

ORIGINAL ARTICLE

Prevalence and Types of Mucocutaneous Disorders, Their Correlation to CD4 Count and Their Impact on Quality of Life in Adults with HIV Infection

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Abstract

Background

Data on prevalence and type of mucocutaneous diseases in HIV-positive patients and their impact on quality of life (QoL) are sparse. We aim to determine prevalence and type of mucocutaneous disorders, their correlation to CD4⁺ counts and impact on QoL for adults with HIV, using the Dermatology Life Quality Index (DLQI).

Methods

A cross-sectional study of HIV-infected adults seen in HIV and Dermatology Clinic.

Results

The majority (90%) of 174 participants recruited was male. Median age at diagnosis of HIV infection was 29 years (IQR 10). Mucocutaneous disorders were present in 90.2%, out of which 58.6% had two or more mucocutaneous disorders. Mean CD4⁺ count was significantly lower in patients with, compared to those without mucocutaneous disorders (363 vs 548 cells/ μ L; $p=0.030$). Infections accounted for 67.2% of all mucocutaneous disorders seen, followed by inflammatory dermatoses (51.7%), cutaneous adverse drug reactions (17.8%) and neoplasm (2.3%). The five most frequent manifestations were eczema (22.4%), anogenital warts (21.2%), candidiasis (16.7%), dermatophytosis (15.5%) and secondary syphilis (12.0%). Oral candidiasis, pruritic papular eruption, drug-induced maculopapular eruption and drug rash with eosinophilia and systemic symptoms were significantly more prevalent in patients with CD4⁺ counts <200 cells/ μ L but anogenital warts were more prevalent in patients with CD4⁺ counts \geq 200 cells/ μ L. The mean DLQI score was 8.39 (SD \pm 6.83). QoL was severely impaired (DLQI >10) in 34.4%.

Conclusion

Mucocutaneous disorders were common in HIV patients causing significant impairment in quality of life. Prevalence co-related with low CD4⁺ counts. Adequate management of HIV may reduce the prevalence of mucocutaneous disorders and improve QoL.

Key words: Mucocutaneous manifestations, Human immunodeficiency virus infection, CD4⁺ T-cell counts, Quality of life

Introduction

Human immunodeficiency virus (HIV) is a retrovirus that cripples immunity by the destruction of CD4⁺ T-lymphocytes.¹ The underlying immunodeficiency predisposes the HIV-infected patient to a variety

of mucocutaneous disorders.^{2,3} Furthermore, the incidence and severity of these disorders increases as the HIV infection worsens.^{2,3} Although mucocutaneous diseases are rarely life-threatening, they can severely impair the patients' quality of life.⁴ The use of combination antiretroviral therapy (ART) may prolong the patient's life but drug-induced adverse reaction is a problem⁵ because they may cause disfiguring facial lipoatrophy.^{5,6,7}

Interestingly, skin diseases may be the first manifestations of HIV infection.⁸ Hence, knowledge of the prevalence of these mucocutaneous disorders, the types and their impact on the HIV-infected patients' life are important aspects for their optimal management. We set out to study the prevalence of mucocutaneous manifestations in these patients, their types and their impact on patients' quality of life (QoL). We also explored the relationship between these disorders and CD4⁺ T-cell counts, a known indicator of disease progression.

Materials and Methods

This was a cross-sectional study involving adults (18 years and above) who were diagnosed with HIV infection based on ICD-10-CM code B20. Study subjects were approached when they attended their scheduled HIV or Dermatology Clinic, Hospital Sultanah Aminah Johor Bahru (HSAJB), a tertiary referral centre in southern Malaysia. All confirmed HIV patients seen consecutively between 1st May 2019 to 31st July 2019 were recruited into the study which was approved by the Malaysian Ministry of Health Institutional Review Board and Medical Research Ethics Committee (NMRR-19-92-46001). Written consents were given by all patients.

Study Procedures

After consent, patients underwent a thorough interview and full physical examination. CD4⁺ T-cell counts and other relevant blood tests and procedures such as skin biopsies, skin scrapings and cultures were performed based on clinical findings. All findings were recorded in a standard Case Report Form (CRF).

Patients with mucocutaneous disorders were asked to fill up the DLQI questionnaire. DLQI is a 10-item dermatology-specific questionnaire that assesses the impact of skin disease and its treatment on the patient's life such as their symptoms of

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itch, embarrassment, interferences with their daily activities, leisure, work and study, personal relationships and problems in taking the treatment. Each question is scored from 0 to 3; 0 for not at all or not relevant, 1 for a little, 2 for a lot, 3 for very much. Questions 3 to 10 offered a “not relevant” response (NRR) option that was scored as an item that had no impact on study participants’ life. A composite score is then calculated by summing the score of each question. It could range from a minimum of 0 to a maximum of 30. A DLQI score of 0 to 1 means the skin disease has no effect on the patient’s life; 2-5 a small effect, 6-10 a moderate effect, 11-20 a very large effect and 21-30 an extremely large effect on patient’s life.⁹

Statistical Analysis

Descriptive statistics were presented as counts and percentages for categorical variables. Means and standard deviation (SD) was used for normally distributed data while median with an interquartile range (IQR) was used for data which were not normally distributed. Chi-square test, Fisher’s exact test or Kruskal-Wallis test are used for univariate analysis depending on data distribution. Statistical significance was set at $p < 0.05$. Statistical analysis was carried out with the Statistical Package for the Social Sciences (SPSS) (version 23; SPSS Inc., Chicago, IL, USA).

Results

Demographic Characteristics

A total of 174 HIV-infected individuals participated in this study. The male to female ratio was 11.4:1. The median age at diagnosis was 29 (IQR: 10) years. In the racial distribution, 48.3% were Malays, 43.1% Chinese, 8.0% Indian and 0.6% others. About 88% of the study participants completed at least secondary school education level. Most of the participants were currently single and employed (Table 1).

Risk Profile, CD4⁺ T-cell Counts and Treatment Status of 174 HIV-positive Patients

The main mode of HIV transmission was through sexual intercourse with 85% of participants having multiple sexual partners. Forty-five percent of them were homosexual.

Twenty-seven participants (15.5%) were

intravenous drug users, five of them being active users and nineteen of them (70.4%) had multiple sexual partners. Twenty-two participants (12.6%) were either using or had a history of using stimulants either in the form of inhalational drugs or pills during engagement of sexual activities (Table 2).

The median duration of HIV infection was 172 (IQR:287) weeks. The median CD4⁺ T-cell counts were 335 (IQR:508) cells/ μ L. Most of the study participants had already commenced on antiretroviral treatment.

Mucocutaneous Manifestations of the Study Participants

Close to 90% of the participants had at least one mucocutaneous manifestation (Table 3). Furthermore, the CD4⁺ T-cell counts were significantly lower in patients with mucocutaneous manifestations when compared to those without (363 ± 338 cells/ μ L vs 548 ± 229 cells/ μ L; $p=0.030$).

Common mucocutaneous disorders were infections (67.2%), followed by inflammatory dermatoses (51.7%), cutaneous Adverse Drug Reactions (cADR) (17.8%) and neoplasm (2.3%). Participants with CD4⁺ T-cell counts <200 cells/ μ L were significantly more likely to develop cADR. Most of the drug eruption in our study were secondary to sulfamethoxazole/trimethoprim (54.8%), followed by antiretroviral therapy (35.5%), anti-tuberculous drugs (6.5%) and antibiotics (3.2%).

Relationship between CD4⁺ T-cell Counts and Mucocutaneous Manifestations

For study participants with CD4⁺ T-cell counts of <200 cells/ μ L, there were 38% of them who had mucocutaneous manifestations compared to only 6% of them without any manifestations ($p=0.008$) (Table 4).

Several dermatoses were noted to be significantly higher among participants with CD4⁺ T-cell counts <200 cells/ μ L when compared to those higher than 200 cells/ μ L (Table 5). These were candidiasis ($p=0.001$), pruritic papular eruption ($p=0.037$), drug-induced maculopapular eruption ($p=0.001$) and drug rash with eosinophilia and systemic symptoms (DRESS) ($p=0.001$).

However, anogenital warts were noted to be

significantly higher in those with CD4⁺ T-cell counts of ≥ 200 cells/ μ L ($p=0.006$). No differences in CD4⁺ T-cell counts was observed for other mucocutaneous manifestations.

Effect of Mucocutaneous Manifestations on Participants' DLQI Scores

The mean (\pm SD) of the total DLQI score was 8.39 ± 6.83 (range:0-27) (Table 6). When further analysed, the mean (\pm SD) DLQI score for participants who had ≥ 3 mucocutaneous disorders was not significantly higher, scoring 8.73 ± 6.54 ($p=0.858$). In all, 54 participants (34.4%) with mucocutaneous manifestations experienced severely impaired quality of life, having DLQI score >10 . Thirty-five participants (22.3%) had moderate effect while 42 participants (26.8%) had a small effect. No effect was seen in 26 participants (16.6%) (Figure 1).

In the questionnaire, Questions 3 to 10 had a “not relevant response” (NRR) option. About two-thirds of participants chose this option at least once from questions 3 to 10. A higher proportion was recorded for questions on sexual difficulties (38.9%), sports (36.3%) and working or studying (22.9%).

Table 1. Demographic characteristics of 174 study participants with HIV infection

Variables		n (%)
Age category in years	18-30	94 (53.7)
	31-40	44 (25.1)
	41-50	26 (14.9)
	51-60	8 (4.6)
	61-70	2 (1.1)
Gender	Male	160 (92.0)
	Female	14 (8.0)
Ethnicity	Malay	84 (48.3)
	Chinese	75 (43.1)
	Indian	14 (8.0)
	Others	1 (0.6)
Education level	Primary	21 (12.1)
	Secondary	86 (49.4)
	Tertiary	67 (38.5)
Marital status	Single	127 (73.0)
	Married	21 (12.1)
	Divorced	19 (10.9)
	Widow / Widower	7 (4.0)
Occupation	Self-employed	33 (19.0)
	Employee	90 (51.7)
	Unemployed	51 (29.3)

Table 2. Risk profile, CD4⁺ T-cell counts and treatment status of 174 HIV-positive patients

Variables		n (%)
Sexual orientation	Homosexual	79 (45.4)
	Heterosexual	61 (35.1)
	Bisexual	33 (19.5)
Number of sexual partners	Multiple	147 (84.5)
	Single	26 (14.9)
Risk factors of HIV transmission	Sexual transmission	147 (84.5%)
	Sexual transmission & Intravenous drug user	26 (14.9%)
	Intravenous drug user	1 (0.6%)
CD4 ⁺ T-cell counts	<200 cells/ μ L	61 (35.1)
	200-349 cells/ μ L	30 (17.2)
	350-499 cells/ μ L	28 (16.1)
	>500 cells/ μ L	55 (31.6)
Participants on antiretroviral treatment (ART)	Yes	129 (74.1)
	No	45 (25.9)

Table 3. Comparison of mean CD4⁺ T-cell counts in 174 HIV-positive patients with and without Mucocutaneous Disorders

Variables	n (%)	Mean CD4 ⁺ T-cell Counts (cells/ μ L \pm SD)		p-value ^a
		Presence of Disorders (n=157)	Absence of Disorders (n=17)	
All mucocutaneous manifestations	157 (90.2)	363 \pm 338	548 \pm 229	0.030
1 Disorder	65 (37.3)	378 \pm 280		
2 Disorders	43 (24.7)	364 \pm 362		
≥ 3 Disorders	49 (28.2)	342 \pm 388		
Infection*	117 (67.2)	381 \pm 360	381 \pm 270	0.991
Inflammatory dermatoses*	90 (51.7)	361 \pm 329	403 \pm 337	0.406
Cutaneous adverse drug reactions (cADR)*	31 (17.8)	194 \pm 249	422 \pm 335	<0.001
Neoplasm*	4 (2.3)	404 \pm 323	381 \pm 334	0.891

SD = Standard deviation; ^aindependent samples T-Test
^{*}One patient may have multiple mucocutaneous manifestations; the percentage reported is based on total patients in each group

Table 4. The effect of CD4⁺ T-cell counts on Mucocutaneous Manifestations

CD4 ⁺ T-cell Counts	Mucocutaneous Manifestations		p-value ^b
	Yes (%)	No (%)	
<200 cells/ μ L	60 (34.5)	1 (0.6)	0.008
≥ 200 cells/ μ L	97 (55.7)	16 (9.2)	

^bChi-Square test

Table 5. Relationship between type of Mucocutaneous Manifestations and CD4⁺ T-cell counts

Variables		n (%)	Participants with CD4 ⁺ T-cell Counts (cells/ μ L) <200 {n=60 (%)}	Participants with CD4 ⁺ T-cell Counts (cells/ μ L) ≥200 {n=97 (%)}	p-value ^b
All mucocutaneous manifestations		157 (90.2)			0.248
	1 Disorder	65 (37.3)	24 (40.0)	41 (42.3)	
	2 Disorders	43 (24.7)	13 (21.7)	30 (30.9)	
	≥3 Disorders	49 (28.2)	23 (38.3)	26 (26.8)	
Infection*					
Viral					
Human papillomavirus	Anogenital warts	37 (21.2)	7 (11.7)	30 (30.9)	0.006
	Palmoplantar warts	6 (3.4)	3 (5.0)	3 (3.1)	0.675 ^c
	Herpes simplex virus	10 (5.7)	6 (10.0)	4 (4.1)	0.183 ^c
	Molluscum contagiosum	6 (3.4)	3 (5.0)	3 (3.1)	0.675 ^c
	Varicella and Herpes zoster virus infection	5 (2.9)	3 (5.0)	2 (2.1)	0.371 ^c
	Oral hairy leukoplakia	3 (1.7)	3 (5.0)	0 (0)	0.054 ^c
Fungal	Candidiasis	29 (16.7)	20 (33.3)	9 (9.3)	0.000
	Dermatophytes	27 (15.5)	9 (15.0)	18 (18.6)	0.566
	Deep fungal infection	3 (1.7)	3 (5.0)	0 (0)	0.054 ^c
Bacterial	Syphilis	21 (12.0)	7 (11.7)	14 (14.4)	0.621
	Cellulitis	12 (6.9)	3 (5.0)	9 (9.3)	0.375 ^c
	Impetigo	5 (2.9)	0 (0)	5 (5.2)	0.157 ^c
	Abscesses / Carbuncle	1 (0.6)	0 (0)	1 (1.0)	1.000 ^c
Parasitic	Scabies	1 (0.6)	1 (1.7)	0 (0)	0.382 ^c
	Pediculosis capitis	1 (0.6)	0 (0)	1 (1.0)	1.000 ^c
Inflammatory dermatosis*					
Inflammatory dermatosis*	Eczema	39 (22.4)	12 (20.0)	27 (27.8)	0.270
	Pruritic papular eruption	14 (8.0)	9 (15.0)	5 (5.2)	0.035 ^c
	Acne vulgaris	11 (6.3)	2 (3.3)	9 (9.3)	0.207 ^c
	Psoriasis	10 (5.7)	2 (3.3)	8 (8.2)	0.320 ^c
	Prurigo nodularis	8 (4.6)	4 (6.7)	4 (4.1)	0.482 ^c
	Seborrheic dermatitis	7 (4.0)	3 (5.0)	4 (4.1)	1.000 ^c
	Urticaria	5 (2.9)	2 (3.3)	3 (3.1)	1.000 ^c
	Hidradenitis suppurativa	4 (2.3)	1 (1.7)	3 (3.1)	1.000 ^c
	Ichthyosis	3 (1.7)	2 (3.3)	1 (1.0)	0.558 ^c
	Xerosis	2 (1.1)	2 (3.3)	0 (0)	0.145 ^c
	Cutaneous vasculitis	1 (0.6)	1 (1.7)	0 (0)	0.382 ^c
	Photodermatitis	1 (0.6)	0 (0)	1 (1.0)	1.000 ^c
	Other inflammatory dermatosis	5 (2.9)	0 (0)	5 (5.2)	0.157 ^c
Cutaneous Adverse Drug Reactions (cADR)*					
Cutaneous Adverse Drug Reactions (cADR)*	Maculopapular eruption	16 (9.2)	12 (20.0)	4 (4.1)	0.001
	Drug rash with Eosinophilia and Systemic symptoms	8 (4.6)	8 (13.3)	0 (0)	0.000 ^c
	Lipodystrophy	5 (2.9)	0 (0)	5 (5.2)	0.157 ^c
	Toxic epidermal necrolysis	2 (1.1)	2 (3.3)	0 (0)	0.145 ^c
	Erythema multiforme	1 (0.6)	1 (1.7)	0 (0)	0.382 ^c
Other cADRs	2 (1.1)	1 (1.7)	1 (1.0)	1.000 ^c	
Neoplasm*					
Neoplasm*	Cutaneous lymphoma	2 (1.1)	1 (1.7)	1 (1.0)	1.000 ^c
	Kaposi's sarcoma	1 (0.6)	0 (0)	1 (1.0)	1.000 ^c
	Bowen's disease	1 (0.6)	0 (0)	1 (1.0)	1.000 ^c

^bChi-Square test; ^cFisher's exact test

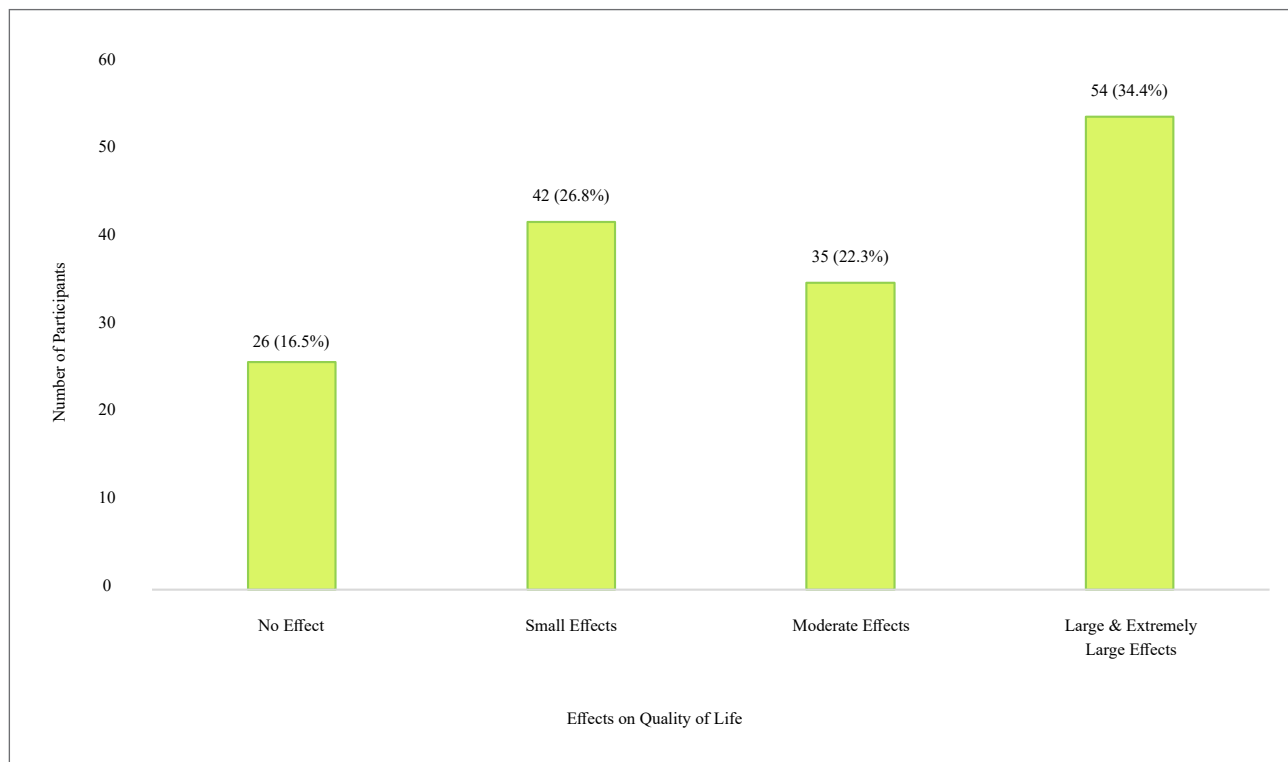
*One patient may have multiple mucocutaneous manifestations; the percentage reported is based on total patients in each group

Table 6. The effect of Mucocutaneous Manifestations on participants’ mean DLQI scores

Variables		Mean DLQI Scores (SD)	p-value ^a
General effect of Mucocutaneous Manifestations	Yes	8.39 (6.83)	
	No		
Infection	Yes	8.65 (6.95)	0.017
	No	6.05 (6.10)	
Inflammatory dermatoses	Yes	7.87 (5.84)	0.892
	No	7.73 (7.69)	
Neoplasm	Yes	6.25 (9.85)	0.645
	No	7.84 (6.73)	
Cutaneous adverse drug reactions (cADR)	Yes	8.71 (6.34)	0.411
	No	7.60 (6.87)	
DLQI components			
Symptoms and Feeling	Yes	2.38 (1.81)	0.001
	No	0.82 (0.95)	
Daily activities	Yes	1.50 (1.89)	0.002
	No	0.06 (0.24)	
Leisure	Yes	1.24 (1.76)	0.009
	No	0.12 (0.49)	
Daily activities	Yes	0.65 (1.15)	0.009
	No	0.12 (0.49)	
Daily activities	Yes	0.65 (1.15)	0.009
	No	0.12 (0.49)	
Treatment	Yes	0.65 (1.15)	0.009
	No	0.12 (0.49)	

^aIndependent samples T-Test

Figure 1. Effects of Mucocutaneous Manifestations on participants’ DLQI



Discussion

Ever since its recognition in 1981, HIV has become a major global public health issue. In 2019, there were 1.7 million newly infected people of whom 690,000 people died from its related causes.¹⁰

Malaysia is no different; by the end of 2018 it is estimated that 87,041 people would have lived with HIV in Malaysia and 55% of these will be receiving antiretroviral treatment (ART).¹¹ Close to 80% of our study participants were below 40 years old of

which, 92% were of males. These figures are similar to those reported by Wang Jing in 2000 in Malaysia who showed that 75% of his study participants were less than 40 years old and with a male preponderance of 87%.¹²

Homosexual contact was the most common mode of transmission in our patients. However, two previous studies from Singapore and Malaysia showed that most of their study participants were heterosexuals.^{12,13} Furthermore, Kanter *et al.*¹⁴ in 2011 screened 517 men who had sex with men in Kuala Lumpur and found that 3.9% of them tested positive for HIV infection. This study shows a change in risk factor for HIV transmission and therefore, targeted interventions should be offered to prevent and control HIV transmission.¹⁵

Mucocutaneous manifestations are common in patients of HIV. They may occur anytime during the course of the disease. Ninety percent of our patients displayed at least one type of dermatological manifestation whereby more than half had 2 or more mucocutaneous disorders. This high prevalence is likely attributed to recruitment of patients done in a tertiary referral centre of HIV and Dermatology Clinic. Consistent with observation documented by Li *et al.*¹⁶, our study showed that patients with mucocutaneous disorders had significantly lower CD4⁺ T-cell counts. However, no significant difference in CD4⁺ T-cell counts was observed between patients with one and more than one mucocutaneous disorders. This contradicted findings by Li *et al.*¹⁶ who showed that significant reduction in CD4⁺ T-cell count occurred with increasing number of mucocutaneous manifestations.

Infections

Human papillomavirus (HPV) infection in the form of anogenital warts was noted to occur frequently among our participants, especially those with CD4⁺ T-cell counts >200 cells/ μ L. In contrast to our findings, Chikandiwa *et al.*¹⁷ showed that anogenital warts were more prevalent among those with lower CD4⁺ T-cell counts (<200 cells/ μ L). HIV infection may have altered the natural history of HPV infection and thus were more common among individuals with HIV infection, regardless of their CD4⁺ T-cell counts.¹⁹ Furthermore, our findings might be related to the fact that 84.5% of our study participants had multiple sexual partners

and 45.4% of them were homosexual. This finding is supported by other workers. Dareng *et al.*¹⁸ showed that anogenital warts were more prevalent among his study participants who had multiple sexual partners. Similarly, Sonnenberg *et al.*¹⁹ found that the diagnosis of anogenital warts were more frequent in men who had sex with men.

On the other hand, candidiasis seemed to be predominant among our participants with CD4⁺ T-cell counts of less than 200 cells/ μ L. Altuntas *et al.*²⁰ and Kore *et al.*²¹ showed similar results. Interestingly, in our study, there was a significant lower prevalence of candidiasis in patients who were on ART treatment. This is in line with the study by Hengge *et al.*²² in which they found a decrease in the prevalence of oral candidiasis after ART administration. This implies that candidiasis infection is related to low immune function. Candidiasis may therefore be an important indicator of progression of the HIV infection and starting ART could decline its prevalence.

Secondary syphilis was present in 12% of study participants, it being the most common bacterial infection with 71.4% occurring among the homosexuals. This finding is not surprising as syphilis is associated with high-risk sexual behaviours and infection substantially increases in association with HIV transmission and acquisition.²³ In Canada, the incidence of syphilis was 300-fold greater among male who had sex with male positive for HIV than the reported case rate in the general male population.²⁴

Inflammatory Dermatoses

Of the inflammatory dermatoses, the most common manifestations were eczema (22.4%), followed by pruritic papular eruption (PPE) (8.0%), psoriasis (6.3%) and acne vulgaris (6.3%). However, of these only pruritic papular eruption was significantly associated with CD4⁺ T-cell counts of less than 200 cells/ μ L. A similar observation was reported by Resnick *et al.*²⁵ and Farsani *et al.*²⁶ and they postulated that PPE reflects an altered and exaggerated immune response to arthropod antigens among HIV-infected individuals.

Eczema was present in 22.4% of our participants. Similar percentage was reported in a group of patients from Thailand.²⁷ It is known that both

eczema and HIV share a similar Th2 cytokine profile characterized by elevated IgE, eosinophils, IL-4 and IL-5 levels. This may explain the relationship between the two diseases.^{28, 29}

Psoriasis was seen in 6.3% of our patients, an incidence much higher than that reported (2.9%) by others from Iran.³⁰ We also found that in about 50% of our patients' psoriasis were aggravated soon after the diagnosis of HIV infection. This may be related to the fact that the HIV, in attacking CD4⁺ T-cells increases the proportion of CD8⁺ T-cells which in turn secrete IFN- γ and aggravates psoriasis.³¹

Cutaneous Adverse Drug Reactions

HIV-infected individuals have both an immunologic dysfunction and do take a diverse set of drugs. A higher incidence of drug eruption among these individuals may therefore be expected.³² Cutaneous Adverse Drug Reactions (cADR) affected 17.8% of the study participants and this was positively correlated with those patients with CD4⁺ T-cell counts of less than 200 cells/ μ L, especially in those with maculopapular eruption and drug rash with eosinophilia and systemic symptoms (DRESS). This shows that drug eruptions are strongly related to the patient's immune function.³³

Most of the cADR were secondary to sulfamethoxazole/trimethoprim, followed by antiretroviral therapy, anti-tuberculous drugs and antibiotics, which was also portrayed in other studies.^{34,35} The frequent occurrence of opportunistic infections among HIV patients³⁶ often leads to concurrent use of sulfamethoxazole/trimethoprim for *Pneumocystis jirovecii* pneumonia prophylaxis and anti-tuberculous therapy, both of which are well-documented instigators of mild to severe cADR. These reactions can seriously impede effective management of HIV and opportunistic infections among HIV-infected individuals.

Dermatology Life Quality Index

HIV patients with mucocutaneous manifestations had a mean (\pm SD) DLQI score of 8.39 ± 6.83 . More than one-third of HIV-infected individuals felt that having mucocutaneous manifestations severely affected their quality of life. This finding was similarly reported by Shittu *et al.*³⁷ Severe impairment of QoL (DLQI >10) was clearly shown affecting our patients presenting with

mucocutaneous disorders regardless of the numbers of manifestations experienced by them.

Not with standing, the mean DLQI scores in our patients may have been underestimated because, about 67% of them chose the "not relevant response". These were in the areas of sexual difficulties (38.9%), sports (36.3%) and working or studying (22.9%). Abstaining from these activities on account of their mucocutaneous diseases might have been the reason for them choosing the NRR option. Rencz *et al.*³⁸ noted similar findings whereby, their participants with psoriasis also picked NRR options for sexual difficulties, sports and working or studying.

The presence of mucocutaneous manifestations also caused significant discomfort in terms of itchiness, pain and embarrassment in our participants. A similar finding was seen in newly diagnosed HIV/AIDS-infected patients in a study from Nigeria.³⁷ Daily and leisure activities were also impaired in our patients with mucocutaneous manifestations as opposed to those with none. In addition, they found it burdensome to seek treatment on account of their mucocutaneous manifestations.

Limitations

This study involved only single centre and had a relatively short study duration of three months. In using convenience sampling, the participants may not have been representative of the target population.

Conclusion

Mucocutaneous disorders were common and diverse among patients with HIV infection. More than one-third of patients with mucocutaneous manifestations had severely impaired quality of life. Hence, early and adequate treatment of HIV patients may reduce the prevalence of mucocutaneous disorders and their impact on patients' QoL. Cutaneous ADR including potentially life-threatening DRESS were significantly higher in patients with CD4⁺ T-cell counts <200 cells/ μ L. This highlights the need for caution in prescribing only absolutely necessary medication for HIV patients with low CD4⁺ T-cell counts.

Conflict of Interest Declaration

The authors have no conflict of interest to declare.

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References

- de Goede AL, Vulto AG, Osterhaus AD, Gruters RA. Understanding HIV infection for the design of a therapeutic vaccine. Part I: Epidemiology and pathogenesis of HIV infection. *Ann Pharm Fr* 2015;73:87-99.
- Chandrakala C, Parimalam K, Wahab AJ, Anand N. Correlating CD4 count with mucocutaneous manifestations in HIV-positive patients: A prospective study. *Indian J Sex Transm Dis AIDS* 2017;38:128-35.
- Raju PV, Rao GR, Ramani TV, Vandana S. Skin disease: clinical indicator of immune status in human immunodeficiency virus (HIV) infection. *Int J Dermatol* 2005;44:646-9.
- Kanmani CI, Udayashankar C, Nath AK. Dermatology life quality index in patients infected with HIV: A comparative study. *Egypt Dermatol Online J* 2013;9:3.
- Masuka JT, Chipangura P, Nyambayo PP, Stergachis A, Khoza S. A Comparison of Adverse Drug Reaction Profiles in Patients on Antiretroviral and Antitubercular Treatment in Zimbabwe. *Clin Drug Investig* 2018;38:9-17.
- Ward HA, Russo GG, Shrum J. Cutaneous manifestations of antiretroviral therapy. *J Am Acad Dermatol* 2002;46:284-93.
- Birbal S, Dheda M, Ojewole E, Oosthuizen F. Adverse drug reactions associated with antiretroviral therapy in South Africa. *Afr J AIDS Res* 2016;15:243-8.
- Mirnezami M, Zarinfar N, Sofian M, Botlani Yadegar B, Rahimi H. Mucocutaneous Manifestations in HIV-Infected Patients and Their Relationship to CD4 Lymphocyte Counts. *Scientifica (Cairo)* 2020;2020:7503756.
- Finlay AY, Khan G. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994;19:210-6.
- Joint United Nations Programme on HIV/AIDS (2020). Global HIV & AIDS statistics - 2019 fact sheet. Available online: <http://www.unaids.org/en/resources/fact-sheet>. Assessed on 19 February 2021.
- Ministry of Health Malaysia. Country Progress Report on HIV/AIDS 2019 Malaysia. Available online: [http://www.moh.gov.my/Umum/Report_GAM_2019_\(Final\)](http://www.moh.gov.my/Umum/Report_GAM_2019_(Final)). Assessed on 19 February 2021.
- Jing W. A Retrospective Survey of Mucocutaneous Manifestations of HIV Infection in Malaysia: Analysis of 182 Cases. *J Dermatol* 2000;27:225-32.
- Goh BK, Chan RKW, Sen P, Theng CTS, Tan HH, Wu YJ et al. Spectrum of skin disorders in human immunodeficiency virus-infected patients in Singapore and the relationship to CD4 lymphocyte counts. *Int J Dermatol* 2007;46:695-9.
- Kanter J, Koh C, Razali K, Tai R, Izenberg J, Rajan L et al. Risk behaviour and HIV prevalence among men who have sex with men in a multiethnic society: a venue-based study in Kuala Lumpur, Malaysia. *Int J STD AIDS* 2011;22:30-7.
- Ramakrishnan L, Ramanathan S, Chakrapani V, Goswami P, Deshpande S, Yadav D et al. Comparison of Sexual Risk, HIV/STI Prevalence and Intervention Exposure Among Men Who Have Sex with Men and Women (MSMW) and Men Who Have Sex with Men Only (MSMO) in India: Implications for HIV Prevention. *AIDS Behav* 2015;19:2255-69.
- Li YY, Yang SH, Wang RR, Tang JT, Wang HM, Kuang YQ. Effects of CD4 cell count and antiretroviral therapy on mucocutaneous manifestations among HIV/AIDS patients in Yunnan China. *Int J Dermatol* 2020;59:308-13.
- Chikandiwa A, Kelly H, Sawadogo B, Ngou J, Pisa PT, Gibson L et al. Prevalence, incidence and correlates of low risk HPV infection and anogenital warts in a cohort of women living with HIV in Burkina Faso and South Africa. *PLoS One* 2018;13:e0196018.
- Dareng EO, Adebamowo SN, Famooto A, Olawande O, Odotola MK, Olaniyan Y et al. Prevalence and incidence of genital warts and cervical Human Papillomavirus infections in Nigerian women. *BMC Infect Dis* 2019;19:27:1-10.
- Sonnenberg P, Tanton C, Mesher D, King E, Beddows S, Field N et al. Epidemiology of genital warts in the British population: implications for HPV. *Sex Transm Infect* 2019;95:386-90.
- Altuntas Aydin Ö, Kumbasar Karaosmanoglu H, Korkusuz R, Özeren M, Özcan N. Mucocutaneous manifestations and the relationship to CD4 lymphocyte counts among Turkish HIV/AIDS patients in Istanbul, Turkey. *Turk J Med Sci* 2015;45:89-92.
- Kore SD, Kanwar AJ, Vinay K, Wanchu A. Pattern of mucocutaneous manifestations in human immunodeficiency virus-positive patients in North India. *Indian J Sex Transm Dis AIDS* 2013;34:19-24.
- Hengge UR, Franz B, Goos M. Decline of infectious skin manifestations in the era of highly active antiretroviral therapy. *AIDS* 2000;14:1069-70.
- Peeling RW, Mabey D, Kamb ML, Chen XS, Radolf JD, Benzaken AS. Syphilis. *Nat Rev Dis Primers* 2017;3:17073.
- Burchell AN, Allen VG, Gardner SL, Moravan V, Tan DH, Grewal R et al. High incidence of diagnosis with syphilis co-infection among men who have sex with men in an HIV cohort in Ontario, Canada. *BMC Infect Dis* 2015;15:356.
- Resneck JS Jr, Van Beek M, Furmanski L, Oyugi J, LeBoit PE, Katabira E et al. Etiology of pruritic papular eruption with HIV infection in Uganda. *JAMA* 2004;292:2614-21.
- Farsani TT, Kore S, Nadol P, Ramam M, Thierman SJ, Leslie K et al. Aetiology and risk factors associated with a pruritic papular eruption in people living with HIV in India. *J Int AIDS Soc* 2013;16:17325.
- Punyaratabandhu P, Prasithsirikul W, Jirachanakul P. Skin manifestation of Thai HIV infected patients in HAART era. *J Med Assoc Thai* 2012;95:497-504.
- Rudikoff D. The relationship between HIV infection and atopic dermatitis. *Curr Allergy Asthma Rep* 2002;2:275-81.
- Garg T, Sanke S. Inflammatory dermatoses in human immunodeficiency virus. *Indian J Sex Transm Dis AIDS* 2017;38:113-10.
- Davarpanah MA, Motazedian N, Jowkar F. Dermatological manifestations of HIV/AIDS individuals in Shiraz, South of Iran. *J Glob Infect Dis* 2018;10:80-3.
- Patel RV, Weinberg JM. Psoriasis in the patient with human immunodeficiency virus, part 1: review of pathogenesis. *Cutis* 2008;82:117-22.
- Tzung TY, Yang CY, Chao SC, Lee YJ. Cutaneous Manifestations of Human Immunodeficiency Virus Infection in Taiwan. *Kaohsiung J Med Sci* 2004;20:216-24.
- Huang XJ, Li HY, Chen DX, Wang XC, Li ZC, Wu YS et al. Clinical analysis of skin lesions in 796 Chinese HIV-positive patients. *Acta Derm Venereol* 2011;91:552-6.

34. Hoosen K, Mosam A, Dlova NC, Grayson W. An Update on Adverse Cutaneous Drug Reactions in HIV/AIDS. *Dermatopathology (Basel)* 2019;6:111-25.
35. Coopman SA, Johnson RA, Platt R, Stern RS. Cutaneous disease and drug reactions in HIV infection. *N Engl J Med* 1993;328:1670-4.
36. Lee CY, Wu PH, Lu PL, Tsai HC. Changing Spectrum of Opportunistic Illnesses among HIV-Infected Taiwanese Patients in Response to a 10-Year National Anti-TB Programme. *J Clin Med* 2019;8:163.
37. Shittu RO, Odeigah LO, Mahmoud AO, Sani MA, Bolarinwa OA. Dermatology Quality of Life Impairments among Newly Diagnosed HIV/AIDS-Infected Patients in the University of Ilorin Teaching Hospital (Uith), Ilorin, Nigeria. *J Int Assoc Provid AIDS Care* 2013; doi: 10.1177/2325957413488207.
38. Rencz F, Poór AK, Péntek M, Holló P, Kárpáti S, Gulácsi L et al. A detailed analysis of “not relevant” responses on the DLQI in psoriasis: potential biases in treatment decisions. *J Eur Acad Dermatol Venereol* 2018;32:783-90.