Demographic, microbiological and management profile of infective corneal ulcer at a tertiary center in Bangladesh

Rajashree Das[1], Nawreen Anwar[2], Bipul Kumer De Sarker[3]

Abstract

Aim: *To assess the demographic, microbiological and management profile of infective corneal ulcer at presentation at a tertiary center in Bangladesh.*

Study design: *Prospective longitudinal study.*

Methods: *Clinically diagnosed corneal ulcer patients were included in this prospective longitudinal study irrespective of their age and gender. Demographic profile, causative organisms, presence of hypopyon, presence of perforation and treatment profile of different infective corneal ulcers were the outcome variables of this study. Patients were clinically diagnosed as bacterial, viral and fungal corneal ulcer after fluorescent dye test and slit lamp examination. Corneal scraping specimen were sent for microbiological examination for Gram staining, KOH initially and Calcofluor White Staining whenever necessary. Culture negative ulcers were treated as per clinical diagnosis.Patients were followed-up to 1 month. Surgical measures were performed in cases with perforation or impending perforation.*

Result: *Overall mean age was 48.72 ± 16.95 years (ranging from 7-81 years). Male female ratio was 1.7: 1. Majority (66.7%) of the patients came from rural areas. Fungal corneal ulcer had the highest incidence (52%) followed by bacterial corneal ulcer (18.1%). Aspergillus was the most common causative organism (38.9%)followed by Fusarium (13.9%), Gram positive cocci (12.5%), virus (4.2%) and candida (4.2%). In about 20.8% cases no causative microorganism could be isolated. Bacterial corneal ulcer had better response (92.3%) to medical management than Fungal corneal ulcer (71.2%). Fungal corneal ulcer required more surgical interventions than other corneal ulcers within 1 and 3 months of their initial presentation. Presence of hypopyon and fungal corneal ulcer were not statistically significant predictive factors for perforation and need of surgical intervention.*

Conclusion: *Fungal keratitis especially Aspergillus keratitis is the most common infective keratitis presented in this study. Males and rural people had higher rate of infective keratitis.*

Keywords: *Infective corneal ulcer, demography, keratitis.*

Introduction

Cornea is the most important refractive media for clear vision. Any disease disrupting the transparency and curvature of cornea leads to vision loss. A corneal ulcer in an ocular emergency which may be defined as a defect in the corneal epithelium involving the underlying stroma.[1] The prevalence of corneal ulcer in India is about 34.18% (95% CI: 31.82, 36.58), in Sri Lanka about 39.39% (95% CI: 27.58, 52.19) and in USA about 6.06% (95% CI: 2.33, 11.31). The prevalence is higher in under-developed and developing countries.[2,3]

1. Assistant Professor, Cornea and anterior segment diseases, BSMMU
2. Assistant Prof, BSMMU.
3. Associate Professor, Ispahani Islamia Eye institute and Hospital

Address of Correspondence: Dr. Rajashree Das, Assistant Professor, Cornea and anterior segment diseases, BSMMU, E-mail: anusharajashree@gmail.com

The major causes of corneal ulcer include bacterial, fungal, protozoal, viral infection and autoimmune disease. The most common corneal ulcer causing bacteria are Staphylococcus aureus, coagulase negative staphylococcus, and Pseudomonas aeruginosa. Staphylococcus epidermidis and Staphylococcus fusarium species usually cause post-traumatic corneal ulcer. The most common ulcer causing fungus include Aspergillus, Fusarium, Candida albicans, and other Candida species. HSV is the most common viral cause of corneal ulcer followed by Varicella-zoster. In contact lens wearers one of the common causes of keratitis is Acanthamoeba which is a free-living protozoa, found in soil and fresh water.Risk factors include contact lens wear, corneal abrasions, ocular trauma, diabetes mellitus, prior ocular surgery, chronic ocular surface disease, corticosteroids, contaminated ocular medications, hot and humid climateand agricultural trauma.[4-6]

The degradation of corneal stromal collagen is the main pathophysiology of corneal ulcer. This degradation is mediated by break down of collagen fibers by extracellular proteases, endocytosis of collagen fragments as a result of their interaction with collagen receptors and intracellular proteolysis within lysosomes.[7] The World Health Organization (WHO)has included infectious keratitisamong neglected tropical diseases.[8]

The causative organisms of infective keratitis depends on the demography, immune status, geographical area and environmental factors. In a subtropical developing country like Bangladesh the causative organisms and presenting conditions of keratitis varies from the developed countries and countries with dry weather. Insufficient treatment or late diagnosis may lead to perforation of the cornea, anterior synechia, posterior synechia, secondary glaucoma, adherent leukoma or even total loss of vision due to endophthalmitis. The rate of disease progression is dependent on the virulence of the infecting organism and on host factors.[9] So, it is essential to diagnose and manage corneal ulcer as early as possible for better outcome.In order to support ophthalmologists' evidence-based practice in the treatment of infective corneal ulcers, this study aimed to assess the demographic profile, etiological agents, corneal ulcer condition at presentation, and treatment profile of patients in a tertiary center in Bangladesh.

Materials and methods:

Participants

After sufficient consent was obtained, clinically diagnosed corneal ulcer patients attending Ophthalmology outpatient department of Bangabandhu Sheikh Mujib Medical university between 1st January, 2021 to 31st October, 2022 were included in this prospective longitudinal study irrespective of their age and gender. Non-randomized purposive sampling was done. Patients with neurotropic keratopathy, history of refractive or intraocular surgery,Diabetes mellitus, Sjögren'ssyndrome, rheumatoid arthritis, Lupus, previously diagnosed with dry eye or ocular surface disorder, cranial nerve palsies, lagopthalmos were excluded.

Methods of Assessment

Demographic profile, causative organisms, presence of hypopyon, presence of perforation and treatment profile of different infective corneal ulcers were the outcome variables of this study. After taking informed consent, relevant history was taken. Patients were clinically diagnosed as bacterial, viral and fungal corneal ulcer after fluorescent dye test and slit lamp examination. Corneal scraping was done and specimen were sent for microbiological examination for Gram staining and KOH initially. Specimens with negative findings for gram stain and KOH were again sent for Calcofluor White Staining. Each patient was treated medically according to the microbiological finding. In cases where causative organisms could not be detected, treatment was given according to clinical diagnosis as fungal, bacterial, viral or protozoal keratitis. In this study the patients were followed-up to 3 months and their response to given treatment were noted. Surgical measures like conjunctival hooding, tenon's patch graft, tenon's patch graft with left-

over tissue, Anterior chamber wash, intra-cameral Amphotericin B administration were performed in cases with perforation or impending perforation whenever needed. All the information were noted in data collection sheets.

Statistical Methods

Continuous variables were reported as mean ± SD. ANOVA and the Wilcoxon rank-sum test were used to compare groups. The Chi-square test or Fisher's exact test were used to compare categorical variables, which were reported as proportions. Confounders that might predict changes were identified using univariate and multivariate regression. All of the data was imported into Microsoft Excel and analyzed with SPSS version 22.

Results

In this study, we assessed 87 patients for eligibility initially. Fourteen patients did not meet all the inclusion and exclusion criteria and 1 patient declined to participate. Seventy-two patients were finally confirmed as eligible (n = 72). As shown in Table I, the overall age was 48.72 ± 16.95 years ranging from 7 years to 81 years. Male female ratio was 1.7:1. About 66.7% of the patients came from rural areas. Male population and people from rural areas had higher incidence of infective corneal ulcers (p <0.01).

Table I : *Demographic profile and laterality of patients with infective corneal ulcer (n= 72)*

Variables	Value	*P* value
Age, mean± SD (years)	48.72 ± 16.95	-
Gender		<0.01 *
Male, n (%)	45 (62.5)	
Female, n (%)	27 (37.5)	
Residence		<0.01 *
Urban, n (%)	24 (33.3)	
Rural, n (%)	48 (66.7)	
Laterality		0.8
Right eye, n (%)	35 (48.6)	
Left eye, n (%)	37 (51.4)	

*Statistically significant

In this study, 52 cases were clinically diagnosed Fungal corneal ulcer after thorough examination. But only 41 cases had positive findings after KOH staining. Although, rest of the 11 cases had no conclusive finding on microbiological examination, they were treated as Fungal corneal ulcer.Thirteen cases were clinically diagnosed as Bacterial corneal ulcer. Gram staining revealed causative bacteria in 10 cases. But the rest of the 3 cases were treated as bacterial corneal ulcer although Gram, KOH& calcofluor white staining revealed no causative organisms. One case revealed acanthamoeba after examining the corneal scrapping with calcofluor white stain. Two cases revealed mixed infection with both fungi and bacteria. As shown in Table II, fungal corneal ulcer was the commonest one (52%) followed by bacterial corneal ulcer (18.1%) among all the infective keratitis.

Table II. *Types of corneal ulcers based on clinical diagnosis (n=72)*

Clinical diagnosis	Frequency	Percentage
Fungal corneal ulcer	52	72.2
Bacterial corneal ulcer	13	18.1
Viral corneal ulcer	3	4.2
Mixed (fungal+ bacterial) ulcer	2	2.8
Healed ulcer at presentation	1	1.4
Acanthamoeba keratitis	1	1.4

As per Table III, Aspergillus was the most common causative organism (38.9%) of infective keratitis followed by Fusarium (13.9%), Gram positive cocci (12.5%), virus (4.2%) and candida (4.2%). There was 1 case of Gram-negative bacilli, 1 case of mixed infection with Fusarium with Gram positive cocci, 1 mixed infection with Aspergillus&Gram-Negative Bacilli and 1 case of Acanthamoeba. About 15 (20.8%) of the corneal scrapping revealed no conclusive isolation of causative organism including 1 case of healed corneal ulcer where corneal scraping was not done. In this study, the rate of presenting with hypopyon was higher in the 2 cases of mixed infection, Gram negative bacilli and Fusarium (p=0.02). Fungal corneal ulcer due to Fusarium had higher perforation rate (30%) than other fungal organisms (p<.001). The only case of Gram-negative bacilli and Acanthamoeba presented with impending perforation.

Table III. ***Spectrum of causative micro-organism isolates and proportion of hypopyon and perforation of infective corneal ulcers at presentation (n=72)***

Causative organisms (n=72)	Frequency, n (%)	Hypopyon, n (% of specific keratitis)	Perforation or impending perforation, n (% of specific keratitis)
Fungal isolates			
Aspergillus	28 (38.9)	7 (25)	3 (10.7)
Fusarium	10 (13.9)	5 (50)	3 (30)
Candida	3 (4.2)	0 (0)	0 (0)
Bacterial isolates			
Gram Positive Cocci	9 (12.5)	5 (55.6)	0 (0)
Gram negative Bacilli	1 (1.4)	0 (0)	1 (100)
Mixed infection			
Fusarium + Gram Positive Cocci	1 (1.4)	1 (100)	0 (0)
Aspergillus+ Gram Negative Bacilli	1 (1.4)	1 (100)	0 (0)
Culture negative clinically suspected fungal keratitis	11 (15.3)	3 (27.3)	1 (9.1)
Culture negative clinically suspected bacterial keratitis	3 (4.2)	2 (66.7)	1 (33.3)
Culture negative healed ulcer	1 (1.4)	0 (0)	0 (0)
Viral	3 (4.2)	0 (0)	0 (0)
Acanthamoeba	1 (1.4)	0 (0)	1 (100)
P value	-	0.02*	<.001*

*Statistically significant

Table IV. ***Treatment regimens of different corneal ulcers (n =72)***

Type of keratitis	Medical treatment only	Conjunctival hooding	Conjunctival hooding with tenon patch graft	Conjunctival hooding and tenon patch graft with left-over tissue	Therapeutic debridement with AC wash	AC wash with I/C Amphotericin B
Total (n=72)	55 (76.4)	4 (5.6)	10 (13.9)	1 (1.4)	1 (1.4)	1 (1.4)
Fungal corneal ulcer (n=52)	37 (71.2)	4 (7.7)	8 (15.4)	1 (1.9)	1 (1.9)	1 (1.9)
Bacterial corneal ulcer (n=13)	12 (92.3)	0 (0)	1 (7.7)	0 (0)	0 (0)	0 (0)
Viral corneal ulcer (n=3)	3 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mixed corneal ulcer						
Fusarium + GPC (n=1)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Aspergillus + GNB (n=1)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Acanthamoeba keratitis (n =1)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
Healed corneal ulcer (n =1)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Table IV displays the treatment regimen to which various corneal ulcers reacted favorably. About 76.4% of total corneal ulcers improved only with medical management. Bacterial corneal ulcer responded more (92.3%) with medical management than Fungal corneal ulcer (71.2%). Fungal corneal ulcer required more surgical interventions than bacterial corneal ulcer within 1 month of their initial presentation.

Table V. ***Multivariate regression analysis of the probable predicting factors for corneal ulcer perforation or for surgical intervention***

Variable	Odds Ratio (95% CI)	*P* value
Presence of hypopyon	5.1 (0.6- 43.4)	0.1
Fungal corneal ulcer	1.3 (0.29- 5.9)	0.7

Multivariate regression analysis showed the presence of hypopyon and the presence of fungal corneal ulcer were not predictive factors for higher rate of perforation or for requirement of surgical intervention.

Discussion

In this prospective longitudinal study, the overall mean age was 48.72 ± 16.95 years ranging from 7 years to 81 years. Male female ratio was 1.7: 1. About 66.7% of the patients came from rural areas. Fungal corneal ulcer had the highest incidence (52%) followed by bacterial corneal ulcer (18.1%) among all the infective keratitis. Aspergillus was the most common causative organism (38.9%) of infective keratitis followed by Fusarium (13.9%), Gram positive cocci (12.5%), virus (4.2%) and candida (4.2%). In about 20.8% cases no causative microorganism could be isolated. Bacterial corneal ulcer had better response (92.3%) to medical management than Fungal corneal ulcer (71.2%). Fungal corneal ulcer required more surgical interventions than other corneal ulcers within 1 month of their initial presentation.

A study by Dunlop et al showed that in the tropics, corneal ulcers tend to occur in adult males more than females. [10] Similarly, in a Bangladeshi study by Ahmed et al reported that 64.63% of corneal ulcer patients were male and 77.6% were from rural area. [11] These studies are consistent with the results of our study. As male population in our country tend to work outside more and the main source of income in rural areas is agriculture based,so the risk of ocular infection and trauma is also higher in men and in rural population.

Similar to the current investigation, Ahmadikia et alrevealed that Aspergillus spp. (32.64%), Fusarium spp. (29.42%), and Curvularia spp. (9.15%) were the top three causal organisms in clinically suspected fungal keratitis. Although the prevalence of Candida-associated keratitis was greater (20.41%) in post-keratoplasty patients, the incidence of candida (5.4%) causing fungal keratitis was lower overall. [12] The lack of post-keratoplasty patients in our sample explains the the lower frequency of candida-associated keratitis in this current study. Furthermore, although Curvularia spp. was listed as the third most prevalent fungus to cause keratitis in prior research conducted in Bangladesh, we had no cases of it in our study. [10]

In contrast to the global pooled prevalence of mixed infections (9.29%) found in the meta-analysis, the incidence of mixed infections was lower (2.8%) in our investigation. According to Mahmoudi et al., there are regional variations within the same country as well as between nations in regards to the epidemiology patterns of FK. In contrast to developed countries with cold or temperate climates, fungal corneal ulcers are more common in developing countries with tropical and subtropical warm and humid climates and economies dependent on agriculture. A comprehensive meta-analysis found that Bangladesh has one of the highest pooled prevalences of fungal corneal ulcers. [12-15]

In this current study among the bacterial corneal ulcer about 69.2% were caused by Gram-positive cocci and 7.7% were caused by Gram-negative bacilli. In a study conducted on Nigerian population by Abubakar et al bacterial growth was seen in 46.8% of the samples, of which 28.6% of the growth were Gram-positive and 18.2% were Gram-negative. The common bacteria isolated were Staphylococcus epidermidis(11.7%),

Staphylococcus aureus (10.4%), Pseudomonas aeruginosa (10.4%), Streptococcuspneumoniae, Proteus species, and Klebsiella pneumoniae. [16] Similarly in a study done in India by Tewari et al showed about 60.3% of the bacterial ulcer causing isolates were Gram-positive cocci and 39.7% were Gram-negative bacilli.[17] These studies remain consistent with the results of this study.

In the study conducted by Ahmed et al micro-organism could not be isolated in 41.2% of the corneal scrapings, but in this current study the rate was lower (20.8%). [18]In a study conducted in Nepal also had 20% negative culture rate. [19]

According to Fong et al., Kredics et al., and Mahmoudi et al., the use of empirical topical antibiotics, surface anesthetics with antimicrobial effects, different sample collection techniques (swabbing vs. corneal scraping), the low number of specimens available for culture, the refractory nature of fungi, and adverse effects of transport devices or media on the viability of microorganisms are possibleconfounders which may influence the results of culture method. [13,14,20] The lower rate of negative cultures in our study may have been due to the smaller number of patients having a history of topical antibiotic use and adequate corneal scraping technique.

According to studies, roughly 50% of cases with severe fungal keratitis result in perforation as a result of a more severe inflammatory response than other corneal ulcers. Fungi have the ability to quickly invade the posterior corneal stroma and weaken and necrose Descemet's membrane, which facilitates early perforation. In our investigation, only about 13% of the clinically diagnosed fungal corneal ulcers resulted in perforation. It should be emphasized that just the patients' first month's condition was reported in this study; if additional follow-ups are considered, the frequency of perforation may rise.

If hypopyon is present at the time of initial presentation, there is a 2.28 times greater risk of corneal perforation and/or the requirement for TPK (95% CI, 1.18-4.40; P =.01), according to Prajna et al. [23] The study's limitations include the small sample size and brief study duration, which prevented the identification of any surgical intervention or perforation predictors that were statistically significant.

Conclusion

Fungal keratitis, Aspergillus spp. related keratitis in particular, is more frequent, advances more quickly, and necessitates immediate treatment. Infectious corneal ulcers are more common in rural areas and among men. To obtain the true picture of the causative isolates and the pattern of each isolate associated keratitis, additional prospective population-based studies in rural regions need to be conducted with a larger sample size.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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