N (%) | On ART N (%) | P value |
|---|---|---|---|
| <200 | 52 (52) | 25 (50) | 0.375 |
| 200-350 | 12 (12) | 13 (26) | 0.232 |
| >350 | 36 (36) | 12 (24) | 0.912 |
| Total | 100 | 50 | |

There was no significant difference in the CD 4 categories between patients on antiretroviral therapy and antiretroviral naive patients. Among anti-retroviral naive patients 52% had dermatological conditions at CD4 count below 200. 12% of antiretroviral naïve patients had dermatological conditions at CD4 count between 200 and 350; while 36% had dermatological conditions at CD4 count above 350. Among patients on antiretroviral therapy, 50% had CD4 count below 200, 26% had CD4 count between 200 and 350, while 24% had CD4 count above 350.

**Table 5: Type of cutaneous manifestation**

| Type of cutaneous lesions | n | 95% CI |
|---|---|---|
| Oral | 78 | 48.50-60.25 |
| Mucosal | 90 | 55.40-65.70 |
| Cutaneous | 85 | 52.28-64.84 |
| STI | 40 | 21.98-31.41 |
| Immunologic | 42 | 22.8-32.10 |
| Tumoral | 12 | 5.35-12.22 |
| Reaction | 1 | 0.08-2.07 |
| Viral | 60 | 32.44-42.76 |
| Bacterial | 20 | 13.15-21.21 |
| Mucotic/parasitic | 90 | 50.40-62.89 |

Our findings were classified into infectious and non-infectious causes based on their etiologies. Viral infections were observed in 60 cases and bacterial infections in 20 cases.

## Discussion

The skin problems here are further compounded by the high prevalence of human immunodeficiency virus (HIV) which commonly causes skin lesions. [12] It was reported that approximately 90% of people living with HIV have skin changes and symptoms during the course of their disease. [13] Skin diseases are significantly higher among HIV-positive than HIV-negative individuals. [14] 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. [15] Skin findings are regarded by the WHO as useful in assessing severity of HIV infection in patients in resource-limited environment. [16]

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. [17] 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. [18] Of the 150 patients included in the analysis, 50 (33.34%) were on antiretroviral therapy while 100 (66.66%) were antiretroviral naive. 74 patients were male while 76 were female. For patients on antiretroviral therapy, the majority were in the age group 45 to 55 years. The majority of antiretroviral naive patients were in the age group 35 to 44 years. The mean duration on ART was 66.94 weeks (95% CI 42.86 to 95.85; standard deviation 102.18) for patients on antiretroviral therapy. The median baseline CD4 count was 154 for antiretroviral naive patients and 122 for patients on antiretroviral therapy. 15 patients tested positive for Syphilis and 5 had positive HbsAg tests.

There was no significant difference in the CD 4 categories between patients on antiretroviral therapy and antiretroviral naive patients. Among anti-retroviral naive patients 52% had dermatological conditions at CD4 count below 200. 12% of antiretroviral naïve patients had dermatological conditions at CD4 count between 200 and 350; while 36% had dermatological conditions at CD4 count above 350. Among patients on antiretroviral therapy, 50% had CD4 count below 200, 26% had CD4 count between 200 and 350, while 24% had CD4 count above 350. 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. [19,20] 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. [21] Dermatologic manifestations can be considered as good clinical indices to predict the status of immunity in HIV‑positive patients in less developed countries. [22] 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. [23] Those involved in health care of HIV patients must therefore know the type, pattern, and prevalence of skin diseases in their locality.

Our findings were classified into infectious and non-infectious causes based on their etiologies. Viral infections were observed in 60 cases and bacterial infections in 20 cases. 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. [24,25]

## 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 the role of the immune system in dermatologic manifestations among HIV patients.

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