TITLE

CLINICAL PATTERNS OF PSORIASIS VULGARIS IN PATIENTS AT KENYATTA NATIONAL HOSPITAL

BY

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A dissertation submitted in part fulfilment for the degree of Master of Medicine Of the University of Nairobi

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DECLARATION

I certify that this is my own original work and has not been presented for a degree at any other University.

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APPROVAL

This dissertation has been submitted with our approval as supervisors.

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ABBREVIATIONS

A & E	-	ACCIDENT AND EMERGENCY.
ACE	-	ANGIOTENSIN CONVERTING ENZYME.
APC	-	ANTIGEN PRESENTING CELL..
AIDS	-	ACQUIRED IMMUNODEFICIENCY SYNDROME.
ARV	-	ANTIRETROVIRAL.
BCC	-	BASAL CELL CARCINOMA.
BMI	-	BODY MASS INDEX.
BSA	-	BODY SURFACE AREA.
CD	-	CLUSTER OF DIFFERENTIATION.
DNA	-	DEOXYRIBONUCLEIC ACID.
ECAM	-	ENDOTHELIAL CELL ADHESION MOLECULE.
ELAM	-	ENDOTHELIAL LEUCOCYTE ADHESION MOLECULE
ELISA	-	ENZYME LINKED IMMUNOSORBENT ASSAY.
ERC	-	ETHICAL RESEARCH COMMITTEE.
H & E	-	HEMATOXIN AND EOSIN.
HAART	-	HIGHLY ACTIVE ANTIRETROVIRAL THERAPY..
HLA	-	HUMAN LEUCOCYTE ANTIGEN.
HIV	-	HUMAN IMMUNODEFICIENCY VIRUS.
IFN	-	INTERFERON.
IL	-	INTERLEUKIN.
KNH	-	KENYATTA NATIONAL HOSPITAL..
KS	-	KAPOSI'S SARCOMA.
LFA	-	LEUCOCYTE FUNCTION ANTIGEN.
NSAID	-	NON-STEROIDAL ANTIINFLAMMATORY DRUGS.
.PCR	-	POLYMERASE CHAIN REACTION.
TGF	-	TRASFORMING GROWTH FACTOR
Th	-	T-helper.
TMP-SMX	-	TRIMETHOPRIM-SULFAMETHOXAZOLE
TNF	-	TUMOUR NECROSIS FACTOR
VCAM	-	VASCULAR CELL ADHESION MOLECULE.

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Above all, to God Almighty for Life and His mercies.

DEDICATION

I dedicate this work to my late Uncle Shem, to my late Dad F. Olungo and my late Grandparents, Cecilia and Jactone Wandhe, Alice and Nyandong Okello.

ABSTRACT

BACKGROUND : Psoriasis Vulgaris is an inflammatory skin disorder with abnormal epidermal differentiation and hyperproliferation. It is a common, chronic relapsing, condition with a strong genetic basis.
It presents with different clinical patterns e.g scalp psoriasis and inverse psoriasis.
There is no data on different clinical patterns of psoriasis in our set up

OBJECTIVE : The main objective was to determine the clinical patterns of psoriasis vulgaris at Kenyatta National Hospital.

DESIGN : This was an hospital based cross-sectional descriptive survey.

SETTING : Kenyatta National Hospital: Dermatology clinic, medical wards, accident and emergency area.

SUBJECTS : Patients who presented with psoriasis vulgaris at Kenyatta National Hospital.

METHOD : History was taken from the patients and physical examination carried out. Biopsy was taken for histology to confirm the diagnosis. ELISA for HIV was done to confirm serostatus.

DATA ANALYSIS : Data obtained was entered, cleaned and analysed using Windows SSPS Version 14.2.
Results were presented in the form of Pie charts, bar graphs and pictures.

RESULTS : A total of 84 patients were screened and 70 fulfilled the criteria for recruitment, ranging from the age of 6 years to 65 years. There were 38 males, out of which two were found to be HIV positive and 32 females.
Patients came from different parts of the country with the majority coming from Nairobi, Central and Eastern provinces. Three patients were found to be related, Nine were alcoholics, 3 were smokers, two were on antihypertensives and one on antimalarial. The sites mostly affected were Trunk, Scalp, Elbow and Knee. Others were thighs, shin, arm and forearm. The most common morphological variant was annular. One of the HIV positive patient had lesions on the mons pubis, face and penile shaft . The duration of psoriasis ranged from 1 month to 467.5 months.

CONCLUSION : The most common variant of psoriasis vulgaris was the annular, affecting the trunk with 17% of body surface area involved. This is unlike the plaque type which affects the knees and elbows.

11. INTRODUCTION

PSORIASIS IN GENERAL.

Psoriasis is a polymorphic disorder with the common variant presenting as a well marginated silvery scaly papules, plaques and patches with erythematous base There are three variants of Psoriasis, namely:

Psoriasis Vulgaris which is also called stable psoriasis. This can transform to unstable variants, pustular and erythrodermic psoriasis following:

- Withdrawal of corticosteroid treatment.
- Pregnancy
- Topical irritants
- Infection.

.It is a common, chronic, relapsing inflammatory skin disorder with a strong genetic basis.

The prevalence is about 2% and involves all races. Men and women are affected equally, the ratio is 1:1.

The age of onset occurs in two peaks, early (20-30) and late (50-60yrs).

Approximately 26,000 dermatological cases are seen in Kenyatta National Hospital per year and psoriasis accounts for approximately 7%.

Disorders in keratinocyte proliferation, differentiation, inflammation and immune dysregulation are the major factors implicated in pathophysiology.

It is a T-cell mediated immune disorder to an epidermal superantigen. T-cell binds to the antigen presenting cell through CD2-intercellular adhesion molecule [ICAM-1]

and leukocyte function associated antigen-3 on the presenting cells.This leads to induction of T-cells and production of type T1 cytokines. The cytokines influence other cells locally to secrete a plethora of proteins including chemokines, TNF-alpha, granulocyte-macrophage colony stimulating factor [GM-CSF], epidermal growth factor and IL-8. These factors regulate the migration of new inflammatory cells into the skin and increase the activity of keratinocytes, resulting in psoriasis plaques.

12. LITERATURE REVIEW

PSORIASIS VULGARIS

INTRODUCTION

Psoriasis Vulgaris is a chronic, polygenic disease with various triggering factors, for example, trauma, infections or medication which may elicit a psoriatic phenotype in predisposed individuals. The characteristic lesion is a sharply demarcated erythematous plaque with silvery white scales.

The impact of psoriasis on quality of life is significant given its chronicity and prevalence. Pruiritus, scaling, and visible plaques are the signs and symptoms of most concern.

Psoriasis Vulgaris is the most common type of psoriasis, also known as plaque psoriasis.

The extent and duration of the disease is also highly variable from patient to patient and upto 10%-20% also experience psoriatic arthritis.

Acute flares or relapses of psoriasis vulgaris may also evolve into more severe disease such as pustular or erythrodermic psoriasis.

Epidemiology

Psoriasis vulgaris is universal in occurrence. The worldwide incidence varies considerably depending on race, geography and environment. Prevalence rates range from 0.6% - 4.8%. It affects men and women equally and is seen in all races **(1-2)**.

It is approximately 0.97% in South America **(3)**, 1.7% in Denmark, 2.3% in Sweden **(4)**, rare in West African and North American blacks **(5-6)**. Kenyan figure is 3.15%.**(7)** It is nearly absent in North America Indians **(8)**.

Age of onset

Although it can begin at all ages, there are two peaks in onset. Ages: 20-30 yrs and 50-60 yrs**(2)**. An early onset predicts more severe disease relative to the percent of body surface involvement with psoriasis and the response to therapy. Also, the earlier the onset, the greater the probability of a positive family history of psoriasis.

Risk factors

Genetic predisposition: Psoriasis is reported to be associated with HLA antigen B13, B17, and B37 all of which are linked to cw6 as well as HLA DR7. Gene linkages have been found to be related to chromosomes 6p, 17q, 4q, 1q, 3q 19p and 1p. Environmental factors.

Obesity and higher body mass index - BMI, (**10-11**).

Smoking (**12-13**) are some of the risk factors.

Alcohol (**14**): Both increased alcohol consumption and smoking cigarettes have been associated with psoriasis, particularly alcohol in middle aged males. However, neither is a major risk factor.

Triggering factors.

These can be both external or systemic and elicit psoriasis in genetically predisposed individuals.

External triggering factors: Psoriatic lesions can be induced by other forms of cutaneous injury, e.g. sunburn, morbilliform drug eruptions or viral exanthems.

Systemic triggering factors

Infections:

Provoking infections have been observed in up to 44% of psoriatic patients. For example, pharyngeal streptococcal infection.(**15**).

HIV infections and Endocrine factors are well known aggravating factors for psoriasis.

Endocrine factors:

Hypocalcemia has been reported as a triggering factor for generalized pustular psoriasis. Pregnancy may alter disease, 50% of the patients in one series reported improvement (**16**).

However, pregnant women may develop pustular psoriasis, also referred to as impetigo herpetiformis in association with hypocalcemia.

Psychogenic stress

Psychogenic stress is a well-established systemic triggering factor for psoriasis (**17**).

Drugs

Lithium, β-blockers, antimalarials, and interferon. Rapid tapers of corticosteroids can induce pustular psoriasis as well as flare of plaque psoriasis (**18**).

Mortality/Morbidity

Mortality in psoriasis is rare except in cases such as pustular and erythrodermic psoriasis provoked by steroids and infections.

Morbidity is a much greater problem and is often related to pruiritus, dry and peeling skin, fissuring, and adverse effects of therapy.

Self-consciousness and embarrassment about appearance, inconvenience, the high cost of antipsoriatic treatment regimens all add to the morbidity.

12.11 PATHOPHYSIOLOGY

Psoriasis was previously viewed as a disease of hyperproliferation primarily, however, more recently it has come to be regarded as an immune mediated disease – **(19)**. It is a complex immune-mediated disease in which T-lymphocytes play a central role. Activated T-lymphocytes produce two different patterns of cytokines. Th1, cells produce IL-2 and IFN-gamma, whereas Th2 cells produce IL-4, IL-5 and IL -10.

Psoriasis is considered to be Th1, dominant disease.

Activated T-cells in psoriatic lesions have been shown to secrete a series of cytokines which may account for many characteristics of the psoriatic lesion.

TNF - α may account for the production of skin associated antileukoproteinase and β defensives by epidermal cells;

IL - 8 may account for neutrophil accumulation **(20)**

Interaction between T-lymphocytes and antigen presenting cells leads to full T-lymphocyte activation through pathways such as LFA - 3 on the surface of the APC and CD2 on the T cells.

Binding of LFA -3 to CD2 results in T-lymphocyte activation **(21.)**

There is accumulation of neutrophils as spongiform pustules of Kogoj and Microabscess of Munro, which are specific to psoriasis and the neutrophils are activated in the psoriatic plaques.

The adhesion molecules on endothelium such as E-selectin, ECAM -1 and VCAM-1 are upregulated on endothelial cells of psoriatic lesion on the skin.

The integrin LFA-1 (CDHa/CD18) is found on all leukocytes and Mac-1 (CD11b/CD18) is found on monocytes, eosinophils and neutrophils. The interaction between the integrins of blood derived cells and ICAM-1/VCAM-1 is crucial in the pathogenesis of psoriasis (**22**).

Keratinocytes also proliferate and differentiate.

Epidermal proliferation in psoriatic lesional skin is characterized by increased recruitment of cycling -cells.

- From resting Go population
- Increased numbers of cells undergoing DNA synthesis
- A shortened cell cycle time for Keratinocytes (36 hrs compared with 311 hours in normal skin.
- A decreased turnover time of the epidermis (4 days from basal cell layer to stratum corneum, compared with 27 days in normal skin.)

In addition to the above mechanisms, there is also cytokine network which includes:

- Interleukins
- Granulocyte and macrophage colony stimulating factor.
- Interferons
- Tumor Necrosis factors
- Chemokines and growth factors

This network is crucial in the control of epidermal proliferation, epidermal differentiation and inflammation (**23**).

T-Lymphocytes can induce epidermal cells to release IL-8 (**24**). IL-8 is chemotactic for neutrophils; IL-10 is released by Th2 lymphocytes and has been shown to inhibit the production of Th1 cytokines. IL - 10 levels in psoriatic lesions have been shown to be decreased (**25**)

TNF - $\propto$ is a Th1 cytokine and is produced by T-lymphocytes, activated keratinocytes and dermal macrophages. TNF - α induces the expression of the adhesion molecules ICAM-1 and ELAM, hence activates leukocytes infiltration into the skin. Epidermal proliferation is stimulated via the induction and expression of TGF - α.

TNF - α induces a large series of effects that are all characteristic for psoriasis. It is increased in psoriatic epidermis – (**26-27**).

IL - 8 is produced by monocytes, T-lymphocytes, endothelial cells, dermal fibroblasts, neutrophils and keratinocytes. It is chemotactic for neutrophils and promotes epidermal proliferation. In the psoriatic lesion, IL-8 is over-expressed.

Genetic factors are also involved in the pathophysiology of psoriasis.

Genes or a gene located within the Major Histocompatibility complex and close to the class 1 HLA loci was the major determinant of the genetic basis of psoriasis (**28**). Among others, HLA CW6 confers an increased risk for developing psoriasis and HLA - B17 may be associated with a more severe phenotype (**29**).

Other putative genetic susceptibility loci have been identified including psoriasis susceptibility 1. (PSOR 1) on chromosome 6, which is associated with up to 50% of cases.

Six other psoriasis susceptibility loci are:

- PSOR 2
- PSOR 3
- PSOR 4
- PSOR 6
- PSOR 7

With regard to the risk of a child developing psoriasis, it was found that if both parents were affected with psoriasis, the risk of the child developing psoriasis was 41%, one parent affected, the risk was 14%, if one sibling was affected, the risk was (**30**).

12.12 HISTOLOGY

A: EPIDERMIS

Mitotic activity of basal keratinocytes increased almost 50 fold with keratinocytes migrating from basal to cornified layers in only 3-5 days.

With hyperproliferation of skin cells, the epidermis becomes thickened or acanthotic in appearance and an increase in size of the rete ridges is observed.

Abnormal keratinocyte differentiation is noted throughout the psoriatic plaques, as manifested by loss of the granular layer.

The stratum corneum is also thickened and the retention of cell nuclei in this layer is referred to as parakeratosis.

Neutrophils and lymphocytes can be observed migrating upwards from the dermis into the acanthotic epidermis. Neutrophils may form localized collections known as Munro microabscesses.

The presence of alternating collection of neutrophils sandwiched between layers of parakeratotic stratum corneum is virtually pathognomonic for psoriasis.

B: DERMIS.

Signs of inflammation can be observed throughout the dermis in persons with plaque psoriasis. Marked hypervascularity and an increase in the size of dermal papillae occur. An activated CD3+ lymphocyte is noted around blood vessels with T cells expressing cutaneous lymphocyte associated antigen, co-stimulatory molecules such as CD2, and LFA -1 adhesion molecules. An aggregation of neutrophils in the dermis occurs that extends up into the epidermis.

12.13 CLINICAL MANIFESTATIONS.

Psoriasis Vulgaris.

Most common type of psoriasis, approximately 75% - 80% of cases. It can be regarded as a spectrum of different cutaneous manifestation with the hallmarks of erythema, thickening and scale. The outline of the lesion is usually circular, oval or polycyclic. During exacerbations, psoriatic lesions often itch.

Plaques are normally symmetrically distributed, involving the scalp, extensor elbows, knees and back. The plaques are erythematous with sharply defined margins that are raised above the surrounding normal skin.

The lesions can be from less than 1 to more than 10cm in diameter. Pinpoint papules surrounding existing psoriatic plaques indicate that the patient is in an unstable phase of disease.

Psoriasis area and severity index (PASI) was formulated to score for body surface area involved, erythema, induration and scaling.

In terms of quality of life, visibility, scaling and itchiness, are important parameters and quality of scores have also been developed.

Clinical Variants of Psoriasis Vulgaris.

A: Gutate Psoriasis. D:Annular psoriasis. G: Mucosal.

B: Nail Psoriasis. E: Scalp Psoriasis.

C: Inverse Psoriasis F: Elephantine

A: Guttate psoriasis:

Accounts for approximately 18% of all cases. Normally predominate in the trunk, proximal of the extremities and are more likely to involve the face. Guttate psoriasis following streptococcal throat infection is thought to originate from streptococcal exotoxin C, which acts as a superantigen and activates CD4+ and CD8+ T cells in the lesions and the areas around them. It is hypothesized that these T-cells persist in the skin of particular patients who go on to develop chronic plaque type psoriasis because the T-cells mistakenly recognize skin autoantigen such as keratin, and carbohydrates.

B: Nail Psoriasis

Typical nail abnormality in psoriasis is pitting, consisting of a few to multiple tiny pits scattered over the nail plate. The pits reflect abnormal nail plate growth resulting from psoriatic involvement of the nail matrix. These changes produce friable areas of cornified nail plate that erode away with normal friction.

In addition to pits, a localized colour change in the nail may occur that resembles the tan-brown colour of new motor oil, "The oil drop sign" . Severe nails involvement results in thick

crumbling nails that can be confused with onychomycosis. Finger nails are more affected than the toe nails.

C: Inverse Psoriasis

Refers to presentation involving the intertriginous areas, including the inguinal, perineal, genital, intergluteal, axillary and intramammary regions. It can easily be misdiagnosed as fungal or bacterial infection because there is no visible scaling.

Psoriasis Vulgaris can also transform into Pustular and Erythrodermic Psoriasis following infection or corticosteroid withdrawal

A: Pustular Psoriasis.

Generalized pustular psoriasis is an unusual manifestation and triggering factors include:

- Pregnancy
- Tapering of corticosteriods therapy
- Hypocalcemia
- Infections
- Topical Irritants

There is widespread erythema, scaling and sheets of superficial pustules with erosions characterizing the most severe forms (the **von Zumbusch** variant). Generalised pustular psoriasis during pregnancy is also referred to as **Impetigo Herpetiformis**.

B: Erythrodermic psoriasis

This is an uncommon manifestation that may be acute or chronic. It is characterized by generalized erythema and scaling from head to toe. Such patients are at risk of complications related to loss of adequate barrier protection such as infection and electrolyte abnormalities secondary to fluid loss.

Acrodermatitis continua of Hallopeauis

This is a rare manifestation of psoriasis. Clinically, pustules are seen as the distal portions of the fingers and sometimes the toes. Postulation is often followed by scaling and crust formation. Pustules may also form in the nail bed.

12.14 Psoriasis in HIV - Infected Patients

Psoriasis may be the presenting sign of HIV infection, however, there is no increased incidence of HIV infection in psoriatic patient.

Normally, it presents with palmar and plantar involvement, nail disease, arthritis and widespread erythrodermic disease with higher PASI score. It may develop at any stage of the disease .

Two groups have been identified,

Group 1: Personal or family history of psoriasis. Normally presents with chronic plaque psoriasis.

Group 2: Develop Psoriasis after infection with HIV. Involvement of palm, soles and joints are common. HIV associated psoriasis may be refractory to topical therapies and systemic retinoid may be required.

Grading Of Severity.

Clinically, psoriasis can be graded according to the percentage of body surface area involved:

Mild Psoriasis: 2% BSA.

Moderate Psoriasis: 2%-10% BSA.

Severe Psoriasis: Greater than 10%.

In addition to Body Surface Area, other parameters for severity are: erythroderma, plaque thickness, pruirutus and scaliness

12.15 THERAPY IN PSORIASIS.

Therapy choice of treatment depends on the severity of disease and response in the individual patients.

Topical Treatments.

These are used in mild to moderate psoriasis.

- Vit D or A anologues e.g Calcipotriene or Tazorotene respectively, are used.
- Phototherapy: This is reserved for patients with widespread lesions involving 10% or more of Body Surface Area.
- Goeckerman Regimen: Broadband UVB (290nm to 320nm) phototherapy and crude coal tar are used.

UVB emitted at 311nm to 313nm is known as narrow band UVB phototherapy and is more effective rapidly.

Systemic Treatment.

- Photochemotherapy: The photosensitizer 8-methoxypsoralen (8-MOP) is taken orally 1.5 to 2 hours before UVA exposure. The drug is excited by UVA irradiation in the 320nm to 340nm wavelength range which produces cross-linking of DNA thereby inhibiting DNA synthesis and epidermal turnover.
- Oral Retinoid Therapy:

Retinoids are naturally or synthetically derived from Vit. A and have anti-inflammatory, anti-keratinizing and anti-proliferative effects on the skin.

Side effects are: Teratogenecity, Dryness of the skin and mucous membrane, hair loss, Nail changes, Hyperlipidemia especially serum triglyceride.

- Methotrexate: Folic acid antagonist that inhibits DNA synthesis. It also acts on mononuclear cells in the skin, blood and lymphatics.
- Cyclosporine: Interferes with T-cell activation and communication with antigen presenting cells. It also inhibits epidermal cytokines network. Reserved for severe psoriasis. Most serious toxicity are nephrotoxicity and hypertension.
- Tacrolimus: Acts on T-lymphocytes.
- Biological Immunomodulators.
- Alefacept: Fusion protein composed of leukocyte function antigen-3 and Fc portion of human IgG.

Reduction in the number of memory-effector (CD45RO+) T-cells is associated with response to therapy.

- Efalizumab:

Humanized monoclonal antibody directed against the CD11a subunit of leukocyte function antigen-1(LFA-1) expressed on the T-cells.

By blocking the interaction of LFA-1 and its ligand intercellular adhesion molecule-1, T-cell activation and migration into psoriatic plaques are decreased.

Tumour Necrosis Factor Inhibitors.

- Etanercept: Fusion protein made of two p75 TNF receptors and the Fc portion of human IgG. It binds and inactivates TNF and prevents its significant proinflammatory effects in the target tissue of the skin and joints.

It is administered as 50mg twice weekly for 12 weeks followed by 25mg twice for maintenance.

- Infliximab: Chimeric monoclonal antibody that binds TNF. Screening for PTB is required before treatment.

Adalimumab: Human anti-TNF monoclonal antibody, currently under development for psoriasis treatment.

12.16 PROGNOSIS.

Psoriasis is a lifelong condition that is not curable but can go into remission. It affects the quality of life and mortality is low unless it is severe e.g erythrodermic and pustular variants with BSA >20%.

12. 17 EFFECTS OF HIV ON PSORIASIS.

A clear relationship exists between psoriasis and the profound immunosuppression of HIV infected patients.

Psoriasis tends to become more severe as the HIV infection progresses and there is even some correlation between low CD4 counts and the severity of psoriasis **(31-33)**.

HIV associated psoriasis is poorly understood because of two main paradoxes it presents:

(A): Psoriasis worsens with dropping CD4 T-cell counts in HIV meanwhile therapies that decrease T-cell count cause psoriasis to improve. **(34-35)**.

(B): HIV is typically characterized by a strong TH2 cytokine profile whereas psoriasis vulgaris is characterized by a strong TH1 secretion pattern. **(36-38)**.

A closer look at the disposition of T cells subsets, cytokine profiles and antigen presentation in HIV and psoriasis provides for better understanding and may clarify these apparent paradoxes.

T-CELLS IN PSORIASIS AND HIV.

T-cells can be divided into many categories such as:

- CD4+ (Helper/suppressor).
- CD8+ (Cytotoxic)
- CD45RA+ -Naïve
- CD45RO+-Memory.
- Th1 or Th2.

The balance of these various cell types is significantly disrupted in HIV infection.

Histological evidence reveals that the accumulation of CD8+ memory lymphocytes in the epidermis is linked to both the onset and exacerbation of psoriasis. **(40)**.

CD8+ subpopulation expresses pro-inflammatory cytokines such as IFN-gamma and TNF-alpha more frequently than the CD4 (**36.40**).

Among CD8 cells, the memory subset is the most active in psoriasis.

Several studies have demonstrated that the memory CD45RO+ T-cells are overwhelmingly predominant in psoriatic lesions. (**41**).

Furthermore, improvement of psoriasis lesions by various therapies including cyclosporine, PUVA, alefacept, methotrexate is preceded by a decrease in epidermal T cells (primarily CD8+, CD45RO+).

Genetically, the strong association of psoriasis with several MHC class 1 antigens provides additional support for the importance of CD8+ cytotoxic T cells in psoriasis. (**42-43**).

HIV progression is characterised by a decrease in the CD4+ Tcell count which leads to a decreased CD4/CD8 T cell ratio.

The HIV also affects the naïve and memory cell subpopulations differently depending on the T cell type.

The majority of studies show that the virus preferentially infects and replicates in CD45RO+(memory/effector) CD4+ T cells whereas in CD8+ T cells, it tends to 'prefer' CD45RA+ (naïve) subtype. (**44-47**).

The decrease in naïve CD8+ subpopulation has been suggested as a possible explanation for the decreased ability of the patients to fight new infections while at the same time suffering from autoimmune diseases such as psoriasis.

In summary, psoriasis in healthy individuals has been described as being mediated by type-1 cytokines, notably IFN-gamma and TNF-alpha with low levels of type-2 cytokines IL-4 and IL-10. HIV is thought to involve a shift from type 1 to type 2 cytokine profile with decreased IL 2 and increased IL 4 and IL 10.

Critical to understanding of psoriasis in HIV patients, however, is the fact that activated CD8+ cells produce increased levels of IFN-gamma compared to healthy controls.

13. Study Justification.

- Psoriasis vulgaris is a common disease with various levels of morbidity, however, there is no published data on the mode of presentation in our institution, Kenyatta National Hospital. This study will generate data on the mode of presentation of psoriasis vulgaris in both HIV negative and HIV positive patients at various stages.

14. Main objective.

To determine the clinical patterns of psoriasis vulgaris in Kenyatta National Hospital patients who are both HIV negative and positive with various CD4 count.

14.11 Specific objectives.

- To determine the sociodemography of patients with psoriasis vulgaris presenting at Kenyatta national Hospital.
- To document precipitating factors, clinical variants lesional surface area and sites affected.
- To determine the clinical patterns of psoriasis vulgaris in Kenyatta National Hospital.

Secondary objectives.

- To describe and compare the mode of presentations of Psoriasis Vulgaris in both HIV negative and HIV positive patients.
- To determine CD4 count and WHO staging of HIV and correlate them with surface area and morphological variants.

14.12 Patients and Methods.

14.13. Study area:

The study was carried out in Kenyatta National hospital which is the largest referral hospital in Kenya. It is based in Nairobi, the capital city of Kenya. Patients were recruited from Dermatology clinics, both Paediatric and Adult which are run on Wednesday and Friday respectively. Other catchment areas were Comprehensive Care Clinic, Accident & Emergency area and Medical Wards

14.14. Study Population:

These were patients presenting to the above named areas for medical care. The ones recruited met the definition critirea set below.

14.15. Study design:

This was an hospital-based Cross-sectional Descriptive survey carried out by the principal investigator and an assistant who assisted in identifying the clients.

14.16. Sample Size

The minimum sample size required was calculated using the formula

$$n=\frac{Z^2xp(1-p)}{d^2}$$

Z: Standard normal deviation at alpha 0.005, equivalent of 95% Confidence Interval.

p: prevalence of the disease, which is 3.15% in Kenya.

d: Degree of precision at 4%.

n: 70.

14.17 CASE DEFINITION

Psoriasis was defined clinically and histologically :

Clinical definition:

Sharply demarcated skin papules, plaques, patches of various sizes and shapes with clear-cut borders, erythema and non-coherent silvery scales in different anatomical regions. Auspitz sign might or might not be present.

Histological confirmation by the pathologist

Variants were defined as follows:

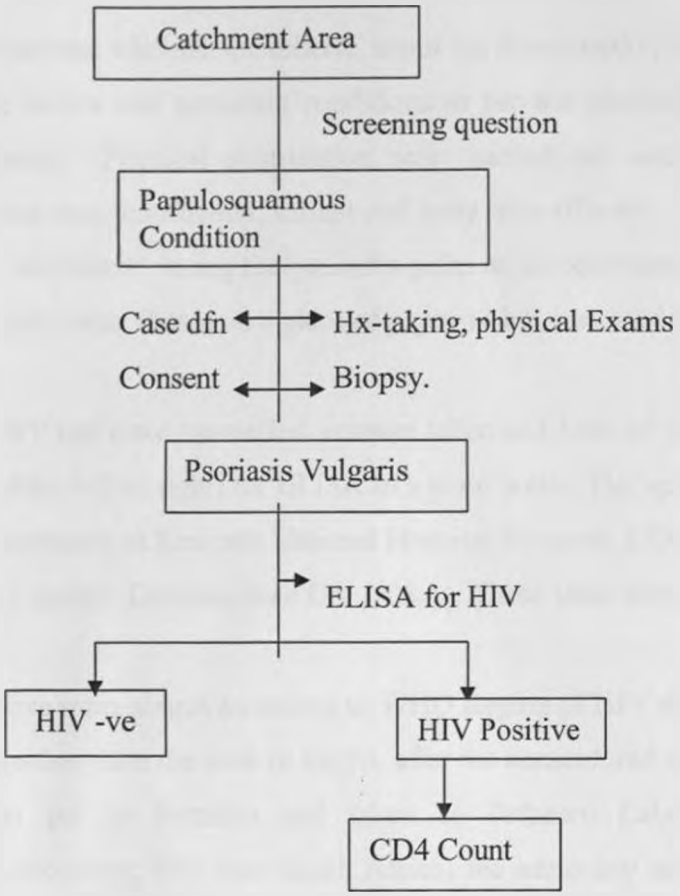
- Gutate: Tear-drop shaped patches on the trunk, arms, legs or scalp.
- Inverse: Smooth inflammed patches without a scaly surface occuring under armpits, breasts or the groin.
- Nail Psoriasis: Tiny white pits scattered across the nails with long ridges across or down the nail.
- Elephantine: Conglomeration of patches and plaques covering approximately 10% of body surface area.
- Scalp: Scaly patches and plaques on the scalp, meeting the above definition of psoriasis.
- Mucosal: psoriatic lesions in the oral mucosa.
- Annular: ringed shaped psoriatic lesions.

HIV test was a laboratory diagnosis.

14.18 Sampling Procedure

This was a consecutive sampling.

Figure 1: Recruitment and study procedure of patients.



14.19 Inclusion criteria

Patients who presented at the study area with active lesions of psoriasis.

Consent was asked for.

14.20 Exclusion criteria

Patients in remission were exempted.

14.21 Data Collection.

I used to attend the Friday and Wednesday dermatology clinics for the recruitment of clients. Patients were picked after I had gone through the file. I would screen the patient and any patient with papular, scaly, plaque-like lesions or referred with a diagnosis of psoriasis was recruited after the consent. My assistant used to identify the patients and refer them to me for evaluation. The dermatologists used to assist in identifying the patients and verifying my diagnosis which was later confirmed by biopsy after recruitment. Monday mornings were set

aside for the CCC(by the principal investigator) and my assistant used to go to CCC on Tuesday and Thursday mornings to look for clients whom I would go and screen. Patients from the wards were seen in the afternoons. The two patients from A & E were referred to me by my colleagues.

History was taken from the patients who met the criteria, about the demography, the duration of the disease, precipitating factors and comorbid conditions as per the attached proforma after the patient had consented. Physical examination was carried out with particular attention to the lesional surface area, distribution, variant and body sites affected.

Lesional surface area was estimated using the patient's palm as an equivalent of 1% of body surface area. Patient's palm was drawn on a piece of paper which was used on the body to estimate the percentage.

Patients who had not done HIV test were counselled, consent taken and 5mls of blood drawn from the antecubital fossa(either left or right) for ELISA in a plain bottle. The specimen was later taken to immunology laboratory at Kenyatta National Hospital the same. CD4 count was measured by FACs counter (Aecton Dickson, rose CA , USA). These tests were done after biopsy results.

Patients who were HIV positive were staged according to WHO staging of HIV disease.

Incisional biopsy was taken(either from the back or thigh), after the consent and under sterile procedure .The tissue was put in formalin and taken to Pathcare Laboratory(an Internationally Accredited Laboratory, ISO from South Africa) the same day and histology was done using H & E staining, however, patients with biopsy results were not asked for biopsy.

All these data were entered into a proforma

14.22 DATA ANALYSIS.

- Data was entered into study proforma, cleaned and verified.
- Statistical analysis using SPSS version 14.2 software
- Determination of means, median, SD and frequency distributions of quantitative variables was done.
- The correlation between CD4 count and psoriasis was not done because the number of HIV positive patients were not statistically significant.
- Categorical variables were analysed using percentages.
- Results were presented in the form of pie charts, graphs and tables.
- The P value was 0.05 with a confidence interval of 95%.

15. ETHICAL CONSIDERATIONS.

- The study was approved by the department of Internal Medicine, Nairobi University and Kenyatta National Hospital Ethical Research Committee.
- Study consent (Appendix 1) explanation was translated into Kiswahili to the clients or guardians(most clients could understand Kiswahili) and voluntary informed consent (Appendix 2) was received.
- Patients were counselled before HIV test was done and after the test. They were advised appropriately.
- There was no exposure to unnecessary risks.
- Full confidentiality was maintained.
- Appropriate referrals were given.
- Freedom to withdraw without prejudicing their care was guaranteed.

16. STUDY UTILITY

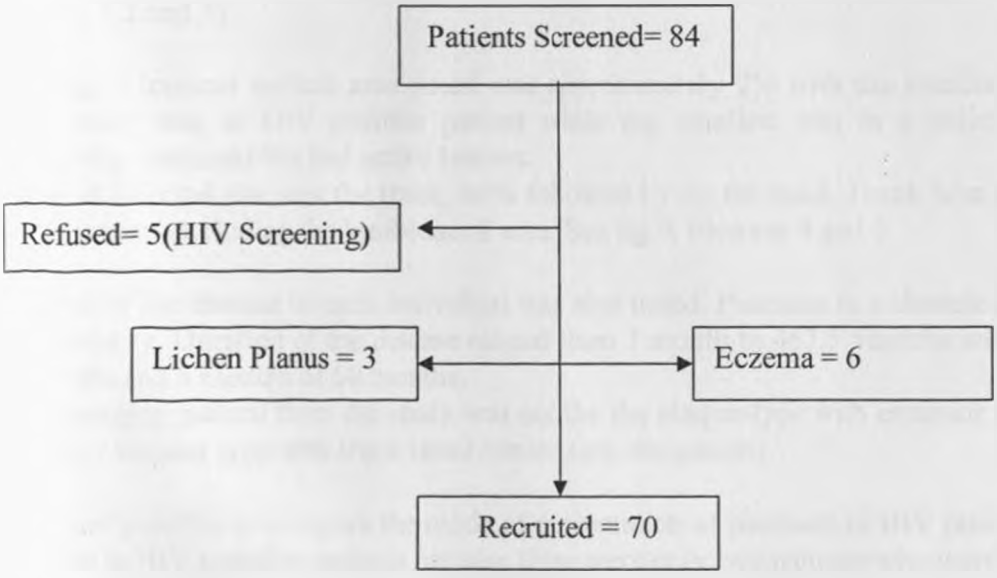
- Information on the burden of psoriasis and HIV formed baseline for assessment of the impact of any future intervention programmes.
- Therapeutic interventions can thus be undertaken to benefit the patients so that the quality of life is improved.

RESULTS

The study was conducted from 24th July 2008 to 2nd OCT 2008. A total of 84 patients were screened. Five (5) declined recruitment because of HIV screening, three (3) were found to have Lichen planus and six (6) had eczema see (fig 2). Two (2) patients were screened from A & E, only one (1) was recruited. Two (2) patients from CCC were all recruited. Four patients were from the wards and were eventually recruited.

The remaining seventy six patients (76) were screened from the dermatology clinics, both adult (70) and paediatric (6) clinics. Out of the seventy patients, two were HIV positives (two males). Thirty had biopsy results ready and forty-nine had biopsy taken. Sixty had blood taken for HIV test while nineteen had the results for HIV ready.

Figure 2: Flow chart of recruitment of patients



Out of the 70 patients recruited successfully, 38 were males and 32 females, (1.2: 1) see Fig 3. Three were from the paediatric clinic.

Majority of the patients were from the adult clinic where the oldest was 65 yrs. Mean age of the patients was 33 yrs the median age being 30 yrs (Standard deviation was 12.3). Fig 4

Patients came from different parts of the country. Grouping them as per region was not easy, therefore, they were grouped as per the province.
Most clients came from Central, Nairobi and Eastern provinces(see Fig 5 and discussion)

Most of the clients had secondary education (n=30), followed by primary (n=23),tertiary colleges(n=9) and university (n=5). Three patients had nil education. See fig 6. Out of the five university graduates, four were still students. The level of education was reflected in the occupation of the clients. Most of them were craftsmen (carpenters, technicians, mechanics and electricians). Farmers were n= 7, Housewives were n= 10, Businesspeople were n= 11, students n= 13, professionals were n= 13 and craftsmen were n= 16. The professinals were teachers, hoteliers, accountants, economists and clerks (See fig 7).

Triggering and risky factors were lumped together because some factors are both triggering and risky (see discussion). Alcohol consumption, cigarette smoking, antihypertensive drugs, antimalarials and throat infection were some of the triggering factors ellicited. Presence of psoriasis in other members of the family was documented in only three cases, 2 nieces and a son.(See Table 1)
No known risk nor triggering factors were documented in the remaining more than 52 cases.

The most common variant noted was annular, n=35 followed by scalp,n= 29.
Nail psoriasis was noted in n=5 cases and inverse psoriasis in n= 1 case. Guttate, mucosal, sebopsoriasis and elephantine psoriasis were not observed during the study. (See table 2 and pictures, 1,2 and 3)

The largest lesional surface area noted was approximately 2% with the smallest 0.5%. this large lesion was in HIV positive patient while the smallest was in a patient who was undergoing treatment but had active lesions.
The most affected site was the trunk, 80% followed by by the head. Trunk here means chest and abdomen, excluding the lumbosacral area. See fig 9, Pictures 4 and 5.

Duration of the disease in each individual was also noted. Psoriasis is a chronic disease with low mortality. Duration of the disease ranged from 1 month to 467.5 months with a mean of 80 months and a median of 60 months.
The emerging pattern from the study was not the the plaque-type with extensor involvement but rather annular type with trunk involvement (see discussion).

It was not possible to compare the mode of presentation of psoriasis in HIV positive patients with that in HIV negative patients because there were only two patients who were positive.
However, it was observed that the lesional surface area and sites affected were different (e,g face, penile shaft in male patients, palms and soles). These areas were not affected in HIV negative patients. The two HIV positive patients were all in Stage 1 disease (WHO staging with CD4 counts of 350 cell/mm and 370cells/mm).

Figure 3: Figure gender distribution

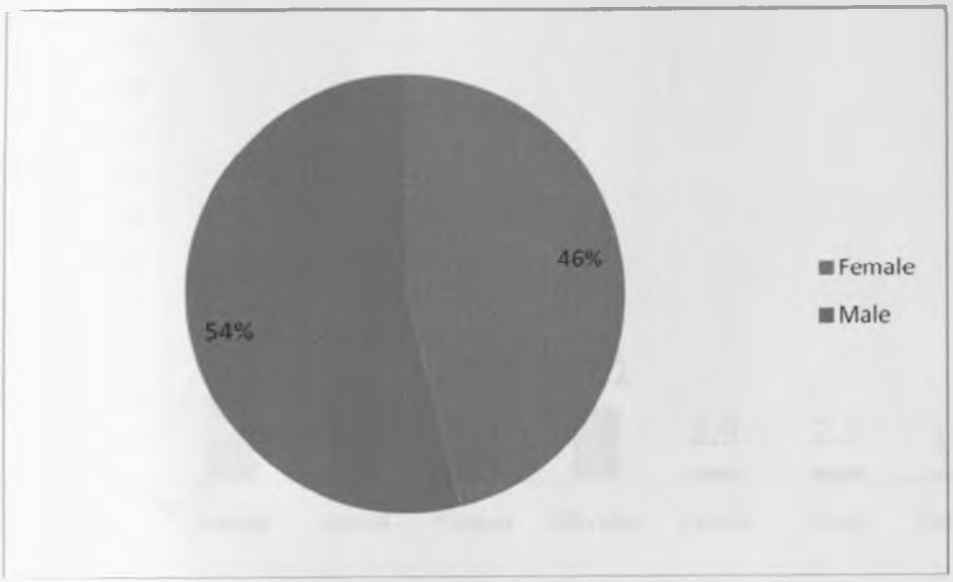


Figure 4: Age distribution of patients.

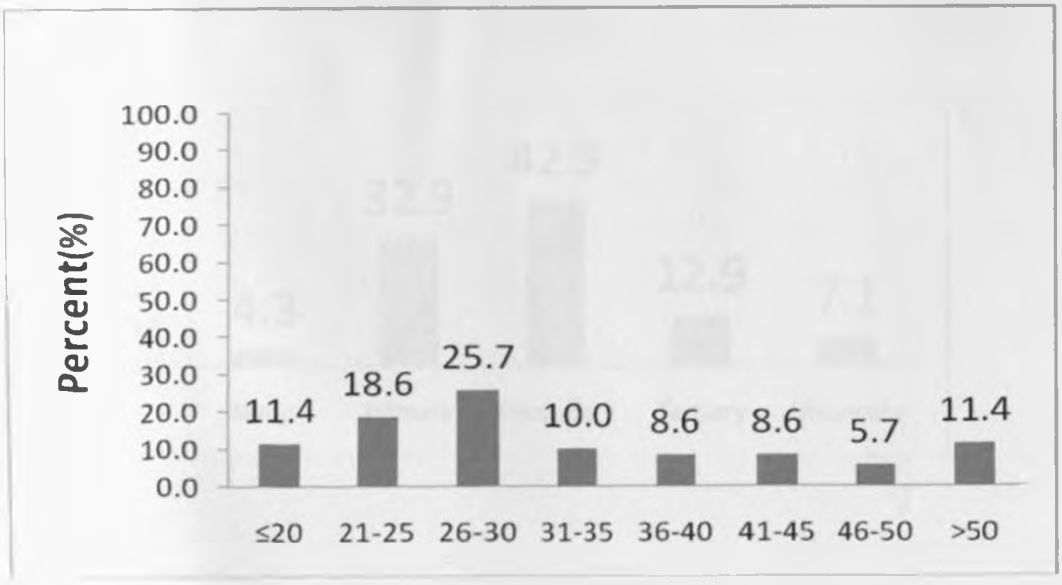


Figure 5: Patients' province of residence

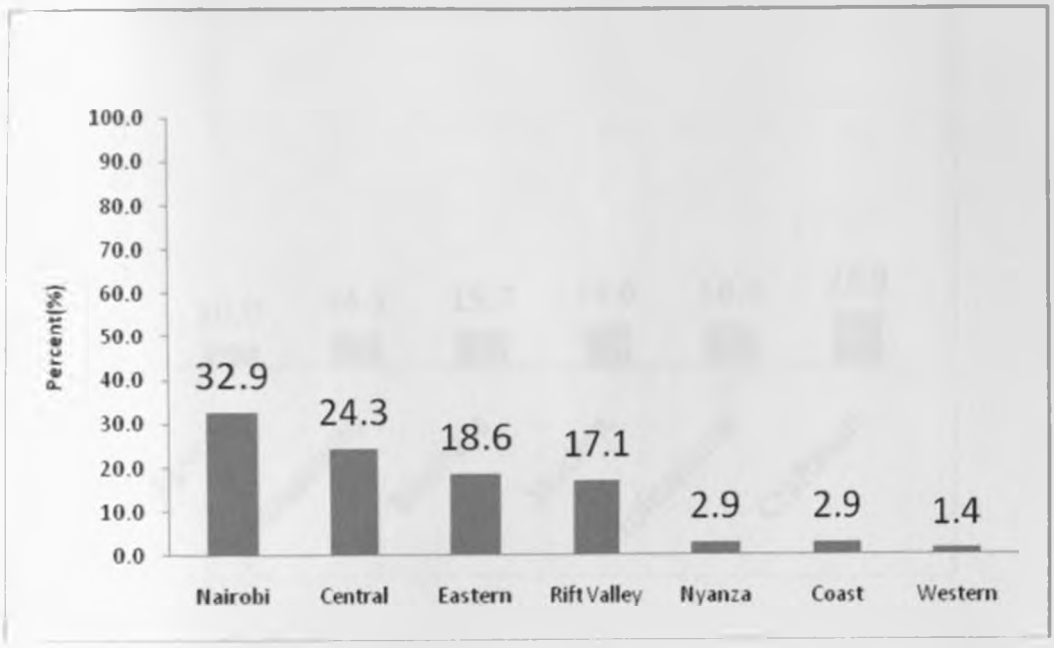


Figure 6: Level of education of patients.

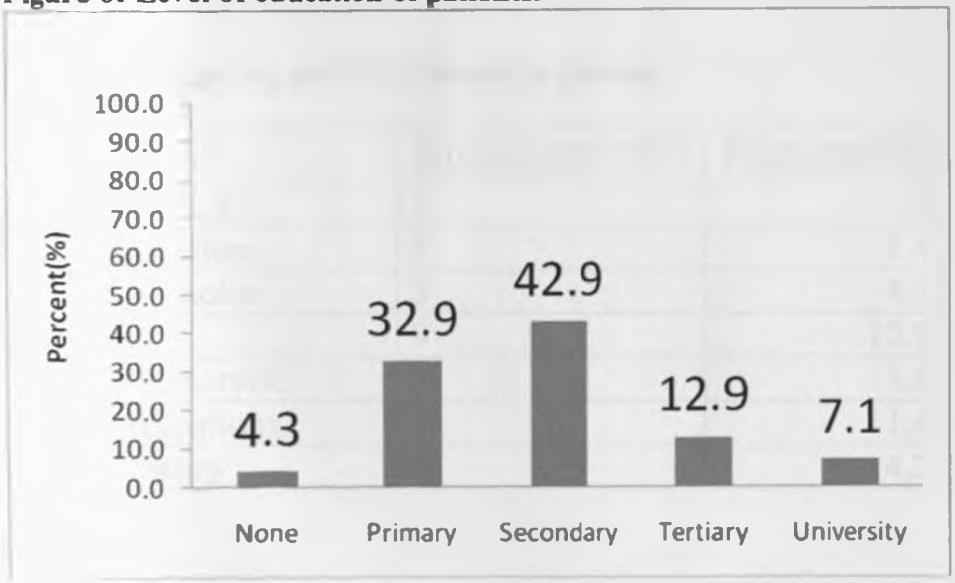


Figure 7: Occupation of patients

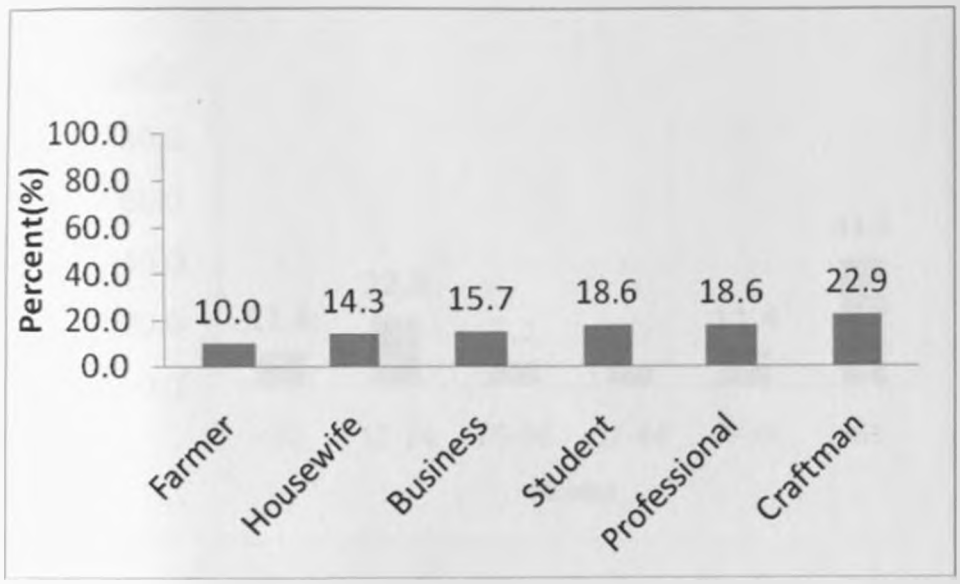


Table 1: Triggering and risky factors in patients

	Number(n=70)	Percent(%)
Malarial drugs.	1	1.4
Throat Infection.	1	1.4
Cigarette Smoke.	3	4.3
Alcohol.	9	12.9
Antihypertensives.	1	1.4
Other medications.	1	1.4
Family history	3	4.3

Figure 8: Duration of the disease in patients

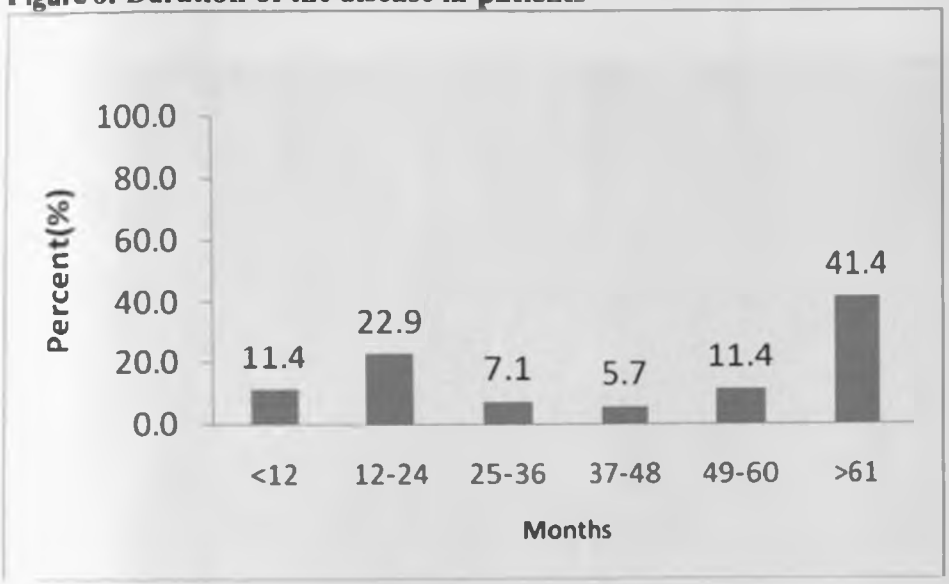
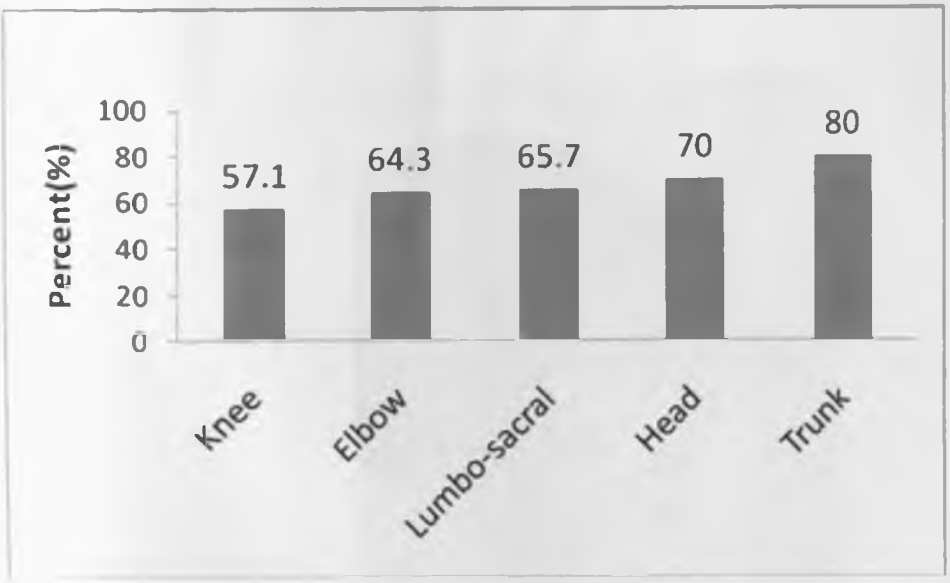
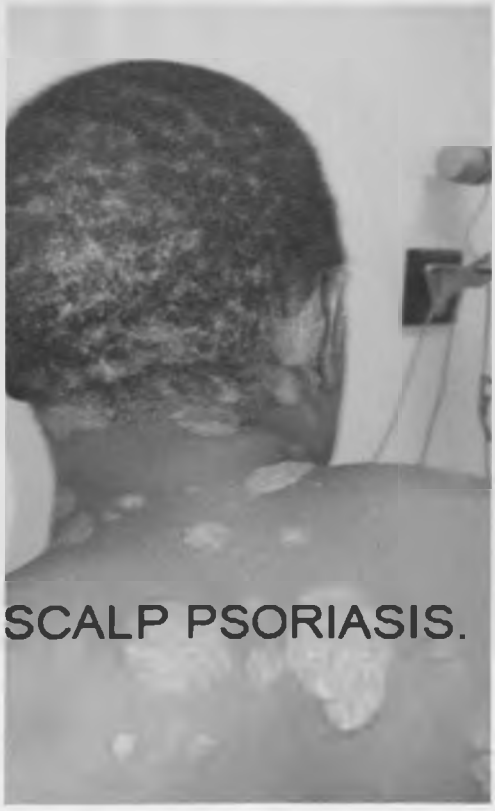


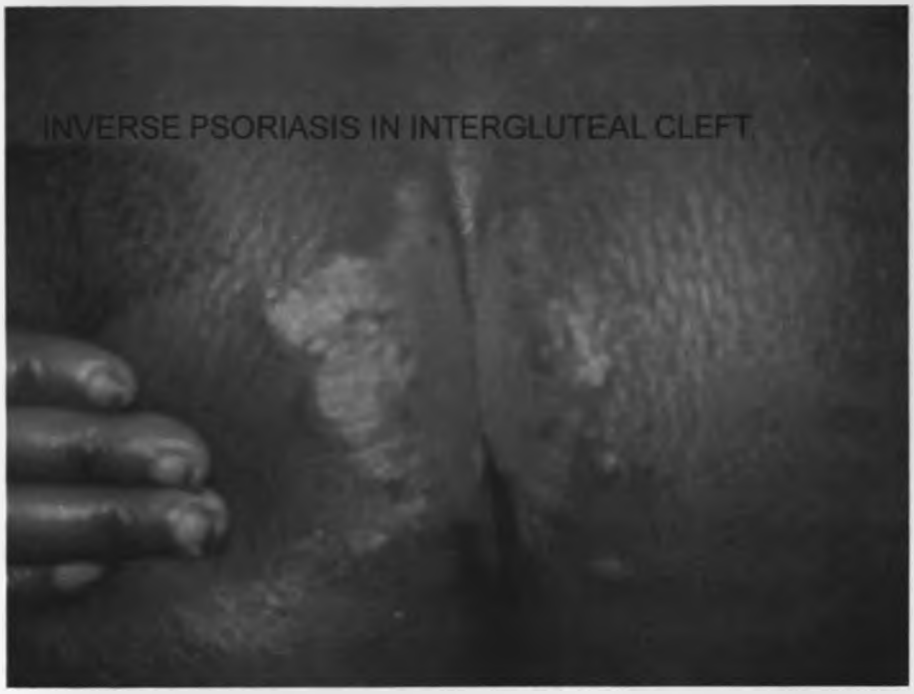
Figure 9: Sites affected in patients



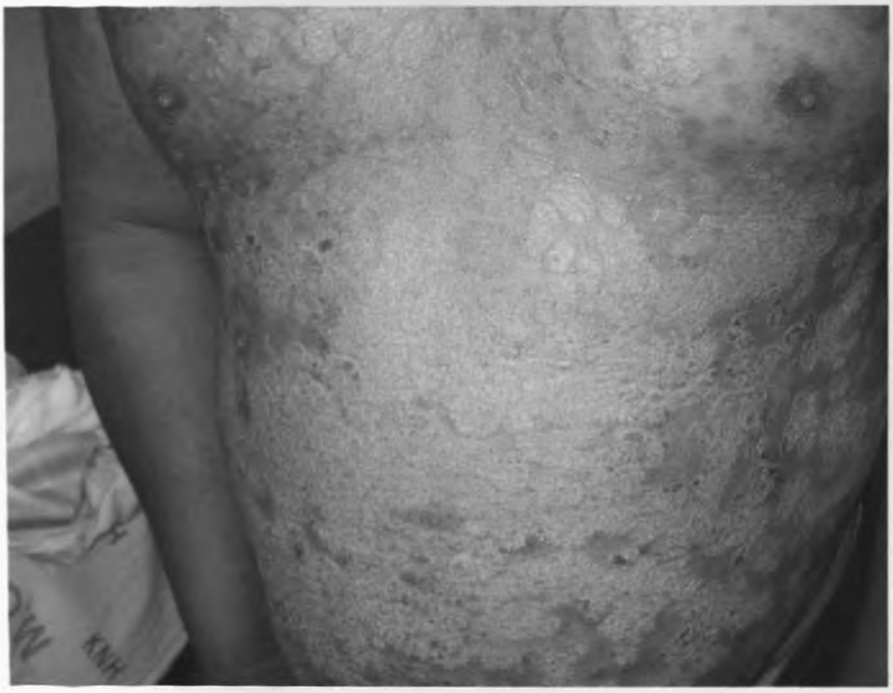
Picture 1: Annular psoriasis



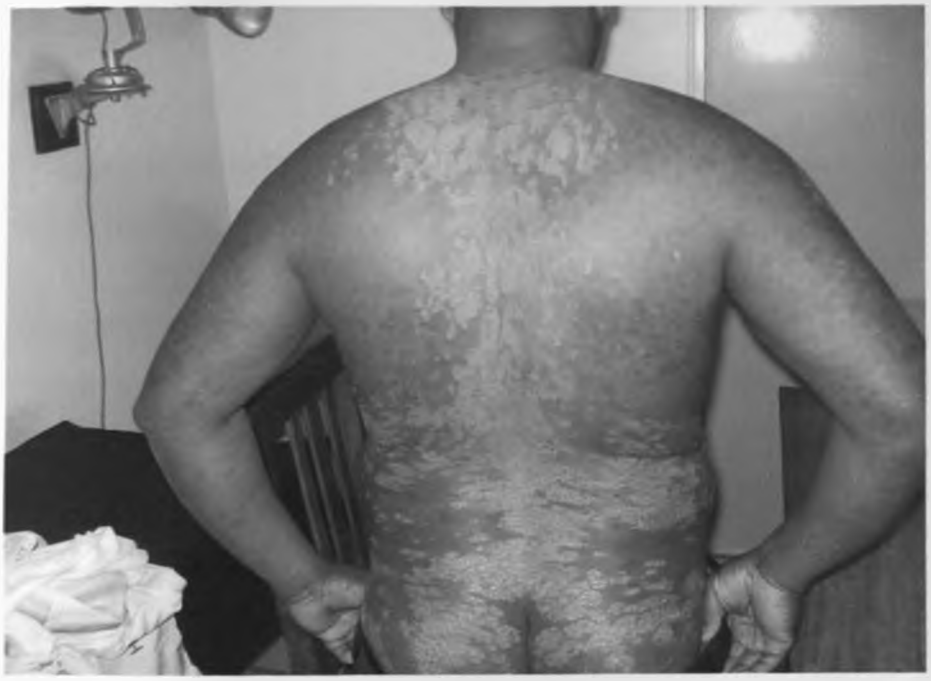
Picture 2: Scalp psoriasis



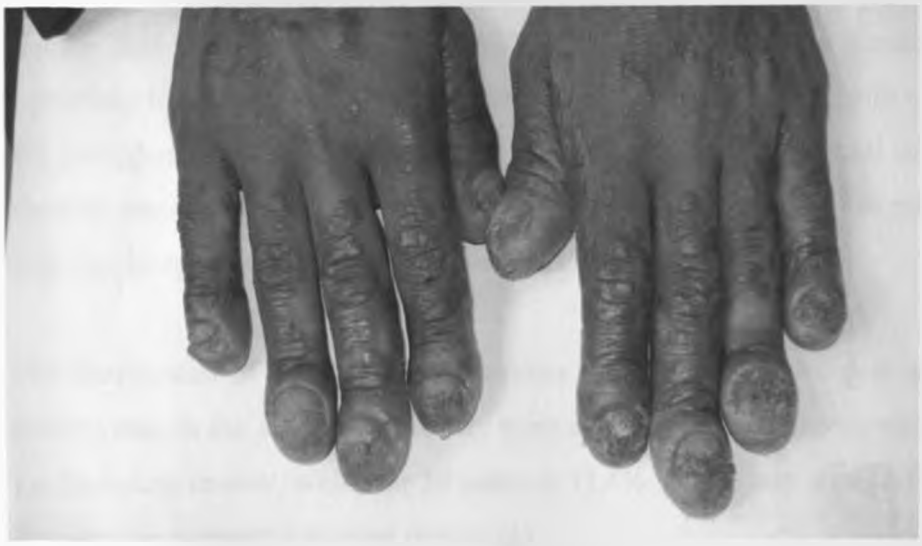
Picture 3: Inverse psoriasis.



Picture 4: Trunk



Picture 5: Lumbo-sacral



Picture 6: Nail psoriasis

Table 2: Clinical variants

	N=70	percentage
Guttate	0	0
mucosal	0	0
Elephantine	0	0
Sebopsoriasis	0	0
Inverse	1	1.4
Nail	5	7.1
Scalp	29	41.4
Annular	35	50.1

DISCUSSION

Data on clinical patterns of psoriasis vulgaris in our set up is lacking and this study was carried out to get data for future reference.

The study was carried on patients who presented to Kenyatta National Hospital with a diagnosis of psoriasis vulgaris, as per the definition criteria and inclusion criteria(i.e active psoriasis). There were some patients who were already on treatment but came in with active lesions. This did not impact negatively on the results as newly diagnosed patients were also noted to have similar pattern as the ones on treatment with active lesions.

Psoriasis is a disease which affects men and women equally. In this study, the number of men who came for treatment were slightly more than women, 54% vs 46%, (1.2:1), however, this was not statistically significant. Psoriasis has profound effects on a patient's self-image, self-esteem and a sense of well being. This was found to affect females more than males according to a retrospective study done in Trinidad and Tobago, with a view to establishing the prevalence of psoriasis. It was carried over 5 years with total of 394 patients and it showed similar results: 54% males, females 46%.(**48**). The females might have shied away from the hospital because of the self-esteem.

The distribution of age at onset in psoriasis is bimodal with two peak ages, 20-30 years and 50-60 years.In the study, the majority were at 20-30 years (44.3%) which is expected as per the literature review, with over 50 years at 11.4%. There was no significant variation in age distribution compared to other studies (**2**).

As indicated earlier in literature review, some of the known risk factors for psoriasis are: genetic predisposition, obesity ,smoking (**49**), stress, HIV infection and alcohol while triggering factors which lead to flaring up of psoriasis in an individual who already has psoriasis are: climatic changes, infections, skin injury, drug reactions and stress. Some of these are both risky and triggerring factors, e.g stress and infection. During the study, both risky and triggering factors were put together. Stress was not looked into because the tools for

objectivity had financial implications. Climatic changes and skin injuries were looked into in terms of area of residence and occupation respectively (see below).

Three(3) patients had family history. Other three(3) patients were on medications, antibiotics, antimalarials and antihypertensives. Nine (9) patients used to take alcohol with a mean duration of 75 months and approximately 400mls of beer per week. Three (3) others were also found to be smokers, a mean duration of three pack years. I was not able to elicit any risk nor triggering factor in the remaining fifty two (52) patients and this can be explained by the fact that psoriasis is multifactorial in origin and associated with multiple genes in an individual patient. Another explanation might have been that the patients forgot what might have triggered the disease because the majority of them had the disease for a mean duration of 80 months (6.7yrs).

From the study, only 18 patients (25.7%) had risk and triggering factors elicited. This might also be due to the few numbers of patients examined .Amongst the 18, only one patient was found to be on anti-hypertensives, enalapril and frusemide. The issue of antihypertensives (b-blockers and ACE inhibitors) acting as trigger factors was challenged in case control study done between 1994 and 2005 on patients 36702 with psoriasis and hypertension **(50)**.

Two patients tested positive for HIV. This was about 2.85% of the total patients studied and it showed that there is low incidence of psoriasis in HIV positive patients as has been shown in other studies. A study carried by Garbe et al from 1983-1992 on 456 patients infected with HIV found that only 29 (6.4%) suffered from psoriasis **(51)**. However, these patients had bigger lesional surface area and had psoriatic lesions on the face, penile shaft and mons pubis.

The low incidence of Psoriasis in HIV positive patients might be explained on the basis of immune reaction.. Psoriasis is an immune reaction involving T-cells especially the subset memory T-cells. Some of the drugs used in treatment of psoriasis lowers T-cell levels.

HIV attacks T-cells and lowers the number, leading to immunosuppresion. Lowering of T-cell levels might ameliorate Psoriasis. However there is still paradox because HIV worsens psoriasis.

The study was carried out in Kenyyatta National Hospital, the largest referral hospital in Kenya. The majority of the clients were from the environs of the hospital (Nairobi, Central and Eastern Provinces). The great distances from, Western, Nyanza and Coast provinces

probably prevented clients from these regions for coming for a review. It could have been good to correlate the area of residence with psoriasis because of climate which plays a major role in the morbidity of psoriasis. Warm and humid weather is known to improve psoriasis while cold and dry weather worsens psoriasis. Gathering data about climatic conditions in these regions and conducting a larger community based study would bring this correlation out clearly. This was not possible from this study because of the time and financial implication.

Most of our clients were form four and primary school graduates hence majority were artisans. This might be attributed to the earnings because Kenyatta Hospital is the only public hospital with fairly reasonable quality care at a cheaper rate. This might bring out bias to insinuate that psoriasis is a poor man's disease. This did not come out clearly because I would have expected cases of Koebner phenomena, which is common in some occupations where trauma is common. Such kind of occupations worsen psoriasis.

Annular variant was the most common type of psoriasis vulgaris (50.1%)., affecting mostly the trunk (80%). This is unusual because the commonest type, the classical plaque type presents with lesions on the extensors of the extremeties, i.e the knees and elbows. This classic type was seen on 57.1% and 64.3% , knees and elbows respectively.

This has an implication on diagnosis and treatment because other lesions which present with annular lesions on the trunk include tinea corporis and lichen planus (as proved by biopsy). Therefore, biopsy should be taken in all patients with such lesions.

In addition to psoriasis vulgaris, around 7.1% of patients also had fingernail changes, mostly onycholysis (see picture 6), not pitting which is the most common nail psoriasis

Guttate which is normally common amongst the paediatric age group was not observed probably because of the small number, n=3. Rare cases like mucosal psoriasis were not observed.

Psoriasis has low mortality though it affects the quality of life leading to psychosocial issues.

CONCLUSIONS

Psoriasis Vulgaris affects the middle age group in our set up.

The most common variant of psoriasis vulgaris from this study is annular, affecting approximatcly 17% of body surface area.

Majority of clients have been having psoriasis for a mean period of 80 months (6.7 years)

The most commonly affected site is the trunk.

RECOMMENDATION

A larger, population based study is required to prove the risk and triggering factors.

Biopsy should be done for all cases of skin diseases presenting as scaly, pustular and plaque-like.

Some of the lesions which satisfied the clinical criteria for psoriasis turned out to be lichen planus and eczema histologically.

LIMITATION

Cross-sectional study may not bring out associations in on-going disease.

Documenting psoriasis Area and Severity Index (PASI) was not possible because of the cost.

I was not able to bring out all the triggering factors of psoriasis e.g. hypocalcemia (cost of test was high) and psychogenic stress (instrument to measure the objectivity was lacking).

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APPENDIX 1

CONSENT EXPLANATION.

STUDY ON: CLINICAL PATTERNS OF PSORIASIS VULGARIS.

I am Francis Omondi Wango, a postgraduate student at the University of Nairobi, department of Internal Medicine and Therapeutics. I will be carrying out a study on: "Clinical Patterns of Psoriasis Vulgaris."This is part of my Master's Degree programme.

AIM OF THE STUDY.

To generate data on the Clinical Pattern of Psoriasis Vulgaris in both HIV negative and HIV positive patients.. This will lead to improvement on the patient's management.

You are under no obligation to either accept or refuse to participate, and your decision will in no way affect your care this institution.

PSORIATIC PATIENTS.

You will participate after understanding the purpose and utility of this study.

You will be required to fill a questionnaire.

After the questionnaire, biopsy of the skin and blood will be taken in case there is no biopsy results and HIV serostatus is not known. The biopsy is to confirm the diagnosis of psoriasis and blood will be taken for HIV Test.. There will be no pain during the procedure (infiltration with lignocaine), however, the wound might heal with a minimal scar. This will not disfigure you nor interfere with your daily life.

The wound will be stitched, dressed and pain killers given. Pre and post test counselling will be done for HIV.

BENEFITS.

The above tests will be done at no cost to you.

You will be advised on the proper mode of treatment available at the institution.

APPENDIX 2

I.....,

have understood the information which has been given to me on the intention and purpose of this study titled "CLINICAL PATTERNS OF PSORIASIS VULGARIS" and have had my questions answered.

I do understand that some of the questions touch on my private life and I have agreed to provide the information in confidence.

I have also been assured that the information gathered from this study will in no way interfere negatively with my clinical care in this hospital or any other institution of medical care but will be used to improve medical care for me and others alike..

I voluntarily agree to participate in the study.

Participant's.

Name.....

Signature.....

Date.

Dr. Omondi (Investigator)

Signature.....

Date.

APPENDIX 3

PROFORMA

PSORIASIS VULGARIS.

Patient no.:_____
DOB:____/____/_____
Gender: [ ]Female [ ]Male
Level of education [ ]None [ ]Primary [ ]Secondary [ ]Tertiary [ ]University
Occupation: _____
Residence: _____

Family Member with similar condition.
[ ] Father [ ]Mother [ ]Brother [ ]Sister [ ] None.
[ ]Other, specify_____

Alcohol intake. [ ]Yes. [ ]No. If yes, duration in months [ ] quantity in mls [ ].

Cigarette smoking [ ]Yes [ ]No. If yes, how many in pack-years [ ].
Any past medical history [ ] Yes [ ]No
If yes, was it
Malaria [ ] Yes [ ]No
Throat infection [ ] Yes [ ]No
Hypertension [ ] Yes [ ]No
Other infection [ ] Yes [ ]No. If yes, specify_____

Medications [ ] Yes [ ]No
If Yes, which ones? [ ] Antihypertensives [ ] Antimalarials [ ] Mood stabilisers [ ] steroids.

Clinical History.
Duration in _____ months

Site:	Percentage affected
[ ] Head	_____
[ ] Elbow	_____
[ ] Knee	_____
[ ]trunk.	_____
[ ] Lumbo-sacral	_____
[ ] other, specify_____	_____

Clinical variants. [ ] Inverse [ ] Nail [ ] scalp [ ] Annular [ ] others.

Comorbid Condition.
[ ] Diabetes [ ] Rheumatism [ ] Inflammatory Bowel Diseases. [ ] Allergic Reactions

HIV TEST. [ ] POSITIVE [ ] NEGATIVE.
CD4 Count_____

Histology. Confirmed psoriasis [ ] Not psoriasis [ ].
WHO HIV/AIDS STAGE: [ ] [ ] [ ] [ ].

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Ref: KNH-ERC/ A/05

22nd July 2008

Dr. F. O. Wango
Dept. of Internal Medicine
School of Medicine
University of Nairobi

Dear Dr. Wango

RESEARCH PROPOSAL: "CLINICAL PATTERNS OF PSORIASIS VULGARIS IN PATIENTS AT KENYATTA NATIONAL HOSPITAL" (P92/05/2008)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your revised research proposal for the period 22nd July 2008 – 21st July 2009.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M.Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
The Dean, School of Medicine, UON
The Chairman, Dept. of Internal Medicine, UON
Supervisors: Dr. T.M. Munyao, Dept.of Internal Medicine, UON
Dr. O. Oyoo, Dept. of Internal Medicine, UON