Prevalence of Selected Cardiovascular Risk Factors Among Patients With Psoriasis Vulgaris At The Kenyatta National Hospital

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DECLARATION:

I, the undersigned, do hereby declare that this dissertation is my original work. It has not been submitted either wholly or in part to any other university for the award of a degree in Masters of Internal medicine.

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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AuAb</td>
<td>Autoimmune antibodies</td>
</tr>
<tr>
<td>CRP</td>
<td>C reactive protein</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>DNA</td>
<td>deoxyribonucleic acid</td>
</tr>
<tr>
<td>HDL</td>
<td>High density lipoproteins</td>
</tr>
<tr>
<td>HLA</td>
<td>Human leukocyte antigen</td>
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<tr>
<td>IL</td>
<td>Interleukin</td>
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<tr>
<td>KNH</td>
<td>Kenyatta National Hospital</td>
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<tr>
<td>MHC</td>
<td>Major Histocompatibility Complex</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial Infarction</td>
</tr>
<tr>
<td>MTX</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Ox LDL</td>
<td>oxidized low density lipoproteins</td>
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<tr>
<td>TH1 cell</td>
<td>T helper one cells</td>
</tr>
<tr>
<td>TNF α</td>
<td>Tumor necrosis factor alpha</td>
</tr>
<tr>
<td>VEGF</td>
<td>Vascular Endothelial Growth Factor</td>
</tr>
<tr>
<td>WHR</td>
<td>Waist Hip ratio</td>
</tr>
<tr>
<td>SSA</td>
<td>Sub Saharan Africa</td>
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ABSTRACT:

**Background:** Psoriasis Vulgaris is a chronic, immune mediated inflammatory disease of the skin associated with a high degree of morbidity and poor quality of life. Psoriasis has been reported to be associated with an unfavorable cardiovascular risk profile. Moreover, the risk of mortality is also increased in patients with severe psoriasis compared to the general population.

**Study Objective:** We set out to determine the prevalence of selected cardiovascular risk factors in patients with psoriasis vulgaris attending the dermatology clinic and dermatology inpatients and healthy controls at the Kenyatta National Hospital.

**Methods:** This was a hospital based cross-sectional study carried out at the Kenyatta National Hospital comparing psoriasis vulgaris cases from the dermatology clinic and dermatology ward with age sex matched healthy controls from the blood transfusion unit over a three month period. Study participants were interviewed using a questionnaire on socio-demographic information, duration of psoriasis and treatment modality used and history of Hypertension, Dyslipidaemia, Diabetes Mellitus, Obesity and Cigarette Smoking. Anthropometric and blood pressure measurements were taken. Blood samples for blood sugar and total cholesterol were drawn.

**Results:** Between July and October 2012 a total of 580 files of patients attending the dermatology clinic and those admitted to the dermatology ward were reviewed. Of these, 92 files identified patients with psoriasis vulgaris and were screened. 75 patients met the inclusion criteria and were recruited as cases into the study. For the controls, a total of 82 healthy blood donors were screened and 77 met the inclusion criteria. The mean age in the psoriasis vulgaris population was 41.1 years and 40.9 years in the controls. There was a slight male preponderance with a male to female ratio of 3.3:2. Hypertension was the most prevalent cardiovascular risk factor in patients with psoriasis vulgaris at 40% and 22% in healthy controls. Hypertension was higher in psoriasis vulgaris cases than healthy controls (OR 2.4 [95% CI 1.2-4.8] p=0.017) The prevalence of other selected cardiovascular risk factors in psoriasis vulgaris patients and healthy age sex matched controls and their odds ratios were as follows: Dyslipidaemia (25.35%, 20.8%, OR 1.3 [95% CI 0.6-2.8] p=0.505), Diabetes (12%, 10.4%, OR 1.2
[95% CI 0.4-3.2] p=0.753), Obesity (12%, 9.1%, OR 1.7[95% CI 0.6-4.8]p= 0.351 ), Abdominal obesity (26.7%, 19.5%, OR 1.5[95% CI 0.7-3.2] p=0.293) and Cigarette smoking (6.8%, 6.5%, OR 1.1 [95% CI 0.3-4.1] p=0.273). There was no difference in the prevalence of these cardiovascular risk factors between psoriasis vulgaris cases and healthy age-sex matched controls.

**Conclusion**: Hypertension was the most prevalent cardiovascular risk factor in psoriasis vulgaris patients and the prevalence was higher in the cases compared to healthy controls. There was a high prevalence of dyslipidaemia, diabetes mellitus, obesity and smoking in psoriasis vulgaris patients but there was no difference between psoriasis vulgaris cases and controls as these did not reach statistical significance. Blood pressure assessment as a primary prevention strategy to prevent development of cardiovascular disease should be emphasized in psoriasis vulgaris patients.
1. **INTRODUCTION AND BACKGROUND:**

Psoriasis is a common chronic immune mediated disease of the skin that affects 1% to 3% of the population [1]

There is increasing awareness that psoriasis is more than skin deep and that it has important systemic manifestations that are shared with other chronic inflammatory diseases, such as Crohn's disease, psoriatic arthritis, and metabolic syndrome [2]. In addition to its clinical symptoms, it is associated with substantial economic costs to the patient and health system, emotional and psychological effects [3]. It is also associated with a poor quality of life of patients affected [4].

There is emerging evidence that systemic inflammation is involved in psoriasis. Several biomarkers of inflammation including C-reactive protein (CRP) and TNFα are elevated in psoriasis [5, 6]. Proinflammatory cytokines and adipokines are responsible for the development of insulin resistance and endothelial dysfunction. An elevated C-reactive protein is associated with increased risk of development of cardiovascular disease [7]. This has major implications for future preventive and therapeutic strategies.

Of emerging significance is the relationship between psoriasis and atherosclerosis. This may be related to the increased prevalence of traditional cardiovascular risk factors as well as to the chronic inflammation [8]. Although psoriasis was not traditionally viewed as a disease associated with mortality, a large population-based study found that patients with severe disease requiring systemic therapy or phototherapy had an increased risk of both cardiovascular mortality and overall mortality [9].
2. LITERATURE REVIEW:

2.1 DEFINITION:

Psoriasis is a disorder of epidermal proliferation characterized by variably sized erythematous plaques with an overlying silvery scale; pinpoint bleeding on removing the scale (Auspitz sign); displays the Koebner phenomenon; has an occasional pustular or erythrodermic presentation and typically affects the scalp, elbows, knees and nails [10].

2.2. BURDEN OF PSORIASIS:

According to the World Psoriasis Day consortium, approximately 125 million people worldwide have psoriasis [11]. The prevalence of psoriasis in various locations in the world ranges from 0.6% to 4.8% [12]. Important factors in the variation of the prevalence of psoriasis include age, gender, geography and ethnicity. This is probably due to genetic and environmental factors. The studies on the prevalence of psoriasis have varied in population studied (general population versus clinic based), definition of prevalence (point versus period versus lifetime) and definition of psoriasis (self reported versus dermatologist reported) [12].

In the United States of America, Gelfand et al carried out a cross-sectional study using the National Health and Nutrition Examination Survey between 2003 and 2004 and estimated prevalence of psoriasis in African-Americans is 1.3% and 2.5% in Caucasians [12].

In the United Kingdom, Gelfand et al carried out a population based study using data from the General Practice Research Data base from 1987 to 2002 and reported a prevalence of psoriasis as 1.5% [1] In Europe, only a handful of population based studies have been done and most prevalence rates are estimates which vary anywhere from 0.6 to 6.5% [2]. The prevalence estimates vary based on the method of assessment, geographic location and ethnicity.

Information on the prevalence of psoriasis in Sub-Saharan Africa is limited. However, data on incidence of psoriasis is readily available [13]. In Kenya, no population survey on psoriasis vulgaris has been carried out. A clinic based survey carried out by Verhagen et al between November 1965 to November 1967 reported the psoriasis incidence rate of 3.15% [14].
Uganda and Tanzania the incidence is reported to be 2.8% and 3%, respectively [13]. In western Africa, a low incidence of psoriasis has been reported at 0.1%. In South Africa, a clinic based survey at the Baragwanath Hospital between 1969 and 1972 found an incidence rate of 1.7% [13].

Psoriasis has serious impact on the quality of life. This impact is more on female and younger patients. Increasing psoriasis severity is associated with seeking care from multiple physicians and having decrements in income [3]. Psoriasis is associated with a lack of self-esteem and increased prevalence of mood disorders, including depression [4]. In SSA, there is no data concerning health care costs, morbidity and mortality and quality of life of these patients.

2.3. AGE OF ONSET:

Psoriasis affects people of all ages and incidence peaks in early adult life (20s) and late adult life (50-60) [15]. An early onset predicts a more severe disease relative to the percent of body surface involvement and response to treatment. Psoriasis affects men and women equally [16].

2.4. RISK FACTORS

2.4.1 PSORIASIS GENETICS

A strong genetic basis for psoriasis has been established and is two times more likely in first-degree relatives than in the general population [17]. Twin studies reveal a higher concordance rate for monozygotic twins than dizygotic twins. A polygenic or a multifactorial pattern is the most likely mode of inheritance [18].

Genome-wide linkage studies reveal the major genetic determinant of psoriasis is *PSORS1* located within the major histocompatibility complex (MHC) on chromosome 6p and probably accounts for 35 to 50% of the heritability of the disease. There is also an association of psoriasis with HLA alleles. The presence of HLA-Cw*0602 is associated with more severe and early onset psoriasis. Other genes involved are *PSORS2*, *IL12B*, *IL23R*, *CDKAL1*, and *LCE3B/3C* [19].
2.4.2 BEHAVIORAL RISK FACTORS:
Smoking cigarettes, exposure to environmental tobacco smoke and alcohol intake have been established as risk factors for psoriasis [20, 21].
Obesity compared with normal weight was associated with a two-fold increase risk for psoriasis onset [21].

2.5. PATHOGENESIS OF PSORIASIS:
The etiology of psoriasis is unknown. It was initially believed to be a disease primarily of epidermal keratinocyte proliferation and the cutaneous inflammatory infiltrate to be a secondary event. However, strong evidence now exists that a dysregulated cell-mediated adaptive immune response is crucial in the pathogenesis of psoriasis [19].

2.5.1. Disease initiation and Maintenance;
The evolution of a psoriatic lesion is based on a complex interplay between environmental and genetic factors that sets the scene for disease initiating events. Stress, micro-organisms, drugs, trauma and smoking are the most common environmental triggers that initiate a cascade of events resulting in disease initiation [19].

During disease initiation, psoriatic keratinocytes are activated by the trigger factors resulting in the production of antimicrobial peptides, including LL-37, β-defensins and psoriasin and cytokines; tumor necrosis factor α [TNF-α], interferon-α, interferon-γ, interleukin-1β (IL 1β), and interleukin-6 (IL 6). The antimicrobial peptides and cytokines activate plasmacytoid cells and myeloid dendritic cells which are responsible for antigen presentation and cytokine secretion. Activated myeloid cells also migrate to lymphoid tissue, secrete cytokines IL 12 and IL 23 and result in differentiation of naïve T cells into effector T cells; type 17 T-helper cells & type 1 helper T cells. Effector cells re-circulate and settle in skin capillaries [19].
During disease maintenance, putative auto antigens presentation to effector T cells occurs and stimulates the release of IL-23 by dermal dendritic cells, the production of proinflammatory mediators such as TNF-α and nitric oxide, cytokines IL-17A, IL-17F, and IL-22, and interferon-γ and TNF-α by Th1 and Tc1 cells. These mediators act on keratinocytes leading to the activation, proliferation, and production of antimicrobial peptides and chemokines which stimulate dendritic cells and T cells to form perivascular clusters and lymphoid like structures around blood vessels and T cells migrate from dermis to epidermis. The more severe the inflammatory response the more severe the disease phenotype [19].

2.5.2. Counter-regulatory Mechanisms:
Regulatory T cells provide the counter-regulatory mechanisms for tissue homeostasis. However, in psoriasis, evidence of defective regulatory T cell suppressive activity and reduced interleukin 10 has been demonstrated [19].

2.5.3. Psoriatic Microvasculature:
In contrast to the microvasculature of normal skin, the psoriatic microvasculature is characterized by tortuous and leaky blood vessels that facilitate leukocyte migration into inflamed skin. Vascular Endothelial Growth Factor (VEGF) and angiopoietins are some of the factors believed to be responsible for these vascular changes in psoriasis. There is evidence of over expression of VEGF in the epidermis in psoriasis and an association of psoriasis with VEGF variants [19].

2.6. CLINICAL MANIFESTATIONS OF PSORIASIS VULGARIS:
Psoriasis Vulgaris is most common type of psoriasis and accounts for approximately 75-80% of cases. It is also known as plaque psoriasis. [22].
The skin lesions are characterized by papulosquamous plaques, well-delineated from surrounding normal skin. The plaques are red or salmon pink in colour, covered by white or silvery scales and may be thick, thin, large or small. They are most active at the edge and rapidly progressing lesions may be annular with normal skin in the centre. The lesions may exhibit the Auspitz sign [22].
Plaques are usually distributed symmetrically and occur most commonly on the extensor aspects of elbows and knees; scalp, lumbosacral region and umbilicus. Active inflammatory psoriasis is characterized by the Koebner phenomenon, in which new lesions develop at sites of trauma or pressure [22].

2.6.1. Clinical variants of Psoriasis Vulgaris:

2.6.1.1 Guttate Psoriasis:
This is an acute form of psoriasis mainly affecting children and adolescents. It is characterized by droplet shaped papules less than 1cm in diameter that erupt on the trunk post-hemolytic streptococcal infection or viral infection. It is self limiting and usually resolves within 3-4 months on onset. One third of patients with guttate psoriasis may develop classical plaque disease [23].

2.6.1.2. Inverse Psoriasis:
This is characterized by shiny, red lesions devoid of scaling that occurs in intertriginous areas. Sebopsoriasis, which is confused with seborrhoeic dermatitis, has greasy scales around the eyebrows, nasolabial folds, post-auricular and presternal sites [23]

2.6.1.3. Nail Psoriasis:
About 50% of patients with psoriasis have distinctive nail changes related to the disease. The commonest is pitting; which is best seen under oblique lighting conditions, onycholysis, oil spots and dystrophy. Psoriatic nail disease occurs most commonly in patients with psoriatic arthritis.

2.6.1.4. Annular Pustular psoriasis:
This is characterized by small, monomorphic, sterile pustules associated with systemic symptoms and fever. It may be severe. Precipitants involved are intercurrent infection, abrupt
withdrawal of systemic/topical steroids and pregnancy. The Von Zumbusch variant is the most severe [23].

2.6.1.5 Uncommon Variants:
These include annular, rupioid, lichenified, elephantine, ostraseous and photosensitive psoriasis.

2.7 CLINICOPATHOLOGICAL CORRELATIONS:
Raised, erythematous, well demarcated oval plaques with adherent silvery or white scales in different size and shape are the hallmarks of psoriasis. Although there are predilection sites such as the elbows, knees and sacral areas, lesions may cover the entire skin [23].

2.7.1 Histologic findings:
Psoriasis has three principal histological features: epidermal hyperplasia; dilated, prominent blood vessels in the dermis; and an inflammatory infiltrate of leucocytes, predominantly into the dermis [23].

2.7.2. Epidermal Hyperplasia:
Epidermal hyperplasia is characterized by an under expression of markers of keratinocyte differentiation; keratins K1 and K10; loss of the granular cell layer; parakeratosis; elongation of rete ridges, and the presence of micro pustules of Cogon and micro abscesses of Munro. Keratinocytes of the hair follicle are unaffected [23].

2.7.3. Micro vascular Dilatation:
Angiogenic factors e.g. VEGF produced by epidermal keratinocytes are now recognized as drivers of abnormal dermal vascular proliferation and angiogenesis. It is the most overlooked and under researched feature of psoriasis.
2.7.4 Inflammatory infiltrate of leucocytes:

T cells are predominantly found around capillaries of dermis and epidermis while dendritic cells are mainly found in the upper dermis.

2.8 CO MORBIDITY IN PSORIASIS:

There is increasing awareness that psoriasis as a disease is more than skin deep and that it has important systemic manifestations. A number of disease entities have been observed more frequently than expected in patients with psoriasis. These disease associations, referred as co morbidities, share similar genetic and environmental risk factors and most often demonstrate an inflammatory background [24].

Co morbidity in psoriasis include Psoriatic Arthritis, Inflammatory Bowel Disease, Pustular disease associated with psoriasis (Generalized pustular psoriasis, Palmoplantar Pustulosis, acrodermatitis continua), Metabolic syndrome, cardiovascular disease and cancer [25-27].

It has also been associated with psychological co morbidities such as depression and suicide, and is known to have a significant impact on patients’ quality of life. [28-29]. Additionally, patients with psoriasis tend to have higher rates of behavioral risk factors including smoking and excessive alcohol intake [20].

2.9. PSORIASIS VULGARIS AND RISK OF ATHEROSCLEROSIS:

Psoriasis is associated with an unfavorable cardiovascular risk profile [30]. Many clinical studies have confirmed this association.

In Sweden, Mallbris et al. carried out a historical cohort study on 8,991 psoriasis vulgaris patients recorded in the Swedish Inpatient registry and 19,757 dermatology outpatients who were members of the Swedish Psoriasis Association between January 1987 and December 1995 to assess the risk for cardiovascular mortality among psoriasis patients. Cardiovascular mortality was subdivided into death from ischemic heart disease, stroke, and pulmonary embolism. Remarkably, patients who were treated at least once as inpatient had a 50% increased overall risk for cardiovascular death compared to the general population Standard
Mortality Ratio (SMR) 1.52; [95% CI: 1.44–1.60] \( p < 0.001 \). The risk appears to be more pronounced among those admitted at a relatively young age (SMR 2.62, [95% CI: 1.91–3.49] \( p < 0.001 \)) at first admission and in several occasions. Patients with mild disease have a lower risk of mortality (SMR 0.94, [95% CI: 0.89–0.99] \( p < 0.001 \)) [31].

Gelfand et al carried out a prospective, population-based cohort study in the United Kingdom in 2006 comparing incident myocardial infarction in patients with and without a diagnosis of psoriasis. Data was collected from the General Practice Research Database between 1987 and 2002 with a mean follow-up of 5.4 years. The incidences per 1000 person-years for control patients and patients with mild and severe psoriasis were 3.58 [95% CI 3.52-3.65], 4.04 [95% CI, 3.88- 4.21], and 5.13 [95% CI, 4.22-6.17], respectively. The risk of MI associated with psoriasis and the frequency of deaths due to cardiovascular disease (CVD) was greatest in young patients with severe psoriasis, is attenuated with age and remains increased even after controlling for age, sex and traditional cardiovascular risk factors (dyslipidaemia, hypertension, smoking, diabetes). The results suggested that psoriasis is an independent risk factor for MI. This is consistent with the hypothesis that greater immune activity in psoriasis is related to a higher risk of MI [32].

A case control study carried out in the United Kingdom in 2006 by Ludwig et al comparing the prevalence and degree of coronary artery calcification in psoriasis patients and age sex matched controls. Psoriasis was shown to be an independent risk factor for coronary artery calcification. An increase prevalence of coronary artery calcification has been detected among psoriasis patients compared to controls (59.4% vs. 28.1%, \( P = 0.01 \)) [33]. An association between psoriasis and stroke has also been established in a population based cohort study carried out in the United Kingdom by Gelfand et al using data from the General Practice Research Database between 1987 and 2002 for patients above 18 years at the time their person years began. The unadjusted incidence of stroke per 1000 person years was higher in severe psoriasis (6.1; 95% CI 4.8-7.6) than in controls (4.4; 95% CI 3.8-5.0). When adjusting for major risk factors for stroke, both mild (HR 1.06, 95% CI 1.0-1.1) and severe (1.43, 95% CI 1.1, 1.9) psoriasis were independent risk factors for stroke [34].
The increase in cardiovascular disease among psoriatic patients is not completely understood and might be a result of multiple mechanisms. One link between psoriasis and cardiovascular disease is the constellation of risk factors for cardiovascular disease such as increased BMI, hypertension, dyslipidaemia, and type 2 DM. A second link is the systemic inflammation involved in psoriasis. Systemic inflammation has been associated with the development of atherosclerosis which suggests that psoriatic patients have a higher risk for cardiovascular disease. Chronic inflammation due to activation of T helper one cells and persistent secretion of proinflammatory cytokines such as TNF alpha, IL1, IL6 and lipid abnormalities is the main causes of excessive risk [35]. A similar inflammatory process is implicated in the development of atherosclerosis. Inflammation has been implicated in the formation of fatty streaks and during the rupture of an unstable atherosclerotic fibrous cap. The activation and up-regulation of T helper one cytokines (TNF alpha, IL1, IL 6, IFN γ) is a probable trigger for acute coronary syndromes [36] Furthermore, local stimulation of smooth muscle cells in the arterial wall amplifies the inflammatory response and promotes a local pre-coagulant milieu. As macrophages, T lymphocytes and smooth muscle cells are activated there is a further progressive amplification of proinflammatory cytokines, chemokines and growth factors that also promote atherogenesis [36]. Biomarkers of inflammation including C-reactive protein (CRP) are elevated in psoriasis [6] CRP levels in patients with psoriasis indicate intermediate to high risk of developing cardiovascular disease [7]. A final link to atherosclerosis is the iatrogenic effects of systemic psoriasis therapies that might also enhance the cardiovascular risk profile [30]

2.10. PSORIASIS VULGARIS AND HYPERTENSION:

A number of published reports demonstrate that hypertension occurs more commonly in patients with psoriasis than in controls.

In Germany, Sommer et al carried out a hospital based case control study to determine the association between psoriasis and metabolic disorders by analyzing data from hospitalized psoriasis patients treated between 1995 and 2002. This study demonstrated a higher prevalence of hypertension in patients with psoriasis (21.9%) as compared to the hospital-based controls.
Arterial hypertension was present in all age groups after controlling for age and sex (OR 3.27, 95% CI [2.43-4.43] p value <0.001 [37].

In the Netherlands, a population case control study carried out in 2005 by Driessen et al compared the prevalence of cardiovascular risk factors in high need psoriasis and other dermatoses. Patients were described as high need if they had severe psoriasis unresponsive to phototherapy, methotrexate and cyclosporin in the past due to lack of efficacy, intolerance or contraindication. The prevalence of hypertension was 34.6% in high need psoriasis patients as compared to 24.4% in controls who had a dermatologic diagnosis [38].

In a large population study carried out in Israel in 2009, the prevalence of hypertension was significantly higher in psoriasis patients than controls (38.8%, 29.1%, respectively, p < 0.001) and hypertension was associated with psoriasis after controlling for age, sex, smoking status, obesity, diabetes, non-steroidal anti-inflammatory drugs (NSAIDs) and use of Cox-2 inhibitors (odds ratio: 1.37, 95% CI [1.29–1.46]) [39].

However, not all data not all current literature supports the association between psoriasis and controls. In the United Kingdom, a cross-sectional population-based study was carried out by Neimann et al to determine the lifetime prevalence of cardiovascular risk factors in patients with mild and severe psoriasis compared to patients without psoriasis. Data was collected by general practitioners as part of the patients’ medical record and stored in the General Practice Research Database between 1987 and 2002. This study did not demonstrate a clinically meaningful relationship between psoriasis and hypertension in patients with mild or severe psoriasis after controlling for risk factors such as obesity (OR1.03 (1.01-1.06 95% CI) [40]. This data suggests that additional studies are needed to delineate the relationship between hypertension and psoriasis.

The pathophysiologic mechanisms that underlie psoriasis and hypertension are unknown. Some mechanisms have been proposed.

Adipose tissue in psoriasis patients serves as a major source of angiotensinogen that is converted to angiotensin II which promotes inflammation through stimulation of T cell proliferation and regulates vascular tone causing vasoconstriction [41]. Increased visceral
adipose tissue may also be associated with perivascular fat that serves as a reservoir of T cells that promote inflammation [41]. The association between psoriasis and hypertension may be due to increased oxidative stress triggered by reactive oxygen species that lead to destruction of nitric oxide resulting in damage endothelial-dependent vasodilatation, inflammation and perpetuation of hypertension [42]. Ultimately, these processes confer a predisposition to atherosclerosis. Another proposed mechanism is the altered expression of endothelin in psoriasis. Endothelin I levels are increased in serum and psoriasis lesions and this is attributed to production of endothelin by keratinocytes and loss of regulatory mechanisms [43]. Increased endothelin levels exert vasoconstrictive effect on blood vessels thus promoting hypertension. Endothelin levels have also been found to correlate with psoriasis disease severity.

2.11. PSORIASIS AND DYSLIPIDAEMIA:

Dyslipidaemia is one of the principle mechanisms causing atherosclerosis and endothelial dysfunction. A number of published reports support the well-established association between psoriasis and dyslipidaemia, including studies that controlled for age, sex, and cardiovascular co-morbidities.

In the United Kingdom, Neimann et al reported a prevalence of dyslipidaemia at 6% in patients with severe psoriasis compared to mild psoriasis at 4.7% and controls at 3.3%. There was a significant association between dyslipidaemia and mild psoriasis (OR 1.16 [95% CI 1.12-1.21]) and severe psoriasis (OR 1.31 [95% CI 1.11-1.56]) after adjusting for age, gender and person years [40].

Mallbris et al carried out a case control study in Sweden between 2001 and 2002 and demonstrated an increase in total cholesterol, HDL; VLDL and apolipoprotein A1 levels at the onset of psoriasis suggesting that dyslipidaemia may precede psoriasis [44].

In Germany, Sommer et al assessed the association between psoriasis and dyslipidaemia and demonstrated an increased risk of dyslipidaemia in psoriasis patients with compared with the hospital based controls. OR 2.09 (95% CI 1.23–3.54) p <0.001[37].
Metabolically, a direct relationship between psoriasis and altered lipid metabolism has not been established.

2.12. PSORIASIS VULGARIS AND DIABETES MELLITUS:

Several cross-sectional studies have reported a possible positive association of psoriasis and the development of insulin resistance and diabetes mellitus.

In Germany, Sommer et al reported a higher prevalence of diabetes mellitus occurred in psoriasis patients at 11.7% as compared to controls at a prevalence of 5.8% with an overall adjusted OR of 2.48 (95% CI 1.70–3.61; P < 0.0001). This was also seen in the younger age groups (40–49 years; adjusted OR 17.2, 95% CI) and an independent association between diabetes mellitus and psoriasis was demonstrated after controlling for age, gender, cigarette smoking and alcohol ingestion (OR 2.61; P < 0.0001) [37].

Neimnn et al found prevalence of diabetes in those with severe psoriasis, mild psoriasis and controls were 7.1%, 4.4% and 3% respectively. Patients with severe psoriasis had a higher risk of diabetes (OR 1.62, 95% CI 1.3–2.01) than mild psoriasis (OR 1.13, 95% CI 1.08–1.18) and controls even after adjusting for age, gender, person-years and each of the other comorbidities [40].

In Israel, a retrospective population study carried out by Cohen et al assessed the association between psoriasis and diabetes using data from Clalit Health Services (CHS), the largest health service provider in Israel. A higher prevalence of diabetes was reported in patients with psoriasis at 13.8% compared with controls at 5.4%. The age-adjusted proportion of diabetes was significantly higher in psoriasis patients as compared to the control group (OR, 1.38, P < 0.05) and was significantly higher in patients above 35 years (P < 0.05). This study also demonstrated that psoriasis was associated with diabetes, even after controlling for age and gender (OR 1.58, P < 0.001) [45].

A retrospective case-control study using the Maccabi Health Service (MHS) database in Israel carried out by Shapiro et al assessed the association between psoriasis and diabetes. This study
demonstrated an association between diabetes and the use of very potent topical steroids (P 0.05) or use of systemic medication for psoriasis (methotrexate, cyclosporine or acitretin) (P 0.001) [46].

A possible explanation for the association between psoriasis and diabetes is the presence of chronic inflammation. Inflammatory cytokines, reactive oxygen species and ectopic lipid deposition are the main mediators of insulin resistance and vascular impairment, which both lead finally to diabetes type 2 and cardiovascular disease. Cytokines, predominantly of the Th1 milieu, including TNF-α, gamma interferon, IL-8, IL-6, and IL-2, are over expressed in individuals with psoriasis [35]. TNF-α is a mediator of insulin resistance through its fat- and obesity-linked secretion [47]. Recent reports reveal inflammatory markers (IL-6, hs-CRP, and TNF-alpha) were independently associated with insulin resistance and fasting glycemia [48].

2.13. PSORIASIS AND OBESITY:

The relationship between obesity and advancing psoriatic disease has been noted in a number of cross-sectional studies in which increased BMI coincides with a greater degree of psoriasis disease severity. Data from large population databases of psoriatic patients found that BMI increased in patients after psoriasis diagnosis, suggesting that obesity is secondary to psoriasis. The risk of psoriasis was directly related to BMI independent from smoking and stressful life events as shown in an Italian case control study by Naldi et al. The study was conducted in three separate periods (1988–1991, 1992–1993, and 1994–1997). The prevalence of obesity in patients with psoriasis and controls was 12.9% and 8.3% respectively with an OR 1.6 (95% CI, 1.1–2.1) for overweight subjects, and 1.9 (95% CI, 1.2–2.8) for obese people [49].

Neimman et al found a prevalence of 20.7%, 15.8, and 13.2% in patients with severe psoriasis, mild psoriasis and controls respectively. Patients with severe psoriasis had a higher adjusted odds of obesity (OR 1.79; 95% CI, 1.55-2.05) than mild psoriasis OR 1.27; 95% CI, 1.24-1.31) Obesity was more prevalent in severe psoriasis than mild psoriasis. (OR, 1.47; 95% CI, 1.32-1.63) and was independently associated with severe psoriasis after controlling for other cardiovascular risk factors [40].
Obesity is associated with a state of chronic low grade inflammation that is triggered by macrophage infiltration of adipose tissue resulting in the release of proinflammatory cytokines mainly TNFα, IL6 and CRP. These cytokines and markers play a key role in the evolution of psoriasis and atherogenesis [50].

Whether obesity is a contributing factor to or a manifestation of psoriasis is still controversial.

2.14. SMOKING AND PSORIASIS VULGARIS:

Several previous reports have associated psoriasis with smoking. Effects of smoking that contribute to atherogenesis have also been reported.

Naldi et al demonstrated the risk of psoriasis was higher in ex- and current smokers than in never-smokers, the relative risk estimates (OR) being 1.9 for ex-smokers and 1.7 for smokers [49].

Neimann et al demonstrated an association between smoking and psoriasis was higher in patients with severe psoriasis at 30% and mild psoriasis at 21% than controls at 21% (OR 1.31) after adjusting for age, gender, person years and other co morbidities [40].

Nicotine alters a wide range of immunological functions, including modulating the functional capacity of dendritic cells and can increase the secretion of proinflammatory TH1 cytokines by dendritic cells and interacting with T cells [51-52].

Additionally, nicotinic cholinergic receptors have been demonstrated on keratinocytes that stimulate calcium influx and accelerate cell differentiation. They can also control keratinocyte adhesion and upward migration in the epidermis. This suggests a biologic explanation for the association between smoking and psoriasis [52].

Smoking is an independent major risk factor for CHD, cerebrovascular disease, and total atherosclerotic cardiovascular disease [53]. The mechanism by which it occurs is not fully understood but multiple factors have been implicated. Free radicals in cigarette smoke damage lipids, resulting in the formation of pro-atherogenic oxidized particles, specifically oxidized low-density lipoprotein cholesterol [54]. Cigarette smoking activates the sympathetic nervous
system, producing an increase in heart rate and blood pressure, and cutaneous and perhaps coronary vasoconstriction [55]. Smoking has been correlated with elevated levels of C-reactive protein and fibrinogen and is associated with endothelial dysfunction leading to impaired prostacyclin and enhanced platelet-wall interactions [56].

2.15. PSORIASIS TREATMENT AND CARDIOVASCULAR RISK:

Antipsoriatic treatments are varied depending on the severity of disease and are aimed at reducing inflammation of the skin. Topical treatments are mainstay of treatment in mild psoriasis. For severe forms of psoriasis, systemic treatments are used.

Topical treatments available for mild-to-moderate psoriasis include dithranol, coal tar and vitamin D analogues; all of these agents are significantly more effective than placebo. Corticosteroids inhibit cytokine production and reduce inflammatory mediators like prostaglandins and leukotrienes. Topical corticosteroid preparations are categorized from Class I to VII according to potency determined by the Vasoconstrictor Assay. The potential systemic side effects of their use include diabetes, hypertension, and hypothalamic-pituitary-adrenal (HPA) axis suppression [57]. The use of corticosteroids, both topical and systemic is only recommended in severe forms of psoriasis especially erythrodermic and pustular psoriasis [58].

Several reports have implicated systemic therapies in enhancing the cardiovascular risk profile in these patients. Methotrexate (MTX) is a frequently prescribed agent. MTX blocks DNA synthesis in rapidly proliferating epidermal cells, T- and B-lymphocytes and disrupts cytokine secretion. MTX also reduces plasma and red blood cell folate levels via reduced activity of dihydrofolate reductase, which subsequently increases homocysteine levels. Hyperhomocysteinemia may constitute an independent risk factor for cardiovascular disease by increasing levels of auto antibodies against oxidized LDL (AuAb-oxLDL) resulting in LDL oxidation [35]

Cyclosporin inhibits T-cell activation and the transcription of IL-2 and other cytokines important in the pathogenesis of psoriasis. Metabolic abnormalities like hypertriglyceridemia and hypercholesterolemia are important adverse effects of cyclosporin [35]
Acitretin is an oral retinoid that by binding to retinoic acid receptors alters the transcription of genes coding for proteins involved in the pathogenesis of psoriasis. Hepatotoxicity and hypercholesterolemia, triglyceridemia and low high-density lipoprotein (HDL) cholesterol are also side effects of Acitretin [35].

Biologic agents are the newer agents used in treatment of psoriasis and include T-cell modifying agents and TNF inhibitors. They have been found to be potentially beneficial in the increase of HDL levels.
3. STUDY JUSIFICATION:

Psoriasis vulgaris affects young adults and the most productive members of our society. There is evidence of a high burden of cardiovascular risk factors and increased mortality due to cardiovascular events especially in patients with severe disease. The burden of cardiovascular risk factors among patients with psoriasis vulgaris attending the Kenyatta National hospital is unknown. Available data emanates from the developed world and this may not directly reflect our situation due to major socio-cultural and economic differences.

3.1 RESEARCH QUESTION:

What is the burden of cardiovascular risk factors in patients with psoriasis vulgaris at the Kenyatta National Hospital?
4. OBJECTIVES:

4.1 BROAD OBJECTIVE:

To evaluate the prevalence of selected cardiovascular risk factors in patients with psoriasis vulgaris.

4.2 SPECIFIC OBJECTIVES:

PRIMARY OBJECTIVE:

To determine the prevalence of the following selected cardiovascular risk factors in patients with psoriasis vulgaris.

1. Hypertension
2. Dyslipidaemia
3. Diabetes mellitus
4. Obesity
5. Smoking

SECONDARY OBJECTIVE:

To compare selected cardiovascular risk factors in patients with psoriasis vulgaris and controls.

5. METHODOLOGY:

5.1 STUDY DESIGN:

Hospital based cross-sectional study.

5.2 STUDY AREA:

The Kenyatta National Hospital (KNH) dermatology clinic, dermatology ward and Blood Transfusion Unit.

5.3 STUDY POPULATION:

The cases were patients attending the dermatology clinic and dermatological in patients.

The controls were healthy blood donors at the Blood Transfusion Unit.
5.4 CASE DEFINITION:

5.4.1 Case:

Patient with a diagnosis of psoriasis based on clinical findings confirmed by a dermatologist and/or confirmed by biopsy.

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 with presence or absence of the Auspitz sign.

Histological: Thickening of the epidermis, parakeratosis, elongated rete ridges, mixed cellular infiltrates of T-cells around capillaries in the dermis and epidermis and dendritic cells in the upper part of the dermis.

5.4.2 Control:

A healthy blood donor at Kenyatta National Hospital Blood Transfusion Unit. Psoriasis vulgaris in these controls was excluded by a thorough history and physical examination.

5.5 PATIENT SELECTION:

5.5.1 INCLUSION CRITERIA:

Cases

Patients above 18 years with a confirmed diagnosis of psoriasis and had signed an informed consent to study participation.

Controls:

Healthy individuals above 18 years, age and sex matched and confirmed not to have psoriasis vulgaris.

5.5.2 EXCLUSION CRITERIA:

All adult patients and healthy donors who declined consent were excluded.

5.6 SAMPLING TECHNIQUE:

Consecutive sampling.
5.7 SAMPLE SIZE:

The number of patients with psoriasis seen in KNH in a month was estimated at 30 patients. Since the study collection ran for a period of three months, the accessible population was expected to be 90 patients. (Daniel, 1999)

\[
n = \frac{DEFF \cdot Z^2 \cdot P \cdot (1-P)}{d^2}
\]

\(n'\) = required sample size

\(Z\) = confidence level at 95% (standard value of 1.96)

\(P\) = estimated prevalence of dyslipidaemia from previous study is 6% (Neimman et al., 2006).

\(d\) = margin of error at 5%

\(DEFF\) = design effect which is equal to 2

Substituting the above in the formula

\(n\) was **86** patients with psoriasis and 86 controls. Total number = 172
5.8 SCREENING AND RECRUITMENT:

5.8.1 Cases:

After approval by the U.o.N Department of clinical medicine and therapeutics and KNH Ethics Research Committee, the investigator and two research assistants reviewed files of patients attending the dermatology clinic and those admitted to the dermatology ward. The files identified patients with a diagnosis of psoriasis vulgaris. The patients were contacted by phone and were scheduled to visit the clinic. The patients who met the inclusion criteria were enrolled into the study. This was the total psoriasis population in KNH over the study period between July and October 2012.

Study questionnaires were administered, a comprehensive history was taken from each patient, physical examination was carried out and blood samples were taken.

5.8.2 Controls:

The investigator went to the Blood Transfusion Unit at the Kenyatta National Hospital placing posters detailing on the study objectives, recruitments and enrollment procedures.

The investigator and trained, supervised research assistants consecutively screened healthy blood donors for eligibility after they had donated blood on all week-days between 0800 and 1700 hrs. The donors who met the inclusion criteria and were enrolled into the study. Age was matched to the nearest 5 years. The controls were selected and matched using the previous week’s cases. A comprehensive history was taken from each patient, physical examination was carried out and blood samples were taken.

5.9 DATA COLLECTION:

5.9.1 CLINICAL METHODS:

The investigator and assistants administered the questionnaire. The socio-demographic data; age, gender, marital status, level of education and occupation was taken. The duration of psoriasis vulgaris, type of treatment and a comprehensive history of diabetes mellitus,
dyslipidaemia, hypertension, cigarette smoking was taken from the patient. A history of any cardiovascular event was taken; myocardial infarction, stroke and heart failure.

Physical examination was carried out. Anthropometric measures taken were weight and height. Height was measured as the standard height to the nearest 0.5cm barefooted, back and scalp against the wall using a standard tape measure.

Weight was measured with the patient standing on a standard bathroom scale and was approximated to the nearest 100gms.

The Body Mass Index The body mass index (BMI) was calculated using the World Health Organization (WHO) criteria as weight (in kilograms) divided by height (in meters) squared.

Waist circumference was measured using the WHO criteria as the midpoint between the lower margin of the least palpable rib and the top of the iliac crest, using a stretch resistant tape that provides a constant 100 g of tension through the use of a special indicator buckle, measured in horizontal plane and to the nearest mm. The measurements were taken at the end of a normal expiration.

Hips circumference was measured using the WHO criteria as the widest portion of the buttocks, in horizontal plane and measured to nearest mm.

Waist-to-Hip ratio was the ratio of the waist circumference to hip circumference.

Blood Pressure measurement: This was in keeping with the WHO criteria: The patient in sitting position, using a cuff covering two thirds of the upper arm circumference and a standard validated mercury sphygmomanometer after an initial rest period of 15 minutes. Systolic blood pressure was determined by the 1st Korotkoff sound. Diastolic pressure was determined by the disappearance of the 5th Korotkoff sound. An average of two readings taken at least 5 minutes apart was noted.

5.9.2 LABORATORY METHODS:

A specimen of blood was obtained aseptically from the antecubital fossa in each patient for measurement of total cholesterol and fasting blood sugar. Study subjects who did not observe
the requisite fast were instructed to observe overnight fasts (10-12 hours) before specimens were collected and presented the following day.

About 5mls of venous blood was drawn aseptically from the antecubital fossa into a lithium heparin tube. Specimens were transported to the Lancet laboratory immediately. The specimens were analyzed under the supervision of a registered senior laboratory technologist. Specimens were centrifuged at 3000rpm for 15 minutes. 1 ml of plasma was collected and transferred into vials for biochemical analyses:

Total cholesterol was estimated using a colorimeter using the enzymatic hydrolysis and oxidation method. Plasma fasting glucose was measured using a glucometer with test strips and using Accu-check glucometer manufactured by Roche diagnostics.

5.10: QUALITY ASSURANCE:

5.10.1: EQUIPMENT:

The equipment used in the physical examination was calibrated according to manufacturer’s specifications.

5.10.2: RESEARCH ASSISTANT TRAINING:

Two Research Assistants who are registered clinical officers were recruited and had a training seminar that was conducted by the investigator that covered:

- Medical ethics including elements of Informed Consent and Disclosure of Medical Information.
- Communication skills
- Medical records abstraction
- Questionnaire administration.
- Data entry
- Procedure of specimen collection
Biohazard and medical waste management

The recommended procedure for specimen collection, proper labeling and storage was followed strictly at all times to minimize source of errors.

5.10.3 The Laboratory

The Lancet laboratory runs internal and external quality controls whereby the internal controls are done daily and the latter monthly. The laboratory is run by well trained qualified staff. Procedures for specimen handling and storage were adhered to. Results were accepted only if the control values were within the expected ranges.

5.11: DATA MANAGEMENT AND ANALYSIS

5.11.1: DATA ENTRY AND MANAGEMENT:

All data was entered into the questionnaires and forms were reviewed by the principal investigator. The data from the questionnaires was coded, entered and managed in a pre-designed Microsoft Access database. Data entry was done continuously in the course of data collection. Data was cleaned and analyzed using SPSS version 18.0

5.11.2: DATA ANALYSIS

The study population was described by summarizing categorical data into proportions and continuous data into means or medians. The prevalence of cardiovascular risk factors was presented as proportions. The Student’s t-test or Mann-Whitney U test was used to compare means or medians respectively. Chi-square test was used to analyze associations between cardiovascular risk factors and other categorical factors. Odds ratios were used to show the likelihood of associations between variables. All statistical tests were performed at 5% level of significance and a 95% confidence interval was applied to the numerical variables that were normally distributed. The findings of this study were presented using tables and graphs.
5.11.3: DATA ARCHIVAL:

The database was locked upon completion of the study and permission to further modify the data was removed from all except the investigator and one supervisor.

5.11.4: FATE OF DATA:

The findings of this study were presented to the Department of Medicine and shall be published in journals.

5.12: DEFINITION OF STUDY VARIABLES:

5.12.1: DEPENDENT VARIABLES:

5.12.1.1 OBESITY:

Waist circumference and waist: hip ratio were classified as per NCEP-ATP guidelines [59]

Waist circumference > 102 cm in men or > 88 cm in women;

Waist: hip ratio >0.9 men, >0.85 in women

BMI was categorized according to the World Health Organization classification [60]

   I. Underweight: BMI of < 18.49
   II. Normal: 18.5-24.9
   III. Overweight: 25 – 29.9
   IV. Obesity > 30

5.12.1.2: DYSLIPIDAEMIA:

Study participants were classified as per the National Cholesterol Education Program/ Adult Treatment Panel III (NCEP/ATP III) guidelines or if they were on treatment for dyslipidaemia.

Hypercholesterolemia: total cholesterol levels > 5.17mmol/l [59]
5.12.1.3 HYPERTENSION:

Study participants were considered hypertensive if they had a systolic pressure greater than 140mmHg and diastolic pressure greater than 90mmHg or if they had been on treatment for hypertension [61]

5.12.1.4: DIABETES MELLITUS:

Diabetes Mellitus was defined according to the American Diabetes Association [62]

Fasting blood glucose >7 mmol/l or

Classic symptoms of hyperglycemia and random blood glucose >11mmols or

Patients on treatment for Diabetes Mellitus.

5.12.1.5: SMOKING:

Study participants were categorized as:

Current smokers were defined as those who had smoked at least 100 cigarettes in their lifetime and were still smoking or had quit smoking within the preceding one year.

Former smokers were those who had smoked at least 100 cigarettes in their lifetime but had quit more than one year earlier

Nonsmokers were those who had smoked less than 100 cigarettes in their lifetime or who had never smoked [63].
5.12.2: INDEPENDENT VARIABLES:

5.12.2.1: SEVERITY GRADING:

The European Medicines Agency criteria were used to assess disease severity in psoriasis. [64]

<table>
<thead>
<tr>
<th>Grade</th>
<th>Skin involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Remission/minimal psoriasis</td>
<td>Stable remission, no lesions/borderline psoriasis/isolated lesions</td>
</tr>
<tr>
<td>Mild psoriasis</td>
<td>&lt;10% total BSA</td>
</tr>
<tr>
<td>Moderate psoriasis</td>
<td>&gt;10% total BSA but on topical therapy</td>
</tr>
<tr>
<td>Moderate to severe psoriasis</td>
<td>&gt;10% total BSA failing on topical therapy</td>
</tr>
<tr>
<td>Severe psoriasis</td>
<td>&gt;20% total BSA with need for systemic</td>
</tr>
<tr>
<td>Psoriasis associated with guarded prognosis</td>
<td>Generalized pustular psoriasis, Psoriatic Erythroderma</td>
</tr>
</tbody>
</table>

5.14: ETHICAL CONSIDERATIONS:

Approval to carry out the study was obtained from the Department of Clinical medicine and Therapeutics and the Kenyatta National Hospital Ethics and Research Committee.

Patients were enrolled into the study only after giving informed consent.

Those who are found to have the cardiovascular risk factors and co morbidities without treatment were referred to the appropriate care givers.

Results of the investigations were communicated to the dermatologists at the dermatology clinic.

Those who gave consent were not exposed to unnecessary risks.

Full confidentiality with each patient was maintained.

Freedom to withdraw without prejudice was observed.
6. RESULTS:

Between July and October 2012, 580 files of patients attending the dermatology clinic and those admitted in the dermatology ward were reviewed. 92 files identified patients with a diagnosis of psoriasis vulgaris. The patients were contacted by phone and out of these, the relatives of 15 patients confirmed that they had died. 2 patients were below 18 years and were excluded. 75 patients met the inclusion criteria and were enrolled into the study. This was the total psoriasis population in KNH over the study period. A total of 82 healthy blood donors were screened for eligibility after they had donated blood. 2 donors were below 18 years and 3 donors declined consent and were excluded. 77 donors met the inclusion criteria and were enrolled into the study. Age was matched to the nearest 5 years.

FIGURE 1: FLOW CHART: CASES
FIGURE 2: FLOW CHART: CONTROLS

82 HEALTHY BLOOD DONORS SCREENED

2 BELOW 18 YEARS

3 DECLINED CONSENT

77 CONTROLS ENROLLED
**SOCIODEMOGRAPHIC CHARACTERISTICS:**

The mean age of the cases was 41.1 years and 40.9 years for the controls. The male to female ratio was 3.3:2. There was no statistically significant difference between the cases and the controls. Table 1 summarizes the socio-demographic characteristics of both populations.

**Table 1: Baseline Demographic Characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Psoriasis patients n=75</th>
<th>Controls n=77</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>28 (37.3)</td>
<td>29 (37.7)</td>
<td>0.967</td>
</tr>
<tr>
<td>Male</td>
<td>47 (62.7)</td>
<td>48 (62.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>20 (26.7)</td>
<td>23 (30.3)</td>
<td>0.209</td>
</tr>
<tr>
<td>Married</td>
<td>55 (73.3)</td>
<td>50 (65.8)</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>0 (0.0)</td>
<td>3 (3.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>4 (5.4)</td>
<td>4 (5.2)</td>
<td>0.456</td>
</tr>
<tr>
<td>Primary</td>
<td>17 (23)</td>
<td>15 (19.5)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>35 (47.3)</td>
<td>30 (39)</td>
<td></td>
</tr>
<tr>
<td>University/college</td>
<td>18 (24.3)</td>
<td>28 (36.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Occupation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>31 (41.9)</td>
<td>29 (37.7)</td>
<td>0.269</td>
</tr>
<tr>
<td>Unemployed</td>
<td>20 (27)</td>
<td>13 (16.9)</td>
<td></td>
</tr>
<tr>
<td>Self-employed</td>
<td>19 (25.7)</td>
<td>29 (37.7)</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>4 (5.4)</td>
<td>6 (7.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean Age (SD)</strong></td>
<td>41.1(16.7)</td>
<td>40.9(16.3)</td>
<td>0.910</td>
</tr>
</tbody>
</table>
AGE DISTRIBUTION:

The ages of both patients with psoriasis vulgaris and healthy controls ranged from 18 years to 82 years. The cases were matched with controls to the nearest five years and were also matched by gender. The age distribution of the cases and controls is summarized by the bar graph below.

FIGURE 3: AGE DISTRIBUTION:
SEVERITY OF PSORIASIS:

The severity of psoriasis was assessed using the European Medicines Agency criteria. 50.7% had very severe disease. 33.3% had moderate to severe disease. 14.7% had mild disease. The mean duration of disease was 10.49 years with a range between 5 months and 37 years. Figure 2: The bar graph below.

FIGURE 4: SEVERITY OF PSORIASIS

![Bar graph showing severity of psoriasis]

- In Remission/ minimal psoriasis: 1.3%
- Mild psoriasis: 14.7%
- Moderate psoriasis: 12.0%
- Moderate to severe psoriasis: 21.3%
- Severe psoriasis: 44.0%
- Psoriasis associated with guarded prognosis: 6.7%
TREATMENT MODALITIES:

The topical agents used were high potency corticosteroids and dithranol. The other alternative agents used were calcipotriol and coal tar. The only systemic agent used was methotrexate. Combination treatment consisted of both topical and systemic agents. A majority of patients (57%) were on combination treatment. A small proportion (12%) was newly diagnosed and treatment naïve. The pie chart below shows the treatment modalities used.

FIGURE 5: TREATMENT MODALITIES
THE PREVALENCE OF CARDIOVASCULAR RISK FACTORS IN PSORIASIS VULGARIS CASES AND HEALTHY CONTROLS:

Hypertension was the most prevalent risk factor at 40% (95% CI 29.2-51.5), followed by Dyslipidaemia at 25.3% (95% CI 15.3-36.1). The prevalence of Diabetes mellitus was 12% (95% CI 4.5-19.7) and Obesity was 12% (95% CI 5.1-20.3). The prevalence of undesirable waist hip ratio (WHR) was 26.7% (95% CI 16.9-36.5) and the prevalence of undesirable waist circumference (WC) was 17.3% (95% CI 9.2-26.5). Current smokers had the least prevalence rate at 6.8% (95% CI 1.5-13.2).

The prevalence of cardiovascular risk factors was compared between psoriasis vulgaris cases and age sex matched healthy controls. The prevalence of hypertension was 40% and 22.1% in the cases and controls respectively. The prevalence of hypertension was higher in patients with psoriasis vulgaris compared to controls and this was statistically significant (OR 2.4, 95% CI [1.2-4.8], p=0.017).

The prevalence of dyslipidaemia in patients with psoriasis vulgaris was 25.35% and 20.8% in the controls. (OR 1.3, 95% CI [0.6-2.8], p=0.505). The proportion of subjects with DM was 12% in patients with psoriasis and 10.4% in controls (OR 1.2, 95% CI [0.4-3.2], p=0.753). The overall prevalence rate of overweight and obese in patients with psoriasis vulgaris was 42.7% compared to an overall prevalence of 29.9% in controls. 26.7% of patients with psoriasis vulgaris and 19.5% of controls had an undesirable waist hip ratio (OR 1.5, 95% CI [0.7-3.2], p=0.293). The prevalence of undesirable waist circumference was 17.3% in the cases and 20.8% in controls (OR 0.8, 95% CI [0.4-1.8], p=0.589). The proportion of current smokers was 6.8% in cases and 6.5% in controls (OR 1.8, 95% CI [0.3-4.1], p=0.273). There was no difference in the prevalence of dyslipidaemia, diabetes mellitus, obesity and smoking between patients with psoriasis vulgaris and healthy controls as these did not reach statistical significance. Table 2 summarizes the findings in both groups.
TABLE 2: THE PREVALENCE OF SELECTED CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH PSORIASIS VULGARIS AND HEALTHY CONTROLS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Psoriasis patients n (%)</th>
<th>Controls n (%)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smoking status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>5 (6.8)</td>
<td>5 (6.5)</td>
<td>1.1 (0.3-4.1)</td>
<td>0.862</td>
</tr>
<tr>
<td>Former</td>
<td>11 (14.9)</td>
<td>7 (9.1)</td>
<td>1.8 (0.6-4.8)</td>
<td>0.273</td>
</tr>
<tr>
<td>Never</td>
<td>58 (78.4)</td>
<td>65 (84.4)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>Waist circumference</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undesirable</td>
<td>13 (17.3)</td>
<td>16 (20.8)</td>
<td>0.8 (0.4-1.8)</td>
<td>0.589</td>
</tr>
<tr>
<td>Normal</td>
<td>62 (82.7)</td>
<td>61 (79.2)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>WHR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undesirable</td>
<td>20 (26.7)</td>
<td>15 (19.5)</td>
<td>1.5 (0.7-3.2)</td>
<td>0.293</td>
</tr>
<tr>
<td>Normal</td>
<td>55 (73.3)</td>
<td>62 (80.5)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (18.5-24.9)</td>
<td>41 (54.7)</td>
<td>53 (68.8)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Underweight (&lt;18.5)</td>
<td>2 (2.7)</td>
<td>1 (1.3)</td>
<td>2.6 (0.2-29.5)</td>
<td>0.445</td>
</tr>
<tr>
<td>Overweight (25-29.9)</td>
<td>23 (30.7)</td>
<td>16 (20.8)</td>
<td>1.9 (0.9-4.0)</td>
<td>0.109</td>
</tr>
<tr>
<td>Obese (&gt;30)</td>
<td>9 (12.0)</td>
<td>7 (9.1)</td>
<td>1.7 (0.6-4.8)</td>
<td>0.351</td>
</tr>
<tr>
<td><strong>Dyslipidaemia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>19 (25.3)</td>
<td>16 (20.8)</td>
<td>1.3 (0.6-2.8)</td>
<td>0.505</td>
</tr>
<tr>
<td>Normal</td>
<td>56 (74.7)</td>
<td>61 (79.2)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive</td>
<td>30 (40.0)</td>
<td>17 (22.1)</td>
<td>2.4 (1.2-4.8)</td>
<td>0.017</td>
</tr>
<tr>
<td>Normal</td>
<td>45 (60.0)</td>
<td>60 (77.9)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td>9 (12.0)</td>
<td>8 (10.4)</td>
<td>1.2 (0.4-3.2)</td>
<td>0.753</td>
</tr>
<tr>
<td>Normal</td>
<td>66 (88.0)</td>
<td>69 (89.6)</td>
<td>1.0</td>
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</tr>
</tbody>
</table>

Abbreviations: BMI=Body Mass Index; WC= Waist circumference; WHR= Waist Hip Ratio

Dyslipidaemia represented by hypercholesterolemia
7. DISCUSSION:

In our study, we set out to determine the prevalence of selected cardiovascular risk factors namely hypertension, dyslipidaemia, diabetes mellitus, obesity and smoking in patients with psoriasis vulgaris at the Kenyatta National Hospital and also compared these factors in healthy controls.

Previous studies done to determine cardiovascular risk factors in patients with psoriasis vulgaris have been done in Europe, UK, Israel and USA. This is the first study done in Africa with respect to cardiovascular risk factors in psoriasis vulgaris patients. This was a hospital based study that enrolled psoriasis vulgaris inpatients and outpatients. The study subjects were relatively young with a mean age of 41 years and half had severe disease. In this study, we demonstrate a high burden of cardiovascular risk factors with hypertension being the most prevalent risk factor at 40% and achieved statistical significance when compared with age sex matched healthy controls with a prevalence of 22%.

The burden of dyslipidaemia, diabetes mellitus, obesity and smoking in psoriasis vulgaris cases and healthy controls is increased. A possible explanation for the association between psoriasis and these risk factors is the presence of chronic inflammation in these patients and the various anti-psoriatic treatments available [30, 35]. However, this study was not powered to show the difference between the cases and healthy controls.

In our study, the prevalence of hypertension was higher than other selected cardiovascular risk factors and was higher in cases than controls. A possible explanation between hypertension and psoriasis is the chronic inflammatory process involving reactive oxygen species and activity of angiotensin II on inflammation and vascular tone and increased production of endothelin by keratinocyte hyper proliferation that may promote development of hypertension and ultimately atherogenesis [41-43]. No published data on prevalence of hypertension in SSA is available. Similar prevalence were reported in The Netherlands at 34.6% in 2005 [37] and in
Israel at 38.8 in 2009[38] where they assessed patients with severe disease. The prevalence of hypertension was higher than that found by Sommer et al in Germany and Neimann in UK who reported the prevalence of hypertension in patients with psoriasis at 21.4% and 19.9% respectively [40]. These were population studies carried out using data bases while we carried out hospital based study.

The high burden of cardiovascular risk factors, with hypertension being the most prevalent risk factor, impact negatively on patients with psoriasis as it increases the risk of atherogenesis and ultimately cardiovascular disease. The risks of stroke, myocardial infarction and cardiovascular mortality have been reported in patients with psoriasis [31-34]. There is evidence of an increasing burden of cardiovascular risk factors in SSA due to the epidemiologic transition [65]. Local data from community based studies done in urban centres report a high prevalence of hypertension in the general population. Hassan et al found 12.6% in urban Garissa [66], Njau et al found a prevalence of 13% in Kibera [67]. These studies were community based and the prevalence of hypertension increased with age.

This is the first study in Africa on cardiovascular risk factors among patients with psoriasis vulgaris in a tertiary hospital where half the patients had very severe disease. Hypertension was the most prevalent and was higher in the cases than controls and the difference was statistically significant. There is a high burden of dyslipidaemia, diabetes mellitus and obesity in these patients even though no difference was demonstrated between the cases and controls. This study was limited by selection bias which was introduced by patients with severe disease being referred to a tertiary institution for management by dermatologist as a majority of the peripheral hospitals lack specialist care. The patients’ selection of the referral hospital is also influenced by the proximity, affordability and attitudes about health services provided by the tertiary institution.

In conclusion, there is an increased burden of cardiovascular risk factors in psoriasis vulgaris patients with hypertension being the most prevalent cardiovascular risk factor. There was a statistically significant difference in the prevalence of hypertension between the cases and
controls. Despite our data showing no statistical difference in the prevalence of the other cardiovascular risk factors between cases and controls, the presence of a high burden of these risk factors in psoriasis vulgaris patients with an underlying chronic inflammation puts them at high risk of developing cardiovascular disease and mortality. Assessment of these cardiovascular risk factors as a primary prevention strategy to prevent development of cardiovascular disease should be emphasized in psoriasis vulgaris patients.

**RECOMMENDATIONS:**
Assessment of cardiovascular risk factors is of importance in patients with psoriasis vulgaris as a primary prevention strategy against cardiovascular morbidity and mortality.
A larger study should be carried out to show the difference of these risk factors in patients and the general population.
8. REFERENCES:


16. Voorhees JJ. The Genetics of Psoriasis. *Archives of Dermatological Research*. 2994;130


23. Feldman S.R et al Epidemiology, pathophysiology, clinical manifestations, and diagnosis of psoriasis *UptoDate* 2011


44. Mallbris L, Granath F, Hamsten A, Sta M. Psoriasis is associated with lipid abnormalities at the onset of skin disease. Journal of the American Academy of Dermatology. 2006;54:614-621


57. Gilbertson E.O. Super potent topical corticosteroid use associated with adrenal suppression: Clinical considerations


66. Hassan A et al Prevalence of cardiovascular disease risk factors in urban Garissa residents. MMed dissertation 2012 University of Nairobi, Department of clinical medicine and therapeutics

APPENDIX I

INFORMED CONSENT EXPLANATION:

Dr CAROLINE SHANGO IRUNGU, a post graduate student in the Department of Clinical Medicine and Therapeutics of the University of Nairobi, am conducting a research on the prevalence of cardiovascular risk factors in patients with psoriasis vulgaris and in individuals without psoriasis vulgaris. Data from this study will therefore serve as a benchmark for future preventive strategies.

Should you accept to join the study, you would be expected to sign a consent form and answer a few questions as indicated in the study proforma. We will measure your blood pressure, weight, height, waist/hip circumference. We’ll require 2mls of blood for measuring your blood cholesterol and blood sugar level. There will be minimal pain while drawing blood.

The results of these investigations will be explained to you and a copy retained in your medical file for access by the primary doctor at the clinic. Participation is voluntary and you are free to withdraw at any time during the course of this study period. Your refusal to participate or withdrawal from the study will not in any way affect the quality of your treatment. All the information obtained will be handled with confidentiality and blood samples discarded after intended use.

For any enquiries or further clarification, please contact:-

Prof. A.N Guantai  Secretary KNH/UoN Ethics 020 02726300 Ext 44355
or
Prof E.Ogola Dept Medicine and Therapeutics Tel. 0722737944
or
Dr. T.Munyao Dept Medicine and Therapeutics tel 0718703330
or
Dr. C. Irungu Principal Investigator Tel 0722643149
APPENDIX II:

CONSENT FORM:

I…………………………………………………………………………………………………………………………………………………………
do hereby give consent/permission to Dr Caroline Shango Irungu (The Principal investigator) to include me in this study on CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH PSORIASIS VULGARIS AT THE KENYATTA NATIONAL HOSPITAL. I have read and understood the contents of this form. I am also aware I can withdraw from this study without losing any benefits or quality of management of my medical problem being affected.

VOLUNTEER NAME……………………………………...SIGNED………………………………………………………………………………

WITNESS……………………………………………………………………………………………………………………………………………..

DATE…………………………………………………………………………………………………………………………. thumb print
APPENDIX 3

STUDY QUESTIONNAIRE:

SERIAL NUMBER....

a) DEMOGRAPHIC DATA;
   a. Age (years).
   b. Sex (M=1, F=2)
   c. Marital status:
      (single=1, married=2, divorced=3, widowed/widower=4)
   d. Place of residence:
   e. Education:
      (never=1, primary=2, secondary=3, university/college=4, other=5)
   f. Occupation:
      (employed=1, unemployed=2, self-employed=3, retired=4, never=5)

b) HISTORY OF PSORIASIS;
   How long have you had the disease?(in years)

c) PSORIASIS TREATMENT
   What medication have you been put on?
   1. Topical
      a=Dithranol
      B=Steroid
      C=Calcipotriol
      D=Other
   2. Systemic
   3. phototherapy

d) History of diabetes Mellitus
   1. Yes
   2. No
   3. Treatment

e) History of Hypertension
   1. Yes
   2. No
   3. Treatment
e) History of dyslipidaemia
   1. Yes
   2. No
   3. Treatment

f) Previous history of chest pain
   1. Yes
   2. No

g) Previous history of Myocardial Infarction
   1. Yes
   2. No

h) Previous history of stroke
   1. Yes
   2. No

i) Previous history of heart failure
   1. Yes
   2. No

f) SMOKING HISTORY:
   a) Do you smoke?
      1. current
      2. former
      3. never

   For current smokers, answer question b & c below, for former smokers ans d & e below

   b) How many cigarettes do you smoke per day?
      1. <5
      2. 5-10
      3. 10-20
      4. 20-40
      5. >40
c) How many years have you been smoking?
   1. <1
   2. 1-5
   3. 5-10
   4. >10

d) Were you a cigarette smoker?
   1. Yes
   2. No

   If yes

e) When did you stop?
   1. <1 year ago
   2. 1-5 years ago
   3. >5 years ago

f) How many cigarettes per day?
   1. <5
   2. 5-10
   3. 10-20
   4. 20-40
   5. >40

g) For how many years have you been smoking?
   1. <1
   2. 1-5
   3. 5-10
   4. >10

g) PHYSICAL EXAMINATION:
   I. Anthropometric Measures
      a) Waist circumference
      b) Hip circumference
      c) Waist : Hip ratio
      d) Weight
      e) Height
      f) Body mass index

   II. Blood pressure:
      a) First reading:
Severity of skin Involvement:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Skin involvement</th>
<th>code</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Remission/minimal psoriasis</td>
<td>Stable remission, no lesions/borderline psoriasis/isolated lesions</td>
<td>1</td>
</tr>
<tr>
<td>Mild psoriasis</td>
<td>&lt;10% total BSA</td>
<td>2</td>
</tr>
<tr>
<td>Moderate psoriasis</td>
<td>&gt;10% total BSA but on topical therapy</td>
<td>3</td>
</tr>
<tr>
<td>Moderate to severe psoriasis</td>
<td>&gt;10% total BSA failing on topical therapy</td>
<td>4</td>
</tr>
<tr>
<td>Severe psoriasis</td>
<td>&gt;20% total BSA with need for systemic</td>
<td>5</td>
</tr>
<tr>
<td>Psoriasis associated with guarded prognosis</td>
<td>Generalized pustular psoriasis, psoriatic erythroderma</td>
<td>6</td>
</tr>
</tbody>
</table>

h) LABORATORY INVESTIGATIONS:

a) Fasting blood sugar

b) Total cholesterol