

A clinic-microbiological study of mycotic corneal ulcers cases

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Abstract

Background: Fungal keratitis is a major ophthalmic problem. It is common in India due to the tropical climate and a large agrarian population that is at risk. **Materials & Methods:** The cases for the present study were selected from the patients attended in the Ophthalmology OPD and/or admitted in Ophthalmology IPD of a tertiary care teaching hospital, Durgapur (West Bengal) during the period from January 2018 to March 2019. Out of all corneal ulcer cases admitted during this period 100 cases clinically suspected to be due to fungal infection were selected for study. Conjunctival swab cultures were carried out from eyes of 10 clinically normal cases to study the fungal flora of conjunctival sac. **Results:** The fungal aetiology in the causation of corneal ulcer varies in relation to age, sex and occupation of the population and climatic condition of the region. The prevalence of mycotic corneal ulcer is more among male agriculture workers in the age group of 30-50 years. Keratomycosis occurs more frequently during the harvesting season of the year. Minor trauma to cornea acts as precipitating factor of keratomycosis mostly by the vegetative origin like paddy leaves straw, etc. Out of topical antifungal agents Fluconazole, Natamycin and Itraconazole, Fluconazole has edge over Natamycin and Itraconazole in treating mycotic corneal ulcer. Development of Fluconazole 0.3% ophthalmic formulation is an innovation in the management of keratomycosis. Fluconazole is more effective and safe than conventional azoles for treatment of ocular fungal infection, especially in the treatment of candida keratitis. 5% Natamycin ophthalmic solutions is effective against aspergillus, fusarium and cephalosporium. It is the drug of choice for Fusarium species. In comparison to Fluconazole, Natamycin is less effective in deep keratomycosis as its corneal penetration is poor. About 1% Itraconazole ophthalmic solution is effective against Aspergillus and other filamentous fungi which are more abundant in our surrounding. **Conclusion:** Instillation of herbal juice, antibiotic and corticosteroid drops in the corneal ulcer aggravate and enhance super added infection by fungus. Aspergillus is the commonest variety among the species of fungus from the mycotic corneal ulcer.

Keywords: Keratomycosis, Corneal ulcer, Conjunctival swab culture, Topical antifungal agents, Complications

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I. Introduction

Corneal ulcer, an inflammatory or more seriously, infective condition of the cornea involving disruption of its epithelial layer with involvement of the corneal stroma, is one of the major causes of monocular blindness after unoperated cataract in many of the developing nations in Asia, Africa and the Middle East.¹ Proper management and treatment of corneal ulcers, a major cause of blindness worldwide requires precise identification of the etiology so that an appropriate antimicrobial agent targeting the organism responsible can be administered on time.³

Corneal ulceration results in 1.5–2 million new cases of corneal blindness annually, posing a major public health problem according to the World Health Organization (WHO) reports.⁴ Fungi are the most common etiological agents which account for 30–40% whereas bacteria account for 13–48% of all cases of suppurative keratitis; this varies by geographical area.⁵ These pathogens lead to corneal damage directly or by release of toxins and enzymes or by activating the host immune system.⁶ Microbial keratitis is an infectious disease of the cornea that is characterized by inflammation, often with stromal infiltration by leukocytes and an ophthalmic emergency requiring immediate attention.⁷

It is an important cause of preventable blindness. All kinds of microorganisms like bacteria, viruses, fungi, and protozoa can cause keratitis leading to corneal ulcers. Keratitis caused by fungi presents as corneal ulcers with an indolent course, stromal infiltrate with a dry texture, feathery borders, satellite lesions, immune ring infiltrates, and unlevelled hypopyon.⁸ Keratomycosis occurs in areas with warm climates and its incidence increases with seasonal increase in temperature and humidity. Trauma by vegetative or soil matter seems to be the predominant risk factor. Injudicious use of tropical corticosteroids and other antibacterial agents for external ocular disease and contact lens use further enhances the risk.

A total of 105 species of fungi, classified in 56 genera have been identified as the etiological agents of fungal Keratitis and *Fusarium spp.* and *Aspergillus spp.* are responsible for 70% of cases.⁹ India being a tropical agricultural country has a higher prevalence of fungal keratitis. The incidence of fungal keratitis lies in the range between 25.6% and 36.7% in various parts of the country.^{10, 11}

Bihar is located in semitropical region. Its climatic condition is humid and moist which helps fungal spores to get widely distributed. This type of weather favours the growth of fungi, therefore in this region the incidence of fungal corneal ulcers appears to be quite high.

II. Materials & Methods

The cases for the present study were selected from the patients attended in the Ophthalmology OPD and/or admitted in Ophthalmology IPD of a tertiary care teaching hospital, Durgapur (West Bengal) during the period from January 2018 to March 2019. Out of all corneal ulcer cases admitted during this period 100 cases clinically suspected to be due to fungal infection were selected for study. Conjunctival swab cultures were carried out from eyes of 10 clinically normal cases to study the fungal flora of conjunctival sac.

Investigations

General: Blood for TC, DLC, Hb%, ESR, blood Sugar

Special Investigations for Fungus: Direct examination of materials from corneal lesions: KOH Preparation and gram's stain; fungal culture of materials from corneal ulcer, conjunctival swab culture for fungus and biochemical study.

After completing the routine clinical examination, the cornea was anaesthetized by instillation of 4% xylocaine drops. Since the commercially prepared 4% xylocaine contains preservative and this preservative is antifungal, so after instillation the eye was washed with normal saline. After that the floor of the ulcer was scrapped with a sterile platinum wire loop. Little amount of the scrapped material was inoculated in Sabouraud's dextrose agar media for culture and the remaining part of the material was smeared on two slides – one for treating with 10% Potassium Hydroxide solution and the other for Gram's staining.

Conjunctival Swab Culture

The presence of fungus in the conjunctival sac was also examined by taking a swab from it and cultured in Sabouraud's dextrose agar media then the culture tubes were incubated at 37°C and at room temperature for 2-3 weeks and examined for the growth of fungus.

Examination of materials from the corneal lesion

A little bit of the material was taken and placed in a clean dry glass slide. Then it was treated with 10% potassium hydroxide solution and examined under microscope for presence of fungal elements.

McGuire's Stain

A little bit of scarping material from the sterile tube was taken over a clean, dry glass slide with the help of a sterile platinum loop. A drop of McGuire's stain was placed over it which was teased with a sterile needle. It was then covered with a clean cover glass. The excess of stain, if any, was mopped away with a filter paper. Then the slide was first examined under low power objective of the microscope and then under high power objective to identify the fungus.

Culture of scrapped material

The other part of the scrapped material from the corneal tissue is taken out from the test tube by a sterile platinum loop. The material is inoculated in Sabouraud's dextrose agar media (in 2 test tube slant). One

tube is kept at room temperature and another is kept in the incubator at 37°C. These tubes were kept for 2-4 weeks for growth of any fungus. If there is the growth of fungus, the morphology of the colony of the fungus is studied for the identification of the species of the fungus. Sometimes, it was examined under low power objective of the microscope and then for further identification of the species, the material from the growth was routinely stained with Gram's stain and examined under the microscope.

III. Results

The present study was carried out in 100 cases of clinically suspected fungal corneal ulcer. All these cases were attended in the Ophthalmology OPD and/or admitted in Ophthalmology IPD of a tertiary care teaching hospital, Durgapur (West Bengal) during the period from January 2018 to March 2019. In all these patients a thorough clinical examinations and laboratory investigations for fungus were done. Conjunctival swab culture for fungi was also done from 10 clinically normal cases as control. During the course of study out of 100 cases fungi could be isolated from 29 cases only. This showed that only 29% of the suspected cases suffered from mycotic keratitis.

In this study, the youngest patient was 8 years old and oldest one was 74 years. The majority of cases were in between 30-50 years. The incidence of corneal ulcer and fungus positive cases in different age groups are tabulated [Table 1] below:

Table 1: Incidence of corneal ulcer and fungus positive cases in different age groups

Age Group (in years)	Total Cases of Corneal Ulcer	Number of Fungus Positive cases	Percentage of Keratomycosis (%)
0-10	8	1	3.44
11-20	13	2	6.89
21-30	15	3	10.34
31-40	23	6	20.68
41-50	19	10	34.48
51-60	13	4	13.79
61-70	6	2	6.89
71-80	3	1	3.44
Total	100	29	99.95

In the present series, it has been observed that incidence of fungal keratitis was more in males than females both in clinically suspected and fungus positive cases. Out of 29 positive cases 18 were male and 11 were female. In the present series it has been observed that the fungal keratitis is much common among the cultivators and farmers both in total suspected cases and positive cases. Out of 100 cases 45 (48.27%) cases are cultivators and among them 14 cases are having fungal keratitis. It has been observed the highest incidence of mycotic keratitis occurred during the month from December to February. There was history of trauma to the eyes in 82 cases which include 28 (96.55%) fungal positive keratitis cases. The injury was mostly caused by paddy leaves. The agents causing injuries are shown below in Table 2.

Table 2: Agents causing injury in fungal corneal ulcer cases

Agents Causing Injury	Total Number of Cases	Fungus Positive Cases	
		Number of Cases	Percentage (%)
Paddy Leaf	16	8	27.58
Wooden Piece	8	2	6.89
Vegetable Matter	10	4	13.79
Other Tree Leaves	8	3	10.34
Straw	10	3	10.34
Bamboo Stick	13	4	13.79
Mud or Soil	7	1	3.44
Miscellaneous	10	3	10.34
Without H/o Trauma	18	1	3.44
Total	100	29	99.95

In this series 4 cases had associated diseases like diabetes mellitus and glaucoma out of 100 cases of suspected cases of fungal corneal ulcer. The nasolacrimal duct was blocked in five cases. Out of 100 cases, 88 cases had mucopurulent discharge. All the cases presented with conjunctival and circum corneal congestion with blepharospasm. In most cases the ulcer was characterized by dry looking, greyish white in colour with elevated irregular rolled out margin. 67 cases out of 100 cases had hypopyon, 4 cases with descemetocoele, 6 cases presented with panophthalmitis and 26 with iridocyclitis.

Out of 29 culture positive cases, all the cases have got conjunctival and circumcorneal congestion and the ulcers were characterized by dry looking, greyish white with elevated rolled out irregular margins. Hypopyon and mucopurulent discharge observed in all culture positive cases. 2 (6.89%) cases had descemetocoele and 4 (13.79%) cases had panophthalmitis.

Out of 100 cases, in the present series only 21 (21%) cases gave history of topical application of either antibiotics or/and corticosteroids in the eye before attending the hospital. Out of these 21 cases, 11 cases showed the growth of fungus in the culture. In the present study, it has been observed that out of 100 cases, 6 cases had history of local application of native drugs (herbal juice) to the eyes. These include 3 positive cases of fungal keratitis.

Laboratory investigations:

Slit Lamp Examination: In the present series hyphate formation were seen in 13 cases (44.82%) near the margin of the ulcer among fungus positive cases. Satellite lesions were seen in 10 cases (34.48%) among the culture positive cases. In the present series descemet’s fold were seen only in 56 cases where all the fungus positive cases are included. Out of 29 fungus positive cases only in 2 (6.89%) cases corneal ring were seen.

Conjunctival Swab Culture

The conjunctival swabs taken from 10 controlled eyes were cultured by inoculating in Sabouraud’s dextrose agar media which were kept at room temperature for 2 to 3 weeks.

Direct microscopic examination of corneal scraping

The corneal scrapings were examined under microscope after treating with 10% KOH solution and Gram’s stain. Out of 100 cases only in 29 cases fungal elements were seen, when species of fungus could not be identifies.

Culture of Corneal Scraping in Sabouraud’s Dextrose Agar Media

The corneal scraping materials inoculated in Sabouraud’s dextrose agar media were kept in room temperature for 3-4 weeks. Out of 100 cases, fungal colonies grew only in 29 (29%) cases. From the character of the colonies and after staining from the growth the different species of fungus were identified. The species identified in the present series are shown in the Table 3 below with their incidence.

Table 3: Fungal species identified in the present series

Types of Fungus	Total Number of Fungus Positive Cases	
	Number of Cases	Percentage (%)
Aspergillus fumigatus	12	41.37
Aspergillus niger	7	24.13
Candida	4	13.79
Penicillium	4	13.79
Fusarium	2	6.89
Total	29	99.97

Anti-fungal Drug Therapy:

In the present series of comparative study of different antifungal agents, three drugs i.e. fluconazole ophthalmic solution (A), natamycin ophthalmic solution (B) and itraconazole ophthalmic solution (C) were used. Out of 29 culture positive cases 9 patients were treated with 0.3% fluconazole ophthalmic solution, 1 drop one hourly for 4 days followed by 1 drop 4 hourly for 3-4 weeks or until there was resolution of the ulcer. About 5% Natamycin ophthalmic solution was given to 7 patients out of 29 cases [Figure 1]. Initially it was given 1 drop at hourly interval for 4 days followed by 1 drop 4 hourly for 3-4 weeks or till resolution of ulcer. 7 patient out of 29 fungal positive cases responded to 1% topical Itraconazole topical solution given 1 drop at hourly interval for 4 days, there after the frequency of application was reduced to 1 drop 4 hourly for 3-4 weeks or upto resolution of ulcer. Combination drugs therapy with Fluconazole topical solution and Natamycin ophthalmic solution were used in 3 culture positive cases. Another combination therapy with topical Natamycin eye drops and topical Itraconazole eye drops were used in 3 culture positive cases with good result.

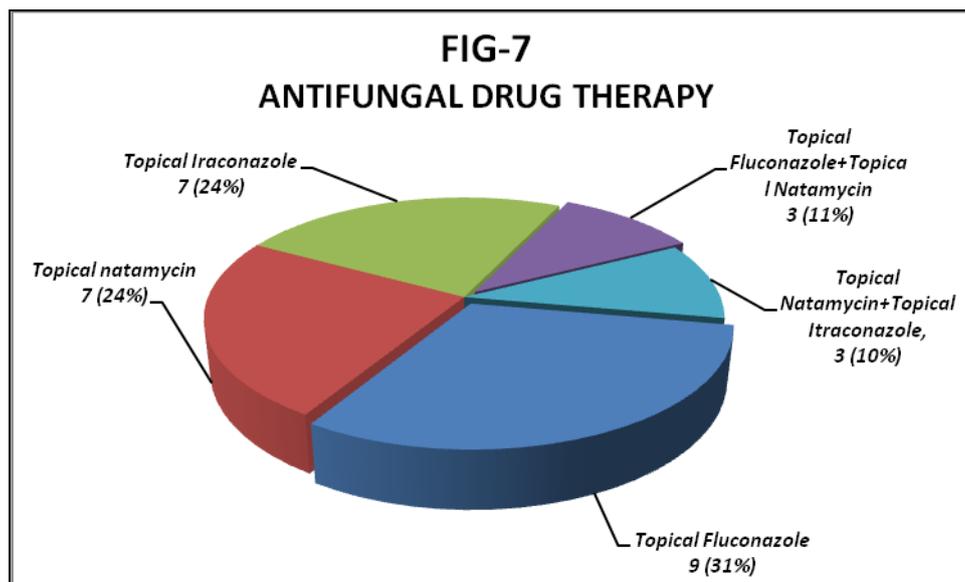


Figure 1: Antifungal drug therapy among mycotic corneal ulcers cases

Complications

Out of 29 culture positive cases the complication of fungal keratitis encountered were, panophthalmitis, perforation of ulcer, descemetocoele, secondary glaucoma, etc. and are shown in the following Table 4.

Table 4: Complications of fungal corneal ulcer

Complications	Total Number of Cases	Total Number of Fungus Positive Cases	
		Number of Cases	Percentage (%)
Panophthalmitis	6	4	13.79
Perforation of Ulcer	1	1	3.44
Descemetocoele	4	2	6.89
Secondary Glaucoma	4	1	3.44
Iridocyclitis	26	7	24.13
Healing with Corneal Opacity	59	14	48.27
Total	100	29	99.96

IV. Discussion

In the present series 100 clinically suspected cases of mycotic corneal ulcer have been selected for undertaking the study. Conjunctival swabs cultures were done in Sabouraud's dextrose agar media from 10 clinically healthy individuals to know the pattern of the fungal flora of normal conjunctival sac. The culture was positive in only one case and the species was identified as aspergillus.

The higher prevalence of corneal ulcer was seen in the agricultural group (57.8%), which was similar to finding reported by Basak et al.¹²; but a marked contrast was seen with the study done in Ghana where only 16.1% corneal ulcer cases were associated with agricultural profession. This could be due to the differences in the occupational pattern between the two countries in consideration.³

Rajesh Somabhai Katara et al¹³ study had shown that the major risk factors for mycotic keratitis were vegetative injury (16, [62%]), followed by conjunctivitis (4, [15%]), and blunt trauma (3, [11%]). Co-existing ocular diseases like conjunctivitis, trachoma and dacryocystitis were major risk factors for bacteria keratitis (8, [57%]). With 20 (70%) isolates *Aspergillus* spp. dominated the fungal keratitis isolate matrix, followed by *Fusarium* spp. with 3 (12%) isolates.¹³

Studies in the South Indian region have shown a higher incidence of *Fusarium* as compared to studies in the northern or western India. *Fusarium* keratitis has a more aggressive course and is less responsive to treatment than *Aspergillus*.¹⁴ Katara et al in Gujarat showed *Aspergillus* as the dominant isolate.¹³ The higher incidence of mycotic keratitis due to *Aspergillus* spp in their study may be due to the high tolerance of their spores to hot and dry weather conditions.¹⁴

USE OF ANTIBIOTICS AND CORTICOSTEROIDS

In the present series it has been found that out of 29 cases of culture positive keratomycosis 10 (34.48%) cases had history of application of antibiotics or/and corticosteroids to their eyes before attending the hospital. This observation is almost similar to that of Sivareddy et al¹⁵ (1972) who had 36% of such cases. From the present study it has been observed that following indiscriminate use of antibiotics and/or corticosteroids the

incidence of keratomycosis is increasing. Various theories have been put forth for aggravation of mycotic corneal ulcer by antibiotics and corticosteroids. They are: Puttanna S T¹⁶ (1967) and Naumann G et al¹⁷ (1967) suggested that antibiotics enhance the fungal growth by inhibition of normal bacterial flora and corticosteroids aggravates the fungal growth by inhibition of inflammation and host resistance. Puttanna S T (1967)¹⁶ and Puttanna¹⁸ (1969) stated that non-pathogenic fungi might be converted into pathogenic one by indiscriminate use of corticosteroid. Suga and Folia¹⁹ (1966) mentioned that corticosteroids might induce corneal hyperglycaemia which aggravates fungal growth.

USE OF HERBAL JUICE

In the present study 3 cases (10.34%) out of 29 cases of keratomycosis had history of application of herbal juice or native medicine to their eyes. Puttanna¹⁸ (1969) reported cases of *Aspergillus* keratomycosis after instillation of herbal juice topically. The herbal juice might carry the fungi which predispose to mycotic corneal ulcer. Sivareddy et al¹⁵ (1972) reported 8.3% cases of keratomycosis following topical instillation of herbal juice. Dutta et al²⁰ (1981) observed 12.5% cases of keratomycosis occur following treatment of corneal ulcer with herbal juice. It has been observed from the present study that topical application of herbal juice in corneal ulcer enhances fungal infection.

ASSOCIATED CONDITIONS

Diabetes Mellitus

In the present series out of 100 clinically suspected cases of keratomycosis only 2 cases of diabetes mellitus were detected during this period. Fungus could be isolated in one case by culture and it was found to be candida species. It is well known fact that keratomycosis is more common in patients with decreased body resistance especially in diabetes mellitus. Baker²¹ (1956) and Sivareddy et al¹⁵ (1972) also reported increased incidence of mycotic keratitis in diabetes mellitus.

The most common associated risk factors in our study were trauma followed by diabetes mellitus and contact lens usage which is comparable with other studies.²² While Yousuf et al²³ reported the use of contact lens as the major cause, Krishna et al²⁴ demonstrated injury to eye as the predominant risk factor followed by the foreign body induced microbial keratitis.

Glaucoma

Two cases of corneal ulcer associated with glaucoma were detected out of 100 clinically suspected cases of keratomycosis and fungus *aspergillus* was isolated from the cornea of one case only. In this particular case, keratomycosis can be attributed to pre-existing corneal lesion by glaucoma where fungus was secondary invader. Nauman et al¹⁷ (1967) reported secondary invasion of fungus to the cornea in long standing cases of glaucoma.

CLINICAL PICTURE

Conjunctival and Circumcorneal Congestion

All the 29 fungus positive cases had conjunctival and circumcorneal congestions which might be due to the reactionary iridocyclitis or due to the secondary bacterial infection. Naumann et al¹⁷ (1967) and Puttanna¹⁸ (1969) stated that reaction of the fungal keratitis is less than that of bacterial corneal ulcer. But it was observed by Duke-Elder²⁵ (1965) that fungal keratitis became more violent when it was super infected by pathogenic organisms like *Staphylococcus*, etc.

Character of the Ulcer

All the culture positive mycotic corneal ulcer possess some common features like greyish white colouration with dry looking appearance and rolled out elevated irregular margins without any vascularization. With all these characters Duke-Elder²⁵ (1965) stated that the clinical picture of mycotic corneal ulcer is so uniform that it can be conveniently described as a type. The same nature of the ulcer was described by Puttanna¹⁸ (1969) and Sivareddy et al¹⁵ (1972). All the 29 cases of keratomycotic eyes had hypopyon which might be a reactional one due to toxins liberated by the fungus resulting iridocyclitis. This fact was also observed by Duke-Elder²⁵ (1965), Kaufman & Wood²⁶ (1965), Puttanna¹⁸ (1969), Sivareddy et al¹⁵ (1972), Grover et al²⁷ (1974) and Dutta et al²⁰ (1981). In addition to the above features Kaufman & Wood²⁶ (1965) described few other features of fungal corneal ulcer. They observed presence of dense white endothelial plaques on the back of the cornea in 4 cases and noted a white ring (immune ring) in 3 of the cases in mid periphery during their study.

Naumann et al¹⁷ (1967) also observed of such ring in fungal keratitis. But in the present series, corneal rings were observed only in 2 (6.89%) cases out of 29 fungus positive cases. This incidence is lower than that obtained by Kaufman & Wood²⁶ (1965). They found it to be 20% in their series. In the present study it has been

observed that out of 29 fungus positive ulcer cases, satellite formation or hyphate were seen only in 8 (27.58%) cases. These might be due to microscopic appearance of hyphae around the edge of the ulcer, which indicate extension of fungus colony. Similar observations were made by Duke-Elder²⁵ (1965), Kaufman & Wood²⁶ (1965), Naumann et al¹⁷ (1967), Puttanna¹⁸ (1969) and Sivareddy et al¹⁵ (1972). Puttanna⁶ (1969) reported that the extension of the hyphate beyond the corneal ulcer margins help in differentiating mycotic corneal ulcer from the bacterial corneal ulcer.

It has been observed in slit lamp examination that out of 100 cases in 48 cases including 29 fungus positive cases; descemet's fold were noticed. Similar features were also stated by Kaufman & Wood²⁶ (1965); Puttanna¹⁸ (1969) and according to them, presence of descemet's fold is an important feature of mycotic corneal ulcer. In the present series vascularization has not been observed in any case of fungus positive corneal ulcer. Similar observation was made by Duke-Elder²⁵ (1965). Greer CH²⁸ (1972) stated that vascularization is invariably absent in mycotic corneal ulcer.

In the present series comparative study of different antifungal drugs were carried out in mycotic corneal ulcer. Nine (31.03%) cases out of 29 fungus positive cases were treated by 0.3% fluconazole ophthalmic solution with significant improvement of corneal ulcer. Treatment was continued upto 4 weeks or till the healing of the ulcer. Panda A et al²⁹ (1996) reported that fluconazole has been shown to be safe and effective in the management of Candida keratitis with deep abscess and effective moderately against aspergillus and fusarium species. Ishibashi Y et al³⁰ (1984) observed that fluconazole is safe and effective in mycotic corneal ulcer. In India at various centres (Ahmedabad, Delhi, Hyderabad, Chennai, Annamally, etc.) multicentric single blind comparative clinical trial has been conducted on 256 cases of smear and culture positive mycotic corneal ulcer. It was observed that the success rate of fluconazole 0.3% ophthalmic solution was 77% for candida, 50% of aspergillus and 64.7% for other (cephalosporium, alternaria, cladosporium, monosporium, aerobasidium etc.). In 7 (24.13%) cases out of 29 culture positive cases; 5% natamycin ophthalmic solution was used which is a fungicidal in nature. It was observed to be effective against filamentous fungi fusarium, aspergillus and candida to some extent. The drug responded excellently to fusarium solani fungus. Treatment was continued upto 4 weeks or till the healing of ulcer. The pooled data from India and abroad in multicentric clinical trials showed natamycin ophthalmic solution (5%) is more effective and safe than conventional azoles for treatment of ocular fungal infection, especially in treating fusarium species. Out of 29 culture positive cases; 7 cases were treated by 1% Itraconazole ophthalmic solution with significant improvement of ulcer. The result was coinciding with the reports of Thomas PA et al³¹ (1988). It is effective against aspergillus and moderately effective against candida, fusarium and other species. The therapy was continued for 4 weeks or till the healing of the ulcer.

In the present study combination drug (0.3% fluconazole eye drops and 5% natamycin eye drops) were used in 3 patients out of 29 culture positive cases with good result. Another combination of drugs (5% natamycin eye drops and 1% itraconazole eye drops) were given in 3 culture positive cases and found to be effective with healing of the ulcer.

V. Conclusion

This study comprises of 100 clinically suspected mycotic keratitis cases, who were attended in the Ophthalmology OPD and/or admitted in Ophthalmology IPD of a tertiary care teaching hospital, Durgapur (West Bengal) during the period from January 2018 to March 2019. The incidence of mycotic keratitis in this series was 29%. The maximum incidence of keratomycosis was observed in the age group from 30-50 years. This is attributed to trauma to the eye in agricultural fields. The disease is more in males than in females and the ratio is 3:2. Incidence of aspergillus keratitis was the highest (65.50%), followed by candida (13.79%), penicillium (13.79%) and fusarium 96.89%). Complications observed among the fungus positive cases were panophthalmitis (3.79%), perforation of corneal ulcer (3.44%), descematocele (6.89%) and secondary glaucoma (3.44%).

All the fungus positive cases were treated with antifungal drugs 0.3% topical fluconazole eye drop, 5% topical natamycin eye drop and 1% topical itraconazole eye drop. fluconazole eye drop which was used in 9 cases out of 29 fungus positive cases (31.03%) responded positively in candida and aspergillus species.

Natamycin eye drop (5%) was active against fusarium, aspergillus and candida and was used in 7 (24.13%) culture positive cases. About 1% itraconazole eye drop was used in 7 (24.13%) fungus positive cases and found to be responded positively in aspergillus and candida species. Combination therapy with (0.3% fluconazole eye drops and 5% natamycin eye drop) and (5% natamycin eye drop and 1% itraconazole eye drops) were also used to treat the mycotic corneal ulcer with good result.

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