A COMPARISON STUDY OF INFECTIVE CORNEAL ULCERATION IN NON HIV AND HIV INFECTED PATIENTS AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM

By

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A dissertation submitted in partial fulfillment of the requirements for the degree of Master of Medicine in Ophthalmology of Muhimbili University of Health and Allied Sciences (MUHAS).

Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance for examination by the Muhimbili University of Health and Allied Sciences a dissertation entitled: **A *comparison study of infective corneal ulceration in non HIV and HIV infected patients at Muhimbili National Hospital, Dar es Salaam,*** in partial fulfillment of the requirements for the degree of Master of Medicine in Ophthalmology at the Muhimbili University of Health and Allied sciences.

---------- 2/12/09

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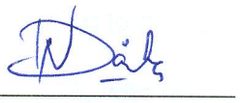
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I, Dr Neema Daniel Kanyaro, here by declare that this dissertation is original work, and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

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DEDICATION

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ABSTRACT

This cross sectional descriptive and comparative study was conducted at Muhimbili National Hospital from May 2007 to May 2008. The study population included 186 patients who attended the ophthalmology department during the study period who were diagnosed to have infective corneal ulceration. The main objective was to determine the clinical presentation of infective corneal ulceration and correlate it to the HIV serological status of the patients.

Social, demographic data and information pertaining to risk factors were recorded. Patients underwent clinical examination to determine the visual acuity, size, depth of the corneal ulcer and the presence of hypopyon and perforation. Corneal scraping was performed and specimen sent for the laboratory analysis. ELISA test to screen for HIV infection after pretest counseling was performed in each participant.

Most (85.9%) affected patients were in the age range between 20-49 years with a peak at 30-39 years comprising 41.9% (Table.1)

There were hundred twenty four (66.7%) males and sixty two (33.3%) females.

More than half of the study populations were petty traders while 19.4% were peasant.

Most (72.0%) of the corneal ulcer patients were either cohabiting or single.

One hundred eleven (59.7%) of the study population were HIV seropositive and seventy five (40.3%) were HIV seronegative.

Bacteria were the most common cause of corneal ulceration affecting (46.24%) of the study population. The second commonest cause of the corneal ulceration was fungal infection which accounted for 39.2%.

The commonest cause of corneal ulceration in HIV seropositive patients was Fungus which occurred in 53.2% of patients.

Most (72.0%) of the 25 viral corneal ulceration were in HIV seropositve patients.

Compared to ulcers in HIV seronegative patients, ulcers in HIV seropositive patients were more severe in clinical presentation and poor post treatment visual outcome.

In conclusion the study has shown that more than half of patients with corneal ulceration are HIV seropositive. The ulcers in these patients are severe in clinical presentation and have poor post treatment visual outcome. Although bacteria are the commonest cause of corneal ulcers, fungal infection dominates in HIV seropositive patients.

Efforts to screen for HIV in all patients presenting with corneal ulceration in order to offer multi-displinary approach to their management is recommended.

ABBREVIATION

AIDS	Acquired Immunodeficiency Syndrome
CPL	Central Pathology Laboratory
ELISA	Enzyme Linked Immunosorbernt Assays
HIV	Human Immunodeficiency Virus
Ig	Immunoglobulin
C/S	Culture and sensitivity
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
WHO	World Health Organization
CMV	Cytomegalovirus
RE	Right eye
LE	Left eye
ART	Ant-Retrovirus Therapy
HSV	Herpes simplex virus
HZV	Herpes zoster virus
IRD	Immune reconstitution disease
HZO	Herpes zoster ophthalmicus
VZV	Varicella zoster virus
PHC	Primary health care.

LIST OF TABLES

Table: 1. Age distribution of 186 patients with infective corneal ulcer by HIV sero status.....40

Table 2: Sex distribution of 186 patients with infective corneal ulcer by HIV sero status.....41

Table: 3. The distribution of 186 patients with infective corneal ulcer by marital status and HIV sero status.....42

Table: 4. The distribution of 186 patients with infective corneal ulcer by occupation and HIV sero status.....43

Figure: I .The distribution of the study population by HIV serological status.....44

Table: 5. The microbial etiology of infective corneal ulcer in 186 patients by HIV sero status.....45

Table: 6. Isolated microorganism's etiology of corneal ulcer in HIV sero status N=186.....46

Table: 7. The clinical presentation of infective corneal ulcer according to HIV sero status N=186.....47

Table 8. Visual acuity on admission in relation to HIV serological status. N =186.....48

Table: 9. The relation ship between etiology of corneal ulceration and post-treatment visual outcome by HIV sero statu.....49

Table: 10.Visual out come at discharge in relation to HIV serological status.....50

TABLE OF CONTENT

0.1. Certification----------i

0.2. Declaration and copyright----------ii

0.3 .Acknowledgement----------iii

0.4 .Dedication----------iv

0.5. Abstract----------v-vi

0.6 Abbreviation----------vi

0.7 List of Tables----------viii

0.8 Table of contents----------ix-x

0.9 Introduction----------1- 10

1.0. Background----------1

2.0. Relevant anatomy----------2-6

3.0. Ocular manifestation of HIV-- ----------7-8

4.0. Literature review----------9-12

5.0. Corneal ulcer----------13-20

6.0. Corneal ulcer and management----------21-25

7.0. Visual outcome----------26

8.0. Problem statement----------27

9.0. Rationale of the study----------28

10.0. Objectives----------29

11.0. Methodology----------30-36

12.0. Results---------- 37-47

13. Discussion----------48-55

14. References----------56-66

15. Data sheet----------67-70

16. Consent forms----------71-75

INTRODUCTION

Background

HIV infection has changed the picture of many diseases in human beings. Though many diseases seen today, in the HIV era had existed even before HIV era. There has been a change in frequency and magnitude of other diseases seen in HIV infected people. The eye like other parts of the body has not been spared by the alarming diseases caused by HIV infection. Many of the eye diseases, we see today ranging from neoplastic conditions to infection, have been modified in terms of aggressiveness of the disease and prevalence as compared to the times of HIV free era. Apart from severity and prevalence changes, the age distribution of affected individuals has also been altered by the deadly HIV infection. Corneal ulcer is one of the eye diseases, which has dramatically changed in terms of causes of the ulcer, age distribution and its prevalence in HIV infected people. First case of HIV in Tanzania was identified in 1983. Studies on corneal ulcer before HIV era showed a different picture from what we see today. Age distribution of the corneal ulcer infected individuals, during HIV free era shows highest frequency at the age below 9 years. Recent studies show however that much of the cornea ulcer is seen in the reproductive age which also corresponds to highest prevalence of HIV infection. Moreover, nutritional related corneal ulcers used to be the most common cause of corneal ulceration[12]. However in the era of HIV, infections caused by bacteria, fungi and virus are the most common cause. In view of this trend, it is vividly seen how much HIV, has modified disease pattern and necessitates a critical account on the subject in the holistic approach of HIV management.

1. 0.ANATOMY OF THE CORNEA.

The corneal is responsible for two-third of the total refractive power of the eye, any slight change in the cornea contour change of corneal, smoothness or corneal tissue may produce visual distortion.

The corneal is transparent, avascular tissue exposed to the external environment. The anterior corneal surface is covered by the tear film and the posterior corneal surface is directly bathed by the aqueous humor.

The corneal is contour with the opaque sclera and semitransparent conjunctiva. The transitional zone between cornea and sclera is the rich vascularized limbus, which contains reservoir of the pluripotential stem cell. The shape of the anterior surface is convex and aspheric. The adult corneal measures approximately, 12mm horizontal and 11.5mm vertically. It is approximately 0.55mm thick at the center and increases gradually toward the peripheral cornea where it is about 0.7mm thick. The radius of the curvature of the corneal surface is not constant over the entire corneal surface. It is steepest at the center of the cornea and becomes flatter in the periphery.

It measures anteriorly 7.8mm, posterior 6.5mm and central 3mm, an optical zone of the cornea. It is composed of:

a) Tear film which covers the outer surface of the cornea.

b) Cornea proper.

Protective mechanisms of the cornea:

Although the cornea is exposed to the atmosphere it has got several defense mechanisms namely:

1. The blinking reflex and the turning of the head away from approaching objects protect the cornea from injury.

2. The tear film provides nutrition to the cornea, lubricates and keeps the cornea epithelium moist. It provides defense by destroying pathogenic bacteria with the aid of lysozyme and by mechanically washing organisms or foreign bodies from the corneal surface. It also contains immunoglobulin: IgG and IgA, which have an indirect antimicrobial role. Transferrin and lactotransferrin are other proteins in the tears, which act by removing iron needed for bacterial multiplication [1, 2 ,3,4]

3. The corneal epithelium provides an efficient protection against most bacteria and fungal infections. The epithelium has to be damaged before these organisms can invade the cornea. However, organisms such as gonococcus, Corynebacterium diphtheria, Koch-Weeks bacillus and viruses can invade a healthy corneal epithelium.[2]

Bowman's membrane is resistant to trauma and acts as a barrier to invasion of the cornea by microorganisms.

Healing of corneal wounds.

Once the cornea has been damaged some reparative process takes place. Usually epithelial wounds heal without leaving scars. Corneal wounds deeper than the epithelium leave varying degrees of corneal opacities. These opacities range from nebulae, maculae to leucoma and leucoma adherens. These scars lead to impaired vision and blindness[3, 4].

(i) Healing of the corneal epithelium.

When the corneal epithelium gets damaged by abrasion, cuts etc., epithelial continuity is restored by the process of epithelial cell migration and mitosis. This process begins within an hour after injury by sliding of adjacent cells, followed by mitosis and thickening of the covering cells and finally, by adhesion of the epithelium to the basement membrane [5]

(ii) Bowman's membrane.

Unlike the epithelium it never regenerates once damaged. Defects involving the Bowman's membrane therefore cause scar formation, this layer act as a mechanical protection of stroma.

(iii) Stromal wound healing.

Stromal wound healing is less rapid than that of the epithelium but there is evidence of the healing process within 12 hours [2, 3]

A superficial defect in the stroma is rapidly covered by the epithelium. However,

in deeper wounds the process is more complex. Initially there is an invasion of the cornea by polymorph nuclear leucocytes which crowd around the injured area within the first 5 hours. They reach the injured site either by the tear film or from the peri-limbal vessels. Some of these cells proliferate and develop into long spindle cells resembling the fibroblasts[3, 9, 21], they also produce mucopolysaccharides.

At a later stage there is invasion by macrophages which initially act as scavengers removing the cellular debris and probably corneal corpuscles. The new collagen fibers formed are arranged irregularly and do not form a perfect optical medium. The irregularly arranged corneal lamella cause scattering of light during refraction and therefore the cornea becomes opaque (corneal scar). In destructive injuries or in the presence of infective corneal ulceration superficial or deep stromal neo-vascularization occurs further contributing to corneal scarring. Depending on the density of the corneal scar, the visual acuity of the affected eye diminishes correspondingly and may cause monocular blindness. Corneal ulcers are the leading cause of monocular blindness.[12, 15]

(iv) Endothelial healing.

Endothelial healing takes place almost entirely by cell sliding. The remaining cells enlarging to cover the defect. Endothelial cells are extremely sensitive to injury so that even a small superficial epithelial wound causes swelling and numerous protrusions in the endothelial cells below the wound. In well apposed wound edges

the endothelial cells slide over the damaged area, this begins about 20 hours after injury and is completed by the fifth day.

Poorly apposed wounds heal by fibrous scarring which is continuous with the stromal scars and are slowly covered by regenerating endothelial cells. The regenerating cells initially present with fibroblast like characteristics but eventually revert to normal endothelial cell morphology[4].

2. OCULAR MAIFESTATION OF HIV

World, AIDS continues to take a devastating toll, particularly in countries of sub-Sahara and in Asia nations with large, impoverished populations. According to the Joint United Nations Program on HIV/AIDS, as of the end of 2002,42 million people are estimated to be living with HIV/AIDS. Of those, 19.2million are women, and 3.2million are children under age 15years [5, 6].

The ocular adnexa consist of the eyelid, the conjunctiva, and the lacrimal drainage system. Common ocular adnexal lesions in patients who are HIV sero positive include; Herpes Zoster Ophthalmicus (HZO), Kaposi's sarcoma, molluscum contagiosum, and conjunctival microvasculopathy [6. 8]

Dr Jeng also disclosed a new finding that has never been published before - that HIV is a risk factor for developing corneal ulceration. For some reason, persons infected with HIV seem to be more predisposed to having corneal ulceration. Even though there have been case reports of spontaneous corneal infections in HIV-infected individuals, it has been generally believed that HIV infection alone does not predispose to bacterial corneal ulcers [9.]

Patients infected with the human immunodeficiency virus (HIV) infection appear to be at increased risk of developing corneal ulcer, confirms a hospital-based cross-sectional study conducted in California. San Francisco ophthalmologist Bennie H Jeng MD presented the results of the new survey of corneal ulceration cases in the general population at the annual meeting of the Association for Research in Vision and Ophthalmology.[7, 8]

The anterior segment is made of the cornea, the anterior chamber, and the iris. More than 50% of HIV-positive patients manifest anterior segment complications, including dry eyes (keratoconjunctivitis sicca), corneal infection (keratitis), and anterior chamber inflammation (iridocyclitis). Common symptoms include irritation, pain, photophobia, redness, and decreased vision.[5]

Posterior segment structures involved in HIV-positive patients include the retina, choroid, and optic nerve. Disorders of at least one of these structures are seen in more than 50% of patients who are HIV seropositive.

Common presenting complaints include floaters, flashing lights, visual field defect, and decreased visual acuity. Presence of an afferent pupillary defect strongly suggests significant retinal or optic nerve involvement. Diagnoses often are based on clinical evidence seen on funduscopic examinations.

More severely Immunocompromised patients with CD4 count of <100 cells/μL may present with Cytomegalovirus virus retinitis, toxoplasmosis retinochoroiditis, Cryptococcus chorioretinitis and other conditions like spontaneous retinal detachment, Kaposi's sarcoma squamous cell carcinoma of the conjunctiva and other benign and malignant tumors of the eye [18,20]

3.0. REVIEW OF LITERATURE

Corneal ulceration and sub sequent corneal scarring are at present a leading cause of ocular morbidity and unilateral blindness in developing countries.[1]

Several studies have been done in different parts of the world on the epidemiology of infective corneal ulcer. The incidence of this condition varies from 11.0 per 100,000 person years in the united state to 799 per 100,000 person years in the developing nations.[8, 11 ,15]

In the developing countries, the incidence of infective corneal ulcer has increased during the last three decades with the widespread use of contact lenses

Studies have shown an increase in the prevalence of corneal ulceration related to HIV infection. Reports from developed countries have shown that contact lens wear is the major cause of corneal ulcer. This contrast to reports from developing countries which show that the major cause of corneal ulceration is ocular trauma[8].

Epidemiological pattern of corneal ulceration varies significantly from country to country and even from region to region. In order to develop a comprehensive strategy for the diagnosis, treatment and ultimately for the prevention of corneal infections, the etiological factors predisposing to ulceration and the pathogenic organisms which are responsible must be determined[11].

Infective corneal ulceration constitutes one of the ophthalmic problem necessitating hospital emergency and attention of ophthalmologist.[16].The cornea being the

outermost covering of the eyeball is exposed to various external factors such as mechanical, chemical, thermal, radiation, electrical and infectious.

Infectious agents may be airborne or waterborne or carried by dust, insects, fingers, towels and other causes of micro trauma to the cornea. Organisms can not generally invade an intact, healthy cornea [5]. However; certain conditions can allow an infection to occur, like mild scratch, micro foreign body and damaged corneal.[22]

Low immunity exposes the body including the cornea to the risk of infection.

The incidences of corneal infection associated with Human Immunodeficiency virus infection have increased dramatically, due to the following factors.[4, 7, 8]

- Decreased body defence mechanism.
- Increased risk for opportunistic infection.
- Increased survival time of HIV pts- on ARV.
- Failure to suppress transient pathogens.

About 40 million individuals are known to be infected with the HIV world wide. Africa is the leading continent with highest prevalence of HIV infected people. Though Africa has only 12% of world's population, 60% of HIV infected people are found in this region, Sub Saharan Africa being the leading part of the continent. Among the individuals who are infected with HIV, approximately 70-80% will be treated for an HIV-associated eye disorder during the course of the illness.[20.]

The acquired immune deficiency syndrome (AIDS) is defined by the centers for disease control (CDC) as a disease that is at least moderately indicative of underlying cellular immune deficiency in a person who has no known cause of

underlying reduced resistance to inflammatory agents reported to be associated with infective corneal ulceration [23.2 7]

The Immunosuppression caused by HIV infection increases the incidence of eye infection. The incidences of infections associated with HIV infection have increased dramatically, as results of incensed survival time of the immunosuppressed patients.

Immune Reconstitution disease (IRD) may affect the eye in patients with advanced HIV disease soon after the initiation of effective ART. It may lead to exacerbation of previously treated opportunistic infection. A new presentation with unusual manifestations of the eye like uncommon retinitis, uveitis, and vitreitis occur during ART. [5,6,7,8]

Spontaneous infective corneal ulceration in the absence of ocular predisposing factors is rare, but known to be manifestation of Human Immunodeficiency Virus (HIV) infection.

Cornea manifestation of AIDS non infectious; peripheral corneal ulcers. Herpes Zoster ophthalmicus, Herpes simplex keratitis, keratoconjunctivitis sicca and corneal ulcers.6,18

Although the clinical characteristics of bacterial ulcers caused by specific individual organisms have been previously described, it is not generally possible to identify the causative agent by clinical examination alone. The microorganisms by virtue of their toxins, adherence capabilities, invasiveness and even strain

differences within each species may produce different types of clinical picture.

The clinical picture may also vary or alter in those patients using contact lenses or with a previous corneal scar due to viral infections, trauma, or surgery.

Clinical observation has shown that the number of patients with infective corneal ulcers attending the Muhimbili National Hospital in eye clinic has increased over the past few years.

Together with the known etiological or predisposing factors to infective corneal ulceration like nutritional, neurological allergic and infectious, several authors have reported an association with acquired Immunosuppression due to HIV-infection [18].

4. 0.CORNEAL ULCER.

When the mechanical defenses of the epithelial layers are breached so as to expose normally sterile areas, if a critical component of the immune system that normally prevent microbial invasion fails, severe infections can result from the normal microbial flora [1,5].

However, even when both the mechanical and immune defense systems are intact, pathogenic microbes can cause infections by means of specific virulent characteristics that allow the microbes to invade and multiply.

A corneal ulcer forms when the surface of the cornea is damaged or compromised. Ulcers may be sterile without infecting organisms or infectious.

A complication resulting from corneal disease is enormous. In the developing word probably about half the uniocular blindness is due to corneal lesions in children [12]. Diseases like trachoma, infective corneal ulcers, and traumatic corneal ulcers, keratomalacia, leprosy and paralytics cause these corneal lesions.

However, there are no global statistics for the incidence and prevalence of corneal ulcers in relation to Human Immunosuppressant Virus.

Etiology of infective corneal ulcer.

The main causes of corneal ulcers in the general population are: Infections-caused by bacteria, viruses, fungi and Chlamydia. Other causes include, Vitamin A deficiency, 7th cranial nerve palsy which leads to exposure keratitis, neuro-trophic corneal ulceration which occurs in 5th cranial nerve palsy which leads to loss of cornea sensation, allergy, trauma and use of contact lens.[9, 11]

1. **Bacterial corneal ulcers.**

Bacteria are the most frequent causative organism of corneal ulcers. The most frequently isolated bacteria being staphylococcus epidermidis in 90%, followed by betahaemolytic streptococcus, pseudomonas, klebsiella pneumonia (Friedlander's bacillus), moraxella liquefactions and gram-negative bacterial. [2]

Studies has reported from San Francisco, California that staphylococcal infection was the most common, followed by pneumococcal infection. Pneumococcus is reported to be the most common cause of bacterial corneal ulcers; they are commonly seen in old and debilitated individuals, and alcoholics [8, 12].

Bacterial corneal ulcers generally follow a traumatic break in the corneal epithelium, there by providing an entry for bacteria.

The traumatic episode may be minor, such as a minute abrasion from a small foreign body, or it may result from such causes as tear insufficiency, malnutrition or contact lens use. [15]

2. **Chlamydia corneal ulcers**:

Chlamydia trachomatis serotype **a, b, c,** and **d** is the offending organism. In trachoma, corneal ulcers usually follow complications of the chronic conjunctiva disease which causes entropion with trichiasis .The constant rubbing action of the inward bending eyelashes rubbing on the cornea causes abrasion and ulceration. These ulcers may then be infected.

3. **Viral corneal ulcers:**

Viruses can penetrate and damage intact corneal epithelium, especially in debilitated individuals. Commonly, viral corneal ulcers may also follow trauma which may be as minor as an abrasion of the epithelium by foreign bodies such as a dust particle or eyelash.

Viral corneal ulcers are less common than bacterial corneal ulcers since most viruses usually cause keratitis without ulceration. Viral corneal lesions are seen following acute febrile illness, overwork, psychological disturbances, minor trauma or condition of immune depression.Viruses of greatest importance in corneal ulceration are herpes simplex and varicella-zoster viruses. Other viruses include vaccinia, measles virus and small pox virus which is extinct. In Herpes simplex, infection follows infiltration of corneal epithelium by viruses. The epithelial cells form white plaques which enlarge to form dendritic lesions. These dendritic lesions have been shown by electron microscopy to be syncytia formed by fusion of rounded and liquefied epithelial cells.[65, 68]

a**: Herpes simplex virus corneal ulcers.**

This is by far the most frequent viral corneal ulcer. The typical lesion is the dendritic ulcers caused mostly by recurrent herpes simplex virus type-I.

In Immunocompromised individuals these dendritic lesions may coalesce to form geographical (amoeboid) corneal ulcers. Failure of dendrite or geographical ulcers to heal may result into trophic ulcers (herpes metaherpatica) in which no viruses can be identified.

have been on the increase due to indiscriminate use of antibiotics and corticosteroids and due to the association with HIV infection.

Reports from different researchers have shown variation in the commonly isolated fungi in corneal ulcers. In Europe and Northern USA, aspergillus fumigatus and other aspergillus species were the most frequently isolated fungi[18, 20, 22]. However, in Nigeria fussarium solani was the most frequently isolated fungus. It is accounted for 12(57.1%) of the 21 identified cases of fungal corneal ulcer. Aspergillus's furrigatus and other species were second in frequency, being responsible for 5(25.8%) of the cases [18]. Aspergillus, fusarium, Cryptococcus, coccidioides, blastomyces, Candida albcans and rhinosporidium have been implicated in corneal ulceration.Fungal corneal ulcers usually follow trauma, especially that due to vegetable matter.

In fungal infection, following disruption of the corneal epithelium, there is replication of fungi, release of mycotoxins, proteolytic enzymes corneal necrosis, antigen-antibody reaction with formation of immune ring and satellite lesions, hypopyon and uveitis.[18, 19]. Considering the importance of ulceration as a worldwide causes of monocular visual loss, there are surprisingly few studies evaluating the microbial etiological factors predisposing a population to corneal infection. Several investigators have reported the prevalence of bacterial and fungal pathogens isolated from ulcerated corneas, but until now there has not been a population based study demonstrating the true incidence of infective corneal ulcers in developing countries.

Pathogenesis of infective corneal ulcer.

Corneal ulcer forms when the surface of the cornea is damaged or compromised. Risk factors include contact lens use, trauma, ocular surface disease, and ocular surgery. Overnight contact lens wear has been shown to be associated with increased risk. Fungal keratitis can occur after a corneal injury involving plant material, or in immunosuppressed individuals.

Corneal damage by microbial organisms may be by one or a combination of the following.

i. Direct corneal invasion

ii. Proteolysis enzyme production or liberation of endo-or exo-toxins in the case of bacteria

iii. Immunological responses, either antigen- antibody reactions or cell- mediated reactions.

iv. Release of mycotoxins, proteolytic enzymes corneal necrosis, and antigen-antibody reaction in fungal infection

v. In viral infections may be replication of bacteria within cells and causes mixed infection.

With disease progression the symptoms of ocular pain, lacrimation and visual loss are experienced. Severe infections may present with hypopyon, impending and for corneal perforation. With specific treatment healing usually occurs leaving various degrees of visual impairment.

Infective corneal ulceration in HIV infected patients.

Reports indicate that more than 50% of HIV infected patients have anterior segment manifestations [27, 30]. Corneal ulcer, Keratoconjunctivitis sicca and irridocyclitis are among the most common complications in the anterior segment of the eye. The Immunocompromised host is at high risk of developing infection. Opportunistic micro organisms are responsible for most of the infections. Others are caused by normal resident flora of the human body. The HIV patients may fail to suppress the transient pathogens [32, 37]

A study from the United Kingdom reported factors associated with an increased risk of a corneal ulcer as invasive events, extended wear of hydro gel contact lenses in which the incidence was about eight times. However in India and sub Saharan countries where the prevalence of HIV/AIDS is high, the incidence of infective ulceration is about 54% of general population in a non contact lens wear [34, 35] More over the clinical symptoms and signs of infective corneal ulceration in patients with HIV infection were very severe lesion requiring inpatient management. Patients are reported to present with sight threatening complications.

A study done in India about polymicrobial keratitis in patients with HIV described the non-responding to treatment in a polymicrobial, and spontaneous corneal ulceration in HIV positive patients, and acanthamoeba was among the microorganism isolated [17]. This study also found that acanthamoeba keratitis is usually associated with local predisposing factors including the opportunistic

infection due to lower immunity of the body caused by Human immunodeficiency Virus.[38, 56.] A study in Singapore showed that topical natamycin and amphotericin B are the first line treatment for suspected fungal corneal ulceration because fusalium in addition to aspergillum species are the most commonly isolated organism's locally.[38]

In more severe cases with impending or presenting corneal perforation or sclera extension systemic antifungal drugs such as fluconazole and intraconazole. [62]

Immunosuppression caused by HIV infection increases the incidence of eye infections. However serious eye problems associated with advanced immunosuppression, such as blindness due to cytomegalovirus retinitis are less common in patient treated with effective antiretroviral therapy.

The infectious processes affecting the eye include herpes simplex virus (HSV), herpes zoster-virus (HZV), and syphilis.[61]

Immune reconstitution disease (IRD) may affect the eye in patients with advanced HIV disease soon after the initiation of effective (ART).[49]

IRD may lead to exacerbation of a previously treated opportunistic infection or a new presentation (often with unusual manifestations) of a previously sub clinical infection (by clinical manual for management of the HIV infected Adult-2006) [45, 59]

5.0. MANAGEMENT OF CORNEAL ULCERS

Knowledge of the sensitivity of the various etiological micro-organisms to commonly used drugs is very important. Accurate management of corneal ulcer depends on early diagnosis of the organisms and knowledge of their culture sensitivity results. Unfortunately, delay in this procedure and emergency of resistant strains has in many times led to failure of therapy and hence resulted into loss of vision of the affected eye.

Treatment of corneal ulcers is divided into medical and surgical treatment.

I. Medical treatment

Immediately following history taking and clinical examination of the patient, the following is done:-

1. Corneal scrapings from the floor or edges of the ulcer for gram stain, culture and sensitivity and KOH.

2. Administration of appropriate antibiotic therapy i.e. broad spectrum antibiotics, antiviral or antifungal drugs either topically, sub-conjunctival or systemically.

The most accepted method of medical approach to corneal ulcers is that patients with ulcers less than 3 mm in diameter and peripherally located should be treated as outpatients on 1 hourly topical antibiotics during daytime and 2 hourly antibiotics at night. Those with ulcers more than 3 mm or those with centrally located ulcers should be hospitalized and subjected to one hourly topical medication and subconjunctival injections. Patients with corneal ulcers more than 3 mm and with hypopyon, regardless of their location should be given topical, subconjunctival and parenteral antibiotics.[57, 58, 62]

Supportive treatment.

3. Analgesics. Which are given to relieve pain.

4. Mydriatics are used to prevent anterior peripheral and posterior synechiae. Cyclopentolate eye drops twice a day.

5. Patching of the eye where there is no eye discharge, keeps the eye in a resting position by minimizing the effect of friction from eyelids

In impending corneal perforation a pressure pad is applied. Drugs such as acetazolamide and/or hyper osmotic agents are also given to lower intraocular pressure.

As soon as culture sensitivity results are obtained the drug of choice is started.

In case of Keratomalacia, on top of the above mentioned the mainstay treatment is immediate administration of Vitamin A and drugs to eliminate secondary bacterial infection.

Vitamin A 200,000IU orally or 200,000 I.U. water soluble Vitamin A intramuscularly start for children 12 months of age or more. 2 days later or on the day of discharge the above dose is repeated orally. For children less than 12 months old half the above dose is given.[66, 68]

ii. Surgical treatment.

Despite intensive medical therapy the ulcer may not respond and surgical treatment is indicated. This may be due to delay in presentation and diagnosis leading to delay in starting specific treatment. Various surgical techniques have been advised and carried out with varying results:

1. Debridement:

This therapy has been used mostly in the treatment of dendritic corneal ulcer. The removal of the necrotic tissue was believed to eliminate the infecting organism and facilitate drug penetration into the tissue. Methods used include chemical debridement using carbolic acid, iodine, and trichloroacetic acid; Mechanical debridement and cryo curettage.[31]

2. Covering of ulcer with conjunctival flap

This method has been used in ulcers threatening to perforate, small perforations and in indolent ulcers. In the latter the aim is to hasten healing by supplying the avascular cornea with nutrients and antibodies through the conjunctival vessels. The outcome of this therapy has been variable. In infective corneal ulcers it has been rewarding.

3. Peritomy.

Alone or combined with cryotherapy and heat cauterization of blood vessels reaching the ulcer. The procedure has been found to be good in Mooren's ulcer and marginal ulcer in which it is aimed at eliminating the conjunctival source of Collagenase and proteoglycanase by interrupting conjunctiva attachment to the cornea.

4. Cauterization: Besides being used in Debridement of ulcers (chemical cauterization) it can be used in the form of heat cautery to severe blood vessels reaching the corneal ulcer with the aim of eliminating toxins or allergens reaching the ulcer. Other studies reported successful treatment of Mooren's ulcer using deep

3. **Lavamisole** (Ketrax): This drug has been used in the treatment of Herpes zoster ophthalmicus and recurrent Herpes simplex both in humans and experimental animals. It is advocated that it does so by its non-specific immunostimulation effect.

4. **Contact Lenses**: Which are therapeutic have been used in the treatment of corneal ulcers alone or in conjunction with antibiotics. The mechanism of the contact lens in this case was thought to be:

a) It acts as a splint to prevent further trauma associated with eyelid movement to the cornea.

b) It maintains an antibiotic-rich tear film over the ulcer.

c) It alters the metabolic environment of the enclosed cornea maybe by changing the pH or reducing the amount of available oxygen, so that the causative organism can no longer multiply or survive.

6.0. VISUAL OUTCOME.

Corneal ulcers are causes of monocular blindness world wide[1, 9].

Following healing of the ulcer a corneal scars ensues and is a cause of varying degrees of visual impairment and blindness in affected eyes[2, 6]

With intensive and early treatment the resultant scar may be reduced so as not to impair visual acuity. Patients with HIV tend to have more severe clinical presentation and therefore form extensive and deep scars leading to monocular blindness.

The leading cause of infective corneal ulceration in HIV infected patient has been reported to be fungal infection. An availability and cost of drugs for fungal infection may leads to inadequate treatment and hence poor visual outcome.

A failure to implement standard therapy at first contact has been reported to be a marker for poor visual outcome in infective corneal ulceration.[20]

The study will highlight the differences between the visual outcome of corneal ulcers in patients with and without HIV infection.

7. 0.STATEMENT OF THE PROBLEM

Infective corneal ulceration is a major cause of uniocular blindness word wide.

In Tanzania there is little information about prevalence of corneal ulcer in HIV infection and causes of spontaneous ulcerative keratitis. The incidences of infective corneal ulceration associated with HIV infection has increased dramatically, as a result of increased survival time of the immunocompromised individuals following the introduction of ARV.

Knowing the clinical presentation and frequency of corneal infection in patients with the acquired immunodeficiency syndrome, together with the changing pattern of infective corneal ulcer and predisposing factors will help us in a proper management of these patients, in our hospital

Efforts on the reduction of blindness need to be directed towards the control of predisposing factors which leads to complication like permanent blindness. Reduction of magnitude of corneal ulcer is not possible if the prevalence and magnitude of the disease is not known. Since corneal ulcer in both HIV and non HIV infected patients, studying the offending organisms in the groups of patients and characteristics presentation will provide light on proper management of the patients. Early detection of causative of ulcerative keratitis will enable proper measures at right time to avoid corneal complications.

8.0. RATIONALE OF THE STUDTY.

Seventy percent of adult AIDS patients will experience an ocular complication of the disease at some point and infective corneal ulceration is one of them, resulting into blindness due to corneal opacities which remain as a public health problem. The eye clinic at MNH has observed an increase in the number and severity of corneal ulcers among its patients. A number of studies including one done in Tanzania [68], have shown the association between HIV infection and infective corneal ulcer.

Results of this study will help in the comprehensive care of a patient with HIV infection. Knowing the aetiology and clinical presentation of corneal ulcer in local setting will help ophthalmologist to decide on the mode of treatment to avoid serious ocular and visual complication of corneal ulceration.

9.0.STUDY OBJECTIVES:

8.1 Broad objective

To compare the clinical presentation of infective corneal ulcer in HIV and non HIV infected patients at Muhimbili National Hospital-Dar-es-salaam.

8.2 Specific objectives.

1. To determine social-demographic characteristics of patients with HIV and non HIV infected with corneal ulcers attending eye clinic at Muhimbili National Hospital.
2. To determine the prevalence of infective corneal ulcer among patients with HIV and Non-HIV at Muhimbili National Hospital.
3. To compare the clinical signs and visual outcome in HIV and Non HIV infected patients.
4. To determine the etiology of infective keratitis in HIV and non HIV patients.

10.0. METHODOLOGY

10.1 Study Design:

This is a Cross-Sectional descriptive and comparative study of infective corneal ulceration which was comparing the clinical presentation of infective keratitis in HIV and non HIV infected patients attending eye clinic at Muhimbili National Hospital May 2007 to May 2008.

The Muhimbili National Hospital (MNH) is a tertiary care hospital which is situated in the middle of the City of Dar-es-salaam, It is a teaching hospital for the Muhimbili University of Health and Allied Sciences (MUHAS).The hospital serves the capital and the surrounding regions and the whole nation at large as the top referral hospital. Dar es Salaam city has three municipal hospitals which refer patients to Muhimbili National Hospital as Out Patients as well as inpatients. It serves about 1000 outpatients per day and admits 1000 patients per week. The hospital has among other departments, the department of Ophthalmology with in patients as well as outpatients services. The eye clinic is one among the specialized clinics, which is conducted every day from Monday to Friday 9.00am to 16.00pm, for outpatients.

10.2 Sample size

The sample size was calculated by the formula given below:

$N=Z^2 P (1-P)/D^2$

Where N=Number of subjects required

Z=95% confidence level (Z-score 1.96)

P= Estimated proportion of the patient with corneal ulcer who have HIV infection (P=83.5%, study done in UK)

1-P= Estimated proportion of subjects without the disease.

E=Desired precision (marginal error) 0.05

Sample was 158. For the purpose of increasing the statistical significance of the study, sample size was raised to 186.

10.3 Inclusion criteria

1. Consenting patients with corneal ulcer
2. All patients with corneal ulcer attending the eye clinic at Muhimbili National Hospital during the study period were eligible for recruitment.
3. Those patients who accepted to test for HIV sero status.

10.4 Exclusion criteria.

1. Patients who did not consent with corneal ulcer.
2. Patients with traumatic injuries, congenital malformation of the cornea, those with chemical injury, nutritional deficiency and exposure corneal ulcers were not included in this study.
3. Patient who refuse HIV testing.

10.5 Data collection:

Patients who presented with clinical signs of corneal ulcers were recruited for the study. An informed consent was obtained before recruitment. A history was taken from patients themselves and from parent/guardian in case of children.

10.6 Data sheet:

For each patient a data sheet was filled on which details about age, sex, occupation, marital status, presenting symptoms and their durations were obtained. The visual acuity was assessed using a Snellen's/illiterate E chart for each eye.

10.7 Description of corneal lesion.

The eyelid was examined for any pathology. A thorough examination of the cornea was done with a torch and slit lamp biomicroscope. Corneal lesions were stained with Fluorescein stain. Size of the corneal lesion was measured using caliper. The infiltrate was measured in square millimeters and its location was determined according to zones (central and peripheral).

The depth was graded as superficial, half thickness and full thickness. Impending perforation, hypopyon and perforated corneal ulcer were ascertained during slit lamp biomicroscopy examination. The anterior and posterior segments of the other eye were examined.

10.8 Specimens collection and transportation.

Corneal scrapping was performed to all patients for Gram stain, KOH and bacterial and fungal culture and microbial susceptibility test.

Eye lids were cleaned with sterile cotton swabs, topical one drop of amethocain 1.0%) was instilled in the conjunctival sac. Under direct visualization and adequate magnification with slit lamp, operating

microscope or magnifying loupe, a kimula spatula or surgical blade no.15 were used to gently scrap the base and edges of the corneal ulcer.

Specimen was immediately placed in Stuarts transport medial and sent to CPL with completed request forms for processing.

10..9 Isolation of microbial pathogens.

The specimen was inoculated into Blood agar, chocolate agar for *Neisseria gonorrhea,* and *Haemophillus influenza* and MacConkey for enteric organisms (*E.coli*, klebsiela species, proteus species) and *Pseudomonas auriginosa.*

Diagnosis of chlamydia and Virus were made on clinical ground. However,even when suspected still corneal scraping were taken for Gram stain and KOH. For chlamydia the following clincal sing were used for diagnosis: The presence of follicals,palpebral scering and trichiasis were used .

For the Virus Dendritic apperence/punctet corneal ulcer were used for diagnosis after excluding bacterial and fungal infection.

10.10 HIV Serology

Counseling for HIV-testing as recommended by the National AIDS Control Program (NACP) of the Ministry of Health was performed.

Three milliliter of venous blood was collected in sterile vacutainers tube without anticoagulant and sent to the virology section at CPL for enzyme immunoassays. Two standards Enzyme Linked Immunosorbernt Assay (ELISA) tests were done, the Wellcozyme HIV Recombinant test (MUREX) and the Enzygonost Anti-HIV1/2 Plus test. A sample was considered HIV positive) if positive on both ELISAs. Results of HIV screening test were recorded on the data sheet.

10.11 Management benefits for the patients.

Treatment was immediately started after the clinical diagnosis on basis of clinical presentation (symptoms and signs) of infective corneal ulceration.

In culture negative cases with poor response on local antibiotics treatment was switched to combined therapy of antibiotics and antifungal.

Since readymade antifungal eye drops were not available in Tanzania cases with smears proven as fungal infection were treated with topical Daktarine 2% suspension locally prepared.

Fresh preparations were reconstituted every 4-5days from Daktarine skin cream Antifungal eye drops were instilled one hourly during working time. e. No any preservatives were used that's why suspension was used for a very limited time.

Duration of hospitalization and follow up after discharge were individualized per patient requirement and response to treatment.

All patients who were suspected of fungal infection from clinical findings and those who had impending perforation under went conjunctival flap immediately after scrapping then they continued with medical treatment.

Patients were then divided into two groups following the ELISA results; they were identified whether they were HIV positive or HIV negative.

Patients in whom laboratory investigations failed to reveal microbial diagnosis were managed based on clinical presentation of the ulcer. Patient with clinical improvement were discharged home in a close follow up at least 3 to5days intervals.

Signs of good response to treatment were decrease in ulcer size, blunting of its margins, and decrease in anterior chamber reaction. Signs of treatment failure were increase in ulcer size and increase in the anterior chamber reaction.

10.12 Data analysis and Management

All questionnaires were coded and data entered into computer using EPI Info 6 software data Cleaning was done before data analysis by using EPI 6. Statistical significance was tested by using the Chi-squared test. A p-value less than 0.05 were considered statistically significant. Frequency distribution was used to summarize data.

10.13 A pilot study:

A pilot study was conducted to check the success of recruiting procedure and collection of data before starting the actual data collection.

10.14 Limitations of the study.

Limited facility of laboratory reagents made it very difficult to screen many different microorganisms especially viral, Chlamydia and sensitivity to isolated fungal organisms.

10.15 Ethical consideration

The study was carried out in accordance with existing ethical guidelines. Ethical and research clearance was obtained from the Muhimbili University of Health and Allied Sciences Senate Research and Publication Committee. Permission to conduct this study was obtained from MNH authority. The aim and benefits of the study were explained to all participants. They were free to pull out of the study any time they wanted and that could not interfere with their treatment schedule. Those who were not ready to participate in the study were managed according to the hospital protocols. A formal written consent was obtained from each participant before enrolment. All patients who were found to be HIV positive were counseled as per hospital protocol and were informed about the possible treatment. Follow up was made until the ulcer healed.

12. RESULTS.

Two hundred and two patients were diagnosed to have infective corneal ulceration during the study period. Sixteen patients refused to be screened for HIV infection. One hundred eighty six patients were recruited for the study.

Description of the study population.

One hundred eighty six patients were diagnosed to have infective corneal ulceration during the study period and they were screened for HIV sero status.

Table: 1 Age distribution of 186 patients with infective corneal ulcer by HIV sero status.

Age group-(years)	Corneal ulcer		HIV positive		HIV negative	
	N	%	N	%	N	%
0-19	17	9.1	2	1.8	15	20.0
20-29	52	27.9	29	26.1	23	30.7
30-39	78	41.9	47	42.3	31	41.3
40-49	30	16.1	28	25.2	2	2.7
50 +	9	4.8	5	4.5	4	5.3
Total	186	99.8	111	99.9	75	100

χ^2=34.20, df=4, P=0.0001

Affected patients in both groups were in the age range between 20-49 years with a peak at 30-39 years which comprised 41.9%.

Fifteen (20.0%) patients with corneal ulcer were below 20 years in HIV seronegative compared to only two (1.8%) patients in HIV seropositive group. (Table 1)

Table 2: **Sex distribution of 186 patients with infective corneal ulcer by HIV sero**

status

Sex	Corneal ulcer		HIV positive		HIV negative	
	N	%	N	%	N	%
Male	124	66.7	89	80.2	35	46.7
Female	62	33.3	22	19.8	40	53.3
Total	186	100	111	100	75	100

χ^2=22.6, df=41 P=0.0002

The study population consisted of hundred twenty four (66.7%) males and sixty two (33.3%) females

There were eighty nine (80.2%) males with infective corneal ulcer in the HIV seropositive group, compared to only thirty five (46.7%) of affected males in the HIV sero negative group. (Table.2).

Table: 3 The distribution of 186 patients with infective corneal ulcer by marital status and HIV sero status.

Marital status	Corneal ulcer		HIV positive		HIV negative	
	N	%	N	%	N	%
Cohabiting	55	29.5	37	33.3	18	24.0
Single	79	42.5	49	44.2	30	40.0
Married	35	18.8	11	9.9	24	32.0
Divorced	11	5.9	10	9.0	1	1.3
Widow	6	3.2	4	3.6	2	2.7
Total	186	99.9	111	100	75	100

χ^2=1.52, df=4, P=0.0001

Most (72.0%) of the corneal ulcer patients were either cohabiting or single in HIV seropositive group.

There were thirty seven (33.3%) cohabiting patients with infective corneal ulcer in HIV sero positive compared to eighteen (29.3%) patients who were HIV sero negative.

About seventy two percent of patients in the HIV seronegative group were either single or married. (Table.3)

Table: 4. The distribution of 186 patients with infective corneal ulcer by occupation and HIV sero status.

Occupation	Corneal ulcer		HIV positive		HIV negative	
	N	%	N	%	N	%
Employed	27	14.5	15	13.5	12	16.0
Unemployed	29	15.6	19	17.1	10	13.3
Petty trader	94	50.5	58	52.3	36	48.0
Farming	36	19.4	19	17.1	17	22.7
Total	186	100	111	100	75	100

χ^2=3.24, df=3, P=0.0004

More than half of the study population were petty traders (50.5%), while 19.4% were farmers.

Fifty eight of the patients (52.2%) patients with infective corneal ulceration were HIV seropositive compared to 36 (48.0%) patients in HIV seronegative.

Farmers were equally affected by infective corneal ulcer. There were nineteen (17.1%) patients in the HIV sero positive groups and seventeen (22.7%) patients in the HIV sero negative group. (Table 4)

Figure 1: The distribution of the study population by HIV serological status.

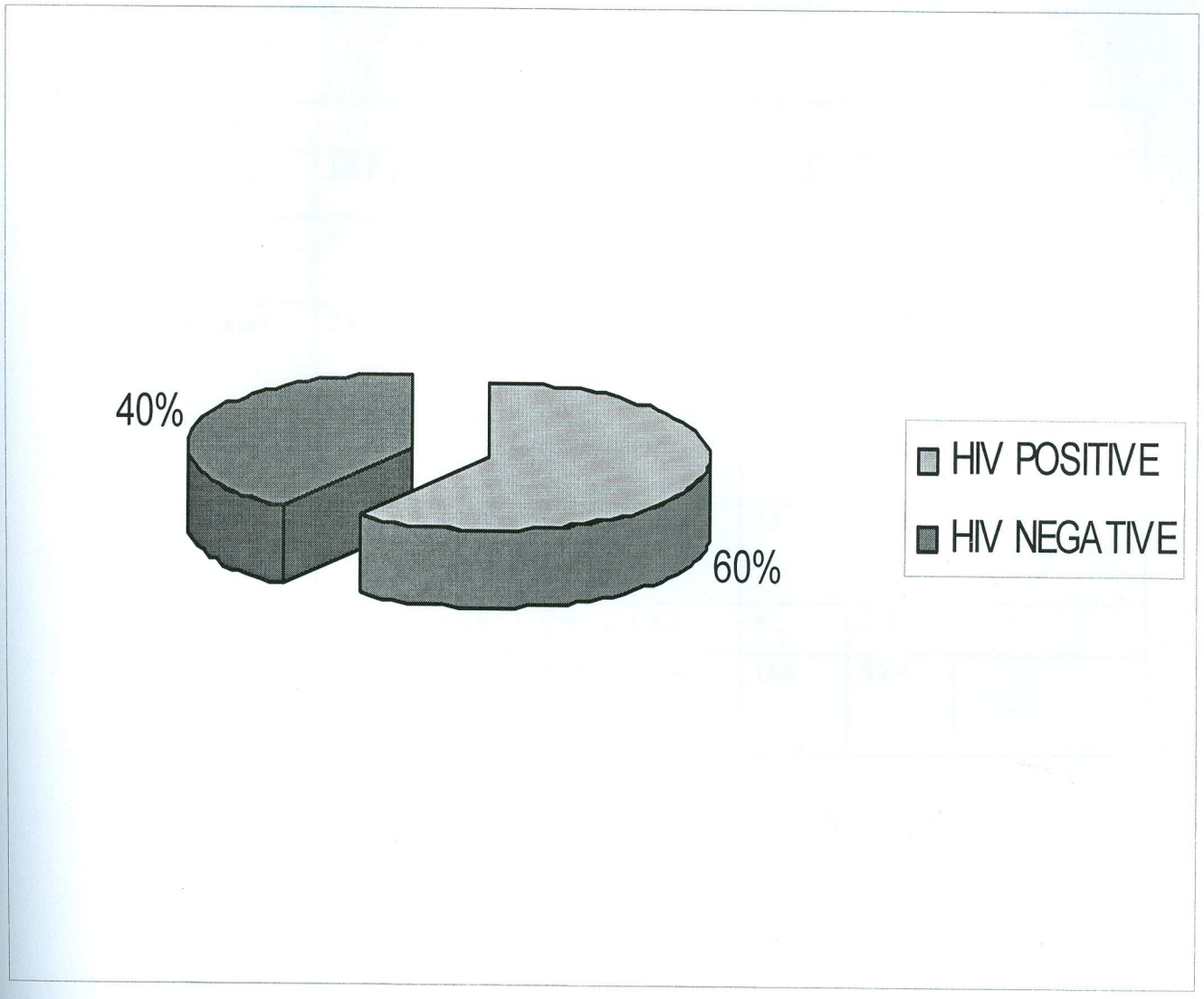


Figure:1

One hundred eleven (59.7%) of the study population were HIV seropositive and seventy five (40.3%) were HIVseronegative.

Table: 5. The microbial etiology of corneal ulcer in 186 patients by HIV sero status.

	HIV status						
Aetiology	HIV-positive		HIV-negative		Total		
	n	%	n	%	n	%	P-value
Bacterial	33	29.7	46	61.3	79	42.4	<0.001
Fungal	59	53.2	18	24.0	77	41.4	<0.001
Viral	18	16.2	7	9.3	25	13.4	0.11
Chlamydia	1	0.9	4	5.3	5	2.7	
Total	111	100	75	100	186	99.9	

Fungal corneal ulceration occurred in 59 (53.2%) of HIV seropositve patients, while it accounted for 24.0% only for HIV seronegative patients.

Bacterial corneal ulceration occurred in 33 (29.7%) of all HIV sero positive patients, while it occurred in 46 (61.3%) in HIV seronegative patients.

Most (72.0%) of the 25 viral corneal ulcers were in HIV seropositve patients.

Table:6. Isolated microorganisms etiology of corneal ulcer in HIV sero status.

Isolated Microorganisms	Number of cases		HIV positive		HIV negative	
	N	%	N	%	N	%
Staphylococcus spp	35	18.8	17	15.3	18	24.0
Streptococcus spp	23	12.4	9	8.1	14	18.6
Candida	41	22.3	33	29.7	8	10.6
Klebsiella spp	9	4.7	5	4.5	4	5.3
Pseudomonas aeruginosa	6	3.2	3	2.7	3	4.0
Bacillus spp	5	2.7	3	2.7	2	2.6
E.coli	9	4.7	4	3.6	5	6.6
Pneumococcus spp	4	2.2	2	1.8	2	2.6
Cornebacteria spp	3	1.6	1	0.9	2	2.6
Moraxella spp	5	2.7	2	1.8	3	4.0
Negative results	46	24.7	32	28.8	14.	18.6
Total	186	100	111	100	75	100

Bacteria were the most commonest cause of corneal ulceration affecting (46.2%) of the study population. The second commonest cause of the corneal ulceration was fungal infection which accounted for 39.2%

The commonest cause of corneal ulceration in HIV sero positive patients was fungal which occurred in 53.2% of patients.

Table 7: The clinical presentation of infective corneal ulcer according to HIV status. N = 186

	HIV status					
Signs	HIV-positive		HIV-negative		Total	
	n	%	n	%	n	%
Hypopyon	57	51.4	33	44.0	90	48.4
Impending perforation	36	32.4	28	37.3	64	34.4
Perforation	15	13.5	9	12.0	24	12.9
Endophthalmitis / Phthisis bulbi.	3	2.7	5	6.7	8	4.3
Total	111	100	75	100	186	100

χ^2=2.53, df=3 P=0.47653

Hypopyon occurred in 48.4% of the study population.

Fifty seven (51.4%) of corneal ulcers in HIV sero positive patients, presented with hypopyon compared to about 44.0% in HIV seropositive patients..

Thirty six (32.4%) ulcers in HIV seropositve patients presented with impending perforation compared to twenty eight (37.3%) of HIV seronegative patients.

Fifteen (13.3%) corneal ulcers in HIV seropositve group had perforation compared to nine (12.0%) ulcers in HIV seronegative group. These findings were not statistically significant.

Table 8 Visual acuity on admission in relation to HIV serological status N=186.

Visual acuity	HIV serological status				
	HIV positive		HIV negative		Total
	N	%	N	%	N
6/4-6/18	1	0.9	3	4.0	4
6/18-3/60	12	10.8	13	17.3	25
<3/60	98	88.3	59	78.6	157
Total	111	100	75	99.9	186

χ^2=12.87, df=2, P=0.0001

There was only one (0.9%) eye with normal vision between 6/6 -6/18 on admission in HIV seropositive patients, compared to three (4.0%) eyes in HIV sero negative patients.

Ninety eight (88.3%) eyes were blind on admission in HIV seropositive group, as compared to fifty nine (78.6%) eyes in HIV seronegative group.

Table 9. The relationship between etiology of corneal ulceration and post treatment visual outcome N=186 by HIV sero status.

Etiology	Visual outcome of infective keratitis on day of discharge.									
	6/6-6/18		6/18-3/60		>3/60		HIV seropositive		HIV seronegative	
	N	%	N	%	N	%	N	%	N	%
Bacterial	18	40.9	42	49.4	19	33.3	33	29.7	46	61.3
Fungal	5	11.4	37	43.5	35	61.4	59	53.2	18	24.0
Viral	21	47.7	3	3.5	1	1.8	18	16.2	7	9.3
Chlamydia	0	0.0	3	3.5	2	3.5	1	0.9	4	5.3
Total	44	100	85	99.9	57	100	111	100	75	99.9

Among the fifty seven blind eyes at discharge, thirty five (61.4%) were due to fungal infection, and among the eighty five eyes with visual impairment thirty seven (43.5%) were due to fungal infection.

Table: 10.Visual acuity at discharge in relation to HIV serological status.

Visual acuity	HIV serological status				
	HIV positive		HIV negative		Total
	N	%	N	%	N
6/4-6/18	25	22.5	19	25.3	44
6/18-3/60	51	45.9	34	45.3	85
<3/60	35	31.5	22	29.3	57
Total	111	100	75	100	186

χ^2=23.4, df=3, P=0.0001

Twenty five (22.5%) eyes in HIV sero positive patients had normal vision at discharge, compared to 19 (25.3%) eyes in HIV seronegative patients.

Thirty five (31.5%) eyes in HIV seropositive patients were blind at discharge compared to 29.3% blind eyes in HIV seronegative patients. (Table .10)

13. DISCUSSIONS

With the emergence of HIV/AIDS epidemic, many studies have been done in India and African countries to associate severity of infective corneal ulceration with HIV infection.[7, 8, 18]

The changes have been noted all over the world[5, 6, 7,8,11].

There is a significant variation in the etiology and clinical presentation of corneal ulceration in different countries. Studies have shown an increase in the prevalence of corneal ulceration related to HIV infection. Reports from developed countries have shown that contact lens wear is the major cause of corneal ulcer. This contrast to reports from developing countries which show that the major cause of corneal ulceration is ocular trauma. Results from our study revealed 59.7% of patients with infective corneal ulceration are HIV seropositive. In a study done at MNH in the era before HIV infection, keratomalacia was reported to be the commonest cause of corneal ulceration, and it was common among children below 9 years. This can be explained by the high prevalence of malnutrition especially vitamin A deficiency in children when the study was conducted. At that time there was a high prevalence of measles in children which led to vitamin A deficiency and subsequent keratomalacia.

Age and Sex distribution.

Studies in pre HIV era had shown the peak age for corneal ulcer was 9 years [5]. This was a time when keratomalacia in relation to measles infection was common. This is in contrast to findings in this study where the peak range for corneal ulceration was 20-49 years. On the other hand successful immunization against measles explains the shift of this trend (Table 1.).The study showed that 59.7% of the study population was HIV seropositive. HIV infection has been associated with increased corneal ulceration as shown in this study [8, 11].The age range for corneal ulceration in this study therefore corresponds to the age range for HIV infection. This study findings are in agreement with other recent studies that found corneal ulcer to be common in reproductive age [1, 18, 20]

Comparatively, since age at which HIV infection is seen more prevalent coincide with the age at which corneal ulcer is most prevalent and the fact that relatively high percentage of corneal ulcer patients were also HIV seropositive, it seems that HIV infection is one of the predisposing factors for corneal ulcer of this age.

Moreover, the age range of 20 -49 years is also the active age for production activities which include farming and other outdoor activities. Such activities expose the population to the development of corneal ulcers.

The study showed that farmers were equally affected by infective corneal ulcer in the HIV seropositive and HIV seronegative groups. There were nineteen (17.1%)

patients in the HIV sero positive groups and seventeen (22.7%) patients in the HIV sero negative group. (Table. 4)

In this study the male female ratio was approximately 2:1 which agrees with that of Panda A and Nayak N in Northern India.[28] In both studies males predominated.

Though it is known that HIV infection is more prevalent in females than in males, the results of this study in which there were more males with corneal ulcers than females may be explained by males being exposed to outdoor activities that predisposed them to corneal ulceration.

As was mentioned above outdoor activities like farming exposes one to contact with vegetation and soil that harbor infective organisms.

HIV sero status.

The study found out that 59.7% of the study population were HIV seropositive.

Most of the patients were not aware of their HIV-status when they first visited the eye clinic due to infective corneal ulceration and they had no other ocular or systemic manifestation. Many of them were diagnosed to be HIV-positive during their course of therapy due to cornea ulceration. Among one hundred eleven (59.7%) in HIV-seropositive patients, only seven patients (3.8%) were on treatment for HIV infection (ARVs).The remaining one hundred and four (55.9%) were not on treatment for HIV, as they were not aware of their HIV status.

Since quite high percentage of the patients who presented with corneal ulcer were not aware of their HIV sero status, then corneal ulceration need to be considered as one of the pointers for the need to screen for HIV infection. It also shows that in some patients corneal ulceration is the first manifestation of HIV infection.

While encouraging screening of all patients for HIV, patients with corneal ulceration in particular need special attention. The findings are similar to those in a study done by Bennie H. Jeng et al in San Francisco on Corneal ulceration and HIV infection, which reported the association between corneal ulcer and HIV infection [8].

Effort to screen for HIV in all patients with corneal ulcer is encouraged in order to detect them early and institute ARV accordingly

Etiology of corneal ulcer.

The commonest microbial aetiology of corneal ulcer in this study was bacteria comprising of 42.4% of the study population. This is in agreement with studies done in Switzerland[7].The second commonest cause was fungus (41.9%) followed by viral infection which occurred in 13.4% of the cases. This is also in agreement with studies done in India and U K [8, 11].

In this study the leading cause of corneal ulceration in HIV seropositive patients was fungus which occurred in 53.2% of cases. This is because in HIV seropositive individuals, fungal infection especially candidiasis is the most common opportunistic infection which affects most of the patients.

Also seventy two percent of all viral ulcers occurred in the HIV seropositive group. These results are in agreement with the studies done in Ghana and South India [11, 15]. The commonest microbial etiology in HIV seronegative patients was also bacterial accounting for 63.7% of the cases.

Chlamydia was the rarest microbial etiology of corneal ulcer comprising only 2.6% of the study population.

In the current study the commonest isolated bacteria in both HIV seropositive and HIV seronegative patients was streptococcus species and staphylococcus aureus, accounting for 57.2% of the patients while Candida albicans was responsible for most of the fungal infections occurring in 61.3% of the patients. These findings are similar to those found by other authors in UK [19, 20] who found staphylococcus species as the commonest cause of infective corneal ulceration comprising 39.3% of the study population.

This is in agreement with the studies done in India in patients from predominantly rural background which found that several traditional eye medicines had been used including vegetable matter which may be a factor in the etiology of corneal ulceration [24].

The author concluded that Health education is mandatory to prevent this avoidable cause of monocular blindness[24]. As emphasized in that study health education for awareness creation on causes and prevention of corneal ulcer is important for the community.

Severity of corneal ulcers.

Ulcers in HIV seropositive patients were severe than those in HIV seronegative group. Hypopyon corneal ulcers in HIV seropositive occurred in fifty seven (51.4%),`in contrast to thirty three (44.0%) in HIV seronegative patients. The proportion of corneal ulcers with impending perforation and those that had perforation were also higher in HIV seropositive group than in HIV seronegative group. This shows that HIV infection is associated with severe corneal ulceration.

The findings are similar to findings in a study done by Bennie H.Jeng in San Francisco in Corneal ulceration and HIV infection, which reported the association between corneal ulcer and HIV infection [8,11]

HIV infection reduces corneal immunity rendering fast multiplication and invasion of microorganisms leading to hypopyon and perforation.

To avoid loss of the eye, deep fungal and perforated ulcers underwent conjunctival flap procedure. A conjunctival flap prevents loss of intraocular contents in a perforated ulcer and prevents perforation in an impending perforation corneal ulcer. Healing of the ulcer is also speeded up by supplying more nutrition and immune cells to the avascular corneal tissue.

It is therefore necessary to create awareness in the community and among health care providers about the importance of early referral of patients with painful and red eyes to centers with ophthalmologist.

Presenting Vision and Post treatment Visual Outcome.

Among the fifty seven blind eye at discharge, thirty five (61.4%) were due to fungal infection, and among the eighty five eyes with visual impairment thirty seven (43.5%) were also due to fungal infection. This shows that corneal infection with fungus leads to poor post treatment visual outcome. (P.value-0.0001)

Of the forty four normal vision eyes at discharge, twenty one (47.7%) had viral infection. The study shows that viral infection is related to good post treatment visual out come. Viral corneal ulceration was related to good visual acuity.

Visual acuity at discharge in relation to HIV serological status showed that twenty five (22.5%) eyes in HIV seropositive patients had normal vision at discharge compared to 25.3% eyes in HIV seronegative patients. Thus HIV seropositive status is related to poor post treatment visual outcome.

Ulcers in HIV seropositive patients were severe with hypopyon and perforation which lead to poor visual outcome.

Thus 35(31.5%) eyes in HIV seropositive patients were blind at discharge compared to 29.3% blind eyes in HIV seronegative patients.

CONCLUSIONS

The study has shown that 59.7% of patients attending the eye clinic at Muhimbili National Hospital with infective corneal ulcers are HIV sero positive. They present mainly with fungal corneal ulcers which are severe in clinical presentation and have poor visual out come.

The common fungus is mainly Candida albicans, and the commonest cause of bacterial corneal ulcer is streptococcal and staphylococcal species.

RECOMMENDATIONS

1. Efforts to screen for HIV sero status for all patients, presenting with corneal ulcer should be instituted in the eye clinic.

2. The initial management of clinically suspected fungal and bacteria corneal ulcers at MNH should target Candida albicans and Streptococcus aureus species, respectively based on local experience.

3. Efforts to reduce complications of infective corneal ulcers in HIV seropositive patients require multi-displinary approach. Strategies have to be made to sensitize HIV seropositive patients, health workers and the general public on the importance of seeking medical help early.

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