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Research Article

Clinical and Microiological Profile of Infective Keratitis in a Tertiary Care Hospital in North India

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Abstract

Design: This was a observational, prospective, interventional study.

Setting: Department of Ophthalmology, Government Medical College, Patiala, Punjab.

Introduction: Infective Keratitis refers to the diseases affecting cornea caused by infective agents which leads to necrosis and suppuration resulting in corneal tissue ulcers. It is a potentially blinding condition that must be treated emergently to preserve vision. Fungal corneal ulcers are the most common, accounting for 30-40% of the cases followed by bacterial, viral and amoebic corneal ulcers.

Methods: It was a prospective, open labelled, interventional study including 75 patients of infective keratitis reporting to the Ophthalmology OPD at Rajindra Hospital, Patiala. Cases diagnosed with microbial keratitis were evaluated clinically using slit lamp biomicroscope and microbiologically using smears and cultures. The patients were treated accordingly and followed up to analyze the treatment response and outcomes in these patients.

Results: Out of 75 patients enrolled in the study, 31 were diagnosed to have fungal keratitis (41.3%), 22 had bacterial keratitis (29.3%) and 6 had mixed infection (8%). 9 patients were diagnosed with viral keratitis based on the clinical picture. *Aspergillus* was the most commonly isolated fungal species followed by *Fusarium* and *Staphylococcus* was the most common isolated bacteria. Fungal keratitis took the longest to heal and had maximum complications compared to other etiologies.

Conclusion: Being an agricultural state the incidence of fungal keratitis is much more in Punjab compared to other microbes. Treating a fungal corneal ulcer is very challenging inspite of the available diagnostic and treatment methods.

Keywords: Infective Keratitis; Microbiology; Bacteria; Fungi

Introduction

In developing countries corneal ulcers are the leading cause of corneal blindness and second leading cause of monocular blindness after unoperated cataract [1]. Keratitis can be caused by a variety of infections like bacteria, fungi, virus or parasitic (Acanthamoeba) [2]. Apart from infections, keratitis can be autoimmune, neurotrophic, toxic, following chemical burns, or even secondary to lid conditions (trichiasis, entropion, blepharitis or lagophthalmos) [3]. Fungal keratitis contributes to nearly 50% of all culture positive cases in India [4]. Irrespective of the causative organism the patient with corneal ulcer may present to the hospital with pain, discharge, watering, redness, foreign body sensation, or blurred vision. Etiological diagnosis is a must to initiate the definitive treatment of the ulcer which is a combination of clinical features and microbiological investigations. Laboratory investigations are carried out to confirm the clinical diagnosis. The gold standard investigations for diagnosis remain the microscopic examination and culture. Another newer technique is molecular diagnosis which has higher sensitivity and specificity.

This study was conducted with the objective to study epidemiology, microbiological profile and treatment outcomes in patients with infective keratitis.

Material and Methods

It was a prospective, open labelled and interventional study including 75 patients diagnosed with infective keratitis from July 2020 to December 2022 in the Out-Patient Department of Ophthalmology, Rajindra Hospital, Patiala, a tertiary care hospital in Punjab, India. Detailed history including the socio-demographic history, history of any trauma or other predisposing factor, occupational history, treatment history, presentation interval was recorded.

Examination included recording visual acuity, intra-ocular pressure, size of ulcer, location, presence of hypopyon, corneal sensation, examination of eyelids, conjunctiva, corneal epithelial defects, infiltrate size, shape, margins and fluorescein staining.

Microbiological investigations were done on the first visit in all patients except those having the clinical picture of viral keratitis.

Image 1: Examination of corneal ulcer showing fluorescein stained epithelial defect and hypopyon.

The scrapings were taken under local anesthesia using topical 0.5% proparacaine eye drops using a sterile #15 Bard-Parker blade or crescent blade or a cotton swab. These scrapings were then sent for assessment in the Department of Microbiology, Government Medical College, Patiala where 2 slides were made- one each for Gram stain and KOH mount. Rest of the sample was used for culture on blood agar, MacConkey's agar and SDA medium. LCB staining was also done in SDA culture positive patients.

Interpretation of results

- Gram's staining
  - Gram-Positive: Purple
  - Gram-Negative: Pink
- KOH mount
  - *Aspergillus*: On KOH mount there were non-pigmented septate hyphae with characteristic acute angled dichotomous branching.
  - *Fusarium*: Direct microscopy showed septate mycelia with conidiospores.
- Identification of bacterial isolates on culture
  - *Staphylococcus aureus*: round, convex colonies surrounded by zones of clear beta-hemolysis.
  - *Streptococcus pneumoniae*: small, grey mucoidal colonies with a zone of alpha-hemolysis

- Pseudomonas species: blue green colonies due to pigment production (pyocyanin)

- Identification of fungal isolates on culture.
  - *Aspergillus flavus*: There were velvety, yellow to green colonies with golden or red brown at reverse.
  - *Aspergillus fumigatus*: There were velvety, white colonies which colorless at reverse.
  - *Fusarium*: There were orange colored colonies which were wooly in the beginning.
- Characteristics of fungi on LCB stain
  - *Aspergillus flavus*: thick walled, unpigmented conidiophores
  - *Aspergillus fumigatus*: short, smooth, flask shaped conidiophores
  - *Fusarium*: septate mycelium, single or branching conidiospores.

Image 2: Gram's staining showing gram positive cocci.

In all of the cases the treatment was initiated on the first visit based upon the predisposing factor and clinical features while waiting for the results of the microbiology.

The topical cycloplegics and antimicrobial agents were the mainstay of the treatment. Fortified antibiotics were prepared by adding required amount of drug to an artificial tear solution.

Image 3: SDA culture tube showing growth of *aspergillus flavus*.

Image 4: KOH mount showing septate fungal hyphae.

Image 5: LCB stain showing aspergillus fumigatus.

Tobramycin was the commonly used fortified antibiotic. Voriconazole eye drops were used in fungal keratitis.

Povidone iodine eye drops were also used in many cases for the purpose of sterilization of the corneal surface and the fornices. In addition to topical drugs, systemic antifungals were given in cases either with large infiltrate size or patients with delayed presentation. The cases, in which definitive microbiological diagnosis was not obtained, were treated as mixed infection and were given the cover of intensive antimicrobial therapy.

The patients were followed up and examined every alternate day during first week, then weekly till 6 weeks and fortnightly later if required. The observations were tabulated and subjected to statistical analysis using appropriate statistical tests.

Observations and Results

Epidemiology

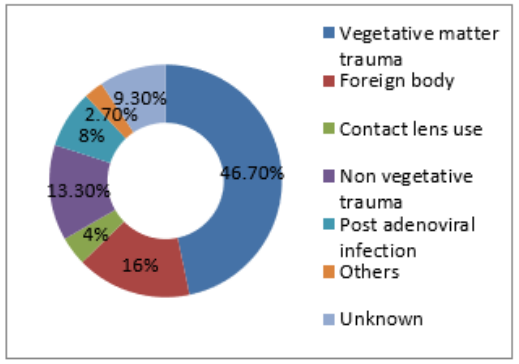
Most common age group in our study was 61-70 years (22.7%), the mean age of all patients was 46.2 years ranging between 13 to 80 years. A male predominance was found in our study with 74.7% males and 25.3% females. 64 percent of the patients in our study belonged to rural background and the major predisposing factor among them was trauma by vegetative matter. Contact lens related infection was reported only among the urban population. 30.7% of the patients in our study presented in the months of August and September combined. 21.3% of the patients reported during the months of October and November combined.

Occupation	Number of patients	Percentage
Farmer	25	33.3%
Laborer	15	20%
Housewife	9	12%
Gardener	3	4%
Student	8	10.7%
Others	15	20%

Table 1: Distribution of 75 patients based on occupation.

Predisposing factor

33.3 percent of the patients in our study were farmers. 20 percent of the cases in our study were labourers. 46.7 percent of the cases in our study were predisposed to trauma by vegetative matter. 16 percent of the patients gave history of foreign body impaction in the eye. 13.3 percent of the patients were predisposed to non vegetative trauma.



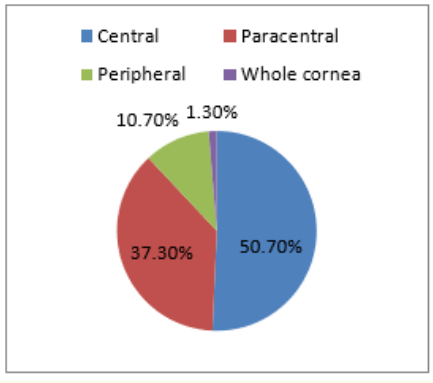
Graph 1: Distribution of 75 patients based on predisposing factor.

Presentation

Only 20 percent of the cases presented within the first week of the onset of symptoms. 56 percent presented later than 15 days of the onset of symptoms. Redness, watering, blurred vision, foreign body sensation and photophobia were the common symptoms at presentation. Pain and discharge were relatively less common presentations. 25.3 percent of the cases had presented with hypopyon in addition to the ulcer. 10.7 percent of the patients had reduced corneal sensation. 50.7 percent of the ulcers were located centrally and 37.3 percent of the ulcers were paracentral in location. One patient had ulcer involving whole of the cornea. 41 patients (54.7%) had baseline visual acuity less than 6\60 and 34 patients (45.3%) had VA better than or equal to 6\60 at presentation.

Presentation interval	Number of patients	Percentage
<7 days	15	20%
7-15 days	18	24%
>15 days	42	56%

Table 2: Distribution of 75 patients based on presentation interval.



Graph 2: Distribution of 75 patients based on location of ulcer.

Microbiological profile

Microbiological investigations form the mainstay in the diagnosis of corneal ulcers. Direct microscopy, staining and culture were the various techniques deployed for the diagnosis. It was observed that KOH mount was positive in 37 cases (49.3%) out of 75 cases and all 37 of them (49.3%) showed growth of various fungi on the SDA medium. Aspergillus was the most common species identified in 23 out of 37 (62.2%) culture positive cases followed by *Fusarium* in 14 cases (37.8%).

21 (28%) out of 75 cases had positive Gram's staining out of which 17 were detected as Gram positive (81%) and remaining 4 were Gram negative (19%). 28 out of 75 (37.3%) cases showed growth on culture plates. Based on their colony characteristics and microscopic examination 13 out of 28 (46.42%) were identified as *Staphylococcus aureus*.

Fungal species isolated from culture	Number of patients	Percentage among 37 cases
Aspergillus flavus	12	32.4%
Aspergillus fumigatus	11	29.72%
Fusarium	14	37.8%
Total	37	

Table 3: Isolated fungi in 37 SDA culture positive cases.

Bacterial species isolated from culture	Number of patients	Percentage among 28 cases
Staphylococcus aureus	13	46.4%
Streptococcus pneumoniae	9	32.14%
Pseudomonas species	6	21.4%
Total	28	

Table 4: Isolated bacteriae in 28 culture positive cases.

Diagnosis

31 patients out of 75 (41.3%) were diagnosed to have fungal keratitis followed by 22 with bacterial keratitis (29.3%) and 6 patients were diagnosed to have mixed infection (8%). In 7 patients no diagnosis could be made as no microbiological evidence was found in these cases. 9 patients out of 75 (12%) were diagnosed as viral keratitis based on the clinical presentation.

Graph 3: Etiological diagnosis in 75 patients based on clinical picture and microbiology.

Complications

24 out of 75 patients in our study developed complications that included corneal perforation (9.3%), anterior staphyloma (8%), non healing ulcer (5.33%), descematocele (4%), post herpetic neuralgia (1.3%) and neurotrophic ulcer (1.3%). Corneal perforation was preceded by corneal melting in 3 out of 8 cases with corneal perforation. Majority of the complications in our study were seen in fungal keratitis- 12 out of 24 (50%) followed by bacterial keratitis- 8 out of 24 (33.3%).

Treatment and its outcomes

In addition to conventional therapy, 24 patients were given fortified antimicrobial drugs, 42 patients were given povidone iodine (5%) eyedrops. Among those developing complications, keratoplasty was done in patients developing corneal perforation and tarsorrhaphy was performed in a patient who had facial nerve palsy.

The mean time for epithelial defect to heal was highest in cases of fungal keratitis- 30.75 days. The least time for epithelial defect to heal was observed in bacterial keratitis- 24.70 days.

With infiltrate size >4 mm only 4 out of 14 patients (28.57%) had final VA better than 6\60 and other 10 (13.3%) had VA equal to or less than 6\60. 8 out of these 14 patients (57.14%) developed complications.

Clinical characteristic	Finding	Percentage
Baseline visual acuity	<6/60	41 (54.7%)
	≥6/60	34 (45.3%)
Final visual acuity	<6/60	28 (37.3%)
	≥6/60	47 (62.7%)
Improvement of 3 lines or more on Snellen's chart	Yes	31 (41.3%)
	No	44 (58.7%)

Table 5: Visual outcomes in 75 patients with infective keratitis.

With infiltrate size <4mm, 35 out of 61 patients had final VA better than 6\60 and 26 patients had final VA equal to or less than 6\60. 16 out of these 61 patients developed complications.

Discussion

38.7 percent of the patients in our study belonged to the age group of 51-70 years. Mean age of the patients enrolled was 46.20 years. Khor WB., *et al*. [5] and Zhang W., *et al*. [6] reported similar findings in their studies.

A male predominance was found in our study with 74.7% males and 25.3% females. Similar to our study Wang JJ., *et al*. [7], Kaliamurthy J., *et al*. [8] and Rautarya B., *et al*. [9] also reported a male predominance in cases of infective keratitis.

64 percent of the patients in our study belonged to rural background and the major predisposing factor among them was trauma by vegetative matter. 33.3% of the patients in our study were farmers The results of our study are also in concordance with study by Bajracharya L., *et al*. [10] in which they reported nearly 64% of the patients belonged to agricultural sector and trauma was the most common predisposing factor in 38.3% patients.

30.7 percent of the patients in our study presented in the months of August and September combined. 21.3 percent of the patients reported during the months of October and November combined. Satpathy G., *et al*. [11] also reported results that were similar to our study as they reported maximum cases in these months.

It was observed that 38 ulcers (50.7%) were located centrally, 29 ulcers (38.7%) were located paracentrally and only 8 ulcers (10.7%) were peripheral. 80 percent of the patients in our study presented later than 7 days after onset of symptoms. The observations were found to be similar to a study conducted by Lim Wen Siang J., *et al*. [12] in which 53.3% of the ulcers were centrally located, 34.7% ulcers paracentral and 12% ulcers were peripheral and 60% patients had presented late.

Among the fungi isolated from the cultures, *Aspergillus* was the most common species identified in 23 out of 37 (62.2%) culture positive cases followed by *Fusarium* in 14 cases (37.8%). *Aspergillus flavus* was the most common identified subspecies in 12 out of 23 (52.17%) tubes followed by *Aspergillus fumigatus* (47.83%). 13 out of 28 (46.42%) were identified as *Staphylococcus aureus*, 9 out of 28 (32.14%) were identified as *Streptococcus pneumoniae* and remaining 6 (21.42%) were Pseudomonas species. Tawde Y., *et al*. [13] and Saha S., *et al*. [14] also reported *Aspergillus* and *Fusarium* to be the most commonly isolated fungal species. Similar results were reported by Basak SK., *et al*. [15] and Wuletaw T., *et al*. [16] as in their studies *Aspergillus* was the most common isolated fungus and among bacterial isolates *Staphylococcus* and *Streptococcus* were the most common identified bacteria.

31 patients out of 75 (41.3%) were diagnosed to have fungal keratitis followed by 22 with bacterial keratitis (29.3%) and 6 patients were diagnosed to have mixed infection (8%). 9 patients out of 75 (12%) were diagnosed based on the clinical presentation with viral keratitis.

Chopra A., *et al*. [17] reported similar results in their study in which they reported fungal keratitis to be most common in 33% patients followed by bacterial keratitis in 16% patients and mixed infection in only 5% patients. Similarly Mohod PN., *et al*. [18] also reported in their study that fungal keratitis was most common (59.09%) followed by bacterial keratitis (19.31%), viral keratitis (17.04%) and mixed infection (4.54%). Our results are also in concordance with the study conducted by Basak SK., *et al*. [16] in which they found that 42.5% of their cases had fungal growth followed by 15.3% having bacterial growth and 9.5% patients had mixed fungal and bacterial growth.

It was observed that the mean time for epithelial defect to heal was highest in cases of fungal keratitis- 30.75 days. The least time for epithelial defect to heal was observed in bacterial keratitis- 24.70 days. Our results are in concordance with the study conducted by Moe CA., *et al*. [19] in which they reported that the median time for re-epithelialization of fungal ulcers was 30 days compared to 25 days for bacterial keratitis.

41 patients (54.7%) had baseline visual acuity less than 6\60 and 34 patients (45.3%) had VA better than or equal to 6\60 at presentation. This observation in our study was in concordance with the study done by Lim Wen Siang J., *et al*. [12] who found that the visual acuity at presentation was worse than 6\60 in 49.33% patients and better than or equal to 6\60 in 50.67% patients.

The final visual acuity recording of the patients showed that 28 out of 75 patients (37.3%) had visual acuity worse than 6\60 while the remaining 47 out of 75 (62.3%) had visual acuity better than or equal to 6\60. Out of these 21 patients (28%) had visual acuity better than or equal to 6\18. All the patients who developed rigorous complications had visual acuity worse than 6\60. The results were again similar to the study by Lim Wen Siang J., *et al*. [12] where they reported that final visual acuity was better than 6\60 in 58.7% of the patients and it worse than or equal to 6\60 in the remaining 41.3% patients.

With infiltrate size >4 mm only 4 out of 14 patients (28.57%) had final VA better than 6\60 and other 10 (13.3%) had VA equal to or less than 6\60. 8 out of 14 patients (57.14%) developed complications. Similar to our study Lim Wen Siang J., *et al*. [12] reported in their study that the final VA achieved was better in smaller infiltrate size. VA was equal to or less than 6\60 in 8 out of 42 patients (19.04%) with infiltrate size <4 mm. In patients with infiltrate size >4 mm 10 out of 33 patients (30%) achieved final VA better than 6\60.

Conclusion

The diagnosis and treatment of the corneal ulcers still remains a difficult task in the developing countries. Owing to illiteracy, ignorance and limited resources, delayed presentation was common among the patients. The diagnostic modalities available need to be upgraded as their availability is limited and also they cannot be relied upon in a major proportion of patients. Apart from being most common, fungal corneal ulcers were also the most difficult to treat. The time for epithelial defect to heal was longest in fungal keratitis. The rate of complications was also highest in fungal keratitis. Visual outcomes depended on a number of factors including etiological agent, infiltrate size, location of ulcer and presence of signs of corneal thinning. Complications in a large share of patients with infective keratitis can be saved with timely diagnosis and proper and timely management. Attempts should be made to lower the rate of complications in patients as even after managing the complications the visual outcomes remain poor. People should be educated about the consequences of the ocular trauma, use of over the counter (OTC) medicines and delaying the visit to eye specialist.

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