

PATTERNS OF PRESENTATION OF FUNGAL KERATITIS IN TERTIARY CARE HOSPITAL*Uday Sridhar Mulgund¹, Ravi Shankar M², Satish Kumar C.S³*¹Associate Professor, Department of Ophthalmology, Karnataka Institute of Medical Sciences, Hubli.²Postgraduate Resident, Department of Ophthalmology, Karnataka Institute of Medical Sciences, Hubli.³Postgraduate Resident, Department of Ophthalmology, Karnataka Institute of Medical Sciences, Hubli.**ABSTRACT****BACKGROUND**

Fungal keratitis is one of the major cause of visual loss in developing countries. A contributing factor for the development of fungal infection is ocular trauma and contamination of corneal lesions by soil and vegetative material. Another factor being widespread use of broad-spectrum antibiotics, steroids and contact lens wear. According to the World Health Organization report, it is estimated that ocular trauma and corneal ulceration result in 1.5 to 2 million new patients of corneal blindness annually. In India, the incidence of corneal ulceration is reported to be 1130 per million population. Corneal infection of fungal aetiology is common in India (19-45%). Corneal infection of fungal aetiology is very common and may represent 30 to 40% of all cases of culture-positive infectious keratitis in South India.⁴ more than 70 species of filamentous fungi have been identified as the aetiological agents of fungal keratitis. Of these, *Aspergillus* and *Fusarium* are responsible for 70% of cases.

The aim of the study is to study the-

1. Clinical presentation, contributing and precipitating factors for fungal keratitis and prognosis with regard to the available mode of therapy.
2. Investigations regarding the type of fungus and the statistical significance regarding the common type of fungi that involve the cornea.

MATERIALS AND METHODS

All cases of keratitis that presented were investigated with KOH wet mount and fungal culture. Histopathological diagnosis was made with the report of fungal culture. All cases of fungal keratitis were treated with antifungal and clinically studied in the Department of Ophthalmology, KIMS, Hubli, from 1st January, 2016 - December 2016.

RESULTS

In the clinical study of fungal keratitis, out of 62 cases, suppurative keratitis 30(48.38%) cases were fungal keratitis on clinical suspicion and fungal staining.

CONCLUSION

India being an agricultural country, the incidence of fungal keratitis is significantly high. Fungal keratitis has tendency to progress slowly with minimal symptoms, hence the patients are provoked to apply local native medicines and approach the doctor very late. Lack of laboratory identification especially in peripheral hospital adds to the problem. With timely specific treatment, one can combat the disease efficiently and thus prevent the eye going in for blindness.

KEYWORDS

Fungal Keratitis, Keratomycosis, KOH, Antifungal Drugs.

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BACKGROUND

The incidence of suppurative corneal ulcers caused by fungi has increased in the recent years due to injudicious use of antibiotics and steroids. Fungal keratitis frequently seen in tropical countries, where the incidence ranges between 14%-40% of all ocular mycoses or of all cases of microbial

keratitis.¹ The incidence in India is 44% to 47%.² Fungal corneal ulcer is common in India due to the tropical climate and a large agrarian population that is at risk.³ It is more common in rural areas and in immune compromised individuals. Fungal keratitis with a worldwide reported incidence varying from 17% to 36% in various studies.² Fungal keratitis are typically seen after injury with vegetable matter such as thorn or woodenstick and are characterised by a relatively indolent course. Fungal keratitis can be caused by as many as 60 species of fungi.⁴ The time interval from trauma to clinical features varies depending on the organism, the size of inoculum and host resistance.

For laboratory diagnosis of fungal keratitis, demonstration of fungal pathogens on direct microscopy (KOH) and their isolation by culture is essential. Fungal

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keratitis should be suspected in every patient with a corneal lesion and should be ruled out promptly to save sight and before commencing steroids and antibiotics. Use of empiric antifungal therapy is discouraged and a confirmatory diagnosis is recommended before institution of therapy.⁵ Such a corneal infection poses a challenge to the ophthalmologist because of its tendency to mimic other types of stromal inflammation.⁶

Aim of the present study is to determine the aetiological agents, predisposing factors and important diagnostic tests in fungal keratitis.

MATERIALS AND METHODS

The clinical study of fungal keratitis was conducted at the Department of Ophthalmology, KIMS, Hubli, from 1st January, 2016 - December 2016.

Inclusion Criteria

All cases with clinical features suggestive of fungal keratitis such as long duration, elevated, plaque like serrated/feathery margins of the ulcer, raised slough, dry surface (texture), satellite lesions, Weiss ring, endothelial plaque, coloration of the ulcer other than yellow (suggestive of diatomaceous fungi) and thick hypopyon were noted and categorised as patients with fungal keratitis.

Exclusion Criteria

Non-suppurative keratitis including viral keratitis, neurotrophic ulcers, degenerative causes were excluded as were Mooren's ulcer, interstitial keratitis, sterile neurotrophic ulcers and any ulcer associated with systemic autoimmune conditions.

After selection of patients, standardised proforma was filled for each patient documenting, age, sex, domicile, education, economic status, occupation and predisposing factors including history of trauma, diabetes mellitus and operation (if any). Detailed clinical history was taken and any previous usage of medications recorded.

Clinical Procedure

Visual acuity was recorded in standard manner. All patients were subjected to a detailed slit-lamp biomicroscopic examination. Size of ulcer was roughly recorded with fluorescent stain and Rose Bengal stain under local anaesthesia.

Depth of the lesion, stromal infiltrate, ulcer margin, thinning, floor, satellite lesions, vascularity, pigmentation, any impacted foreign body and hypopyon were noted. Associated ocular conditions like blepharitis, conjunctivitis, dacryocystitis, spheroidal degenerations, bullous keratopathy, dry eyes, preexisting viral keratitis, lid abnormalities, Bell's palsy, lagophthalmos, trichiasis, suture infiltrates and adherent leucoma were noted. Usage of contact lenses, topical corticosteroids or any other topical or systemic medications were noted. Material was collected from conjunctiva, sac area and corneal ulcer scrapings. Materials used by patients (eye drop bottles, lens solutions)

and corneal button after therapeutic keratoplasty were collected. The collected material was submitted for Gram staining, Giemsa staining and KOH wet mount preparation. Fungal elements are observed under microscope. Rest of the material was sent for culture. Commonly used media were blood agar plate (bacteria 35-37 degrees and fungi room temperature), chocolate agar plate (aerobes and facultative anaerobes, 35 degrees), SDA without cycloheximide, SDA with cycloheximide (fungus), thioglycollate broth (anaerobes 35-37 degrees). Remaining scrapings were utilised for histopathology.

By convention to indicate the site of inoculums on a solid medium, harvested material is inoculated in the form of a 'C' streak on each medium from separate scrapings. Almost, all fungal isolates grow and become evident in 48-72 hrs. Cultures were examined daily up to one week before declaring a culture negative for fungi.

Anyone of the following criteria if fulfilled suggest a significant growth-

1. If smear results are consistent with culture.
2. The organism is grown on more than one media.
3. Growth of the same fungus in decreasing gradation at multiple sizes of inoculation on the solid medium.

Interpretation of Fungal Results

Smears- 10% KOH wet mount is useful in detecting for hyphal elements, budding cells and fungal morphologies.

Gram stain is useful in identifying bacteria and fungi. Fungal hyphae stain variable as their cell walls do not stain well and often be seen as negative outlines.

Culture- Smear examination gives preliminary evidence, culture isolation gives diagnostic information. Culture report ideally should include the growth appeared and its diagnostic significance. More than 10 colonies on only 1 solid medium or growth in only 1 liquid medium is usually equivocal. All isolates were considered in the light of clinical relevance and lab significance.

Lab criteria for definite infection include growth on 2 or more media, growth on at least one medium of the same organism identified in smears, confluent growth at the inoculation site in at least one solid medium or repeat isolation from same patient. These criteria are more applicable to bacteria and fungi.

Treatment- The standard treatment protocol was followed based on KOH staining categorising causative fungal element as filamentous and non-filamentous. Epithelium was debrided every 24-48 hrs. to increase drug penetration and to reduce fungal load along with debris. One drop of natamycin suspension 5% was used every hour during daytime and every 2 hours at night time used for filamentous fungi. Dosing was tapered according to the clinical response. It was also used in mycotic keratitis with yeast infection after regular follow up nystatin ointment was supplemented in nonresponsive cases. Oral fluconazole 150mg OD added when ulcer was more than

6mm in diameter deeper than the anterior one half of the stroma or if anterior chamber exudates were present.

Antifungal treatment was supplemented with broad-spectrum antibiotics, cycloplegic, anti-inflammatory agents, vitamin C and lubricating eye drops. For mycotic keratitis with secondary glaucoma, antiglaucoma medications were prescribed. For corneal ulcer with small perforation, bandage contact lens, cyanoacrylate glue and conjunctival hooding was done. For larger perforations, therapeutic keratoplasty was done.

Follow Up- Patients are followed weekly for one month. Then, every 15 days up to 6 months. Thorough examination was done at each visit. Treatment was decided upon further based on clinical response.

Main outcome measures- Symptomatic improvement, comfort of patient, remission of signs, reduction in size of ulcer and improvement in visual acuity.

OBSERVATIONS AND RESULTS

The clinical study of fungal keratitis conducted in the Department of Ophthalmology at KIMS, Hubli, from 1st January 2016 -December 2016.

During this period, the following observation were made.

Total Number of Patients with Suppurative Keratitis	Clinically-Suspected Fungal Keratitis	Percentage
62	30	48.38%

Table 1. Incidence of Keratomycosis

Thus, the total number of cases included in the present study was 30 (48.38%) patients, male 19 patients and female 11 patients.

Age Group	Patients	Percentage
Below 12 yrs.	1	3.33%
13-20 yrs.	2	6.66%
21-40yrs.	6	20%
41-60yrs.	18	60%
Above 60yrs.	3	10%

Table 2. Age Distribution

Occupation	Patients	Percentage
Agriculturists	18	60%
Labourers	4	13.33%
Gardeners	3	10%
Housewife	2	6.66%
Student	2	6.66%
Businessmen	1	3.33%

Table 3. Incidence Based on Occupation

Modes	Fungal Corneal Ulcer	
	Number	Percentage
Vegetative matter	15	50%
Stones	4	13.33%
Finger nail	9	30%
Nil	2	6.77%
Total	30	100%

Table 4. Modes of Trauma

Associated Factors	Fungal Corneal Ulcer	
	Number	Percentage
Diabetes mellitus	3	10%
Chronic dacryocystitis	1	3.33%
Alcoholism	6	20%
Malnutrition	18	60%
Immunocompromised state	2	6.67%

Table 5. Associated Factors

Site	Number of Cases	Percentage
Central	21	70%
Peripheral	1	3.33%
Diffuse	8	26.67%
Total	30	100%

Table 6. Site of the Ulcer

Size of Ulcer	Number of Cases	Percentage
<2 mm	2	6.67%
2 to 5 mm	10	33.33%
>5 mm	18	60%
Total	30	100%

Table 7. Size of Ulcer

	Number of Cases	Percentage
Superficial stromal	12	40%
Deep stromal	18	60%
Total	30	100%

Table 8. Depth of Ulcer

Vision at Presentation	No. of Cases	%
6/18-6/60	4	13.33%
CF 1-5 mts.	10	33.33%
HM+ve	8	26.27%
PL+ve	7	23.33%
PL-ve	1	3.33%
Total	30	100%

Table 9. Vision at Presentation

KOH Results	Fungal Culture Results	
	Culture Positive	Culture Negative
+ve	12(92.30%)a	17(34.70%)
-ve	1(7.7%) b	32(65.30%)
Total	30	100%

Table 10. Sensitivity of KOH Wet Mount

Organisms	Fungal Corneal Ulcer	
	Number of Cases	Percentage
Fusarium	8	61.53%
Aspergillus	4	30.77%
Candida	1	7.70%
Total	13	100%

Table 11. Different Species Identified in Culture Positives

Associated Bacteria	Fungal Corneal Ulcer	
	Number	Percentage
Staphylococci aureus	4	36.36%
Streptococci	5	45.45%
Enterobacter	1	3.33%
Pseudomonas	1	3.33%
Total	11	100%

Table 12. Associated Bacterial Infections

	Number of Cases	Percentage
Antifungal topical	30	100%
Antifungal oral	16	53.33%

Table 13. Medical Treatment

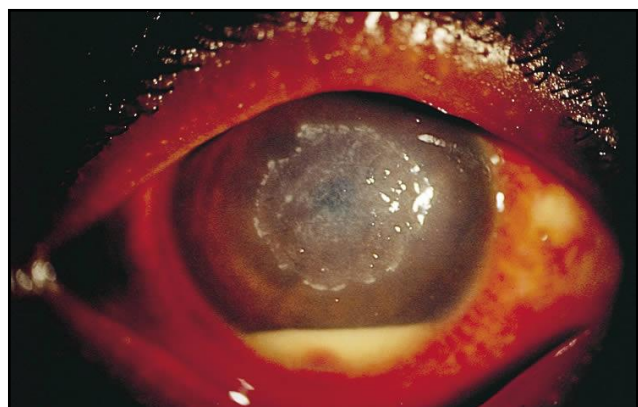
	Number of Cases	Percentage
Perforation	1	3.33%
Secondary glaucoma	4	13.33%
Endophthalmitis	1	3.33%

Table 14. Fungal Corneal Ulcer with Complications

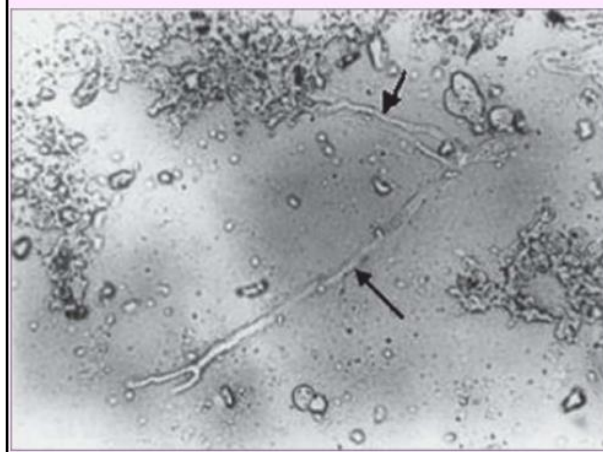
Visual Acuity	Number	Percentage
6/24-6/36	4	13.33%
6/36-6/60	14	46.67%
CF 1-5 mts.	8	26.67%
HM +ve	2	6.67%
PL +ve	1	3.33%
PL -ve	1	3.33%

Table 15. Visual Outcome at Last Follow Up

In the present study of fungal keratitis, out of 30cases 4 (13.33%) cases had fairly good vision, i.e. 6/24-6/36, 14(46.67%) had 6/36 to 6/60, 8(26.67%) patients had CF 1-5mts.and 2(6.67%) cases had only HM positive. One case (3.33%) was left with only perception of light and 1(3.33%) cases were with no perception of light.

**Figure 1. Fungal Keratitis with Hypopyon****Figure 2. Central Fungal Keratitis with Hypopyon**

KOH preparation

**Figure 3. KOH Wet Mount Showing Fungal Hyphae**

DISCUSSION

In the clinical study of fungal keratitis, out of 62 cases, suppurative keratitis 30(48.38%) cases were fungal keratitis on clinical suspicion and fungal staining. Earlier studies by Leck AK⁷ and others in Ghana and South India reported incidence of fungal keratitis 42% in South India. The higher incidence of males is probably due to the fact that males were mostly involved in outdoor activities, which predispose them to trauma with vegetative matter and other types of traumas with causative agent contaminated with fungus. Male preponderance was noted in study done by Dr. S.L.Sharma.⁸ 57.9% in males and 42.1% in females. We had 36.66% of female patients with keratomycosis in this area women are also equally engaged in field works. Among 30 cases of fungal keratitis, 18(60%) cases were in the age group of 41-60yrs., 6(20%) cases were in the age group of 21-40 yrs., 3(10%) were above 60years. 1 (3.33%) were below 12 years and 2(6.67%) in the age group of 13-20years. Maximum incidence was noted in the age group 21-60 yrs. This age group is usually engaged in outdoor work and more predisposed to trauma. In our study, we had 23 (76.67%) patients from rural background and 7(23.33%) from urban background. The higher incidence of mycotic keratitis in rural area maybe due to their exposure to outdoor agricultural work, lack of education, illiteracy and poverty may play a role in higher incidence of fungal keratitis. In the study by Dr. Sandu and others, the maximum incidence is seen among labourers (41.38%) and farmers (34%).Our findings also confirms with the results of earlier workers. In the present study, incidence of fungal keratitis in farmers and labourers found higher, which almost correlates with studies by LC Dutta⁹ and Dr. Sandu. In the present study of fungal keratitis, prior injury with vegetative material accounted for 15 cases (50%). Other modes of injury were trauma with nail in 9cases (30%) with stone in 4 cases (13.33%).

In the study of fungal keratitis, 18 cases had malnutrition, 6 cases had alcoholism, 3 cases had diabetes

mellitus, 2 cases had immune compromised status and 1 case of chronic dacryocystitis.

Reports in earlier studies, done by Gopinathan,¹⁰ Agarwal PK and Mohanthy PK have shown similar associated factors with fungal keratitis.

Signs of Fungal Keratitis

The incidence of central fungal keratitis was accounted to 70%. Peripheral fungal keratitis accounted to 26.67%. Diffuse fungal keratitis was seen in 3.33% of cases. Diffuse corneal ulcers had poor prognosis. One case had gone for perforation.

In the present study of fungal keratitis, size of the fungal keratitis varied from 1mm to the total corneal involvement. In 6.67% of cases, the corneal ulcer was smaller than 2mm; in 33.33% of cases, the extent of ulcer varied from 2 to 5mm; in remaining 60% of cases, the corneal involvement was more than 5mm, it varied from more than 5mm to total corneal involvement. The prognosis of ulcers, which have size of more than 5mm was not good due to corneal scarring. In the present study of fungal keratitis, 12 (40%) of cases had superficial stromal involvement and 18 (60%) of cases had deep stromal involvement. 55.33% of cases had hypopyon in the present study. 83.33% of cases had feathery margins, 60% of cases had dry surface, 40% cases had elevated surface, 73.33% cases had satellite lesions. Whitish round lesion with surrounding infiltration was seen in 3.33% cases. In the study of fungal keratitis, 4 (13.33%) cases had visual acuity of 6/18 to 6/60, 10 (33.33%) cases had vision of counting fingers 1-5mts. and 8 (26.67%) with perception of hand movements. 7 (23.33%) patients had perception of light and one (3.33%) with no perception. Sensitivity of KOH wet mount preparation in our study is 92.30%. In the study by Jayahar BM and others, Tamil Nadu, KOH sensitivity 97.23%. In studies by Gopinathan U.¹⁰ and Panda A.,¹¹ sensitivity of KOH is 91% and 90.20%, respectively.

Sensitivity of KOH wet mount preparation in our study is almost similar to other studies. So, KOH wet mount preparation is liable criterion for the diagnosis of fungal keratitis.

Mode of Therapy- In the present study of fungal keratitis, all 30 patients treated medical treatment, i.e. natamycin 5% sups. hourly with cycloplegics and broad-spectrum antibiotics for 4-6 weeks or till there is complete resolution of clinical picture, vitamin C and lubricating eye drops were also supplemented. 18 (60%) cases of deep stromal fungal corneal ulcer with or without hypopyon were treated with natamycin 5% suspension hourly along with systemic Tab. Fluconazole 200-600mg/day q.i.d. for 2-3 weeks. Timolol eye drops BD and/or Tab. Diamox 250 mg BD was prescribed along with antifungals in patients with secondary glaucoma.

In the present study, treatment of one case out of 30 cases was modified based on culture results and nonresponsiveness to topical natamycin and oral

fluconazole. Nystatin eye ointment was used 5 times daily along with cycloplegics and broad-spectrum antibiotic eye drops.

In the present study of fungal keratitis for all 30 cases, treatment started with debridement of ulcer. 2 (6.66%) cases were prescribed bandage contact lens. Therapeutic keratoplasty was done in 1 (3.33%) case and 1 (3.33%) evisceration was done for a patient presented late with fungal keratitis with panophthalmitis without perception of light.

Overall, 70.68% were treated with medical line of treatment and 29.32% with surgical line of treatment.

Response to the Treatment

Corneal ulcer with perforation was seen in 1 (3.33%) patients. 4 (13.33%) patients developed secondary glaucoma. Panophthalmitis was seen in one (3.33%) patient.

In the present study of fungal keratitis, 4 (13.33%) cases had fairly good vision, i.e. 6/24-6/36, 14 (46.67%) cases had 6/36 to 6/60, 8 (26.67%) patients had CF 1-5mts. and 2 (6.67%) cases had only HM positive. Visual prognosis at the end of follow up was poor as corneal scarring was the predominant outcome in most of the cases. One case (3.33%) was left with only perception of light. It was a case with deep stromal fungal corneal ulcer with perforation presented after one month of history of trauma treated with conjunctival hooding along with medical line of treatment, but did not respond and 1 (3.33%) cases with no perception, in that one had undergone therapeutic keratoplasty, which was failed. Another case presented with panophthalmitis, which evisceration was done to avoid dissemination of infection.

CONCLUSION

India being an agricultural country, the incidence of fungal keratitis is significantly high. Fungal keratitis has tendency to progress slowly with minimal symptoms, hence the patients are provoked to apply local native medicines and approach the doctor very late. Lack of laboratory identification especially in peripheral hospital adds to the problem.

This study signifies the importance of keeping in mind fungus as one of the inflicting agent in causation of corneal ulcer, especially when predisposing factors like corneal trauma with organic matter, chronic dacryocystitis, diabetes mellitus, etc. are present and also by looking at the clinical features and taking help of rapid diagnostic tests like Gram stain, KOH stain, one can predict the diagnosis and treat early. With timely specific treatment, one can combat the disease efficiently and thus prevent the complications and prevent eye going in for blindness.

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