THE PATTERN OF MUCOCUTANEOUS DISORDERS IN HIV INFECTED CHILDREN ATTENDING CARE AND TREATMENT CENTRES IN DAR ES SALAAM

By

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation titled: ***The Pattern of Mucocutaneous Disorders in HIV Infected Children Attending Care and Treatment Centres in Dar es Salaam***, in partial fulfilment of the requirements for the degree of Master of Medicine (Paediatrics and Child Health).

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DECLARATION AND COPYRIGHT

I **Milembe F. Panya**, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature 

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Last but not least, thanks to the almighty GOD for making this possible. Glory, praise and honour to his name. AMEN.

DEDICATION

To my parents Mzee Panya and Nyamate.

My brothers Ipilinga and Senema.

My sisters Yande, Hoka and Mwalu.

My nieces Bhoke, Minza, Neema.

My nephew Panya Junior.

ABSTRACT

Background

Human Immunodeficiency Virus (HIV) infects millions of people worldwide. It causes severe immunodeficiency resulting in a greater susceptibility to infections, inflammatory disorders and tumorous conditions. HIV/AIDS is associated with a wide range of mucocutaneous disorders, some of which are used in staging of the disease. Patterns of mucocutaneous disorders in children could be modified by the various drugs the patient is taking, especially the Antiretrovirals (ARVs). There is lack of information about the magnitude of the problem in Dar es Salaam.

Objective

To determine the pattern of mucocutaneous disorders in HIV infected children aged 0 to 17 years attending Care and Treatment Centres (CTC) at Muhimbili National Hospital (MNH) and the Municipal Hospitals in Dar es Salaam.

Study design and Setting

Cross sectional descriptive study at CTCs at MNH and the three Municipal Hospitals in Dar es Salaam; Ilala, Temeke and Mwananyamala.

Methodology

Data was collected using a structured questionnaire. A complete dermatological examination was carried out in daylight. Investigations such as skin biopsy, skin scrapings and CD4+ count were taken. Data was analysed using Statistical Package for Social Science (SPSS) program version 10.0. Chi-square and Fisher exact statistical test were used to determine association between variables and p-value of less than or equal to 0.05 was considered statistically significant.

Results

A total of 347 children were recruited into the study, of these 52% were males and 48% were females. Mucocutaneous disorders were found in 294 (85%) HIV infected children. There was no gender difference in the occurrence of mucocutaneous disorders except for non infectious inflammatory dermatoses in which males were more affected (p=0.02). The most frequently encountered dermatoses were infections followed by non infectious inflammatory dermatoses. All types of mucocutaneous disorders were more prevalent in advanced stage of the disease. Children with severe immunosupression had significantly increased viral and fungal cutaneous infections (p=0.01). Most children (75%) with mucocutaneous disorders were using ART. However, there was no statistical significant in the distribution of types of mucocutaneous disorders between those on ART and those not on ART.

Conclusion and Recommendation

Mucocutaneous disorders are common in HIV infected children despite the use of ART. These disorders are more common when HIV infection advances and the immune function deteriorate. Therefore, comprehensive care and management of HIV infected children should emphasize on mucocutaneous disorders. Health care providers need to be on the look to identify various types of mucocutaneous disorders, as they may be a pointer of HIV infection as well as an indication of advanced disease.

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ARV	Anti-Retroviral
ART	Anti-Retroviral Therapy
CDC	Centres for Disease Control and Prevention
CTC	Care and Treatment Centre
DPX	Dextrene Polystyrene Xylene
ELISA	Enzyme Linked Immunosorbent Assay
HAART	Highly Active Anti-Retroviral Therapyay
HAART	Highly Active Anti-retroviral Therapy
HHV	Human Herpes Virus
HIV	Human Immunodeficiency Virus
ILDS	International League of Dermatological Societies
IRD	Immune Restorative Disease
KOH	Potassium Hydroxide
KS	Kaposis Sarcoma
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
PCR	Polymerase Chain Reaction
PPE	PruriticPapular Eruption
TMP/SMZ	Trimethoprim/Sulphamethoxazole
UNAIDS	United National Joint Programme on HIV/AIDS
WHO	World Health Organisation

DEFINITION OF TERMS

HIV infected children defined as those children aged 17 years and below who have a positive test for HIV antibodies and / or a positive HIV DNA PCR.

Macule: a flat lesion usually circumscribed with a change in colour and less than 1 cm in diameter.

Papule: a small, elevated lesion above the surface of the skin less than 1cm in diameter.

Nodule: a small, solid, palpable and elevated above the skin with mirror image in duration below the skin.

Plaque: a lesion slightly raised over a large area (larger than 1cm in diameter).

Blister: an elevated papule or plague containing fluid.

Ulcer: a depressed lesion with loss of surface epithelium.

Scale: flakes of stratum corneum that has become visible as flaking or peeling skin often on an erythematous papule.

Crust: a mixture of scale and serum, yellowish secretion on the surface of a lesion.

Pustule: an elevated papule containing pus.

1.0 INTRODUCTION AND LITERATURE REVIEW

1.1 HIV and AIDS

Human Immunodeficiency Virus (HIV) belongs to the Lentivirinae sub family of retroviruses. The infection causes predominantly severe immunodeficiency characterized by depletion of helper T lymphocytes (CD4+ cells).[1] This results in a greater susceptibility to infections, non infectious inflammatory dermatoses and malignant conditions.[1, 2]

Disease due to Human Immunodeficiency Virus (HIV) was unknown until the early 1980's when previously healthy individuals presented with generalized lymphadenopathy and/or Kaposi's sarcoma.[2] Since then HIV has infected millions of people worldwide which has already resulted in the death of over half of its victim.[3]
By the end of 2006 UNAIDS (United National Joint Programme on HIV/AIDS) estimated that about 39.5 (34.1 - 47.1) million people were living with HIV/AIDS in the world; of these 1.7 - 3.5 million were children under the age of 15 years. Sub Saharan Africa is the region most affected by the HIV/AIDS pandemic; where 24.7 (21.8 - 27.7) million (63%) people with HIV live. Children and adolescents have higher prevalence of the infection. [4]

In Tanzania the prevalence of HIV infection in the general population is 6.4%-11.9%[5]. By the end of 2005 the number of adults and children living with the disease was estimated to be 1.4 (1.3 - 1.6) million, of these the number of children under the age of 15 years living with HIV/AIDS was estimated to be 85,000 – 230,000. [5]

In Dar es Salaam, Tanzania the prevalence of HIV infection among children admitted at Muhimbili National Hospital was found to be 19.2%, and the mortality rate among these infected children was 21.4%.[6]

The skin is the largest organ of the body. It has multiple functions including temperature regulation, fluid balance, sensation, immunological, protection e.g. from ultraviolet light damage and expression of racial and sexual characteristics[7]
Mucocutaneous disorders in children are common both in HIV infected and non-HIV infected children. There is no single mucocutaneous disease in children that is pathognomonic of HIV infection. In early stages of the disease, most of the manifestations in HIV infected children cannot be distinguished from similar manifestations in non-HIV infected children except for the differences in the degree of severity, persistence and frequency of recurrence, atypical presentation and difficult in their response to treatment.[8, 9] Nonetheless pathological conditions of the skin are most frequently observed in HIV infected patients, which correlates well with depletion of CD4+ cells and may be the first signs of HIV related immunosupression.[7] Some authors have pointed out that as many as 90% of patients with HIV infection will have dermatological manifestations at some stage during the course of the disease.[10, 11] With progressive deterioration of the immune system, cutaneous infections become more specific and include organisms or disease patterns typically not seen in immunocompetent children. [12]

The cutaneous conditions are frequently related to the sequalae of impaired immunity, including opportunistic infections and neoplasm as well as dramatic

exacerbations of pre – existing normally benign dermatoses.[13] The most commonly reported dermatological manifestations in paediatric HIV/AIDS patients include infectious disease (fungal, bacteria, viral and parasitic), non- infectious inflammatory dermatoses, tumorous proliferation and other miscellaneous or non-specific cutaneous disorders. Conditions like oral hairy leukoplakia and Kaposi's sarcoma, which are frequently observed in adults, are quite rare among children.[14]

In adults the sequence of characteristic mucocutaneous manifestations occurring with deteriorating immune function has been well characterized. However, this is less clear in children.[15] Mucocutaneous disorders are present in almost all stages of the disease in children.[16] This fact has justified the inclusion of mucocutaneous manifestations of HIV infection in both adults and children in the Centres for Disease Control and prevention (CDC) staging system. [17, 18]

The most important markers used in the follow-up of clinical progression to AIDS are CD4 + T cells counts, plasma viral load and viral phenotype.[1, 19] Studies in children have not addressed the relationship between mucocutaneous manifestations and virological, immunological markers and the impact of antiretroviral therapies.[7] Immune reconstitution with Anti-Retroviral Therapy (ART) significantly reduces the prevalence of many dermatological diseases. It causes profound suppression of viral replication with consequent increase in CD4+ T cell lymphocyte but on the other hand has associated cutaneous side effects.[7, 20]

Children, unlike adults have an immature immune system.[21, 22] They have higher CD4 + T cells count than adults because they have lymphocytosis at birth. [23, 24] Children also have higher viral load levels which leads to both severe cellular and humoral immune deficiency with greater susceptibility to various infectious,

inflammatory diseases and tumorous conditions.[7, 12] The normal value of the absolute CD4+T lymphocyte count is relatively higher in normal infants and declines steadily until they reach six years of age, while the CD4 percentage of the total lymphocyte count remains constant. The immunological categories according to the 1994 revised paediatric human immunodeficiency (HIV) classification based on CD4+ percentage of the total lymphocyte count is classified into three categories; no evidence of suppression (CD4 T-lymphocytes >25%), moderate suppression (CD4 T-lymphocytes 15-24%) and severe suppression (CD4 T-lymphocytes 1-14%) .[18]

A study was done in Madrid Spain to assess the role of antiretroviral therapies in mucocutaneous manifestations in different treatment periods. Mucocutaneous disorders were diagnosed in 119/210 (56.7%) of HIV infected children, 17% in untreated children. Among children receiving anti-retroviral drugs at different treatment periods, 22% in the monotherapy period, 25% in the combined therapy period and 10% in the HAART (Highly Active Antiretroviral Therapy) period had some type of mucocutaneous manifestations. Mucocutaneous disorders of infectious aetiology were observed most frequently. They were detected in 13% of the children during the first calendar period when no treatment was offered, 16% during the second (monotherapy) and third (combined therapy) periods and only 5% in the last period (HAART period). [7] Fungi, mainly *candida albicans* caused the most frequent infections. Oral candidosis was the most prevalent mucocutaneous disorder present in 78% of the affected children. Among the viral infections, *varicella zoster* infected 42%, *molluscum contagiosusm* 14% and *herpes simplex* 4%. Low incidence of bacterial infections was observed. Exanthema of various aetiologies, infections or

secondary to drugs affected 36%. Seborrhoeic dermatitis appeared in 20% whereas atopic dermatitis was observed in 13% and leiomyosarcoma was observed in one child. [7]

A study done in Bangkok, Thailand where 120 HIV infected children were prospectively examined, showed a significant increase in the prevalence of mucocutaneous disorders in those with moderate to severe immunosupression.[25] The prevalence of mucocutaneous manifestations was 52%. The prevalence among those with severe, moderate and no immunosuppression was 62%, 43% and 20% respectively. The prevalence of mucocutaneous disorders increased as the CD4 + percentage of the total lymphocyte count decreased.[25]

Infection was the most common mucocutaneous manifestation found in 50% of patients. Fungal, viral and bacterial infections were found in 44%, 10% and 8% respectively. Oral candidosis was the most common manifestation in 33% of patients. In the non-infectious group, pruritic papular eruption of HIV/AIDS (PPE of HIV/AIDS) was the most common (63%). Seborrheic dermatitis was found in four patients. Drug rash caused by cotrimoxazole was found in three patients and in one, it was caused by ampicillin. [25]

Studies to look into clinical manifestations of HIV infected children in Africa found skin disorders to be prevalent. In Nigeria, it was found that 37% of the 63 children studied had a form of skin manifestations.[26] In Ethiopia, 46.1% of the 89 HIV infected children had skin manifestations. [27]

Studies carried out in Tanzania looking into cutaneous manifestation of HIV infection have been done mainly in adults and have shown increased prevalence of mucocutaneous disorders in HIV infected individuals. A study done on Kaposi's Sarcoma (KS) before and during HIV epidemic found a significant increase in disseminated KS during the AIDS epidemic and that children younger than five years were at high risk of developing KS, possibly reflecting low resistance to human herpes virus (HHV) type 8 infection. It is also likely that an increased susceptibility to HHV8 infection and morbidity is related to progressive immunodeficiency. The increase in HIV-related paediatric KS appears to reflect a direct or indirect promoting effect of HIV on the development of KS lesion. [28]

1.2 Mucocutaneous Disorders

1.2.1 Infectious Dermatoses

1.2.1.1 Fungal Infections

Yeast Infections

Candida infection usually due to *Candida albicans* is the most common and often the first manifestation of paediatric HIV infection. Oral thrush and recalcitrant monilial diaper dermatitis are the most common mucocutaneous manifestations of HIV infection in children. Clinically, oral candidosis manifests with white, curd-like material that on being scraped off reveals an erythematous mucosa. Angular chelitis, fissuring, maceration and erythema of the corners of the mouth may accompany the thrush.[14, 29, 30]

Children may also present with severe napkin dermatitis (diaper rash) due to *Candida albicans*, which may present as a rash, that is slightly raised, which can involve the skin fold and often shows satellite lesions outside the affected area.[15, 27] Pityriasis versicolor (formally incorrectly referred to as tinea versicolor) is caused by *Mallasezia furfur*. It presents as hypo pigmented macular lesions often on the shoulders, neck and face.[14, 29, 30]

Dermatophyte Infections

HIV infected children may become infected with any of the three dermatophyte genera (Trichophyton, Epidermophyton and Microsporon), which may lead to severe or widespread tinea corporis, tinea capitis or tinea unguim.[14, 29, 30]

Tinea corporis presents as a single or multiple scaly oval patches on the trunk that are often hyper pigmented with raised margins.[14, 29, 30]

Tinea capitis can present as an area of flaking within the scalp, with or without hair loss or a weeping or crusting lesion (kerion). It can also present as a diffuse flaking throughout the scalp. Children may also present with more severe inflammatory lesions, which may be complicated with golden crusts on the surface of the scalp. Tinea unguium (Onychomycosis) is a dermatophytic infection of nails. It usually presents as yellow, darkened, thickened or pitted nails.[14, 28, 30]

Diagnosis is mainly clinical, but can be verified by 10% potassium hydroxide (KOH) preparation of skin scraping or nail clipping or fungal culture. HIV infected children

are also at risk of infection with atypical fungi that tend to be dependent on the fungal species endemic in the country where the child lives. [14, 29]

1.2.1.2 Viral Infections

Molluscum contagiosum is a common childhood infection caused by a poxvirus called *Molluscum contagiosum* virus. It may occur even without the presence of severe CD4+ cell depletion. It manifests as umbilicated flesh coloured shiny papules of 2-3 mm in diameter. The papules contain creamy- cheese like material often on the face, shoulder or back. They tend to be more widely spread, confluent, larger and persistent in HIV infected children and may cause considerable disfigurement. It occurs in approximately 10 to 20% of HIV infected individuals.[14, 29, 30]

Extensive cutaneous molluscum contagiosum is a cutaneous marker of advanced HIV disease. Diagnosis is made based on typical clinical presentation. Direct microscopic examination of unstained curreted lesion crashed on a slide also establishes the diagnosis. Diagnosis can be confirmed histologically or by electron microscopy.[14, 29, 30]

Herpes simplex infection may manifest with extensive, recurrent ulcerated lesions on the mouth, nose, lips and perianal areas. Children may also present with acute herpetic gingivostomatitis associated with high fever, malaise and dehydration. In HIV infected children the virus can be persistent and recurrent presenting as crusting erosion of the lips, gums and tongue. Vesicular and ulcerative lesions of the fingers can also occur. Diagnosis is made on the basis of clinical presentation. [14, 29, 30]

Varicella zoster virus is a causative agent for chicken pox and herpes zoster (shingles). Chicken pox presents as vesicular and ulcerative lesions all over the child's body in multiple different stages. Herpes zoster is a relatively rare disease in immunocompetent children. It presents with painful or pruritic-blistering lesions, usually in a single dermatome on one side of the body. At time of presentation may look more ulcerative and occasionally in severe immunosuppressed children, multiple dermatomes and/or both sides of the body may be affected.[14, 29, 30]

Diagnosis of Herpes zoster is mainly clinical, but culture or immunoflourescent antibody test can be done if the diagnosis is uncertain. [14, 29]

Viral warts caused by *Human papilloma* virus are also more common in HIV infected children. These may be common warts presenting as hyperkeratotic papules on the fingers or flat plane warts. They are commonly, seen on the face, neck and hands. They may be quite extensive presenting with hypo pigmented or hyper-pigmented macules which may become confluent when extensive.[14, 27, 28] Anogenital warts (condylomata acuminata) may be huge and extensive in HIV infected children and are resistant to treatment. Diagnosis is clinical and can be confirmed by whitening of the mucosa when acetic acid is applied. [14, 29, 30]

1.2.1.3 Bacterial Infections

Paediatric HIV infection is associated with high prevalence of pyogenic infections. Cutaneous bacterial manifestations include impetigo, ecthyma, folliculitis, abscesses and cellulitis. The common causative organism is *Staphylococcus aures.* This is

probably secondary to the high rate of nasal carriage in HIV positive children. Less frequently implicated organism includes streptococcus, pseudomonas and rarely atypical Mycobacterium.[14] Characteristically present with redness, pustules, blisters and abscess. [29, 30]

1.2.2 Infestations

Infestation with *Sarcoptes scabiei* that causes scabies is common in immunocompetent children. Atypical and severe forms of scabies may accompany HIV infection. There may be vesicles, itchy papules and excoriations all over the body. Burrows may be seen in the classic sites such as the wrists, web spaces, feet, ankles, axillae and genitalia. The lesions may somehow be disguised by self-inflicted scratch marks. Patients may also present with a crusted form of scabies known as Norwegian scabies. Presenting with widespread eczematous eruption, no characteristic papules and burrows and may easily go undiagnosed. It is associated with huge number of mites. Diagnosis is clinical supported by opening of the burrows and looking for mites. [14, 29, 30]

1.2.3 Non Infectious Inflammatory Dermatoses

Seborrhoeic Dermatitis

Seborrhoeic dermatitis is seen in a high percentage of adults and children with HIV infection up to 85%. Severe form of the disease has been noted in children. It may present at any CD4+ cell count but usually becomes extensive and refractory as CD4+ cell count declines. ART therapy has decreased the number of refractory cases. HIV related seborrheic dermatitis occurs predominantly on the scalp, usually

with mild involvement on the face (particularly in the eye brows, around the eyelashes, down the nasolabial folds and in and around the ears). The chest and genital organs might be involved as well. It presents as yellow-white greasy scales on erythematous patches. Diagnosis is mainly clinical. [14, 28, 30]

Psoriasis

This is primarily an inflammatory skin disease of acute exanthematic or chronic stationary course. The skin lesions are red, sharply delimited plaques of various shapes, with characteristic silvery lustrous scaling. The erythematous changes can be restricted to a few patches, confluent over a large area or occasionally universal in occurrence. It has a familiar tendency. The first appearance of psoriasis has often been described following an acute disease such as streptococcal infection in the upper respiratory tract (Acute tonsillitis or bronchitis). HIV infection can also provoke Psoriasis. It can affect almost the entire body from the scalp to nails. Diagnosis is mainly clinical.[31]

Napkin Dermatitis

Napkin dermatitis (also known as Ammonical dermatitis) is very commonly seen in HIV infected babies. This is usually an irritant dermatitis caused by ammonia due to continuous contact with faeces and urine as a result of the chronic diarrhoea. Seborrhoeic dermatitis and candida infection also play a role in napkin dermatitis, the latter may present with typical satellite lesions around the irregular border of the affected area. [14, 29, 30]

Pruritic Papular Eruption of HIV/AIDS

Papular pruritic eruption (PPE) is a common manifestation of HIV in Africa, in both adults and children. It is characterised by multiple, chronic, pruritic, hyper-pigmented and hypo pigmented lesions. They can either be follicular and non-follicular, macules and papules distributed symmetrically on the trunk and extremities. The primary lesion is an erythematous discrete pruritic papule, which once excoriated leads to chronic hyper-pigmented papule with scars [14, 29]. The exact aetiology of PPE is unknown. The distribution of lesions could probably represent interplay between the effect of gravity, sun exposure and vulnerability of these areas to bites by insects like mosquitoes. Such insect bites could be responsible for initiation of an allergic phenomenon with formation of immune complexes whose deposition could be determined by forces of gravity and the ultimate manifestation as PPE of HIV/AIDS being influenced by the effects of sunlight. [32, 33] PPE has been found to be an AIDS defining illness in the majority of individuals. [33] PPE is primarily a clinical diagnosis, but on histology mixed perivascular lymphocytic infiltrate with eosinophils can be seen. [14, 29, 30]

Atopic Dermatitis (Eczema)

This is a chronic disorder characterized by severe itching with scratch marks, eczematous papulovesicular lesions with crusting and pruriginous papules, nodules and lichenification. In early childhood, exudative eczematous lesions usually predominate, whereas at school age and in adult life pruritus, pruriginous linchenoid papule and lichenification are prominent. The site of predilection for the lesions varies depending on the age of the affected individual. In neonates the sides of the

cheeks and the scalp are mostly affected. In childhood the sites commonly affected are large joint flexures and the nape of the neck, dorsum of the feet and hands. In adolescents skin lesions are symmetrical, mostly on the face (forehead, eyelids, and perioral region), upper chest and shoulder girdle, large joint flexure and backs of hands. [30, 31]

The disease tends to run in families or the affected individuals themselves have other atopic disorders. HIV infected children may present with severe and generalized eczematous eruptions in the absence of a clear family history of atopy. [14]

1.2.4 Neoplasms

Kaposi's sarcoma, lymphoma and other cutaneous malignancies are rarely seen in HIV infected children. Kaposis sarcoma was the first reported malignancy associated with HIV infection. The worldwide prevalence of KS in patients with HIV/AIDS approaches 35%. It begins, as pink macules that become nodular, mucosal involvement are common. The clinical progression of KS patients infected with HIV is more aggressive than the other clinical types of KS. [7, 14, 30]

1.2.5 Miscellaneous Cutaneous Conditions

Drug Reactions

Pharmacological drug reactions are more common in HIV infected children than in the general population. The incidence of reaction to drugs increases in proportion to the degree of the host's level of immune dysfunction.[33] The most common causes of drug-induced rashes are antibiotics and ARV drugs. Among antimicrobial, drug

reactions resulting from Trimethoprim/Suphamethoxazole (TMP/SMZ) are relatively common although they are much less common in HIV infected children than adults. Although skin reactions are fairly common with ARV drugs, the most serious drug reactions that may be life threatening have been ascribed to nevirapine, abacavir, amprenavir and lopinavir/ritonavir (kaletra). [29, 30]

In many cases of AIDS, iatrogenic cutaneous disorders associated with toxic or allergic drug reactions are seen. With therapeutic prolongation of survival, certain cutaneous manifestations (especially drug reactions) are likely to become more common. [14]

Most common presentation is morbilliform rash, less common is diffuse redness, papule or targeitoid lesions and rarely blisters and skin desquamation. Stevens-Johnson syndrome and toxic epidermal necrolysis may occur.[14, 29]

In this era of ART exacerbation of opportunistic infection in HIV infected patients shortly after initiation of highly active antiretroviral therapy is common. This has been named immune restorative disease (IRD) or syndrome (IRIS). This can present as mucocutaneous manifestation such as herpes zoster (HZ). The risks of developing HZ include absence of protective varicella specific antibody despite previous varicella infection. Patients with severe immunodeficiency at baseline and vigorous immunological and biological response to ART are also at increased risk. [34] However, there are few reports on how antiretroviral therapy affects the skin in HIV infected children. [7]

2.0 PROBLEM STATEMENT AND RATIONALE

2.1 Problem Statement

HIV/AIDS is a major cause of infant and childhood morbidity and mortality. In children under five years of age HIV/AIDS now accounts for 7.7% of mortality worldwide. AIDS already accounts for a rise of more than 19% in infant mortality and a 36% rise in under five mortality. [16] Disorders of the skin were among the main features of the acquired immune deficiency syndrome (AIDS) in the initial description of the disease.[13] Most patients with HIV/AIDS develop mucocutaneous disorders at some stage during the course of the disease. In some cases, mucocutaneous disorders may lead to the diagnosis of HIV infection. With increasing HIV infection, dermatological conditions are also on the increase. Mucocutaneous disorders related to HIV infection are polymorphous and can be classified as infectious diseases (fungal, bacterial, viral, parasitic), either directly related to HIV or secondary to the resulting immunodeficiency. Other disorders are non infectious inflammatory dermatoses (seborrheic dermatitis, PPE, atopic dermatitis, psoriasis etc) and tumorous proliferation. With the increasing availability and access to ARVs, manifestations of various diseases are likely going to be different and the skin is no exception. Familiarity with the various dermatological presentations of paediatric HIV/AIDS is important for earlier diagnosis and treatment of the disease and hopefully, the prolongation of patient's life.

However, many clinicians are unfamiliar with the various dermatological and changing presentations of paediatric HIV/AIDS. In the current situation where there is an increased ability to diagnose, monitor and prevent disease progression, it is important that the clinicians are able to identify undiagnosed children with HIV. An

increased awareness of the varied clinical presentation of mucocutaneous disorders may serve this goal.

Early diagnosis and treatment protocols have been based on data extrapolated from adult studies. Researches into paediatric specific aspects of HIV are needed to improve the ability of clinicians to make rational diagnostic and management decisions regarding HIV infected children.

2.2 Rationale of the Study

There are number of studies in the world on mucocutaneous disorders in HIV infected children but not as yet for Tanzania. In fact there has been little information documenting paediatric dermatological disorders in Tanzania. No studies have been done to describe the mucocutaneous disorders in HIV infected children.

Given the lack of data on the prevalence of mucocutaneous disorders in HIV infected children in Dar es Salaam and Tanzania as a whole, it was necessary to undertake a study that will address this deficiency, a study that will also provide baseline data for future studies.

The study aimed at describing mucocutaneous disorders in HIV infected children. This will help to familiarize clinicians with the various dermatological and changing presentations of paediatric HIV/AIDS and to equip the clinicians with information and knowledge on the problem. This will help improve the best care possible for HIV infected children.

3.0 OBJECTIVES

3.1 Broad Objective

To describe the patterns of mucocutaneous disorders in HIV infected children attending Care and Treatment Centres at Muhimbili National Hospital (MNH) and Municipal Hospitals in Dar es Salaam.

3.2 Specific Objectives

1. To determine the prevalence of mucocutaneous disorders in HIV infected children by age and sex.
2. To determine the prevalence of mucocutaneous disorders in HIV infected children by WHO clinical staging and level of immunosupression.
3. To determine the distribution of types of mucocutaneous disorders in HIV infected children by age and sex.
4. To determine the distribution of types of mucocutaneous disorders in relation to level of immunosupression and WHO clinical stage in HIV infected children.
5. To compare the distribution of types of mucocutaneous disorders among HIV infected children on ART and those not on ART.

4.0 METHODOLOGY

4.1 Study Design

A descriptive cross sectional hospital based study.

4.2 Study Area

The study was conducted at the paediatric HIV Care and Treatment Centre (CTC), Muhimbili National Hospital and the municipal Hospitals CTCs (Temeke, Amana and Mwananyamala) in the city of Dar es Salaam. The city has four government hospitals, one being the Muhimbili National Hospital (MNH) and the three Municipal Hospitals. Muhimbili is one of the four tertiary hospitals in the country and it serves as a referral hospital from the municipal hospitals in Dar es Salaam and from other regions in the country. It also serves as a University teaching hospital for the Muhimbili University of Health and Allied Sciences (MUHAS). The municipal hospitals are public and serve the respective municipals/districts i.e. Temeke (Temeke), Amana (Ilala) and Mwananyamala (Kinondoni). Dar es Salaam has a population of about 2.5 million people with children under 15 years accounting for 32.8% of the whole population. Kinondoni municipal is the most populated district (1,088,862 people) followed by Temeke (771,500 people) and Ilala (637,573 people).[35]

4.3 Study Population

All HIV infected children aged 0- 17 years inclusive attending HIV Care and Treatment Centres at Muhimbili National Hospital and the three Municipal hospitals.

4.3.1 Inclusion Criteria

The inclusion criteria were:

-Children who were already confirmed to have HIV infection.

-Children aged 0- 17 years inclusive.

-Children whose parents/guardians gave informed consent to participate in the study.

4.3.2 Exclusion Criteria

-Unwillingness of the parent/guardian to participate in the study.

4.4 Study Duration

The duration of the study was twelve weeks between April and July 2006.

4.5 Sample Size Estimation

The sample size was calculated from the following formula,

$$N = \frac{4\,p\,(100-p)}{\varepsilon^2}$$

Where

N = sample size

P = prevalence (52%). The prevalence of mucocutaneous manifestations of HIV in 91 children born to HIV-seropositive women in Thailand.[38]

ε = marginal error (6%)

Therefore the minimum sample size was 277 children.

4.6 Sampling Technique

Sampling proportional to size technique was used. The number of children to be included from each clinic depended on the predetermined number of children attending the centre. The centre with a large number of children was represented by a larger number than those with a fewer in number. A sampling fraction of 24% was used to determine the minimum number of children at each hospital. At Muhimbili National Hospital 120 children were recruited. Ninety, 75 and 62 children were recruited from Mwananyamala, Temeke and Ilala hospitals respectively. Patients attending these Centres and meeting the inclusion criteria were enrolled consecutively until the required sample size was obtained. An average of 6-10 patients was recruited per day. A sticker was put on a file to avoid a repeated recruitment.

4.7 Data Collection and Instrument Used

4.7.1 Clinical work - up

Recruitment was done daily from Monday to Friday starting at 9am to 3pm.

A structured questionnaire designed for the purpose of the study was used to obtain the relevant information (Appendix i). HIV status was confirmed from patients file.

A complete dermatological examination of the scalp, face, mouth, neck, trunk, genitalia and extremities was carried in daylight. The main morphological features and the distribution of the lesions were recorded. Lesions were described according to the nomenclature committee of the International League of Dermatological Societies (ILDS) as macule, papule, nodule, plaque, blister, ulcer, scale and crust (Appendix ii).

Diagnosis of most conditions was done clinically and where necessary skin scrapings and skin biopsies were done for confirmation of the diagnosis. Patient's files were used to get the information about the HIV status. Photographs of striking conditions were taken whenever appropriate and a discussion with a dermatologist was done.

4.7.2 Laboratory Investigations

Skin Scraping

Skin scraping of lesions suspected to be scabies was done by using a blunt side of a surgical blade on the burrows. The scrapings were put on a glass slide that had a drop of mineral oil; a cover slip was applied on top and then examined under low power microscope for presence of mites.

Skin Biopsy

Skin biopsy was done on lesions suspected to be malignant to establish histological diagnosis. The site chosen represented both the pathological part and the normal tissue for comparison. Local anaesthesia (2% lignocane) was injected around the lesion and incisional or wedge biopsy was done according to the presentation of the lesion using a sharp scalpel. Specimen was immediately placed in the bottle containing fixative 10% buffered formalin in the volume ratio of 1:10 (tissue: fixative). The specimen was then submitted to the histopathology laboratory for processing. The tissue sections were stained by Haematoxylin and Eosin and mounted on Dextrene Polystyrene Xylene (DPX) and then examined under microscope.

CD_4+ T cell Count Determination

Lymphocytes subsets were determined using a FACS calibur (Becton-Dickinson USA 2005). About 2-3 mls of whole blood was collected and put in sterile ethylene diamine tetra –acetic acid (EDTA) tube mixed well and sent to laboratory for analysis by flow cytometry. Interpretations of the results were done according to CDC immunologic classification for HIV infected infants and children (Appendix iv). For children above 12 years the immunological classification of adults and adolescents was used. Those with CD4+ cell counts of more than 350 were taken as having no evidence of immunosupression. While those with counts of 200-350 and less than 200 were taken as having moderate and severe immunosupression respectively.

4.8 Ethical Issues/ Consideration

Objectives and details of the study were explained to the parents/guardians before they gave their consents. Patients were managed according to the National guidelines for management of HIV infection. Children found to have mucocutaneous disorders were treated according to the HIV CTC protocol. Patients meeting the criteria for starting ARVs and were not on ARVs were started according to the available regimen at the centres.

4.9 Ethical Clearance

Ethical clearance to carry out this study was obtained from the Research and Publication Committee of the Muhimbili University of Health and Allied Sciences.

4.10 Data Management and Analysis

Data was entered into a computer, cleaned to ensure accuracy of all entries and was analysed using Statistical Package for Social Science (SPSS) program version 10.0.[36] Results were presented using cross tabulation tables and figures of illustrative coloured photographs. Chi square statistical test was used to determine association between categorical variables and Fisher exact test was used when the number was less than 5. P-value of less than or equal to 0.05 was considered statistically significant.

5.0 RESULTS

This study recruited a total of 347 HIV infected children who were attending Care and Treatment Centres for HIV/AIDS in Dar es Salaam. Of these 180 (52%) were males and 167 (48%) were females. The male to female ratio was almost 1:1 (1:0.9). The age ranged from six months to sixteen years with a mean age of 7.8 years (SD $\pm$ 3.8) years. About 45% (77/347) of the children were in the age group of 6-10 years and the age group with fewer patients 12/347 (3.4%) was those above 15 years (Table 1).

Table 1: Distribution of HIV infected children attending HIV CTC by age and sex. n=347

Age group (years)	Males n (%)	Females n (%)	Total n (%)
0-5	61 (33.9)	44 (26.3)	105 (30.3)
6-10	77 (42.8)	78 (46.7)	155 (44.7)
11-15	36 (20.0)	39 (23.4)	75 (21.6)
>15	6 (3.3)	6 (3.6)	12 (3.4)
Total	180 (51.9)	167 (48.1)	347 (100)

Of the 347 children with HIV infection attending HIV CTCs, 294 (84.7%) were found to have mucocutaneous disorders. Overall, mucocutaneous disorders were found in 156/180 (86.7%) males and 138/167 (82.6%) females and the difference was not statistically significant (p=0.29) (Table 2).

Children aged 5 years and below had a highest prevalence of mucocutaneous disorders, 92/105 (87.6%). This was followed by those aged between 6 and 10 years, 130/155 (83.9%). Children aged between 11 and 15 years had the lowest prevalence of mucocutaneous disorders, 62/75 (82.7%). However, the difference in the prevalence of mucocutaneous disorders between the age group was not statistically significant (p=0.59) (Table 2).

Table 2: Prevalence of mucocutaneous disorders among HIV infected children in relation to age and sex.

Characteristic	Total patients	Patients with mucocutaneous disorders	p-value
	n=347 (%)	n=294 (%)	
SEX			0.29
Male	180 (51.9)	156 (86.7)	
Female	167 (48.1)	138 (82.3)	
AGE (years)			0.59
0-5	105 (30.3)	92 (87.6)	
6-10	155 (44.7)	130 (83.9)	
11-15	75 (21.6)	62 (82.7)	
>15	12 (3.4)	10 (83.3)	

When considering patients in different HIV stages, the prevalence of mucocutaneous disorders was highest in children in the WHO paediatric stage 4, 10/10 (100%), followed by those in stage 3, 166/177 (93.8%). Children in WHO paediatric stage 1 had the lowest prevalence 2/7 (28.6%). The difference in the occurrence of mucocutaneous disorders in relation to WHO paediatric staging was statistically significant ($p<0.01$) (Table 3).

Likewise children with severe immunosupression had the highest prevalence of mucocutaneous disorders, 111/114 (97.4%), followed by those with moderate immunosupression 109/129 (84.5%). Children with no evidence of immunosupression had the lowest prevalence of mucocutaneous disorders, 74/104 (71.2%). The difference in the prevalence of mucocutaneous disorders in relation to level of immunosupression was statistically significant ($p<0.01$) (Table 3).

Table 3: Prevalence of mucocutaneous disorders among HIV infected children by disease progression.

Characteristic	Total patients	Patients with mucocutaneous disorders	p-value
	n=347 (%)	n=294(%)	
WHO PAEDIATRIC STAGE			<0.01
1	7 (2.0)	2 (28.9)	
2	153 (44.1)	116 (75.6)	
3	177 (51.0)	166 (93.8)	
4	10 (2.9)	10 (100)	
LEVEL OF IMMUNOSUPRESSION			<0.01
No evidence	104 (29.9)	74 (71.2)	
Moderate	129 (37.2)	109 (84.5)	
Severe	114 (32.9)	111 (97.4)	

A wide range of mucocutaneous conditions were seen as shown in table 4. Non infectious inflammatory dermatoses were the most frequently encountered conditions occurring in 63% (186/294). PPE of HIV/AIDS was found in 123/294 (41.8%) patients, followed by atopic dermatitis 31/294 (10.5%) and seborrheic dermatitis 24/294 (8.2%). Other non infectious inflammatory dermatoses encountered were purpular urticaria 10/294 (3.4%), non specific dermatitis 10/294 (3.4%) and prurigo nodularis chronicus which was found in one child (Table 4).

Fungal mucocutaneous infections were found among 118/294 (40.1%) patients. The most prevalent condition was Tinea capitis 47/294 (15.9%), followed by Tinea unguim 31/294 (10.5%) and Tinea corporis 28/294 (9.5%). The least encountered condition was Tinea cruris 1/294 (0.3 %) (Table 4).

Viral cutaneous infections were found in 68/294 (23.1%) patients. The most frequently encountered conditions were plane warts 58/294 (19.7%) followed by molluscum contagiosum 13/294 (4.4%). Herpes zoster and Herpes simples were found in 2/294 (0.7%) and 4/68 (1.4%) of HIV infected children respectively (Table 4).

A total of 36/294 HIV infected children had different forms of bacterial skin infections. Impetigo was the commonest, it was found in 28/294 (9.5%) followed by abscesses 6/294 (2.0%) and the least bacterial infection found was cellulitis 3/294 (1.0%) (Table 4).

Scabies was the only parasitic infestation found among 34/294 (11.6%) patients (Table 4).

Only one child was found to have Kaposis sarcoma (0.3%); he was 10 years old with stage 3 disease and had moderate immunosupression and had been on ART for a month.

Other miscellaneous mucocutaneous conditions found in 3/294 (1.0%) HIV infected children were hyper pigmentation of nails in two children (0.7%) and one child (0.3%) had Stevens-Johnson syndrome which was related to taking sulphur containing drug (Cotrimoxazole).

Table 4: Classification of mucocutaneous disorders in HIV infected children. n= 294

Mucocutaneous disorder	n	%
Non infectious inflammatory dermatoses	**186**	**63.3**
Pruritic papular eruption	123	41.8
Atopic dermatitis	31	10.5
Seborrheic dermatitis	24	8.2
Non specific dermatitis	10	3.4
Purpular urticaria	10	3.4
Prurigo nodularis chronicus	1	0.3
Infectious dermatoses		
Fungal	**118**	**40.1**
Tinea capitis	47	15.9
Tinea unguim	31	10.5
Tinea corporis	28	9.5
Pityriasis versicolor	11	3.7
Oral candidosis	11	3.7
Tinea cruris	1	0.3
Viral	**68**	**23.1**
Warts	58	19.7
Molluscun contagiosum	13	4.4
Herpes simplex	4	1.4
Herpes zoster	2	0.7
Bacterial	**36**	**12.2**
Impetigo	28	9.5
Abscess	6	2.0
Cellulitis	3	1.0
Infestations	**34**	**11.6**
Scabies	34	11.6
Neoplasm	**1**	**0.3**
Kaposis Sarcoma	1	0.3
Miscellaneous	**3**	**1.0**

The occurrence of various types of mucocutaneous disorders varied among age groups as shown in table 5. Non infectious inflammatory dermatoses were more prevalent in children aged more than 15 years 8/12 (66.7%). Children aged between 11 and 15 years had the lowest prevalence 38/75 (45.3%). There was no statistically significant difference in occurrence of non infectious inflammatory dermatoses among the age groups (p=0.71) (Table 5).

Fungal cutaneous infections were more prevalent in the older children 7/12 (58.3%), children aged 5 years and below were the least affected 21/105 (20%). The difference in the prevalence of fungal cutaneous infections between the age groups weredifference in the prevalence of fungal cutaneous infections between the age groups was statistically significant (p=0.01) (Table 5).

Viral cutaneous infections were also more prevalent in children aged 11 to 15 years 22/75 (29.3%). Those aged between 6 and 10 years were least affected 28/155 (14.1%). However, the difference was not statistically significant (p=0.35) (Table 5).

Bacterial cutaneous infections were more common 9/75 (12%) in the age group between 11 and 15 years, followed by those aged 6 to 10 years. There was no child above 15 years who had bacterial infection. However this finding was not statistically significant (p= 0.93) (Table 5).

Scabies was more prevalent in children aged more than 15 years 2/12 (16.7%) and the prevalence was lowest on those aged between 6 and 10 years 11/155 (7.1%). The difference was not statistically significant (p=0.25).

Table 5: Distribution of types of mucocutaneous disorders among HIV infected children by age.

MUCOCUTANEOUS DISORDER	AGE GROUP (years)				Total	p-value
	0-5 n=105 (%)	6-10 n=155 (%)	11-15 n=75 (%)	>15 n=12 (%)		
Inflammatory dermatoses	66 (62.9)	78 (50.3)	34 (45.3)	8 (66.7)	186	0.71
Fungal infections	21 (20.0)	60 (38.7)	30 (40.0)	7 (58.3)	118	0.01
Viral infections	15 (14.3)	28 (14.1)	22 (29.3)	3 (25.0)	68	0.35
Bacterial infection	10 (9.5)	17 (11.0)	9 (12.0)	0 (0.0)	36	0.93
Infestation (scabies)	14 (13.3)	11 (7.1)	7 (9.3)	2 (16.7)	34	0.25
Miscellaneous	1 (0.9)	0 (0.0)	2 (2.7)	0 (0.0)	3	0.76

Table 6 shows the distribution of various types of mucocutaneous disorders encountered in relation to sex. Of the 186 children with non infectious inflammatory dermatoses, 107/180 (59.4%) were males and 79/167 (47.3%) were females. Non infectious inflammatory dermatoses were significantly frequent in males compared to females and the difference was statistically significant (p=0.02) (Table 6).

In almost all types of mucocutaneous disorders males had the highest proportions except for fungal cutaneous infections where females were more affected 57/167 (34.1%) compared to males 61/180 (33.9%). However the difference was not statistically significant (Table 6).

Table 6: Distribution of types of mucocutaneous disorders among HIV infected children by sex.

MUCOCUTANEOUS DISORDER	MALE n=180 (%)	FEMALE n=167 (%)	Total	p-value
Bacterial infection	19 (10.6)	17 (10.2)	36	0.91
Fungal infections	61 (33.9)	57 (34.1)	118	0.96
Viral infections	39 (21.7)	29 (17.4)	68	0.31
Infestations (scabies)	19 (10.6)	15 (9.0)	34	0.62
Inflammatory dermatoses	107 (59.4)	79 (47.3)	186	0.02
Miscellaneous	2 (1.1)	1 (0.6)	3	0.94

All types of mucocutaneous disorders were more prevalent in advanced WHO paediatric stage, which is stage 3 and 4 combined (Table 7).

Non infectious inflammatory dermatoses were found more in children with advanced WHO paediatric stage 112/187 (59.9%) when compared to those in early stage which was 74/160 (46.3%) and the difference was statistically significant (p=0.01) (Table 7).

Cutaneous fungal infections were the second commonest mucocutaneous disorders encountered in 80/187 (42.8%) followed by viral infections 47/187 (25.1%). The occurrence of these two conditions in advanced WHO paediatric stage were statistically significant with p value of <0.01 and 0.01 respectively (Table 7).

In both advanced and early WHO paediatric stage the distribution of various types of mucocutaneous disorders followed the same trend, differing only in proportions. Non infectious inflammatory dermatoses were commonest in both stages followed by fungal infections, viral infections, bacterial infections and scabies in descending order (Table 7).

Table 7: Distribution of types of mucocutaneous disorders among HIV infected children in relation to WHO paediatric stage.

MUCOCUTANEOUS DISORDERS	WHO STAGE		p-value
	Early stage (1 and 2) n=160 (%)	Advanced stage (3 and 4) n=187 (%)	
Inflammatory dermatoses	74 (46.3)	112 (59.9)	0.01
Fungal infections	38 (23.8)	80 (42.8)	<0.01
Viral infections	21 (13.1)	47 (25.1)	0.01
Bacterial infections	13 (8.1)	23 (12.3)	0.22
Infestation (scabies)	11 (6.9)	23 (12.3)	0.09
Miscellaneous	0 (0.0)	3 (1.6)	0.30

Table 8 shows the prevalence of various types of mucocutaneous disorders in different levels of immunosupression. Children with severe immunosupression had more of non infectious inflammatory dermatoses (64%), fungal infections (49.1%) as well as viral infections (30.7%). The distribution of the above three types of mucocutaneous disorders between the levels of immunosupression was statistically significant, (p - value of 0.02, 0.01 and 0.01 respectively).

Bacterial cutaneous infections were found more in children with moderate immunosupression 14/129 (10.9%), followed by those with severe immunosupression 12/114 (10.5%). The difference in the occurrence of bacterial cutaneous infections between the different levels of immunosupression was not statistically significant (p=0.95) (Table 8).

Table 8: Distribution of types of mucocutaneous disorders among HIV infected children in relations to level of immunosupression.

MUCOCUTANEOUS DISORDER	LEVEL OF IMMUNOSUPRESSION No evidence n=104 (%)	Moderate n=129 (%)	Severe n=114 (%)	Total 347	p-value
Inflammatory dermatoses	49 (47.1)	64 (49.6)	73 (64.0)	186	0.02
Fungal infections	27 (26.0)	35 (27.1)	56 (49.1)	118	0.01
Viral infections	7 (6.7)	26 (20.7)	35 (30.7)	68	0.01
Bacterial infections	10 (9.6)	14 (10.9)	12 (10.5)	36	0.95
Infestation (scabies)	7 (6.7)	11 (8.5)	16 (14.0)	34	0.16
Miscellaneous	0 (0.0)	2 (1.6)	1 (0.9)	3	0.91

Overall, 256/347 (73.8%) HIV infected children were on ART. Of the patients with mucocutaneous disorders 219/294 (74.5%) were on ATR. Majority of the patients were on first line ARV regime according to Tanzanian guidelines that is 35.2% were on Zidovudine, Lamivudine and Niverapine; 21.3% were on Stavudine, Lamivudine and Nevirapine and 10.7% were on Stavudine, Lamivudine and Efavirenz.

Children on ART had the highest proportions of bacterial and viral cutaneous infections and scabies. Children who were not on ART had the highest proportions of inflammatory dermatoses and fungal cutaneous infections. These differences were not statistically significant (Table 9).

Table 9: Distribution of types of mucocutaneous disorders among HIV infected children in relation to HAART use.

MUCOCUTANEOUS DISORDER	HAART USE		Total	p-value
	Yes n=219 (%)	No n= 75(%)		
Inflammatory dermatoses	136 (62.1)	50 (67.0)	186	0.48
Fungal infections	84 (38.4)	34 (45.3)	118	0.29
Viral infections	54 (24.7)	14 (18.7)	68	0.29
Bacterial infections	27 (12.3)	9 (12.0)	36	0.94
Infestation (scabies)	26 (11.9)	8 (10.7)	34	0.77
Miscellaneous	2 (0.9)	1 (1.3)	3	0.98

6.0 DISCUSSION

This was a cross sectional descriptive study addressing mucocutaneous disorders involving 347 HIV infected children. Patients with HIV/AIDS infection suffer from a wide range of mucocutaneous disorders, some of which correlate well with the degree of immunosupression.[37] Therefore information about the magnitude of the problem, different types occurring and other factors related to mucocutaneous disorders are important to ensure comprehensive care is given to HIV infected children.

Mucocutaneous disorders occurred with high frequency in HIV infected children in this study. About 85% of the children were affected. Other studies have found similar findings differing in magnitude.[7, 9, 25, 38, 39] The high prevalence was also reported by Montri et al (83%) in Thailand and De carvalho OV et al (82.5%) in Brazil in survey involving 47 and 40 children respectively[9, 39] In these two studies their sample size was smaller compared to the one used in this study however, the prevalence of mucocutaneous disorders is almost similar to that in the present study. This shows that in any group of HIV infected children one is likely to find a high proportion of mucocutaneous disorders. Siriwan W. et al in two studies found the prevalence of 52% and Seona R. et al found it to be 56.7% in a study involving 210 children.[25, 38, 7] Those findings are lower compared to the current study. It could be due to the fact that, studying children from patient care settings could result in overestimation of prevalence of mucocutaneous disorders, since children receiving care are generally symptomatic.

Mucocutaneous disorders cut across all ages in HIV infected children almost in the same magnitude. Almost all age groups were affected equally by mucocutaneous disorders, though those aged five years and below appeared to be more affected (87.6%). The difference among the age groups was not statically significant ($p>0.005$). This is contrary to the findings of Luminous LM et al where they found children of less than five years being least affected compared to the older ones.[40] There is no sex difference in the prevalence of mucocutaneous disorders since males and females were affected almost in the same magnitude. The slight male preponderance found in this study was not statistically significant.

Among the numerous manifestations of human immunodeficiency virus (HIV) disease, mucocutaneous disorders remain one of the most important clinical markers from the time of seroconvension.[41] The skin being the most visible and largest organ, often shows early manifestations of internal disease. This is true of HIV/AIDS.[40] Mucocutaneous disorders function as visual markers in assessing the progression of HIV disease. In WHO clinical paediatric staging of HIV/AIDS almost each clinical stage has a form of mucocutaneous disorders.[17, 18] Pruritic papular eruption of HIV/AIDS, fungal nail infection, angular cheilitis, molluscum contagiosum and herpes zoster are found in stage 2 disease.[17, 18] Oral candidosis and oral hairy leukoplakia are markers of stage 3 disease. Cutaneous herpes simplex infection and kaposis sarcoma are markers of stage 4 disease.[17, 18] These disorders are not limited to one stage, as the patient progresses from one stage to another so do mucocutaneous disorders. Indeed more than 90% of HIV infected patients develop skin or mucus membrane disorders at some time during their disease.[10, 12]

The prevalence of mucocutaneous disorders increased with the advanced stage of HIV disease as well as the as the severity of immunosupression. All children who were in WHO paediatric stage 4, 10/10(100%) had mucocutaneous disorders of one type or another, while those in stage 1 only about 29% had the disorders. Almost all children with severe immunosupression (97.4%) had mucocutaneous disorders, and the prevalence decreased in those with moderate and no evidence of immunosupression, (84.5% and 71.2% respectively). These findings were statistically significant ($p< 0.05$). This shows that for children with advanced stage of the disease, almost all of them will have one or more types of mucocutaneous disorders, but more important is the fact that mucocutaneous disorders occur at all stages of the disease. These findings are consistent with the observation in other studies that have shown increased incidence of mucocutaneous conditions in Paediatric AIDS patients during the course of the disease. [10, 11, 25, 39] A study done by Siriwan W et al, [25] showed a significant increase in the prevalence of mucocutaneous disorders in HIV infected children with moderate to severe immunosupression. The prevalence in those with severe, moderate and no evidence of immunosupression was 62%, 43% and 20% respectively.[25] Similar findings were found by De carvalho OV et al in Brazil.[39]

Lim W et al, observed that as the CD4 + cell count declines more severe and multiple cutaneous manifestations appeared and the occurrence of certain skin manifestations has been noted to correlate with the CD4+ cell count.[42]

Mucocutaneous disorders caused by opportunistic and other infections and non infectious inflammatory dermatoses of the skin can result in serious complications in

patient with HIV disease. The mucous membranes and the skin are the first lines of defence in the body.[41] Infections are a frequent cause of mucocutaneous disorders. In this study mucocutaneous disorders due to infections were the most common findings. This could be due to alteration of skin barrier function resulting from the disease leading to reduction in the Langerhans cells responsible for presenting antigens that reach the skin through the immunological system.[39] Fungal infections were more prevalent (40%) followed by viral (23%) and bacterial (12%) infections. These findings are consistent with those found by Seone R et al where low incidence of bacterial infections was found while fungal and viral infections were more prevalent.[7] The same was also observed by Luminous LM et al.[40]

Similarly, non infectious inflammatory dermatoses were found to be highly prevalent in HIV infected children.[40] Pruritic papular eruptions (PPE) of HIV/AIDS, atopic dermatitis and seborrheic dermatitis were the common conditions among the non infectious inflammatory dermatoses. PPE have been found to be a common presentation of AIDS both in adults and children in Africa.[9] In this study PPE accounted for about two thirds of the non infectious inflammatory dermatoses. PPE of HIV/AIDS is a common and important clinical manifestation of HIV disease indicating advanced level of immunosupression.[33] In Africa PPE of HIV/AIDS is found in HIV infected children with the same frequency as in adults.[38] Montri et al,[9] found 30% of HIV infected children to have PPE of HIV/AIDS which is lower compared to the 40.1% found in this study but this can partly be explained by the different methodology used.

Although the pattern of mucocutaneous disorders in this study is compatible with that of other studies, there was a striking lower prevalence of cutaneous neoplasm and drug eruption. Kaposi's sarcoma (KS) was seen only in one child. Other studies have reported a significant rise in childhood KS. Amin H et al, [28] found a significant increase in anatomically disseminated KS during the AIDS epidemic. Ziegler et al, [43] found that the incidence of KS had risen more than 40-fold in the era of HIV and 78% of the 63 cases of KS tested positive for HIV. Similarly Athale OH et al, [44] found the same in Zambian children. Nevertheless, Mocroft A et al, [45] found that most individuals who develop KS while receiving ART, begun treatment with low CD4+ cell count and developed KS within six months of the initiation of ART. Generally the incidence of KS has been reduced with the introduction of ART. [45] Other studies which had found a rise in cases of KS when comparing with the pre-AIDS period, they were done well before the widely use of ART.

It is surprising that, with the wide use of cotrimoxazole for Pneumocystis Pneumonia (PCP) prophylaxis, only one child was found to have a drug reaction associated with taking sulphur-containing drugs. This may not reflect a true picture as it is expected that a child with any severe reactions will be admitted through emergency service and will rarely present at the clinic with the acute reactions. In a study done by Oliveira V et al, they found 4 (10%) children with drug reaction related to taking cotrimoxazole.[39] Other studies have also found the prevalence almost in the same range, that is 11%[46] and 12%. [10]

Generally, HIV infected children suffer from common mucocutaneous disorders, but they also present with rare dermatoses unique to HIV infection such as PPE of HIV/AIDS. Common dermatoses often present with atypical presentation and may pose a diagnostic dilemma. For example, Herpes simplex, one of the viral cutaneous infections may present as large superficial erosions or deeply ulcerating lesion (Appendix vi figure 1 and 2) rather than the classical small vesicles on the erythematous base.

Older children above 15 years were found to have the highest proportion of different types of mucocutaneous disorder. This could be due to the progressive disease process associated with a decrease in CD4+ cell count. Luminus LM et al observed similar findings, although a different age category was used but older children were affected more than the younger age group.[40] Generally all children at any age could be affected by one or more types of mucocutaneous disorders as it has been found in this study. However, there were no statistically significant differences in the presence of different types of mucocutaneous disorders among different age groups ($p>0.05$).

Gender does not appear to have an influence on the presence of different types of mucocutaneous disorders with the exception of non infectious inflammatory dermatoses where there was a male predominance. This finding was statistically significant ($p < 0.05$). This could be explained by a large number of male children who had non infectious inflammatory dermatoses when compared to female children.

An increase in CD4+ T cells is associated with a decrease in mucocutaneous disorders.[7] It is therefore right to say that advanced clinical stage of HIV disease and severe immunosupression will be associated with highest prevalence of mucocutaneous disorders. This speculation has been found to be true in this study where the largest proportion of different types of mucocutaneous disorders were found in children who were in WHO paediatric stage 3 and 4. Those with severe immunosupression had the highest proportion of almost all types of mucocutaneous disorders. These findings are similar to those found by S. Wananukul et al.[25] Cutaneous infections can also be seen in immunocompetent patients early in the course of HIV infection in children, [12] this has also been found in this study. Children with no evidence of immunosupression, 71% of them had mucocutaneous disorders of one type or another.

The use of ART has shown a significant reduction in the prevalence of mucocutaneous manifestations in HIV infection with an increase in CD4+ T cells lymphocytes.[7] A study which has compared types of mucocutaneous manifestations in different treatment periods has found that manifestations were higher in the monotherapy and lower in the ART period. [7] In this study about 75% of children with mucocutaneous disorders were on ART. There was no significant decrease in the occurrence of mucocutaneous disorders for those who were on ART. This could be explained by the fact that those children with mucocutaneous disorders either already had severe immunosupression or were in paediatric stage 3 or 4 which are WHO recommended criteria for initiating antiretroviral therapy.[42] Therefore, it could be said that when one sees an HIV infected child with one or more types of

mucocutaneous disorders, it is a pointer towards the need for initiating antiretroviral therapy.

Despite the use of ART, mucocutaneous disorders still persist although they may change in their clinical presentation. Fungal infections in which oral candidosis used to be a common presentation was found to be up to 78% by Seona R et al.[7] Wananukul S et al in another study found it to be 41.9% [38] and De carvalho OV et al found it to be 42.3%. [39] In this study only 4.3% had oral candidosis. Hyper pigmentation of nail plates was seen in two children which is the effect of ART (Nevirapine is implicated) but also could be the effect of HIV itself.[31] Although the majority of the children with mucocutaneous disorders were on ART, their duration of use varied widely. Many children (36.3%) had used the drugs between six months and one year, while about 23% had used the drugs for less than six months and only about 15% had used for more than a year. For ART to be effective, adherence is very important. In this study, adherence on treatment was not studied. Poor adherence could be another reason why so many children, despite being on ART still had mucocutaneous disorders. Therefore it could be speculated that for ART to have significant effect on mucocutaneous disorders, it needs to be taken for a longer period. In a study done by Donic I. et al, it was found that the use of ART for about two years (22 months) reduced significantly the presence of oral candidosis and seborrheic dermatitis.[48] To asses the effect of ART on mucocutaneous disorders, a follow-up study of HIV infected children with mucocutaneous disorders on ART is important rather than a cross sectional study like this one. Children with mucocutaneous disorders may give a clue to the need to start ART early as they will

either have severe immunosupression or be at advanced WHO paediatric stage of the disease.

Mucocutaneous manifestations, which may be the initial signs of virus related immunosupression frequently, occur in patients who are infected with HIV. More than one type of mucocutaneous disorders was not an uncommon findings, similar findings were found in other studies.[9, 25] Recognizing HIV related skin changes may lead to the diagnosis of HIV infection at the early stages which will allow timely initiation of antiretroviral therapy and hence improvement in the immune system.

7.0 CONCLUSION

1. Mucocutaneous disorders are common among HIV infected children attending care and treatment centres in Dar es Salaam.
2. Mucocutaneous disorders are more common at advanced levels of immunosupression and WHO stage.
3. Various types of mucocutaneous disorders among HIV infected children are encountered throughout the course of HIV infection.
4. There is no gender or age spared of mucocutaneous disorders among HIV infected children.
5. Despite the use of ART in the management of HIV infection, mucocutaneous disorders are almost equally prevalent in those using ART and those not on ART.

8.0 RECOMMENDATIONS

1. Comprehensive care and management of HIV infected children should emphasize on mucocutaneous disorders because they are very common.
2. Health care providers should be on the look for various types of mucocutaneous disorders since they may not only be a pointer of HIV infection but also of advanced HIV disease.
3. Further studies are needed to address different aspects of mucocutaneous disorders among HIV infected children and the effect of ART.

9.0 STUDY LIMITATIONS

1. Being a hospital based study the prevalence observed does not reflect the true prevalence of mucocutaneous disorders in HIV infected children in the community population.
2. The fact that the study design was cross sectional it was not possible to assess the effect of ART on mucocutaneous disorders and the response to treatment among HIV infected children.

9.0 REFERENCES

1. Brooks GF, Butel JS, Morse SA; Jawtz, Melnick & Adelbergs Medical microbiology.23rd Edition. Appleton & Lange 2004;605-618.
2. UNAIDS/WHO epidemiological fact sheet, UNAIDS/WHO working group for global HIV/AIDS and STD surveillance Dec 1998. www.unaids.org (Accessed March 2006).
3. UNAIDS/WHO epidemiological fact sheet on HIV/AIDS and STI 2002 Update.
4. UNAIDS epidemic update December 2006. Report on Global AIDS Epidemic.
5. www.aegis.com/fies/unaids/june_2005/Tanzania.en.pdf (Accessed March 2006).
6. Kawo G, Karlson K, Lyamuya E, Kalokola F, Fataki M, Kazimoto T, et al. Prevalence of HIV type 1 infection associated clinical feature and mortality among hospitalised children in Dar es Salaam Tanzania. *Scandinavia Journal of Infectious Disease* 2000; **32**:357-363.
7. E.Seoane Reola, JM Bellon, D Gorbindo et *al*, Role of Antiretroviral Therapy in mucocutaneous manifestation in HIV infected children over a period of two decades. British Journal of Dermatology 2005;**153**:382.
8. Myskowski PL, Ahkami R. Dermatolgical complications of HIV infection. *Medical Clinics of North America* 1996;**80**:1415-1435.
9. Montri U, Tarunotai U. Cutaneous Manifestation in Children with HIV infection. A 5-year study in Vachira Hospital. *Thai Journal of Dermatology* 2001;**17**:167-174.

10. El-Hachem M, Bernadl S, Pianosi G, et al. Mucocutaneous manifestation in children with HIV infection and AIDS. *Paediatric Dermatol* 1998;**15**: 429-434.

11. Cockerel C, Friedman-Klein A. Cutaneous signs of HIV infection. *Clinical Dermatol* 1993;**4**:507-524.

12. Rennet WP. Infectious manifestations of HIV in children. *AIDS read* 2005;**15**:619-622.

13. Nance KV, Smith ML, Josh VV, Cutaneous manifestation of Acquired Immunodeficiency Syndrome in Children. *British Journal of Dermatology* 2005;**153**:382.

14. Salim A, Lawrence P. Mucocutaneous manifestation in children with HIV infection. *Current Allergy & Clinical immunology* 2003;**16**:48-52.

15. Geusau A, Tschahler E. HIV related skin disease. *Journal of Royal College of Physician of London* 1997;**31**:374-379.

16. WHO, 2004, Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for surveillance for Africa Region, Geneva/Harare.

17. Centres for Disease Control and Prevention. Revision of the CDC Surveillance case definition for acquired immunodeficiency syndrome. MMWR 1987;**36**:Suppl35:135.

18. Centres for Disease Control and Prevention. Revised classification system for HIV–1 infection in children less than 13 years of age. MMWR 1994;**43**:1-13.

19. Schuitemaker H, Koot M, Kootstra NA et al. Biological phenotype of human immunodeficiency virus type 1 clones at different stages of

infection: progression of the disease is associated with a shift from monocytotropic to T- cell-tropic virus population. *Journal of Virology* 1992;**66**:1354-1360.

20. German ME, Tyring SK. The cutaneous manifestation of HIV infection. *Clinics in Dermatology* 2002;**20**:193-208.

21. Dickover PE, Garralty EM, Herrnan SA et al. Identification of level of maternal HIV-1 RNA associated with risk of perinatal transmission. Effect of maternal Zidovudine treatment on viral load. *JAMA* 1996; **275**:606-610.

22. Shearer WT, Quinn TC, La Russia Petal. Viral load and disease progression in infants. Transmission study Group. *New England Journal of Medicine* 1997;**33**:1337-1342.

23. Mofenson LM, Korelitz J, Meyer WA et al. The relationship between serum human immunodeficiency virus type 1 (HIV-1) RNA level, CD4 lymphocyte percent and long-term mortality risk in HIV infected children. National Institute of child health and human development intravenous immunoglobulin. *Clinical Trial Study Group* 1997;**175**:1029-1038.

24. Nance KV, Smith ML, Joshi V, Cutaneous manifestations of acquired immunodeficiency syndrome in children. *International Journal of Dermatology* 1991;**30**:531-539.

25. Siriwan W, Tawatchai D, Chitsanu P et al. Mucocutaneous findings in Paediatric AIDS related to degree of immunosupression. *Paediatric Dermatology* 2003;**20**:289.

26. Emondi I.J, Okofor G.O. Clinical Manifestations of HIV Infection in Children at Enugu, Nigeria. *Journal of Tropical Paediatric* 1998;**44**:73-76.

27. Sebhat A, Solomon A. Clinical Manifestations of HIV/AIDS in Children in Northwest Ethiopia. *Ethiopian Journal of Health Development* 2005;**19**:24-28.

28. Amin H, Kaaya EE, Manji KP. Kaposis Sarcoma before and during HIV epidemic in Tanzanian children. *Paediatric Infectious Disease Journal* 2001;**20**:518-521.

29. Dermatological manifestation. www.hivguidelines.org/public_htm/p-derm-tbls.pdf (Accessed February 2006).

30. Stefanaki C, Stratigos AJ, Stratigos JD. Skin Manifestations of HIV-1 Infection in Children. *Clinics in Dermatology* 2002;**20**:74-86.

31. Braun-Falco O, Plewing G, Wolff HH, Wenkelmann RK. Dermatology 3rd ed. Springer-Verlag-Berlin 1991;348-356;417-429.

32. Mgonda YM. Pruritic popular eruption of HIV disease versus cutaneous epidemic kaposis sarcoma: could it be used as an AIDS defining illness. *Tanzania Medical Journal* 2003;**18**:5-8.

33. Mgonda YM, Urassa WK, Lyamuya EF, Pallangyo KJ, Mbena EC. The clinical characteristic of pruritic popular eruption (PPE) of HIV disease: Experience from Dar es salaam, Tanzania. *Tanzania Medical Journal* 2001;**16**:1-4.

34. Manking TN, Kamchaisation W, Ziiberma L et al. Varicella Zoster as manifestation of immune restoration disease in HIV infected children. *Allergy Clinical Immunology* 2004;**133**:742-746.

35. United Republic of Tanzania. 2002 Population and Housing Census. General report.

36. SPSS Inc version10.0. The Statistical Package for the Social Sciences. Chicago,11:SPSS Inc, 2004.

37. Goldstein B, Berman B, Sukenik F. Correlation of skin disorders with CD4+ lymphocyte counts in patients with HIV/AIDS. *Journal of American Academy Dermatol* 1997;**36**:262-264.

38. Wananukul S, Thistakom U. Mucocutaneous manifstation of HIV infection : 91 children Born to HIV seropositive women. *Paediatric Dermatology* 1999;**16**:359-363.

39. Oliveira de Carvalho V, Marinoni LP, Martin F, Giraldi S, Taniguchi K, Bertogna J. Dermatological alterations in children with AIDS and their relation to clinical-immunological categories and viral load. *An Bras Dermatol* 2003;**78**:679-692.

40. Luminus LM, Mardaresu M, Petrea S. Et al. Cutaneous disorder in HIV infected children. *International conference on AIDS* 1998;**12**:574.Absract No 32273.

41. Jing W, Ismail R. Mucocutaneous manifestations of HIV infection : a retrospective analysis of 145 cases in a Chinese population in Malaysia. *International Journal of Dermatology* 1999;**38**:457-463.

42. Lim W, Sadick N, Gupta A et al. Skin disease in children with HIV infection and their association with degree of immunosupression. *International Journal of Dermatology* 1990;**29**:24-29.

43. Ziegler JL, Katongole-Mbidde E. Kaposi's sarcoma in childhood : an analysis of 100 cases from Uganda and relationship to HIV infection. *International Journal of Cancer* 1999;**65**:200-203.

44. Athale OH, Patil PS, Chintu C, Elem B. Influence of HIV epidemic on the incidence of Kaposi's sarcoma in Zambian children. *Journal of Acquired Immune Deficiency Syndrome Hum Retrovirol* 1995;**8**:96-100.

45. Mocroft A, Kurk O, Clumeck N, Gargalianus-Kakolyris P, Trocha H, Chentsova N, et al. The changing pattern of Kaposi's sarcoma in patient with HIV, 1994-2003. The EUROSIDA study. *Cancer* 2004;**100**:2644-2654.

46. Leaute-Laubreze C, Niamba P, Douard D, Taieb A. Cutaneous manifestation of paediatric HIV infection: a cohort study of 35 patients. *Ann Dermatol Veneorol* 1998;**125**:80.

47. WHO HIV/AIDS Treatment and Care Protocol for Countries of Commonwealth of Independent states 2004.

48. Donic I, Vesic S, Jertoric DJ. Oral candidosis and seborrheic dermatitis in HIV infected patients on highly active antiretroviral therapy. *HIV medicine* 2004;**5**:50.

10.0 APPENDICES

Appendix i

QUESTIONARE

PATTERN OF MUCOCUTANEOUS DISORDERS IN HIV INFECTED CHILDREN CARE AND TREATMENT CENTRES IN DAR ES SALAAM

A. PATIENT PROFILE

ID NO_____

NAME (initial) _____

DATE OF BIRTH_____

AGE_____

SEX_____

B. HISTORY

1. Is the child on ARV
   (a) Yes
   (b) No
2. If yes, which combination
   (a) Zidovudine, lamivudine, niverapine
   (b) Stavudine, lamivudine, niverapine
   (c) Stavudine, lamivudine, efavirenz
   (d) Zidovudine, lamivudine, efavirenz
   (e) Didanosine, Abacavir, kaletra
3. How long has the child being on ARVs_____
4. Other medication the child is using apart from ARVs and that for

Mucocutaneous condition_____

5. Is the child allergic to any medication?

(a) Yes

(b) No

6. If yes, which medication_____

C. PHYSICAL EXAMINATION

Dermatological examination

7. Is there mucocutaneous lesion_____

(a) Yes

(b) No (IF NO GO QNS 12)

8. Duration of the lesion(s)_____

(a) One week

(b) Two weeks

(c) More than two weeks but less than a month

(d) More than one month

9. Location of the lesion(s)

(a) Scalp

(a) Face

(c) Mouth

(d) Trunk

(e) Genitalia

(f) Extremities

(g) Generalized

10. Morphological description of the lesion

(a) Macule

(b) Papule

(c) Nodule

(d) Plaque

(e) Blister

(f) Ulcer

(g) Scale

(h) Crust

(i) Papulosquamous

11. Staging of HIV/AIDS (WHO Staging) _____ (End here if no mucocutaneous disorders)

D. INVESTIGATIONS

12. Skin scraping

Date specimen taken_____

Results_____

13. Skin biopsy_____

Date specimen taken_____

Results_____

14. CD4 count_____

Date specimen taken_____

Results_____

E. **FINAL DIAGOSIS**

15. Candidosis
16. Pityriasis versicolor
17. Tinea corporis
18. Tinea capitis
19. Tinea unguim
20. Molluscum contagiosum
21. Herpes simplex
22. Herpes zoster
23. Chicken pox
24. Warts
25. Cellilitis
26. Impertigo
27. Abscess
28. Scabies
29. PPE
30. Seborrheic dermatitis
31. Atopic dermatitis
32. Napkin dermatitis (Diaper rash)
33. Kaposis sarcoma
34. Toxic epidermal necrosis
35. Steven Johnson syndrome
36. Psoriasis
37. Non specific dermatitis

38. Purpular urticalia

39. Others (specify).....

THANK YOU FOR YOUR COOPERATION.

Appendix ii

Consent form for participation in the study of pattern of mucocutaneous disorder in HIV infected children attending care and treatment centres in Dar es Salaam.

My name is Dr Milembe Panya
I am a Senior Resident in Paediatric and Child Health at MUCHS. I am doing a study to determine the pattern of mucocutaneous disorder in HIV infected children. I would like to ask you permission for your child to participate in this study. First I will explain about the study and answer any question you have.

Study aims.

This study will determine the patterns of mucocutaneous disorder in HIV infected children aged 17 years and below attending CTCs at MNH and Municipal hospitals.

How to participate in the study

The child will be examined fully for any mucocutaneous disorder after you have agreed to participate in the study. Depending on the type of lesion found, I would need to perform a skin biopsy or scrapping for investigations. A small amount of blood will be taken to check for CD4+ count.
Photography of some of the conditions will be taken and this may be used while writing a report of this study. If photography is taken, the face will be covered and if the face will be included then the eyes will be covered,
Participation in this study is completely voluntary. Even if you will not participate in this study your child will continue to receive the same service from this centre like other children.

Confidentiality

Your child's name and other particulars will not be made public in any way and so your participation will be anonymous. Only the chief investigator and dedicated laboratory staff will handle the specimen and information obtained.

Benefits

Parents and guardians whose children will participate will benefit by knowing their children mucocutaneous problem and treatment will be provided according to the center protocol and for some of the condition patient will be referred to appropriate clinic

Risks

The procedures that will be done in this study are common for patients in hospital and we don't expect your child to experience any problems as a result of this study.

For any questions or problems contact the following persons :

1. The Investigator
   Dr. Milembe Panya
   Department of Paediatric and Child Health
   Mobile 0744 303 284
2. Dr. Mgonda Y
   A Senior lecturer and Dermatologist
   Department of Internal Medicine
   Muhimbili University of Health and Allied Sciences
   P.O.Box 65011
   Dar es Salaam.
3. Dr. Massawe A
   A Senior lecturer and Neonatologist,
   Department of Paediatric and Child Health
   Muhimbili University of Health and Allied Sciences
   P.O.Box 65011
   Dar es Salaam.

I .....have read or been told the content of this form and undestand.My quoestions have been answred. I agree my child to take part in this study.

_____	_____	_____
Date	Participant signature	Investigator signature

Appendix iii

CLINICAL DEFINITION OF MUCOCUTANEOUS DISORDERS

Oral candidosis: White curd like material with or without angular cheilitis, fissuring. Sometimes only hyperaemia of oral mucosa / tongue.

Diaper rash (napkin dermatitis)

Slightly raised rash (papule) involving skin fold, satellite lesion outside the affected region.

Pityriasis versicolor

Hypo pigmented macular on the face, shoulder and neck.

Tinea corporis

Single/multiple scale patches on the trunk; hyperpigmented with raised margin.

Tinea capitis

Flaking area within the scalp, hair loss may be present. There may be weeping or crusting.

Tinea unguium

Yellow or darkened or pitted nails.

Molluscum contagiosum

Umbilicated dome shaped flesh coloured shiny papules found on the face, shoulder and back.

Herpes simplex

Grouped erthematous base vesicles and pustules.

Chicken pox

Vesicular and ulcerative lesion in different stages has centripetal distribution.

Herpes zoster

Painful/pruritic blistering lesion usually affects single dermatome.

Viral warts

Hyperkeratotic papule on fingers or flat plane on face, neck or hands. There may be hyper pigmented or hypo pigmented macules which may become confluent and may involve anal region.

Scabies

Vesicles, itchy papules, excoriation all over the body, burrows or eczematous eruption (Norwegian). Sites commonly involved are wrists, web spaces, feet, ankles, axilae and genitalia.

Serborrheic dermatitis

Yellow-white greasy scales, erthematous patches seen on the face (eyebows, eyelashes, nasolabial fold ears), chest, and genital organ.

Psoriasis

Inflamed skin, sharply delimited plaque silvery lustrous scaling.

Pruritic Papular Eruption (PPE)

Pruritic hypepigmented/hypopigmented follicular, macules, papules with scars found on trunk and extremities.

Eczema (Atopic dermatitis)

Itchy eczematous papulovesicular or crusting papule and lichenification. Affects cheeks scalp, flexures nape of the neck, dorsum of the feet and hands.

Kaposis Sarcoma

Pink/bluish macules or plaque or nodular lesion.

Toxic epidermal necrolysis

Skin is dusky purple, mucosal involvement may occur. Sheets of skin are shed leaving weeping red areas like that of burn.

Impertigo

Yellowish brown crust, which is roundish accompanied by erosion and pustules.

Appendix iv

WHO Paediatric staging of HIV/AIDS disease

WHO Paediatric Stage 1	• A symptomatic • Persistent generalised lymphadenopathy (PGL) • Hepatosplenomegaly
WHO Paediatric Stage 2	• Papular pruritic eruption • Seborrheic dermatitis • Fungal nail infection • Angular chelitis • Lineal gingival erythema • Extensive HPV or molluscum infection (>5% of body area/face) • Recurrent oral ulceration (>2episode/6months) • Parotid enlargement • Herpes zoster (>1 episode/ 12 months) • Recurrent or chronic upper respiratory infection (URI): otitis media,otorrhea,sinusitis (> 2 episode/ 6 months)
WHO Paediatric Stage 3	• Unexplained moderate malnutrition (-2 SD or Z score) not responding to standard treatment • Unexplained persistent diarrhoea (> 14 days) • Unexplained persistent fever (intermittent or constant, >1 month) • Oral candidosis (outside neonate period) • Oral hairy leukoplakia • Pulmonary tuberculosis • Severe recurrent presumed bacterial pneumonia (>2 episode /12 moths) • Acute necrotizing ulcerative gingivitis/periodonitis • Lymphoid interstitial pneumonitis(LIP) • Unexplained anaemia (<8gm/dl),neutropenia(<1000/mm^3) or thrombocytopenia(<30000/mm^3) fo >1 month • HIV related cardiomyopath • HIV related nephropthy
WHO Paediatric Stage 4	Symptomatic HIV antibody positive infant age <18 months • Two or more of the following: • Oral candidosis • Failure to thrive • Severe pneumonia • Sepsis

	Presumptive diagnosis of stage 4 disease in HIV antibody positive infants <18 months require confirmation with virologic tests when possible or by Antibody tests after age 18 months.
WHO Paediatric Stage 4 (Any Age)	• Unexplained severe wasting or severe malnutrition (-3 SD or Z score) not responding to standard therapy. • Pneumocystis pneumonia • Recurrent severe bacterial infections (>2 episodes/12 months, excluding pneumonia) • Chronic orolabial or cutaneous HSV (lasting>1 month) • Extra pulmonary tuberculosis • Kaposis sarcoma • Oesophageal candidosis • CNS toxoplasmosis • Cryptococcal meningitis • Any disseminated endemic mycosis • Cryptosporidiosis or isosporiasis (with diarrhoea>1 month) • CMV infection of organ other than liver, spleen, lymphnodes (and onset age >1 month) • Disseminated mycobacterial disease other than tuberculosis • Candida of trachea, bronchi or lungs • Acquired recto-vesico fistula • Cerebral or B cell non- Hodgkin's lymphoma • Progressive multifocal leukoencephalopathy (PML) • HIVencephalopathy

Source: WHO, 2004, Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for surveillance for Africa Region, Geneva/Harare.

Appendix v

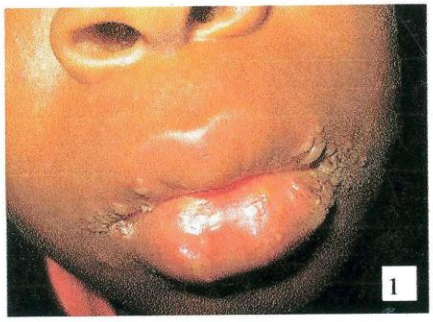
IMMUNOLOGICAL CLASSIFICATION FOR HIV INFECTED INFANTS AND CHILDREN

Immunological category	Age of child		
	< 12 months	1- 5 years	6- 12 years
	Cells/ul (%)	Cells/ul (%)	Cells/ul (%)
1. No evidence of suppression	≥1500 (≥ 25)	1000(≥ 25)	500 (≥ 25)
2. Evidence of moderate suppression	750-1499 (15-24)	500-999 (15-24)	200-499 (15-24)
3. Severe suppression	<750 (<15)	<500 (<15)	<200 (<15)

Source: Centre for Disease Control and Prevention. 1994 Revised classification system for HIV infection in children < 13 years of age

Appendix vi

Plates of different mucocutaneous manifestations in HIV infected children.



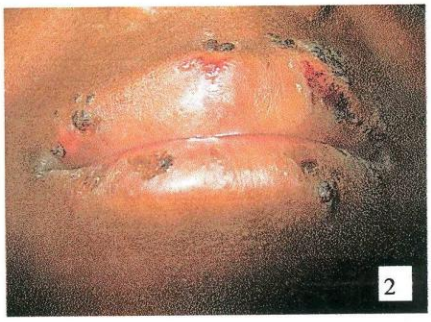
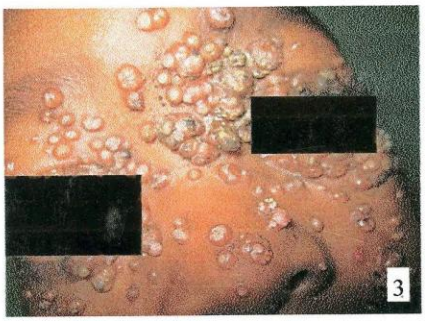


Figure 1 and 2 Herpes simplex: Extensive herpetic lesions undergoing ulceration and crusting.



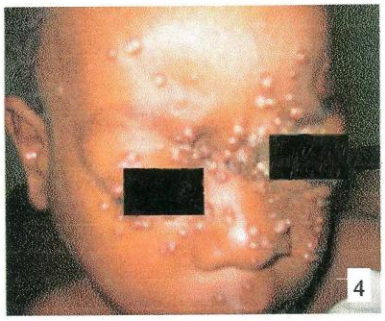
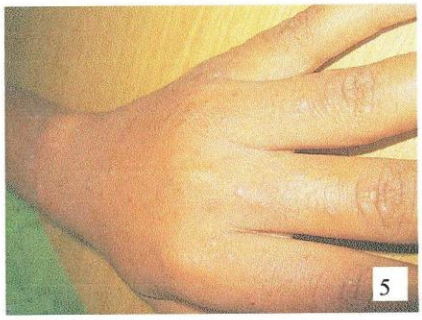


Figure 3 and 4 Molluscum contagiosum: Confluent lesions of various sizes, some are obviously shiny, dome shaped with central umbilication; while others are irregular in shape and crusted.



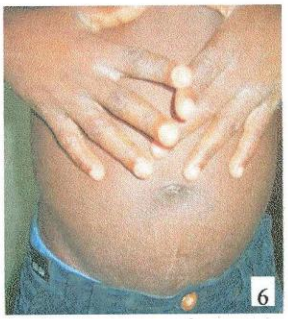


Figure 5 and 6 Scabies: Pin head sized papules, vesicles on the fingers and finger webs (5) also involving periumbilical area (6). Note the extensive scratch marks in the sub umbilical areas

Plates of different mucocutaneous manifestations in HIV infected children (*cont.*)

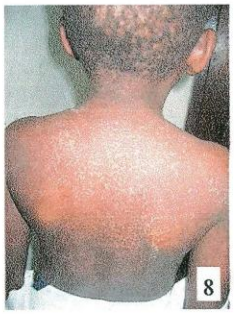
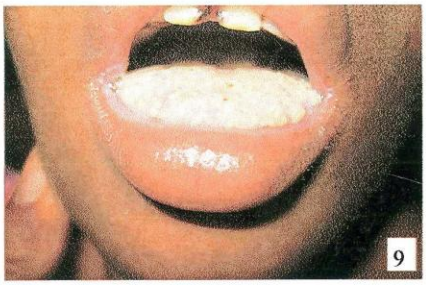


Figure 7 and 8 Plane warts: Caused by Human papilloma virus serotype 3 and 10 as seen on the face and back. Köbner's phenomen is seen in both figures. The condition is very difficult to treat.



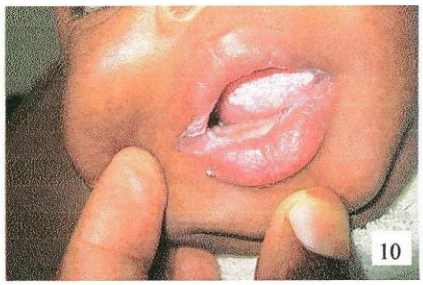
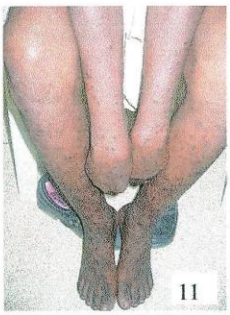


Figure 9 and 10 Oral candidiosis: Extensive pseudomembraneous and cheilitis presentation.



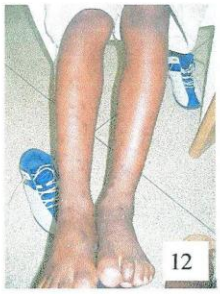


Figure 11 and 12 Pruritic papular eruption (PPE): There is predominant involvement of the legs and forearms. On the forearms lesions are more on extensor surfaces while on the legs there is circumferential distribution. Repeated scratching due to intense itching has lead to hyperpigmentation and lichenification of the skin.

Plates of different mucocutaneous manifestations in HIV infected children (*cont.*)

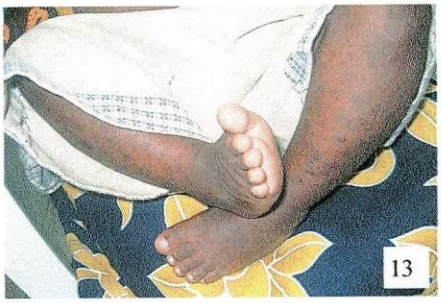


Figure 13 Papular urticaria: Common condition in children. Not always associated with HIV infection.

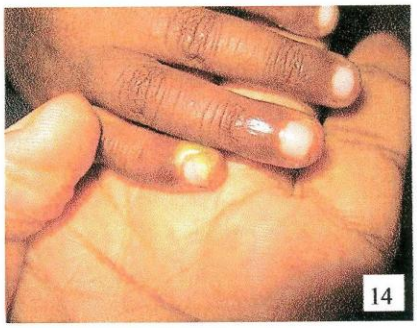


Figure 14 Paronynchia: Yellowish/ greenish discoloration of the nail plate with an intact pus pocket on the lateral nail fold.

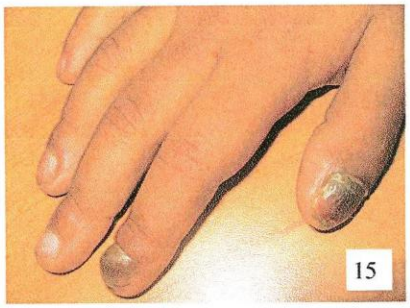


Figure 15 Onychomycosis: The nail plates of the thumb and index fingers showing hyperpigmentation and dystrophy of the nail plates. Note the sparing of other fingers which is characteristic of fungal nail infection.

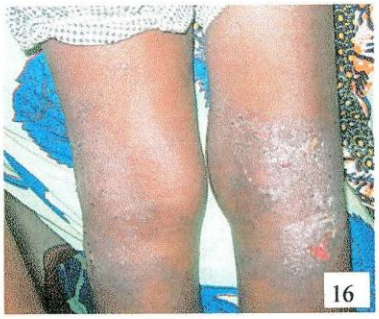


Figure 16 Atopic eczema: Extensive itching leading to ulceration.

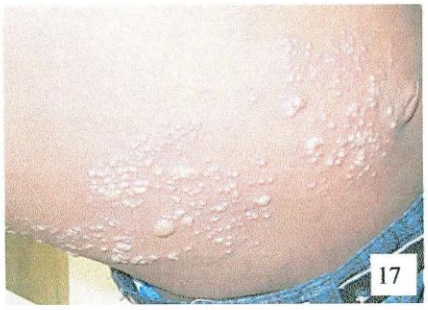


Figure 17 Herpes zoster: Vesicles arranged in dermatome distribution around T10.

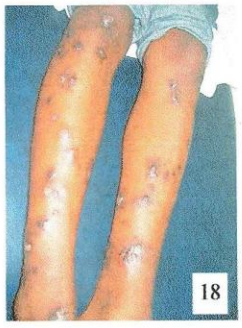
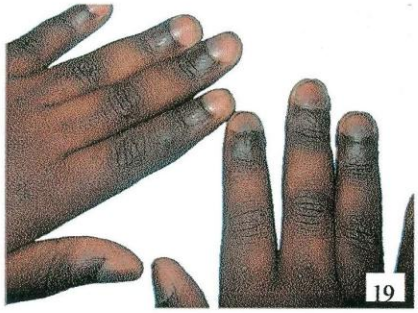


Figure 18 Prurigo nodularis chronicus: Presenting with extensive secondary infection and ulceration.

Plates of different mucocutaneous manifestations in HIV infected children (*cont.*)



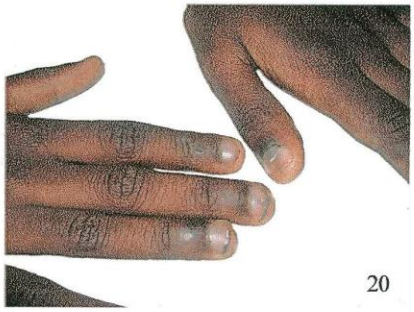
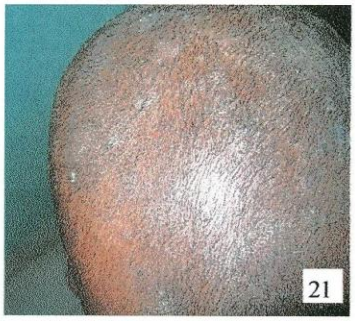


Figure 19 and 20 Hyperpigmentation of nail plates: This is increasingly seen in patients on ARV especially Nevirapine.



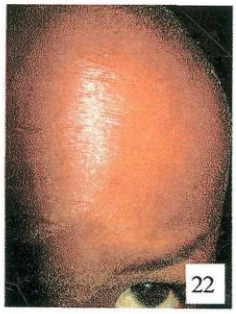
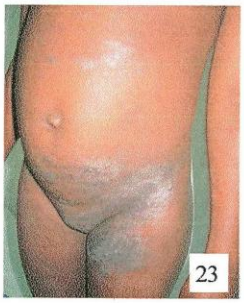


Figure 21 and 22 Seborrheic dermatitis: Extensive stuck on scales which could be confused with psoriasis (21), sometimes the two conditions do co-exist. On the right (22) stuck on scales with dandruff on hairs.



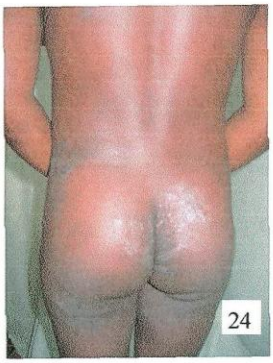


Figure 23 and 24 Tinea cruris: Extensive lesion with well dermacated margins, note the asymmetrical distribution, (23). The buttocks, intergluteal area and the belt line have been involved (24).