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**Original Article**

# Demography, Clinical Features and Outcome of Bacterial Keratitis Presenting in Tertiary Eye Care in Nepal

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**ABSTRACT**

**Background and Objectives:** Bacterial keratitis is an important cause of ocular morbidity in developing country like Nepal and this warrants a detail study of it including its outcome.

**Material and Methods**: Data of demography, clinical features and risk factors of bacterial keratitis were segregated from our previous cross-sectional study of microbial keratitis and retrospective data of treatment and outcome were taken from electronic medical record.

**Results**: Among 123 cases of bacterial keratitis, 111 had bacteria isolated in the culture whereas 12 had bacteria seen only in Gram stain. Average age of patients was 52.6 years; 65(52.8%) were female; 68.3% of total subjects were farmers. Patients had visited the tertiary hospital at an average of 12.9 days since onset of symptoms. Of culture isolates, 55 were *Streptococcus pneumonia* followed by *Staphylococcus aureus* (n=25) and *Streptococcus viridians* (n=14). Regarding clinical characteristics, 78(63.4%) cases had hypopyon; 24.3% (n=30) had infiltrate size of >¼ of corneal surface; 16(13.0%) were either perforated or impending to perforate at presentation. Trauma was the main risk factor in 35% (n=43), followed by topical steroid (19.5%, n=24) and dacryocystitis (16.2%, n=20). Patients were treated with combination of fortified cefazoline and amikacin or monotherapy with moxifloxacin or ofloxacin. Overall, 90(73.2%) responded to medical treatment, 19(15.4%) underwent therapeutic penetrating keratoplasty and 3(2.4%) needed evisceration. Smaller sized ulcers had better healing rates (81%) with statistical significance.

**Conclusion:** Patients with bacterial ulcers present late in tertiary eye center causing increased morbidity and even loss of eyes. Awareness, protective measures from trauma and proper

treatment has to be undertaken for controlling its occurrence and for better prognosis of the ulcers.

**Keywords**: Bacterial keratitis, bacterial ulcer, outcome

## INTRODUCTION

Microbial keratitis is common corneal pathology in developing countries [1]. Bacterial keratitis requires rapid and proper intervention. Delay in presentation, improper treatment, lack of facility for culture, antibiotic-resistant microbes, and delay in referral, all contribute to complications like perforated or non-healing ulcers which would necessitate therapeutic penetrating keratoplasty (TPK). Corneal perforation can occur in less than 24 hours in the presence of particularly invasive pathogens such as Pseudomonas aeruginosa and Staphylococcus aureus [2]. In hospital based studies of most developing countries, number of bacterial ulcers closely followed fungal ulcers [3].

Prognosis of bacterial ulcers depends on virulence of the bacteria. Pyogenic bacteria can cause rapid lysis of the corneal stroma, and perforation. Our study intended to find out demography, clinical features and outcome of bacterial keratitis along with prognostic factors related to the outcome. The study was done in Tilganga Institute of Ophthalmology (TIO) which is a tertiary referral center, located in Kathmandu, Nepal.

## MATERIALS AND METHODS

This was a retrospective study of all cases of bacterial ulcers that presented in TIO between November 2013 and April 2015 (18 months duration). Data of bacterial keratitis were segregated from our previous descriptive study of 602 presumed microbial keratitis presenting during that period. For more information, readers are referred to our prior publication [3]. Ethical approval was obtained from Institutional Review Committee of Tilganga Institute of Ophthalmology (Ref no: 24/2021)

Bacterial ulcers were selected for this study on the basis of i) positive corneal cultures for bacterial or ii) presence of bacteria in Gram stain. Cases with mixed bacterial and fungal growth were not included in the study. Data were collected about demographic parameters and clinical features of the bacterial ulcer. From Electronic medical records of the institution, detail information was taken about treatment of bacterial keratitis and its outcome. Initial treatment was hourly dose of combination of fortified topical cefazoline and amikacin or flouroquinolones (moxifloxacin or ofloxacin). The drops were modified according to the culture and sensitivity report. Slow tapering of the medication was done when ulcer showed signs of improvement. Oral ofloxacin 200 mg twice a day was given for a) ulcers extending to the limbus or sclera; b) ulcers associated with endophthalmitis or c) perforated ulcers. For endophthalmitis, vitreous tap and intravitreal antibiotic injection was given. Infection was considered as responding to treatment if there had been decrease in size of infiltrate, hypopyon, epithelial defect, congestion and anterior chamber reaction.

Topical steroids were given to those patients who improved and who could follow up. Infection was considered as healed if there was epithelization of the ulcer, resolution of the hypopyon and infiltrate. Ulcers not responding to treatment or those perforated

underwent TPK or evisceration (when eye was not salvable). A number of ulcers who did not come for follow up and whose status could not be known are kept in "lost to follow-up" group. Outcome of the bacterial ulcers was evaluated on the basis of how many responded to medical treatment and healed, how many underwent surgical intervention and how many lost their eyes (eviscerated). Visual outcome was evaluated for those that healed or responded to treatment. The outcome of bacterial ulcer was evaluated with respect to clinical prognostic factors like size of ulcer, duration of symptoms and presence of hypopyon.

Data entry and analysis was done using Microsoft excel. For the categorical data analysis, Chi square /Fisher Exact test were used wherever applicable. P value <0.05 was considered as statistically significant.

## RESULTS

Total number of presumed non-viral infective keratitis in the study period was 602, out of which 111 had pure bacterial growth, 7 cases had mixed bacterial and fungal growth and 12 cases had bacteria only in Gram stain with no growth in culture A total of 121 bacteria were isolated from 118 culture positive cases of which 95% isolates were Gram-positive and 5% were Gram-negative organisms.

The isolates were *Streptococcus pneumoniae* 55(45.5%), *Staphylococcus aureus* 25 (20.6%), *Streptococcus viridans* 14(11.6%), *Corynebacterium* species 10(8.2%), *Bacillus* species 5(4.1%) and 3(2.5%) each of *Nocardia* species, *Staphylocoocus epidermidis*, *Pseudomonas* and *Moraxella* species.

(As Clinical Ophthalmology 2020:14 3219-3226, with permission from the original publisher Dove Medical Press Limited. Reference No. ACQ212109) The sensitivity and specificity and the predictive value of Gram stain had been calculated and discussed in our previously published article [3]. Seven cases which had concomitant fungus growth were excluded from the study thus making total cases of bacterial keratitis under study to be 123. Ninety-four patients were from rural area, 23 patients were from city and 6 were from India.

Average age of patients with bacterial ulcer was 52.6 years. 65(52.8%) patients were female. Seventy-one (57.7%) were illiterate and another 19(15.45%) were just literate. Eighty-four (68.3%) of 123 patients with bacterial ulcers were farmers followed by housewives (10.6%). Bacterial keratitis presented throughout the year with slight preponderance in winter (Figure 1).

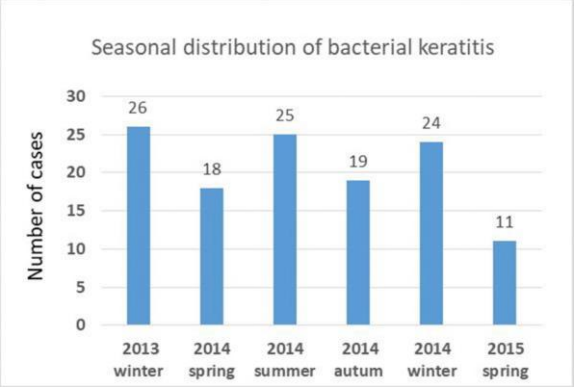


**Figure 1: Seasonal distribution of bacterial keratitis**

Place where the cases were first treated is shown in Table 1. It is inferred from this table that 80 (65%) of cases had some form of treatment before they came to TIO. Overall, the cases had sought medical help at an average of 5.7 days of symptoms, but for

those who were referred to TIO (n=80) had average duration of symptoms of 12.9 days.

Table 2 shows the risk factors associated with bacterial keratitis. Risk factor was detected in 103 cases (79 cases had one risk factor; 24 had two risk factors). 31 out of 43 trauma were due to vegetative matter.

**Table 1: Places where patient visited at first hand for treatment**

| First place where patients first visited for treatment | Number (%) |
|---|---|
| Trained eye care worker or Ophthalmologist ( primary or secondary eye care centers ) | 27 (21.9 ) |
| Tilganga Institute of Ophthalmology (tertiary care center) | 43(35) |
| Pharmacy shop | 35(28.5) |
| Traditional healers | 11(8.9) |
| General health post | 7(5.7) |
| **Total** | **123 (100)** |

**Table 2: Risk factors for bacterial ulcers**

| Risk factors* | Number ( %) |
|---|---|
| Trauma | 43(35) |
| Topical steroid | 24(19.5) |
| Dacryocystitis | 20(16.2) |
| Herpetic keratitis | 19(15.4) |
| Past ocular surgery | 11(8.9) |
| Others (diabetes, lagophtahlmus, bullous keratopathy ) | 10 ( 8.1) |
| No risk factors noted | 20(16.2) |

**24 patients have more than one risk factors*

Out of 123, 77 (73.3%) of ulcers had infiltrate in the visual axis (4 mm in the pupillary area). Regarding ulcer size, 93 cases (75.6%) of bacterial keratitis had infiltrate size of ≤ ¼ of corneal surface; 12(9.8%) had ulcers with infiltrate size >½ of the cornea. In total, 78 (63.4%) were with hypopyon, 6 case were perforated and 10 cases were impending to perforate at the time of presentation. 54.6% of 123 bacterial keratitis had received combination therapy and the rest received monotherapy.

**Table 3: Outcome of bacterial keratitis**

| Outcome of bacterial keratitis | Number (%) |
|---|---|
| Healed | 90 (73.2) |
| Needed therapeutic keratoplasty | 19 (15.4) |
| Needed Evisceration | 3 (2.4) |
| Lost to follow up, outcome unknown | 11 (8.9) |
| Total | 123 (100 ) |

Table 3 shows the outcome of bacterial keratitis under study.

**Table 4: Best corrected vision of 90 cases that healed**

| Best corrected vision after keratitis healed | Number (%) |
|---|---|
| ≥ 6/18 | 18 (20.0) |
| < 6/18 ≥ 6/60 | 12 (13.3) |
| <6/60 ≥ 3/60 | 13 (14.4) |
| < 3/60 | 47 (52.2) |
| Total ulcers healed | 90 (100) |

Table 4 shows best corrected vision of 90 cases which had healed completely. Table 5 shows outcome with respect to ulcer characteristics with statistical analysis. It shows that smaller size ulcers (≤¼ of corneal surface) were more likely to heal, less likely to need TPK or eviscerations than larger ulcers with statistical significance (P values <0.05) whereas hypopyon has no prognostic significance in the outcome of bacterial ulcer. Ulcers presenting earlier (within 7 days or less) had less chance of undergoing TPK than those presenting later than 7 days with statistical significance.

**Table 5**: **Outcome of bacterial ulcers with respect to clinical parameters**

| **Outcome** / **Characteristics of ulcer** | | **Responded to treatment (%)** | **Needed TPK* (%)** | **Needed Evisceration (%)** | **Lost to follow up (%)** | **Total (%)** |
|---|---|---|---|---|---|---|
| Size of ulcer | Ulcer size ≤ 25% of corneal surface (N=93) | 76 ( 81.7) | 10 (10.8) | 0 (0) | 7 (7.5) | 93 (100) |
| | Ulcer size > 25% of corneal surface ( N=30) | 14 ( 46.7) | 9(30.3) | 3(10.0) | 4(13.3) | 30 (100) |
| | **P value** | **<0.001** | **0.019** | **0.013** | **0. 460** | |
| Hypopyon | Presence of hypopyon ( N=78) | 55(70.5) | 14(17.9) | 2(2.6) | 7(9.0) | 78(100) |
| | Absence of hypopyon ( N=45) | 35(77.8) | 5(11.1) | 1(2.2) | 4(8.9) | 45(100) |
| | **P value** | **0.381** | **0.312** | **1.00** | **1.00** | |
| Duration of symptoms | ≤ 7 days ( N=59) | 47(79.7) | 5(8.5) | 2(3.4) | 5(8.5) | 59(100) |
| | >7 days (N=64) | 43(67.2) | 14(21.9) | 1(1.6) | 6(9.4) | 64(100) |
| | P value | 0.119 | 0.04 | 0.607 | 0.861 | |

***TPK:** Therapeutic keratoplasty*

## DISCUSSION

In our institute, 20.4% of all presumed microbial keratitis had been bacterial. In India, 21.4 to 32.7% of infective keratitis was of bacterial etiology [4, 5]. In hospital based studies of developing countries, fungal ulcers were more commonly isolated in culture than bacterial [3]. Bacterial keratitis is more common than fungal in temperate climate such as Britain and North USA and in subtropical urban climates of Hong Kong [4]. Bacterial keratitis showed lower incidence from June to September in the study of Bharathi et al [4]. In our study, lower incidence was noticed in spring (February to April) and in autumn (August to October) Figure 1.

In our study, 52.8% of our patients were female. But contradictory to our study, proportion of male was 56.7 to 71.3% in the study done in India, Saudi Arab and Iran [4-7]. In a study (done in Portugal) by Ferreira et al, 55.1% of people with bacterial keratitis were female [8]. Contact lens was an important risk factor (28.9%) in the study of Ferreira et al [8]. which could be the reason

for more female in their study. In our study (Table 2), chronic dacryocystits was the risk factor in 16.2% of bacterial ulcers. Chronic dacrycocysitis is the condition more common in female than in male [9]. This could be the reason for more female in our country.

The incidence of bacterial keratitis was 54.07% in rural area in India [4]. In our study, rural population accounted even more of upto 76.4%. In our study, 68.3% were farmers. In India, farmers accounted for 42.3 % in the study of Rautaraya et al [5].

In our study 52.6 years is the average age which was similar to the study done by Bharathi et al (in India) and of Rahimi et al (in Iran) but in France average age of bacterial keratitis was 46 years [4,7,10]. Younger age was affected in France because the commonest risk factor was contact lens [10].

Rahimi et al mentioned that the mean number of days between the onset of symptoms and referral to tertiary hospital in Iran was around 13 days, which is very similar to that of our study [7]. But in Sweden, people presented within 2.7 days of symptoms [11]. In France, 76% of bacterial ulcers reached immediately in emergency department [12].

In our study 83.8% has at least one risk factor versus 95.7% in the study by Ferrira et al in Portugal [8]. Trauma was the main predisposing factor for bacterial keratitis in other Asian countries, ranging from 17.6 to 43.3% of cases [4-7]. But in France, contact lens was the main factor responsible for up to 39.6% and trauma accounted for only 11.7% [13].

In our study, 73.3% of ulcers had involvement of visual axis. 61% to 67% of ulcers were located in the central region of cornea in the study of Rahimi et al and Ancele et al [7, 10]. The most common site of bacterial infiltration was paracentral (45.9%) and in inferior region (46%) in the study of Almizel et al and Bourcier et al respectively [6, 12] which could be related to contact lens being risk factor in their study. This shows the trauma is relating to mostly central corneal ulcers with significant impact in vision.

In our study, 13% of cases were either perforated or impending to perforate at presentation. Rahimi et al mentioned 11% percent of the patients had corneal perforation at admission in his study [7]. In ours as well as in his study, late presentation of the cases to the hospital or the high rate of topical steroid use prior to admission could be the reason for poor condition of the ulcers at presentation. In the study of Schaefer et al, at presentation, the diameter of bacterial ulcer was ≤ 2mm in 76.5% of ulcers [2]. This implied an early presentation of the ulcers.

Like in our study *Streptococcus pneumoniae* was the most common isolate in India in the study of Bharathi et al and Rautaraya et al [4, 5]. In Saudi Arab, it was *Staphylococcus epidermidis* followed by *Streptoccocus pneumonia* [6]. In the study of Schaefer et al, 62% were *Staphylococcus* species [2]. In the study of Bourcier et al, 17% of the bacteria were Gram negative compared to 5 % in our study [12].

In the study of Darugar et al in France, resolution of infection was obtained in 77.5% with only medical treatment; amniotic membrane transplantation was performed in

16.2% and emergency keratoplasty in 8.1% [13].

In the study of Rautaraya et al in East India, 15.5% underwent penetrating keratoplasty, 2.6% underwent evisceration and 11% were lost to follow up; findings was very similar to our study (Table3) [5]. Their analysis showed that older age, stromal infiltrate size more than 25 $mm^2$ and poor visual acuity at the time of presentation were significantly associated with poor outcome, but presence of hypopyon and Gram-negative bacterial etiology did not influence outcome [5].

In the study done in France by Bourcier et al, 0.6% underwent keratoplasty and 0.6% underwent evisceration [12]. Similarly, healing rate of 91% was obtained with medical treatment alone in a multicentric study done in England by Kaye et al [14]. Like in our study (Table 5), in the study of Kaye et al, patients with larger ulcers tended to have a significantly worse outcome and a greater risk of loss of the eye [14].

At discharge, 61% eyes had visual acuity ≤ Hand Movement in the study of Rahimi et al whereas in our study, 52.2 % of cases which healed had vision of less than 3/60 (Table 4)[7].

In the study of Schaefer et al, 1–15% of strains were resistant to fluoroquinolones, 13–22% to aminoglycosides, 37% to cefazolin and hence fluoroquinolones appear to be the therapy of choice for bacterial keratitis [2].

In the study by Aurell et al, 66% received monotherapy and 34% received combination therapy; majority responded to this empirical therapy [11]. In our study, 54.6% received combination therapy. Higher rate of combined therapy in our study is because, either the ulcers were large or most of the patients who were referred to our center already had had monotherapy.

In the study of Rautaraya et al, the most prescribed antibiotic before and after culture was gatifloxacin as it was found effective in 87% of Gram positive and 95% of Gram negative organisms [5]. As per our previous published paper, vancomycin, cefazoline, moxifloxacin and gatifloxacin were > 85% sensitive against Gram positive organisms. Gentamycin and tobramycin were 100 % and amikacin was 83.3% sensitive against Gram negative organisms [3]. Limitations of our study were that cases which were lost to follow-up were not traced for analysis and that the outcome of cases that underwent TPK was not analyzed in this study.

## CONCLUSION

Late presentation of the bacterial ulcers makes the prognosis of worse, needing surgical intervention and even loss of eye. Prevention of trauma, prompt and appropriate treatment of bacterial ulcers as well as timely referral to tertiary center can decrease the morbidity due to bacterial ulcers. Necessary antibiotics have to be made available in primary health centers.

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### *Author's Contribution*

*Concept, design, intellectual content, literature review, data acquisition and analysis, manuscript writing (major) and manuscript review-**LB;** data acquisition and analysis, literature review, manuscript writing-**ARB;** Critical analysis of the manuscript-**RG***

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