Original Research Article

Aetiology and risk factors of bacterial corneal ulcer

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Abstract

Introduction: Bacterial corneal ulcer or bacterial keratitis is an infection of the cornea that is caused by bacteria that causes rapid visual loss and pain. The incidence of microbial keratitis (MK) is variable worldwide with an estimated 1.5–2 million cases of corneal ulcers in developing countries.**Materials and Methods**: This is a prospective study conducted over a period of six months at the Department of Ophthalmology. Inclusion Criteria: Patients above the age of 18 years presenting with suspected corneal ulceration and having symptoms of pain, redness, watering, photophobia and decreased vision were included in the study. Exclusion Criteria: Patients with typical features of viral infection and healing ulcers were excluded as were Mooren's ulcers, interstitial keratitis, sterile neurotropic ulcers, and any ulcer associated with autoimmune conditions.**Results:** The keratitis was induced by foreign body particles were most common risk factor 22.3%. Trauma with vegetative material was by far the second most common risk factor; this was encountered in 16 (12.3%) patients. History of non-vegetative trauma in 14(10.7%) patients. Anterior chamber inflammation was absenting in 10 (7.6%) patients. A1+ to 2+ Tyndall effect with 1+ to 2+ cells were present in 30 (23.1%) patients, and severe anterior chamber inflammation (3+ to 4+ Tyndall effect and cells, with or without hypopyon) was present in 90 (69.3%) patients. 102 (77.6%) patients, bacteria were isolated from the corneal smears. Gram positive bacteria isolated, most of them 62 (47.6%) were staphylococcus aureus. Gram negative bacteria were isolated in patients, most of them were pseudomonas and yersina. **Conclusion:** Bacterial Corneal ulcers are a vision-threatening ocular emergency. It is imperative that health care providers across specialties work together so that these patients may have the best possible outcome and avoid the many potential complications.

Keywords: Bacterial Corneal ulcers, Toxins, Contact lens.

Introduction

Bacterial corneal ulcer or bacterial keratitis is an infection of the cornea that is caused by bacteria that causes rapid visual loss and pain. Types of bacteria that commonly caused bacterial keratitis include: Pseudomonas aeruginosa and Staphylococcus aureus. [1] Bacterial keratitis is a major cause of preventable monocular morbidity and blindness globally. [2] The severity usually depends on the underlying condition of the cornea and the pathogenicity of the infecting bacteria. Hence, bacterial keratitis is an ophthalmic emergency that needs immediate treatment. [3] However, antibiotic resistance among ocular pathogens is increasing worldwide. [4] Resistance increases the risk of treatment failure with potentially serious consequences. [5] The incidence of microbial keratitis varies from 11.0 per 100,000 persons/year in the United States to 799 per 100,000 persons/year the developing countries. Moreover, it has been estimated that 1.5 to 2 million cases of corneal ulcers occur in the developing countries. [6] Until recently, most cases of bacterial keratitis were associated with ocular trauma or ocular surface diseases. However, the widespread use of contact lenses has dramatically increased the incidence of contact lens related keratitis. [7] Besides, the pattern of risk factors predisposing to bacterial keratitis varies with geographical regions. [8] A wide range of bacteria can cause bacterial keratitis. However, Pseudomonas aeruginosa is the most frequent and the most pathogenic ocular pathogen, which can cause corneal perforation in the absence of predisposing factors in less than 24 hours after onset. [9] Besides, the bacteriological profile and their susceptibility as well as resistant patterns vary from place to place and in the same place from time to time. [10] With advances in the understanding of its pathogenesis, laboratory investigations like immunohistochemistry,fluorescent microscopy,enzyme immunoassays and molecular biology, and the availability of fourth generation antibiotics, the overall visual outcome in bacterial keratitis has improved with time. [11] Particular attention should be given to this condition as it can progress very rapidly with complete corneal destruction occurring within 24–48 hours. Early diagnosis, which is primarily clinical and substantiated largely by microbiological data, and prompt treatment are needed to minimise the possibility of permanent visual loss and reduce structural damage to the cornea. [12]In India, there is a scarcity of published data on the spectrum of etiologic agents and risk factors of bacterial keratitis. Thus, this study was conducted to identify the spectrum of bacterial aetiology and risk factors of bacterial keratitis and to assess the in-vitro antimicrobial susceptibility of these bacterial isolates at our center.

Materials and methods

This is a prospective study conducted over a period of six months at the Department of Ophthalmology.

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Inclusion Criteria: Patients above the age of 18 years presenting with suspected corneal ulceration and having symptoms of pain, redness, watering, photophobia and decreased vision were included in the study.

Exclusion Criteria: Patients with typical features of viral infection and healing ulcers were excluded as were Mooren's ulcers, interstitial keratitis, sterile neurotropic ulcers, and any ulcer associated with autoimmune conditions.

The following data were collected from each chart: patient age and sex, and duration of the symptoms at the time of the presentation. History and examination were focused on the following risk factors: corneal trauma, contact lens wear, ocular surface diseases (that is, previous herpetic infection, bullous keratopathy, dry eye syndrome,blepharitis,or other eyelid abnormalities),corneal surgery (refractive surgery, penetrating keratoplasty). There were few cases in which contact lens wear was associated to ocular surface disease.Those cases were classified as ocular surface diseases. The size of the infiltrate was measured in square millimetres and its location was determined according to five zones: central, nasal superior, nasal inferior, temporal superior, and temporal inferior. The ulceration depth was evaluated as <⅓, ⅓–⅔, and >⅔ of the total corneal thickness. Anterior chamber inflamma-tion, when present, was scored from 1 to 4 + for Tyndall effect and cells. We recorded the antibiotics and other treatments that were administered before examination. 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,ceftazi -dime,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.

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 25th.

Results

Total 120 patients were enrolled with a corneal infiltration that was clinically compatible with the diagnosis of bacterial corneal ulcer during the study period. The bacterial corneal ulcer was identified in 130 patients.

Table 1: Distribution of Gender

Gender	No. of patients	Percentage
Male	86	66.15
Female	44	33.84
Total	130	100

In table 1, Majority of them were male 86 (66.15%) and female 33.84%.

Table 2: Distribution of Gender

Age (Years)	No. of patients	Percentage
1-20	25	19.2
21-40	52	40.0
41-60	43	33.0
>60	10	7.7
Total	130	100

In table 2, the age of patients ranged from 1 to >60 years. Majority of 21-40 years age group (40%).

Table 3: Clinical features of corneal ulcer

Risk factor	No. of patients	Percentage
Foreign body	29	22.3
Vegetative trauma	16	12.3
Non-vegetative trauma	14	10.7
Ocular surface disorder	10	7.6
Ocular surgery	15	11.5
Contact lenses	18	13.8
Keratopathy	15	11.5
Blepharitis	13	10
Total	130	100

In table 3, the keratitis was induced by foreign body particles were most common risk factor 22.3%. Trauma with vegetative material was by far the second most common risk factor; this was encountered in 16 (12.3%) patients. History of non-vegetative trauma in 14(10.7%) patients. In 10 (7.6%) patients, ocular surface disorder was observed, eighteen (13.8%) patients were affected by contact lenses. Keratopathies (including herpetic, bullous and post-operative keratopathies) were presented in 15 (11.5%) patients. Blephritis was noted in 13(10.0%) patients.

Table 4: Location of bacterial corneal ulcer

Location	No. of patients	Percentage
Central	70	53.8
Peripheral	60	46.2
Total	130	100

In table 4, corneal localization of the ulcers was distributed as in 70(53.8%) patient's central and in 60 (46.2%) peripheral.

Table 5: Diameter of bacterial corneal ulcer

Size (mm)	No. of patients	Percentage
1-2	34	26.2
3-4	40	30.7
5-6	38	29.2
7-8	10	7.7
Entire	8	6.2
Total	130	100

The diameter of the corneal ulceration was of 1-2 mm in 34 (26.2%), 3-4mm in 40 (30.7%), 5-6 mm in 38 (29.2%), 7-8 mm in 10 (7.7%) patients, 8 (6.2%) patients had entire corneal involvement.

Table 6: Depth (corneal thickness) of bacterial corneal ulcer

Depth (corneal thickness)	No. of patients	Percentage
<1/3	65	50.0
1/3-2/3	42	32.3
>2/3	23	17.6
Total	130	100

In table 6, ulceration depth was less than 1/3 conreal thickness in 65 (50.0%), between 1/3 to 2/3 in 42 (32.3%) patients and over 2/3 in 23 (17.6%) patients.

Table 7: Anterior chamber reaction of bacterial corneal ulcer

Anterior chamber reaction	No. of patients	Percentage
1-2 tyndall and 1-2 cells	90	69.3
3-4 tyndall and 3-4 cells or hypopyon	30	23.1
Nil	10	7.6
Total	130	100

In table 7, Anterior chamber inflammation was absent in 10 (7.6%) patients. A1+ to 2+ Tyndall effect with 1+ to 2+ cells were present in 30 (23.1%) patients, and severe anterior chamber inflammation (3+ to 4+ Tyndall effect and cells, with or without hypopyon) was present in 90 (69.3%) patients.

Table 8: Microorganisms isolated from bacterial corneal ulcers

Organisms cultured	No. of patients	Percentage
Staphylococcus aureus	62	47.6
Pseudomonas aeruginosa	13	10
Streptococcus pneumonia	19	14.6
Yersina	3	2.3
Moraxella spp	1	0.7
Proteus spp	2	1.5
Klbsiella pneumonia	1	0.7
No growth	29	22.3
Total	130	100

In table 8, 102 (77.6%) patients, bacteria were isolated from the corneal smears. Gram positive bacteria isolated, most of them 62 (47.6%) were staphylococcus aureus. Gram negative bacteria were isolated in patients, most of them were pseudomonas and yersina. Infection with Gram negative organisms associated with severe anterior chamber inflammation and depth more than 2/3 of cornea. 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 (Moxifloxacin).

Table 9: Visual acuity of bacterial keratitis patients at initial presentation (admission) and discharge.

Visual Acuity	On admission	On discharge
	No. of patients (%)	No. of patients (%)
6/6-6/18	31 (23.8)	39 (30)
6/24-6/60	57 (43.8)	67 (51.5)
Counting fingers	0	0
Hand movement	23 (17.6)	22 (16.9)
Perceived light	19 (14.6)	1 (0.7)
Did not perceive light	0	1 (0.7)
Total	130	100

In table 9, the visual acuity of keratitis patients at initial presentation and discharge is indicated. At initial presentation, among the bacterial keratitis, majority (43.8%) had visual acuity of 6/24- 6/60. At the end of the treatment, 39 patients (30.0%) had attained vision of 6/6 to 6/18, 67 patients (51.5%) had visual acuity of 6/24 to 6/60. Twenty-three patients had visual acuity of hand movement and another one with light perception.

Discussion

Bacterial corneal ulcers may follow a break in the corneal epithelium, thereby providing an entry for bacteria. The traumatic episode may be minor, such as a minute abrasion from a small foreign body, or may result from such causes as tear insufficiency, malnutrition, or contact lens use. Increased use of soft contact lenses in recent years has led to a dramatic rise in the occurrence of corneal ulcer, particularly due to Pseudomonas aeruginosa and

Staphylococcus aureus. 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. [13]In our study male were predominance (66.15%), in line with other studies 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 outdoor activities, which subsequently increased their vulnerability to this blinding disease. [14,15] In our study, 40% of patients were 21-40 years older individuals were more frequently affected in this study. Age profile in our patients is comparable to Khor WB study. [16] In general, older age, delay in referral, topical steroid treatment, past ocular surgery, poor vision at presentation, large size of ulcer, and central and deep ulcer are all major risk factors for evisceration and enucleation in patients with bacterial corneal ulcer. [17]In our study, Bacterial corneal ulcer was diagnosed in 130 patients. Although it is rare in the absence of a predisposing factor, most of the cases of microbial keratitis were associated with Foreign body and ocular trauma. In this study, 86 (55.0%) were associated with various types of ocular injuries and vegetative trauma Accounts 22.3% and 12.3% patients respectively. According to Chidambaram JD 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. [18] Moreover, the climate is mild and humid, and malnutrition is common. Foreign body induced corneal ulcer was the most common (29 cases, 22.3%) 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 7.6% and 11.5% of cases respectively. Motukupally SR reported 21% of cases of bacterial corneal ulcer were with ocular surface disorder. [19] Contact lenses remained the least common cause of bacterial corneal ulcer in our study. In contrast Kumar R 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. [20] Many physiopathological effects of contact lenses wear have been reported. The most important of which is an induced hypoxia and hypercapinia of the cornea. The success rate of bacterial isolation was high in the present study, with 77.6% of smear positive on blood, chocolate and Mac-Conkey agar. While Srinivasan W, reported 70% of isolation of organism on same medium. [21] As with most published studies there was a high prevalence of Gram positive bacteria with staphylococcus aureus accounting for 62 (47.6%). [22] Sharma N reported higher incidence of streptococcus pneumonia (20%) in his study. [23] While Hafezi F reported high (27%) incidence of Staphylococcus epidermidis in their study. [24] 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. [25] However, the use of fortified antibiotics was 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. 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 microorganisms. In addition, it penetrates well in the anterior chamber and remains fairly stable for at least 12 hours. [25] 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 was 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.

Conclusion

Corneal ulcers are a vision-threatening ocular emergency. It is imperative that health care providers across specialties work together so that these patients may have the best possible outcome and avoid the many potential complications. The patient will often first present in a clinic or emergency department setting and so primary care, and emergency health care professionals must be able to rapidly identify this disease and communicate effectively with their ophthalmology colleagues. Pharmacists should be consulted to help with antimicrobial selection or, in the case of peripheral ulcerative keratitis, immunosuppressants. Nurses are essential for successful treatment plans and patient education.

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