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Original Article

# Clinical and Microbiological Profile and Treatment Outcome of Infective Corneal Ulcers: A Study in Central India

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## Abstract

**Background:** Corneal ulceration is a leading cause of corneal blindness world over. The underlying microbiological etiology of infective corneal ulcer shows a wide regional variation. An understanding of the clinical and microbial profile of corneal ulcers in a particular region helps us in improved management of this sight-threatening condition.

**Materials and Methods:** Our study is a prospective, analytical, hospital-based study conducted in the Eye Department of R. D. Gardi Medical College, Ujjain, India. 60 patients with a clinical diagnosis of infective corneal ulcer were enrolled for the study. A complete demographic profile, associated risk factors, and microbial etiology were studied. Treatment outcome was also noted.

**Results:** In our study, 60 patients with infective keratitis were enrolled. 46 (76.7%) were male patients while 14 (23.3%) patients were females. A history of vegetative injury during crop harvesting was the leading cause seen in as many as 17 (28.3%) patients. 47 (78.3%) patients in our study had an ulcer involving the center of the cornea. 43 (71.67%) patients were found to be culture positive. Among the 43 culture positive patients, 29 (67.44%) patients were positive for fungi, while 14 (32.56%) patients gave a positive yield for bacteria. The majority of our patients, i.e., 37 (61.66%) out of 60 showed clinical improvement, while 11 (18.36%) patients recovered. 4 (6.66%) of our patients worsened even after appropriate management.

**Conclusion:** Fungal corneal ulcers were the most common type found in our study. Timely detection and appropriate management are recommended to prevent prolonged ocular morbidity and blindness.

**Key words:** Bacterial, Blindness, Corneal ulcer, Fungal, Infective keratitis, Microbial

## INTRODUCTION

Corneal blindness ranks next to cataract among the major causes of blindness. Ocular trauma, as well as corneal ulceration, is responsible for most of these cases of corneal blindness. In the developing world, infectious corneal ulcer is a leading cause of prolonged ocular morbidity and visual loss.[1] Corneal blindness is responsible for 1.5-2 million new cases of monocular blindness every year.[2] In India, approximately 6.8 million people are suffering from corneal blindness. Out of these, about 1 million have bilateral corneal blindness. It has been estimated that the number of people afflicted from corneal blindness in India will increase to 10.6 million by 2020.[3]

There is a significant variation in the prevalence of corneal ulceration in different parts of the world. This can be attributed to difference in climatic conditions, difference in occupation as well as other socioeconomic factors.[4,5] Population-based studies conducted in India and in the USA have found that the incidence of corneal ulceration is 10 times higher in India as compared to the incidence of corneal ulceration in USA.[6,7]

The causative organism responsible for infective corneal ulcer varies considerably by region. In the Western population, viral corneal infections account for the majority of cases of corneal blindness. On the other hand, fungal and bacterial infections of the cornea predominate in the Asian sub-continent. Thus, practitioners need to

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be aware of local epidemiological patterns of corneal infection.

In this study, we aim to understand the epidemiology, the predisposing factors, microbiological profile and the outcome of management of infective corneal ulcers presenting to our hospital, which is a tertiary care hospital located in the state of Madhya Pradesh in Central India.

## MATERIALS AND METHODS

This study is a prospective, hospital-based study that was conducted at R. D. Gardi Medical College, Ujjain, Madhya Pradesh, India, over a period of 1-year from April 2015 to March 2016. Before the commencement of the study, approval was sought and obtained from the Institutional Ethics Committee. 60 patients with a clinical diagnosis of infective suppurative corneal ulcer were enrolled in the study.

Corneal ulceration was defined as a loss in the continuity of corneal epithelium with underlying stromal necrosis along with associated signs of inflammation, with or without hypopyon.

### Exclusion Criterion

- Cases presenting as non-infectious keratitis such as peripheral ulcerative keratitis due to systemic auto-immune diseases, Mooren's ulcer, phlyctenular keratitis, vernal keratoconjunctivitis associated shield ulcer, contact lens related sterile infiltrates, marginal keratitis, interstitial keratitis, and atheromatous corneal ulcer were excluded from this study.
- Cases of corneal ulcer who presented with excessive corneal thinning and impending perforation, as well as perforated corneal ulcers were excluded, as taking a corneal scraping and subsequently establishing a microbiological etiological diagnosis was not feasible in such patients.
- Typical viral corneal ulcers.
- Pediatric patients, as corneal infection in the pediatric age group differs from the adult disease in risk factors, treatment and complications.[8]

A detailed history was obtained from each patient, with special emphasis on the patient's occupation and any prior history of trauma. If present, the mode of injury, as well the details of previous treatment taken, was noted. Special inquiry was made regarding the use of steroid eye drops, use of indigenous medications and if any self-medication had been resorted to. History of any antecedent febrile illness as well as the history of contact lens wear was also sought. History of any associated systemic illness such as diabetes was taken. The nature and duration of complaints was noted.

The best-corrected visual acuity (BCVA) was recorded. Each patient was subjected to a detailed slit-lamp biomicroscopic examination, with special emphasis on the cornea. The details of the corneal ulcer - including the location, size, shape, depth of the ulcer, nature of infiltrate, margins of the ulcer, presence of any satellite lesions, immune ring, corneal vascularization, and hypopyon - were noted. Photographic documentation of the corneal ulcer on slit-lamp imaging system was done at the time of initial presentation, as well as on each follow-up visit. Ocular adnexal structures were also examined to look for meibomianitis, trichiasis, lagophthalmos, chronic dacryocystitis, etc. All the relevant ocular investigations were carried out. This included lacrimal syringing and testing for corneal sensation. Intraocular pressure by non-contact tonometry was recorded whenever feasible. Fluorescein stain of the corneal ulcer was also performed. B-scan ultrasound examination of the posterior segment was done to rule out endophthalmitis in suspicious cases.

Corneal scraping was performed with full aseptic precautions, after anesthetizing the cornea with 4% lignocaine, under slit-lamp visualization with a sterile No. 15 Bard-Parker blade. The material was obtained by gently scraping the leading edge and base of the ulcer. The material was smeared on two slides - One for Gram-stain and other as 10% potassium hydroxide (KOH) wet mount.[9,10] For culture and sensitivity, the material was also directly inoculated by multiple C-shaped streaks, on blood agar, chocolate agar, nutrient agar and two tubes of Sabouraud dextrose agar (SDA) with chloramphenicol (50 mg/ml). The laboratory diagnosis was performed using standard protocols. All the inoculated media, i.e., blood agar, chocolate agar, and nutrient agar were inoculated at 37°C and were evaluated at 24 and 48 h. They were subsequently discarded at 48 h if no growth was observed. The inoculated SDA media for fungi was incubated at 25°C and 37°C and examined daily. It was discarded after 10 days if no growth was present. Identification of growth on SDA was done by lactophenol cotton blue stain, by pigment production and by the morphological appearance of hyphae and spores.[11]

All routine systemic investigations, including fasting blood glucose to rule out diabetes mellitus, were performed. Systemic examination to rule out any septic focus in the body was also done.

After obtaining the corneal scraping, the patient was empirically put on broad-spectrum antibiotic eye drops and/or antifungal eye drops depending on the clinical

presentation. Corneal ulcers with regular margins, wet appearance, mobile hypopyon, and with greater symptoms were primarily considered to be bacterial in nature and treated with broad-spectrum antibiotic eye drops. On the other hand, corneal ulcers having feathery margins, dry appearance, thick cheesy hypopyon, satellite lesions or with a history of vegetative injury were initially put on antifungal eye drops. The initial therapy was also guided by Gram-stain/KOH mount findings. Cycloplegic drops/ointment was started in all patients. The anti-microbial therapy was reviewed after obtaining the culture and sensitivity report. If no growth was obtained on culture, then the treatment of the patient was continued according to the clinical appearance of the ulcer (as discussed) as well as the clinical response to treatment.

Follow-up of the patient was documented at 1 week, 2 weeks and 1 month, respectively, though the actual follow-up was done more frequently.

On follow-up, we recorded the patient's BCVA, corneal ulcer size, hypopyon (present/absent/decreased), infiltration (increased/decreased) and symptomatic relief as reported by the patient. The patient was said to have improved if the size of the ulcer, hypopyon, infiltration had decreased and patient's symptoms had improved.

All the data obtained was entered in a pre-tested performa, and statistical analysis was performed using Statistical Package for Social Sciences version 16.0.

## RESULTS

Our study was a prospective, hospital-based study of 60 patients suffering from infective suppurative corneal ulcer. 46 (76.7%) were male patients while 14 (23.3%) patients were females. 47 (78.3%) out of 60 patients belonged to age group 51-60 years while 7 (11.7%) patients belonged to age group of 41-60 years. Only 5 (8.3%) patients belonged to >60 years of age (Figure 1). 55 (91.7%) patients in our study belonged to the rural area, and only 5 (8.3%) patients were from urban background.

Socioeconomic status plays an important role in the causation as well as management of patients with corneal ulcer. Access to medical facilities as well as affordability of treatment becomes significant in the final visual outcome. In our study, 51 (85%) out 60 patients belonged to low socioeconomic group as they mostly came from surrounding rural areas, whereas only 9 (15%) patients belonged to the middle-income group. Occupation of a person also has a bearing on the causation of corneal ulcer in many cases. In our study, we found that 37 (61.7%) out of 60 patients were involved in farming activities and were thus predisposed to vegetative injury. 19 (31.6%) patients were involved in other outdoor activities such as manual labor or were employed in industries, and only 4 (6.7%) patients were working indoors such as in offices/shops or were home-makers (Figure 2).

Climatic conditions play a significant role in epidemiology of corneal ulcers. We found that 20 (33.3%) out of the 60 patients in our study presented during the months of March-April and 16 (26.6%) patients presented during the months of September-October (Figure 3). These four months (March-April, September-October) coincide with the harvesting season in Ujjain district, Malwa region. Thus, the large farming populace is more prone to suffer occupational injury to the eye during this period.

There are a large number of risk factors associated with the causation of corneal ulcers. Ocular injuries remain one of the major pre-disposing causes of infective corneal ulcers. In our study, we found that an antecedent history of ocular trauma before the onset of symptoms was seen in 40 (66.66%) out of 60 patients of corneal ulcer. Co-existing ocular disorders, such as chronic dacryocystitis and bullous keratopathy, were seen in 15 (25%) patients. In 3 (5.1%)

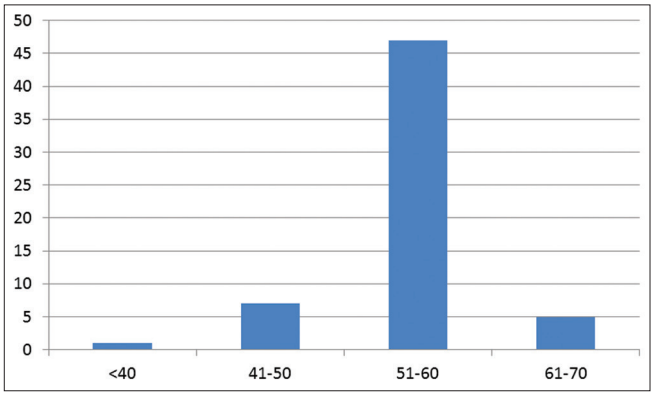


**Figure 1: Age distribution in the study group (*n* = 60 patients)**


**Figure 2: Distribution of cases according to the occupation (*n* = 60 patients)**

patients, there was a history of inadvertent use of topical steroids. 2 (3.3%) patients were found to be suffering from diabetes mellitus. Both of them were on irregular treatment with consequent very high blood sugar levels at the time of presentation.

Among the cases of ocular trauma, history of vegetative injury such as accidental thorn injury, by the stalk/leaf of wheat plant during crop harvesting was the leading cause seen in as many as 17 (28.33%) patients. A history of injury by other wooden material such broomstick and wooden splinter was seen in 15 (25%) patients. History of injury by animal matter, such as from the tail of domestic animals such as cow and goat or from accidental fall of cow-dung in the eye, was seen in 4 (6.66%) patients. Injury by materials such as stone/sand particles was seen in 3 (5%) patients. Among the coexisting ocular disorder, lid margin abnormalities like severe blepharitis/meibomianitis, trichiasis and entropion accounted for 7 (11.67%) cases. Pre-existing corneal opacity/degeneration such as climatic droplet keratopathy was present in 4 (6.67%) patients. In 1 (1.67%) patient bullous keratopathy was present and 2 (3.3%) patients were found to be having coexisting chronic dacryocystitis in the eye with corneal ulcer (Table 1).

Corneal ulcers profoundly affect the visual function of an individual, and if appropriate treatment is not administered in time irreversible loss of vision will occur. In our study, we found that 50 (83.4%) patients had an unaided visual acuity of <3/60 in the affected eye while only 10 patients had visual acuity of >3/60 in the affected eye. Location of corneal ulcer also influences the final visual outcome as central corneal ulcers are usually associated with marked visual impairment. 47 (78.3%) patients in our study had an ulcer involving the center of the cornea. This led to severe visual impairment in these patients. 6 (10%) patients had peripheral ulcers while 7 (11.7%) patients had ulcers involving the paracentral cornea. Decreased immunity from a comorbid systemic condition usually aggravates the clinical course of corneal ulcer. In our study, we found that 20 (33.3%) of our patients were anemic. This can be attributed to the poor nutritional status of the rural farming population. 2 (3.3%) patients suffered from diabetes mellitus, and 11 (18.4%) patients were found to be hypertensive.

In our study, 43 (71.67%) patients were found to be culture positive. While the remaining 17 patients failed to give a positive yield on culture examination (Figure 4). Among the 43 culture positive patients, 29 (67.44%) patients were positive for fungi, while 14 (32.56%) patients gave a positive yield for bacteria (Figure 5). *Aspergillus* species was identified in 16 (37.21%) patients, while *Fusarium* species was detected in 13 (30.23%) patients. Among the 14 patients testing positive for bacteria, *Staphylococcus aureus* was isolated in 9 (20.93%) patients, *Streptococcus pneumoniae* was identified in 3 (6.98%) patients, while 2 (4.65%) patients tested positive for *Pseudomonas* species (Table 2).

**Table 1: Risk factors associated with corneal ulcer (*n*=60 patients)**

| Risk factor | Number of patients (%) |
|---|---|
| Trauma | 40 (66.66) |
| Vegetative trauma (leaf/grass/thorn) | 17 (28.33) |
| Animal matter (cow dung/tail of animal) | 04 (6.66) |
| Sand/stone | 03 (5) |
| Wooden object (stick/chip) | 15 (25) |
| Others | 01 (1.67) |
| Coexisting ocular disorder | 15 (25) |
| Lid margin abnormalities | 07 (11.67) |
| Lagophthalmos | 01 (1.67) |
| Associated corneal opacity/degeneration | 04 (6.67) |
| Bullous keratopathy | 01 (1.67) |
| Chronic dacryocystitis | 02 (3.33) |
| Use of steroids | 03 (5) |
| Diabetes mellitus | 02 (3.33) |
| Total | 60 (100) |

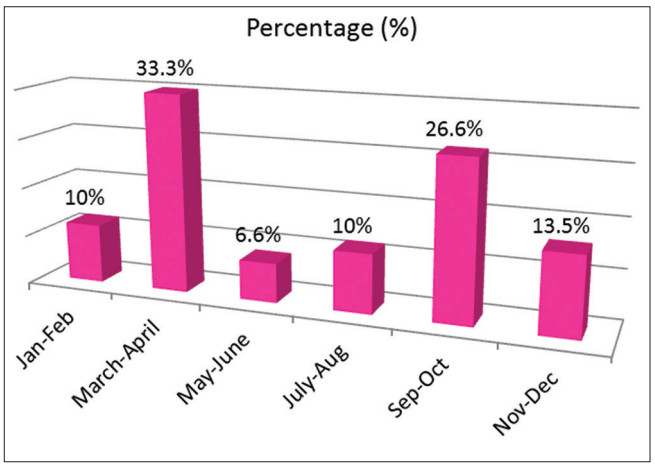


**Figure 3: Seasonal distribution of cases in study group (*n* = 60 patients)**

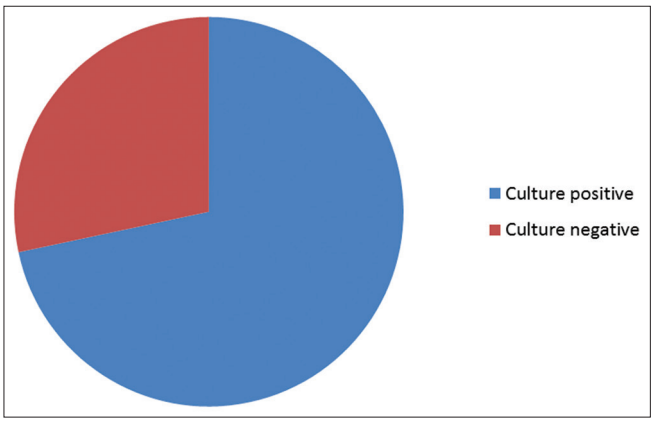


**Figure 4: Culture results in the study group (*n* = 60 patients)**

Treatment of corneal ulcers has always posed to be a challenging task for the treating clinician. In our study, 29 (48.33%) patients were treated with antifungals + cycloplegics + intraocular pressure lowering agents. Topical antibiotics remained the primary anti-microbial therapy in 14 (23.33%) patients. 2 (3.33%) patients underwent therapeutic keratoplasty as they failed to respond to medical anti-microbial therapy and showed progressive clinical deterioration (Table 3).

The majority of our patients, i.e., 37 (61.66%) out of 60 showed clinical improvement, while 11 (18.36%) patients recovered. In 8 (13.3%) patients, the condition remained stationary. 4 (6.66%) of our patients worsened even after appropriate management (Figure 6).

## DISCUSSION

Cornea, being the most anterior part of the eyeball, is exposed to the atmosphere and thus remains prone to infections. Corneal ulcer is a major health problem in developing world causing prolonged ocular morbidity and loss of vision. The major morbidity from infectious keratitis is due to corneal ulceration and subsequent perforation which can lead to endophthalmitis, or visual loss from severe scarring and vascularisation.[12] Even with appropriate treatment, there is a high incidence of visual loss due to the development of dense corneal scar.

In our study, 46 (76.7%) patients were male while 14 (23.3%) patients were females. A similar male preponderance was found in the study by Titiyal *et al.,* in which 75% patients were males.[13] However, an almost equal distribution among both the sexes was found in a study by Upadhyay *et al.* in Nepal.[14] The higher incidence of corneal ulcers in female population in the Nepal study could be due to greater involvement of females in outdoor activities there, especially farming.

In our study, 47 (78.3%) out of 60 patients belonged to age group 51-60 years. Li *et al.* too found in their study that the age group with the highest prevalence of corneal infections was 50-59 years, accounting for 83.21% of all corneal disease.[15] 55 (91.7%) patients in our study belonged to the rural area. This is chiefly because our hospital caters to a large extent to the villages in and around Ujjain district. A similar propensity of rural patients was found in a study conducted in Jammu by Gupta *et al.* where 65% patients came from a rural background.[16] In our study, 51 (85%) out 60 patients belonged to low socioeconomic group, whereas only 9 (15%) patients belonged to the middle-income group. Bhushan *et al.* also found in their study conducted in Uttar Pradesh and Bihar that the majority of patients (71.3%) belonged to the low socioeconomic group.[17] This could be due to the fact that people belonging to lower socioeconomic status are mostly engaged in manual labor and outdoor work and thus have a higher occupational risk of corneal injury.

In our study, we found that 37 (61.7%) out of 60 patients were involved in farming activities. Similar results were also

**Table 2: Etiological distribution of microbial keratitis in study group (*n*=43 patients)**

| Etiology | Number of patients (%) |
|---|---|
| Fungal | 29 (67.44) |
| *Aspergillus* | 16 (37.21) |
| *Fusarium* | 13 (30.23) |
| Bacterial | 14 (32.56) |
| *S. aureus* | 09 (20.93) |
| *S. pneumoniae* | 03 (6.98) |
| *Pseudomonas* | 02 (4.65) |

*S. aureus: Staphylococcus aureus, Streptococcus pneumoniae: S. pneumoniae*

**Table 3: Management of patients in study group (*n*=60 patients)**

| Management | Number of patients (%) |
|---|---|
| Antibiotics+cycloplegics+IOP lowering agents | 14 (23.33) |
| Antibiotics+cycloplegics+IOP lowering agents+antifungals | 15 (25.00) |
| Antibiotics+cycloplegics+IOP lowering agents+antifungals+surgery | 02 (3.33) |
| Antifungals+cycloplegics+IOP lowering agents | 29 (48.33) |
| Total | 60 (100) |

IOP: Intraocular pressure

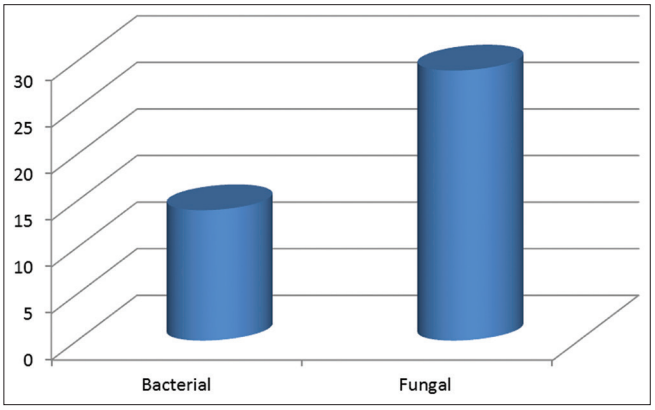


**Figure 5: Type of isolates in the study group (*n* = 43 patients)**

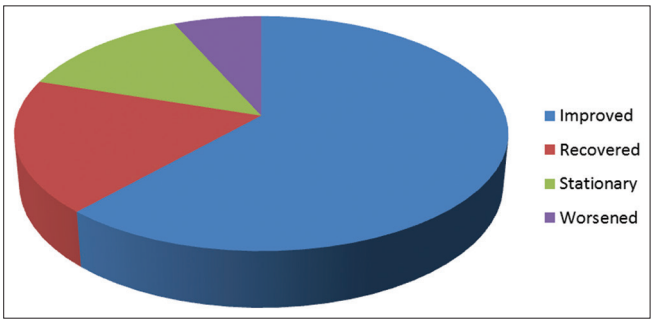


**Figure 6: Treatment outcome in study group (*n* = 60 patients)**

found in the studies by Jatoi *et al.* and Gopinathan *et al.*, thus suggesting that corneal ulcers are more prevalent in farmers and other outdoor workers.[18,19]

In our study, 36 (60%) patients presented during the harvesting months of September-October, March-April. Lin *et al.* too found in their study a higher incidence of fungal keratitis during the months corresponding to windy and harvesting seasons, during which time infection from vegetative corneal injury may be more likely.[20] In our study, we found that an antecedent history of ocular trauma was seen in 40 out of 60 patients of corneal ulcer. Trauma was also found to be the major predisposing cause in the studies by Assudani *et al.*, Sethi *et al.*, and Ranjini and Waddepally.[1,21,22] A history of injury by other wooden material was seen in as many as 15 (25%) patients in our study group. A similar high incidence of vegetative injury was seen in the study by Chhangte *et al.* done in Kumaon region of Uttarakhand, where 23.7% patients reported injury with vegetative matter.[23] 2 (3.3%) patients were found to be suffering from diabetes mellitus in our study group. A similar prevalence of diabetes in the study population was found in the study of Krishna *et al.*[24] Contact lens use has been found to be a major predisposing factor causing infective ulcerative keratitis in a large number of studies conducted among the Western population. However, in our study, there were no contact lens users among the corneal ulcer patients. This is due to the fact that the majority of patients in our study group belonged to rural areas. This finding is similar to the study by Basak *et al.* who also found the number of contact lens users to be negligible.[25]

In our study, 43 (71.67%) patients were found to be culture positive. In a study by Tewari *et al.*, microbiological etiology on culture examination could be determined in 60% patients presenting with corneal ulcer.[26] In another study by Gupta *et al.*, 87.5% cases showed growth on culture media.[16] Among the 43 culture-positive patients in our study, 29 (67.44%) patients were positive for fungi, while 14 (32.56%) patients gave a positive yield for bacteria. Nath *et al.* in their study conducted in Assam found that a fungal etiology could be established in 60.6% cases.[27] The preponderance of culture positive fungal corneal ulcers in our study can be attributed to hot climatic conditions conducive to the growth of fungi and agriculture being the main occupation of the large farming populace in our study group. On the other hand, a study conducted in Nepal by Suwal *et al.* found bacterial isolates (56%) outnumbering the fungal isolates (44%). Furthermore, in their study, *S. pneumoniae* (31.1%) was the commonest among the bacteria, while *Fusarium* (13.4%) was the mos common fungus isolated.[28] Thus, the microbiological etiology differs not only from region to region but also varies with the occupational exposure of the study population to different microbes.

Among the 29 patients testing positive for fungus in our study group, *Aspergillus* species was identified in 16 (37.21%) patients, while *Fusarium* species was detected in 13 (30.23%) patients. Amatya *et al.* in their study conducted in Nepal found that the commonest fungal pathogen was *Aspergillus* species (33% cases), followed by *Fusarium* species (12.66% cases). *S. aureus* (44.53% cases) was isolated as the most common bacterial agent.[29] These results are comparable to our study.

In our study, 6.66% patients worsened or progressed even with appropriate medical line of management. In a study by Prakash and Kemisetty., 10% patients worsened with treatment and 4% patients required emergency keratoplasty due to perforation.[30] 3.33% patients underwent therapeutic keratoplasty in our study due to non-responsiveness to treatment.

Corneal ulcer leads to permanent visual impairment in the vast majority of cases due to corneal scarring. In our study, we found that 50 (83.4%) patients had a visual acuity of <3/60 in the affected eye. Keshav *et al.* also found in their study that 65% patients had a visual acuity of <3/60.[31]

## CONCLUSION

Infective suppurative keratitis is a major cause leading to prolonged ocular morbidity and loss of vision. This is more so in developing countries like India, where the vast majority of people are socially and economically backward, dwelling in rural areas and pursuing agriculture and other manual work as their main source of livelihood. These individuals are at an increased occupational risk of ocular trauma. In addition, the problem is compounded by frequent late presentation of the patient due to lack of awareness, and inaccessibility to specialist ophthalmic care. It has been seen that the microbiological etiology of infective keratitis shows a wide regional variation. In our study, we found that that in our region fungal corneal ulcers predominate, as the majority of patients present with a history of antecedent vegetative trauma. The occurrence of corneal ulcers peaks during the harvesting season. Treating infective suppurative corneal ulcers as an ophthalmic emergency and quick administration of appropriate anti-microbial therapy is the need of the hour for saving the eye of the patient and preventing the catastrophe of life-long blindness.

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