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# Histopathological Study of Dermatological Lesions in HIV Patients

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**Original Research Article**

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**Abstract:** HIV-related cutaneous manifestations are very common and can be easily detected. If studied systematically, they can serve as diagnostic and prognostic markers. It is aimed to study the skin biopsies of various dermatological manifestations that occur in HIV seropositive patients attended to a tertiary care centre. This is a prospective study of cases of 104 were studied histopathologically who were Seropositive for HIV. Majority are of 31- 40 years (32.69%), and closely followed by the age group 21-30 years (28.84 %). Patients of both sexes were affected with males females ratio of 1.19:1. The most common cutaneous manifestation observed was Papulosquamous lesions with 37.5% cases and in this 53.84% cases were pruritic papular urticaria. Infections observed were 25%, among which majority were of bacterial infections. Drug reactions were observed in 15.3% of cases and majority of patients presented with Stevens Johnson syndrome. Dermatitis was seen in 11.53% of patients and seborrheic dermatitis is the common non-infectious dermatosis. Other cutaneous manifestations like vascular involvement, neoplasms contributed minority of cases. Most of the patients presented with cutaneous manifestations having CD4 count in the range of 350-500. It was conclude that the dermatological lesions are extremely common and may present with early, severe, unusual and atypical manifestations in the course of HIV infection. Awareness of the varied pattern of these manifestations would help in the early diagnosis and management of HIV infection, which would in turn decrease the morbidity and improve the quality of life of HIV-infected patients.
**Keywords:** HIV infection, histopathological study, CD4 counts, neoplasms.

## INTRODUCTION

It is now 32 years since Acquired Immune Deficiency Syndrome (AIDS) was first recognized as a novel disease. Within 2 years of defining AIDS as a distinctive syndrome in 1981, the human immunodeficiency virus (HIV) was identified as the causative agent. HIV-1 infection now represents a global pandemic [1].

Globally, an estimated 35.3 (32.2–38.8) million people were living with HIV in 2012. There were 2.3 (1.9–2.7) million new HIV infections globally, and the estimated number of AIDS deaths were 1.6 (1.4–1.9) million in 2012[2].

The first case of AIDS in India was reported in May 1986 from Mumbai in Maharashtra, the source of which was traced to blood transfusion given in USA during coronary bypass surgery. There after increasing number of cases have been reported by many workers from different parts of the country. In India there is an estimated 2.5 million people infected with HIV. The most rapid and well-documented spread of infection has occurred in Mumbai and the State of Tamilnadu.

AIDS is the problem faced not only by the medical community, but has become a major social problem. The rapid emergence of disease has forced intensive debates regarding health care issues, sexual practices in the community, immigration policies and also as regards formation of new laws for the affected people[3].

It has become evident that the medical personnel will be required to face HIV positive patients and their problems in every day practice. Thus it has become necessary to be well acquainted with the pathophysiology and histopathology of various lesions seen in HIV seropositive patients.

Dermatological disorders are a frequent presenting feature of HIV infection and/or AIDS. More than 90% of HIV-infected patients will suffer from one or more skin diseases during the course of their illness. This trend is reflected in the increasing number of skin biopsies from HIV-positive patients in those parts of the world where HIV infection/AIDS is highly prevalent.

Histopathologists are therefore required to possess a working knowledge of the broad spectrum of cutaneous manifestations of HIV infection. These include the range of dermatoses that are specific to HIV infection, the more common dermatoses occurring with greater frequency (or modified by) HIV infection/AIDS, the spectrum of infectious diseases (often opportunistic) caused by viruses, bacteria, fungi, protozoa and even arthropods, and neoplastic conditions such as Kaposi sarcoma and B-cell non-Hodgkin lymphoma. The risk for adverse skin reactions to certain drugs is also greatly increased. Although the introduction of highly active antiretroviral therapy has resulted in a dramatic decrease in opportunistic infections, several of these drugs may result in adverse reactions in the skin.

Skin biopsies play a vital diagnostic role when different diseases present with clinically similar skin lesions31. Biopsy material should always be examined carefully to exclude dual pathology. The diagnosis may need to be confirmed with histochemical and immunohistochemically stains, and/or molecular studies. Where indicated, additional biopsies for microbiological culture should always be recommended. The examination of multiple serial sections often proves invaluable. A diagnostic approach is given based on the predominant histological reaction pattern, with an emphasis on clinic pathological correlation

## MATERIALS AND METHODS

It is a prospective study of cases attended to the Government General Hospital, Vijayawada who was seropositive for HIV. Skin biopsy was taken from the lesions and the biopsies were processed in the Department of Pathology to carry out histopathological examination and correlating the diagnosis with clinical history and clinical diagnosis. This study comprised of 104 cases that were received during the period of August 2011 to September 2013.

Inclusion criteria: HIV seropositive patients with cutaneous lesions attending the Department of Dermatology and ART center, Government General Hospital, Vijayawada.

Exclusion criteria: Non co-operative patients, Severe ill patients, Patient not counseled, and Patients with severe thrombocytopenia or other bleeding disorders.

## METHOD OF COLLECTION OF DATA

Pertinent clinical history like age, duration of the lesion, site of the lesion, significant family and personal history, history of associated diseases and any drug intake was taken and entered in the proforma. After detailed general and local examination, the site of the biopsy was selected. The selected patients consent was taken after explaining the details of the biopsy procedure. The biopsy is done on the lesion along with the surrounding area.

### Biopsy Techniques

Punch biopsy is the standard procedure for obtaining samples of skin biopsy. It is important to select a proper site for biopsy. Biopsy is taken from the active lesion. A specimen obtained with a 4mm biopsy punch is adequate for histological study. A 3 mm punch may be preferable for small lesions or biopsy from face for cosmetic reasons.

A representative area on the skin was chosen, cleaned with 70% alcohol. The area was anaesthetized by infiltrating 2% lignocaine deep into the skin and subcutaneous tissue. The punch was pushed into the skin with a downward twisting movement and then removed. The tissue specimen biopsy material was placed in a bottle containing 10% formalin and was lifted and separated from the underlying tissue and removed from the biopsy punch. The biopsy site was then dressed maintaining asepsis. The biopsy specimen taken was placed in a fixative (10% formalin) immediately after removal from the patient to prevent autolysis.

### Gross examination of the skin biopsy

The three dimensional size and shape of the skin biopsy was assessed including the circular or elliptical shape of the biopsy. The entire skin biopsy was submitted for routine processing and embedded in paraffin wax. From each block, ribbons containing 3 serial sections each 5 microns in thickness were taken. Sections of the skin biopsy were stained with haematoxylin and eosin routinely. The sections were examined under microscope. Pathological findings were noted at the level of epidermis, dermis and sub-cutis and were segregated into different histological patterns. Special stains are done wherever required.

Processing of tissue: After fixation in 10% formalin for 12-24 hours, the tissue was processed in graded alcohols and embedded in paraffin to make blocks. The biopsy was oriented such that the section obtained passed vertically through the skin. Sections of 3-5µ thickness were cut with rotary microtome and stained with haematoxylin and eosin. The special stains were used where ever necessary.

## HAEMATOXYLIN AND EOSIN STAIN

Paraffin sections were placed in Xylol for 2 minutes. Transferred to absolute alcohol for 1 minute. Section drained and placed in 90% alcohol for 1 minute. Section transferred to hematoxylin for 10-40 minutes. Slides are transferred to slide washing tray for bluing for 10 minutes. Section dipped in acid alcohol, agitated for few second for differentiation. Section transferred to slide washing tray for 3-4 min to differentiate eosin. After draining, section transferred to 90% alcohol agitated for 10-15 seconds. Slides

transferred to absolute alcohol agitated for 10-15 seconds. Slides transferred to absolute I and then to absolute II for 30 seconds. Sections transferred to Xylol I and Xylol II until completely cleared. Sections mounted with DPX.

**Special stains**

Periodic Acid Schiff's stain for fungi, Gomori's Methenamine Silver stain for fungi, Ziehl Neelsen stain for Acid fast bacilli and Grams stain for bacteria were analysed.

**RESULTS**

The present study is "Histopathological study of dermatological lesions in HIV patients" carried out from August 2011 to September 2013, included 104 skin biopsies from HIV seropositive patients attending the Dermatology OPD and ART centre of Government General Hospital, Vijayawada. In the present study, patients in the age group of 31 to 40 years were affected more with 34 cases ( 32.69%), followed by 21-30 years with 30 cases ( 28.84.4% ) , 41-50 years 27 ( 25.96% ), 10-20 years 09 (8.65%) and patients above 50 years of age 4 (3.84%). Males were most commonly affected with M: F ratio 1.19:1. Majority of the patients were males. Out of 104 cases 57 were males and 47 were females. The male to female ratio, M: F of 1.21:1 with slight male preponderance.

In case of males the peak incidence was noted in 31-40 years of age and in females the peak incidence was noted in 21-40 years of age group. Only few patients were in the age group of 10 – 20.

**Table-1: Histopathological diagnosis**

| Histopathological Diagnosis | n = 104 | Percentage |
|---|---|---|
| A. Dermatitis | 12 | 11.53% |
| B. Papular lesions | 39 | 37.5% |
| C. Viral lesions | 06 | 5.7% |
| D. Bacterial infections | 17 | 16.3% |
| E. Fungal infections | 03 | 2.8% |
| F. Drug Reaction | 16 | 15.3% |
| G. Vascular lesion | 02 | 1.9% |
| H. Malignant lesions | 03 | 2.8% |
| I. Vesiculobullous | 05 | 4.8% |
| J. Autoimmune lesions | 01 | 0.9% |
| Total | 104 | 100 |

In the present study the most common skin lesions found in HIV seropositive patients were papulosquamous lesions followed by bacterial infections, drug reactions and dermatitis.

**Table-2: Distribution of papulosquamous lesions**

| Disease | Number | Percentage |
|---|---|---|
| Papular urticaria | 21 | 53.8% |
| Eosinophilic folliculitis | 3 | 7.69% |
| Pytiriasis rubra pilaris | 2 | 5.12% |
| Lichen planus | 2 | 5.12% |
| Lichen simplex chronicus | 2 | 5.12% |
| Psoriasis | 5 | 12.8% |
| Para psoriasis | 2 | 5.12% |
| Prurigo nodularis | 1 | 2.56% |
| Nonspecific inflammation | 1 | 2.56% |
| Total | 39 | 100% |

In the present study papulosquamous lesions were the most common type with papular urticaria type being the most common and over all the cutaneous lesions constituting 20.19% and 53.84% in Papulosquamous lesions, followed by psoriasis with 12.82%.

Out of 12 cases of dermatitis, seborrheic dermatitis constituted the most common type in 5 cases.

**Drug reactions in hiv patients**

Adverse drug reactions were seen in 16 patients (15.3%). Stevens Johnson syndrome were seen in 6 patients (37.5%) & Toxic epidermal necrolysis seen in 5(18.75%) cases, Erythema multiforme in 3(18.75%) and fixeddrug eruption seen in 2 patient (12.5%). Most of the adverse effects were seen in patients using Nevirepine.

Out of five cases of vesiculobullous lesions 3 were pemphigus vulgaris and Pemphigus foliaceous and Bullous pemphigoid were one each.

In the present study viral lesions due to human papillomas virus constitute the major group with verruca vulgaris in 2 cases followed by molluscum contagiosum and herpes zoster of one each case.

**Table-3: Distribution of bacterial infections**

| Disease | Number | Percentage |
|---|---|---|
| Tuberculous verrucus cutis | 4 | 23.52% |
| Lupus vulgaris | 4 | 23.52% |
| Papulo necrotic TB | 1 | 5.88% |
| Secondary syphilis | 3 | 17.64% |
| Folliculitis | 2 | 11.76% |
| Furuncle | 1 | 5.88% |
| Erysipelas | 1 | 5.88% |
| Acute suppurative inflammation | 1 | 5.88% |
| Total | 17 | 100% |

Out of 17 cases of bacterial lesions, most of the lesions were due to tuberculous infection constituting about 9 cases with tuberculous verrucous cutis and lupus vulgaris each being 23.52%.

**Disease distribution of fungal infections**

Three cases of cutaneous fungal infections were come across, two cases of Chromoblastomycosis and a single case of Tinea was seen.

**MALIGNANT LESIONS**

Three cases of malignant lesions were observed out of which two cases were well differentiated squamous cell carcinoma. One case of cutaneous lymphoma was diagnosed.

**Disease distribution of vascular lesions**

Two cases of vascular lesions have been observed which comprised of Urticarial vasculitis and a single case of Nodular vasculitis

**Autoimmune diseases**

A single case of autoimmune disease of SLE in a 45 year old female has been identified and CD4 is more than 200. She presented with maculopapular rash over the extremities. Histopathology showed vacuolar degeneration of basal layer with dermal edema and perivascular inflammatory infiltrate and fibrinoid necrosis.

**CD4 COUNT**

In the present study skin lesions were seen most commonly in the patients having CD4 count in range of 350-500. More than 500 of CD4 count observed in 16 cases.

**Table-4: CD4 count in relation to lesions**

| Histopathological diagnosis | CD4 count <350 | CD4 count 350-500 | CD4 count >500 |
|---|---|---|---|
| Dermatitis | 0 | 9 | 3 |
| Papular lesion | 3 | 31 | 5 |
| Viral | 1 | 4 | 1 |
| Bacterial | 7 | 9 | 1 |
| Fungal | 1 | 1 | 1 |
| Vascular | 1 | 1 | 0 |
| Drug reaction | 4 | 10 | 2 |
| Neoplasm | 1 | 1 | 1 |
| Vesiculo bullous | 0 | 4 | 1 |
| Autoimmune | 0 | 0 | 1 |
| Total | 18 | 70 | 16 |

Most of the patients presented with cutaneous manifestations having CD4 count in the range of 350-500. Bacterial infections were most common in patients having CD4 count less than 350.

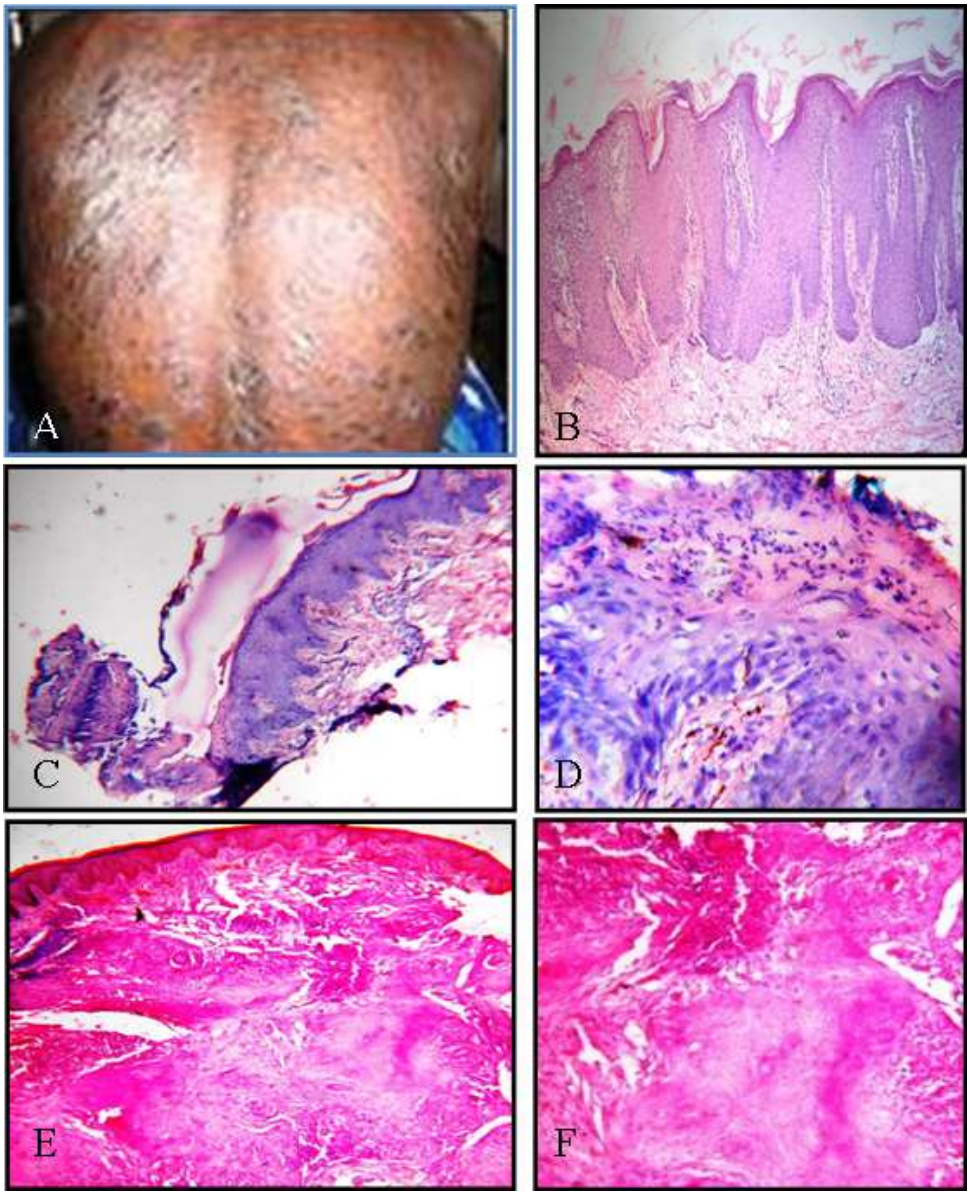


**Fig-1: A. PSORIASIS. Clinical picture showing silvery scales. B. PSORIASIS. Low power view of psoriasis showing elongated rete ridges. C. STEVENS JOHNSON SYNDROME. Low power view of Stevens Johnson Syndrome showing epidermal necrosis and dermal edema. D. STEVENS JOHNSON SYNDROME. High power view showing neutrophilic infiltration. E. TUBERCULOUS VERRUCOUS CUTIS. Low power view showing central caseating necrosis and langhans giant cells. F. TUBERCULOUS VERRUCOUS CUTIS. High power showing central caeseous necrosis**

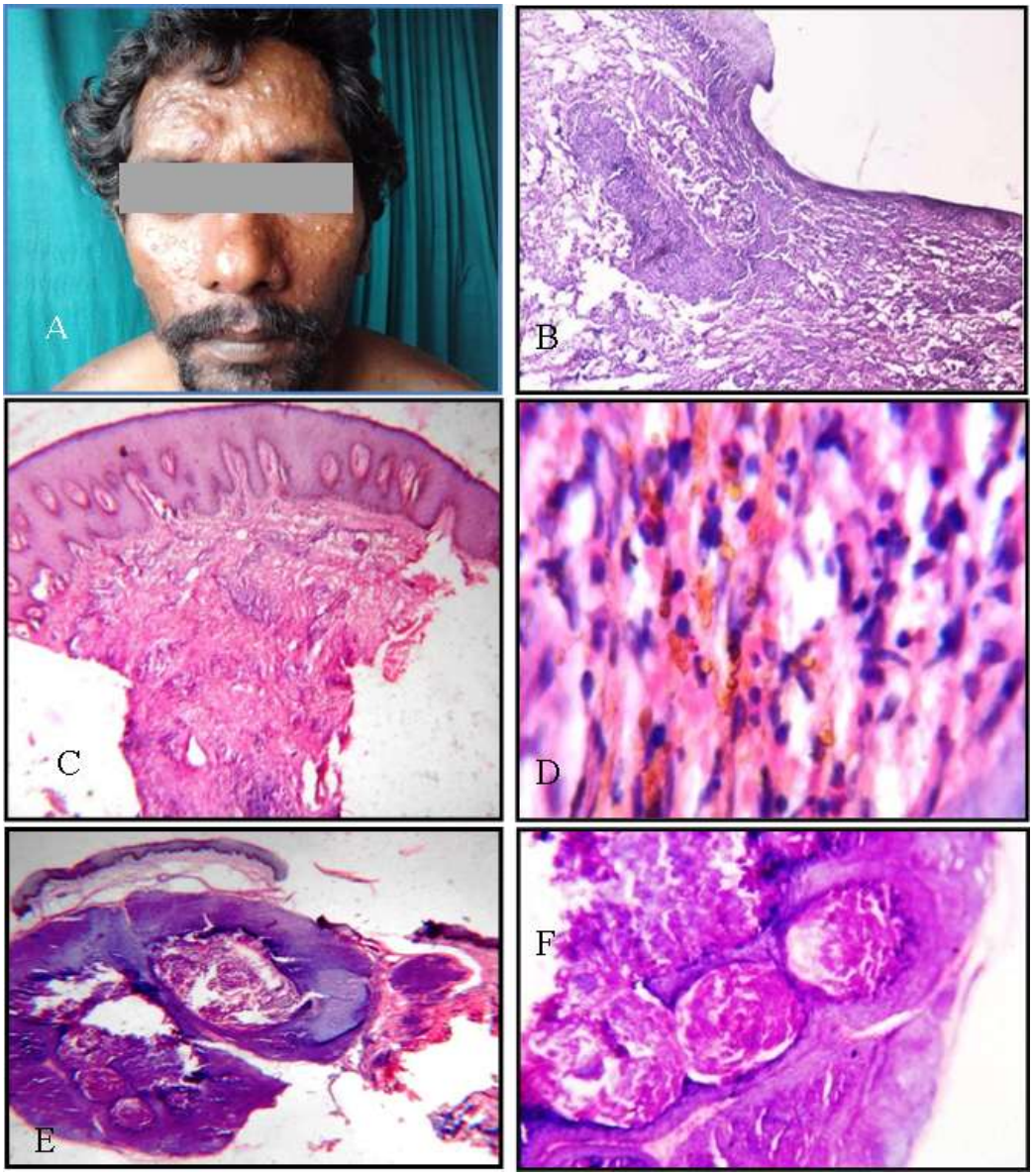


**Fig-2: A. SYPHILIS. Clinicalpicture of syphilis. B. SYPHILIS. Dense lymphoplasmacytic infiltrate in upper dermis. C. CHROMOBLASTOMYCOSIS. Low power view showing pseudoepitheliomatous hyperplasia and dermal inflammatory infiltrate. D. CHROMOBLASTOMYCOSIS. High power view showing copper penny appearance of spores. E. MOLLUSCUM CONTAGIOSUM. low power view showing central disintegration of stratum corneum and release of molluscum bodies. F. MOLLUSCUM CONTAGIOSUM. High power view showing molluscum bodies**

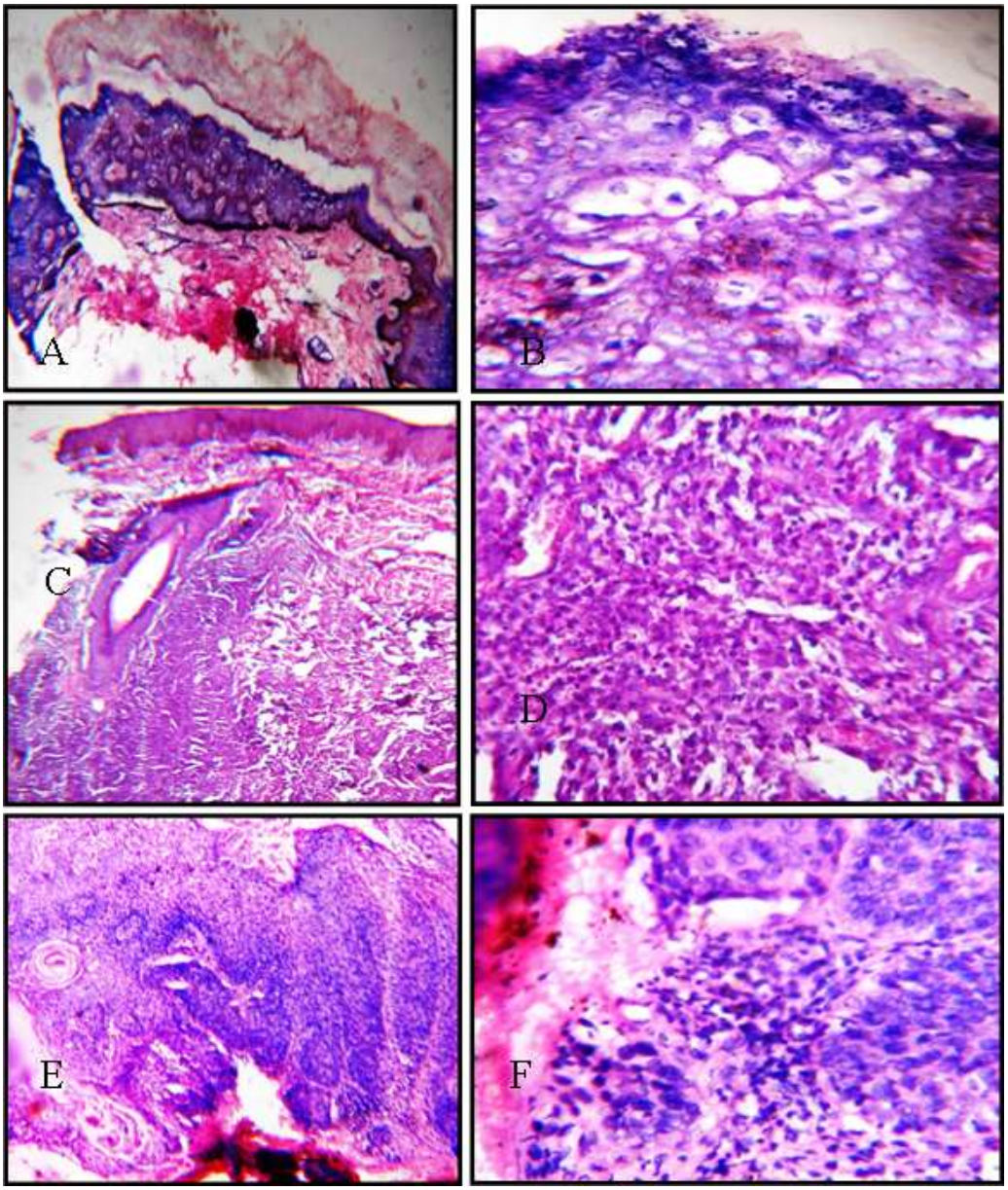


**Fig-3: A. EPIDERMODYSPLASIA VERRUCIFORMIS. low power view showing hyperkeratosis and mild acanthosis with vacuolated cells. B. EPIDERMODYSPLASIA VERRUCIFORMIS. High power view of keratinocytes with basophilic cytoplasm and prominent Keratohyalin granules. C. CUTANEOUS LYMPHOMA. Low power view showing atypical lymphocytes infiltrating sub epidermal region. D. CUTANEOUS LYMPHOMA. High power view of cutaneous lymphoma. E. SQUAMOUS CELL CARCINOMA. Low power view of Squamous Cell Carcinoma. F. SQUAMOUS CELL CARCINOMA. High power view showing invasion of tumor cells in to dermis**

## DISCUSSION

HIV infection represents a global pandemic and worldwide more than 35.3 million people are believed to be living with the HIV infection[2]. In India there are an estimated 2.5 million people are infected with HIV.

Skin is the most commonly affected organ in HIV. Cutaneous findings in HIV are frequent and include viral, fungal, bacterial and non-infectious aetiologies, which not only serve as marker of HIV infection but also a marker of stage of HIV disease.

However the morphological pattern of skin lesion in HIV is often non-diagnostic. Histopathological correlation is therefore pivotal in the accurate diagnosis of many HIV induced skin diseases.

The study was done to observe the morphological lesions where confirmed clinical diagnosis could not be made and skin biopsies of

lesions are taken to do the histopathological confirmation.

In the present study, we received 104 skin biopsies in the histopathology section of Department of pathology, patients in the age group of 31 to 40 years were affected more with 34 cases (32.69%), followed by 21-30 years with 30 cases (28.84.4%) together constituting 61.53%.

This study correlates with the study conducted by Nirja jindal[4] where most affected age group was 21-40 years constituting 73.7% and a second peak in the age group more than 40 years with 21%. In the study done by Saswathi *et al.* patients were mostly in 26-35 years age group which constituted to 50%.

The patients were mostly in 21-40 years age group (61.53%). In the present study, patients in the age group of 31 to 40 years were affected most with 34 cases(32.69%), followed by 21-30 years with 30 cases(28.84.4%), 41-50 years 27 (25.96%), 10-20 years 09 (8.65%) and patients above 50 years of age 4 (3.84%).

In the present study majority of patients were males with male to female ratio of 1.19:1. This is similar with studies by Saswathi *et al.*[5] where the male to female ratio is 1.38:1. In the present study papular lesions did the most common type constitute about 39 cases (37.5%).

In the present study out of 104 we observed 21 cases of Pruritic Papular eruption constituting overall about 20.1% and 53.84% of papular lesions. This is similar to study of Ajay Sharma *et al.* [6], and Saswati Halder *et al.* where Pruritic Papular eruptions were 21.5% and 28% respectively[5].

The study done by Ajay Sharma *et al.* showed 40% infections and noninfectious cutaneous lesions of 60% out of which Pruritic Papular eruptions were the most common which were similar to our study.

Psoriasis constituted the next peak with 5 cases out of which 4 cases showed near normal psoriatic pattern and 1 case showed atypical presentation. The study by Saswathi *et al*. showed about 10% of the cases.

The other Papulosquamous lesions were Eosinophilic folliculitis, Pytiriasis rubra pilaris, Lichen planus, Lichen simplex chronicus, Para psoriasis, Prurigo nodularis which constituted the minor group.

Seborrheic dermatitis was present in 4.8% of cases and is the most common form of dermatitis constituting 41.66%. This is similar to the study by Ajay Sharma et al. which showed 2.5% cases.

This is followed by 2 cases of atopic dermatitis and a single case of subcorneal pustular dermatoses, 4 cases showed features of nonspecific dermatitis.

Out of five cases of vesiculobullous lesions 3 were pemphigus vulgaris and Pemphigus foliaceous and Bullous pemphigoid constituted one each. Ajay Sharma et al. observed only a single case of Pemphigus vulgaris.

In the present study infections constituted 24.8% and it similar to studies by Ajay Sharma et al. And Saswathi *et al.* where noninfectious cutaneous lesions dominated over infectious lesions.

However, the studies by Nirja jindal *et al.* and Rosemary spira et al. showed more cases of infective cutaneous manifestation.

Only Bacterial infections constituted 16.3% whereas the other infections together constituted 8.5%, similar to Saswathi *et al.*

The study done by Sanjay M Chawhan *et al.* and Nirja jindal *et al*. viral infections were predominant.

Tuberculosis is widely prevalent in our country. In the present study Mycobacterium tuberculosis is the most common bacterial infection with 52.92%.

The study conducted by Sanjay *et al.* showed mycobacterial infections of which M. leprae were common followed by M.tuberculosis[7].

In this study we observed 4 cases of each Tuberculous Verrucous cutis and Lupus vulgaris and we came across a single case of Papulonecrotic TB. The diagnosis was done based on the histopathological findings and confirmed by acid fast staining. Out of 9 cases only 6 cases showed positive staining.

Viral lesions due to human papillomas virus constitute the major group with verruca vulgaris comprising of 33.33% cases followed by verruca palana(16.66%) and epidermodysplasia verruciformis(16.66%).

Munoz-Perez *et al*. in their study mentioned that HIV infection itself predisposes to an increased risk of HPV infection that is not directly related to the degree of immunosuppression [8].

Molluscum contagiosum is the most common viral infection in the study done by Sanjay *et al.* [7]. This difference in the results noted in the present study could have been due to difference in geographical distribution.

Three cases of cutaneous fungal infections were come across, two cases of were of Chromoblastomycosis and a single case of Tinea was seen. There is no literature showing Chromoblastomycosis in relation to HIV. There is no single case of fungal infection in the study done by Saswathi *et al.*

Sanjay M Chawhan *et al.* and Nirja Jindal *et al.* observed candidiasis as the common fungal infection.

This difference may be due to site of biopsy as in our cases mucosal involvement was very low when compared with the cutaneous involvement in the patient. The improvement in the anti-retroviral treatment may have reduced the prevalence of these infections.

Adverse drug reactions were seen in 16 patients (15.3%). Stevens Johnson syndrome were seen in 6 patients (37.5%) & Toxic epidermal necrolysis seen in 5(18.75%) cases, Erythema multiforme in 3(18.75%) and fixed drug eruption seen in 2 patient (12.5%).

Most of the adverse effects were seen in patients using Nevirepine. The incidence of adverse drug reaction is high in HIV patients. Also generally, utility of drugs is more in HIV due to various illnesses.

The drug reactions were 15.3% in our study which were near to study by Ajay Sharma et al and Saswathi *et al*. Nevirepine was the main offending drug for cutaneous manifestations in our study.

A single case of autoimmune disease of SLE in a 45 year old female has been identified and CD4 is more than 200. She presented with maculopapular rash over the extremities.

In the present study two cases of squamous cell carcinoma were observed and both the cases showed the histopathological features of well differentiated squamous cell carcinoma, both patients presented with ulcerative growth in anogenital region.

A single case of cutaneous lymphoma was observed which showed features of non-Hodgkin lymphoma. Cutaneous involvement of NHL is uncommon in HIV-infected patients. However, cutaneous lymphoma has encountered with more frequency in the study by Sidhu *et al*. [9], which reported four cases of HIV-related lymphomas and reviewed eight other patients published in the medical literature.

No cases of Kaposi sarcoma were found in our study although it has been reported by Rosemary Spira *et al*. and Ramadhan *et al.*

The studies by Nirja Jindal *et al*., Sanjay M Chawhan *et al*. Ajay Sharma *et al*. and Saswathi et al., also did not show any case of Kaposi sarcoma. This difference may be due to geographical variation where the prevalence is very less in our country.

It is evident from the above table that the results of present study varies considerably when compared with other study. In present study mean CD4 cell count was low in individuals with skin infections and malignancy.

The study done by Farrokh Rad et al, shows CD4 cell count higher than that of our study and the study done by Rosemary et al are lower than that of our study [10,11].

In general, our study showed no strong correlation between CD4 cell counts and this could be due response to Anti-Retroviral treatment in our patients. However we concluded that skin disorders can be seen with higher CD4 cell counts in HIV patients. Cutaneous manifestations in HIV seropositive patients may be localised or generalised but a biopsy only provides the pathologist with a small sample, which may not be representative of the disease as a whole.

Incorrect diagnosis may arise because of inadequate information on the request form; different diseases with similar pathology may present at different ages or in different body sites.

Certain dermatological conditions may present with very subtle histological alterations. The microscopy may appear normal despite quite obvious clinical disease. Changes may be too subtle to diagnose if the lesion is very early in its development.

## CONCLUSION

HIV-related cutaneous manifestations are very common and can be easily detected. If studied systematically, they can serve as diagnostic and prognostic markers.Cutaneous adverse drug reaction may reflect involvement of internal organs. Many of the infectious and non-infectious manifestations respond well to ART. The possibility of an adverse drug reaction should always be considered, especially if a biopsy shows a combination of reaction patterns. We conclude that the dermatological lesions are extremely common and may present with early, severe, unusual and atypical manifestations in the course of HIV infection. Awareness of the varied pattern of these manifestations would help in the early diagnosis and management of HIV infection, which would in turn decrease the morbidity and improve the quality of life of HIV-infected patients.

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