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Clinical Profile and Predisposing Factors for Infective Keratitis in Dar es Salaam

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Abstract

Background

Infective keratitis is a commonly encountered ocular emergency and it is a major cause of corneal related blindness. The etiology and predisposing factors tend to vary with time and by geographic locations.

Methods

A hospital based cross sectional study was conducted at Muhimbili National Hospital (MNH) & Comprehensive Community Based Rehabilitation in Tanzania (CCBRT) hospitals among adult patients with infective keratitis from July to December 2020. Consecutive sampling was used to recruit 58 participants. A structured questionnaire was used to capture the demographics and predisposing factors for infective keratitis of the participant, and cornea-scrapping specimens were taken for microbiology laboratory tests. Data was analyzed using SPSS version 23.

Results

This study involved 58 participants who were attended and diagnosed to have infective keratitis at MNH and CCBRT during the study period. Majority (65.5%) of them were males. The median age of the participants was 36.30 years with a range of 18 years to 80 years. More than half (56.9%) of the participants presented to these tertiary eye hospitals late with blind eyes having visual acuities of less than 1.301 log MAR. Microbial etiology for infective keratitis in this study was bacteria in 84.5% of the participants. There was no single fungal isolate in both KOH mount and culture growth. The commonest bacteria isolate was *Staphylococcus aureus* in 36.1% of the participants. The leading predisposing factor for infective keratitis was a history of topical steroid use in 41.4% of the participants.

Conclusion and Recommendations

Microbial etiology for infective keratitis in Dar-es-Salaam is mostly bacterial and the leading predisposing factor for infective keratitis is topical steroid use. Therefore, initiatives should be taken to control irrational corticosteroid use to the eyes.

Key words: *Infective keratitis, Over the Counter Topical Cortical Steroids, Late presentation.*

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Introduction

Infective keratitis is the leading cause of cornea related blindness which is responsible for 1.5-2 million new cases of monocular blindness every year (1). Infective keratitis is the second common cause of ocular blindness after cataract in the developing world (2). The predisposing factors for and causative organisms responsible for infective keratitis vary considerably with time and by region (1). Ocular morbidities such as corneal scarring and subsequent visual loss can be significantly reduced by prompt institution of appropriate therapy guided by the knowledge of the causative agents, predisposing factors and drug susceptibility (3). Despite having many patients with infective keratitis in our facilities, there are limited studies in this topic in Tanzania. According to the study done at Kilimanjaro Christian Medical Center (KCMC) more than 10 years ago, the proportion of culture positive infective keratitis was 54% (4). Infective keratitis is treated empirically in most health facilities in Tanzania due to inadequate diagnostic resources. The use of empirical treatment in treating infective keratitis often leads to treatment failure and also prolonged hospitalization. The available local research findings on the clinical profile and predisposing factors for infective keratitis are outdated and may no longer be reliable. This may be due to possibilities of having new microbial etiologies, rapidly growing resistances to the available antimicrobials, and availability of new antimicrobial agents. This study was conducted to document current data on the clinical profile, antimicrobial susceptibility pattern and predisposing factors for infective keratitis at Muhimbili National Hospital (MNH) and Comprehensive Community Based Rehabilitation in Tanzania (CCBRT).

Methodology

Study design and Site

This was a hospital based descriptive cross-sectional study, which was conducted from June to December 2020 at tertiary ophthalmology departments of MNH and CCBRT.

Study area

MNH is a national referral and University teaching hospital in Dar es Salaam, Tanzania. The hospital has an Ophthalmology department among the other departments, which provide outpatient and inpatient, services. MNH has a well-

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equipped Clinical laboratory where a variety of investigations including microbiological tests are routinely performed.

CCBRT is a zonal referral hospital located in Dar-es-Salaam city serving both in-patients and outpatients from different parts across the country. Currently it serves as one of the high-volume hospitals providing ophthalmic care in Tanzania with an average of 6,200 monthly eye consultations. The hospital outsources laboratory services to the Lancet laboratory located few kilometers from the hospital.

Study population, Sample size and Sampling Technique

The study population included all adult patients with a provisional diagnosis of infective keratitis who were admitted or attended as outpatients at the two centers. Consecutive sampling was used to recruit the study participants. The sample size was calculated based on an average number of patients attended at the two centers for past six months. All adult patients aged 18 years and above with a provisional diagnosis of infective keratitis were enrolled. Patients with typical dendritic viral keratitis, interstitial keratitis and those with severe rapidly progressing infective keratitis (These were the patients with severe ocular inflammatory symptoms associated with keratitis which subjectively were worsening and objectively had poor progress) who were already on antibiotic use within 72 hours from the time of recruitment were excluded from study.

Data collection procedure

A structured questionnaire was used to collect information on social demographics, associated factors, and clinical findings. A structured laboratory form was used to collect laboratory findings for patients with infective keratitis.

On daily basis, the investigator and a well-trained research assistant visited the outpatient clinics and wards to identify patients who were attended for a clinical diagnosis of infective keratitis and informed them about the study. Infective keratitis was defined as an inflammation of the cornea characterized by an ulcer or epithelial defect with an infiltrate associated with any of the following signs and symptoms; pain, photophobia, redness of the conjunctiva, tearing, reduced vision, eye discharge with or without hypopyon. After signing a written informed consent, patients were consecutively recruited into the study.

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Duration of symptoms before presentation to MNH or CCBRT was defined as early presentation <7 days, delayed presentation 7-21 days, and late presentation >21days.Visual acuity (VA) of the affected eye(s) were assessed using illuminated Snellen charts for both literate and illiterate patients to establish the severity of visual impairment caused by infective keratitis. Visual acuity recordings were as per WHO categories of visual impairment of year 2019 (normal vision [<6/18-6/6], visual impairment [6/18-6/60], severe visual impairment [<6/60-3/60] and blind<3/60-No Perception of Light). Slit lamp examination was performed using Haag Streit BM 900 to obtain the clinical status of anterior segment of the eyes with infective keratitis that were used to guide on initial treatment and during cornea scrapping procedure.

Examination with a slit lamp biomicroscope included cornea staining with fluorescein under cobalt blue light filter to locate and estimate the size of corneal lesion. Staining was done by applying a wet fluorescein impregnated paper strip in the inferior conjunctiva fornices and asking the patient to blink in order to spread the dye on the ocular surface. Wetting of fluorescein impregnated paper strip was done with a drop of tetracaine 1.0% eye drop.

The visual acuity, slit lamp examination findings and corneal staining were used to assess the extent and severity of infective keratitis as the part of routine ocular examination of all patients with infective keratitis to guide their initial treatments.

Corneal scrapings were obtained from patients while viewing through the slit lamp. A sterile cotton swab was used to clean the conjunctiva fornices. Corneal scrapings were taken before administration of any antimicrobials. Those who already were on antimicrobials and did not meet exclusion criteria were requested to withhold the medication for 12 hours prior to scrapping in order to enhance recovery of viable organisms. Scrapings were taken from the edges and bases of the ulcers using a sterile number 15 blade after instillation of topical tetracaine 1.0% anesthesia eye drops to numb the corneal surface in order to make the procedure painless**.** The samples were placed in well-labeled thioglycolate broth containers immediately and taken to Muhimbili University of Health and Allied Sciences (MUHAS) microbiology laboratory for processing.

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Laboratory procedures

Direct microscopy was performed by taking the scrapings from the transport media on two glass slides, one for Gram stain and the other for 10% Potassium hydroxide (KOH) mount. Corneal scrapings samples were cultured on blood agar and chocolate agar for isolation of *Staphylococcus aureus,* coagulase negative *staphylococcus*, *Neisseria gonorrhoeae* and *Haemophilus influenzae*. MacConkey agar was used to isolate pathogenic organisms (Enterobacteriaceae and *Pseudomonas species* etc.) and Sabouraud's dextrose agar (SDA) for fungal culture in multiple C shaped streaks. Incubation was done at 37 °C for 48 hours, initially all plates were examined for growth after 24 hours and if no growth observed were further incubated up to 48 hours. Cultures were considered positive if they met the following criteria: i) the same organism isolated on two or more media with exception of fastidious organisms ii) an isolate present on one media and associated with the identification of the same organism on gram-stained direct smears iii) heavy growth at the inoculation site on one solid media [for enteric organisms]. Bacterial isolates were identified based on colonial morphology, Gram stain and biochemical tests. For Gram-positive, catalase, coagulase and DNase test and for Gram-negative bacteria oxidase, Citrate, Urea, Kligler iron agar (KIA), Sulfide, Indole and Motility (SIM) were performed.

Inoculated SDA were inspected daily for up to ten (10) days and declared as fungal culture negative thereafter. Fungal growths would be grossly identified by their colony morphology on observation, pigment production, and microscopically by lacto phenol cotton blue stain. The criteria for laboratory diagnosis of fungal keratitis was based on correlation between direct Potassium hydroxide (KOH) examination and growth on SDA and growth on more than one C streak lines.

Ethical consideration

Ethical approval to conduct the study was granted by the Research and Publication Committee of MUHAS. Permission to conduct the study at MNH was obtained from the Executive Director. Patients were recruited only after signing an informed consent and all were managed appropriately regardless of whether they participated or withdrew from the study.

Data analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 23. SPSS was used to generate frequency distribution tables for social demographic characteristics, microbial etiologies, and factors associated with infective keratitis. The comparison within variables was performed using the Chi-square test to observe the proportion differences. The P-value <0.05 was considered statistically significant.

Results

A total of 58 participants were enrolled in the study. Majority (65.5%) of the study participants were males and 74.1 % were residents of Dar-es- Salaam. The mean age of the participants was 39.95 with standard deviation of ±16.86 years. More than half of the participants (58.7%) had primary education level and had nonspecific employments (51.7%) (Table 1).

Table 1: The Socio-demographic characteristics of the study population (N=58)

Character	Frequency	Percentage (%)
Age group (Years)		
18 to 25	15	25.9
26 to 35	13	22.4
36 to 45	13	22.4
≥ 46	17	29.3
Sex		
Male	38	65.5
Female	20	34.5
Education level		
Informal	9	15.5
Primary school	34	58.6
Secondary school	11	19
University/college	4	6.9
Occupation		
Employed	13	22.4
Peasant	15	25.9
Others * informal employments*	30	51.7
Residence		
Dar es Salaam	43	74.1
Other regions	15	25.9

Majority of the participants 33/58 (56.9%) presented to MNH/CCBRT more than one week after the onset of symptoms. More than a two-third of affected eyes were blind (VA <3/60) with centrally located ulcers (Table 2).

Table 2: Clinical characteristics of the study population (N=58)

Characteristic	Frequency	Percentage (%)
Type of referral		
Self-referral	35	60.3
Referral from primary health facility	23	39.7
Duration of symptoms (weeks)		43.1
<1	25	34.5
1 to 3	20	22.4
>3	13	
History of using topical antimicrobials before cornea scraping		
Yes	38	65.5
No	20	34.5
Visual acuity of the affected eye		
<6/18 – 6/6	7	12.1
6/18 – 6/60	9	15.5
<3/60 – PL	42	72.4
Location of ulcer		
Central	36	62.1
Para central	15	25.9
Peripheral	4	6.9
Extensive ulcer	3	5.2
Depth of ulcer		
Superficial	27	46.6
Stromal	29	50
Presence of desmatocele	2	3.4
Hypopyon		
Present	19	32.8
Absence	39	67.2

Predisposing factors for infective keratitis

Topical steroid use 24(41.4%) was the reported leading predisposing factor for the infective keratitis followed by ocular trauma 12(20.7%). Only one patient reported history of contact lens wearing, and the use of traditional eye medication, respectively and none had history of eye surgery. Only 2(3.4%) of participants had HIV/AIDS in this study (Table 3).

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Table 3: Frequency of predisposing factors for infective keratitis (N=58)

Predisposing factor	Frequency	Percentage (%)
Topical eye steroid use	24	41.4
Ocular trauma	12	20.7
Diabetes mellitus	6	10.3
Contact lens use	1	1.7
Traditional eye medication	1	1.7
HIV/AIDS	2	3.4
Others	12	20.6
Total	**58**	**100**

Majority of the corneal scraping specimens 49 (84.5%) had bacterial growth whereby, half of cornea scraping specimens was a gram-positive bacterium. Out of 49-culture positives specimen, 37 (75.5%) cultures grew single bacterial isolates and 12 (24.5%) grew two bacterial isolates each making a total of 61 isolates. Most of the bacteria isolates were gram-positive *Staphylococcus aureus* and the least-isolated bacteria were *Enterobacter spp* (Figure 1). There was no single fungal isolate in both KOH mount and culture growth.

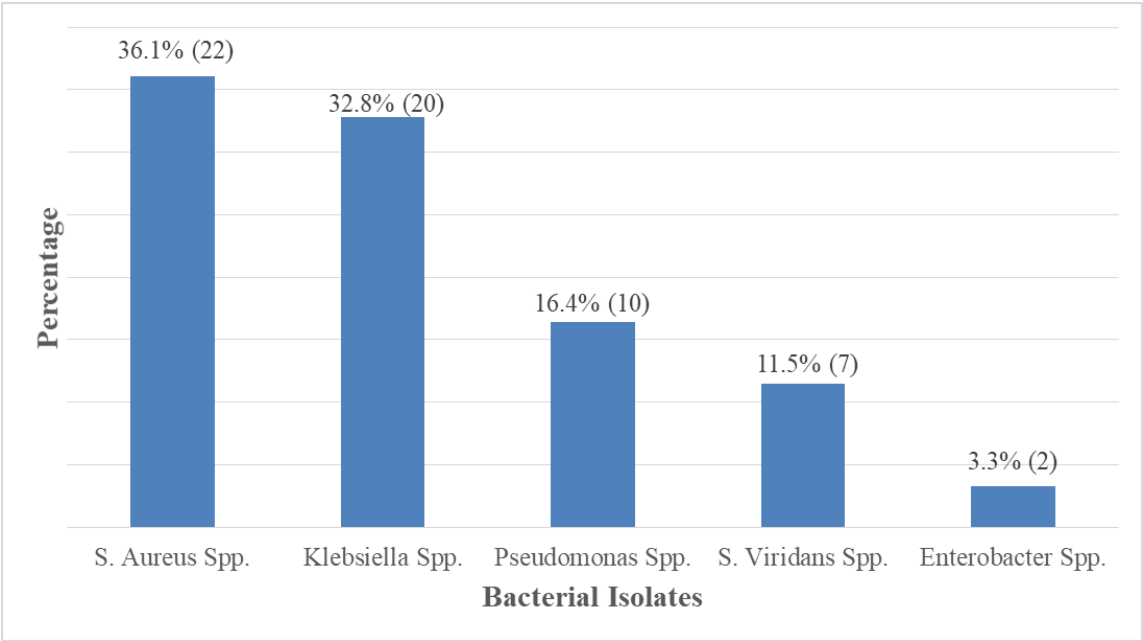

Figure 1. Bacteria Isolated from Corneal Scrapping Specimens

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Highest sensitivity was shown by ciprofloxacin and moxifloxacilin by 100% each with all bacteria isolates, whereas highest resistance was shown by ampicillin and cloxacillin by 50 % and 100%, respectively. Of all the bacteria isolates, *Pseudomonas aeruginosa* was the most resistant organism to most of the tested antibiotics (Table 4).

Table 4: The susceptibility pattern of the isolated bacteria from participants with infective keratitis (N=61)

Bacteria Isolated	CHL n (%)	TE n (%)	TOBRA n (%)	CIP n (%)	CN n (%)	AMP n (%)	CRO n (%)	DOX n (%)	CLOX n (%)	MOX n (%)
Enterobacter spp N=2	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	1 (50)	2(100)	2 (100)	NA	2 (100)
Klebsiella spp N=20	19 (95)	20 (100)	20 (100)	20(100)	2(100)	0 (0)	20 (100)	19 (95)	NA	20 (100)
Pseudomonas aureginosa N=10	1 (10)	1 (10)	8 (80)	10 (100)	8 (80)	4 (40)	9 (90.9)	0 (0)	NA	10 (100)
Viridans streptococci N=7	7 (100)	7 (100)	7 (100)	7 (100)	0 (0)	3 (42.9)	3 (42.9)	7 (100)	0 (0)	7 (100)
S. aureus N=22	18 (81.8)	16 (72.7)	22 (100)	22 (100)	20 (90.9)	9 (40.9)	22 (100)	21 (95.5)	0 (0)	22 (100)

NA-Not Applicable; NI-No interpretation; CHL-Chloramphenicol; CIP-Ciprofloxacin; TE-Tetracycline; TOBRA-Tobramycin; CN-Gentamycin; AMP-Ampicilin; CRO-Cefriaxone; DOX-Doxycycline; CLOX-Cloxacillin; MOX-Moxifloxacilin;

Discussion

The demographic characteristics for infective keratitis vary considerably with time and by region; many patients who get infective keratitis are young, working adults who develop an unexpected infection from various causes (19). The median age of the participant in this study was 36.30 years with a range of 18 years to 80 years. This is in consistence with the Tanzania age structure distribution by age and sex where most active adults are between 25 to 54 years of age (5). This is the group that probably because of its activeness is likely to encounter ocular micro trauma, which may predispose them to infective keratitis.

Late in seeking care, with severe forms of infective keratitis is a common finding in most of the eye units in developing countries (4). The reasons for late presentation are similar to those of other health conditions, which include remoteness of the services, poor healthy seeking behaviors, poor referral systems, and financial constraints among others (20).

Majority of the participants in this study came more than 1 week after the onset of symptoms and most of the affected eyes were blind (VA <3/60) with centrally located ulcers. Late presentation for the individuals with infective keratitis is among the causes of poor visual outcome and blindness. These findings are similar to the findings of the studies, which were done in tertiary eye hospitals in Tanzania and Nepal (4, 6).

Topical corticosteroids use in the eye without medical prescription generally has a deleterious effect. A corticosteroid can enhance the stromal growth of some bacteria, such as Pseudomonas aeruginosa, but may not produce detectable effects after inoculation with staphylococci or streptococci (7). Moreover, topical corticosteroid use significantly increases the risk of developing infective keratitis and result into poor subsequent outcomes of treatment (8, 9).

In this study topical corticosteroid use was the most common predisposing factor for infective keratitis identified in 41% of study participants. This is probably because most of the participants were from Dar es Salaam city where there are many pharmacies from which corticosteroids are easily accessible over the counter without ophthalmologist's prescription. Additionally, topical steroids are sometimes prescribed inappropriately by primary health care providers due to their poor knowledge on ocula pharmacology this is according to the pilot study which was done in Dar-es-Salaam 2010 -2011 by Mafwiri et al (10). Due to the grave complications of inappropriate steroid use in the eye, strategies must be established to create awareness among the community on good health seeking behavior and avoiding using over the counter medications to the eyes. Awareness creation among health care providers on appropriate prescription of steroids in the eye cannot be overemphasized.

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The finding of only one participant with infective keratitis had a history of using contact lens in this study, is contrarily to the study by Bourcier T et al which was done in Paris France in which the leading risk factor for bacterial keratitis was contact lens wear (11). This difference can be explained by differences in treatments options for refractive errors whereby there is extensive use of contact lenses in developed countries compared to sub-Saharan Africa.
Moreover, the results of associated factors for infective keratitis in this study are also different from studies by Chidambaram et al and Tesfayegebremariam T et al where the leading risk factor for infective keratitis was trauma (12,13). The difference can be accounted for by differences in ecological distribution of the populations. Most of the participants in these two studies were from rural areas where there were higher chances for sustaining farm related ocular trauma; whereas most of the participants of this study were from Dar-es-Salaam city with minimal farming activities.

Cornea scrapping and culture continues to be an imperative utility in the diagnosis of infective keratitis. However because of predilection of fungi to penetrate into deeper layers of the cornea, tissue scrapping is usually inadequate in confirming a fungal agent (14). The finding that bacteria were the leading culture isolates that accounted for 84.5% of positive culture growth is similar to a multi-center study by Peng et al in the United States of America and a study by Usman et al in Kano Nigeria between year 1996 and 2015 where they had predominant of bacteria growth (15)(16). However, the findings of 84.5% bacterial growth are different from studies done earlier by Burton et al and Furlanetto et al between year 2001 and 2010 which showed a leading microbial isolate to be fungus (4)(17). This is probably due to changes in the predisposing factors for infective keratitis from HIV infection and trauma in the past studies to topical corticosteroid use in this study. *Staphylococcus aureus* and *Klebsiella spp* were the common isolated bacteria in 36.1% and 32.8%, respectively. This finding is similar to what was found by previous studies in Tanzania by Burton et al at KCMC and Mafwiri et al at MNH and also in India by Mehta et al and Ranjin et al) (1)(3)(4)(18). This is probably due to similarities in geographical and climatic factors where these studies were conducted.

On antimicrobial susceptability tests in this study, the highest senstivity of 100% were seen with ciprofloxacilin and moxifloxacilin followed by gentamycin, tobramycin and doxycline about 80-100%, and highest resistance was shown by ampicilin and cloxacilin with resistance of 50% and 100%, respectively. The findings are similar to the studies which were

done in India by Ranjin et al and Biradar et al. whereby floroquinolone and aminoglycosides had high senstivity (3)(21). Also these findings are consistent with the study which was done in Kano Nigeria by Usman et al on the senstivity of floroquinolones and aminoglycosides (15). This is probably because floroquinolones and aminoglycosides are newer drugs in our market and probably recently there has been rational use of antibiotics due to on going campaigns on proper antibiotics use to slow down the on going antimicrobial resistances. The highest resistance with penicilins (ampiclin and cloxacillin) is probably due to their prolonged extensive use in our clinical practices at MNH and CCBRT.

Limitations

The study did not establish the nature of ocular trauma in assessment of predisposing factors for keratitis; this could have some explanations for the laboratory results.

Conclusion

The main cause of infective keratitis in Dar-es-Salaam is bacteria in which the leading predisposing factor is irrational topical corticosteroid use. Most patients with infective keratitis present to tertiary centers late with blind eyes. Therefore initiatives should be taken to control over the counter corticosteroid use for ocular pathologies. Also there should be more efforts to avoid delays and improve access to appropriate treatment for patients with infective keratitis

Ethics approval and consent to participate

The aim of this study was clearly explained to all patients who signed an informed consent to participate before enrollment in the study. Permission to conduct this study at the selected facilities was granted by the Executive Directors of MNH and CCBRT.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

PB participated in conception, research design, data collection and data analysis and preparation of the manuscript. CM and MM participated in research design, data analysis and interpretation, and revising the manuscript. AJ participated in research design, data

collection and data analysis and revision of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analyzed are available from the corresponding author on a request.

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Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
AST	Antimicrobial Susceptibility Test
CCBRT	Comprehensive Community-Based Rehabilitation In Tanzania
CLSI	Clinical Laboratory Standard Institute
HIV	Human Immunodeficiency Virus
KCMC	Kilimanjaro Christian Medical Centre
MNH	Muhimbili National Hospital
MUHA	Muhimbili University of Health and Allied Sciences
SDA	Sabouraud's Dextrose Agar
SPSS	Statistical Package for Social Sciences
VA	Visual Acuity
WHO	World Health Organization

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