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Original Research Article

Change in profile of cutaneous manifestations of HIV after the advent of antiretroviral therapy: a retrospective analysis

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ABSTRACT

Background: To date, there has been no study conducted in Zambia to determine the prevalence of mucocutaneous conditions among HIV positive patients on antiretroviral therapy.
Methods: The aim of the study was to determine the differences in cutaneous manifestations of HIV between HIV positive adult patients on antiretroviral therapy and antiretroviral naïve patients.
Results: A total of 143 adult HIV/AIDS patients with dermatological manifestations, and fulfilling inclusion criteria, were included. Among the 58 patients on antiretroviral therapy, the most common dermatoses were hyper-pigmentation (18.97%), fungal dermatitis (17.24%) genital herpes (8.62%), papular pruritic eruption (8.62%), oral candidiasis (8.62%) and Kaposi's sarcoma (6.9%). The most common dermatoses among the 85 antiretroviral naive patients were oral candidiasis (34.12%), herpes Zoster (17.65%), hyper pigmentation (8.24%), eosinophillic folliculitis (7.06%), abscesses (5.88%), herpes labialis (4.71%) and Kaposi's sarcoma (4.71%). Among patients in Stage III of HIV infection, the proportion of patients with infectious dermatoses was significantly greater than the proportion of patients with non-infectious dermatoses (47.5% versus 28.6%; p=0.036).The odds of having an infectious dermatosis were 28% lower for patients on antiretroviral therapy as compared to antiretroviral naive patients (p=0.001).
Conclusions: There is a changing profile of muco-cutaneous conditions in HIV infected patients. Infectious dermatoses such as oral candidiasis and Herpes Zoster infections occur more frequently in antiretroviral naïve patients, as compared to patients on ART. Prevention of infectious dermatological conditions occurs with the use of ART.

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

INTRODUCTION

With development of antiretroviral drugs, human immunodeficiency virus (HIV) infected individuals live longer and better, both in developed and developing countries.[1] In 2010, 7.7 million HIV-infected population of the world were on antiretroviral therapy which rose to 24.5 million at the end of June, 2019. 62% of HIV infected adult population accessed antiretroviral therapy.[2] Dermatologic conditions are common in individuals with HIV and can be an initial or presenting manifestation of HIV infection.[3] Antiretroviral therapy has changed the profile of mucocutaneous manifestations of HIV. Incidence, prevalence and severity of some of the

dermatological conditions have changed. However, these conditions are still common among HIV patients. For instance, cutaneous drug reactions and non-infectious dermatological conditions are still encountered frequently among HIV patients receiving antiretroviral therapy.[4,5] A phenomenon that is increasingly seen in patients on antiretroviral therapy is immune reconstitution inflammatory syndrome (IRIS). IRIS may present with new cutaneous manifestations, or worsening of pre-existing skin disease.[6]

IRIS represents a paradoxical worsening of patients' clinical condition weeks to months after commencing antiretroviral therapy. This is despite improvements in the CD 4 count and decline in the HIV viral load.[7] Most cases of IRIS occur within 3 months of commencing antiretroviral therapy.[8] IRIS is most frequently seen in HIV patients who are co-infected with *Mycobacterium tuberculosis* (TB), *Mycobacterium avium complex* (MAC), *Cryptococcus neoformans* and Cytomegalovirus infection (CMV).[9] About 52-78% of the cases of IRIS involve the skin.[9] Paradigm shift due to immune restoration after antiretroviral therapy may risk them to methicillin resistance *Staphylococcus aureus* (MRSA) infections, HPV-related neoplasia, and other cutaneous infections.[10]

In addition, trichodysplasia spinulosa (TS); a rare disease of immunosuppressed patients caused by *trichodysplasia-associated polyomavirus* (TSPyV) where dermatological features are of folliculocentric papules and keratin spicules; may get unmasked after antiretroviral therapy.[11-13] HIV-pruritus may increase due to drug reactions because of ART.[14] The prevalence of these conditions among antiretroviral therapy patients in Zambia is unknown. A previous study, done by Hira et al assessed dermatological manifestation of HIV in patients who were not on antiretroviral therapy as it was not available at that time.[15] Zambia, like many other African countries, has adopted the 'test and treat' strategy of antiretroviral therapy, in order to facilitate the epidemic control of HIV/AIDS.[16] Using this strategy, more people will have access to antiretroviral therapy. As a result, more people may present with cutaneous symptom that are related to antiretroviral therapy. This study will enable the characterization of dermatological conditions in patients on antiretroviral therapy in Zambia, in order to develop guidelines that can be used by health care workers to manage these conditions.

Objectives

The primary objective of this study is to evaluate cutaneous manifestations of HIV in patients on antiretroviral therapy, as compared to patients who are not on antiretroviral therapy. This will help to formulate differential diagnoses that health care workers in Zambia should consider when they encounter dermatological conditions in patients on antiretroviral therapy.

METHODS

Study design

This was a retrospective medical record review of patients attending an out-patient antiretroviral clinic at Levy Mwanawasa university teaching hospital, Lusaka, Zambia, from the period 2002-2019. At enrolment, each patient was given a unique patient identifying number. HIV testing was done by using Determine Rapid HIV test kits, followed by confirmation with Standard Diagnostics (SD) Bioline HIV 1/2 test kit. CD 4 count was measured by flow-cytometry using the PD-FACS count machine. Testing for syphilis was done using Bioline 3.0 syphilis Rapid test. We tested for the Hepatitis B surface antigen (HBsAg) using Standard Diagnostics Bioline HBsAg 3.0 Elisa test kits. Biochemistry tests were done using the Pentra 2000 machine. Hematological tests were done using Sysmex-XT-1800i machine. Data was collected during the period November 2019 to April 2020.

Inclusion criteria

Only medical records belonging to patients aged 18 and above, who had a dermatological diagnosis, were considered for inclusion in the analysis. All medical records were required to have results of CD 4 count at baseline, and at the time of dermatological diagnosis, in order to be included.

Exclusion criteria

Medical records of patients who had dermatological disorder prior to the diagnosis of HIV and/or had undergone dermatological treatments in the 6-12 weeks prior to commencement of antiretroviral therapy were excluded. Patients with co-existent diabetes or kidney disease were not included in the study. Patients having co-existent peripheral vascular disease, connective tissue disease or internal malignancy were excluded.

Sample size and data extraction

143 records were included in the analysis. These were classified as antiretroviral naïve (85 medical records) and antiretroviral experienced (58 medical records). Data was extracted from the medical records using a structured data collection tool. A copy of this is included in the appendix. Data was collected during the period November 2019 to April 2020.

Statistical analysis

Data was analyzed using SPSS version 23. The primary outcome variable was the difference in the frequency and type of cutaneous diseases between patients on antiretroviral therapy, and patients not on antiretroviral therapy. The secondary outcome variable was the relationship between dermatological conditions and the CD4 cell count, and the relationship between

dermatological conditions and the clinical stage of the disease. Descriptive statistics were use to describe the demographic and baseline laboratory parameters of the study population. Chi-square test was used to determine association between categorical variables. A P-value less than 0.05 were considered as statistically significant. Fischer's exact p value was used where at least one of the cells had expected frequencies less than 5. For bivariate analysis, cutaneous lesions were classified as either infectious or non-infectious. Eosinophillic folliculitis, papular pruritic eruption, allergic dermatitis, alopecia and hyper pigmentation were classified as noninfectious. The rest of the cutaneous conditions were classified as infectious.

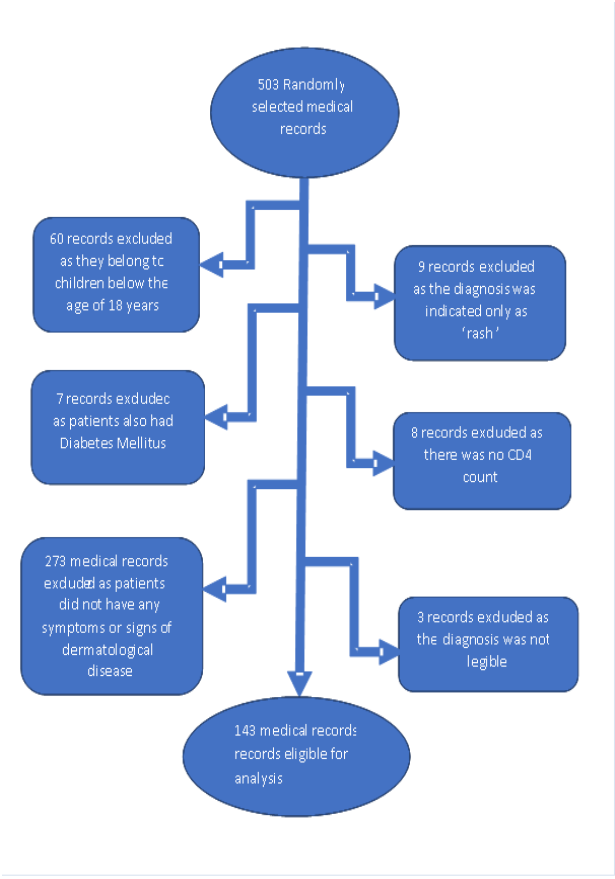

Figure 1: Medical record selection process.

RESULTS

Sociodemographic characteristics of study population

Of the 143 patients included in the analysis, 58 (40.6%) were on antiretroviral therapy while 85 (59.4%) were antiretroviral naive. 69 patients (48%) were male while 74 (52%) were female. For patients on antiretroviral therapy, the majority (33%) were in the age group 45 to 55 years. The majority of antiretroviral naive patients (39%) were in the age group 35 to 44 years. Demographic characteristics of the study population like marital status, occupation, income, education level are described in (Table 1).

Baseline ART duration and laboratory parameters of study population

The mean duration on ART was 68.98 weeks (95% CI 41.84 to 96.82; standard deviation 103.22) for patients on antiretroviral therapy. The median baseline CD4 count was 152 for antiretroviral naive patients and 121 for patients on antiretroviral therapy. The baseline hematological and biochemical laboratory test results of the study population are shown in (Table 2).

Hepatitis B and syphilis among study participants

9% of the study population tested positive for Syphilis. 3 % had positive HbsAg tests, as shown in (Table 3).

CD4 counts of study participants

There was no significant difference in the CD 4 categories between patients on antiretroviral therapy and antiretroviral naive patients. Among anti-retroviral naive patients 58% (49) had dermatological conditions at CD4 count below 200. 18% (15) of antiretroviral naïve patients had dermatological conditions at CD4 count between 200 and 350; while 24% (21) had dermatological conditions at CD4 count above 350. Among patients on antiretroviral therapy, 50% (29) had CD4 count below 200, 26% (15) had CD4 count between 200 and 350, while 24% (14) had CD4 count above 350. The association between CD4 count and antiretroviral status is shown in (Table 4).

Most frequently occurring dermatoses in study population

Among the 58 patients on antiretroviral therapy, the most common dermatoses were hyper pigmentation (18.97%), fungal dermatitis (17.24%) genital herpes (8.62%), papular pruritic eruption (8.62%), oral candidiasis (8.62%) and Kaposi's sarcoma (6.9%). Other conditions that were encountered include eosinophillic folliculitis (5.17%), pruritus (3.45%), nodular prurigo (3.45%) and herpes Zoster (3.45%). The most common dermatoses among the 85 antiretroviral naive patients were oral candidiasis (34.12%), herpes Zoster (17.65%), hyper pigmentation (8.24%), eosinophillic folliculitis (7.06%), abscesses (5.88%), herpes labialis (4.71%) and Kaposi's sarcoma (4.71 %). Other conditions that occurred among antiretroviral naive patients include genital warts (2.35%), genital ulcers (2.35%), fungal dermatitis (2.35%), molluscum contagiosum (2.35%), Angular cheilitis (2.35%), genital herpes (1.18%), hair changes (1.18%), nodular prurigo (1.18%) and papular pruritic eruption (1.18%). The most frequently occurring dermatoses in patients on antiretroviral therapy and in antiretroviral-naïve patients is shown in (Table 5).

Table 1: Demographic characteristics of study participants.

Parameters		Not on ART		On ART		Total
		N	%	N	%	
Age groups (years)	15-24	4	5	2	3	6
	25-34	20	24	10	17	30
	35-44	33	39	18	31	51
	45-55	18	21	19	33	37
	56+	10	12	9	16	19
Sex	Female	42	49	32	55	74
	Male	43	51	26	45	69
Marital status	Divorced	15	18	5	9	20
	Married	34	40	28	48	62
	Single	23	27	11	19	34
	Widowed	7	8	5	9	12
	Unknown	6	7	9	16	15
Occupation	Formal Govt	12	14	8	14	20
	Formal Private Sector	13	15	10	17	23
	Self Employed	35	41	21	36	56
	Student	6	7	3	5	9
	Unemployed	9	11	5	9	14
	Unknown	10	12	11	19	21
Income	No income	11	13	6	10	17
	ZMK 1-499	5	6	0	0	5
	ZMK 500 +	43	51	17	30	60
	Unknown	26	30	35	60	61
Education Level	College/University	33	39	22	38	55
	Never been to school	2	2	3	5	5
	Primary	8	9	4	7	12
	Secondary	34	40	17	29	51
	Unknown	8	9	12	21	20

Table 2: Baseline parameters of study participants.

Parameter	On ART	Mean	SE	95 % CI for mean		Median	SD	Skewness	Kurtosis
Weeks on ART	Yes	68.98	13.55	41.84	96.82	32	103.22	1.904	5.938
Baseline Hb	No	11.36	0.269	10.83	11.90	11.4	2.49	-0.152	0.634
	Yes	11.35	0.289	10.77	11.93	11.6	2.21	-0.926	2.705
Baseline ALT	No	32.01	3.24	25.56	38.45	25.5	29.34	3.714	18.5
	Yes	26.45	1.89	22.66	30.24	22.2	14.01	1.325	1.401
Creatinine	No	97.77	7.51	82.8	112.74	88.64	64.61	6.690	52.153
	Yes	87.53	4.966	77.58	97.47	83.28	37.49	3.396	17.502
Baseline AST	No	43.72	3.603	36.54	50.90	33.70	31.21	2.452	6.982
	Yes	42.79	4.051	34.62	50.96	34.75	26.87	1.697	2.857
Baseline CD4 count	No	214.41	21.595	171.47	257.36	152	199.1	1.195	1.808
	Yes	165.3	20.393	124.44	206.11	121	155.31	1.430	1.782

Table 3: Baseline parameters of study participants (categorical).

Parameters		Not on ART N (%)	On ART N (%)	Total
Baseline RPR	Negative	42 (49)	22 (38)	64 (45)
	Not tested	34 (40)	32 (55)	66 (46)
	Positive	9 (11)	4 (7)	13 (9)
	Total	85 (100)	58 (100)	143 (100)
Baseline HBSAg	Negative	37 (44)	19 (33)	56 (39)
	Not tested	45 (53)	38 (65)	83 (58)
	Positive	3 (3)	1 (2)	4 (3)
	Total	85 (100)	58 (100)	143 (100)

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

CD4 cell count	Not on ART N (%)	On ART N (%)	P value
<200	49 (57.64)	29 (50.00)	0.367
200-350	15 (17.65)	15 (25.86)	0.236
>350	21(24.71)	14 (24.13)	0.938
Grand Total	85 (100)	58 (100)	143

Association between dermatological condition and treatment status

It was not possible to determine whether there were significant differences in the frequency of all the individual dermatological conditions between patients on antiretroviral therapy and antiretroviral naïve patients. This is because of the small relative frequencies for most conditions. For the conditions were there were adequate frequencies of the dermatological conditions, the associations are highlighted in table six. Analysis in (Table 6) shows that the odds of having oral candidiasis were 20% higher for ART naïve patients as compared to patients on antiretroviral therapy (p=0.002). The odds of having herpes zoster were approximately 17% higher for ART naïve patients as compared to patients on antiretroviral therapy (p=0.01). The table also shows that there was no significant difference in the odds of developing hyper pigmentation between ART naïve patients, as compared to patients on antiretroviral therapy (p=0.3). Similarly, there was no significant difference in the odds of developing Eosinophillic folliculitis between ART naïve patients, as compared to patients on antiretroviral therapy (Fischer's exact p=0.73).

Association between dermatological conditions andCD4 count

The CD4 counts at which the various dermatological conditions occurred in patients on antiretroviral therapy and antiretroviral naïve patients are shown in (Table 7).

Association between dermatological conditions and clinical stage of HIV

There were significant differences in the number of patients in stage II and stage III among patients on antiretroviral therapy and antiretroviral naïve patients (p=0.000). There was no significant difference in the number of patients in stage I and stage IV between patients on antiretroviral therapy and antiretroviral naïve patients (p value 0.085 for stage I and 0.944 for stage IV). Association between dermatological conditions and clinical stage of HIV is shown in (Table 8).

Association between CD4 count, clinical stage and dermatological conditions for infectious dermatoses compared to noninfectious dermatoses

There were no significant differences in the proportion of patients with infectious dermatoses as compared to non-infectious dermatoses for patients in stage I, II and IV disease (p values 0.28, 0.054 and 0.715 respectively) while significant difference was noted in favour of infectious dermatoses for patients in stage III (p=0.005). Patients in stage III were more than twice more likely to have an infectious dermatosis (OR 2.26, 95% CI 1.04-4.9). There were no significant differences in the proportion of patients with CD4 count below 200 and above 350 between patients with infectious dermatoses as compared to patients with non-infectious dermatoses (p=0.283 and 0.33). There was a significant difference in favour of non-infectious dermatoses as compared to those with infectious dermatoses for patients with CD4 count between 200 and 350 (p=0.005). The odds of being of having an infectious dermatosis were28% lower for patients on antiretroviral therapy as compared to antiretroviral naive patients (p=0.001). The results of the bivariate analysis are highlighted in (Table 9).

DISCUSSION

This research was undertaken to study differences in skin manifestations between two cohort of patients who attended an out-patient antiretroviral clinic at University

Teaching Hospital of Zambia, Africa from the period 2002-2019; those "ART naïve"; a group of 85 patients who did not access ART because of various reasons; and another group of 58 patients who were who were on ART.

Table 5: Dermatological conditions in both groups.

Type of skin condition at diagnosis	Not ART (n=85)		On ART (n=58)		Total (n=143)	
	Frequency	% of not ART patients	Frequency	% of on ART	Frequency	% of total patients
Abscess	5	5.88	0	0	5	3.5
Allergic dermatitis	0	0	2	3.45	2	1.4
Angular cheilitis	2	2.35	0	0	2	1.4
Eosinophilic folliculitis	6	7.06	3	5.17	9	6.29
Fungal dermatitis	2	2.35	10	17.24	12	8.39
Genital herpes	1	1.18	5	8.62	6	4.2
Genital ulcers	2	2.35	1	1.72	3	2.1
Genital warts	2	2.35	1	1.72	3	2.1
Hair changes	1	1.18	0	0	1	0.7
Herpes labialis	4	4.71	1	1.72	5	4.2
Herpes zoster	15	17.65	2	3.45	17	11.89
Hyper pigmentation	7	8.24	11	18.97	18	12.59
Kaposi sarcoma	4	4.71	4	6.9	8	5.59
Molluscum contagiosum	2	2.35	0	0	2	1.4
Nodular prurigo	1	1.18	2	3.45	3	2.1
Oral candidiasis	29	34.12	5	8.62	34	23.78
Oral hairy leucoplakia	0	0	1	1.72	1	0.7
Oral ulcers	0	0	1	1.72	1	0.7
Pruritic papular eruption (PPE)	1	0.7	5	8.62	6	4.2
Pruritus	0	0	2	3.45	2	2.8
Pityriasis versicolor	1	1.18	0	0	1	0.7
SJS	0	0	2	3.45	2	1.4
Grand total	85 (59.5)	100	58 (40.5)	100	143	100

Table 6: Association between dermatological conditions and ART status.

Condition	Total	ART naive	On ART	Bivariate	
	N (%)	N (%)	N (%)	OR (95% CI)	P value
Oral candiasis	34 (24)	29 (34)	5 (9)	0.19 (0.066-0.5)	0.002
Hyper pigmentation	18 (13)	7 (8)	11 (19)	1.733 (0.885-2.9)	0.3
Eosinophillic Folliculitis	9 (6)	6 (7)	3 (5)	0.55 (0.546-1.4)	0.73
Herpes zoster	17 (12)	15 (18)	2 (3)	0.167(0.37-0.76)	0.01

As this long period had witnessed changes in ART guidelines, new recommendations for HIV related diagnosis and practices, as well as in epidemiology of HIV/AIDS related/unrelated dermatological conditions, findings of this study may give better insights for future dermatology practice.[18-20] Turning point of HIV pandemic was highly active antiretroviral therapy (HAART), which not only changed the mortality statistics but also the profile of the disease.[21] In olden times, in pre-ART era, skin manifestations were considered to be important "tell-tale" signs, to suspect HIV infection and more than 90% would present with skin manifestations.[22] These manifestations were present as presenting feature and could forecast the immune status of a patient.[23] Since the advent of antiretroviral therapy, these classic skin manifestations, severity and incidence of such manifestations have decreased.

Table 7: Association between CD4 count and dermatological conditions.

Skin condition	Not on ART			On ART		
	CD4<200	CD4 200-350	CD4>350	CD4<200	CD4 200-350	CD4 >350
Allergic dermatitis	0	0	0	0	1	1
Eosinophilic folliculitis	4	2	0	2	0	1
Fungal dermatitis	2	0	0	3	2	5
Genital herpes	1	0	0	3	0	2
Genital ulcers	0	0	2	1	0	0
Genital warts	2	0	0	1	0	0
Abscess	3	0	2	0	0	0
Hair changes	1	0	0	0	0	0
Herpes labial	2	0	2	1	0	0
Herpes zoster	4	7	4	0	1	1
Hyper pigmentation	5	1	1	4	5	2
Kaposi's sarcoma	2	1	1	4	0	0
Molluscum contagiosum	2	0	0	0	0	0
Oral candidiasis	19	2	8	4	1	0
Oral hairy leucoplakia	0	0	0	1	0	0
Oral ulcers	0	0	0	1	0	0
Pruritic papulareruption (PPE)	0	0	0	4	1	0
Pruritus	0	0	0	0	1	1
Nodular pruritus	1	0	1	0	1	1
Stevens-Johnson syndrome (SJS)	0	0	0	0	2	0
Angular cheilitis	1	1	0	0	0	0
Pityriasis versicolor	0	1	0	0	0	0
Grand total	49	15	21	29	15	14

However other "newer" skin lesions have resulted either due to the drugs themselves or due to the altered immune status due to these drugs.[5,23] research and review papers in literature do mention of decreased incidence of skin manifestations due to ART.[24] Co-existent diabetes and/or kidney disease were excluded from the study because diabetes itself increases the frequency and severity of cutaneous conditions.[25] Various other parameters like demographic profile, stages of illness and CD4 count of patients were analyzed in lieu of dermatological features in both groups. HIV infection typically affects young and middle age men and women in the reproductive age group was also finding of this study like other studies.[26,27] More than 50% of the study population can be classified as having AIDS, as they had a CD4 count less than 200. The study showed that patients on antiretroviral therapy had lower baseline median CD4 count as compared to those on antiretroviral therapy. This may have been due to previous guidelines which recommended antiretroviral therapy only for patients with CD4 count below 200.[28] The study showed that co-infection with syphilis and/or hepatitis B is frequent in HIV infected patients. Screening of these conditions is required for comprehensive care and may give information about the mode of transmission of HIV in the study population.

Oral candidiasis and herpes zoster were statistically significantly higher in antiretroviral naïve patients in comparison to patients who received ART. Many studies have shown infectious mucocutaneous preponderance than non-infectious complications in antiretroviral naïve patients.[29,30] In this study, oral candidiasis was the most common dermatoses which was present in 29 out of 85 (34.12%) in antiretroviral naïve group while it was present in 5 out of 58 (8.62%) in ART group; total patients being 34 of 143 patients (23.78%). Oral candidiasis is one of the common prevalent mucocutaneous complications in HIV-infected patients in the present era also, prevalence being reported from 0.9 to 83%.[31] Our study suggests that ART may lead to decrease in prevalence of this common infective condition. In this study, a total 8 (9.59%) patients had Kaposi's sarcoma; 4 (4.71%) in antiretroviral naive patients, and 4 (6.9%) of patients on antiretroviral therapy. This is similar to the findings in the study by Boushab et al 2017.[32] In this study, the prevalence of Kaposi's sarcoma among antiretroviral naïve patients was 3.5%; while papular pruritic eruptions were the most frequent conditions among antiretroviral naïve patients.[32] our study, the prevalence of papular pruritic eruption was found to be 8.62% among patients on antiretroviral therapy and 1.18% among antiretroviral naïve patients. Papular pruritic eruption can be the first markers of HIV infection.[33]

Table 8: Association between dermatological conditions and clinical stage of HIV.

Skin condition	Not on ART				On ART			
	Stage I	Stage II	Stage III	Stage IV	Stage I	Stage II	Stage III	Stage IV
Abscess	0	2	3	0	0	0	0	0
Allergic dermatitis	0	0	0	0	1	1	0	0
Angular cheilitis	0	0	2	0	0	0	0	0
Eosinophilic folliculitis	0	2	4	0	0	3	0	0
Genital ulcers	0	0	1	1	0	1	0	0
Genital warts	0	1	1	0	0	1	0	0
Hair changes	0	0	0	1	0	0	0	0
Genital herpes	0	1	0	0	0	2	1	2
Tinea corporis	0	1	1	0	0	7	3	0
Herpes labialis	0	1	3	0	0	0	0	1
Herpes zoster	0	9	4	2	0	2	0	0
Hyperpigmentation	0	1	3	3	1	6	3	1
Kaposi sarcoma	0	0	0	4	0	0	0	4
Molluscum contagiosum	0	0	1	1	0	0	0	0
Nodular pruritus	0	0	1	0	0	2	0	0
Oral candidiasis	0	1	23	5	0	0	4	1
Oral hairy leucoplakia	0	0	0	0	0	0	0	1
Oral ulcers	0	0	0	0	0	0	1	0
Pruritic papular eruption	0	0	0	1	0	5	0	0
Pityriasis versicolor	0	1	0	0	0	0	0	0
Pruritus	0	0	0	0	0	1	0	1
Stevens-Johnson syndrome	0	0	0	0	0	0	1	1
Grand total	0	20	47	18	2	31	13	12

Table 9: Association between clinical stage, CD4 count and ART status in patients with infectious as well as non-infectious conditions.

Factors		Total		Infectious		Non-infectious		Bivariate	
		N	%	N	%	N	%	OR (95% CI)	P value
Clinical stage	Stage I	2	1.4	0	0	2	4.8	0.28 (0.218-0.37)	0.085
	Stage II	51	35.7	31	30.7	20	47.6	0.48 (0.23-1.02)	0.054
	Stage III	60	42	48	47.5	12	28.6	2.26 (1.04-4.9)	0.036
	Stage IV	30	21	22	21.8	8	19	1.18 (0.48-2.9)	0.715
CD4 Count	< 200 cells	78	54.5	57	56.4	21	50	1.48 (0.72-3.05)	0.283
	200 - 350 cells	30	21	16	15.8	14	33.3	0.38 (0.16-0.87)	0.019
	> 350 cells	35	24.5	28	27.7	7	16.7	1.55 (0.63-3.76)	0.33
ART Status	On ART	58	42	32	32	26	62	-	-
	Not on ART	85	58	69	68	16	38	0.28 (0.13-0.6)	0.001

The cutaneous hyperpigmentation in patients were generalized, symmetrical and perifollicular. This was most likely post inflammatory hyperpigmentation, secondary to other infectious or inflammatory conditions such as papular pruritic eruption, eosinophilic or bacterial folliculitis. The frequency of genital lesions in our study population may have been higher than reported. There is a lot of stigma and shame associated with genital lesions in our setting. Consequently, many patients do not seek medical attention for them. There were two cases of adverse drug reaction in this study. There were 2 cases of Steven Johnson Syndrome (SJS) associated with the use of co-trimoxazole prophylaxis. This is contrary to what is expected in patients on antiretroviral therapy. Hoosen et al, report a prevalence of adverse cutaneous drug reactions (ACDR) of 43% among HIV positive individuals and up to 69% in patients with AIDS.[34] Most resource constrained settings have poor pharmacovigilance systems.

Consequently, most adverse cutaneous drug reactions are not reported or documented. Our study findings are similar to the findings in the study by Hira et al.[15] Their study was also done in Zambia, in a setting that is similar to the one in which the current study was done. Hira found that multi-dermatomal herpes zoster was one of the most frequently encountered dermatological conditions. Their study population was predominantly antiretroviral

naïve.[15] This was a well conducted prospective study with an adequate sample size. However, the study by Hira et al found that Kaposi's sarcoma and pruritic maculopapular rashes were also frequently encountered. This was not the case in the current study. Kaposi's sarcoma was only encountered in 4.71% of the antiretroviral naïve patients. Pruritic maculopapular rashes were encountered in only 1.18% of antiretroviral naïve patients.

The observed differences in skin changes in the Hira et al study and ours maybe because of better awareness of HIV/AIDS; and thus, early diagnosis and treatment of HIV such that natural history of HIV infection leading to skin conditions reported of the past maybe not seen. There was a statistically significant difference in the frequency of infectious conditions among antiretroviral naïve patients as compared to patients on ART ($p<0.001$). This is similar to findings in a study by Sailo et al.[36] When two cohorts; one having infectious dermatoses and another having non-infectious dermatoses were compared (irrespective of ART status) (Table 8); there was a significant difference in the patients in stage III; who were more than twice more likely to have an infectious dermatoses. There was also significant difference in the proportion of patients with infectious dermatoses as compared to those with non-infectious dermatoses for patients with CD4 count between 200 and 350. Again, the odds of being of having an infectious dermatosis were 28% lower for patients on antiretroviral therapy as compared to antiretroviral naive patients ($p=0.001$).Our findings suggest that ART plays a significant role in preventing infectious dermatoses. It also indirectly suggests that patients will remain in stage 2 for longer time, and that progression to stage 3 will be less likely; as patients in stage III were more likely to have infectious dermatoses ($p=0.036$). Our study had several limitations. One of the main limitations of our study is the restrospective design.

Though medical records available of "ART naïve patients having skin conditions" were more in number than "on ART" (59.4% Vs 40.6%), it is difficult to conclude than incidence of skin manifestations have decreased due to ART. It is because of retrospective nature of this study. Consequently, the diagnosis of IRIS syndrome was not possible in our study. It was not possible to fully investigate factors that increase the risk of IRIS, such as rapid decline in the HIV viral load.[35] In addition, patients in this study were not followed up. This made it difficult to differentiate IRIS syndrome from actual opportunistic infections. The sample size was not large enough to determine whether they were significant differences in the frequency of many of the individual dermatological conditions between patients on antiretroviral therapy, and antiretroviral naïve patients. Another limitation of the study is that all the diagnoses were clinical. There was no biopsy confirmation of diagnoses. This study shows that there are still a significant proportion of patients presenting with advanced HIV infection. There is need to conduct further qualitative and quantitative research in order to identify factors that are preventing patients infected with HIV from seeking care early in the course of the infection.

CONCLUSION

There is a changing profile of mucocutaneous conditions in HIV infected patients. Infectious dermatoses such as oral candidiasis and Herpes Zoster occur more frequently in antiretroviral naïve patients, as compared to patients on ART. Prevention of infectious dermatological conditions is anticipated with the use of ART.

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