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A Study of Infective Keratitis and its Response to Treatment

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Abstract: *Corneal infection is the leading cause of ocular morbidity and blindness worldwide. Despite advances in treatment, infective keratitis remains clinically challenging and although the outcome can be favorable with appropriate management. The aim of the present study is to study the prevalence and distribution of bacterial and fungal keratitis and assessment of their response to treatment. Corneal scrapings were inoculated in to various media after collection and identified, assessed their antibiotic susceptibility pattern. All the patients were treated appropriately according to the etiology of infective keratitis. Out of 100 suspected cases, 40 (40%) were bacterial etiology of infective keratitis and 36 (36%) were fungal cause of infective keratitis. Both Gram positive and Gram Negative isolates was treated according to antibiotic sensitivity pattern. Fungal isolates were treated according to the type of fungus, by using eye drops of various antifungals. 52.5% of bacterial corneal ulcers recovered on treatment, while 30% deteriorated with loss of vision or perforation or corneal vascularization. 72.22% of fungal corneal ulcers deteriorated in spite of treatment with scarring and cicatrisation of corneal and total corneal ulceration. To avoid complications of corneal ulcers there is a need of appropriate treatment to start as early as possible.*

Keywords: *Bacterial Keratitis, Fungal Keratitis, Treatment*

I. Introduction

Keratitis is an inflammation of the cornea. The term keratitis was first introduced by James Wardrop. Corneal infection is the leading cause of ocular morbidity and blindness worldwide. Corneal ulceration is a major cause of monoocular blindness in developing countries. Corneal infection or microbial keratitis is a condition caused by various pathogens like bacteria, fungi, viruses or parasites.

The unique structure of the human eye as well as exposure of the eye directly to the environment renders it vulnerable to a number of uncommon infections and diseases caused by fungi, bacteria, parasites or viruses.Bacterial keratitis is an acute or chronic infection of the eye, can results in severe disability [1]. Staphylococcus aureus, Pseudomonas aeruginosa and Streptococcus pneumoniae account for 80% of all bacterial corneal ulcers. Keratitis should be regarded as an emergency since corneal perforation and loss of vision can occur within 24 hours when organisms such as Pseudomonas aeruginosa and Staphylococcal aureus were involved [2].

Fungal keratitis or Keratomycosis are ubiquitous and responsible for 6% to 53% of all corneal infections. Due to a large agrarian population and tropical environmental factors, Keratomycosis is common in India [3]. The common etiological agents implicated in Mycotic keratitis are saprophytic fungi like Fusarium solani, Aspergillus spp, Acremonium and Curvularia [2].

Predisposing factors such as corneal injury, contact lens wear, ocular adnexal dysfunction, corneal abnormalities, systemic diseases and immunosuppression may alter the defense mechanisms of eye and permit the bacteria and fungi to invade the cornea. Once anatomical barriers are breached, host defenses directed against these microorganisms are often insufficient to prevent loss of vision. Therefore, timely identification and treatment of disease is of paramount importance. If appropriate therapy is not initiated promptly will result in poor clinical outcome [4-6].

Despite advances in treatment, infective keratitis remains clinically challenging and although the outcome can be favorable with appropriate management, there is potential for significant and permanent visual impairment in addition to social and healthcare costs [7,8].

This is a small Endeavour done to study the prevalence and distribution of bacterial and fungal keratitis among out patients attending ophthalmology clinics and assessed their response to treatment.

II. Material And Methods

A prospective study was done for one year in Microbiology department at Government General Hospital, Vijayawada. Ethical committee has approved to do this study.

All patients who attended the hospitals with corneal ulcers were examined by an ophthalmologist by slit lamp. A detailed history from 100 selected patients was taken in the form of a proforma and recorded after obtaining informed consent. From each patient, corneal scrapings were collected following strict aseptic

measures, after instillation of anesthetic (4% lignocaine) drops into the eyes, under the magnification of slit lamp using sterile Bard-Parker Blade (No.15), the material was scrapped from the base and margins of the ulcer.

The scrapings were subjected to direct microscopy by grams stain and 10% KOH wet mount and were inoculated on to blood agar, chocolate agar, Mac conkey agar, Nutrient agar and Sabouraud dextrose agar (SDA) with antibiotics, in a row of C-shaped streaks. They were incubated at 370C. Another set of inoculated Sabouraud dextrose agar slants are incubated in BOD (Biological Oxygen Demand) at 250C. Bacterial growth were observed for 24-48hrs and fungal growth for 3 weeks.

Colony characteristics has observed. For identification of bacteria, a single colony was taken, inoculated in peptone water broth and then subjected to relevant Biochemical tests and Gram staining along with controls. All the bacterial isolates were subjected to antibiotic sensitivity testing on Mueller Hinton Agar by Kirby Bauer disc diffusion technique.

The fungal isolates were identified by gross morphology by their colony characteristics, any pigmentation on the obverse and reverse. The filamentous fungi were identified by tease mount technique & stained with Lacto phenol cotton blue (LPCB). When required, further study of fungi was done by Slide culture technique.

All the patients were treated appropriately according to the etiology of infective keratitis. Those patients were assessed after treatment.

III. Results

Out of 100 corneal ulcer patients, culture positivity was seen in 76 (76%) patients. Among them 40 (40%) were bacterial etiology of infective keratitis and 36 (36%) were fungal cause of infective keratitis. Bacterial isolation was predominant in the age group of 31-40 years followed by 21-30 years, whereas fungal isolates were predominant in 51-60 years of age group followed by 61-70 years. Male predominance was seen in both bacterial and fungal keratitis.

Among 40 bacterial isolates Pseudomonas aeruginosa was the predominant bacterial isolate (22.5%). The second predominant isolates were Staphylococcus aureus (20%), Streptococcus pneumoniae (20%) and Micrococcus species (20%) (Table.1).

Among 36 isolates of fungi predominant was Aspergillus species (36.11%) followed by Fusarium species (25%) (Table.2) (Fig.1&2)

Out of 76 isolates, both bacterial and fungal isolate were obtained from five patients. These mixed organisms growth from corneal ulcers were represented in Fig.3

Out of 100 patients, most of the corneal ulcers (54) were resulted because of traumatic injury (Table.3).

Among Gram positive isolates 100% were sensitive to Levofloxacin, Tetracycline, Amikacin, Cefuroxime. More than 60% of isolates shown sensitive to Cefoxitin, Erythromycin. (Table. 4)

Among Gram Negative Organisms Pseudomonas aeruginosa was isolated which were 88.88% sensitive to Amikacin and Ofloxacin, 77.77% sensitive to Gentamicin, 55.55% sensitive to Ceftazidime+Clavulanic acid, 44.44% sensitive to Ceftazidime, 33.33% sensitive to Piperacillin.

Fungal isolates were treated according to the type of fungus, by using either ketoconazole or itraconazole or amphotericin B or other antifungals. Alternate therapy and prolongation of therapy were based on the tolerance of topical medications and improvement of signs in cornea and reduction in inflammatory signs.

Treatment response were assessed in those patients who came for follow up (Table.5). 52.5% of bacterial corneal ulcers recovered on treatment, while 30% deteriorated with loss of vision or perforation or corneal vascularization. No follow up was present in 17.5% of the cases. 72.22% of fungal corneal ulcers deteriorated in spite of treatment with scarring and cicatrisation of corneal and total corneal ulceration, and no follow up was present for 13.88% cases. Response to treatment for the culture positive corneal ulcers was statistically significant ($P<0.05$).

IV. Discussion

Microbial keratitis is a common potentially vision threatening ocular infection that may be caused by bacteria, fungi, viruses or parasites. Timely identification and treatment of microorganisms are paramount.

In this study bacterial isolates were 40. fungal isolates were 36. Bacterial isolation was predominant in the age group of 31-40 years followed by 21-30 years, whereas fungal isolates were predominant in 51-60 years of age group followed by 61-70 years. Male predominance was seen in both bacterial and fungal keratitis.

Pseudomonas aeruginosa was the predominant bacterial isolate in the present study (22.5%) followed by Staphylococcus aureus (20%), Streptococcus pneumoniae (20%) and Micrococcus species (20%) each. The other bacterial isolates included Staphylococcus epidermidis (10%) and Corynebacterium species (7.5%). As etiological agents, bacterial isolates were more common when compared to fungal isolates. In line with this study Bharathi et al [9], Alexandrakis et al [10] reported that Pseudomonas aeruginosa was the predominant

isolate followed by Staphylococcus aureus from corneal ulcers. Khanaal et al [11] and Schaefer et al [7] observed that Staphylococcus aureus and Staphylococcus epidermidis was the predominant isolate from infective keratitis respectively.

Aspergillus species was the predominant fungal isolates in the present study (36.11%), followed by Fusarium species (25%). Other isolates included Pseudallescheria boydii (8.33%), Cladosporium spp, Penicillium spp, Acremonium spp (5.55%) each. Bipolaris spp, Curvularia lunata, Paecilomyces lilanicus, Alternaria alternata (2.77%) each. Isolates from 2.77% remain unidentified. This study was supported by Khanal et al [11], Mohapatra et al [12], Kumari et al [13], observed that Aspergillus species was the predominant pathogen from infective keratitis. In contrast to this Xie et al [14], Bharathi et al [15] documented that Fusarium species was the predominant isolate.

Mixed growth for bacterial and fungal isolates were obtained in 5% cases in the present study. This coincides with Kumari et al[13] - 4.9%. Bharathi et al [15] and Mohapatra et al [12] reported an incidence of 3.9% and 8.9% respectively. Khanaal et al[11] reported higher incidence of 18.2%.

Among Gram positive isolates 100% were sensitive to Levofloxacin, Tetracycline, Amikacin, Cefuroxime. Both Gram positive and Gram Negative isolates was treated according to antibiotic sensitivity pattern. Eyes drops of appropriate antibiotics Ciprofloxacin, Ofloxacin, Gentamicin, Levofloxacin were advised to use frequently depending on the severity for one or two months. Fungal isolates were treated according to the type of fungus, by using eye drops of either Natamycin, ketoconazole or itraconazole or amphotericin B or other antifungals. Natamycin 5% suspension is the first choice for treatment of filamentous fungal keratitis [16]. Effective gaent against yeasts is amphotercin B [17].

As per this study, 52.5% of bacterial corneal ulcers recovered on treatment, while 30% deteriorated with loss of vision or perforation or corneal vascularization. No follow up was present in 17.5% of the cases. 72.22% of fungal corneal ulcers deteriorated in spite of treatment with scarring and cicatrisation of corneal and total corneal ulceration, and no follow up was present for 13.88% cases. Lack of awareness and late presentation to ophthalmic clinics are also responsible deterioration of the condition.

More number of cases were deteriorated among fungal keratitis patients, most of the fungal isolates are very less to respond to treatment and needs prolonged treatment with appropriate antifungal agent. Almost around 20% of fungal ulcers won't respond to medical therapy [18].

V. Figures And Tables

Table No:1 Various Bacterial isolates from Corneal ulcers

S.No.	Bacterial Isolates	No. of isolates	Percentage (%)
1	Pseudomonas aeruginosa	9	22.5
2	Staphylococcus aureus	8	20
3	Streptococcus pneumoniae	8	20
4	Micrococcus spp	8	20
5	Staphylococcus epidermidis	4	10
6	Corynebaterium spp	3	7.5
Total		40	100

Table No:2 Various fungi isolated from Corneal ulcers

S.No.	Fungal Isolates	No. of isolates	Percentage (%)
1	Aspergillus species	13	36.11
2	Fusarium species	9	25
3	Pseudallescheria boydii	3	8.33
4	Pencillium species	2	5.55
5	Cladosporium species	2	5.55
6	Acremonium species	2	5.75
7	Curvularia lunata	1	2.77
8	Bipolaris species	1	2.77
9	Paecilomyces lilanicus	1	2.77
10	Alternaria alternata	1	2.77
11	Unidentified	1	2.77
Total		36	100

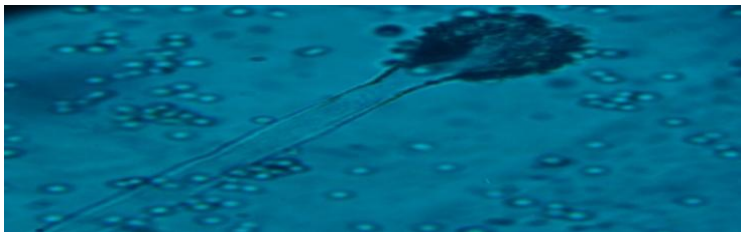

Fig No.1 Showing LPCB stain of Aspergillus flavus

Fig No.2 Showing LPCB stain of Curvularia lunata

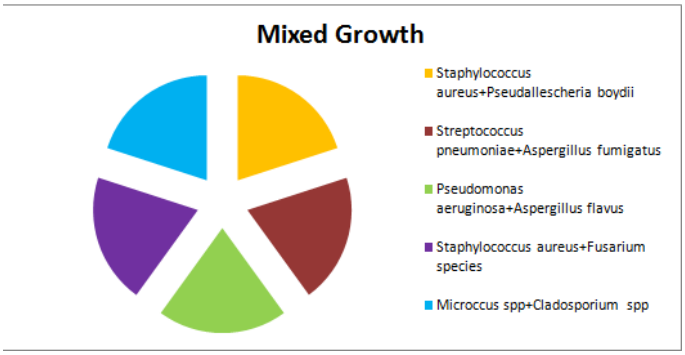

Fig No. 3 Representing mixed growth of Bacteria and Fungi isolates from corneal ulcers.

Table No:3 Prevalence of Traumatic and Non traumatic injury among corneal ulcers

Factor	Bacterial	Fungal	Total
Traumatic	26	28	54
Non Traumatic	14	8	22
Total	40	36	76

Table No.4 Antibiotic sensitivity pattern of Gram Positive isolates

Organism	No.of strains	Amoxycillin		Cloxacillin		Erythromycin		Levofloxacin		Tetracycline		Amikacin		Cefoxitin		Cefuroxime	
		No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
S.aureus	8	3	37.5	4	50	6	75	8	100	8	100	8	100	7	87.5	8	100
S.pneumoniae	8	6	75	8	100	7	87.5	8	100	8	100	8	100	8	100	-	-
Micrococcus	8	7	87.5	6	75	7	87.5	8	100	8	100	8	100	8	100	8	100
S.epidermidis	4	2	50	4	50	1	25	4	100	4	100	4	100	3	75	4	100
Corynebacterium spp.	3	3	100	3	100	2	66.6	3	100	3	100	3	100	3	100	3	100

AMX - Amoxicillin, CX - Cloxacillin, E - Erythromycin, LE - Levofloxacin, TE - Tetracycline, AK - Amikacin, CN - Cefoxitin, CU - Cefuroxime.

Table No.5 Assessment of response of treatment among bacterial and fungal keratitis

Category	Bacterial (n=40)		Fungal (n=36)	
	No	%	No	%
Responded to treatment	21	52.5	5	19.44

Deteriorated	12	30	26	72.22
No Follow up	7	17.5	5	13.88
Total	40	100	36	100

VI. Conclusion

To avoid complications of corneal ulcers there is a need of appropriate treatment to start as early as possible. Both bacterial and fungal keratitis are ocular emergencies has to start empirical therapy to avoid various complications. As bacterial emergence of resistance towards antibiotics has became more common worldwide, has to test antibiogram and advice appropriate antibiotic. As most fungal isolates are refractory to medical therapy, need to give prolonged therapy by notifying the improving signs of the eye. Health education is necessary to improve the personal hygiene, eye protective measures during work, early presentation to ophthalmic clinics.

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