THE SPECTRUM OF DERMATOLOGICAL MANIFESTATIONS AMONG HIV INFECTED PATIENTS AT AMPATH CLINIC IN ELDORET, KENYA

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A RESEARCH THESIS PRESENTED IN PARTIAL FULFILLMENT FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE

THE SPECTRUM OF DERMATOLOGICAL MANIFESTATIONS AMONG HIV INFECTED PATIENTS AT AMPATH CLINIC IN ELDORET, KENYA

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Student's Declaration:

I declare that this research thesis is my original work and that it has never been presented for a degree in any other university. No part may be reproduced without prior permission of the author or Moi University.

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DEDICATION

This thesis is dedicated to my grandmother

ABSTRACT

Background: Skin and mucocutaneous diseases are common among HIV infected patients. The introduction of antiretroviral therapy (ART) has changed the spectrum of skin and mucocutaneous disorders among HIV infected patients. There is need to assess the changing spectrum of skin diseases after the introduction of antiretroviral. Currently there are few studies, which have assessed the spectrum of skin diseases in HIV infected patients in Western Kenya.

Objective: To determine the spectrum of skin disorders among ART naive and ART experienced HIV infected patients attending Academic Model Providing Access to Health care (AMPATH) clinic Eldoret, Kenya.

Method: This was a cross-sectional study that recruited 490 HIV infected patients who attended AMPATH clinic from October 2016 to September 2017.A systematic random sampling was used to select the patients in the study. The socio-demographic and clinical data was collected using a structured questionnaire. Full body examination was done under adequate light by the investigator and confirmed by a dermatologist. All findings were entered in to a questionnaire and digital photography was captured. A total of 13 patients had unclear diagnosis, which was confirmed with a biopsy. The data was analyzed using STATA version14, the categorical variables summarized as frequencies and percentages. Continuous variables were summarized as median and interquartile range. Pearson's Chi Square test was used to assess association between categorical variables.

Results: The prevalence of skin disorders in this study was 51.42% (95% CI 46.90, 55.93). The median age was 39 years (IQR: 32, 46) with female preponderance (70.4% vs. 29.6%). Majority of the participants, 59.30% were in WHO clinical stage I and II. The median baseline CD4 cell count was 302 (IQR 160,479) with a plasma viral load 108log10 copies/ml (IQR 0,1120log10 copies/ml). Most of the patients (60.4% 296) were on ART. The antiretroviral-naive patients had a higher proportion of dermatological disorders than antiretroviral- experienced patients (62.89% vs. 43.92%, P <0.001).

Infectious disorders were more common among ART-naive, 58.1% while eczematous conditions were frequent among ART-experienced patients, 51.85 %. The median duration of skin disorder was 3months (IQR 2, 5).

Conclusions: Eczematous skin disorders were more frequent among antiretroviral-experienced patients while infections related skin disorders were more common among antiretroviral naive patients. A higher viral load was associated with increased frequency of skin diseases.

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ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
AMPATH	Academic Model Providing Access to Healthcare
ART	Antiretroviral therapy
CD4	Cluster of differentiation 4
HAART	Highly active antiretroviral therapy
HIV	Human Immunodeficiency Virus
IREC	Institutional Research and Ethics Committee
MTRH	MOI Teaching and Referral Hospital
WHO	World Health Organization

DEFINITION OF TERMS

ART-experienced	HIV-infected patient on antiretroviral therapy
ART-naïve	HIV-infected patients not on antiretroviral therapy
Critically sick	In-patient
Dermatologic skin manifestation	All of skin, nail, hair and mucocutaneous diseases. Can be divided into five groups: Eczematous, Infectious, adnexal, malignancy and miscellaneous skin disorders

CHAPTER ONE: INTRODUCTION

1.1 Background

The HIV infection is an uphill task faced by the whole world and it is a calamity that has affected many countries (WHO, 2017). There were 37.9 million people living with HIV in 2017 with 23.3 million people accessing antiretroviral therapy by June 2017 (WHO, 2015). 0.8 Million people have died of AIDS-related illnesses including skin disorders (WHO, 2017).

In 2017 it was estimated that 20.6 million people were living with HIV infection in Sub-Saharan Africa. Women account for more than half of the total number of people living with HIV in sub-Saharan Africa (WHO, 2016). Sub-Saharan Africa accounts for 66% of the global total of new HIV infections. In 2017, there were an estimated 1 million new HIV infections in sub- Saharan Africa (USAIDS 2017).

Kenya is ranked fourth among countries with the highest HIV infection in the world (WHO 2016). The prevalence of HIV/AIDS in Kenya is 4.9% (NASCOP update 2017) while the prevalence of HIV/AIDS in Eldoret is estimated at 4.2% (NASCOP update 2017).

A healthy individual has a CD4 count of 1200-1400. The declining CD4 count often is associated with the appearance of certain cutaneous conditions. The number of T-helper lymphocytes (CD4 count) is a useful measure of a patient's immune-competence or, by inference, disease progression. In patients with HIV infection, a CD4 cell count below 200 correlates with a number of skin conditions, including severe systemic and cutaneous infections caused by viruses, bacteria, parasites or fungi (Kumarswamy N, 2000). The level of CD4 cell count is useful measure of an individual's immunity which determines the risk for skin disorders including severe

systemic and cutaneous infections caused by viruses, bacteria or fungi (Aftergut K, 1999).

Dermatologic skin manifestation includes all skin, nail, hair and mucocutaneous diseases. This can be divided into five groups: Eczematous, Infectious, adnexal, malignancy and miscellaneous skin disorders (Preawphan. 2012).

Mucocutaneous diseases are the first identifiable manifestation in HIV infected patients. It could be the earliest sign and reflects the progression of HIV disease. In the Pre-HAART era, most of the mucocutaneous diseases were opportunistic infections such as oral candidiasis, neoplasm such as Kaposi's sarcoma, and inflammatory disorder, which were caused by diminution of patient's immunity such as oral hairy leukoplakia and Pruritic Papular eruption (Hengge UR, 2000).

In the Pre-HAART era HIV related skin disorders were frequent and regular among HIV infected individuals (Reynand- Mendel B, 1996) and after the introduction of HAART the frequency of dermatological disorders decreased and this is thought to be due to immune reconstitution while reappearance of mucocutaneous disorders is due to immunological and virological failure (Montazeri A, 1996).

The effectiveness of HAART, has led to a significant change in epidemiology and clinical manifestation skin diseases in HIV patients. In the HAART era, mortality rate has reduced markedly and the patient's immunity has increased significantly. The ART has been proven to enhance CD4 restoration and suppress viral replication, which in turn decreased in AIDS-defining illness, including Kaposi's sarcoma and esophageal candidiasis.

Mucocutaneous complications in HIV infected persons can be disfiguring and life threatening (Rigopoulos D, 2004). The HIV infected individuals may present with skin disorders or may develop during the course of the illness. Skin signs give an indication of the degree of immune depletion. Skin signs are a common component of drug reactions and immune reconstitution and inflammatory syndrome (IRIS) (Casioglia JW, Woo S-B, 2004).

It is noted that 80-95% of HIV infected individuals present with some sort of skin disorders (Tschachler E, 1996). These skin disorders are seen in all stages of infection and range from opportunistic infections and inflammatory dermatoses to cutaneous malignancies. They may also be due to the drug treatment given to the patient (Uthayakumar S, 1997). Alteration in the immune status of the patient along with a low CD4 count has been found to be associated with an increased occurrence of skin disorders (Uthayakumar S N. R., 1997). The normal CD4 cell count in adults ranges from 500-1500 cells per mm. (Erdar E, 2009),.

Seborrhoeic dermatitis, candidiasis and hairy leukoplakia may be strong indicators of underlying HIV infection (Osborne GEN, 2003). The T-helper cells are burdened by HIV infection, where the normal Th1 mediated immune response is converted to Th2 mediated response resulting in severe skin disease (Raju PV, Rao GR, Ramani TV, Vandaman S, 2005). The reduced immune function in the skin is correlated with many HIV related non- infectious skin diseases (UNAIDS, WHO, 2015).

Skin disorders can be elicited in every stage of human immunodeficiency virus (HIV) infection Skin lesions can often be the first indication that an individual is infected with HIV (Munoz Perez MA, 1998). The different types of skin manifestations in HIV infected individuals' shows to be correlated with the degree of

immunodeficiency (Gao U, 2008). Several skin disorders may act as indicators for the diagnosis and monitoring of HIV infection.

1.2 Problem Statement

There is high burden of skin disorders among HIV patients and the diagnosis of skin and mucosal conditions is often difficult. More than 90% of HIV-infected patients develop skin lesions at some time throughout the course of the disease (Kumarswamy N, 2000).

In Eldoret there are many HIV infected patients attending the AMPATH HIV clinic and skin disorders are regularly seen as a sign of HIV infection and conversion to AIDS.

Patients may present with atypical signs and a single etiologic agent may cause diverse clinical features. (Kumarswamy N, 2000).

Several skin diseases have proved to be sensitive and useful indicators of progression of HIV infection. Although these conditions may be seen in general healthy population, their occurrence in patients with acquired immunodeficiency syndrome is often atypical and more severe.

Thus proper diagnosis of skin manifestations is very important as it may serve as the earliest manifestation to suspect a case of HIV infection.

Infectious agents can produce skin lesions even though the classic of involvement for that agent does not include the skin. HIV/AIDS infection is a highly stigmatized disease that causes an immense psychosocial effects on affected individuals.

HIV/AIDS has a lot of human suffering socially, psychologically and aesthetically and when it coexists with skin disorders it has unfavorable and unpleasant blow on health programs. Mucocutaneous conditions are appreciably high in HIV patients than non-HIV patients. The proficiency to diagnose skin disease is inadequate in sub-Saharan Africa, Kenya included.

However, despite the hefty number of patients enrolled at AMPATH HIV clinic, there are no studies on the spectrum of dermatological manifestation in HIV infected patient attending this AMPATH clinic in Eldoret.

1.3 Justification

The information skills and understanding of the range of skin disorders in HIV-infected patients is of great importance to the health care providers, this will assist in prompt diagnosis and treatment. The intervention of early treatment will also reduce stigma as HIV/AIDS infections is highly stigmatized and causes an immense psychosocial effects on the affected individuals especially when it co-exists with skin disorders.

Special HIV clinics are available with few dermatologists with no proper referral systems. Careful skin examination of HIV infected patients who present at primary health care facilities have received limited attention.

Dermatological manifestations differ among countries and currently there is insufficient data on skin disorders among patients attending AMPATH HIV clinic in Eldoret, Western Kenya.

This study therefore assessed the spectrum of dermatological manifestation among HIV infected patients attending the AMPATH HIV clinic in Eldoret, Kenya.

1.4 Objectives

1.4.1 Broad Objective

To assess the spectrum of skin disorders among HIV infected patients attending AMPATH clinic Eldoret, Kenya

1.4.2 Specific Objectives

1. To establish the spectrum of skin disorders in HIV infected patients.
2. To find out the proportion of HIV infected patients with skin disorders on ART (experienced) to ART-naive patients.
3. To compare the skin disorders of ART experienced and ART-naive with their CD4 cell count and viral load.

CHAPTER TWO: LITERATURE REVIEW

The burden of skin conditions in developing countries is vast and huge with severe impact on quality of life and loss of output at work and school with aesthetic defacement (NACO, India), (NACO, 2006), (Bravo, 2004). Infectious dermatoses are the most common skin ailments due to overcrowding, poor sanitary conditions, sharing of personal effects or formites with poor access to medical supplies and treatment (Ranganathan K, 2004), (Moniaci D, 1990).

The skin ailments are further compounded by the soaring prevalence of HIV, which frequently cause skin lesions (Wiwanikti V, 2004), (Kumarasany N, 2000). Nearly 90% of people living with HIV have skin condition during the course of the disease (Coopman SA, 1993).

Mucocutaneous conditions are appreciably high in HIV patients than non-HIV patients (Tschachler E, 1996). The variation in climate, hygiene, genetic, pigmentation, demographic and behavioral factors cause disparity in clinical features in HIV-associated skin manifestation in Africa (Uthayakumar S N. R, 1997), (Goldstein B, 1987). Unpleasant drug reaction is reportedly common among HIV infected individuals than the non-HIV patient (Nadia Ali Azfar, 2011).

HIV propels the capacity to be photosensitive and most of the individuals with HIV use photosensitizing drugs like cotrimoxazole thus augment the photosensitivity (Wiwanikti V, 2004).

Mucocutaneous conditions are highly prevalent in patients with HIV but the pattern varies from region to region, therefore all patients with HIV are examined for mucocutaneous disorders (Sanjay M, 1997).

The acquaintance of mucocutaneous signs of HIV/AIDS is vital as these are the earliest manifestation of HIV; it ensures timely diagnosis and quick treatment and detects complications as HIV causes atypical and harsh features of this ailments (Smith KJ, 1993), (Goodman DS, 1987). Those in the health care provision must therefore have knowledge in the recognition of common skin diseases and the prevalence in their locality (Colddiron BM, 1989), (AIDS, USAIDS, 2010).

A total 37% of patients present with mucocutaneous lesions as a sign of HIV infection (Coopman SA J. R., 1993). As the immunity declines, the severity of the skin conditions increase and the tendency to relapse wheels. The patient often shows feature of atypical presentation, which fails respond to commonly used medications.

It’s approximated that 50-70% of the patients will have acute syndrome after infection, they present with fever, sore throat, myalgia, headache and cervical lymphadenopathy. The cutaneous presentation include maculopapular rash with central petechiae (Coopman SA J. R., 1993).

Dermatological diseases are both individual and public health problems worse in HIV patients who present in atypical manner (Coopman SA. J.R., 1993). Extensive HIV related literature has focused on unique clinical presentation such as Kaposi sarcoma, oral hairy leukoplakia and oral candidiasis (Colddiron BM, 1989).However, the findings on careful skin examination of HIV infected patients who present for primary care have received limited attention.

The HIV attacks the CD4 cells resulting in destruction of these immune cells with slow but progressive demolition of the CD4 cells. As these cells decline in population patient develops diverse mucocutaneous disorders thus revealing failing immune system. HIV infection is a challenge faced by the entire world. It is a devastating human crisis that has affected many countries including Kenya.

The normal CD4 cell count in adults ranges from 500-1500 cells per mm (Goodman DS, 1987) low CD4 count is associated with raised occurrence of skin conditions, (Goodman DS, 1987) these disorders may be due to the medications given to the patient. The skin presentation may be acute, recurrent, explosive and atypical thus resulting in appreciable morbidity and aesthetically challenging leading to psychomotor disorders and poor value of life (Nadia Ali Azfar, 2011).

Skin conditions have been correlated with CD4 counts in many studies (Goodman DS, 1987). Skin conditions may be the initial signs of immunosuppression and cause considerable morbidity (Uthayakumar SN.R, 1997) and it’s the only organ affected

during most of the course of HIV disease (Goodman DS, 1987). Some skin conditions may be a sign of HIV progression (Coopman SA J.R. 1993).

Skin disorders provide a hint to the degree of immune deficiency and prognosis of the patient; the skin is a site for drug reaction and immune reconstitution and inflammation syndrome. The number of CD4 cell count is valuable measure of a patient's immune competence and to an extent the disease progression; falling CD4 cell count is associated with worsening of skin disorders (Uthayakumar S N. R., 1997). In resource limited community where CD4 count is not readily available, skin conditions serve as indicators of HIV/AIDS which correlates with WHO clinical stages can be use to assess HIV patients (Ranganathan K, 2004).

CHAPTER THREE: METHODOLOGY

3.1 Study setting

The study was conducted at AMPATH HIV Clinics at Moi Teaching and Referral Hospital, Eldoret between October 2016 and September 2017. Eldoret is the headquarters of Uasin Gishu county lying south of the Cherangani Hills. The altitude of Uasin Gishu varies from 2100metres to 2700 metres above sea level. Eldoret is the second largest urban centre west of the Great Rift Valley after Kisumu and the fifth largest urban centre in the country with a population of about 400,000 persons. It is currently the fastest growing town in Kenya.

The AMPATH is a joint program for Moi University, Moi Referral Hospital and a consortium of North American universities led by Indiana University working in partnership with the Government of Kenya. AMPATH treats over 180000 HIV-

positive persons in over 500 clinical sites throughout Western Kenya. It is estimated that 2000 new patients are being enrolled in these clinics monthly.

3.2 Study population

HIV infected adults above 18 years who were enrolled into care at AMPATH clinic.

3.3 Eligibility

3.3.1 Inclusion criteria

HIV-infected patients above 18 years of age

3.3.2 Exclusion criteria

Critically sick patient as defined in the study

3.4 Study design

This was a cross-sectional study

3.5 Sample size

$N=Z^2p\ (1-p)/d^2$

N: minimum sample size

z: statistic for a level of confidence set at 95% confidence interval

p: prevalence 40%(Calista D et al 2002)

$$N = \frac{(1.96^2)*0.40*0.60}{(0.05)^2}$$

N= 369 participants

3.6 Sampling technique

Systematic random sampling was used to carry out the study at AMPATH clinic.

Every Eighth patient who consented to the study was recruited, examined for skin lesions and recorded the ART status.

Every eighth interval was arrived at by considering that an average of eighty patients was seen on a daily basis and the study target was to recruit ten participants per day. Eighty divided by ten gives an interval of eight.

The recruitment was done until the desired sample size was achieved.

A total of 490 participants, comprising 190 ARV-naive and 300 ARV-experienced were recruited into the study.

3.7 Study procedure

The study was conducted at AMPATH HIV clinic in MTRH. Recruitment of participants into the study was done in the clinic. The purpose of the study and potential benefits was explained to individual participants in a language they comprehended and all their concerns were addressed.

The participants who met the inclusion criteria and consented to participate in the study were enrolled after signing the consent forms. The participants were free to terminate their participation at any stage of the study without affecting the health care services they received in the institution.

A structured questionnaire was administered to participants to determine the demographic characteristics and history of HIV testing. A standardized clinical history was recorded and full dermatologic examination was performed by the study doctor, as part of a comprehensive clinical evaluation including WHO clinical staging.

The diagnosis of each skin condition was made according to the characteristic clinical appearance and photography of the lesions was captured and reassessed by the consultant dermatologist. Diagnostic biopsies were taken in few cases where the clinical diagnosis was not clear. The skin disorders were classified into eczematous disorders, infections, malignancies, adnexal and miscellaneous disorders

3.8 Data collection and management

Interviewer administered questionnaire was used to collect the demographic, socioeconomic and clinical data of the study participants. Data was entered into MS Access database and validated.

3.9 Data analysis

The completed questionnaires were coded and entered into an MS Access database and later exported into STATA version 14 for analysis. Categorical variables were summarized as frequencies and percentages.

Continuous variables were summarized as median and inter quartile range; Pearson's Chi Square test was used to assess association between categorical variables.

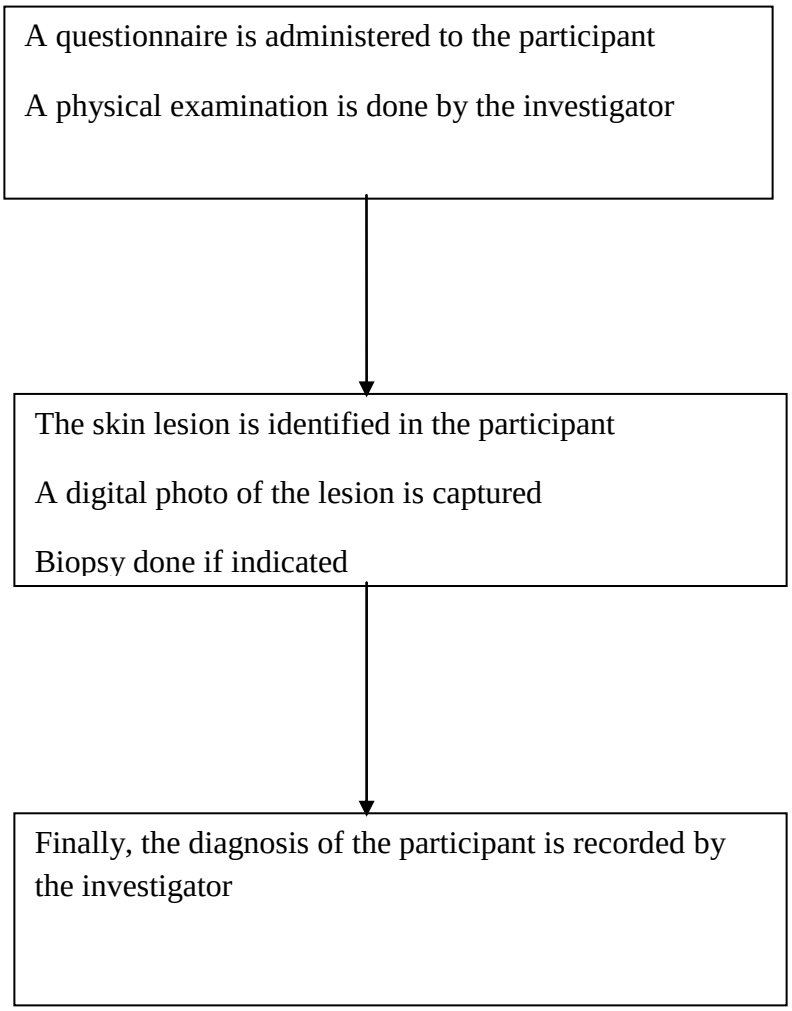
3.10 Ethical consideration

Ethical approval was obtained from Moi University Institutional Research and Ethical Committee (IREC). Permission to conduct the study was obtained from the management of AMPATH in Eldoret. Written informed consent was obtained from every participant before enrolling in the study. All patients with medical conditions were treated or referred accordingly.

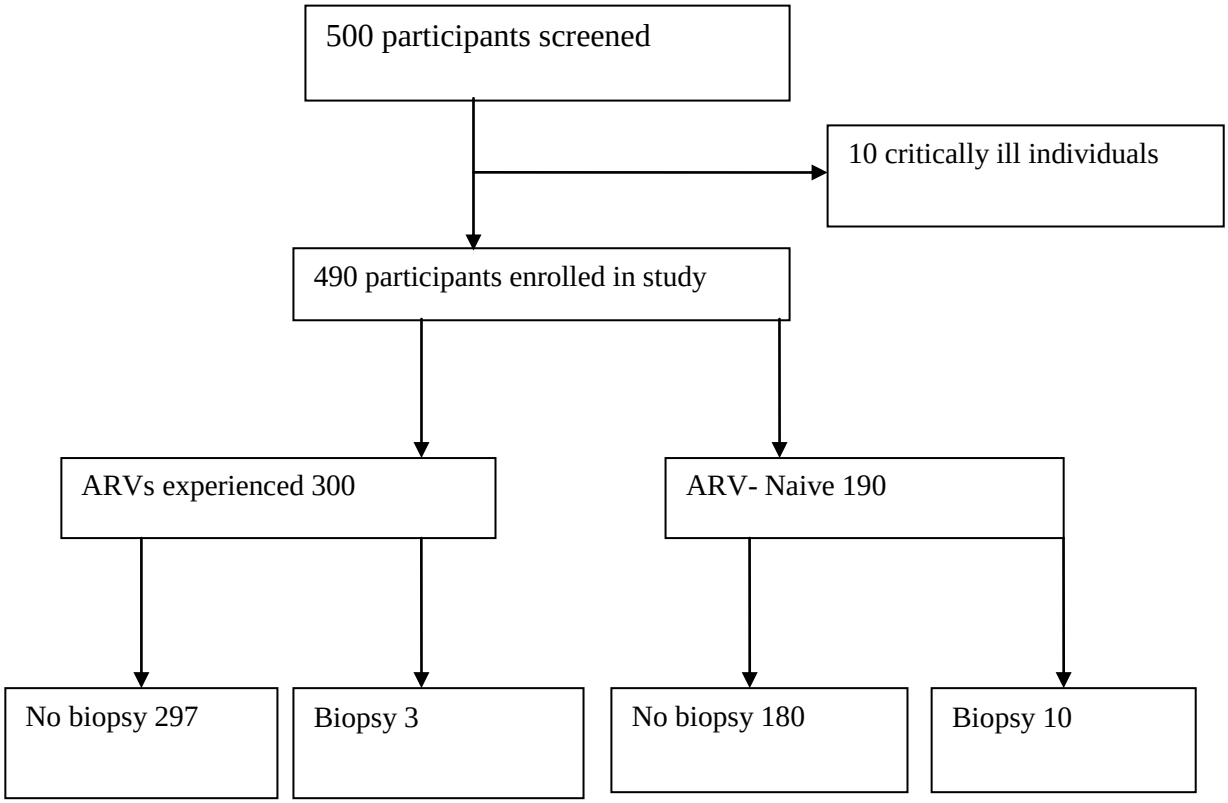
All the information obtained from the study was kept confidential. The investigator did not have any conflict of interest to declare.

Algorithm of study procedure

Study process



Recruitment Process



CHAPTER FOUR: RESULTS

Four hundred and ninety participants were recruited with median age of 39, the majority were female 70.4% with more than half married, 51.6%. Majority of the participants 83.7% had primary and secondary education and 59.4% of the study subjects' were casual laborers and farmers.

The median age of study subjects was 39 years (IQR: 32, 46 years). The median duration of cutaneous symptoms was 3 months, IQR: 2, 5 months and only 13 participants were done punch biopsy which revealed 10 Kaposis sarcoma, 2 discoid lupus erythromatosus and one Melanoma.

Most of the participants were on antiretroviral therapy 60.4% vs.39.6%, majority were on first line regimen 85.5% vs. 15.5% and most have never changed or switched the antiretroviral medication 83.3% vs. 16.7%, the median duration of antiretroviral therapy among the participants was 88 months (54, 120) and only 1.1% of the participants experienced drug reaction, 1.1% vs. 99.1%.

4.1Socio-demographic and clinical characteristics

The participants, 84% (n=309) had either primary or secondary level of education while 14.4% (n=7) had tertiary level of schooling and the remaining number of participants 1.6%, (8) had no formal level of teaching. Greater part of the participants, 52% (253) were married, 29.2 %(142) were single while the remaining 18.8 % (n=92) were either widow, divorced, widower or separated. The participants were largely casual laborers and peasant farmers, 59.3 %(290), small scale businesses accounted for 23.5% (115) while 17.2% (84) were either government or nongovernmental employees (Table1).

Table1: Demographic Characteristics

Variable	Freq /median	%/ IQR
Age in years	39	32, 46
Gender		
Female	345	70.40
Male	142	29.60
Education level		
None	9	1.80
Primary	212	43.30
Secondary	198	40.40
Tertiary	71	14.50
Marital		
Divorced	20	4.10
Married	253	51.60
Separated	6	1.30
Single	142	29.00
Widow	59	12.00
Widower	10	2.00
Occupation		
Business	115	23.50
Casual	208	42.70
Farmer	82	16.70
Government	62	12.70
Other	22	4.50

The participants were predominantly on ARVs, 60.4% (296) and 39.6% (194) were on first line regimen while 15.3% were on second line regimen. The majority of the participants on ARV were swallowing ARVs for a long duration, median 88 months (IQR: 54, 120), (Table2).

Table 2: Anti-retroviral characteristics of participants

	Frequency/Median	%/ IQR
On ART		
Yes	296	60.4
No	194	39.6
ARV regimen (n=296)		
First line	250	84.5
Second line	46	15.5
Duration on ART (n=296)	88	54, 120
Ever changed meds (n=296)		
Yes	50	16.7
No	246	83.3
Experienced drug reaction (n=296)		
Yes	26	5.3
No	270	94.7

The median CD4+ cell count at baseline was 302 cells/ll (IQR: 160,479 cells/ll), while the median plasma HIV RNA level at baseline was 108 log10 copies/ ml (IQR: 0, 1120 log10 copies/ml).

Pertaining to world health organization (WHO) clinical staging, 59.3% were either WHO stage I or stage II, 32.9% of the subjects had WHO clinical stage III disease, and 7.8% had WHO stage IV disease (Table 3).

4.2 HIV-infected patients and markers of Immunity

Table 3: Markers of Immunity (N=490)

	Freq/Median	%/ IQR
Baseline CD4	302	160, 479
Latest Viral Load	108	0,1120
WHO staging		
Stage 1	171	35.0
Stage 2	119	24.3
Stage 3	161	32.9
Stage 4	39	7.8

In relation to the type and area of skin lesion, 82% (187) were localized skin lesions while 18% (41) were generalized skin disorder.

The study participants, majority 54.7% (268) when asked whether they had any skin disorders at the time of the study reported not to have dermatological disorder contrary to the clinical examination performed while 45.3% (222) reported they had skin disorder.

The duration of skin disorders among the study participants with dermatological disorders was a quarter year (median, 3 months, IQR: 2, 5. (Table 4)

4.3 Skin disorder, duration and the type of lesion

Table 4: Presence of skin disorder, duration and type of lesion

	Frequency/Median	%/ IQR
Type of lesion		
Localized	187	82.0
Generalized	41	18.00
Duration in months	3	2, 5

Eczema and infections were more frequent among individuals who were ARV-experienced, this accounted for 52% (42) and 42% (36) respectively, while infections 58% (50) was more common among the participants who were ARV-naïve. (Table 5).

Skin disorders were frequent in ART- naive patients, 63% compared to 44% in the participants on antiretroviral medications (P-value 0.001).

4.3 ART status and the skin disorder

Table 5: ART status and Skin disorder

	ARV status (n, %)	
Diagnosis	**No**	**Yes**
Adnexal	8 (32.0)	17 (68)
Drug	1 (33.3)	2 (66.67)
Eczema	39 (48.2)	42 (51.85)
Infection	50 (58.1)	36 (41.86)
Malignancy	9 (90.0)	1 (10)
Miscellaneous	15 (31.9)	32 (68.09)

The prevalence of skin disorders among the participants was 51.4% (95% CI: 46.9,55.9), the most common skin disorders were infections 34% followed by eczematous disorders 32% and the least common was malignant disorders which accounted for 4 %.(Figure 1)

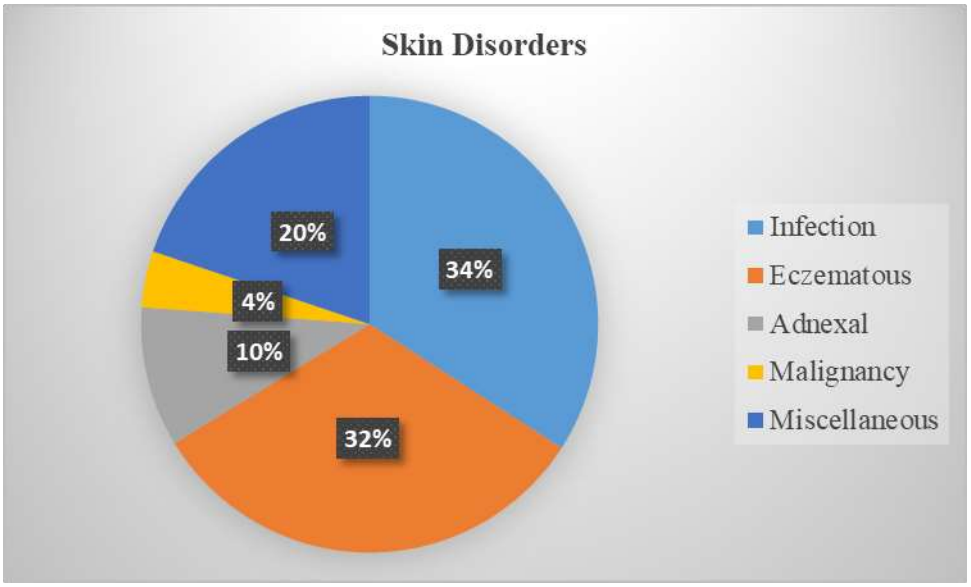


Figure 1: Showing classification of skin disorders

The range of mucocutaneous disorders among the participants included eczematous conditions, infection dermatosis, adnexal disorders, malignancies, drug reaction and miscellaneous disorders as depicted in the tables 6-11.Papular pruritic eruption was the commonest eczematous dermatosis 54% (42) while tinae coporis 20% (21) and oral candidiasis 18% (19) were the commonest cutaneous infection among the study participants. (Table 6, 7)

Acne was the most frequent adnexal disorders 59% (16) whereas Kaposi's sarcoma 91% (10) was the commonest malignancy elicited among the participants and fixed drug reaction was common among the participants who experienced drug reaction and it accounted for 67% (2) (Table 8).The most prevalent viral cutaneous infection was genital herpes 7% (7) while herpes zoster accounted for 3% (3) and furuncle, bacterial infection accounted for 3% (3). (Table 7) Aphthous ulcer and HIV xerosis accounted for 21% (10) and 14% (7) respectively among the participants in the study. (Table 11).

4.3 Spectrum of skin disorders

Table 6: Eczematous Disorders

Eczematous disorder	Frequency/%
Papular pruritic eruption	42 (54)
Actinic cheilitis	7 (9)
Seborrhoeic dermatitis	6 (8)
Lichen simplex chronicus	5 (6)
Stasis eczema	3 (4)
Actinic dermatitis	3 (4)
Urticaria	2 (3
Atopic eczema	2 (3)
Asteotatic eczema	2 (3)
Areolar dermatitis	2 (3)
Prurigonodularis	1 (1)
Acrodermatitis enteropathica	1 (1)
Nikel contact dermatitis	1 (1)
Total	77

Table 7: Infection Disorders

Infection disorders	Frequency/%
Tinae coporis	21 (20)
Oral candidiasis	19 (18)
Scabies	15 (15)
Verucca vulgaris	10 (10)
Tinae ungium	8 (8)
Genital ulcer	7 (7)
Paronychia	6 (6)
Pityriasis vesicolor	5 (5)
Herpes zoster	3 (3)
Furuncle	3 (3)
Pityrosporum folliculitis	2 (2)
Herpes labialis	2 (2)
Tinae incognito	1(1)
Total	102

Table 8: Adnexal, Malignancies and Drug reaction disorders

Adnexal, Malignancies and Drug Reaction disorders	
Adnexal	Frequency/%
Acne	16 (59)
Melanochyia	8 (29)
Perioral dermatitis	1 (4)
Folliculitis keloidalis nuchae	1(4)
Folliculitis decalvans	1 (4)
Total	27
Malignancy	
Kaposis sarcoma	10 (91)
Melanoma	1 (9)
Total	11
Drug Reaction	
Fixed drug eruption	2 (67)
Stevens John’s syndrome	1 (33)
Total	3

Table 9: Miscellaneous disorders

Miscellaneous Disorder	Frequency/%
Post herpetic scar	15 (31)
Apthous ulcer	10 (21)
Xerosis	7 (14)
Discoid lupus erythromatosus	5 (10)
Dermatosis papulosa nigra	3 (6)
Skin tag	2 (4)
Vitiligo	2 (4)
Pellagra	1 (2)
Melasma	1 (2)
Post inflammatory hypopigmentation	2 (4)
Alopecia areata	1 (2)
Total	49

Eczema and infections were more frequent in WHO clinical stage 2 and 3 which accounted for 72.8% (59) and 70.9% respectively, while malignancies were common in participants classified in WHO clinical stage4.(Table 10).

4.4 The association of the skin disorder and markers of Immunity

Table 10: Skin disorder by WHO clinical staging

	WHO staging			
Diagnosis	**Stage1**	**Stage2**	**Stage3**	**Stage4**
Adnexal	9 (36)	10 (40)	5 (20)	1 (4)
Drug	0 (0)	0 (0)	3 (100)	0 (0)
Eczema	19 (23.46)	29 (35.8)	30 (37.04)	3 (3.7)
Infection	19 (22.09)	32 (37.21)	29 (33.72)	6 (6.98)
Malignancy	0 (0)	0 (0)	3 (30)	7 (70)
Miscellaneous	12 (25.50)	15 (31.90)	17 (36.20)	3 (6.40)

The participants on antiretrovirals therapy (ART) with no skin disorders had a median baseline CD4 332(200,458) while those with skin disorders had a median, 319(169,480), (P-value, 0.639). The antetroviral (ARV) -naive participants with no skin disorders had a baseline CD4 count, median 318(158.5, 525) whilst ARV-naive with skin disorders, baseline CD4, median204.5 (125,474), (P-value 0.048).

The individuals in the study who were ART experienced with skin disorders had viral load, median 48(0, 1144) compared to those with no dermatological disorders, median viral load 0(0, 163), (P-value 0.002).ART-naive individuals in the study with skin disorders had viral load, median 1100(134, 2890) in contrast to those with no skin disorders but were ART-naïve who had median viral load, 193 (33.5, 1153.50), (P-value 0.002). (Table11).

Table 11: The association between ART and skin disorder

Variable		Skin disorder		p-value
		No	**Yes**	
On ARV	**No**	72 (37.1)	122 (62.9)	**<0.001**
	Yes	166 (56.1)	130 (43.9)	
Baseline CD4 and on ARV		332 (200, 458)	319 (169, 480)	0.639
Baseline CD4 and not ARV		318 (158.5 , 525)	204.5 (125, 474)	**0.048**
Viral Load and on ARV		0 (0, 163)	48 (0, 1144)	**0.002**
Viral Load and not ARV		193 (33.5, 1153.50)	1100 (134,2890)	**0.002**

CHAPTER FIVE: DISCUSSION

Antiretroviral therapy has changed the natural course of HIV infection through immune restoration of HIV infected patients by decreasing viral loads and increasing CD4 level. The present study was to examine the spectrum and frequency of skin diseases in patients with HIV/AIDS. The mean age of the study subjects was 39 years (range: 32, 46 years). The median duration of cutaneous symptoms was 3 months (IQR: 2, 5 months) this was similar to Daud R. Mavura 2015.

Increased proportion of female participants, 70.80% was prominent in this study similar to the trend depicted in India Kore SD et al 2013.

This is accredited to the increased promotion on voluntary testing and detection among the females. General statistics from health institutions show that more women report and use public health services than men Alemnii GA 2002.The participants were largely casual and peasant farmers, 59.30 %(290). This is comparable to study by Billy Mayanja et al 1999, which revealed mucocutaneous disorders were prominent among the poor.

The study subjects had early progressive HIV disease as revealed by WHO stage I or II clinical manifestations, such early presentation of HIV infection is uncommon and differs from previous description by other studies where individuals presented with late HIV infection, stage III and IV MoHSW Tanzania 2005. This difference could be the due to the longstanding advocacy on HIV/AIDS prevention; care and ART scale up by the country's health programs.

Skin lesions were regular among individuals who were in stage II or III WHO clinical staging while malignancy was common among individuals in WHO clinical stage IV, 70% (7), however skin disorders were more frequent among antiretroviral naïve patients, 63% (P value 0.000).

The population under study demonstrated abnormal skin findings in both the patients on antiretroviral and those who were antiretroviral-naive individuals.

Skin disorders were more frequent among antiretroviral naive patients than those who were antiretroviral experienced. This was similar to J. Han et al 2012 who revealed that skin disorders were less common among patients receiving antiretroviral therapy.

The dominance of certain skin disorders has decreased in HIV⁄ AIDS patients since antiretroviral therapy has become accessible and reachable Zancanaro PC et al 2006 and Maurer T et al 2004.

This study exposed that infection related skin diseases were common among ARV-naive individuals while non-infectious disorder; eczema was frequent among patients on antiretroviral therapy. This was similar to Preawphan Punyaratabandhuin et al 2012.This finding is also comparable to past studies which demonstrated the range of skin disorders, had changed from infection to non-infectious skin disorders among individuals on antiretroviral.

The occurrence of eczema was higher than previous studies. Since antiretroviral medications perk up HIV infected patient's immunity, the skin immunity also had developed protection to various skin infectious diseases; therefore, eczema could be a sequel or complication from infection or xerosis, which cause severe itching.

Infectious skin disorders and malignancy (Kaposis) were less common among individuals on antiretroviral therapy.

The most common dermatological disorders were mainly infections and Eczema similar to an account by HIV-infected cohort in Dar es Salaam in which fungal infections represented the most common disorder, WHO 2006.

Relating to the spectrum of skin disorders; the commonest eczematous disorder was papular pruritic eruption while tinae coporis and oral candidiasis were the most regular cutaneous infection among the study participants. This was similar to Calista et al 2012.

Pertaining to infectious disorders in this study, tinea coporis and oral candidiasis were the most frequent cutaneous infections among the study participants albeit lower than in the pre ART era, Ulrich et al 2000 revealed a decreasing trend in some of the infection dermatosis (oral candiadiasis) after antiretroviral therapy administration.

Furuncle, bacterial infection was rare this was inconsistent with a study by Leslie KS et al 2011 which revealed a higher prevalence and this could be in this study, the participants had higher individuals on ART as this is related to decrease in cutaneous bacterial infections in patients on antiretroviral therapy.

The most prevalent viral cutaneous infection was genital herpes (2.8%) this incomparable with study by Mignard and Dabis et al 1998 which revealed 10.2% this could be due to the amplified effort and the deliberate focus on the prevention and support of sexually transmitted diseases by the health ministry.

Herpes zoster accounted for 1.2% and it was infrequent among patients initiated on antiretroviral therapy, this is dissimilar to Domingo P 2001, which illustrated an increase in herpes zoster among patients commenced on antiretroviral therapy due to immune reconstitution.

In relation to adnexal disorders, melanonychia (3.2%) was the most frequent and this was due to zidovudine therapy this was similar to Spira R et al 1998.

Concerning the miscellaneous disorders, Xerosis was less frequent in this study, this similar to Sachin D Kore et al 2012 but differ from another study Smith KJ et al which revealed a high prevalence in HIV xerosis. There is a relation between HIV xerosis and advance WHO clinical stage, since most of the participants in this study were in WHO clinical stage 1 and 2 there was likelihood of low prevalence of xerosis.

Cutaneous drug reaction was rare among the participants in the study which caused considerable morbidity this was lower than a study by Sachin D Kore 2012 this was because mild drug reaction rarely reports to the hospital to seek for help.

In this study adverse drug reaction was infrequent in spite of using trimethoprim/sulfamethoxazole and a nevirapine- containing anteritroviral regimen; this is in agreement with study done by Daud R. Mavura 2015 in Tanzania. This was because mild form of drug eruption, resolved on terminating drug use thus might be under represented in the present study. The study also focused on HIV-infected patients who came to the outpatient clinic.

Participants with low CD4 count, high viral load and were ART-naive had significant skin disorders in this study similar to Preawphan Punyaratabandhuin et al 2012. This is because immunosuppression increases the risk of cutaneous infections and malignancies,

5.1 Limitations of this study

The drawback in this study was specific disease could not be correlated with CD4 count and viral load due to the few numbers per disease.

CHAPTER SIX: CONCLUSION AND RECOMMENDATION

6.1 Conclusion

The most common spectrum of dermatological manifestation encountered in this study was eczema and infectious disorders

Antiretroviral therapy-naïve participants had a higher prevalence of skin disorders

The non-infectious inflammatory skin disorders were frequent among ART-experienced patients and infectious mucocutaneous disorders were regular among ART-naïve individuals

A low viral load among the participants was associated with reduction in skin disorders

6.2 Recommendations

Healthcare providers and patients with cutaneous problems should consider antiretroviral therapy as promising in the management of HIV infected patients

The healthcare providers should assess the viral load of patients who develop mucocutaneous disorders despite using antiretroviral therapy.

The healthcare providers should be trained in common skin disorders among HIV-infected patients.

The healthcare workers must be encouraged to use clinical imaging or digital photography to gain experts opinion and for treatment monitoring of patients with dermatological manifestations.

The study recommends future research that correlate specific disease with CD4 count and viral load.

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APPENDICES

Appendix I: Consent form

Appendix II: Data collection form

Appendix III: Skin biopsy consent form

Appendix IV: MU-MTRH IREC Approval

Appendix V: MTRH Permission to conduct study

Appendix VI: AMPATH Permission to conduct study

Appendix I:Letter To Respondents /Introduction Letter/Consent Forms

Investigator: My name is Dr. Mohamed A Abdille.I am a qualified doctor, registered by the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Master's degree in Internal Medicine at Moi University. I would like to recruit you into my study which entails the spectrum of skin disorder among HIV infected patients attending AMPATH clinics at Moi Teaching and Referral Hospital.

Purpose: This study will seek to assess the common skin disorder among HIV infected patients.

Benefits: The study will be used to assess the common skin disorder among HIV infected individuals and to use the data for posterity to aid programs.

However there will be no direct benefits to the participants but they will be given same quality of care as the non-participants.

Risk: There are no anticipated risk to the participants attributable with extreme confidentiality and shall not be divulged to any unauthorized person.

Rights to decline: Taking part in the study is voluntary and each participant has right to decline or withdraw at any stage of the research. This study has been approved by the institutional Research and Ethics Committee (IREC) of Moi \University /Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study

Participant …….Investigator…… Date ……

Appendix II: Questionnaire

Part A: demographic characteristics

Age……..

Gender Male ☐ Female ☐

Education level

Primary ☐ Secondary ☐ Tertiary ☐ None ☐

Marital status

Single ☐ Married ☐ Divorced ☐ Widowed ☐

Widower ☐ others
Specify…….

OCCUPATION

1. Business ☐
2. Government Employee ☐
3. Casual laborer ☐
4. Farmer ☐
5. Others specify ☐

Part b HIV DATA

1. When were you first diagnosed to have HIV?.....
2. When were you enrolled to HIV care ?.....
3. Are you on antiretroviral ARVs Yes ☐ No ☐
4. If yes ,when were you initiated/started ARV medication?.....
5. Which regimen (ARVs) are you taking ?.....(check the patient records)
6. For how long have you used the antiretroviral medication?(ARV)

Has your doctor ever changed your ARVS regimen

Yes ☐ No ☐

7. Have you ever experienced drug reaction Yes No ☐
   If yes, which drug (s) did you react to?(list drug)……..
8. What is your baseline CD4 count level?.....Check or refer to the patient clinic
9. What is your last or viral load?.....(check or refer to the patient clinic record.

   part c data on skin diseases
10. Did you had any skin disorder by the time you were diagnosed with HIV/AIDS?
    Yes ☐ No ☐
    If yes the skin lesion (s)
    1. Localized ☐
    2. Generalized ☐

       If localized which part of the body was affected
11. Presently do you any skin lesion(s)
    Yes ☐ No ☐
    If yes which part of your body has skin lesion(s)……...
    ……
    ……
12. If yes Q 10how long did you had the skin lesion (s)……

Part D:physical examination

13. What is the world Health Organization (WHO)clinic staging
    i. ☐
    ii. ☐
    iii. ☐
    iv. ☐

14. Clinical findings at presentation (examine the patient)……

    ……

    ……

    ……

    ……

15. What is the previous

    diagnosis……

16. What is the /biopsy

    result…..

    ……

17. Final diagnosis

    ……

Thank you

Appendix III:Dermatology biopsy consent form

Patient name _____

A skin biopsy involves removal of a small piece of skinn under local anesthesia. The piece of skin is then processed and examined under a microscope or is tested in some other fashion to obtain diagnostic information.

Possible complications include bleeding, scarring, infection, never damage, recurrence, or the need for further procedures. I have been informed, to my satisfaction, regarding the nature of the procedure and why it is being performed.

I understand that a biopsy does not guarantee complete removal of a lesion or that a diagnosis will be obtained.

In a small percentage of cases, even with the biopsy information ,a diagnosis may not be arrived at and another biopsy or special stains may have to be done.

I also realized and understand that there are no cost related to the biopsy, pathology, cultures or other lab work and that I am not responsible for those cost.

I give consent for any lab pathology results to be called to the following phone number

Phone number: 0722213061

I hereby consent to a skin biopsy

Patient Signature_____ Date _____

Thank you for participating in this study

Appendix IV: MTRH Permission to conduct study

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke
P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008

30th September, 2016

Dr. Mohamed A. Abdile,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"The Spectrum of Dermatological Manifestations among HIV Infected Patients at AMPATH Clinic in Eldoret, Kenya".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

30/09/2016

DR. WILSON ARUASA
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM

Appendix IV: MU-MTRH IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2016/193
Approval Number: 0001760

27th September, 2016

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
27 SEP 2016
APPROVED
P. O. Box 4606-30100 ELDORET

Dr. Mohamed A. Abdille,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Mohamed,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"The Spectrum of Dermatological Manifestations among HIV Infected Patients at AMPATH Clinic in Eldoret, Kenya".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1760*** on 27th September, 2016. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 26th September, 2017. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix V: AMPATH Permission to conduct study

Academic Model Providing Access To Healthcare
Telephone: 254 53 2033471/2P.O. BOX 4606, ELDORET Fax: 254 53 2060727

RESEARCH

Ref: RES/STUD/4/2017

April 12, 2017

Mohammed A. Abdille
Moi University
School of Medicine
P.O Box 4606-30100
Eldoret

Dear Dr. Abdille,

RE: PERMISSION TO CONDUCT RESEARCH AT AMPATH

This is to inform you that your study "***The Spectrum of Dermatological Manifestation in Patients with HIV attending AMPATH Clinic***" *has* been reviewed by the AMPATH Research Program Office. Permission is therefore granted to begin collecting your data at AMPATH.

Please note that your research activities should not in any way interfere with the care of patients. This approval does not support access to AMRS data at AMPATH.

You are required to submit a final report of your findings to the AMPATH Research Program Office.

Should you wish to publish your research findings, permission has to be sort from AMPATH Publications Committee. Please contact the AMPATH Research Office research.manager@ukenya.org in case of any enquiry regarding this matter.

Thank you,

Prof. Winstone Nyandiko
AMPATH Executive Director, Research

CC: AMPATH Executive Director, Care

Appendix VI: Proposed Budget

Item			Total
Laboratory	100	2000	200,000
Stationary		20000	20000
Internet services			10000
Biostacian services			30,000
Research assistant	2		100,000
Total			360,000

Appendix VII: Time frame

Activity	Start	End
Proposal concept development	October	December 2025
Proposal writing	January 2016	April 2016
IREC Approval	May 2016	June 2016
Data collection	November 2016	June 2016
Data analysis	November 2017	December 2017
Thesis	January 2018	March 2018

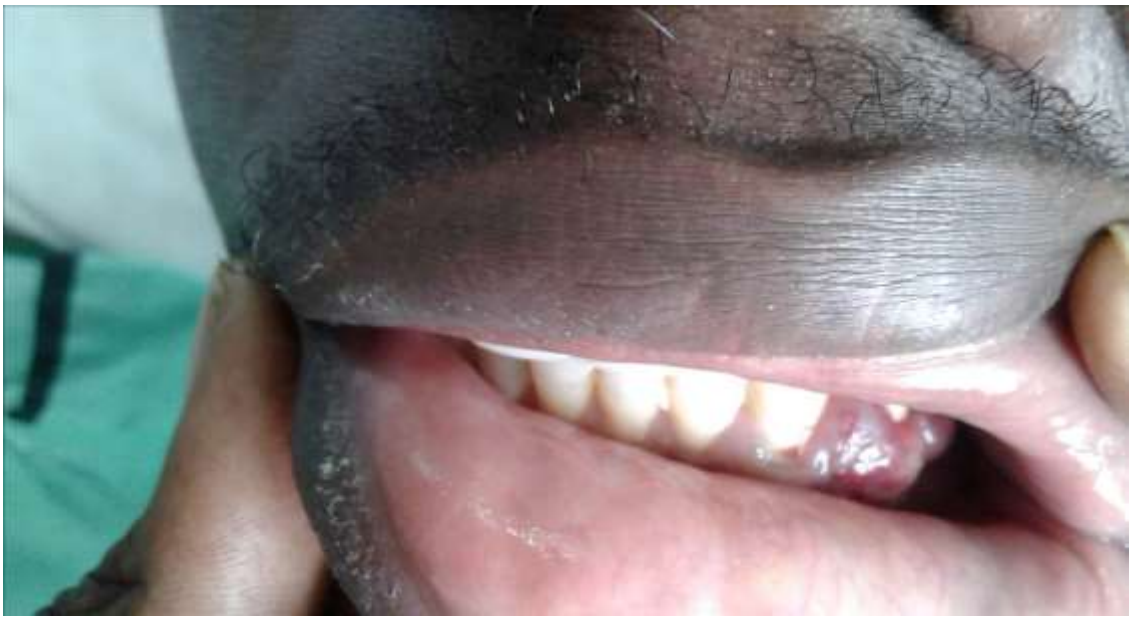

Figure 2: a 33 year old man with oral Kaposis Sarcoma

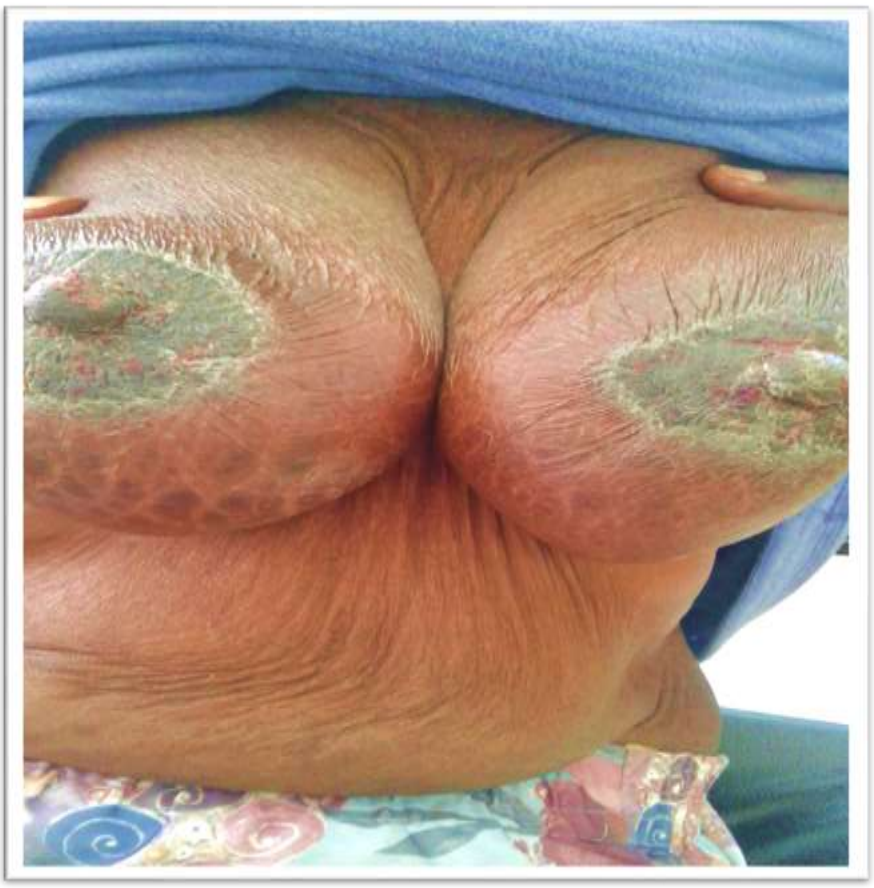

Figure 3: a 44 year old woman with Areolar Dermatitis

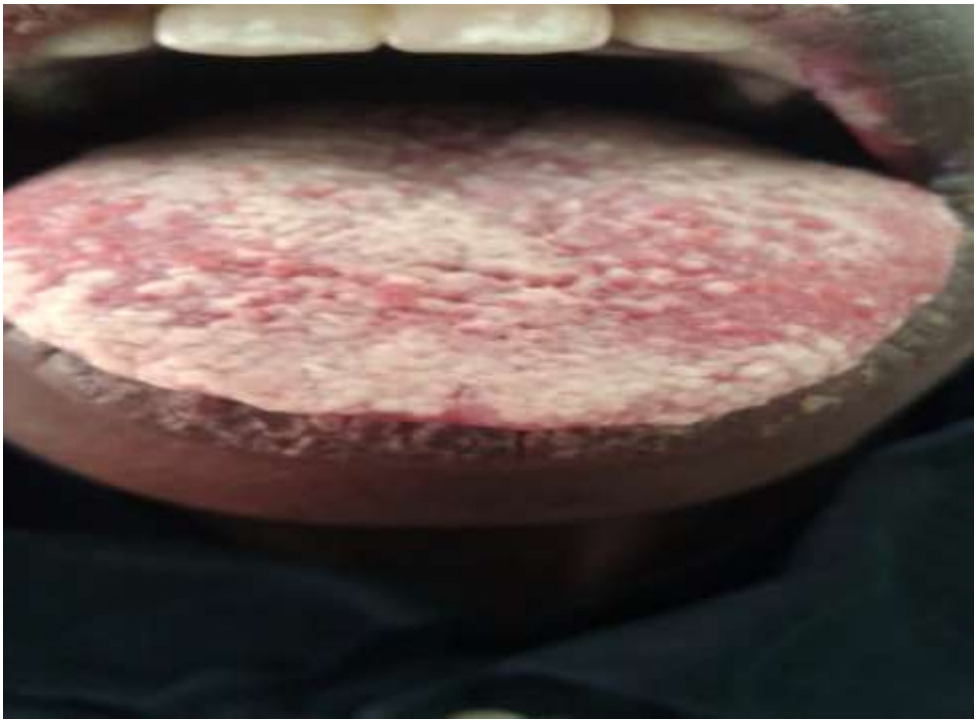

Figure 4: a 21 year old male with Oral Candidiasis

Figure 5: a 38 year old man with Urethral wart

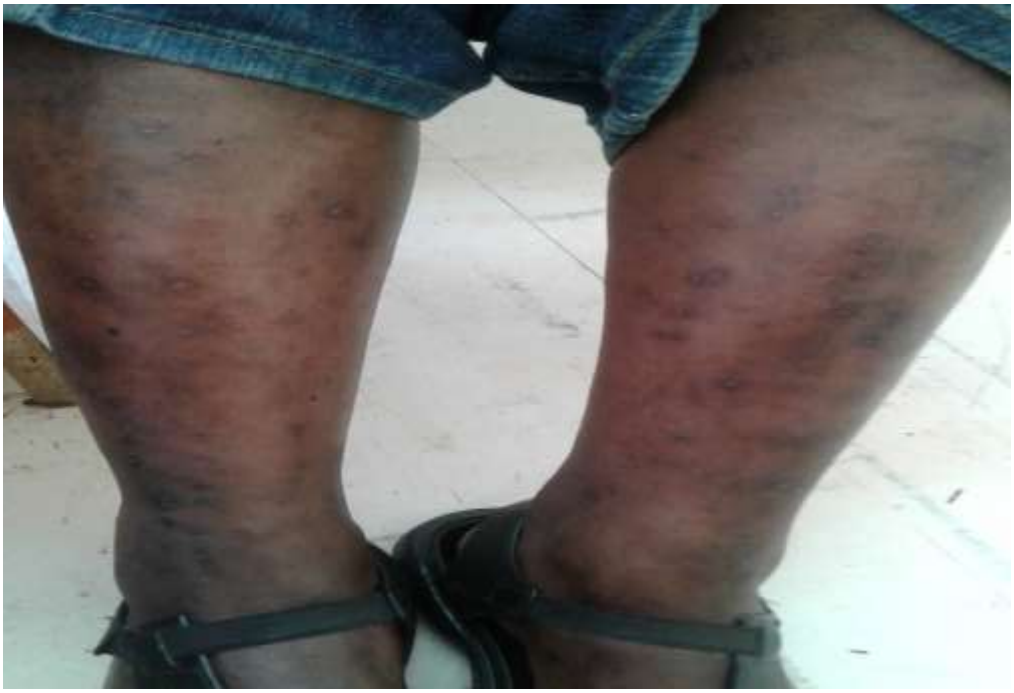

Figure 6: a 44 year old man with Pruritic Papular Eruption

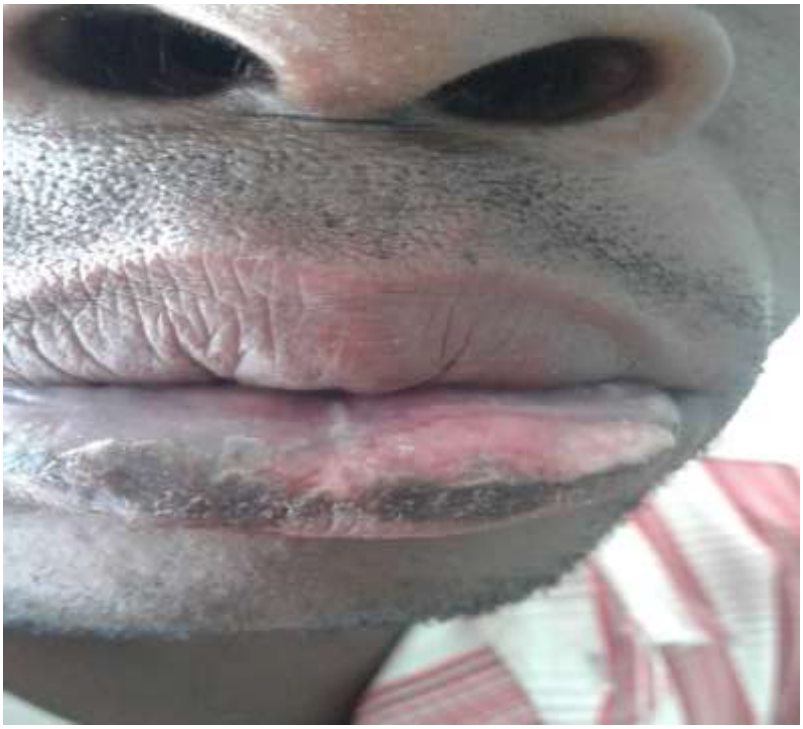

Figure 7: A 37 year old male with Actinic cheilitis

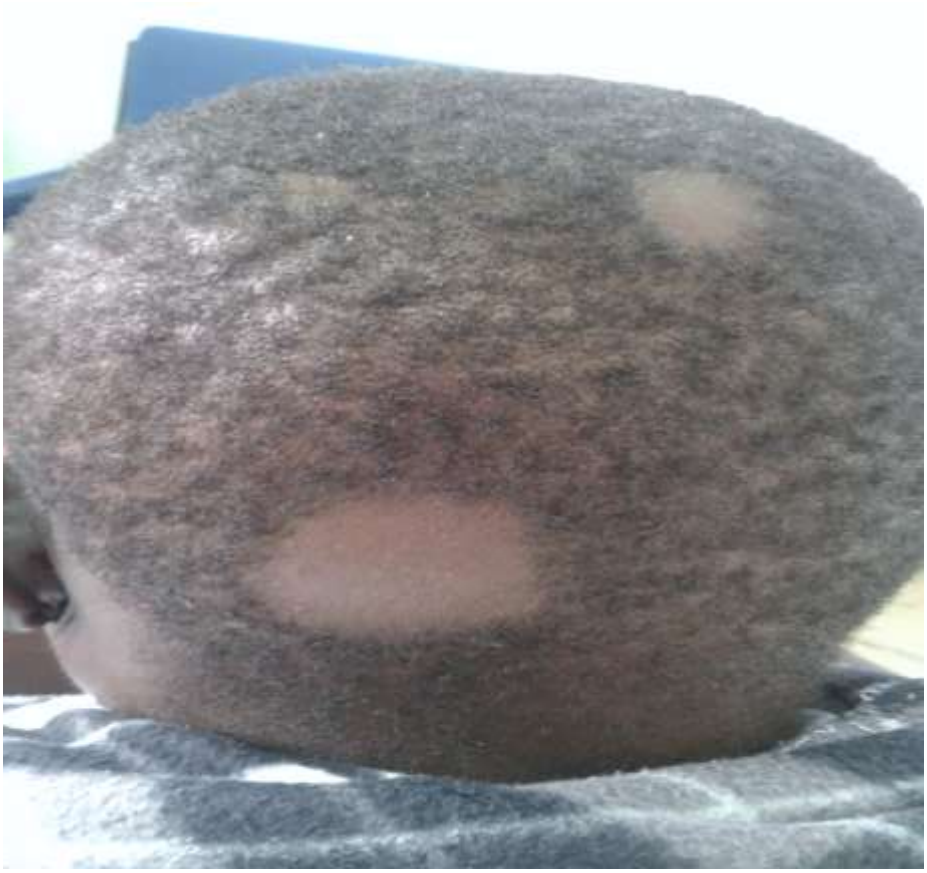

Figure 8: 23 year old female with alopecia

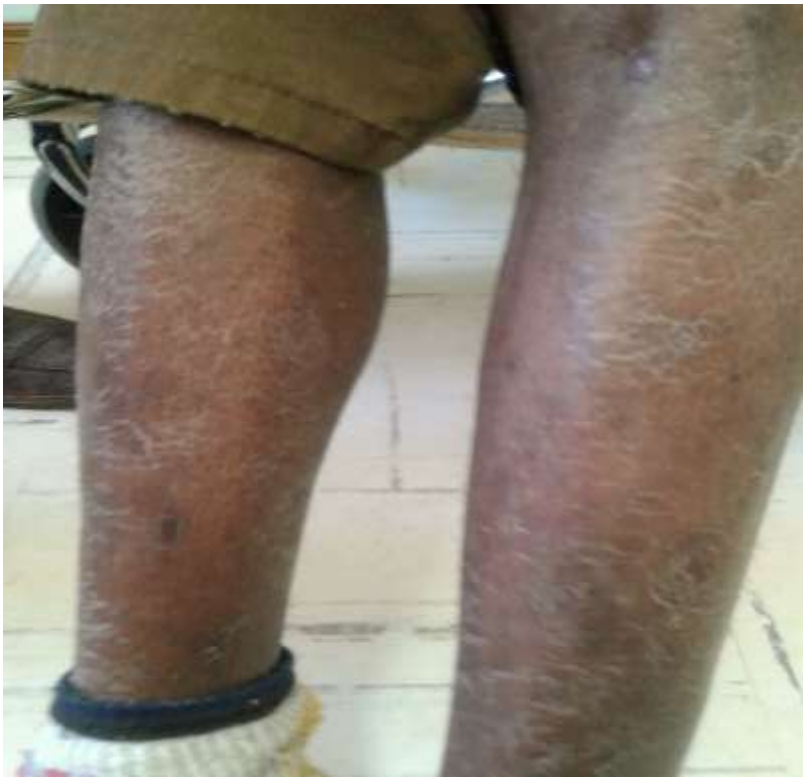

Figure 9: 35 year old man with HIV xerosis

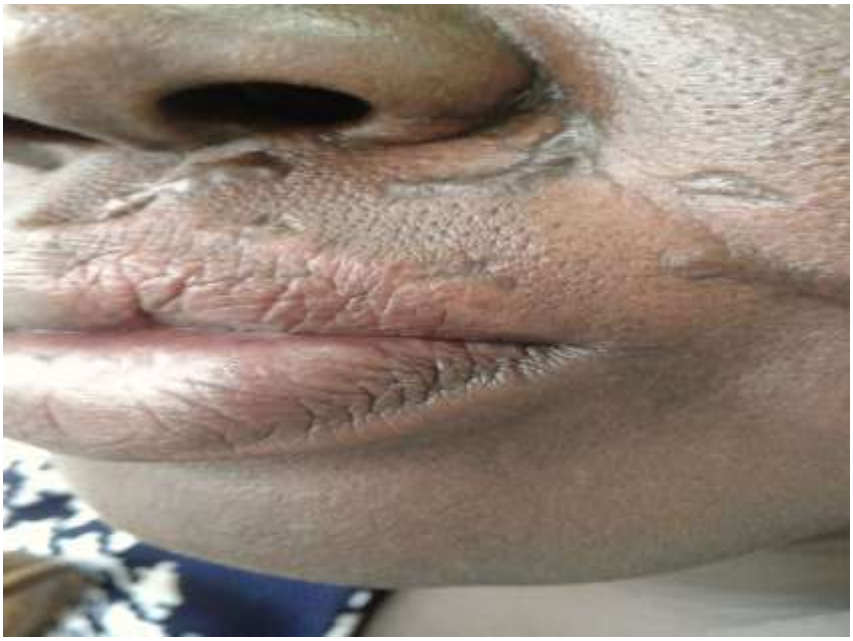

Figure 10: 40 year old woman with post herpetic scar

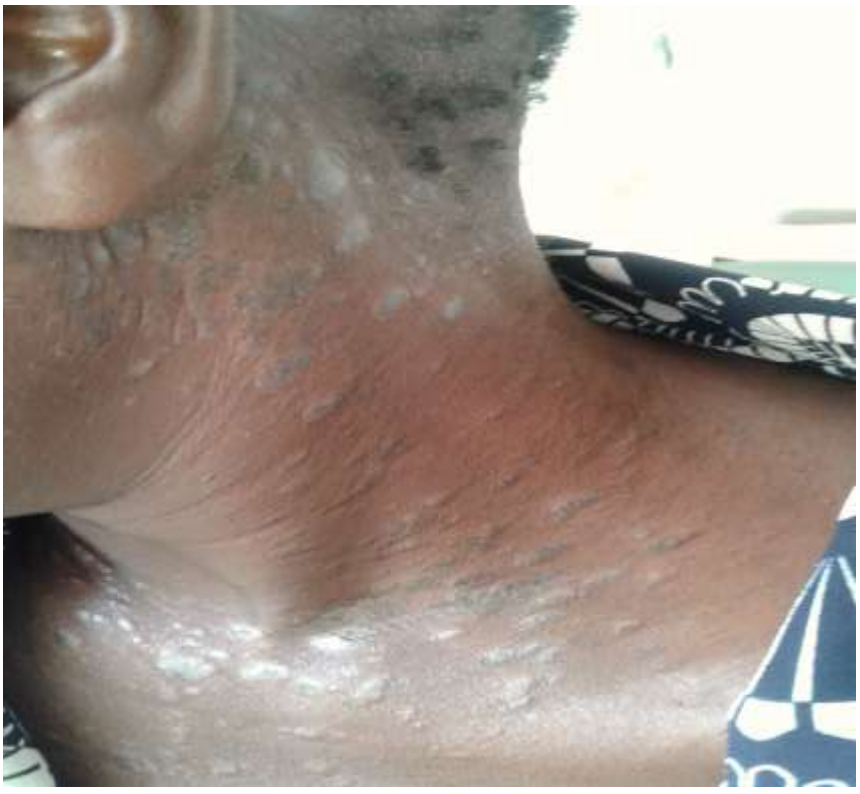

Figure 11: 27 year old female with lichen planus