



SKIN – A PREDICTOR OF HIV - WARNING BELLS

Tina Priscilla Katta

Associate Professor, Department of DVL, Apollo Institute of Medical Sciences, Hyderabad.

Aruna Kumari Badam*

Associate Professor, Department of Respiratory Medicine, ESIC Medical College, Hyderabad. *Corresponding Author

K Vinod Kumar

Senior Medical Officer, ART Centre, Hyderabad.

ABSTRACT

Introduction: Human immunodeficiency virus infection (HIV) infection is associated with numerous cutaneous changes. There are various documentations in the literature about the high incidence of cutaneous manifestations in HIV. This study is focused on the cutaneous manifestations and its role as a marker or warning bell of advanced disease process. There is a varied prevalence of these disorders owing to regional distribution. So, we are studying the seroprevalance, clinicoepidemiological spectrum of mucocutaneous disorders in patients attending. **Aim:** The present study aimed to evaluate occurrence of various cutaneous manifestations (CM) in patients with HIV. **Methods:** HIV positive patients attending with definite CM attending OPD were studied. Demographic details including age, sex, height, weight, department, occupation status, laboratory parameters, marital state, and type of HIV was noted. HIV transmission mode and history of comorbidities was also recorded. **Results:** Among 71 HIV positive patients, 84.5% of patients belonged to <50 years age group. Of these, 52.1% were men and 47.9% were women. Most common occupation group, was housewives (25.4%), followed by daily wage workers (23.9%), students (8.5%), clerks (7.0%), farmers (5.6%), tailors (5.6%), engineers (4.2%), actors (4.2%), teachers (2.8%), barbers (2.8%), and others (9.9%). Hypothyroid and diabetes mellitus were the most common comorbidities. Heterosexual route was most common mode of transmission. Most common CM were papules (? Eosinophilic folliculitis), anal warts, scrotal swelling, maculopapular rash (?-IRIS-reconstitution inflammatory syndrome), itching, scaly hyperkeratotic plaques (eczema) and oral thrush. **Conclusion:** Majority of patients belonged to young age group. Pallor and papules were the most common reported CMs.

KEYWORDS : Daily wage workers, housewives, pallor, papules.

INTRODUCTION

Utilization Human immunodeficiency virus infection (HIV) has emerged as a modern pandemic which remains a major challenge in healthcare. Globally, approximately 7 million people have died from HIV-related causes and 1.7 million people were newly infected [1]. As per India's HIV Estimation 2019 report, 23.49 lakhs peoples were living with HIV, with an HIV prevalence of 0.2% [2].

HIV is transmitted primarily by unprotected sexual intercourse, contaminated blood transfusions, hypodermic needles, and congenital transmission, or breastfeeding. During the initial period, a person may experience brief influenza-like illness [3]. As the infection progresses, it interferes with the immune system, thus making the person vulnerable to common infections like tuberculosis, opportunistic infections, and tumors [4]. Cutaneous manifestations (CM) are commonly encountered in HIV-infected patients [5]. Identifying the cutaneous symptom associated with HIV infection and investigating them can be helpful in early diagnosis of the disease [4].

Among HIV-infected individuals, cutaneous disorders may cause significant morbidity. They affect between 80 and 95% of HIV-infected patients, occurring at any time in the course of infection. Chronic herpes simplex virus, molluscum contagiosum, oral hairy leukoplakia, oral candidiasis, and Kaposi's sarcoma are the most common HIV-associated CM [6]. Cutaneous infections such as eosinophilic folliculitis and Kaposi's sarcoma are highly suggestive of HIV [7]. Pruritic papular type of chronic eruptions is associated with a high cluster of CD4 T helper cell count. It has been reported to be the most common during the initial CM of HIV. Eosinophilic folliculitis usually occurs with advanced stages of HIV infection [8]. Nag D, et al, revealed that lymphadenopathy is a very common manifestation of HIV infection [9]. Apart from other causes such as tuberculosis, opportunistic infections such as non-tuberculous mycobacteria and non-Hodgkin

lymphoma, HIV itself can cause follicular hyperplasia, which manifests as persistent generalized lymphadenopathy [9].

However, the findings on careful dermatological examination of patients with HIV who present for primary care setting have received limited attention. The present cross-sectional study aimed to analyze the clinical characteristics of patients with HIV presenting with common skin complaints.

METHODS

This is cross sectional, hospital based descriptive study, which was conducted. Patients with known HIV positive status according to NACO guidelines having an opportunistic infection or patients with different opportunistic infection admitted to the hospital and later found to have HIV positive status were included in the study. Patient data were collected from outpatient department, in ward, and from radiology center, and all participants testing positive for HIV at screening were enrolled for the present study. There were no specific eligibility criteria. All participants were administered an informed consent.

Detailed history, clinical examination, and investigations were done. Information on demographics including age, sex, height, weight, department, occupation status, laboratory parameters, marital state, and type of HIV was noted. Patient information such as HIV transmission method, and history of comorbidities was recorded. Routine investigations, complete clinical history, systemic and dermatological examination were performed. PR, RR, and T count was done. Histopathological study was done in the pathology department.

Data were analyzed using Statistical Package for The Social Sciences (SPSS) software, version 22.0. Qualitative data was presented as number and percentages, while quantitative data was presented as mean (standard deviation [SD]) or median (range).

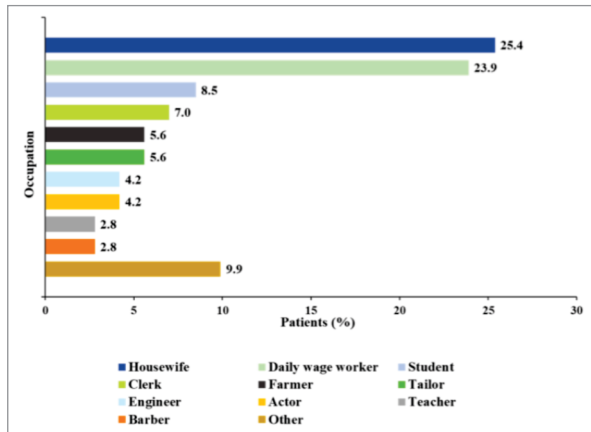
RESULTS

A total of 71 HIV-infected patients were enrolled in the present study. Of these, most of the patients, (84.5%), were < 50 years of age, while 11 (15.5%) of patients were > 50 years of age. Of these, 52.1% were men and 47.9% were women. Regarding the occupations of the patients, the largest group were constituted by housewives (25.4%), followed by daily wage workers (23.9%), students (8.5%), clerks (7.0%), farmers (5.6%), tailors (5.6%), engineers (4.2%), actors (4.2%), teachers (2.8%), barbers (2.8%), and others (9.9%) (Figure 1).

Hypothyroid (21.0%) and diabetes mellitus (21.0%) were the most common comorbidities observed followed by hypertension (10.5%), pulmonary tuberculosis (5.2%), chronic kidney disease (5.2%), hepatitis B (5.2%).

The predominant mode of transmission was heterosexual contact (97.2%), only two patients (2.8%) were infected through congenital (mother to child) transmission. There was no history of intravenous drug abuse and homosexuality (Table 1).

Figure 1. Occupation data across patients with HIV infection



Other, Accountant (n = 1, 1.4%); businessman (n = 1, 1.4%); construction worker (n = 1, 1.4%); lab technician (n = 1, 1.4%); driver (n = 1, 1.4%); mason (n = 1, 1.4%).

Table 1. Demographic characteristics of patients with HIV infection

Parameters	Number of patients (N=71)*
Age [years], median (range)	40.0 (10.0-70.0)
Age coding [years]	
<50	60 (84.5)
>50	11 (15.5)
Sex	
Men	37 (52.1)
Women	34 (47.9)
Height [cm], mean (SD)	155.7 (15.1)
Weight [kg], median (range)	50.0 (15.0-77.0)
Department	
CTB	8 (11.3)
Dermatology, venereology and leprosy	4 (5.6)
General medicine	34 (47.9)
General Surgery	9 (12.7)
Obstetrics and gynecology	8 (11.3)
Otorhinolaryngology	1 (1.4)
Pediatrics	2 (2.8)
Orthopedics	5 (7.0)
Systolic pressure [mmHg], mean (SD)	112.3 (15.5)
Diastolic pressure [mmHg], mean (SD)	71.5 (10.9)
PR, median (range)	81.0 (60.0-150.0)
RR, median (range)	20.0 (16.0-26.0)
T, mean (SD)	98.9 (1.3)

Comorbid conditions	[n = 19]
Hypothyroid	4 (21.0)
Diabetes mellitus	4 (21.0)
Hypertension	2 (10.5)
Pulmonary TB	1 (5.2)
Chronic kidney disease	1 (5.2)
Hepatitis B	1 (5.2)
Asthma	1 (5.2)
Marital state	
Married	62 (87.3)
Unmarried	9 (12.7)
Type of HIV	
HIV 1	58 (81.7)
HIV 2	3 (4.2)
HIV 1 HIV 2	10 (14.1)
Mode of transmission	
Heterosexual	69 (97.2)
Congenital	2 (2.8)
History of addiction	
Alcohol consumption	8 (11.3)
Smoking	4 (5.6)
Data shown n (%). n=71 unless otherwise specified. CTB, computerized tomography brain.	

Most common HIV-related dermatological manifestation was papules (? Eosinophilic folliculitis), anal warts, scrotal swelling were observed in 9.9, 1.4, and 1.4% of patients respectively. Skin lesions associated with HIV infection were maculopapular rash (4.8%) (IRIS), itching (1.4%), Scaly hyperkeratotic plaques (1.4%) (? eczema), oral thrush (1.4%).

Table 2. Cutaneous manifestation in patients with HIV infection

Parameters	Number of patients (N=71)*
Signs	
Pallor	27 (38.0)
Icterus	1 (1.4)
Clubbing	1 (1.4)
Edema	1 (1.4)
Lymphadenopathy	1 (1.4)
Genitals	
Papules	7 (9.9)
Anal warts	1 (1.4)
Scrotal swelling	1 (1.4)
Skin lesions	
Maculopapular rash	2 (4.8)
Itching	1 (1.4)
Dry hyperkeratotic plaques	1 (1.4)
Oral thrush	1 (1.4)
System involved	[n = 41]
Respiratory	17 (41.5)
Gastrointestinal tract	12 (29.3)
Genitourinary	8 (19.5)
Dermatology, venereology and leprosy	3 (7.3)
Cardiovascular system	1 (2.4)
Symptoms	
Fever	37 (52.1)
Weight loss	32 (45.1)
Weakness	21 (29.6)
Dyspnea	16 (22.5)
Cough	16 (22.5)
Loss of appetite	11 (15.5)
Diarrhea	11 (15.5)
Pain in abdomen	7 (9.9)
Chest pain	7 (9.9)
Vomiting	3 (4.2)
Headache	1 (1.4)
Altered sensorium	1 (1.4)
Data shown as n (%). n=71 unless otherwise specified. TB, tuberculosis.	

The most common presenting symptoms were fever (52.1%), weight loss (45.1%), followed by weakness (29.6%), dyspnea (22.5%), cough (22.5%), loss of appetite (15.5%), diarrhea (15.5%), pain in abdomen (9.9%), chest pain (9.9%), vomiting (4.2%), headache (1.4%), and altered sensorium (1.4%) (Table 2).

DISCUSSION

The CM in patients with HIV are quite common. This study was mainly evaluated CM of HIV positive patients. In this present study, 71 patients with HIV were examined for various CM. The most common age group affected was <50 years. This was followed by the age group of >50 years. Higher prevalence among men with men to women ratio of 1.1:1. Regarding the occupations of the patients, housewives and daily wage workers formed the major group in the study. The predominant mode of transmission was heterosexual contact. On examination of the patients for CM related to HIV, 38.0% and 9.0% of total study population had pallor and papules, related to HIV.

Skin often acts as a mirror of many internal pathology including HIV. Skin manifestation may herald the recurrence of dermatoses associated with HIV infection [10]. Skin disease can be uniquely encountered with HIV infection and these infections are often due to common disorders and it may prone to more severe form [11]. The spectrum of skin conditions has helped the clinician to diagnose systemic diseases. Saravanabhavan et al reported that approximately 82% patients with HIV have at least one associated cutaneous change [12].

The patient's age in the study ranged from 10 to 70 years and the most common age group was <50 years (84.5%). The mean age of patients was 40.0 years which was compatible with the studies done by Davarpanah MA, et al (40.9 years) and Lahoti S, et al (37.5 years) [7,13]. The previous study conducted in north India reported the prevalence of cutaneous dysfunction associated with HIV and 50.8% of patients belonged to the age group of 31-40 years [14]. Another evidence-based study from Indian literature reported the prevalence of CM in HIV infected patients and 51% of patients belonged to the age group of 30-39 years [15].

In the present study, the men-to-women ratio was 1.1:1, which showed a slight preponderance of men over women, whereas Kumari et al had observed 1.9:1 men-to-women ratio [8]. Moreover, studies carried out by Patjoshi et al and Shehu et al reported men-to-women ratio of 1.8:1 and 2.3:1, respectively [16,17]. These results are considered alongside the research of Neerja et al in which 90 HIV infected patients with CM were studied and men preponderance was observed with men to women ratio of 2.1:1 [18]. This distribution differed from a study carried out in Indian settings by Mohammed et al who reported a men-to-women ratio of 1:2 [19]. Similarly, Neerja et al and Sud et al also observed a women predominance in their series [18, 20]. However, the men preponderance was observed in this study which agrees with previous studies. This wide variation in the distribution of prevalence among men and women is possibly due to a lower recovery rate in women and it may be related to the fact that they are less educated with lower monthly income [21]. The exact cause of this sex variation is not clearly understood.

Majority of the patients (24.5%) were daily wage workers. Among women, majority (37.0%) of patients were housewives. This emphasizes the main route of contact was through heterosexual contact [21]. In parallel to these results present study also revealed that CM associated with HIV were prevalent among housewives and daily wage workers. The incidence of HIV infection among students was 8.5% while Kumari et al reported a relatively low prevalence among students (0.8%) [14]. The possible factors responsible for this

are illiteracy, lack of awareness, and delay in diagnosis.

CM can occur in majority of patients with HIV infection during the course of the disease [12]. Severe infections, atypical presentation, treatment failure, recalcitrant and lesion, presence of >4 concurrent oral lesions, multiple sites of involvement, chronic pruritus, associated systemic symptoms are characteristics of skin conditions in HIV patients [11,22,23]. The above-mentioned issues states that importance of awareness of these manifestations. Early identification and treatment would help in early management of HIV infection which would reduce all-cause mortality and improve the patients' quality of life [11]. Early diagnosis of cutaneous dysfunction in patients with HIV has become a fundamental step to allow initiation of appropriate antiretroviral therapy.

The heterosexual route was the most common mode of transmission (97.2%), followed by congenital (2.8%) which was compatible with the studies done by Kumari et al and Kumawat et al wherein they reported heterosexual route as the most common route of transmission i.e., 85.8% and 87.7% respectively [14,24]. Patients who acquired HIV through heterosexual contact had the highest risk of developing advanced HIV disease [25].

The most common manifestation observed was pallor seen in 38.0% of patients which is different from the other studies done by Kumar et al where pallor was the commonest opportunistic infection but they reported in a higher number of patients as they reported pallor in 75.0% patients of their study populations [26]. Similarly, in a previous Indian report, the prevalence of pallor was found to be associated with HIV ($P < 0.001$) [27]. Similarly, study papules were reported as the most common skin manifestation in 9.1% patients with HIV. These findings agree with previous Indian study [28]. Maculopapular rash was the second most common CM occurring in 4.8% of patients. Oninla et al. reported maculopapular rash occurred in 25.3% of his study group of HIV patients [29].

The cluster of differentiation 4 (CD-4) count indicates the degree of weakened immune system or disease progression [17]. Larger forms of lesions may be associated with the severity of endoscopic findings and which may result into worsen clinical output. These lesions are generally associated with the viral load and CD-4 count [30]. Previous prospective study by Rane et al evaluated the comparison between histopathological findings with CD-4 cell count. The results demonstrated that prevalence of skin lesions in HIV infected patients was associated with lower CD-4 cell count ($< 220/\mu\text{L}$) [28]. In parallel to these studies, Yang et al revealed that CMs in HIV infection were significantly associated with increase in ratio of CD-4 to cluster of differentiation-8 cells ($P = 0.006$). Furthermore, decrease in the number of CD4 cells was associated with in the dermis of HIV ($P = 0.044$) [31]. The present study did not record CD-4 cell count of the patients which could have added valuable data while inferring the observations.

The present study has few limitations. Small sample size and short study period are the limitations of this research. Large-scale, well-designed studies are needed.

CONCLUSION

In the present study, most of the affected population was from age group of <50 years which increases the economic burden. Housewives and daily wage workers were the most common occupation found to be affected. Heterosexual route was the commonest mode of transmission. Pallor and papules were the most common CM reported by patients with HIV.

REFERENCES:

- [1] HIV/AIDS. WHO. <https://www.who.int/news-room/fact-sheets/detail/hiv-aids#:~:text=Due%20to%20gaps%20in%20HIV,million%20people%20were%20newly%20infected.> Last accessed on 04 April 2021.
- [2] India HIV Estimates 2019 Report. Available from <https://www.aidsdatahub.org/sites/default/files/resource/india-hiv-estimates-2019.pdf>. Last accessed on 04 April 2021.
- [3] Blood Donor Counselling: Implementation Guidelines. Geneva: World Health Organization; 2014. Annex 5, HIV infection: information for blood donors. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK310571/>. Last accessed on 04 April 2021.
- [4] Vora RV, Jivani NB, Kota RS, Gandhi SS, Patel T. A clinico-epidemiological profile of HIV positive patients with muco-cutaneous manifestations. *IP Ind J ClinExp Dermatol* 2017;3(2):80-84.
- [5] Systems Review. 21. Dermatologic Manifestations InHiv Disease. Available from: <https://www.aids.gov.hk/pdf/g190htm/21.htm>. Last accessed on 04 April 2021.
- [6] Khondker L. Dermatological Manifestations of HIV/AIDS Patients. *J Enam Medical College* 2019;9(3):185-188.
- [7] Davarpanah MA, Motazedian N, Jowkar F. Dermatological Manifestations of HIV/AIDS Individuals in Shiraz, South of Iran. *J Glob Infect Dis.* 2018;10(2):80-83.
- [8] Kumari N, Krishan K, Bist JS, Mehta AK, Kumari N, et al. Study of cutaneous manifestation of HIV disease in correlation with CD4 lymphocyte count. *Int J Res Dermatol.* 2019 Aug;5(3):587-592.
- [9] Nag D, Dey S, Nandi A, Bandyopadhyay R, Roychowdhury D, Roy R. Etiological study of lymphadenopathy in HIV-infected patients in a tertiary care hospital. *J Cytol.* 2016;33(2):66-70.
- [10] Lewis DJ, Feldman SR. Cutaneous manifestations of human immunodeficiency virus/acquired immunodeficiency syndrome: A comprehensive review. *J Dermatol Dermatol Surg.* 2020; 24: 66-73.
- [11] Cedeno-Laurent F, Gómez-Flores M, Mendez N, Ancer-Rodriguez J, Bryant JL, et al. New insights into HIV-1-primary skin disorders. *J Int AIDS Soc.* 2011; 14: 5.
- [12] Saravanabhavan S, Vellaisamy SG, Gopalan K, Kandasamy M. The pattern of mucocutaneous disorders in pediatric HIV patients in a tertiary care center. *IJPD.* 2020; 21: 301-6.
- [13] Lahoti S, Rao K, Umadevi HS, Mishra L. Correlation of mucocutaneous manifestations of HIV-infected patients in an ART center with CD4 counts. *Indian J Dent Res.* 2017;28(5):549-554.
- [14] Kumari N, Krishan K, Bhat B, Gupta G, Bist JS, Mehta AK. Study of cutaneous manifestations in HIV infection. *IAIM,* 2017;4: 99-106.
- [15] Nkwoemeka NE, Anyamene CO, Okwelogu IS, et al. Fungal Isolates in HIV positive and negative subjects attending Chukwuemeka OdumegwuOjukwu University Teaching Hospital, Amaku, Awka, Anambra State, Nigeria. *J Med Res Surg.* 2020; 1(2):1-9.
- [16] Patjoshi SK, Chandra TJ. A study to find the correlation between mucocutaneous manifestations and CD4 counts among the newly diagnosed HIV individuals. *Int J Med Res Rev.* 2020;8(1):130-135.
- [17] Shehu E, Harxhi A, Simaku A. Cutaneous Manifestations of Human Immunodeficiency Virus/AIDS Patients in Albania. *Int J Appl Basic Med Res.* 2019;9(4):197-200.
- [18] Neerja J, Aruna A, Satwinder K. HIV seroprevalence and HIV associated dermatoses among patients presenting with skin and mucocutaneous disorders. *Ind J Dermatol Venereol Leprol* 2009;75(3):283-286.
- [19] Mohammed S, Vellaisamy SG, Gopalan K, Sukumaran L, Valan AS. Prevalence of pruritic papular eruption among HIV patients: A cross-sectional study. *Indian J Sex Transm Dis AIDS.* 2019;40(2):146-151.
- [20] Sud N, Shanker V, Sharma A, Sharma NL, Gupta M. Mucocutaneous manifestations in 150 HIV-infected Indian patients and their relationship with CD4 lymphocyte counts. *Int J STD & AIDS,* 2009;20(11):771-774.
- [21] Conger RD, Conger KJ, Martin MJ. Socioeconomic Status, Family Processes, and Individual Development. *J Marriage Fam.* 2010;72:685-704.
- [22] Vellaisamy, Kannan G, Muthusamy K, Bajpai S, Pazare AR. Oral manifestations of HIV. *Contemp Clin Dent.* 2010;1:1-5.
- [23] Kaushik SB, Cerci FB, Miracle J, Pokharel A, Chen SC, Chan YH, et al. Chronic pruritus in HIV-positive patients in the southeastern United States: its prevalence and effect on quality of life. *J Am Acad Dermatol.* 2014; 0:659-64.
- [24] Kumawat S, Kochar A, Sirohi P, Garhwal J. Socio-demographic and clinical profile of HIV/AIDS patients in HAART era at a tertiary care hospital in North-West Rajasthan, India. *Int J Community Med Public Health* 2016;3:2088-93.
- [25] Chen Q, Zeng D, She Y, Lyu Y, Gong X, Feinstein MJ, et al. Different transmission routes and the risk of advanced HIV disease: A systematic review and network meta-analysis of observational studies. *E Clinical Medicine.* 2019;16:121-128.
- [26] Kumar BM, Thippeswamy T, Shankar R, Prathima C. Hematological Abnormalities in Early and Advanced HIV Infection Patients. *Int J Sci Stud* 2016;3(11):1-5.
- [27] Antwal M, Gurjar R, Chidrawar S, Pawar J, Gaikwad S, Panchal N, et al. Clinical profile of HIV infected patients attending a HIV referral clinic in Pune, India. *Indian J Med Res.* 2014;140:271-277.
- [28] Rane SR, Agrawal PB, Kadgi NV, Jadhav MV, Puranik SC. Histopathological study of cutaneous manifestations in HIV and AIDS patients. *Int J Dermatol.* 2014;53(6):746-51.
- [29] Oninla OA. Mucocutaneous Manifestations of HIV and the Correlation with WHO Clinical Staging in a Tertiary Hospital in Nigeria. *AIDS Res Treat.* 2014;2014:360970.
- [30] Nagata N, Shimbo T, Yazaki H, Asayama N, Akiyama J, Teruya K, et al. Predictive clinical factors in the diagnosis of gastrointestinal Kaposi's sarcoma and its endoscopic severity. *PLoS One.* 2012;7:e46967.
- [31] Yang C, Mosam A, Mankahla A, Dlova N, Saavedra A. HIV infection predisposes skin to toxic epidermal necrolysis via depletion of skin-directed CD4⁺ T cells. *J Am Acad Dermatol.* 2014;70:1096-102.