

Mucocutaneous manifestations in HIV and their correlation with WHO clinical staging

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Abstract-

Introduction

Mucocutaneous infections have played a myriad role in early diagnosis of HIV infection and in clinical staging of the disease. The frequency and associated etiological factors of complications can be varied.

Aim

This study focuses on various patterns and presentations of mucocutaneous manifestations in HIV patients and its correlation with WHO clinical staging.

Material methods

270 diagnosed asymptomatic HIV patients and those who reported for care after testing HIV-positive were assessed for skin findings and were divided according to the WHO clinical stages at presentation.

Results

Mean age of HIV positive patients was 40.04 ± 10.77 years from the rural area (55.19%) taking ART (91.85%) with most common regimen Tenofovir Disoproxil, Lamivudine and Dolutegravir(TLD) (53.33%). Male preponderance (58.52%) was reported. Prevalence of mucocutaneous manifestations in present study was 22.96% with sex predilection for males(23.27%). Commonest were Onychomycosis(8.06%), Scabies(8.06%), Oral Candidiasis(6.45%) and infection of Tinea Cruris, Corporis(4.84%). Majority of the patients pertained to WHO clinical staging of 1 (48.89%) while both males and females were highest in WHO stage of 1 (47.17%, 51.35%).

Conclusion

Regular skin examinations are recommended as routine in HIV-infected patients.

Keywords- HIV, AIDS, Mucocutaneous, Onychomycosis, scabies.

Introduction

Human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) is a fatal illness caused by a retrovirus known as human immunodeficiency virus (HIV), affecting not only the developed nations but also the developing nations like India.^[1] HIV is transmitted primarily via unprotected sexual intercourse (including anal and oral sex), contaminated blood transfusions, hypodermic needles, and from mother to child during pregnancy, delivery, or breastfeeding. Following initial infection, a person may experience a brief period of influenza-like illness. This is typically followed by a prolonged period without symptoms. As the infection progresses, it interferes more and more with the immune system, making the person much more susceptible to common infections like tuberculosis, as well as opportunistic infections and tumors that do not usually affect people who have working immune systems.^[2]

Currently, India has the third largest number of people living with HIV in the world, because of its huge population, even though it has a low HIV prevalence. The total number of people living with HIV is equates to 2.1 million with a prevalence of 0.26% in 2017. Overall, India's HIV epidemic is slowing down. Between 2010 and 2017 new infections declined by 27% and AIDS-related deaths more than halved, falling by 56%.^[3] Knowledge of the skin and mucosal signs of HIV/AIDS is important, as mucocutaneous infections are usually the first manifestation of HIV, plays an important role in early diagnosis and prompt treatment, and reveals complications as HIV causes atypical and severe presentations of these conditions.^[4]

Mucocutaneous manifestations in HIV infected individuals are myriad and can serve as a main indicator of other problems. These manifestations are seen in any stage of World health organisation (WHO) clinical HIV staging, but are more common in the advanced stages of HIV infection. Few selected dermatoses serve as sensitive and useful clinical indicators of HIV infection and disease progression. Certain dermatoses like herpes simplex virus infection are more severe, chronic in nature and present with atypical manifestations.^[5]

Differences in skin pigmentation, demographic, racial factors, behavioural factors, environmental, and climate causes different clinical presentations and epidemiological patterns of HIV-associated skin conditions. Health care personnel involved in HIV health care must therefore have a clear idea of type, pattern, and prevalence of skin diseases in their locality.^[6]

Progressive immune dysfunction is the hallmark of this viral infection. The ribose nucleic acid (RNA) retrovirus infects cluster of differentiation (CD4) cells, most notably T helper cells, and leads to a profound alteration of immune system function that predisposes patients to numerous opportunistic infections, malignancies, and neurologic disease. Patients progress to AIDS when CD4 cell counts fall below 200cells/cumm or certain clinical diseases manifest.^[7]

CD4 cell count is one of the essential markers in monitoring HIV disease progression in patients on anti-retroviral treatment. It predicts the degree of immunosuppression and occurrence of specific dermatoses at specific CD4 counts. However, the standard test for CD4 cell count requires sophisticated laboratory facilities, expertise and is expensive. It is not readily available in resource-poor settings.^[8] Mucocutaneous conditions have been correlated with CD4 counts in many studies. But correlation of CD4 counts, clinical manifestations with WHO staging's are only few and limited.^[9] Therefore, present study was conducted to find out the various patterns and presentations of mucocutaneous manifestations in HIV patients and its correlation with WHO clinical staging.

Material and methods-

This single centre, hospital based cross-sectional observational study was conducted in ART-Plus centre at department of Medicine at DR. B.R.A.M.H Raipur located in Central India. 270 asymptomatic HIV patients visiting ART centre and those who reported for care after testing HIV-positive at screening centre for a period of 1.5 year from January 2020 to June 2021 were included in this study. Patients who were seriously ill with HIV infection and pregnant were excluded from the study. After explaining the study procedure, written informed consent obtained from all the subjects selected for the study. Case records were collected from the medical records department after availing necessary ethical approval from the institution and were meticulously looked for various skin findings and were categorized according to the WHO clinical stages at presentation using skin and findings in other body systems. Diagnosis was mainly clinical and when necessary confirmatory mycological and haematological test was done. The collected data were tabulated and statistically analysed using IBM SPSS (SPSS Inc., Chicago, Illinois-USA) ver. 20 software. Quantitative data were expressed as mean and standard deviation. Categorical data was expressed as number and percentage. Oneway ANOVA / independent sample t test was used to compare the mean. Categorical data was compared using Chi Square test. P-value <0.05 was considered as statistically significant.

Observations and Results-

In present study, majority of the patients with HIV had age interval between 41-50 years (32.59%) followed by those between 31-40 years of age (30.37%) and 21-30 years (20%). Mean age of HIV positive patients was 40.04±10.77 years. Males' preponderance (58.52%) was reported in our study compared to females (41.11%). Majority of the HIV positive patients were from the rural area (55.19%) followed by the urban area (44.81%). Majority patients were put on ART (91.85%), rest patients did not take ART (8.15%). Most common regimen followed was Tenofovir Disoproxil, Lamivudine and Dolutegravir (TLD) (53.33%) and Tenofovir Disoproxil, Lamivudine and Efavirenz (TLE) (30%). This was followed by cases who weren't started on any ART regimen (8.15%) and Zidovudine + Lamivudine + Nevirapine (ZLN) regimen (5.93%). Rest categories of patients included cases with various different regimens (all<1%) like abacavir + Lamivudine + Efavirenz, Zidovudine + Lamivudine + Nevirapine, Atazanavir and Atazanavir / Ritonavir.

Prevalence of mucocutaneous manifestations in present study was 22.96%. Male preponderance was noted with prevalence in males was 23.27% and females was 22.52%. Most common Mucocutaneous manifestations in present study were Onychomycosis (8.06%) and Scabies (8.06%) followed by Oral Candidiasis (6.45%) and infection of Tinea Cruris and Corporis (4.84%). Majority of the patients were categorized as WHO clinical staging of 1 (48.89%) followed by stage 2 (21.85%). Genderwise, majority of the males belonged to WHO clinical stage of 1 (47.17%) followed by stage 2 (20.75%). Similarly, majority of the females belonged to WHO clinical stage of 1 (51.35%) followed by clinical stage 2 (23.42%).

Out of 5 patients with Scabies, 3 were in WHO clinical stage 3 whereas 2 were in clinical stage 4. Out of 5 patients with Onychomycosis, 2 each were in clinical stage 3 and 4 respectively and 1 belong to the WHO clinical stage 2. Out of 3 patients having Tinea Cruris and Corporis infection, 1 each belonged to WHO clinical stage 2, 3 and 4 respectively. Out of 4 patients with Oral Candidiasis, 3 belonged to clinical stage 3 and 1 belong to clinical stage 4. Out of 5 patients with Scabies, 4 were female and 1 was male. Out of 5 patients with Onychomycosis, 1 was female and 4 were males. Out of 3 patients having Tinea Cruris and Corporis infection, all were males. Out of 4 patients with Oral Candidiasis, 2 each were male and female respectively.

Discussion-

1) Demographic Parameters-

In the present study, majority of the patients with HIV had age between 41-50 years (32.59%) with mean age of 40.04±10.77 years. Males' preponderance (58.52%) was reported. Mirnezami M et al., showed that out of the 84 HIV patients, who aged 23–53 years with a mean age of 34.6 ± 6.3 years, 20 (23.8%) were female and 64 (76.2%) were male supporting our study findings. Seventeen patients (20.2%) had CD4 counts < 200, twenty-six (30.8%) had CD4 counts of 200–500, and 41 (49%) had CD4 counts > 500. Sixty-two patients had been infected by the virus through drug abuse, four of which reported a history of suspected sexual contact, as well.^[10] Oninla OA et al., found that there were 71 males and 144 females with a ratio of 1 : 2. The age ranged between 18 and 77 with a mean of 35 years.^[11] A higher female preponderance was also reported by Salami et al.,^[12] in Nigeria. These gender wise findings were not in consensus with our data. Santosh k et al., supported us with 148 males (59.2%) and 102 females (40.8%) with age range was 18 to 64 years with a mean of 38 years.

2) Prevalence of Mucocutaneous manifestations-

In present study, most common manifestations were Superficial fungal infections(27.37%), [Tinea Cruris & Corporis (9.66%), Onychomycosis (8.06%), Oral Candidiasis(6.44%), Pityriasis Versicolor (1.61%)] followed by Scabies (8.06%) . Mirnezami M et al., showed that the most common skin disorders were xerosis (54.8%) and seborrheic dermatitis (54.4). In the infectious category, the most common cutaneous infection was by herpes simplex virus (52.4%), followed by oral candidiasis (47.6%) while in hair it was telogen effluvium (19%) and nails it included nail hyperpigmentation (26.2%), nail dystrophy (7.1%), cyanosis clubbing (4.2%), and onychomycosis (2.4%).^[10] Oninla OA et al., found most common skin disorders as oropharyngeal candidiasis (32.1%), pruritic papular eruptions (25.3%), vaginal candidiasis (9.0%), dermatophytic infections (8.9%), herpes zoster(3.9%), carbuncles(2.6%), herpes simplex(2.6%), and seborrheic dermatitis(1.9%). More than half (52.6%) of the newly diagnosed HIV patients had dermatoses.^[11] Sivayathorn et al., found that oral candidiasis (34.3%), pruritic papular eruption (32.7%), seborrheic dermatitis (21%), herpes zoster (16.1%), oral hairy leukoplakia(14.9%), herpes simplex(10.9%), onychomycosis(9.3%), cutaneous ringworm(7.7%), psoriasis(6.5%), and folliculitis (5.6%) were the most prevalent skin conditions among HIV seropositives.^[14] Lowe et al., found skin disorders in 88% of 301 HIV-positive patients, while pruritic skin lesions and plane warts were the most observed ones.^[15] these results were in accordance with the studies reported by Levy et al.,^[16] Foroughi et al.,^[17] Josephine et al.,^[18] and Noruka et al.^[19] Conversely, in a study conducted in Tanzania, Kaposi sarcoma was reported one of the most common cutaneous lesions in HIV-positive patients.^[20]

Santosh k et al., observed that amongst fungal infections, Candidiasis was the commonest (62.14%) followed by Onychomycosis (19.42%).^[13] These findings were on contrary with findings of Raju et al.,^[21] who reported the prevalence as 22.17% in his study, but similar to Kumaraswamy et al.,^[22] who reported as 37% in his study. Followed in next order, generalized pigmentation was observed with 19.61% prevalence and Seborrheic dermatitis in 23.53%. The prevalence of pigmentation and seborrheic dermatitis was considerably less than in other studies.^[13,21-22]

3) WHO clinical staging

Santosh K et al., showed that there were 33 cases in WHO Clinical stage 1, 72 in Stage 2, 96 in stage 3 and 49 in stage 4.^[13] Oninla OA et al., noted that the proportion of the total number (156) of cutaneous diseases occurring in stage 1 was 4.5% and 21.8% in stage 2, 53.2% in stage 3, and 20.5% in stage 4.^[11] A similar report was obtained in Nigerian children by Okechukwu et al.^[23]

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Tables-

Table 1: Baseline characteristics of patients included in the study (n=270)

Categorical variables	Percentage
Age (Years)	
≤20	1.85
21-30	20.00
31-40	30.37
41-50	32.59
51-60	11.85
>60	3.33
Sex	
Males	58.52
Females	41.11
Residential area	
Rural	55.19

Urban	21.3
On ART	
Yes	91.85
No	8.15
Patients ART regime	
ABC, 3TC, EFV	0.37
TL and ATVr	0.74
TLD	53.33
TLE	30.00
ZL and EFV	0.74
ZL and ATVr	0.37
ZLN	5.93
ZLN and EFV	0.37
Not taking	8.15
Continuous variables- Mean age (years)	Mean + SD 40.04±10.77

ART- antiretroviral therapy, SD- standard deviation, ABC- Abacavir ,3TC- Lamivudine, EFV- Efavirenz, TL- Tenofovir Disoproxil + Lamivudine, ATV- Atazanavir, ATVr- Atazanavir / Ritonavir, TLD- Tenofovir Disoproxil + Lamivudine + Dolutegravir, TLE- Tenofovir Disoproxil + Lamivudine + Efavirenz, , ZL- Zidovudine + Lamivudine , ZLN- Zidovudine + Lamivudine + Nevirapine.

Table 2 : Mucocutaneous manifestations in study population (n=270)

Mucocutaneous manifestations	Percentage (%)
Onychomycosis	8.06
Scabies	8.06
Oral Candidiasis	6.45
Tinea Cruris and Corporis	4.84
Chelitis	3.23
Molluscum contagiosum	3.23
Tinea Corporis	3.23
Prurigo Simplex	3.23
Squamous cell Carcinoma	1.61
Acne vulgaris	1.61
Acniform eruption	1.61
Acute eczema	1.61
Acute Urticaria	1.61
Albinism	1.61
Bald Tongue	1.61
Dermatitis	1.61
Diffuse hairfall with pruritis	1.61
Discharging sinuses	1.61
Fissure on angle of mouth	1.61
Fissure Tongue	1.61
Generalised pruritis	1.61
Genital wart	1.61
Intertrigo	1.61
Lichenoid Photodermatitis	1.61
Melasma	1.61
Molluscum contagiosum& Oral candidiasis	1.61
Multiple Pustularbullae with infraauricular swelling	1.61
Nutritional Dermatitis	1.61
Onychomycosis SUH + Onycholysis	1.61
Oral Lichen planus	1.61
Oral Malignancy	1.61

Papular Eruption d/t retroviral infectrion	1.61
Papular Pruritic eruption of HIV	1.61
Perforating Dermatosi	1.61
Pityriasis Versicolor	1.61
PMLE	1.61
Post Anasarca skin exfoliation	1.61
Prurigo Simplex+Onychomycosis	1.61
Scabies+Xerosis	1.61
Sebaceous Hyperplasia (Acne)	1.61
Seborrheic Dermatitis	1.61
secondary syphilis	1.61
Senile purpura	1.61
Stasis Dermatitis	1.61
Tinea Faciei	1.61
Grand Total	100.00
Gender wise prevalence-	
Male	23.27
Female	22.52
WHO Clinical Staging	
WHO stage 1	
<i>Males</i>	47.17
<i>Females</i>	51.35
WHO stage 2	
<i>Males</i>	20.75
<i>Females</i>	23.42
WHO stage 3	
<i>Males</i>	15.72
<i>Females</i>	17.12
WHO stage 4	
<i>Males</i>	16.35
<i>Females</i>	8.11

SUH- Subungal hyperkeratosis, PMLE- Polymorphous light eruption, WHO- world health organization, HIV- human immunodeficiency virus

Table 3: Correlation of Mucocutaneous manifestations with WHO staging (n=270)

Mucocutaneous manifestations	WHO staging				Total
	1	2	3	4	
Squamous cell Carcinoma	0	0	0	1	1
Acne vulgaris	0	0	1	0	1
Acniform eruption	0	1	0	0	1
Acute eczema	0	0	0	1	1
Acute Urticaria	0	0	0	1	1
Albinism	0	1	0	0	1
Bald Tongue	0	0	1	0	1
Chelitis	1	0	1	0	2
Dermatitis	0	1	0	0	1
Diffuse hairfall with pruritis	0	1	0	0	1
Discharging sinuses	0	0	0	1	1
Fissure on angle of mouth	0	1	0	0	1
Fissure Tongue	0	0	1	0	1
Generalised pruritis	0	0	0	1	1
Genital wart	0	0	0	1	1

Intertrigo	0	1	0	0	1
Lichenoid Photodermatitis	0	0	0	1	1
Melasma	1	0	0	0	1
Molluscum contagiosum	0	1	0	1	2
Molluscum contagiosum& Oral candidiasis	0	0	0	1	1
Multiple Pustularbullae with infraauricular swelling	0	0	1	0	1
Nutritional Dermatitis	0	1	0	0	1
Onychomycosis	0	1	2	2	5
Onychomycosis SUH + Onycholysis	0	1	0	0	1
Oral Candidiasis	0	0	3	1	4
Oral Lichen planus	0	0	0	1	1
Oral Malignancy	0	0	1	0	1
Papular Eruption d/t retroviral infectrion	0	0	0	1	1
Papular Pruritic eruption of HIV	0	1	0	0	1
Perforating Dermatitis	0	1	0	0	1
Pityriasis Versicolor	0	1	0	0	1
PMLE	0	0	0	1	1
Post Anasarca skin exfoliation	0	0	1	0	1
Prurigo Simplex	0	0	1	1	2
Prurigo Simplex+Onychomycosis	0	1	0	0	1
Scabies	0	0	3	2	5
Scabies+Xerosis	0	0	1	0	1
Sebaseous Hyperplasia(Acne)	0	0	1	0	1
Seborrheic Dermatitis	0	0	1	0	1
Secondary syphilis	0	0	1	0	1
Senile purpura	0	1	0	0	1
Stasis Dermatitis	0	0	1	0	1
Tinea Corporis	0	1	1	0	2
Tinea Cruris & Corporis	0	1	1	1	3
Tinea Faciei	1	0	0	0	1
Grand Total	132	59	44	35	270

SUH- Subungal hyperkeratosis,PMLE- Polymorphous light eruption, WHO- world health organization, HIV- human immunodeficiency virus

Table 4: Correlation of Mucocutaneous manifestations with sex (n=270)

Mucocutaneous manifestations	Sex		Total
	F	M	
Squamous cell Carcinoma	0	1	1
Acne vulgaris	1	0	1
Acniform eruption	1	0	1
Acute eczema	0	1	1
Acute Urticaria	0	1	1
Albinism	0	1	1
Bald Tongue	0	1	1
Chelitis	2	0	2
Dermatitis	0	1	1
Diffuse hairfall with pruritis	0	1	1
Discharging sinuses	0	1	1

Fissure on angle of mouth	0	1	1
Fissure Tongue	1	0	1
Generalised pruritis	0	1	1
Genital wart	0	1	1
Intertrigo	0	1	1
Lichenoid Photodermatitis	0	1	1
Melasma	1	0	1
Molluscum contagiosum	1	1	2
Molluscum contagiosum& Oral candidiasis	1	0	1
Multiple Pustularbullae with infraauricular swelling	1	0	1
Nutritional Dermatosi	1	0	1
Onychomycosis	1	4	5
Onychomycosis SUH + Onycholysis	0	1	1
Oral Candidiasis	2	2	4
Oral Lichen planus	0	1	1
Oral Malignancy	0	1	1
Papular Eruption d/t retroviral infection	1	0	1
Papular Pruritic eruption of HIV	1	0	1
Perforating Dermatosi	0	1	1
Pityriasis Versicolor	1	0	1
PMLE	1	0	1
Post Anasarca skin exfoliation	1	0	1
Prurigo Simplex	1	1	2
Prurigo Simplex+Onychomycosis	1	0	1
Scabies	4	1	5
Scabies+Xerosis	1	0	1
Sebaceous Hyperplasia (Acne)	0	1	1
Seborrheic Dermatitis	0	1	1
Secondary syphilis	0	1	1
Senile purpura	0	1	1
Stasis Dermatitis	0	1	1
Tinea Corporis	0	2	2
Tinea Cruris & Corporis	0	3	3
Tinea Faciei	0	1	1

SUH- Subungual hyperkeratosis, PMLE- Polymorphous light eruption, WHO- world health organization, HIV- human immunodeficiency virus.