·Clinical Research·

# Hospital –base epidemiology, risk factors and microbiological diagnosis of bacterial corneal ulcer

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## Abstract

• AIM: To determine the predisposing factors, clinical and microbial characteristics of bacterial corneal ulcer.

• METHODS: Three hundred patients (300 eyes) of clinically suspected microbial corneal ulcer were included in the study. Data was collected through history and slit lamp examination. Using standard techniques, corneal scraping was performed. A portion of each scraping was examined by direct microscopy for the presence of bacteria, fungi and acanthamoeba by using 100g/L potassium hydroxideand also by Gramand staining. Another portion was inoculated directly on the surface of solid media such as blood agar, Mac-Conkey agar, chocolate agar and Sabouraud's agar. A bacterial corneal ulcer was defined as a suppurative corneal infiltrate and overlying epithelial defect associated with presence of bacteria on corneal scraping examination and cured with antibacterial therapy.

• RESULTS: Of the 300 patients, sixty were lost in follow up, they were excluded from study. Of the remaining 240, bacterial corneal ulcer was identified in 156 (65.0%) patients. The age of patients ranged from 14 to 74 (mean age of 48) years. Majority of them were male (102). Corneal localization of the ulcers was distributed as central in 96 (61.5%) patients and peripheral in 60 (38.5%) patients. Ulcer depth in 82 (52.6%) patients was less than 1/3 of corneal thickness. In 64 (41.0%) patients, anterior chamber inflammation was 1+ to 2+ Tyndall effect with 1+ to 2+ cells present. Bacteria were isolated in 125 (80.0%) patients from the corneal smears. Sixty-nine percent of isolated bacteria were Grams' positive, and 39% were Grams' negative. Gram negative bacteria were associated with severe anterior chamber inflammation ($P$=0.003) and depth more than 2/3 of cornea ($P$ =0.001). The most frequent organism isolated was Staphylococcus aureus. Forty percent of patients had good visual outcome with visual acuity same or better than the level at admission. Among the others 60% patients, final outcome was poor.

• CONCLUSION: Bacterial corneal ulcer is aserious ocular infectious disease that remains a therapeutic challenge and vision threatening ocular condition. Rapid isolation of bacteria and treatment with intensive ocular antibiotics represent decisive steps in the management of such pathologies.

• KEYWORDS: bacterial keratitis; agriculture trauma; organism

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## INTRODUCTION

Microbial keratitis is a serious ocular infectious disease that can lead to significant vision loss and ophthalmic morbidity [1]. Bacteria's are the most common infective organisms responsible for this morbidity. The severity of corneal infection depends on the underlying condition of the cornea and pathogenecity of the infecting bacteria [2]. It is rare in the absence of predisposing factors, and hence most commonly associated with ocular trauma or ocular surface disease. However the increasing prevalent with the use of contact lenses in the general community has resulted well established association between keratitis and contact lens[3].

The spectrum of bacterial keratitis can also be influenced by geographic and climatic factors. Many differences in keratitis profile have been noted between populations living in rural or in urban areas in western, or in developing countries [4]. Gram positive bacterial species are more frequently recovered in temperate zones, and Gram negative species in tropic climates. Untreated, infective keratitis may lead to opacification and, ultimately, to perforation of the cornea. The associated morbidity is the result of several factors and is directly affected by difficulties in patient's management because of a lack of diagnostic facilities and

appropriate treatment. Specific treatment requires prompt and accurate identification of causative micro-organisms[5]. This study is an effort to analyze the epidemiologic features, predisposing factors and the main causative organisms for bacterial corneal ulcer in this part of Asia to provide a useful guide for the practicing ophthalmologists. This two years Quasi-experimental study (from April 2006 to March 2008) of bacterial corneal ulcer was conducted at Liaquat University Eye Hospital, Hyderabad, a Tertiary Referral Center in Southern Pakistan.

## MATERIALS AND METHODS

**Subjects** Patients above 15 years of age presenting with suspected corneal ulceration and having symptoms of pain, redness, watering, photophobia and decreased vision were registered for the study. Patients written consent was obtained and a standardized proforma was used to record the data. Detailed history and examination of the patients was taken regarding demographic features, time of onset of symptoms, pre-disposing factors including corneal injuries (agriculture, non agriculture, foreign bodies), contact lens wear, keratopathies (due to previous herpetic infection, corneal dystrophy or surgical procedure, as in bullous keratopathy), dry eye syndrome, eye lid abnormalities (blephritis, entropion, ectropion, lagophthalmos, and others). Visual acuity was measured with Snellen chart. All patients underwent through slit lamp examination to locate the site, size and depth of ulcer. Anterior chamber inflammation, when present, was scored, according to Hoagan and associates, a 0+ to 4+ for Tyndall effect and cells.

After the instillation of local anesthetic 5g/L proparacaine hydrochloride, corneal scrapping was obtained aseptically with a sterile No.15 surgical blade from the base and edges of each ulcer. A portion of each scrapping was examined microscopically for the presence of bacteria, fungi or acanthamoeba by using Gram staining, 100g/L potassium hydroxide (KOH) and Giemsa staining methods. Another portion was inoculated on to blood agar, chocolate agar, Mac-Conkey agar, Sarboraud's agar, brain heart infusion broth respectively, in C-shaped streaks and cultured for the potential growth of, bacteria, fungi or acanthamoeba. Sarboraud's agar slants were incubated at 28℃ while others at 37℃. All media were cultured for a period of seven days and observed daily. Isolated bacteria were tested by chemical reaction for identification. Further the bacteria were tested for their resistance against the following ocular antibiotics: cefuraxime, cefazolin, moxifloxacin, gentamycin, tobramycin, ceftazidime, norfloxacin, ofloxacin, levofloxacin, gatifloxacin. The resistance to antibiotics was evaluated with the standard disc diffusion method according to the modified test recommended by the NCCLS.

**Treatment Protocol** Ninety-five (61%) patients were treated as an out patients department basis and 61 (39%) patients were hospitalized for treatment. The decision to admit patients and use of fortified antibiotics were influenced by the severity of the corneal ulcer and patients compliance. The standard fortified therapy consisted of topical cefuraxime 50g/L and fortified tobramycin 9g/L, where as commercially available antibiotics used were topical fluoroquinolones (Moxifloxacin). The antibiotic eye drops, administered alternately every fifteen minutes during the first 4 hours then every hour for the next 48 hours. Later, drops were progressively tapered according to the clinical response. Bottles of fortified antibiotics drops were freshly prepared and cefuraxime, was changed every 72 hours. This standard treatment protocol was started for every patient and modified on patients response and the bacterial susceptibility.

**Statistical Analysis** Univariate analysis was used to evaluate the possible association between bacterial type, clinical characteristics, risk factors and clinical outcomes. Data was analyzed on SPSS version 10.0.

## RESULTS

**General Situation** Three hundred patients (300 eyes) were enrolled with a corneal infiltration that was clinically compatible with the diagnosis of bacterial corneal ulcer during the two years study period. Of these 60 patients were lost in follow-up, excluded from study. Of the remaining 240 cases, bacterial corneal ulcer was identified in 156 (65.0%) patients. Among these, 60 (38.5%) patients were examined first time in the out patients department, where as 96 (61.5%) were previously treated by general practitioners and ophthalmologists and were already being treated with topical antibiotics, corticosteroids and antifungal eye drops. The age of patients ranged from 14 to 74 (mean age of 48) years. Majority of them were male 102 (65.4%) with male to female ratio of 1.9:1 (Table 1). One hundred and two (69.2%) patients belonged to rural and 48 (30.0%) were from urban population. Trauma with vegetative material was by far the most common risk factor; this was encountered in 46 (29.5%) patients. History of non-vegetative trauma in 16 (10.3%) patients is shown in Table 2. In 18 (11.5%) patients, ocular surface disorder was observed, the keratitis was induced by foreign body in 24 (15.4%) patients. Eleven (7.1%) patients were affected by contact lenses. Keratopathies (including herpetic, bullous and post operative keratopathies)

were presented in 17 (11.0%) patients. Blephritis was noted in 8 (5.1%) patients, while 16 (10.3%) patients had no significant prior history.

Corneal localization of the ulcers was distributed as in 96 (61.5%) patient's central and in 60 (38.5%) peripheral. The diameter of the corneal ulceration was of 1-2mm in 24 (15.4%), 3-4mm in 78 (50.0%), 5-6mm in 24 (15.4%), 7-8mm in 26(16.7%) patients, 4 (2.6%) patients had entire corneal involvement. Ulceration depth was less than 1/3 conreal thickness in 82 (52.6%), between 1/3 to 2/3 in 60 (38.5%) patients and over 2/3 in 14(9.0%) patients (Table 3).

Anterior chamber inflammation was absent in 42 (26.9%) patients. A 1+ to 2+ Tyndall effect with 1+ to 2+ cells was present in 64 (41%) patients, and severe anterior chamber inflammation (3+ to 4+ Tyndall effect and cells, with or without hypopyon) was present in 50 (32.1%) patients (Table 3). In 125 (80%) patients, bacteria were isolated from the corneal smears (Table 4). Sixty-nine percent of isolated bacteria were Gram positive, most of them 75(60%) were staphylococcus aureus. Gram negative bacteria were isolated in 39 (31%) patients. Most of them were pseudomonas and yersina. Infection with Gram negative organisms associated with severe anterior chamber inflammation ($P$=0.003) and depth more than 2/3 of cornea ($P$=0.001). All isolated bacteria were tested on currently used 10 antibiotics.

One hundred and fourteen (73.1%) patients were treated according to the standard protocol by using fortified antibiotic drops for Gram positive and Gram negative organisms. The remaining 42 (26.9%) patients who did not stay at hospital and had small infiltration were, treated by commercially available antibiotic fluoroquinolone (Moxi-floxacin).

**Clinical Outcome** Visual acuity on presentation ranged from 6/6 to no light perception. Mean visual acuity was 2.67 (SD 1.01). Forty percent of patients had good visual outcome with visual acuity same or better than the level at admission (Figure 1). Among the others 60% patient's final outcome was poor. Complications of bacterial corneal ulcer were noted in 45 (28.8%) patients. Among them, glaucoma in 11 patients, endophthalmitis in 3 patients, anterior staphyloma in 3 patients and corneal perforation, descmetocele, cataract each develops in 3 (4.5%) patients. Where as one hundred and eleven (71.2%) patients had no severe complications, except scaring at the site of lesion. In our study statistical analysis revealed that poor visual outcome was correlated with history of ocular surface disease ($P$<0.01), large size and central localizations of the ulcer ($P$< 0.01), and depth of infiltrate more than 1/3 corneal thickness ($P$<0.01).

**Table 1 Demographic data of 156 patients with bacterial corneal ulcer**

| Age (year) | Sex *n*(%) | | Total *n*(%) |
|---|---|---|---|
| | Male | Female | |
| 1-10 | 0 | 0 | 0 |
| 11-20 | 0 | 6 (3.8) | 6(3.8) |
| 21-30 | 24(15.4) | 0 | 24(15.4) |
| 31-40 | 30(19.2) | 0 | 30(19.2) |
| 41-50 | 12(7.7) | 12(7.7) | 24(15.4) |
| 51-60 | 24(15.4) | 24(15.4) | 48(30.8) |
| >60 | 12(7.7) | 12(7.7) | 24(15.4) |
| Total | 102(65.4) | 54(34.6) | 156(100) |

**Table 2 Frequency of risk factors in bacterial corneal ulcer**

| Risk factor | Population type *n*(%) | | Total *n*(%) |
|---|---|---|---|
| | Rural | Urban | |
| Vegetative trauma | 44(28.2) | 2(1.3) | 46(29.5) |
| Non-vegetative trauma | 6(3.9) | 10(6.4) | 16(10.3) |
| Ocular surface disorder | 12(7.7) | 6(3.8) | 18(11.5) |
| Ocular surgery | 6(3.8) | 2(1.3) | 8(5.1) |
| Foreign body | 18(11.5) | 6(3.9) | 24(15.4) |
| Contact lenses | 6(3.8) | 5(3.2) | 11(7.0) |
| Keratopathy | 5(3.2) | 4(2.6) | 9(5.8) |
| Blepharitis | 5(3.2) | 3(1.9) | 8(5.1) |
| Nill | 6(3.9) | 10(6.4) | 16(10.3) |
| Total | 108(69.2) | 48(30.8) | 156(100) |

**Table 3 Clinical features of corneal ulcer**

| Feature | *n* | Percentage (%) |
|---|---|---|
| Location | | |
| Central | 96 | 61.5 |
| Peripheral | 60 | 38.5 |
| Size (mm) | | |
| 1-2 | 24 | 15.4 |
| 3-4 | 78 | 50.0 |
| 5-6 | 24 | 15.4 |
| 7-8 | 26 | 16.7 |
| Entire | 4 | 2.6 |
| Depth (corneal thickness) | | |
| <1/3 | 82 | 52.6 |
| 1/3-2/3 | 60 | 38.5 |
| >2/3 | 14 | 9.0 |
| Anterior chamber reaction | | |
| 1-2 tyndall &1-2 cells | 64 | 41.0 |
| 3-4 tyndall & 3-4 cells or hypopyon | 50 | 32.1 |
| Nill | 42 | 26.9 |

**Table 4 Organisms isolated in bacterial corneal ulcers**

| Organisms cultured | *n* | Percentage (%) |
|---|---|---|
| Staphylococcus aureus | 75 | 48.1 |
| Streptococcus pneumonia | 11 | 7.1 |
| Pseudomonas aeruginosa | 13 | 8.3 |
| Yersina | 9 | 5.8 |
| Moraxella spp | 4 | 2.6 |
| Proteus spp | 9 | 5.8 |
| Klbsiella pneumonia | 4 | 2.6 |
| No growth | 31 | 19.9 |
| Total | 156 | 100 |

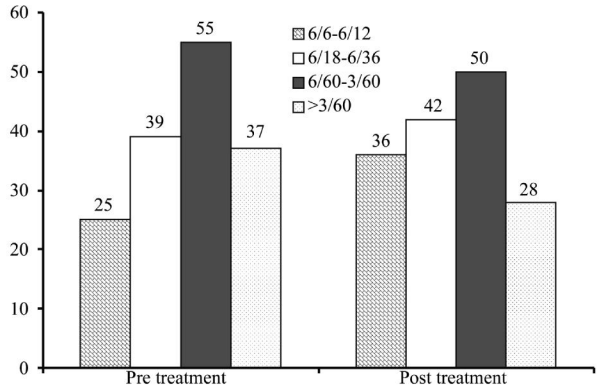


**Figure 1 Pre and post treatment visual status of patients**

## DISCUSSION

Corneal infection is the leading cause of ocular morbidity and blindness worldwide. In the published reports, bacterial corneal ulcer has been found to be 13.0% to 29.3% of all cases of ulcerative corneal ulcer[6].

Of the remaining 240 patients with infective keratitis from April 2006 to March 2008 presenting at our department, bacterial corneal ulcer was diagnosed in 156 (65.0%) eyes. Although it is rare in the absence of a predisposing factor, most of the cases of microbial keratitis were associated with ocular trauma. In this study, 86 (55.0%) were associated with various types of ocular injuries. Vegetative trauma accounts 46(29.5%) patients. Vajpayee *et al* [7] reported 77.5% of cases of bacterial corneal ulcer occurred by trauma in low income countries, where a large number of population were concerned to agriculture. Moreover, the climate is mild and humid, and malnutrition is common. Foreign body induced corneal ulcer was the second most common (24 cases, 15.38%) predisposing factor in our study. Most of these patients had also history of foreign body removal by own or by other family members and followed by self-medications.

Ocular surface disorders such as dry eye syndrome and eye lid pathologies and keratopathies accounted 17.3% of cases. Bourcier *et al* [2] reported 21% of cases of bacterial corneal ulcer were with ocular surface disorder. Contact lenses remained the least common cause of bacterial corneal ulcer in our study. In contrast Radford et al reported contact lenses had greatly increased the risk of bacterial keratitis which was estimated to be 10-15 times higher with the use of extended wear disposable contact lenses. Many physiopathological effects of contact lenses wear have been reported. The most important of which is an induced hypoxia and hypercapinia of the cornea. In line with other studies [8,9] males (65.4%) were predominant in our study. The increased risk in males in our population was probably due to their more active involvement in out door activities, which subsequently increased their vulnerability to this blinding disease. The duration from the onset of symptoms to the presentation at our department ranged from 7 to 105 (mean 41) days. This delay presentation to tertiary center might be due to the fact that the patient already received the therapy from their nearest ophthalmologists or doctor and were referred when the ulcers did not respond. Xie *et al*[7] reported the first visit of 41.0% between 16 and 30 days.

In this study, the most common signs on slit lamp examination were epithelial defect, stromal infiltrate and suppuration presents in every case, while anterior chamber reaction and hypopyon was observed in 73% of patients. This is in accordance with another European study [2]. Older individuals were more frequently affected in this study, majority (61%) of patients were fifth or more decades. Age profile in our patients is comparable to Schaefer *et al* and Cohen *et al* study. In general older age, delay in referral, topical steroid treatment, past ocular surgery, poor vision at presentation, large size of ulcer [10], and central and deep ulcer are all major risk factors for evisceration and enucleation in patients with bacterial corneal ulcer. The situation in this study was not too different.

The success rate of bacterial isolation was high in the present study, with 80% of smear positive on blood, chocolate and Mac-Conkey agar. While Waxman *et al*[11] reported 70% of isolation of organism on same medium. As with most published studies there was a high prevalence of Gram positive bacteria with staphylococcus aureus accounting for 75 (60%) of all 125 bacterial isolates. Our study matches to the Hyderabad study. Stephen *et al* reported higher incidence of streptococcus pneumonia (20%) in his study. Jayahar *et al* [12] study also reported the same. While Maske *et al* reported high (27%) incidence of Staphylococcus epidermidis in their study. Thus etiology of the

corneal ulcers varies significantly from region to region.

The standard treatment of bacterial corneal ulcer in majority 114 (73.1%) of our patients consists of topical instillation of fortified antibiotics (cefuraxime 50g/L and fortified tobramycin 9g/L). Which has been the "gold standard" for the therapy of bacterial corneal ulcer [6]. However the use of fortified antibiotics were associated with complain of ocular irritation or intense conjunctival reactions during drop instillation. This was due to the local corneal and conjunctival toxicity to the fortified drops. The same issue was raised by Cutarelli *et al* in 1991. We also treated 42 (26.9% ) patients by fluoroquinolones (Moxifloxacin) antibiotics. The antibacterial action results from inhibition of topoisomerase II (DNA gyrase) and topoisomerase IV. This is a new fourth generation fluoroquinolone with a broad spectrum of activity against Gram positive (including methicillin resistant Staph-ylococcus aureus and ciprofloxacin resistant Staphylococus aureus) and Gram negative micro-organisms. In addition, it penetrates well in the anterior chamber and remains fairly stable for at least 12 hours [13]. This treatment was advised to those patients who did not stay at hospital and had small infiltration.

Visual prognosis after bacterial corneal ulcer depends on the size, locality, and depth of the ulcers as well as on the risk factors, bacteria isolated, age and general health of patient. In our study, poor outcome were seen in patients having chronic surface ocular disorder, large size of ulcers, involving more than 2/3 of depth of the cornea and poor visual acuity at presentation. Patient presented very late or previously treated by topical steroids has also poor end result in our study. Only forty percent of patients had good visual out come with visual acuity better than the level at admission. Among the others 60% patient, final outcome was same or poor than time of presentation.

In conclusion, bacterial corneal ulcer is a serious ocular infectious disease that remains a therapeutic challenge and vision threatening ocular condition. Rapid isolation of bacteria and treatment with intensive ocular antibiotics represent decisive steps in the management of such pathologies.

**REFERENCES**

1 Stapleton F, Keay LJ, Sanfilippo PG, Katiyar S, Edwards KP, Naduvilath T. Relationship between climate, disease severity, and causative organism for contact lens-associated microbial keratitis in Australia. *Am J Ophthalmol* 2007;144(5):690-698

2 Bourcier T, Thomas F, Borderie V, Chaumeil C, Laroche L. Bacterial keratitis: predisposing factors, clinical and microbial review of 300 cases. *Br J Ophthalmol* 2003;87(7):834-838

3 Keay L, Edwards K, Naduvilath T, Taylor HR, Snibson GR, Forde K, Stapleton F. Microbial keratitis predisposing factors and morbidity. *Ophthalmology* 2006;113(1):109-116

4 Schaefer F, Bruttin O, Zografos L, Guex-Crosier Y. Bacterial keratitis: a prospective clinical and microbiological study. *Br J Ophthalmol* 2001;85 (7):842-847

5 Khanal B, Kaini KR, Deb M, Badhu B, Thakur SK. Microbial keratitis in eastern Nepal. *Tropical Doctor* 2001;31(3):168-169

6 Chaudhuri PR, Godfrey B. Treatment of bacterial corneal ulcers with concentrated antibiotics eye drops. *Trans Ophthalmol Soc UK* 1982;102(1):11-14

7 Xie L, Zhong W, Shi W, Sun S. Spectrum of fungal keratitis in north China. *Ophthalmology* 2006;113(11):1943-1948

8 Chowdhary A, Singh K. Spectrum of fungal keratitis in north India. *Cornea* 2005;24(1):8-15

9 Gopinathan U, Garg P, Fernandes M, Sharma S, Athmanathan S, Rao GN. The epidemiological features and laboratory results of fungal keratitis: a 10-year review at a referral eye care centre in south India. *Cornea* 2002;21(6):555-559

10 Poole TR, Hunter DL, Maliwa EM, Ramsay AR. Aetiology of microbial keratitis in northern Tanzania. *Br J Ophthalmol* 2002;86(8):941-942

11 Waxman E, Chechelnitsky M, Mannis MJ, Schwab IR. Single culture media in infectious dermatitis. *Cornea* 1999;18(3):257-261

12 Jayahar BM, Ramkirshan R, Vasu S, Meenakashi R, Palaniappan R. In vitro efficacy of antibacterials against bacterial isolates from corneal ulcers. *Ind J Ophthalmol* 2002;50(2):109-114

13 Kampougeris G, Antoniadou A, Kavouklis E, Chryssouli Z, Giamarellou H. Penetration of moxifloxacin into the human aqueous humor after oral administration. *Br J Ophthalmol* 2005;89(5):628-631