THE PREVALENCE OF SCABIES AND OTHER CUTANEOUS MANIFESTATIONS AND THE PERFORMANCE OF THE MedMira RAPID HIV TEST; AN EXPERIENCE AMONG HOSPITALIZED HIV -INFECTED ADULTS AT MUHIMBILI MEDICAL CENTER, DAR ES SALAAM, TANZANIA

BY

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Results

Five (3.84%) out of 131 HIV-positive patients had scabies while five (2.57%) out of 194 HIV-negative patients had scabies. A hundred and thirty-seven (42) 2% patients out of the 325 patient enrolled in the study had cutaneous manifestation. Superficial fungal infection was the commonest manifestations, and it was significantly more common among HIV seronegative compared to HIV seropositive patients ($P<0.001$). Overall, cutaneous manifestation was significantly more common among HIV-positive patients compared to HIV-negative patients ($P<0.001$). And, cutaneous manifestation among HIV-positive patients increased with advancing stage of HIV infection ($P=0.02$). In addition, generalized hyperpigmented post-inflammatory macules were significantly more common among HIV-positive compared to HIV-negative patients ($P<0.01$). Using blood samples from Tanzanian adults, the MedMira rapid HIV test was found to have 97% sensitivity and 34.4% specificity.

Conclusions

From this study it can be concluded that scabies, is rare in HIV infected adults as well as among adult patients without HIV infection admitted to medical wards at MMC. It can also be concluded that the odds of getting a skin disease is higher among HIV-infected adult patients than those without HIV infection and it increases with increasing clinical stage of HIV infection. Furthermore, generalized hyperpigmented post inflammatory macules were found to be associated with HIV infection. The current study also suggests that using blood samples from Tanzanian adults, the MedMira rapid HIV test is highly sensitive but less specific.

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DECLARATION

"I declare that the whole of this dissertation is my own original work, and has not been submitted for a similar degree in any other University".

Date: 7th JUNE, 1999

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INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

Scabies, the contagious skin condition caused by the itch mite, has been known to humanity for centuries.[1] Known as "seven-year itchy" scabies, had been observed to be associated with wars, social upheaval and poverty.[2] Epidemics of scabies were associated with both the first and the second world war, and rampant scabies was thought to have affected Napoleon troops during his Russian campaign.[1] These observations suggested that, poverty, poor hygiene, overcrowding, malnutrition and sexual promiscuity were contributory factors. In Africa including Tanzania, scabies is endemic and is commonly seen among the poor, overcrowded and those living under unhygienic condition.[3]

Disregarding the occurrence of social upheavals, epidemics of scabies have been observed to appear in cycles of 12 to 15 years.[2] This cyclic pattern of occurrence, could be due to changing levels of immunity against scabies in the human population.[4,5] The immunity against scabies is cell-mediated.[6] HIV infection predominantly affect cell-mediated immune mechanisms therefore, with the current AIDS pandemic, it seems logical to study any relationship, that may exist between scabies and HIV/AIDS.

1.2 Biology and medical importance of the itch mite

Sarcoptes scabiei, the itch mite, is the aetiological agent for scabies. It is classified under the Sub-order Acaridida. There are three families under this sub-order, but only one of them is of medical importance, that is, family sarcoptidae. *Sarcoptes scabei* causing scabies in man, belongs to the sarcoptidae family. The itch mite does not only infest man, but also other mammals causing a condition known as mange. Despite diversity of potential hosts, at species-level, no difference in structure has been noted between mites from different hosts. The differences noted have been more physiological than anatomical.[7,17] As a result, *Sarcoptes scabiei* is currently considered one species in which different forms of the organism differing only physiologically exist.[4,1] The form that infests man for instance, is referred to as *Sarcoptes scabiei* var hominis and that for dogs *sarcoptes scabiei* var canis.

Mites from one host species do not establish themselves on another, however, humans can become infested from other mammals and get what is known as animal scabies. Infestations such as these, however, are mild and disappear spontaneously.[7,4,17]

The life cycle of scabies mites encompasses four stages: egg, larva, nymph and the adult stage. The entire life cycle from egg to egg takes about ten to fifteen days.[3,4] The mite at the nymph stage has three pairs of legs while at the adult stage has four pairs.

The most conspicuous difference between the adult male and the adult female mite is

their size. The adult male is smaller than the adult female, measuring about 0.2mm in length compared with 0.4 mm for the female adult mite.

Both adult male and female mites, possess striated cuticle bearing various specialized dorsal scales and short stiff hair-like structures (bristles). The legs are arranged in two groups: the anterior and the posterior pairs. In both sexes, the anterior pairs end in stalked pulvilli which because of their disc-shaped appearance are called suckers. The suckers are considered to be used by the mites to grip host's skin in order to aid their movement. The adult female mite, has two posterior pairs of legs ending in long bristles, while in the adult male only the third pair ends in bristles; the fourth pair resembles the anterior pairs in that it has stalked pulvilli.

In scabies, the newly fertilized female mite is the infective agent.[4] It moves rapidly about on the skin surface, progressing up to 2.5 cm per minute and selects a suitable site to make a burrow. Using its chelicerae and the sharp edges of its first two pairs of legs, the mite cuts the skin to make the burrow. The burrows are driven parallel to the skin surface, and are always confined within the horny layer of the skin. The burrow made by the adult female mite is usually about a centimeter long while that made by the adult male, is usually no more than a millimeter long. Shortly after being fertilized by the adult male - which comes out of its burrow searching for a female `partner' and dies after mating - the female mite, lays a few relatively large eggs while further excavating her burrow and hides among faeces at the burrow end. The hexapod larvae that hatch from the eggs, move to the skin surface to find shelter and presumably food in the host

follicles. The larvae moult to reach the nymph stage. Female mites in the nymph stage moult twice to reach the adult stage, while male mite-nymphs moult once to reach the adult stage.

1.3 Clinical presentation of scabies

Scabies can be acquired through direct contact with the skin of infested persons and or their recently worn clothes and beddings. The disease is so contagious that minimal contact such as handshaking with an infested person may be enough to cause infestation.

Scabies is common among people living in close proximity under adverse social and hygienic conditions, particularly under conditions of shortage of water leading to infrequent washing. Such conditions can be found in prisons, dormitories, mental institutions, refugee camps and nurseries. Although individuals who frequently wash are less likely to get infested, scabies is known not to respect social class,[2,4] and is found among people in the high social class as well. But in such people, the disease is likely to be mild with few lesions. Because of the highly contagious nature of scabies, it is not uncommon to find all members of a family affected at the same time and epidemics of scabies may also occur in hospitals. An index case of scabies, may cause an epidemic among other patients and/or nursing staff, as casual contact of nursing attendants is adequate for transmission of the disease. Sexual contact is also an important mode of transmission of scabies.[4,3]

Itching is the cardinal symptom of scabies. After infestation with the mite, normally, a period of three to four weeks elapses before itching starts.[7] Itching in scabies, is considered to be an immunologically mediated response to the presence of mites and/or mite faeces.[9] The itching is intense and worse at night; because warmth produced by beddings or a hot bath taken before going to bed, increases mite activity.[7]

Because of the immunological nature of the itching in scabies, the high intensity of itching and its widespread presence on the body, is not in line with the localized presence of mites and their small number in a typical case of scabies. There could be as few as twenty mites in a typical patient of scabies.[4,3]

Itching leads to scratching which may offer some temporary relief to the patient, since it causes removal of mites from the body by rupturing burrows and subsequently mites falling off the body. In addition, some mites may die in the process of scratching. However, scratching may be hazardous too. Scratch marks may be infected by bacteria leading to pyoderma and may ease burrowing of other mites.

Scabies mites have a predilection of burrowing on areas of the skin, where the skin is thin and wrinkled.[1] As a result, the presence of mites and the associated eruption in a typical case is normally limited or more marked on such areas of the skin as the: inter-digital web spaces; anterior surface of the wrists, extensor surfaces of the elbows; the axillae, and the sides of the soles. Other areas include the thighs and external genitalia in men, and under the breasts, the nipples, the abdomen and the lower portions of the buttocks in women.[2] Despite this wide range of areas which can be affected, up to two-

thirds of mites in a typical case are to be found in the hands and flexor surfaces of the wrists.[7]

The characteristic eruption of scabies, is an important sign of the disease. It starts with a small (1-3 mm) slightly raised papule which develop at the site of each mite.[4] Local sensitization of the skin (a hypersensitivity phenomenon) resulting from mite infestation is followed by the appearance of an erythematous rash of scabies resulting from a type IV hypersensitivity reaction.[2,6] Except in children, the scabies eruption characteristically spares the face and the scalp.[2]

A more severe form of scabies is seen among people who are mentally retarded (who cannot care for themselves properly), debilitated, and immunosupressed. It has been rarely described in healthy individuals.[8]

This form of scabies, is characterized by a generalized, hyperkeratotic and crusting eruption. Indeed, it is sometimes described as a highly infectious exfoliative dermatitis.[9] Millions of mites may be present, itching is often mild or absent and burrows are not formed in this severe form of scabies.[4] In patients who present with this severe form of scabies, the mites escape immunological control and multiply considerably leading to encrustation of the skin.[3] Itching is immunologically mediated, and since there is immunodeficiency among patients presenting with this form of the disease, itching is mild or absent.

The first epidemics of this severe form of scabies were reported from Norway. Therefore, this form of scabies has been named "Norwegian scabies". However, some people have found this name derogatory to Norwegians, and prefer to call it crusted scabies.

Since the advent of HIV and AIDS, Norwegian or crusted scabies has been widely reported among patients with AIDS.[10] Indeed, at present, HIV/AIDS is the commonest disease, which can trigger crusted scabies.[11] Crusted scabies in institutions has been reported to be on the increase[12] and since this form of scabies is more infectious than ordinary scabies, strict barrier nursing is required to prevent nosocomial transmission. If not treated promptly "Norwegian" scabies, can be associated with high morbidity and bacterial skin sepsis which may lead to life-threatening bactereamia.[8]

Crusted or Norwegian scabies is an important dermatological condition in today's clinical practice, but its magnitude at Muhimbili Medical Centre is unknown. It is essential that the prevalence of crusted scabies at Muhimbili Medical Centre is established and vigilance for its occurrence is observed.

1.4 Diagnosis of scabies

The diagnosis of scabies is based on the presence of an erythematous and excoriating papular eruption which is symmetrically distributed on predilection areas. Normally, there is associated intense itching which tends to be worse at night. Burrows made by mites on the cornified layer of the skin, can be seen with the naked eye. However, better visualization of burrows can be achieved by the help of a magnifying glass. Burrow identification can be improved further by application of blue or black ink on the suspected burrow; by capillary action, the ink will be pulled into the burrow; the burrow will be demonstrated by the ink remaining in it after removal of the excess external ink, with an alcohol swab.[1]

By themselves, burrows identified on a patient with a suggestive eruption have been considered pathognomonic.[2,13] Burrows in African patients are rarely seen;[3] in fair-skinned people burrows are commonly seen,[2] and under a magnifying glass, they look like tunnels resembling pepper owing to the accumulation of faecal pellets. The adult female mite can be found at the end of the tunnel, where it appears as a pearl-shaped structure with a dark object - its mouth parts. When the mite is seen in this way, it can be removed using a point of a needle, and the diagnosis of scabies is confirmed. Confirmation of scabies can also be done by scraping over a burrow. Skin scrapings are transferred onto a drop of 10% potassium hydroxide or mineral oil; with a cover-slip applied on top of the drop; examination under the low-power of a microscope allows identification of mite, their eggs and/or faecal pellets. In a patient with ordinary or typical scabies, the number of mites is normally small and in many such patients skin - scraping can give negative results.[14]

Punch skin biopsy over a burrow or burrow-suspected areas is another method for identifying mites. It has been found to give better results than skin scraping [15], and is recommended in a suspected case of scabies with negative skin scrapings. Haematoxyline and Eosin stained sections of the epidermis can reveal mites, sectioned mite parts, as well as eggs, larvae and nymphs.

The use of epiluminescence microscopy, has revolutionarised mite detection. It allows a detailed inspection of the skin from the surface to the superficial papillary dermis, at which the mites appear as dark points, and can be proven by scraping in the usual manner. Epiluminescence microscopy has proved to be a very useful tool for in-vivo diagnosis of scabies in that it has been associated with a very low number of false-negative results; it permits mite detection in only a few minutes; and causes no discomfort to the patient.[14]

1.5 Treatment of scabies

Scabies is a curable condition, and a number of effective agents are available for treatment. Gamma benzene hexachloride (Kwell) is the drug of choice.[1] Other effective preparations include sulfur in petroleum jelly, 10% crotamiton (Eurax), 25% benzyl benzoate emulsion (BBE), Permethrin 5% dermal cream and oral ivermectin.

In non-pregnant adults, lindane lotion is applied from the neck to toes and left on for twelve hours whereas in pregnant women and children, the drug is left on for six hours. Lindane is not recommended in children aged below one year, and in patients with underlying cutaneous disorders that allow greater absorption of the drug into the blood stream. For example, when a patient has widespread dermatitis or scaly lesions, gamma benzene hexachloride or lindane, has a great potential for neurotoxicity.[1] Greater absorption of lindane into the blood stream, could also result from repeated applications. For this reason, patients are instructed not to apply the drug more than twice in a one-month period.[1]

Crotamiton (Aurax) is also applied from the neck to the toes, but is left on for 24 hrs, and a second application is recommended the next day. Benzyl benzoate (BBE) is applied in a similar fashion, left on for twelve hours, and re-applied after one week. On the other hand, sulfur in petroleum jelly (precipitated sulfur), is applied daily for three days. The multiple application of scabicides is designed to kill any mites, which may have evaded death at the time of first application because of being in the form of egg.

Either crotamiton 10% cream or lotion, or 5% precipitated sulfur is safer to use in pregnant women and children below one year. However, their safety has not been established in clinical trials, and treatment with these preparations is associated with a high failure rate.

Currently, scabies has been characterized by less frequent cases of classic or ordinary scabies and an increasing frequency of atypical scabies.[16] This observation could be attributed to the concurrent HIV/AIDS pandemic. Crusted and atypical (exaggerated) scabies, the unusual forms of scabies, have been widely reported among patients with HIV disease. Because of underlying immunodeficiency, the unusual forms of scabies are characterized by heavy mite-load and are resistant to the previously effective scabicides.[17]

The problem of drug resistance in atypical cases of scabies, has led to the discovery of new preparations that are effective against scabies. Permetrin 5% dermal cream has been shown to be more effective than lindane in the treatment of such cases.[18] However, ivermectin, the anti-helminthic agent that has been used for oncho-cerciasis, is the most recent to be used in drug resistant cases. It is given as a single oral dose, 20μg per kilogram body weight, and has been found to be quite effective in typical and atypical cases.[19]

Patients with scabies could also be treated symptomatically with an oral antihistamine and a soothing topical preparation, to control itching. Even so, pruritis probably caused by retained mite parts may persist up to two weeks after adequate treatment.[1,3] The use of topical corticosteroids to decrease inflammation and pruritus, is an area of controversy. They can be used because of their potent anti-inflammatory action, but they carry the risk of potentiating the scabies infestation from possible immunosuppression, which they are known to cause.

1.6 HIV infection and scabies

A clear immunologic link exist between HIV infection and scabies; HIV infection impairs the effectiveness of the body's cell-mediated immune mechanisms, while it is the very same cell-mediated mechanisms the body needs to defend itself against scabies.[5]

When development of the immune system takes place during foetal life in humans, lymphocyte precursors migrate from the bone marrow to two principal sites: the thymus and the liver. Lymphocyte precursors migrating to the thymus gland are modified by the environment in this organ into lymphocytes responsible for cellular immunity. Lymphocyte precursors, which migrate to the foetal liver or to the bone marrow after birth, become transformed into B lymphocytes responsible for humoral immunity.

$CD4^+$ cells, the helper/inducer T cells, make one of the subsets of T cells that have been identified.[20] They are called $CD4^+$ T cells because, they have on their surface the $CD4^+$ glycoprotein molecule. However, they could also be simply called T4 cells. Of the four groups of T cells, helper/inducer T cells and suppressor T cells ($CD8^+$ or T8), are involved in the regulation of antibody production by B lymphocytes. Although T cell effector mechanisms play a relatively minor role in the defence against all parasitic infections[21], T cells play a critical role in the immune mechanism against scabies. Immunity against scabies is IgE-based with eosnophils being the principal effector cells, and as a result, the cardinal pathological change in scabies-parasitized skin is

eosinophilic infiltrations. However, T lymphocytes are behind all this IgE-based immune reaction against scabies. Eosinophil production itself, is dependent on T-lymphocytes, and T-lymphocytes, through the T-lymphocyte chemotactic factor attract eosinophils.[22] In addition, when naive and sensitized animals are challenged with the scabies mite, there is a significant increase in helper/inducer T cells expressing $CD4^+$ antigens in the epidermal cellular infiltrate.[23] This suggests, a key role by $CD4^+$ T cells in a successful immune response against scabies.

The central immunological lesion in HIV infection is the progressive loss of $CD4^+$ T cells, but the precise mechanisms responsible for this depletion and functional defects of $CD4^+$ T cells are complex and not well understood.[24] However, in vitro studies have elucidated two possible mechanisms which cause HIV-associated immunodepression; including mechanisms associated with increased HIV expression, and those associated with quantitative reduction of $CD4^+$ T cells.

Antigens and mitogens, form the first group of agents which initiate up-regulation of HIV expression. These are basically, genes from heterologous viruses; such as cytomegalovirus, Herpes simplex virus, Human herpes virus type 6, and Human T - lymphocytic virus type 1.[24] Activating DNA binding proteins such as NF-KB, initiates viral expression through interaction with specific sequences within the HIV long terminal repeats (LTR). This is the presumed mechanism through which antigens and mitogens cause increased HIV expression.[24]

Through the induction of a wide variety of endogenous soluble factors (cytokines), which are otherwise responsible for normal immune homeostasis, mycoplasma and other co-infecting organisms form the second group of agents associated with increased HIV expression. Tumour necrosis factors alpha and beta (NF and TNF), interleukin 6 (IL-6), transforming growth factor beta (TGF-β), and granulocyte-macrophage colony stimulating factor (GM-CSF); have been associated with increased HIV expression among HIV-infected $CD4^+$ T cells.

HIV can cause a quantitative reduction of $CD4^+$ T cells through a number of direct and indirect mechanisms:

$CD4^+$ T cells death from direct viral mechanisms.

i) Budding off from activated $CD4^+$ T cell surfaces of large amount of virus, causes massive increase in cell membrane permeability and, thus, eventual cell death.

ii) The accumulation of large amounts of unintergrated viral DNA, heterodisperse RNA, and viral core proteins in the intracellular environment interferes with cell functions leading to cell death.

iii) The binding of newly synthesized HIV-envelope glycopreteins to $CD4^+$ molecules within the host cell may lead to cell death.

$CD4^+$ T cell death from indirect viral mechanisms:

i) HIV-infected $CD4^+$ T cells, express gp 120 molecules on their surfaces which bind to CD4 molecules of uninfected cells. The resulting multi-nucleated giant cells (syncytia) are associated with cell death.

ii) Free gp 120 molecules, may bind to the surface of uninfected $CD4^+$ T cells leading to their destruction by antibody-dependent cellular cytotoxicy responses.

iii) Uninfected $CD4^+$ T cells, that have captured and processed soluble gp 120; functioning as class II major histocompatibility (MHC) restricted antigen presenting cells, may mistakenly be destroyed by HIV specific cytotoxic T cells.

Other cytopathic autoimmune reactions, may contribute to the $CD4^+$ T cell depletion, because HIV gp 120 and gp 41 proteins, share some degree of homology with certain class II MHC molecules.

$CD4^+$ cell death by apoptosis has also been hypothesized.

Through the above-outlined mechanisms HIV, causes progressive loss of $CD4^+$ T cells

leading to a slowly developing immuno-deficiency with four currently well-known stages: Primary infection, clinical latency, cytopathicity and clinical disease.[24]

There is a state of increased levels of HIV and a decreased number of circulating $CD4^+$ T cells, in the peripheral blood during the period of primary infection. In some patients the primary infection, is associated with an acute, flue-like syndrome.

The clinical latency period is characterized by the dissemination of HIV to the lymphoid organs, the principal organ being the lymphnode. There are very few HIV-infected $CD4^+$ T cells in peripheral blood during this period, and the number of HIV-infected $CD4^+$ T cells may be as low as 1 in 1,000 to 1 in 10,000.[25,26] However, gradual attrition of circulating $CD4^+$ T cells, has been observed among patient in clinical latency.[24] Therefore, although patients are asymptomatic, immune deterioration continues, and HIV replication in the lymphnodes continues throughout the course of the disease.

Marked pathological changes among $CD4^+$ T cells and their subsequent death, characterize cytopathicity stage, while clinical disease, develops when the $CD4^+$ T cells falls below 200 cells per ml of blood, leading to the appearence of life threatening opportunistic infections and specific tumours.[21]

At an advanced stage the lesion of HIV infection does not only involve $CD4^+$ T cell depletion, but also extends to antibody responses and ability to sustain antibody responses against polysaccharide antigens. The defective antibody response against

polysaccharide antigens, is associated with increased susceptibility to bacterial infections which have been reported to be especially common among paediatric and African adult patients.[21] Indeed, HIV infection affects cellular immunity, as well as the humoral immune mechanisms. Polyclonal activation of B lymphocytes leads to hypergammaglobulinaemia, which is not protective to the infected host. It is also reckoned that at some stage even the HIV specific antibodies produced are not protective.

Leishimaniasis is an obvious example of a parasitic disease, which is exacerbated by HIV infection,[21] and scabies could be another example. *Leishimania donovani* infection among immune competent individuals, is localized to a superficial lesion at the site of parasite entry (oriental sore) with features of a cell-mediated immune reaction. In patients with HIV/AIDS, with failure of such T cell localization, leishmaniasis usually presents with disseminated or visceral disease.[21] Similarly, the chronic cellular immunodeficiency of HIV is thought to be the underlying cause of crusted or "Norwegian" scabies, the severe form of the disease. However, the clinical presentation of scabies in HIV disease has been reported to be extremely variable, and suspicion of scabies to any atypical itching or non-itching rash has been recommended in HIV-positive patients.[11] Scabies in HIV/AIDS may present as atypical (exaggerated) scabies with absent classic distribution of lesions or itching, and may also present as a generalized papulo-squamous dermatitis.[17] Therefore, while it is clear that Leishmaniasis in HIV/AIDS, usually presents with disseminated or severe disease, it is not so with scabies.

1.7 MedMira rapid HIV test

During the planning of the current study, a rapid HIV test, MedMira rapid HIV test (MedMira laboratories Inc.), was made available to Muhimbili Medical Centre. Although the test had been used elsewhere, it had not been used in Tanzania before. And since the current study was going to involve HIV testing, an additional objective to validate the MedMira rapid HIV test was adopted.

The use of rapid HIV tests in the developing world is absolutely appropriate. These tests are inexpensive, simple to do; require no sophisticated equipment; and the duration of waiting for results is reduced for both HIV-positive and HIV-negative patients. However, for HIV-positive patients, confirmatory tests may be required. On the other hand, standard non-rapid enzyme immuno-assays, like those in use at Muhimbili Medical Centre, require expensive equipment; need personnel with a considerable laboratory experience; and there is usually a delay between blood collection and the availability of test results when standard enzyme immuno-assays are used.

The MedMira rapid HIV test, is a three-minute membrane-based immunodot assay utilizing synthetic peptides derived from both the HIV-1 and HIV-2 virus. The peptides, are immobilized on an immuno-reactive test membrane, and when a drop of human plasma, serum or whole blood is placed on the membrane; the synthetic peptides capture the antibodies to HIV-1 and HIV-2, present on the specimen. The membrane is then washed to remove any non-specific binding, and the captured antibodies are visualized through a calorimetric reaction with a proprietary protein, a Colloidal gold conjugate.

The conjugate binds to HIV antibodies to produce a distinctive red dot on the test membrane, and this represents a positive test. Absence of HIV antibodies does not yield a red dot, and is indicated by a clear white test membrane.

2.0 STUDY RATIONALE

The magnitude of HIV disease, has been on the increase since the pandemic started in 1981. The World Health Organization (WHO), had estimated 7.7 million AIDS cases Worldwide by July 1996, an increase of 7.9% compared to estimated cases for 1995.[27] Since then, the incidence of HIV infection has increased tremendously and a total of 30.6 million people living with HIV/AIDS Worldwide had been reported by the end of 1997.[28] Twenty-one million (68.6%) out of the reported people were from Sub-saharan Africa.[28] Therefore, the AIDS problem is greatest in this region whose countries include Tanzania.

By 1992 in Sub-Saharan Africa, Tanzania was ranked sixth in terms of total estimated number of HIV-infected persons, and the rates were higher than those in north-Africa and most Sahalian countries.[29] In addition, the cummulative number of reported AIDS cases in Tanzania, increased from 44,195 in 1991 to 103,185 in 1997.[30] Certainly, this could be an under estimate because, late and incomplete reporting; and the problems involved in AIDS Surveillance; are the major problems in developing countries like Tanzania.

Anecdotal reports suggest, at Muhimbili Medical Centre today, HIV-related medical conditions are the commonest reason for admission to medical wards. Of the associated medical condition among HIV-positive patients, skin disease is extremely common.[29]

However, the prevalence of scabies among HIV-positive patients at MMC is unknown and, in fact, even the prevalence in the general population is unknown.[1]

The literature on scabies and HIV has been primarily from descriptive case reports, and prospective studies designed to determine the prevalence of skin diseases among HIV/AIDS patients, do not report of scabies as one of the common skin diseases in HIV/AIDS. But skin diseases among HIV positive patients, may vary from one locality to another.[32]

In a study in Togo which involved 120 AIDS patients who were followed-up for thirteen months, none of the patients developed scabies despite 100% prevalence of skin disease at 6 months.[33] A wide spectrum of skin disorders was seen among HIV-positive patients in a prospective study in Dublin, but scabies was not among the top ten most frequent disorders.[34] In Bangkok, Thailand, scabies was not among the skin conditions with a prevalence, higher than 5%.[35] And, a ten-year documentation of HIV associated dermatoses and their prevalence in Berlin, did not show scabies as one of the HIV associated conditions.[36]

Scabies, especially crusted or "Norwegian" scabies, is highly contagious, and may easily lead to outbreaks of epidemics of common scabies among hospitalized patients as well as health care workers.[37,11] However, scabies is a treatable condition and in the majority of patients, beneficial effects especially diminished pruritus, are evident within hours

after treatment.[17] The relief afforded by the cessation of itching; and the ability to sleep soundly; are benefits of any successful scabies therapy, and the patient's well being is dramatically improved.

A number of HIV testing techniques which are rapid and simple to use have been developed. Indeed, rapid HIV tests have been commercially available for over 10 years now.[37] Although rapid-HIV tests have been proven to be highly sensitive and specific when compared with standard enzyme immunoassays, there are incidences where they have been withdrawn from the market. For instance, Nine tests were withdrawn from the market in France following an investigation, which showed some of the tests to have low sensitivities when used against reference serum.[39] It was essential, as part of this study therefore, to validate the MedMira rapid HIV test, and to determine its performance characteristics and suitability for use in Tanzania.

3.0 OBJECTIVES

3.1 Broad

To study the association between scabies and HIV infection.

3.2 Specific

1. To determine the prevalence of scabies among HIV-positive patients.

2. To determine the clinical types of scabies among HIV positive patients.

3. To determine the frequency of scabies in the four different WHO clinical stages of HIV infection.

4. To determine the cutaneous manifestations and their frequency among HIV-infected adult patients at different stages of HIV infection in patients at MMC.

5. To evaluate the performance of MedMira rapid HIV test using blood samples from Tanzanian adults.

4.0 METHODOLOGY

4.1 Study design and setting

This was a descriptive study conducted at Muhimbili Medical Centre (MMC) located in Dar es Salaam city, a city with a population currently estimated to be close to three million people. Muhimbili Medical Centre, is one of the only four tertiary care centers in Tanzania, but it also functions as a primary care center for the people in and around Dar es Salaam city. The public health service in Dar es Salaam include Muhimbili Medical Centre itself; three district hospitals; several health centers; and many dispensaries. In the city, parallel to public health facilities are, few private hospitals and

a multitude of private dispensaries. The referal system to Muhimbili Medical Centre is so weak that, simple cases like uncomplicated malaria, acute diarrhoea and even acute alcohol intoxication could be referred.

4.2 Study subjects and methods

The study was conducted between February and April of 1998. For practical reasons, data collection was not done every day. It was done on three consecutive days and skipped on the fourth day, and eligible subjects included all adults admitted in the medical wards, who fulfilled the following criteria.

(i) Aged between 15 and 56 years.

(ii) A verbal informed consent to participate in the study.

Patients aged above 56 years, and those who declined to participate were excluded from the study.

4.3 Clinical evaluation

A detailed history and thorough physical examination were done by the author (AS) on all patients included in the study, and information recorded on a specially designed questionnaire (appendix I). Using the current WHO system (appendix II), the author

also determined the clinical stage of HIV infection on all study subjects. Patients found with skin lesions were afterwards evaluated by a dermatologist (MB), in order to confirm the diagnoses.

Patients suspected to have scabies were clinically classified as having:

(a) Definitive scabies if they had the following lesions:

i. Itchy, erythematous papules or papulo-pustular lesions on predilection areas for scabies, or generalized but more marked on predilection areas.

ii. Generalized itchy hyperkeratotic and crusting lesions.

iii. Generalized non-itching hyperkeratotic and crusting lesions.

(b) Probable scabies, if they had any other atypical rash itching or non-itching, which could not be assigned to any other diagnosis.

Patients with lesions under a(i) above were considered to have typical scabies. "Norwegian" scabies was considered in patients with lesions consistent with a(ii) and a(iii) above, while patients with lesions falling under category (b), were considered to have atypical scabies if mites were identified in them.

4.4 Confirmation of scabies infestation

The following procedures were performed on patients suspected to have scabies. First, burrow identification was done with the aid of a magnifying glass, and presence of a burrow was confirmed by application of blue ink to the suspected burrow; and after removing excess external ink by an alcohol swab. Second, using a sterile surgical blade, scraping was done over the burrows allowing scrapings to drop on a filter paper until some minimal bleeding occurred. The scrapings were transferred onto a drop of 10% potassium hydroxide placed on a clean glass slide, and a cover-slip was applied on top of the drop. The slides were microscopically examined under low power magnification. Thirdly, a punch skin biopsy was taken from another burrow suspected area, and specimens were sent for histological examination, where Hematoxyline and Eosin stains were used on cut-sections of the epidermis for mite identification. However, only sixteen punch biopsies were done because of limited supply of needles. All these procedures were done on the hands and wrists, except when the patient had no lesions on them, and in that case, the procedures were done on areas of the skin where most of the lesions were located.

4.5 HIV testing

The National AIDS Control Programme (NACP) of the Ministry of Health (MOH) recommends, HIV testing to be done after pre-test counselling and the test should be

followed by a post-test counselling. In the absence of counselling facilities NACP, recommends anonymous testing. In agreement with the ethical committee, anonymous unlinked HIV testing protocol was adopted in the current study. Blood collection tubes had only a study number written on them; samples were sent to the laboratories, clinical research laboratory for the MedMira test and Virology reference laboratory for the enzyme immunoassays; test results were recorded separately and then, were linked to the patient's records (questionnaires) bearing study numbers at the end of the study.

Two standard enzyme linked immunosarbent assay (ELISA) tests, were used as the golden standard in the evaluation of the MedMira rapid HIV test (MedMira laboratories inc. Canada). The wellcozyme HIV Recombinant test (Murex) and the Enzygnost anti-HIV 1/2 Plus test (Behring).

A standard sequencial testing procedure was adopted. Serum samples were tested with the rapid test (MedMira), reactive samples were tested with the first ELISA (Enzygnost) which has a high sensitivity. Samples reactive on the first ELISA were then tested by the second ELISA (Wellcozyme), which has a high specificity. A sample was considered reactive (HIV-positive) if positive on both ELISAs. No discondant results were observed.

4.6 Statistical analysis

Data were analysed using the Epi Info Software (version 6.02, October 1994). The proportions of HIV-seropositivity between age groups, and the prevalence of cutaneous manifestation between HIV-positive and HIV-negative patients were compared using Chi-square test. Prevalences of superficial fungal infection and generalized post-inflammatory hyperpigmented macules among HIV-positive and HIV-negative patients, were also compared using the chi-square test, and the statistical significance level of P-value less than 5% was used for all comparisons.

The statistical significance of an observed trend of cutaneous manifestation among HIV-positive patient in different clinical stages of HIV infection, was assessed using Chi-square test for trend. While, the performance of the MedMira HIV test was evaluated by calculating its sensitivity and specificity.

5.0 RESULTS

5.1 Sociodemographic characteristics of the study population.

5.1.1 Age and Sex distribution.

A total of 325 patients were recruited in the study. Of these 191 (58.8%) were males and 134 (41.2%) were females. The mean age (SD) for the study population was 33 (10) years. Majority of the patients (35.1%) were in the age group of 25 to 34 years (Table 1).

5.1.2 Marital status

Marital status was determined for 308 patients. Of these 111 (36%) were single, 153 (49.7%) were married, 31 (10%) were divorced, while 11 (3.6%) were widowed.

5.1.3 Occupation

Of the 301 patients whose nature of work was determined, 37 (12.3%) were engaged in office work, 64 (21.3%) were doing petty business, and 80 (26.6%) were involved mainly with household chores. 7 (2.3%) were prison inmates.

5.1.4 Living environment and hygienic behaviour

Since very sick patients and those in coma were included in the study, some information was impossible to obtain in some patients. As a result, some data is not available for all 325 patients included in the study.

The type of housing was determined for 235 patients. A hundred and ten (46.8%) patients came from families which shared houses with other families. While, 125 (53.2%) patients came from families which did not share houses with any other family. Generally, study subjects came from large families, with an average number of six people per family. However, the average number of children aged below fifteen years was low - two children per family. Two hundred and sixty-five patients gave information on bathing frequency. Thirty-three patients (12.5%) had been bathing once daily, while 169 (63.8%) had bathed twice daily and 63 (23.3%) bathed thrice daily. Therefore, majority of the study subjects had healthy bathing behaviour.

Two hundred and twenty-nine patients reported about the source of water. Of these, 63 (27.5%) obtained water from inside or within the household compound while 166 (72.48%) obtained water from outside the house compound. However, the exact distance between the household compound and the water source was not determined in the current study. Nevertheless, the finding suggest that water source, was not within easy reach to the majority of the study subjects.

Two hundred and seventeen patients responded to the question regarding cleanliness of bedlinen and clothes. Eighty-five (39%) patients reported changing and washing their bedlinen every three days while 51 (23.5%) did wash and change once per week.

Regarding ironing, two hundred and seven out of two hundred and sixty-four patients (78.4%) ironed their clothes, while fifty-seven out of the two hundred and sixty-four patient (21.6%) did not iron their clothes. A hundred and fifty patients (72.5%) of the 207 who ironed their clothes did so always. And, the percentages were similar to those about beddings where, 68.2% ironed their beddings while 31.4% did not. Of those who ironed their beddings, 71% did so always. Hence, the cleanliness of clothes and bedlinen was satisfactory in majority of the study subjects.

5.2 Referral diagnosis

A total of 436 referral diagnoses (one patient could have more than one diagnosis) were recorded (Table 2), in which, suspected tuberculosis was the leading reason for admission, making 13.7% of all the diagnoses. Malaria ranked second with 11.4%, and suspected HIV infection came third with 10.5% of all the referral diagnoses recorded. Involvement of the skin was recorded in eleven out of three hundred and twenty-five (3.3%) patients included in the study. Indeed, scabies was not recorded at all, even among the few patients who presented with classic clinical presentation.

Table 1: Age and sex distribution of study subjects.

Age group	Male	Female	Total
	n (%)	n (%)	n (%)
15-19	15 (51.7)	14 (48.3)	29 (100)
20-24	29 (53.7)	25 (46.3)	54 (100)
25-29	33 (56.9)	25 (43.1)	58 (100)
30-34	31 (56.4)	24 (43.6)	55 (100)
35-39	19 (52.8)	17 (47.2)	36 (100)
40-44	17 (60.7)	11 (39.3)	28 (100)
45-49	19 (73.0)	7 (27.0)	26 (100)
50-54	20 (66.7)	10 (33.3)	30 (100)
55-59	6 (100)	0 (0)	6 (100)
Total	189 (58.7)	133 (41.3)	322 (100)

3 patients had missing age.

Table 2: Referral diagnoses recorded among the study subjects.

Referral diagnosis	Frequency	Percentage
Pulmonary Tuberculosis	60	13.7
Malaria	50	11.4
Suspected HIV infection	46	10.5
Anaemia	42	9.6
Diabetes mellitus	19	4.3
Hypertension	19	4.3
Pleural effusion	13	2.9
Congestive heart failure	11	2.5
Others	176	40.3
Total	436	100

5.3 The prevalence of HIV infection.

Three hundred and twenty patients were tested for HIV antibodies while five patients refused blood testing. Of the 320 patients whose blood samples were tested for HIV-antibodies by ELISA, 131 (40.9%) were HIV seropositive (Table 3). There was a significantly higher HIV sero-prevalence among patients aged 25 to 34 years when compared to patients aged below 25 years (P<0.001) and compared to patients above 34 years of age (P=0.01). In addition, there was a significantly higher HIV sero-prevalence among female (47.7%) than male (35.6%) patients (P=0.03).

Table 3: Prevalence of HIV infection by age group.

Age group years	HIV ELISA test		Total
	+ve	-ve	
	n %	n %	n %
15-19	3 (10.3)	26 (89.7)	29 (100)
20-24	13 (24.07)	41 (75.93)	54 (100)
25-29	31 (56.36)	24 (43.64)	55 (100)
30-34	32 (58.18)	23 (41.82)	55 (100)
35-39	16 (44.40)	20 (55.60)	36 (100)
40-44	16 (57.14)	12 (42.86)	28 (100)
45-49	12 (46.15)	14 (53.85)	26 (100)
50-54	5 (17.86)	23 (82.14)	28 (100)
59	1 (16.67)	5 (83.33)	6 (100)
Total	(40.69)	188 (59.31)	317 (100)

* Two HIV-positive patient and one HIV-negative patient had missing age.

5.4 The prevalence of scabies

Out of the 325 enrolled patients, 137 (42.8%), had skin manifestations. Among these, only ten (7.3%) satisfied the clinical criteria for definitive scabies. Five were HIV-positive and the remaining five were HIV-negative. Thus, of the 131 HIV-positive patients in the study, only five (3.8%) had scabies. Scabies was confirmed by skin scraping in only one of the ten patients with scabies (Fig. 1,2; Appendix III). She was a 40 years old, HIV-negative patient, who presented with ascending motor polyneuropathy and was found to have Norwegian scabies. The four remaining HIV-negative patients with scabies had lesions consistent with typical scabies. Two of the five HIV-positive patients with scabies had Norwegian scabies, and the remaining three had typical scabies. All the five HIV-positive patients with scabies were found to be in WHO Stage III of HIV-infection. However, overall, majority of HIV positive patients were in Stage III, and because of the small number of HIV-positive patients with scabies, no firm conclusion could be drawn with regards to the prevalence of scabies and the clinical stage of HIV infection.

Of the ten patients with scabies, nine reported whole body washing at least once daily and one bathed after every-three days. Seven of these patients did not iron their clothes, four were prison inmates, and four came from families with more than five people each. Since scabies was not confirmed in any of the patients with probable scabies, further analysis could not done, and because the number of patients found with scabies in the study was small, the influences of the living environment and hygienic behaviour on the prevalence of scabies could not be assessed.

5.5 Other cutaneous manifestations

Of the 325 patients recruited in the study 137 (42.2%) had cutaneous manifestations and six of these patients had more than one manifestation. Seventy-five out of the 137 patients with cutaneous manifestation (54.7%) were HIV-positive, while 62 (45.3%) were HIV-negative (Table 4). Cutaneous manifestation was significantly more common among HIV-positive than HIV-negative patients ($P < 0.001$).

The proportion of patients with skin manifestation was 32.1% among asymptomatic HIV-infected patients; 70.76% among HIV-positive patients in clinical stage III; and 56.8% among patients in clinical stage IV of HIV infection (Table 5). The increasing trend of cutaneous manifestation with advancing clinical stage of HIV infection, was statistically significant (P=0.02).

Table 4: Presence/absence of cutaneous manifestation among study subjects as related to HIV serostatus.

		HIV-ELISA test			
		Positive	Negative	Total	
		n (%)	n (%)	n (%)	P value
Cutaneous manifestation	Yes	75 (54.7)	62 (45.3)	137 (100)	< 0.001
	No	56 (30.6)	127 (69.4)	183 (100)	
	Total	131 (40.9)	189 (59.1)	320 (100)	

Among the 137 patients with skin disease, superficial fungal infection was the commonest finding, while generalized post-inflammatory hyperpigmented macules was the second commonest finding. There was a significantly higher prevalence of superficial fungal infection among HIV seronegative compared to HIV seropositive patients (P < 0.001; 95% CI 0.1, 0.44). On the other hand, the prevalence of generalized post-inflammatory hyperpigmented macules was significantly higher among HIV seropositive compared to HIV seronegative patients (P=0.006; 95% CI 1.6, 16.9), while no difference was observed in the prevalence of scabies between HIV seropositive and HIV seronegative patients (Table 6).

Table 5: Presence/absence of cutaneous manifestation in HIV-infected patients as related to WHO clinical staging.

	WHO clinical stage				
Cutaneous-manifestation	I n (%)	II n (%)	III n (%)	IV n (%)	Total n (%)
Yes	9 (32.1)	0 (0)	41 (70.7)	25 (56.8)	75 (57.3)
No	19 (67.9)	1 (100)	17 (29.3)	19 (43.2)	56 (42.7)
Total	28 (100)	1 (100)	58 (100)	44 (100)	131 (100)

Table 6: Comparison of presumptive skin diagnosis and HIV serostatus.

Pressumptive skin diagnosis	HIV-ELISA test		
	+ve	-ve	Total
	n (%)	n (%)	n (%)
Superficial fungal infection	18 (31.58)	39 (68.42)	57 (100)
Post-inflammaory hyperpigmented macules	16 (84.21)	3 (15.79)	19 (100)
Scabies	5 (50)	5 (50)	10 (100)
Kaposi's Sarcoma	7 (100)	0 (0)	7 (100)
Pruritic papular eruption (P.P.E)	3 (42.86)	4 (57.14)	7 (100)
Herpes zoster scar	3 (75.0)	1 (25.0)	4 (100)
Other	30 (66.67)	15 (33.33)	45 (100)
Total	82 (55.03)	67 (44.97)	149 (100)

5.6 Performance of the MedMira rapid HIV test

In the current study, a total of 320 serum samples were tested for HIV antibodies using two different test, the rapid test (MedMira) and the two ELISA tests. A hundred and twenty-seven out of the 320 serum samples tested positive for both of the ELISA tests and the rapid test (MedMira). While 65 samples tested negative for all three tests (Table 7). The sensitivity of the rapid test (MedMira) was therefore calculated to be 96.9% and its specificity was 34.4%. The positive predictive and the negative predictive values of the rapid test (MedMira) were 50.6% and 94.2% respectively.

Table 7: Specificity and sensitivity of the MedMira rapid HIV test.

	HIV-ELISA test		
MedMira test	Positive	Negative	Total
Positive	127	124	251
Negative	4	65	69
Total	131	189	320

* Sensitivity = Probability of the MedMira test, to test positive if HIV infection is truly present:

$$\frac{127}{251} \times 100 = 96.94\%$$

* Specificity = Probability of the MedMira test, to test negative if HIV infection is truly absent:

$$\frac{65}{189} \times 100 = 34.39\%$$

* Positive predictive value = When a serum sample test positive with the MedMira test, what is the probability that HIV infection is truly present?

$$\frac{127}{251} \times 100 = 50.59\%$$

* Negative predictive value = When a serum sample tests negative with the MedMira test, what is the probability that HIV infection is truly absent?

$$\frac{65}{69} \times 100 = 94.20\%$$

6.0 DISCUSSION

The results of the current study do not only suggest that scabies is rare among patients admitted to medical wards at MMC, but also suggest scabies to be very uncommon among HIV-positive patients. Only five (3.84%) out of 131 HIV-positive patients had clinically definitive scabies, and only ten (3%) out 325 patients had scabies. Because such a small number of patients with scabies was found, statistically significant differences between HIV-positive and HIV-negative patients in relation to scabies could not be observed. Healthy bathing behaviour reported by the majority of patients included in the present study, could partly explain the observed low prevalence of scabies. However, the finding of a low prevalence of scabies among HIV/AIDS patients did not contrast the finding of other studies, that could be traced in the available literature. Hendrick J. Halsebosch, reported only 14 cases (2.6%) of scabies out of 530 AIDS patients, in a study to determine the causes of itch among AIDS patients.[40] By 1986 scabies, had been found in only 4 (2%) out of 206 HIV-infected patients who had been treated at the Division of Dermatology of the Cornell University College, New York.[17] Despite an approximately three-year follow-up period, scabies was found in only 28 (4%) out of 684 HIV-infected members of the Harvard Community Health Plan (New England, USA) in a study aimed at determining the frequency of dermatological diagnosis among HIV infected members.[41] At one center in Spain, 1,100 HIV-infected patients had been seen between 1983 and 1995, and only 6 cases (0.5%) of Norwegian scabies had been found.[37] Therefore, the finding of the current study is consistent with previous studies.

Turning to the diagnosis of scabies, the current study suggest that, the confirmation of the clinical diagnosis of scabies may be difficult. Scabies was confirmed in only one of the ten patients with scabies. The finding could be attributed to two main factors making the limitation of the current study. First, the study involved patients being admitted at a referral hospital, and since it may take a long time between the onset of the illness and arrival to a referral hospital, majority of the patients with scabies could have presented with old scabies lesions in which mites are hard to find.[42] Secondly, patients with scabies in the current study, may have received treatment before admission since it is more likely that the current admission was made only after other medical conditions had developed. Mites are also difficult to identify in previously treated cases.[3]

On the other hand, the inability to confirm the diagnosis of scabies in the current study, could be attributed to the very nature of scabies at the present time, currently classic scabies is seen less frequently and atypical forms of scabies are on the increase. The well-known scabietic burrow is seen only rarely today.[16] Indeed, with a negative skin scraping, the diagnosis of scabies may prove to be a great challenge to clinicians. However, with the prevailing paucity of diagnostic facilities and limited resources, skin scraping remains the most practical, and ideal bedside method for screening patients with suspected scabies as opposed to doing-punch skin biopsies.

None of the sixteen punch skin biopsies, which were done was positive for mites. This does not mean that punch skin biopsy is less useful in the diagnosis of scabies, but the limitations of the current study could explain the observation. Characteristic burrows were not identified and the small size of the punch biopsy needles used in the study, could have made the punch biopsy technique less accurate.

Although the use of the 2-mm punch biopsy technique has been shown to produce specimens, which allow an accurate histological diagnosis to be made in a wide range of skin conditions,[43] it may not be true for scabies. The 3-mm punch biopsy technique (the only available at the time) used in the current study, could have produced specimens without the adequate size for histological diagnosis of scabies: The adult female mite is normally found at the end of the burrow which is usually about a centimeter long. And therefore, if a 3-mm punch biopsy is used in the absence of clearly identified burrows, the accuracy of histological diagnosis could be reduced.

Punch skin biopsy with Haematoxyline and Eosin Staining has a place in the diagnosis of scabies, and adult mites and/or larvae have been identified using the technique, in as high as 49% of the patients with clinical manifestation of scabies.[44] Indeed, the diagnostic utility of skin biopsy sections has increased in recent years: The exoskeleton of *sarcoptes scabiei*, in Fungifora Y (known to stain fungi) stained deparaffinized skin biopsy sections, has been found to produce a characteristic greenish-blue fluorescence when put under incident illumination with ultraviolet light,[45] easying the identification

of the parasite. In addition direct immunofluorescence staining of histological sections allows to study, the immunopathological status of the skin infested with scabies.

Although the prevalence of scabies among medical-ward patients is low, it made about 6.7% of all the cutaneous manifestations observed in the current study. This makes scabies, an important cutaneous manifestation. Without delay, specific treatment need to be administered in patients with scabies, and vigilance for occurrence of "Norwegian scabies" is needed, if nosocomial infestation is to be avoided.

At Muhimbili Medical Centre, as well as elsewhere, skin manifestation is extremely common among HIV/AIDS patients. In the current study, 42% of all the study subjects had cutaneous manifestation; 56% of the HIV-positive patients had cutaneous manifestations compared with 34% of the HIV-negative patients and the difference was statistically significant.

Serge Coopman and Colleagues, demonstrated skin disease, to be present in 79% of the 684 HIV-infected members of the Harvard Community Health plan.[41] While workers in Zambia, revealed a prevalence of 54% among HIV-infected patients and 98% among patients who had already developed AIDS.[46] The reasons why, the finding of the current study is not quite consistent with the findings of the two quoted studies; could be partly, the different study environments and the difference in the study subjects. While the current study was purely hospital-based, the study in Zambia involved only outpatients,

and the USA-study involved both in-patients and out-patients. However, both studies and the current study show, a prevalence of cutaneous manifestation above 50%, among HIV-infected patients. Thus, cutaneous manifestation is extremely common in HIV disease.

The current study shows an increasing frequency of skin manifestation with advancing stage of HIV infection. This is in agreement with previous studies, which have shown skin diseases in HIV/AIDS, to be more frequent as immunodeficiency progresses.[47,41,36,33] Oral candidiasis, seborrhoeic dermatitis and kaposi's sarcoma, are by far, the commonest skin diseases encountered in HIV/AIDS.[48,36,3,33] However, what skin disease is seen in HIV/AIDS may depend on the stage of immunodeficiency. Oral candidiasis, oral hairly leucoplakia, kaposi's sarcoma and molluscum contagiosum have been associated with marked disease progression with very low $CD4^+$ cell counts,[49,36] while dermatophytes (tinea), Human papilloma viruses (warts) bacterial skin infections (Pyodermas) and Herpes Zoster develop early in the course of HIV infection, when there is still a satisfactory immune situation.[35]

The present study looked at cutaneous rather than mucocutaneous manifestations, thus, oral candidiasis is not considered. However, other studies done at Muhimbili Medical Centre have shown high prevalence of oral candidiasis among HIV infected patients. In the current study, superficial fungal infection, which included *dermatophytes* (tinea), *pityriasis versicolor,* and cutaneous candidiasis, was the commonest manifestation

among HIV-positive patients making 22% of the HIV-positive patients with cutaneous manifestation. However, it was also the commonest manifestation (58%) among HIV-negative patients. And, infact, superficial fungal infection was significantly more common among HIV-negative than HIV-positive patients (P=0.00001). The warm and humid climate of Dar es Salaam which equally affects HIV-positive and HIV-negative individuals, could explain this observation. Indeed, cutaneous manifestation other than superficial fungal infection in the current study, were significantly more common among HIV-positive than HIV-negative patients (table 6).

On the other hand, 78% of the HIV infected patients included in the present study were in advanced stage of immunodeficiency (Table 5). But, in HIV-positive patients, superficial fungal infection commonly occur in the early stage of immunosuppression, and the observation of higher superficial fungal infection in HIV-negative patients could be a result of the biased nature of hospitalized patients as far as the degree of immunodeviciency is concerned.

Nevertheless, fungal infections are a major cause of morbidity and mortality among HIV infected patients. The yeasts, candida and *cryptococcus neoformans*; the dimorphic fungi, *Histoplasma capsulutum* and *sporothrix schenckii*; and the dermatophyte fungi are the most common pathogenic fungi in HIV/AIDS.[50] *Tinea cruris* has been shown to be significantly more common in HIV-positive patients compared to HIV-negative controls in some studies.[32] But, although the prevalence pattern of skin diseases in

HIV/AIDS is generally similar among different studies, there has been notable differences from one locality to another.[35] In the present study, 19.5% of the HIV-positive patients with skin manifestation presented with generalized post-inflammatory hyperpigmented macules without any other active lesions. Kaposi's sarcoma was present in 8.5%, while seborrhoeic dermatitis was seen in only 1.2% of the HIV-positive patients with cutaneous manifestation.

The findings of the current study, suggest that at Muhimbili Medical Centre, the presence of superficial fungal infection poorly predict HIV infection. However, when superficial fungal infection is diffuse and resistant to treatment, HIV infection need to be seriously considered. HIV infection must also be considered, in patients with generalized post-inflammatory hyperpigmented macules, as the current study has shown such macules, to be significantly more common among HIV-positive than HIV-negative patients (P=0.006).

Skin manifestation is very important in HIV infection. It may not only represent the first clinical sign of HIV infection[51], but also may indicate progression of HIV disease. Skin disease in HIV infection, may be disabling, disfiguring, or even life threatening. Yet, in the current study, cutaneous manifestation was found to be rarely stated as a diagnosis or as an additional diagnosis on referal forms.

Therefore, there is a need through continuing education of health care workers, to emphasize the importance of skin disease, especially with the current AIDS pandemic.

Although the MedMira rapid HIV test has been validated and used elsewhere, validation in the current study at Muhimbili Medical Centre, reveals low specificity (34.4%). However, as in previous studies, its sensitivity in the current study was satisfactory (97%). The finding of such a low specificity with the current study, was not comparable to the studies quoted in the marketing profile for the test. A total of fourteen studies are quoted, and none of them reported specificity below 98%. Since no technical reasons could be traced to explain the low specificity with the current study, independent local studies are needed to corroborate the findings of the previous studies. Nevertheless, the current study suggest that the MedMira rapid HIV test, has a problem of labelling patients HIV-positive, while infact, they are truly HIV-negative. If the test is to be used, confirmatory tests need to be performed on MedMira HIV-positive samples. Alternatively, the test could be used in series with other rapid HIV screening tests, that is, for every MedMira HIV-positive result, other rapid HIV screening test(s) are performed, and the sample considered positive only when, it is positive for all the tests. This strategy would improve, the specificity of the MediMira test.

7.0 CONCLUSION AND RECOMMENDATIONS

The following conclusions can be drawn from the current study:

- Scabies is rare among HIV-infected adult patients as well as among adult patients without HIV infection admitted to medical wards at MMC.

- The odds of getting a skin disease is higher among HIV-infected patients than patients without HIV infection, and it increases with advancing stage of HIV infection.

- Using blood from Tanzanian adults, the MedMira rapid HIV test is highly sensitive but less specific.

- HIV infection is a common underlying problem among adult patients admitted to medical wards, at Muhimbili Medical Centre in whom HIV sero-prevalence is about 41%.

Further studies are recommended as follows:

- Since scabies is a rare disease, the relationship between HIV infection and scabies, could be better studied by employing a carefully designed case-control study.
- Further studies need to be carried out to validate the MedMira rapid HIV test, because the finding of the current study sharply contrast, that of previous studies.

8.0 SUMMARY

Since the advent of HIV/AIDS, HIV-related medical conditions have become the commonest reason for admission to medical wards at Muhimbili Medical Centre (MMC). Of the associated medical conditions among HIV-positive patients, skin disease is extremely common. But it was not clear whether scabies is among the commonest skin conditions in HIV-positive patients. The immunity against scabies is cell-mediated, and HIV infection predominantly affect cell-mediated immune mechanisms. This would suggest an association between scabies and HIV infection. However, a number of prospective studies designed to determine prevalence of skin disease among HIV/AIDS patients, do not report of scabies as one of the common skin diseases in HIV/AIDS patients. But the type of skin diseases among HIV/AIDS patients has been shown to vary from one locality to another. The prevalence of scabies among HIV-positive patients at MMC is unknown, and scabies, especially crusted or Norwegian scabies, is highly contagious and may easily lead to outbreaks of epidemics in hospital setting. In addition, scabies is a treatable condition and in the majority of patients beneficial effects especially diminished pruritus are evident within hours after treatment. It seems logical therefore, to study any association that may exist between scabies and HIV infection.

The objective of the current cross-sectional descriptive study was to determine the prevalence of scabies among HIV-infected patients. The study involved 325

consecutive adult patients admitted to medical wards between February and April 1998, also aimed at determining other cutaneous manifestations among HIV-positive patients, as well as to determine the performance characteristics and suitability for use in Tanzania, of the MedMira rapid HIV test (MedMira laboratories Inc. Canada).

Five (3.84%) out of 131 HIV-positive patients had scabies while five (2.57%) out of 194 HIV-negative patients had scabies. A hundred and thirty-seven (42%) patients out of the 325 patient enrolled in the study had cutaneous manifestation. Superficial fungal infection was the commonest manifestations, and it was significantly more common among HIV seronegative compared to HIV seropositive patients ($P<0.001$). Overall, cutaneous manifestation was significantly more common among HIV-positive patients compared to HIV-negative patients ($P<0.001$). And, cutaneous manifestation among HIV-positive patients increased with advancing stage of HIV infection ($P=0.02$). In addition, generalized hyperpigmented post-inflammatory macules were significantly more common among HIV-positive compared to HIV-negative patients ($P<0.01$). Using blood samples from Tanzanian adults, the Medmira rapid HIV test was found to have 97% sensitivity and 34.4% specificity.

From this study it can be concluded that scabies, is rare in HIV infected adults as well among adult patients without HIV infection admitted to medical wards at MMC. It can also be concluded that the odds of getting a skin disease is higher among HIV-infected adult patients than those without HIV infection and it increases with increasing clinical stage of HIV infection. Furthermore, generalized hyperpigmented post inflammatory

macules were found to be associated with HIV infection. The current study also suggests that using blood samples from Tanzanian adults, the MedMira rapid HIV test is highly sensitive but less specific.

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