ORIGINAL ARTICLE

HIV-Related Skin Disease in Kaduna, North-West Nigeria: A 20-Year Experience

Yahya H.

ABSTRACT

Background: Skin diseases are common in African patients with HIV infection. They are often the first clinical manifestations of immune deficiency and their frequency increases as impaired immunity worsens and decreases as immunity improves with antiretroviral drugs (ARV). **Objective:** To report the relative incidence and clinical presentation of HIV-related skin disease over 20 years when diagnosis and treatment availability varied. **Methods**: Records of patients with HIV-related skin disease attending a dermatology clinic in Kaduna, Nigeria from 2001 to 2021 were reviewed. **Results:** HIV-related skin disease was diagnosed in 525/29,278 (1.8%) patients with 610 episodes of skin disease: Mean age 36.2 years (range:4 – 68 years), 60% age < 40, males 55%. Almost 72% of patients were seen between 2001 and 2010 and only 9.3% were seen after 2015. Patients seen between 2001 and 2010 were significantly less likely to know their HIV status (19.9% vs. 80.1%, P = 0.000) and be receiving ARV (21.5%, vs. 51.4%, P = 0.000) than those seen between 2011 and 2021. The most common skin conditions were: pruritic papular eruption 33%, herpes zoster 19.7%, Kaposi sarcoma 11%, atopiform dermatitis 8.9%, and seborrheic dermatitis 3.8%. Plane warts, adverse drug reactions, folliculitis, furunculosis, genital herpes simplex, psoriasis, dermatophyte infection, and molluscum contagiosum were also seen. Almost 60% of patients a had CD4 count < 200 cells/ml at presentation. **Conclusion:** We noted a marked change in the frequency and pattern of disease between 2001-2010 and 2011-2021 likely due to the increased availability of care and treatment over the period.

Keywords: HIV, Skin disease, Relative incidence, Kaduna-Nigeria, sub-Saharan Africa

[1]Dermatology Unit, Department of Internal Medicine, Barau Dikko Teaching Hospital/Kaduna State University, Kaduna, Nigeria and Habbat Medical Centre, Kaduna, Nigeria

Corresponding Author:

Dr Husain Yahya

Address of corresponding author: Department of Internal Medicine, Barau Dikko Teaching Hospital, PO Box 9727, Kaduna, Nigeria

Email address: husainyahya@yahoo.co.uk

Introduction

Skin diseases are common in Africans infected with the Human Immunodeficiency virus (HIV).[1-3] These diseases are often the first clinical manifestations of immunodeficiency and their frequency increases as impaired immunity worsens. HIV infection is associated with a marked fall in Langerhans cells, macrophages, monocytes, Natural Killer (NK) cells and CD4 lymphocytes, with an accompanying increase in turnover of CD8 lymphocytes, and B cells and a shift from T helper (TH) 1 cytokine to TH2 cytokine profile leading to immune activation and dysregulation, and subsequent impairment of the immune system.[4,5] The skin, like the gut and other mucosal surfaces, is an active immunological organ that not only serves as a physical barrier to microorganisms and other noxious substances but also mounts a robust innate and adaptive immune response to microorganisms and tumour cells.[6] It is not surprising, then, that the skin is affected early and throughout the period of infection with HIV. A severe and rapidly-progressive Kaposi sarcoma (KS) was one of the first diseases to be linked to an as yet undefined immune deficiency-causing disease in previously healthy young homosexual men,[7] which was later identified by Barre-Sinoussi and colleagues in France to be caused by a retrovirus, Human T-cell Leukemia Virus (HTLV) 1,[8] which was subsequently

Access this article online

QuickResponse Code

website:www.bornomedicaljournal.com

DOI: 10.31173/bomj.bomj_2214_19

renamed HIV.[9] Skin diseases have been associated with HIV infection right from the onset of the epidemic.[10-12]

HIV-related skin diseases are of four types: infectious, inflammatory, neoplastic disorders, and hypersensitivity reactions to drugs or Highly Active Antiretroviral Therapy (HAART)-induced immune reconstitution syndrome (IRS). Opportunistic infections such as herpes zoster and neoplastic disorders such as Kaposi sarcoma result from the progressive destruction of antigen-presenting cells in the skin (Langerhans cells and dermal dendritic cells) and CD+ cells, monocytes, macrophages and natural killer cells. They are more common and more severe as immunodeficiency worsens.[5] Inflammatory disorders including eczematous (atopiform) dermatitis, seborrheic dermatitis, and psoriasis result from a shift from TH1 to TH2 cytokine response which triggers an inflammatory response in keratinocytes.[5]

Although skin disease is common in patients infected with HIV, their prevalence, pattern and severity differ depending on the location and prevalence of endemic diseases.[13-15] It's also clear that the availability of HAART has reduced and modified the kind of skin diseases observed – rates of many diseases fall but some may develop or become worse because of immune reconstitution inflammatory syndrome, IRIS.[16]

A lot of progress has been made to control the HIV epidemic in Nigeria. It was estimated that 3.2 million Nigerians lived with HIV in 2011, one of the highest in the world at that time,[17] but a new survey, The Nigeria HIV/AIDS Indicator and Impact Survey (NAIIS) using improved methodology conducted in 2018, projected the figure to 1.9 million.[18] The national HIV Seroprevalence Sentinel Surveys (HSSS) conducted biennially in Nigeria since 1991 to track the epidemic has shown that Kaduna State, with a prevalence of 5.6%, had one of the highest prevalence of the disease in 2001 which had remained steady over the decade.[19] Still, the new data from NAIIS found the rate to be 1%.[18] There is a scarcity of data on HIV-related skin disease in the Northern part of Nigeria, with most published reports coming from the South.[2,3, 20] Our study looks at the relative frequency and pattern of HIV-related skin disease in patients presenting to an outpatient dermatology clinic in Kaduna, North-West Nigeria over 20 years in which HIV testing, care and support were not initially widely available but later became more accessible. We hope this will further foster understanding of this disease.

Methods

Study type and setting

This is a retrospective review of records of consecutive patients presenting for the first time to the outpatient skin clinic of Habbat Medical Centre in Kaduna, North-West Nigeria from September 2001 to November 2021. The study was approved by the Health Research Ethical Committee of Kaduna State Ministry of Health on 22 June 2022 with approval number MOH/ADM/744/VOL.1/941. A trained dermatologist saw all patients. Patients were referred to the clinic from within or outside Kaduna from public, private or faith-based hospitals or by patients or their relatives. Diagnosis of skin disease was made clinically, supplemented by histology and other tests where required. A patient was considered to have HIV-related skin disease if they presented with a skin disease known to be strongly associated with HIV infection [1-3, 10-16] and if an infection is established by proof of a previous positive antibody test or a positive new test. HIV tests were conducted according to the Nigeria national guidelines.[21] All patients were requested to perform CD4 count tests whenever this was possible - tests were conducted in secondary and tertiary health facilities within and outside Kaduna. Many of the patients came from cities outside Kaduna and elected to do CD4 count tests and enrol in care for HIV infection in their various stations. Nucleic acid (HIV viral load) testing was unavailable for most patients at the time of presentation or subsequently.

Data Retrieval

Medical records of patients diagnosed with HIV-related skin disease were retrieved and demographic data, year of the first presentation, type and number of skin diseases, knowledge of HIV status at presentation, most recent CD4 cell count and whether or not patients had started antiretroviral therapy (ART) and how long for, were obtained.

Statistics

IBM SPSS Version 22 (Armonk, New York, USA, 2013) was used to obtain descriptive statistics. Chi-Squared or Fisher's Exact tests were used to assess the significance of differences in categorical

variables. A P value of < 0.05 was interpreted as significant.

Results

Over 20 years, 525 new patients out of 29,278 (1.8%) presenting to the skin clinic of Habbat Medical Centre, Kaduna, Nigeria were diagnosed with 610 episodes of HIV-related skin disease. Table 1 summarizes the demographic and clinical characteristics of the patients. Their mean age was 36.2 years, the majority (60%) were below the age of 40 and most patients (86.6%) were between the ages of 20 and 50. There were more males than females with a male-female ratio of 1.2. More than 70% of the patients were seen in the first 10 years of the period under review, with the number falling sharply after 2010 and even more so after 2015 (Fig 1). Most patients presented with only one skin condition when they were first seen. Overall, almost two-thirds of patients did not know their HIV status at presentation; patients seen between 2001 and 2010 were significantly less likely to know their status than those seen between 2011 and 2021 (80.1% vs. 19.9%, X^2 28.928, P = 0.000). Only about 30% of patients received or had received antiretroviral drugs (ARV) at the time of presentation (median 18 months, interquartile range 6 – 60 months). Patients seen during 2010 – 2021 were significantly more likely to be receive ARV than those seen between 2001 – 2010 (51.4% vs 21.5%, X^2 45.224, P = 0.000). Pruritic papular eruption of HIV (PPE) (fig 2a) was the most common condition seen, accounting for 33% of skin disease. PPE was significantly more likely to affect females than males (table 2) and those not receiving ARV, and also significantly more common during the 2001 – 2010 period than 2011 – 2021 (table 3). Herpes zoster (fig 2b), Kaposi sarcoma (fig 2c) and atopiform (atopic dermatitis-like) dermatitis (fig 2d) constituted 19.7%, 11%, and 8.9% of cases respectively. Atopiform dermatitis was significantly more likely to affect patients above the age of 40 years than those younger and those who had received ARV. Plane wart, which appeared as extensive lesions on the face, scalp, neck (fig 2e) and upper body, on the other hand, was significantly more likely to affect patients who were younger than 40 years, who presented during the 2011 -2021 period and in those who received ARV. Herpes zoster was significantly more common during the 2011 – 2021 period than in 2010 – 2010 and also significantly more likely to affect those not receiving ARV. Herpes zoster was recurrent in 26/120 (21.7%) episodes.

Sixteen episodes of adverse drug reactions (ADR) were seen in patients who had received ARV: Exanthem was the most common reaction occurring in 7 (43.8%) of patients followed by eczematous dermatitis, Stevens-Johnson syndrome, erythroderma which constituted 12.5% each. One person each was seen with hyperpigmentation, extensive bullous fixed drug eruption (fig 2f) and peripheral neuropathy. Co-trimoxazole and nevirapine were the commonest offenders, implicated in 11/16 of the episodes. Others drugs implicated included antituberculosis drugs, griseofulvin and tetracycline. Adverse drug reactions were significantly more common during 2001 – 2010 than in 2011 – 2021. Folliculitis was mainly bacterial, although a few cases were diagnosed as probably caused by demodex folliculorum.

There was a trend for pyoderma, which presented mainly as extensive and recurrent furunculosis, to affect more patients seen between 2001 and 2010 but did not reach statistical significance. Genital herpes simplex presented as a large number of recurrent and persistent genital ulcers which took a long time to heal (fig 2g). Psoriasis tended to affect male patients (fig 2h), was generalized in all cases (≥ 10% body surface area affected) and in four cases was erythrodermic. Dermatophyte infection affected predominantly female patients and presented with extensive well-marginated scaly plaques affecting the neck (fig 2i), back, arms and thighs. All ten cases of extensive molluscum contagiosum were seen in patients who had not received any ARV.

The most recent CD4 cell count results were available for only 178 patients: Almost 60% had a count of less than 200 cells/ml indicating advanced immune suppression.

Analysis of the CD4 count results shows that a greater proportion of patients with extensive genital herpes simplex infection, PPE, plane wart, Kaposi sarcoma and seborrheic dermatitis had CD4 counts < 200 than patients with other conditions.

Table 4 shows relative frequency of various skin diseases in patients with HIV infection and those without. Herpes zoster, seborrheic dermatitis, plane wart and molluscum contagiosum were more common in HIV-infected patients.

Legends for Tables and Figures

Table 1 - Demographic and clinical characteristics of 525 patients with HIV-related Skin disease. Figures in parentheses are percentages unless otherwise indicated.

Table 2 - Age and gender comparison of relative frequency of HIV-related skin disease. Figures in parentheses are percentages.

Table 3 – Relative frequency of HIV-related skin disease according to period seen and ARV status. Figures in parenthesis are percentages

Table 4 - Skin disease in HIV-infected and non-HIV infected patients. Figures in paratheses are percentages

Figure 1. Number of patients with HIV-related skin disease seen over a 20-year period

Figure 2 – HIV-related skin disease: **(a)** Pruritic papular eruption – PPE, **(b)** Herpes zoster, **(c)** Kaposi sarcoma, **(d)** Atopiform dermatitis, **(e)** Plane warts, **(f)** Fixed drug eruption – FDE, **(g)** Herpes simplex, **(h)** Psoriasis, **(i)** Tinea corporis – note also plane warts on cheeks.

Tables and Figures

Table 1 – Demographic and clinical characteristics of 525 patients with HIV-related Skin disease. Figures in parentheses are percentages unless otherwise indicated

Age group	**n (%)**
1 – 9	12 (2.3)
10 – 19	9 (1.7)
20 – 29	114 (21.7)
30 – 39	178 (34.2)
40 – 49	160 (30.7)
50 – 59	40 (7.7)
60 - 69	8 (1.5)
Gender	
Male	289 (55)
Female	236 (45)
Year seen	
2001 – 2005	168 (32)
2006 – 2010	209 (39.8)
2011 – 2015	99 (18.9)
2016 – 2021	49 (9.3)

Number of skin disease at presentation	
1	449 (85.5)
2	67 (12.8)
3	9 (1.7)
Skin disease	
(n = 610)	
Pruritic papular eruption	201(33)
Cutaneous malignancy:	
Kaposi sarcoma	67 (11)
Eczematous dermatitis:	
Atopiform dermatitis	54 (8.9)
Seborrhoeic dermatitis	28 (4.6)
Viral infections:	
Herpes zoster	120 (19.7)
Plane wart	23 (3.8)
Extensive genital herpes simplex	11 (1.8)
Molluscum contagiosum	10 (1.6)
Bacterial infections:	
Folliculitis	15 (2.5)
Pyoderma	14 (2.3)
Fungal infections:	
Dermatophyte infection	11 (1.8)
Adverse Drug reactions:	16 (2.6)
Papulo-squamous disease:	29 (4.8)
Psoriasis	11 (1.8)
Others	29 (4.8)

HIV status at first visit	199 (37.9)
Known	326 (62.1)
Unknown	
Receiving/received ARVs when first seen	
Yes	157 (29.9)
No	368 (70.1)
CD4 cell count (cells/ml)	
n = 178	
< 200	103 (57.9)
200 – 499	58 (32.6)
500 +	17 (9.6)
Skin disease and CD4 count < 200	
Pruritic papular eruption	50 /71(70.4)
Herpes zoster	15/30 (50)
Kaposi sarcoma	15/24 (62.5)
Atopiform dermatitis	10/20 (50)
Seborrhoeic dermatitis	8/13 (61.5)
Plane wart	9/14 (64.3)
Folliculitis	5/9 (55.6)
Extensive genital herpes simplex	4/5 (80)
Psoriasis	1/3 (33.3)
Dermatophyte infection	2/4 (50)
Molluscum contagiosum	1/2 (50)

Table 2 - Age and gender comparison of relative frequency of HIV-related skin disease. Figures in parentheses are percentages

Skin disease	Overall (n =610)	Age < 40 (n = 313)	Age ≥ 40 (n = 208)	*P* value	Male (n = 289)	Female (n = 236)	*P* value
Pruritic papular eruption	201(33)	116 (37.1)	84 (40.4)	0.445	95(32.9)	106 (44.9)	0.005
Herpes zoster	120 (19.7)	72 (23)	46 (22.1)	0.813	74 (25.6)	46 (19.5)	0.097
Kaposi sarcoma	67 (11)	40 (12.8)	25 (12)	0.797	42 (15.5)	25 (10.6)	0.178
Atopiform dermatitis	54 (8.9)	22 (7)	32 (15.4)	0.02	34 (11.8)	20 (8.5)	0.217
Seborrhoeic dermatitis	28 (4.6)	14 (4.5)	14 (6.7)	0.263	15 (5.2)	13 (5.5)	0.872
Plane wart	23 (3.8)	21 (6.7)	2 (1)	0.02	13 (4.5)	10 (4.2)	0.884
Adverse drug reaction	16 (2.6)	9 (2.9)	7 (3.4)	0.751	8 (2.8)	8 (3.4)	0.680
Folliculitis	15 (2.5)	11 (3.5)	4 (1.9)	0.287	8 (2.8)	7 (3)	0.892
Pyoderma	14 (2.3)	9 (2.9)	5 (2.4)	0.744	7 (2.4)	7 (3)	0.700
Genital herpes simplex	11 (1.8)	6 (1.9)	5 (2.4)	0.761	7 (2.4)	4 (1.7)	0.762
Psoriasis	11 (1.8)	8 (2.6)	3 (1.4)	0.538	8 (2.8)	3 (1.3)	0.360
Dermatophyte infection	11 (1.8)	9 (2.9)	2 (1)	0.213	2 (0.7)	9 (3.8)	0.014*
Molluscum contagiosum	10 (1.6)	6 (1.9)	4 (1.9)	0.617	8 (2.8)	2 (0.8)	0.098*

Table 3 – Relative frequency of HIV-related skin disease according to period seen and ARV status. Figures in parentheses are percentages

Disease	Overall (n = 610)	2001 - 2010 (n = 377)	2011 – 2021 (n = 148)	*P* value	Received ARV (n = 157)	Not received ARV (n = 368)	*P* value
Pruritic papular eruption	1201 (33)	165 (43.8)	36 (24.3)	0.000	44 (28)	157 (42.7)	0.002
Herpes zoster	120 (19.7)	71 (18.8)	49 (33.1)	0.000	21(13.4)	99 (26.9)	0.001
Kaposi sarcoma	67 (11)	49 (13)	18 (12.2)	0.796	20(12.7)	47 (12.8)	0.992
Atopiform dermatitis	54 (8.9)	39 (10.3)	15 (10.1)	0.493	23 (14.6)	31 (8.4)	0.032
Seborrhoeic dermatitis	28 (4.6)	21 (5.6)	7 (4.7)	0.700	8 (5.1)	20 (5.4)	0.874
Plane wart	23 (3.8)	10 (2.7)	13 (8.8)	0.002	14 (8.9)	9 (2.4)	0.001
Adverse drug reactions	16 (2.6)	15 (2.9)	1 (0.2)	0.034*	13 (8.3)	3 (0.8)	0.000*
Folliculitis	15 (2.5)	11 (2.1)	4 (2.7)	0.578*	8 (5.1)	7 (1.9)	0.047
Pyoderma	14 (2.3)	13 (3.4)	1 (0.7)	0.061*	4 (2.5)	10 (2.7)	0.912
Genital herpes simplex	11 (1.8)	7 (1.9)	4 (2.7)	0.377*	5 (3.2)	6 (1.6)	0.206*
Psoriasis	11 (1.8)	8 (3.1)	3 (0.6)	0.623*	4 (2.5)	7 (1.9)	0.428*
Dermatophyte infection	11 (1.8)	5 (1.3)	6 (4.1)	0.058	5 (3.2)	6 (1.6)	0.206*
Molluscum contagiosum	10 (1.6)	6 (1.6)	4 (2.7)	0.302*	0	10 (2.7)	0.037*

*Fisher's Exact test, ARV – Antiretroviral drugs

Table 4 - Skin disease in HIV-infected and non-HIV infected patients. Figures in paratheses are percentages

Disease	HIV-infected N = 610	Non-HIV-infected N = 28,668
Herpes zoster	120 (19.7)	56 (0.2)
Kaposi sarcoma	67 (11)	-
Atopic/atopiform dermatitis	54 (8.9)	4115(14.4)
Seborrhoeic dermatitis	28 (4.6)	675 (2.4)
Plane wart	23 (3.8)	67 (0.2)
Adverse drug reactions	16 (2.6)	648 (2.3)
Pyoderma	14 (2.3)	1402 (4.9)
Psoriasis	11 (1.8)	183 (0.6)
Dermatophyte infections	11 (1.8)	3590 (12.5)
Molluscum contagiosum	10 (1.6)	81 (0.3)

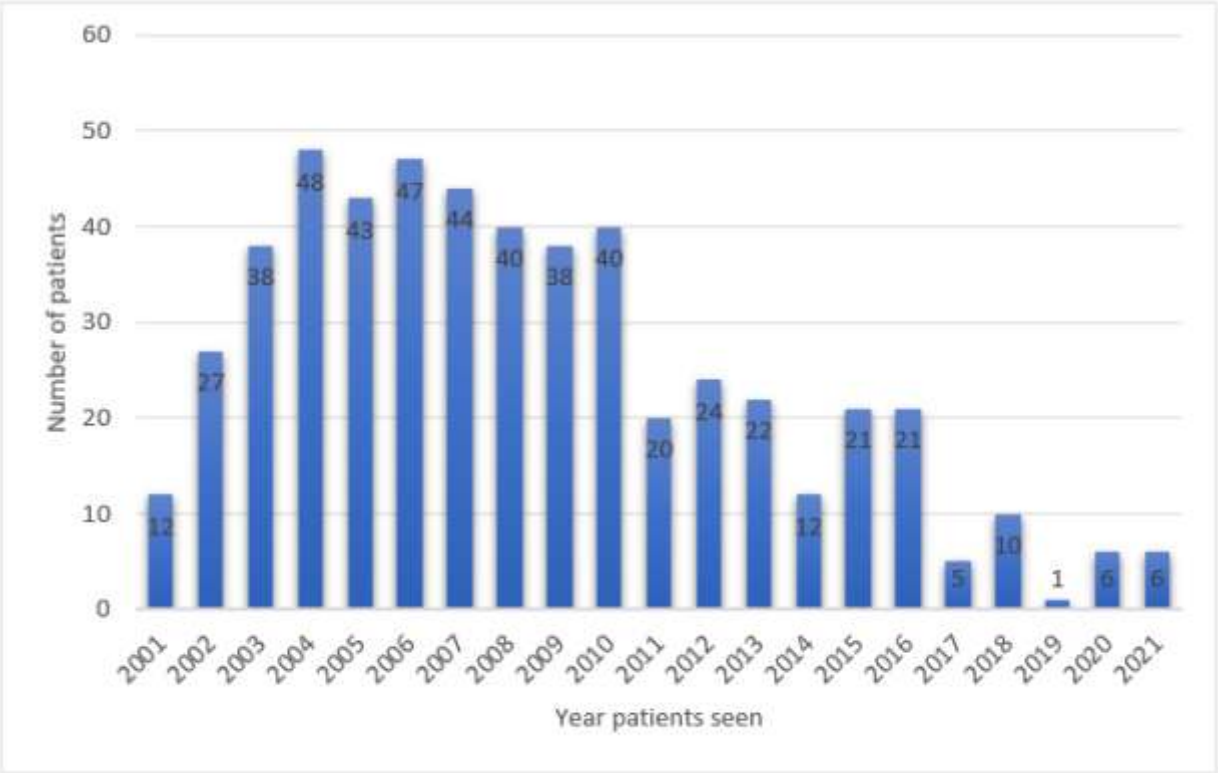

Figure 1. Number of patients with HIV-related skin disease seen over a 20-year period

Legend for Figure 2

Figure 2 – HIV-related skin disease: **(a)** Pruritic papular eruption – PPE, **(b)** Herpes zoster, **(c)** Kaposi sarcoma, **(d)** Atopiform dermatitis, **(e)** Plane warts, **(f)** Fixed drug eruption – FDE, **(g)** Herpes simplex, **(h)** Psoriasis, **(i)** Tinea corporis – note also plane warts on cheeks.

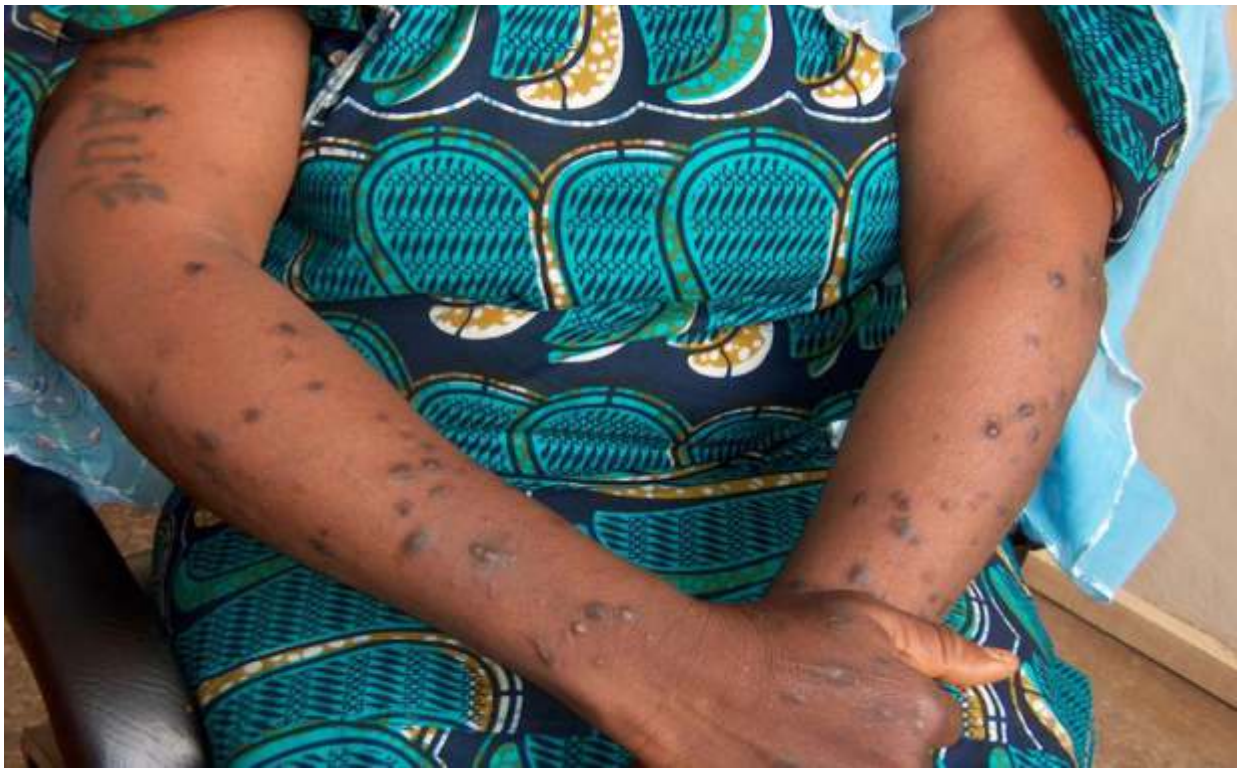

Fig 2a

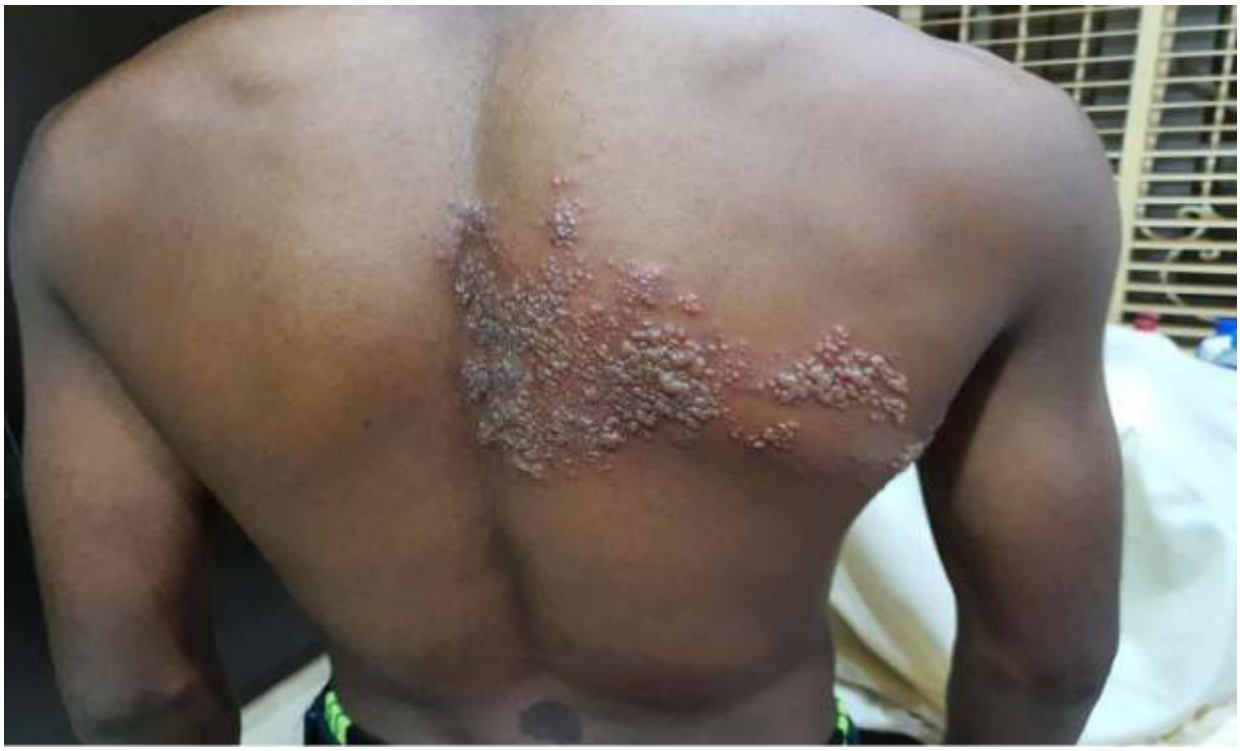

Fig 2b

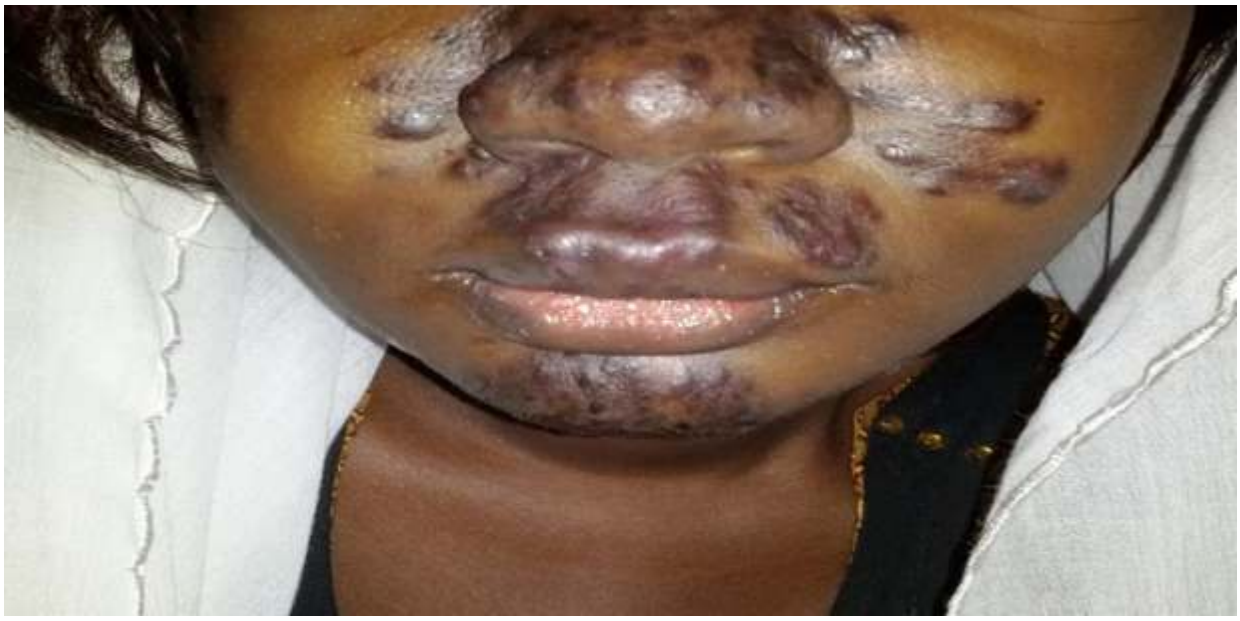

Fig 2c

Fig 2d

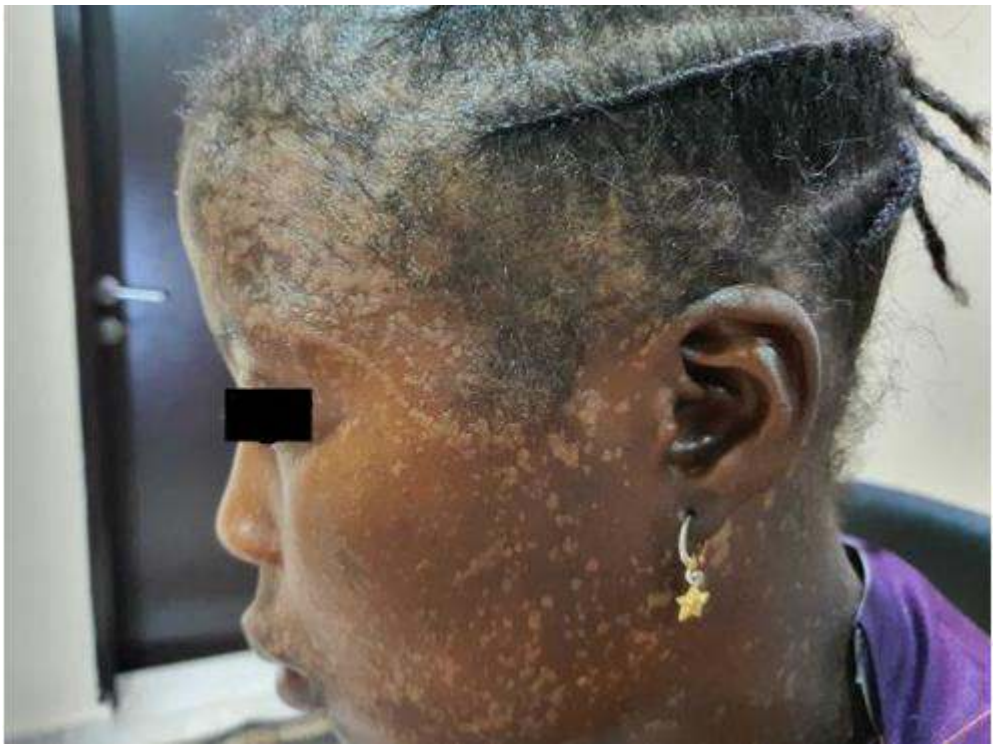

Fig 2e

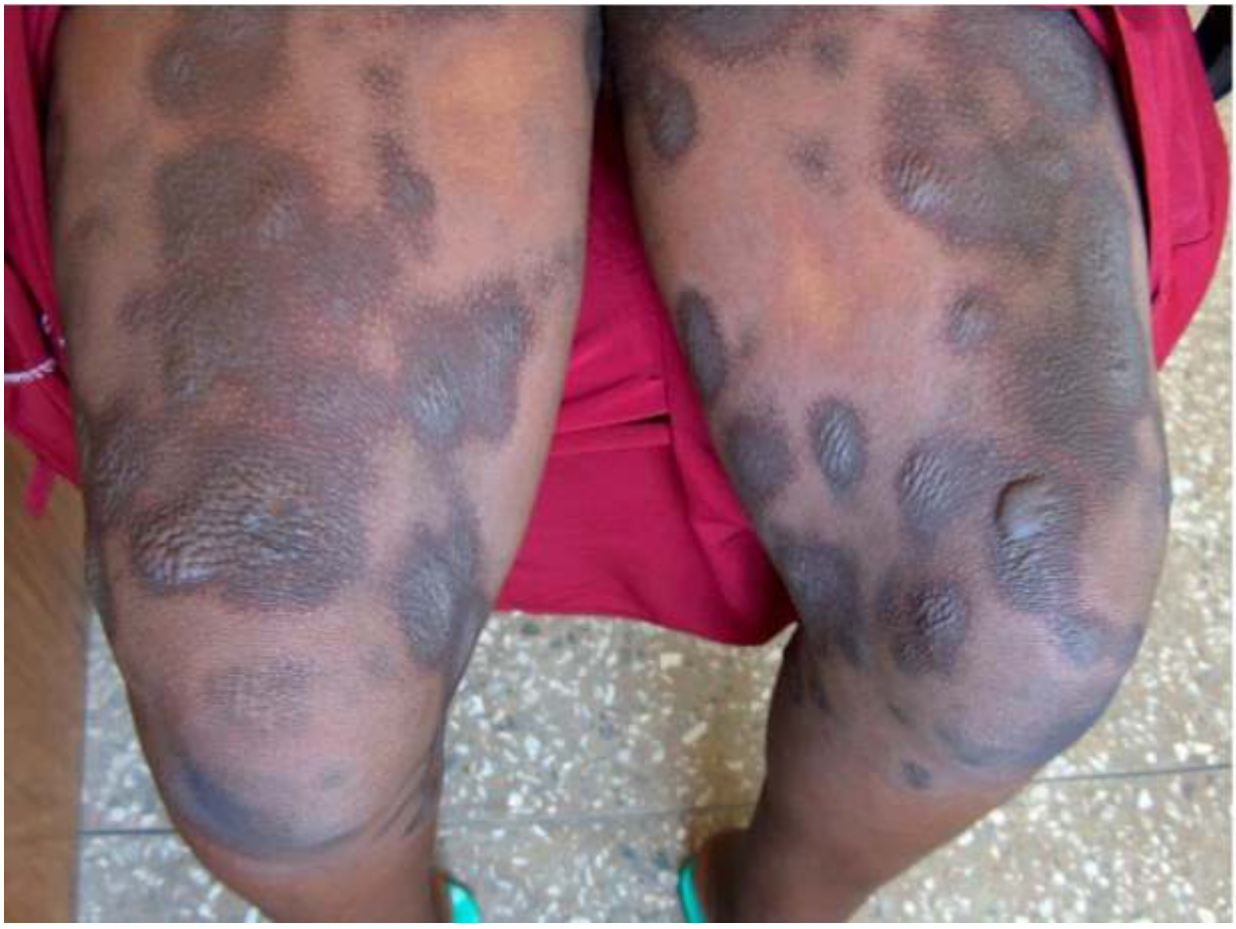

Fig 2f

Fig 2g

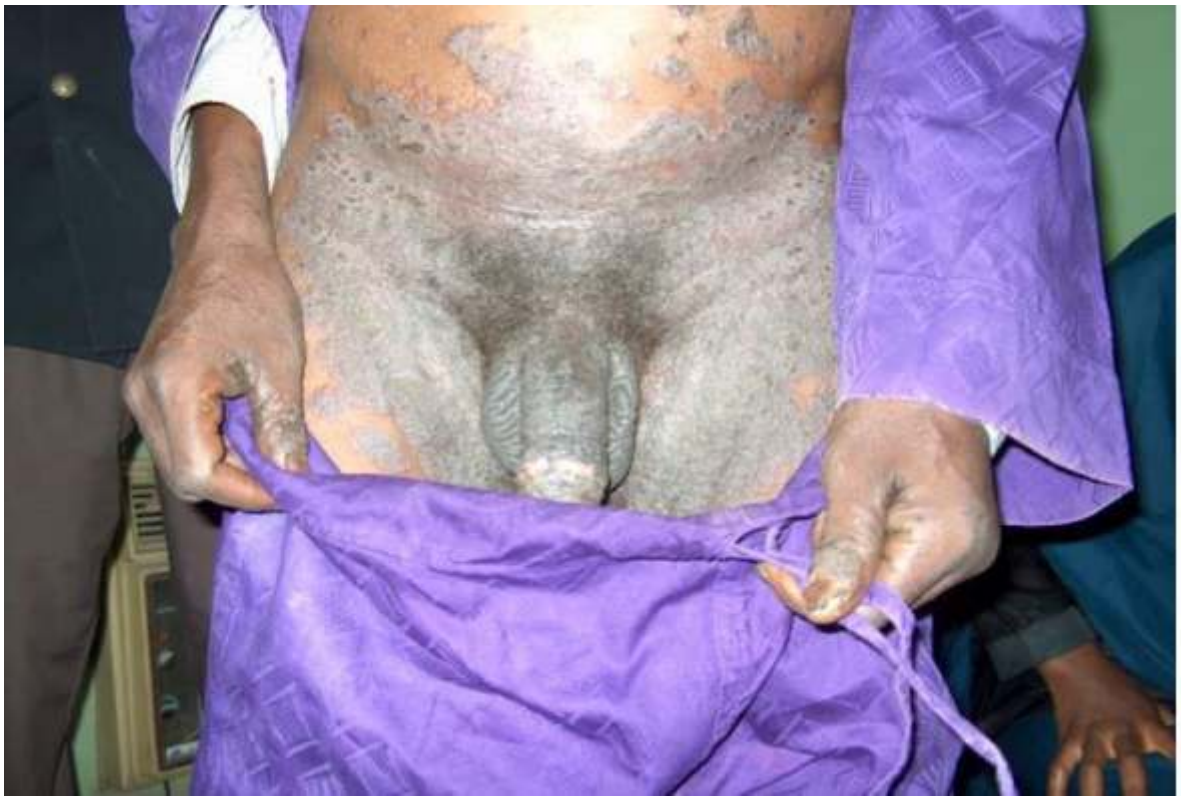

Fig 2h

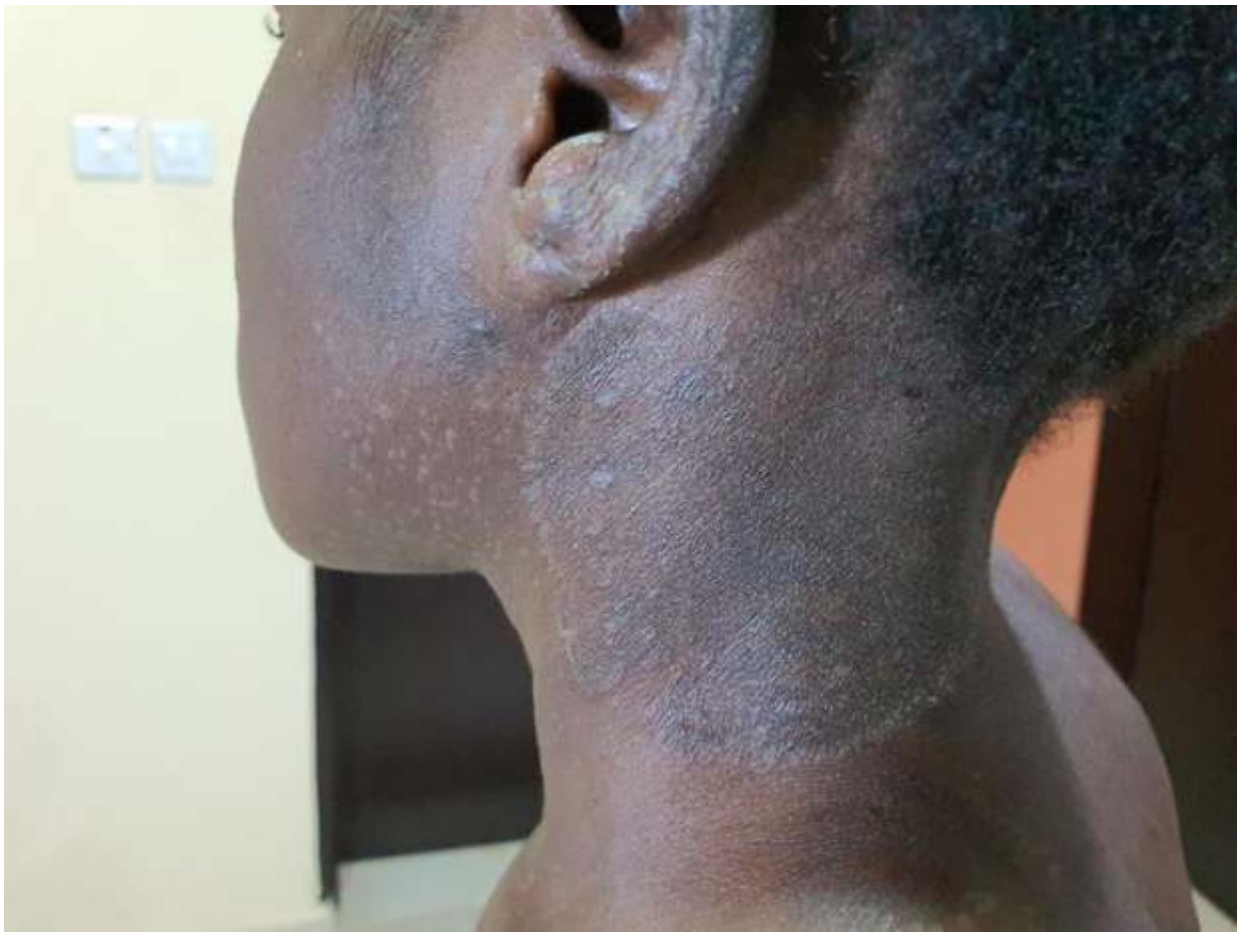

Fig 2i

Discussion

Our data, spanning 20 years, shows a change in the relative frequency and type of HIV-related skin disease in Kaduna, North-West Nigeria from the first decade of the study (2001 – 2010) to the second (2011 – 2022). Almost two-thirds of the patients were seen during the first decade, a period when HIV testing, treatment and care in Kaduna State were not widely available and HIV prevalence rates were above 5% and rising. [19] The number of patients with HIV-related skin disease fell sharply after 2010, typified by the significant drop in the most common skin disease seen in these patients, PPE, which constituted over 40% in the first decade but less than a quarter of cases in the second. Increasing access to testing, treatment and care is the most likely explanation for this observation – our data shows that four times as many patients knew their status and received treatment in 2011 – 2021 than in 2001 – 2010. HIV care, treatment and support became more widely available in Kaduna State in 2007 when several secondary care facilities, supported by donor agencies, started providing and augmenting services. According to UNAIDS – Joint United Nations Program on HIV/AIDS – there was a 20-fold worldwide rise in access to HAART from 2003 to 2011, and with the adoption of the test and treat policy in 2016,[21] HIV treatment coverage in Nigeria increased from 55% in 2016 to over 85% in 2020.[22] Availability of HAART has had a major impact in the frequency and pattern of HIV-related skin disease worldwide [16] and our study highlights some of the similarities and differences.

The pruritic papular eruption, first described in African patients by Colebunders et al.,[23] is caused by hypersensitivity to insect bites [24] resulting from immune dysregulation in HIV infection and is a marker of immune deficiency - 70% of our patients with PPE had a CD4 cell count less than 200 at presentation - and is often the first indication of HIV; its prevalence mirrors the underlying immune deficiency and has been used as a surrogate for HIV diagnosis during the early period of the pandemic

when testing was not widely available. [25] PPE resolves within 24 months of instituting ARV, and its recurrence or worsening suggests ARV failure.[26] The characteristic itchy, excoriated, lichenified, hyperpigmented papules and nodules on exposed parts of the body, and the subsequent scarring, were well known to be associated with HIV infection in the hospital setting and the community leading to stigmatization.[25] It is far more common in the tropics than in temperate climates reflecting differences in exposure to insect bites. [11-15, 20, 23-27] It is interesting that PPE occurred significantly more frequently in our female patients than males (43% vs 29.8%), an observation also made in Uganda [24, 26] and India.[27] Differences in clothing and exposure to insect bites between the sexes may explain these findings.

Herpes zoster occurs throughout the course of HIV infection, but is more common as immune function deteriorates; [28] although its incidence falls with treatment, the disease is three times more likely to occur in HIV infected patients than in the general population [29] and the risk may remain constant.[30] Our findings agree with these observations: herpes zoster was significantly more common in our patients who had HIV infection than those who did not. It was also more common in those who had not received ARV irrespective of the period when they were seen but the relative incidence of the condition was, nevertheless, higher in the 2011 – 2021 period when treatment was more widely available. Vanhems *et al*. have suggested that viral latency in nerve root ganglia might limit exposure of varicella-zoster virus to immune restoration and patients continue to be at risk of developing herpes zoster.[30] Herpes zoster in patients receiving ARV may also represent an IRS.[28, 29] Kaposi sarcoma was seen exclusively in those with HIV infection, and given that HIV-related Kaposi sarcoma is also known to occur as immune deficiency worsens, and the incidence falls when HAART is started, [16] the proportion of cases in our study was the same in the decade before ARVs were more widely available. Reasons for this observation may also include Kaposi sarcoma presenting as IRS when ARVs are introduced or as a manifestation of ARV failure. Kaposi sarcoma has also been noted to occur even when CD4 count is high and viral load is low, although these cases tended to have less severe and indolent disease; [31] this phenomenon has been attributed to immunosenescence similar to Kaposi sarcoma in elderly non-HIV infected patients.[32] Clinicians should be vigilant to diagnose and promptly treat both herpes zoster and Kaposi sarcoma even in patients receiving ARV to prevent complications.

Almost all our patients diagnosed with HIV-related atopiform (atopic dermatitis-like) eczematous reaction (96.3%) were 20 years of age or above, in contrast to patients with atopic dermatitis in the general population who are considerably younger.[33] There are three main putative mechanisms through which HIV infection increases the risk of atopiform dermatitis, a condition which, unlike atopic dermatitis, is not associated with Ig E-mediated hypersensitivity to environmental allergens:[34] The immune dysregulation in HIV infection causes a shift from TH2 cytokine response (upregulation of interferon-gamma, interleukin (IL) 2 and tumor necrosis factor beta) to TH1 cytokine response (mainly IL 4 and IL5) which triggers an inflammatory reaction in keratinocytes leading to eczematous dermatitis. HIV infection is also associated with cutaneous xerosis; the associated disruption in epidermal barrier function allows environmental allergens to penetrate the skin and are taken up by Langerhans and dendritic cells, which initiate the recruitment of inflammatory cells and release of cytokines resulting in inflammation.[34] Lastly, *Staphylococcus aureus* colonization of the skin is widespread in patients with HIV infection,[34] and exotoxins produced by these organisms are believed to have superantigen activity by binding to the T cell receptor and inducing T cell activity leading to inflammation. Seborrhoeic dermatitis, another inflammatory disorder, was a lot less common in our patients than has been reported worldwide although it is similar to most other African reports [1,3,25,35], and in Asia.[15,36] Another inflammatory condition, psoriasis, was more severe in our patients but its relative frequency was similar irrespective of the period or ARV use.

While the numbers of patients with infectious conditions such as extensive plane warts, genital herpes simplex and dermatophyte infection were small, and it is difficult to reach any firm conclusions on their occurrence, they were relatively more common in the second period than in the first. They were more likely to affect patients who had received or were receiving ARV probably suggesting they may be markers of failing immunity due to ARV

failure. Molluscum contagiosum was, however, significantly more common in those who had not received ARV and was relatively more common in HIV infected patients than those without. Although prevalence of psoriasis did not differ according to period or ARV use, it was relatively more frequently diagnosed in patients with HIV infection that those who were not infected, underscoring the influence of immune dysregulation and immune deficiency in this inflammatory disease. Adverse drugs reactions (ADR), which are more frequent and more severe in patients with HIV infection as a result of immune dysregulation,[37] occurred mostly in the 2001 – 2010 period and in patients who received ARV, a period when testing and care were not easily available, and when nevirapine was a major component of first line treatment regimens. Nevirapine, a frequent offender in our patients, as was of others,[38] was replaced entirely by efavirenz as a first-line drug in 2016 on the recommendation of the World Health Organization because of its cutaneous and hepatic toxicity and lower efficacy.[39]

Our study has some limitations. It is a retrospective study from a private healthcare provider, and this may explain why males outnumber females, although the latter constitute a greater percentage of patients with HIV in Nigeria.[18] Also, CD4 count results were only available for a third of patients as our centre did not perform this test and patients often did not return with test results when requested. This also applies to viral load tests which were available in very few centers until recently. Nonetheless, our center was an open-access center where patients with skin disease were seen almost every day and is only one of two centers in Kaduna where a trained dermatologist was available over this extended period. We believe our observations improve our understanding of time trends in frequency and type of HIV-related skin disease in Northern Nigeria, an area from whom similar reports are scanty.

Conclusion

We have reported a marked reduction in the relative frequency and a change in the pattern of HIV-related skin disease in Kaduna, North-West Nigeria from the first ten years (2001 – 2010) to the second (2011 – 2021). We attribute these changes to greater access to testing, care and treatment for patients in the second period, thus highlighting the positive influence of treatment on changing the epidemiology of the disease.

References

1. Mbuagbaw J, Eyong I, Alemnji, G, Mpoudi N, Same-Ekobo A. Pattern of skin manifestations and their relationships with CD4 counts among HIV/AIDS patients in Cameroon. Int. J. Dermatol. 2006; 45: 280 - 284.
2. Nnoruka EN, Chukwuka JC, Anisuiba B. Correlation of mucocutaneous manifestations of HIV/AIDS infection with CD4 counts and disease progression. Int. J. Dermatol. 2007; 46(Suppl 2): 14 - 18.
3. Oninla OA. Mucocutaneous Manifestations of HIV and the Correlation with WHO Clinical Staging in a Tertiary Hospital in Nigeria. AIDS. Res. and Treat. 2014; 2014: 360970.
4. Moir S, Chun TW, Fauci AS. Pathogenetic mechanisms of HIV disease Annu. Rev. Pathol. Mech. Dis 2011; 6: 223 - 248.
5. Cedeno-Laurent F, Gomez-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.
6. Richmond JM, Harris JE. Immunology and Skin in Health and Disease. Cold. Spring. Harb. Perspect. Med. 2014; 4: a015339.
7. CDC. Kaposi Sarcoma and Pneumocystis Pneumonia Among Homosexual Men – New York City and California MMWR 1981; 30: 305 - 308.
8. Barre-Sinoussi F, Chermann JC, Rey F, Nugeyre MT, Chamaret S, et al. Isolation of T-Lymphotropic Retrovirus from a Patient at Risk for Acquired Immune Deficiency Syndrome (AIDS). Science. 1983; 220: 868 - 871.
9. Case K. Nomenclature: Human Immunodeficiency Virus. Ann. Int. Med. 1986; 105: 133.
10. James WD, Redfield RR, Lupton JP, Meltzer MS, Berger TG, et al. A papular eruption associated with T cell lymphotrophic virus type III disease. JAAD. 1985; 13: 563 - 566.
11. Coldiron BM, Bergstresser PR. Prevalence and Clinical Spectrum of Skin Disease in Patients Infected with Human Immunodeficiency Virus. Arch. Dermatol 1989; 125: 357 - 361.
12. Pallangyo KJ. Cutaneous findings associated with HIV disease including AIDS: Experience

from Sub Saharan Africa. Trop. Doct. 1992; 22(suppl 1): 35 - 41.

13. Motswaledi MH, Visser W. The Spectrum of HIV-Associated Infective and Inflammatory Dermatoses in Pigmented Skin. Dermatol. Clin. 2014; 32: 211 - 225.
14. Tschachler E, Bergstresser PR, Stingl G. HIV-related skin diseases. Lancet. 1996; 348: 659 - 663.
15. Huang X, Li H, Chen X, Wang Z, Li Z, Wu, Y, et al. Clinical Analysis of Skin Lesions in 796 Chinese HIV-positive Patients. Acta. Derm. Venereol. 2011; 91:552 - 556.
16. Chelidze K, Thomas C, Chang AY, Freeman EE. HIV-related Skin Disease in the Era of Antiretroviral Therapy: Recognition and Management. Am. J. Clin. Dermatol. 2019; 20: 423 -442.
17. Federal Ministry of Health (FMOH). Technical report on National HIV Sero-prevalence sentinel Survey Among Pregnant Women Attending Antenatal Clinics in Nigeria. Abuja, 2010.
18. NAIIS National Fact Sheet. Nigeria HIV/AIDS Indicator and Impact Survey, 2019; p. 2
19. Bashorun A, Nguku P, Kawu I, Ngige E, Ogundiran A, Sabitu K, et al. A description of HIV prevalence trends in Nigeria from 2001 to 2010: What is the progress, where is the problem? Pan. Afr. Med. J. 2014; 18(Suppl 1): 3
20. Ekpe O, Onunu AN, Forae GD, Okwara B. Clinicopathological Features of Pruritic Papular Eruption of HIV Patients Seen in Benin-City, Nigeria. West. Afr. J. Med. 2020; 37: 53 -57.
21. Federal Ministry of Health, Abuja, Nigeria. National Guidelines for HIV Prevention, Treatment and Care. 2016; p 17 - 26.
22. UNAIDS. Five questions about the HIV response in Nigeria, 31 October 2021. Available at: Five questions about the HIV response in Nigeria | UNAIDS [Last accessed 30 July 2022].
23. Colebunders R, Mann JM, Francis H, Bila K, Izaley L, Kakonde, N, et al. Generalized papular pruritic eruption in African patients with HIV infection. AIDS. 1987; 1: 117 - 121.
24. Resneck JS, 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 - 2621.
25. Lowe S, Ferrand RA, Morris-Jones R, Salisbury J, Mangeya N, Dimairo, M, et al. Skin disease among Human Immunodeficiency Virus-infected adolescents in Zimbabwe: a strong predictor of underlying HIV infection. Pediatr. Infect. Dis. J. 2010; 29: 346 - 351.
26. Castelnuovo B, Byakwaga H, Menten J, Schaefer P, Kamya M, Colebunders R. Can response of a pruritic papular eruption to antiretroviral therapy be used as a clinical parameter to monitor virological outcome? AIDS. 2008; 22: 269 - 273.
27. Farsani TT, Kore S, Nadol P, Ramam M, Thierman SJ, Leslie K, et al. Etiology and risk factors associated with a pruritic papular eruption in people living with HIV in India. J. Int. AIDS. Soc. 2013; 16: 17325.
28. Shearer K, Maskew M, Ajayi T, Berhanu R, Majuba P, Sanne I, et al. Incidence and predictors of herpes zoster among antiretroviral therapy-naïve patients initiating HIV treatment in Johannesburg, South Africa. Int. J. Infec. Dis. 2014; 23: 56 - 62.
29. Grabar S, Tattevin P, Selinger-Leneman H, de La Blanchardiere A, de Truchis P, Rabaud C, et al. Incidence of Herpes Zoster in HIV-Infected Adults in the Combined Antiretroviral Therapy Era: Results From the FHDH-ANRS CO4 Cohort. Clin Infect Dis 2015; 60: 1269 - 1277.
30. Vanhems P, Voisin L, Gayet-Ageron A, Trepo C, Cotte L, Peyramond, D, et al. The Incidence of Herpes Zoster is Less Likely Than Other Opportunistic Infections to Be Reduced by Highly Active Antiretroviral Therapy. J. Acquir. Immune. Defic. Syndr. 2005; 38: 111 - 113.
31. Crum-Cianflone NF, Hullsiek KH, Ganesan A, Weintrob A, Okulicz JF, et al. Is Kaposi Sarcoma Occurring at Higher CD4 Counts Over the Course of the HIV Epidemic? AIDS. 2010; 24: 2881 -2883.
32. Unemori P, Leslie KS, Hunt PW, Sinclair E, Epling L, Mitsuyasu, R, et al. Immunosenescence is associated with presence of Kaposi's sarcoma in antiretroviral treated HIV infection. AIDS 2013; 27: 1735 - 1742.
33. Emanuel PO, Scheinfeld N, Williams HC. The Epidemiology of Atopic Dermatitis. In: Rudikoff R, Cohen S, Scheinfeld N, editors. Atopic Dermatitis and Eczematous Disorders. Boca Raton: CRC Press (Taylor & Francis Group); 2014, p. 25 - 38.
34. Friedman A, Rudikoff D, Lacobellis F. HIV Infection and Atopic Dermatitis. In: Rudikoff R,

Cohen S, Scheinfeld N, editors. Atopic Dermatitis and Eczematous Disorders. Boca Raton: CRC Press (Taylor & Francis Group); 2014, p. 341 - 350.

35. Bakari M, Lyamuya E, Mugusi F, Aris E, Chale S, Magao P, et al. The prevalence and pattern of skin diseases in relation to CD4 counts among HIV-infected police officers in Dar es Salaam. Trop. Doct. 2003; 33: 44 - 48.

36. Punyaratabandhu P, Prasithsirikul W, Jirachanakul P. Skin Manifestations of Thai HIV Infected Patients in HAART Era. J. Med. Assoc. Thai. 2012; 95: 497 - 504.

37. Peter J, Choshi P, Lehloenya R. Drug hypersensitivity in HIV infection. Curr. Opin. Allergy. Immunol. 2019; 19: 272 - 282.

38. Sarfo FS, Sarfo MA, Norman B. Incidence and determinants of nevirapine and efavirenz-related skin rashes in West Africans: nevirapine's epitaph? PLoS. One 2014; 9: e94854.

39. World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. Recommendations for a Public Health Approach. 2nd Ed. Geneva: WHO Press; 2016, p. 98.

Cite this Article as: Yahya H. HIV-Related Skin Disease in Kaduna, North-West Nigeria: A 20-Year Experience. **Bo Med J** 2022;19(2):110-127 **Source of Support:** Nil**, Conflict of Interest:** None declared