ANALYSIS OF CASES OF MICROBIAL KERATITIS IN A MEDICAL COLLEGE IN VISAKHAPATNAM

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ABSTRACT

AIM

To analyse the epidemiological characteristics, microbiological profile and treatment outcome of patients with microbial keratitis.

SETTINGS AND DESIGN

This was a prospective study done on infective keratitis patients who attended OPD in our teaching institute over a period of one year. The purpose of our study was to assess the risk factors, clinical and visual outcome of treatment of microbial keratitis.

METHODS AND MATERIALS

136 patients who were clinically diagnosed as infective keratitis presenting between January 2014 and January 2015 were included in our study. Standard microbiological evaluation of their corneal scrapings was done and visual and clinical outcome of treatment was assessed.

STATISTICAL ANALYSIS

Statistical analysis of the data was performed using Chi-square test. Odds ratio and 95% confidence intervals were calculated wherever essential.

RESULTS

In our study, fungal keratitis was predominant (65.44%) as compared to bacterial keratitis. Trauma was the commonest predisposing factor in fungal keratitis patients (80%) and co-existing ocular disease was commonest predisposing factor for bacterial keratitis (53.19%). Majority of fungal infections were caused by Fusarium species (39.72%). The commonest bacterium isolated was Staphylococcus aureus (36.36%). The incidence of complications was higher in fungal keratitis group (34.83%) as compared to bacterial keratitis. Corneal scar was the final clinical outcome in 74.15% and 78.72% of fungal and bacterial keratitis patients respectively.

KEYWORDS

Keratitis, Evisceration, Penetrating keratoplasty, Phthisis bulbi.

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INTRODUCTION: Blindness constitutes one of the major health problems haunting developing and developed nations. Cataract and glaucoma are the leading causes of blindness accounting for 72.2% & 4.4%[1] respectively according to RAAB survey conducted in 2006-07. Corneal opacities including trachoma account for 6.5% of blindness. About 37 million are blind due to eye diseases in the world. While the problem of blindness is global, its magnitude is much higher in India. More than 50% of world's blind due to eye diseases live in India (9 million), Africa (7 million) and China (6 million). The prevalence of blindness according to a recent survey conducted in India by RAAB is 1%.[1] Corneal scarring including trauma accounts for 1.3 million (3%) of global blindness. In India, it accounts for 6.5% of blindness. Of 6.8 million people who have visual acuity <6/60 in at least one eye due to corneal disease, a million have bilateral involvement.[2,3] The number is expected to increase to 10.6 million by 2020. According to NPCB estimates,[3] there are currently 1,20,000 corneal blind people in the country. There is an addition of 25,000-30,000 corneal blindness cases every year in our country.

Corneal blindness could be due to eye conditions that alter the transparency of cornea leading to corneal scarring and eventually blindness. Causes include infection, keratitis, xerophthalmia, trauma, trachoma, corneal degeneration. The incidence of microbial keratitis varies from 11/1,00,000 persons per year in US[4] to 799/1,0000 in Nepal.[5] In tropical countries like South Florida,[6] Bangladesh[7] and South India,[8] fungal keratitis is predominant. In developed countries like Britain,[9] US,[10] bacterial keratitis is more predominant.

Infective keratitis may be caused by bacteria, fungi, protozoa and virus. The spectrum of microbial pathogens

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causing keratitis varies according to geographical factors. The ocular surface is normally protected from microbial invasion through an intricate biochemical and anatomical relationship between cornea, conjunctiva, tear film and eyelids. Corneal injury due to vegetative material is the main predisposing factor for fungal keratitis while co-existing ocular disease for bacterial keratitis. The purpose of this study was to study the risk factors, clinical and visual outcome after treatment in our study group. The cases of viral keratitis were excluded from our study.

MATERIALS AND METHODS: The present study was done on 136 patients in the Department of Ophthalmology, NRIIMS, Sangivalasa, Visakhapatnam from January of 2014 to 2015 for a period of 12 months. Infective keratitis is defined as suppurative infection of corneal stroma with an associated overlying epithelial defect and signs of infiltration and is characterised by the presence of white or yellowish stromal inflammation, with an associated epithelial defect with or without hypopyon. The demographic features, information about predisposing factors, history of injury, associated ocular diseases, contact lens usage, usage of drugs, presence of systemic disease like diabetes were documented.

Visual acuity was recorded using Snellen's Visual acuity chart, ocular examination was done by slit-lamp biomicroscope. Corneal scraping was performed under aseptic conditions by an ophthalmologist using a Bard parker blade 15 or a 26 gauge needle after instillation of 0.5% proparacaine hydrochloride. The scraped material was smeared onto a clean sterile labelled glass slide for 10% KOH wet mounting, gram staining and Giemsa staining procedures. The material obtained from next scrapes was inoculated onto surface of media such as blood agar, Sabouraud's dextrose agar and non-nutrient agar in a row of C-shaped streaks.

STATISTICS: Statistical analysis of the data was performed using Chi-square test. Odds ratio and 95%, confidence intervals were also presented for 2 x 2 containing tables. The statistical significance level was taken as $\alpha = 0.05$ and at 95% confidence level.

RESULTS: From January, 2014 to January 2015, 136 cases of corneal ulcer were evaluated.

Demographic Profile: The demographic profile of the 136 patients with microbial keratitis is documented in table-1. Of 136 patients, 94 (69.11%) were male and 42 (30.88%) were females. The male to female ratio was 2.29:1 in patients with fungal keratitis and 2.13:1 in patients with bacterial keratitis. The youngest in patients affected with fungal keratitis was 10 years old and oldest was 75 years old. The mean age was 44 years and median age was 42 years. In patients with bacterial keratitis, the youngest patient was 15 years old and oldest patient was 70 years old. The mean age was 44 years and median age was 43 years. Males were affected more in both bacterial (69.66%) and fungal keratitis (68.08%) {OR 1.08, Cl: (0.50-2-31, P < 0.001)}. Though a majority of patients were in the age group of 25-55 years and the patients above 40 years of age (80/136); 58.82%) were more than patients below 40 years of age (56/136, 41.17%), it was not statistically significant {OR 1.38 with CI (0.66-2.85)}. The incidence of bacterial keratitis (76/89) and fungal keratitis (33/47) was more in patients belonging to rural areas which was statically significant (P=0.03).

Age Group	Fungus (n=89)	Bacteria (n=47)	P Value
10-24	12(13.48%)	03(6.38%)	P > 0.05
25-39	27(30.33%)	14(29.78%)	
40-54	24(26.96%)	21(44.68%)	
55-69	20(22.47%)	08(12.02%)	
70-84	06(22.47%)	01(2.12%)	
Gender			
Male	62(69.66%)	32(68.08%)	P > 0.05
Female	27(30.33%)	15(31.91%)	
Residence			
Rural	76(85.39%)	33(70.21%)	P = 0.03 OR(2.48)
Urban	13(14.60%)	14(29.78%)	

Table 1: Demographic profile of our study group

Predisposing Factors: The predisposing factors are summarised in table-II. Corneal injury was identified as major risk factor for causation of fungal keratitis (72/89; 80%) as compared to other predisposing factors (17/89) 19.10%). The correlation between fungal keratitis and trauma was statistically highly significant. (P <0.001) The incidence of fungal keratitis secondary to co-existing ocular disease was 13.48%, usage of steroids 2.2%, post pterygium surgery 1.1% and diabetes 2.2%. The major aetiological factor predisposing to bacterial keratitis was co-existing ocular disease (25/47, 53.19%). This correlation of bacterial keratitis with co-existing ocular disease was just statistically significant (P=0.05). The incidence of bacterial keratitis secondary to trauma was 38.29%, contact lens 4.22%, and diabetes 2.12%.

Sl. No.	Aetiology	Fungus	Bacteria
1	Ocular injuries (Vegetative matter, dust/soil/stone/sand, animal material, metallic foreign body	72(80.98%)	15(31.91%)
2	Co-existing ocular diseases:	12(13.48%)	28(59.57%)
	a. Chronic dacryocystitis	-	1(2.12%)

	b. Corneal disorders degeneration oedema, epithelial defect	4(4.49%)	14(29.78%)
	c. Lid disorders (Lagophthalmos, blepharitis	3(3.37%)	5(10.63%)
	d. Suture infiltration (Post PKP)	1(1.12%)	1(2.12%)
	e. Dry eye	2(2.24%)	2(4.25%)
	f. Conjunctivitis	2(2.24%)	2(4.25%)
3	Contact lens wear	-	2(4.25%)
4	Usage of steroids	2(2.24%)	1(2.12%)
5	Post surgery	1(1.12%)	-
6	Systemic diseases – Diabetes	2(2.24%)	1(2.12%)

Table 2: Predisposing factors

In our study cultures were positive in 106/136(77.94%). Mixed bacterial and fungal growth was obtained in 8 patients (5.88%), in 22 patients (16.17%) culture was negative. Pure bacterial isolates were obtained in 70.21% of patients. The most commonly isolated fungus was Fusarium in 21 cases (44.65%), followed by Aspergillus in 13 cases (27.65%). The commonest bacterium that was identified was staphylococcus aureus in 12 patients (36.36%), followed by staphylococcus epidermidis in 7 patients (21.21%).

Sl. No.	Name	No. s.	%
1	Fusarium	29	39.72%
2	Aspergillus	22	30.1%
3	Curvularia	4	5.47%
4	Pencillium	2	2.73%
5	Alternaria	5	6.84%
6	Candida	11	15.06%

Table 3: Microbiological profile (Fungi)

Sl. No.	Name	No. s.	%
1	Staphylococcus aureus	12	36.36%
2	Staphylococcus epidermidis	7	21.21%
3	Streptococcus pneumonia	4	12.12%
4	Streptococcus pyogenes	1	3.03%
5	Nocardia	1	3.03%
6	Pseudomonas	3	9.09%
7	Moraxella	1	3.03%
8	E. coli	2	6.06%
9	Proteus	1	3.03%
10	Klebsiella	1	3.03%
Total		**33**	

(Bacteria)

Visual Outcome: In patients with fungal keratitis visual improvement on treatment was observed in 51.69% (46 patients), decrease in vision noted in 22.47% and no change of vision in 21.34%. Amongst 89 patients, 30 patients (33.70%) presented within 24 hours, 37 patients (41.51%) in 3 days, 13 patients (14.60%) between 4-7 days, 9 patients (10.15%) after 1 week. There was visual improvement in 83.58% (56/67 patients) who presented within 3 days to the hospital, 53.84% (7/13 patients) who presented between 4-7 days, 22.22% (2/9) who presented after 1 week after the onset of symptoms. There was visual deterioration in 14.92% (10/67) of patients who presented to the hospital within 3 days, in 30.76% (4/13) of patients who presented between 4-7 days after the onset of symptoms, in 66.66% with presentation after 1 week.

In patients with bacterial keratitis, after treatment vision improved in 51.06%; vision decreased after treatment in 23.47% and there was no change of vision in 17.02%. Amongst 47 patients, 18 patients (59.94%) presented to the hospital after the onset of symptoms within 24 hours, 11 patients (32.35%) in 3 days, 8 patients (17.02%) between 4-7 days, 5 patients (10.63%) after 1 week. The visual prognosis was good in (85.29%, 29/34) patients and visual deterioration in 4/34 patients (11.76%), who presented to the hospital within 3 days after the onset of symptoms As the presentation of the patient to the hospital was delayed ,the chances of visual improvement decreased {(4-7 days (2/8, 25%); (>1week(1/5, 20%)}.

Healed scars was the final clinical outcome in 66 cases (74.14%) in fungal keratitis and 78.72% in bacterial keratitis. The visual and clinical outcome were better in patients who presented within 3 days to the hospital after the onset of symptoms in both fungal (83.58%) and bacterial (85.29%) keratitis patients. Though the figures showed that the response to treatment in both bacterial and fungal keratitis was almost the same and beneficial the rate of complications were higher with fungal keratitis. There was perforation in 23 cases of fungal keratitis patients (25.84%) as compared to bacterial keratitis (4/47) 8.51%. Surgical intervention was required in 6 cases (6.74%) in fungal keratitis patients as compared to bacterial keratitis 6.38% (3 cases). The response to treatment was much slower in fungal keratitis. This study reiterates the fact that though fungal keratitis can be treated effectively, the treatment of fungal keratitis still remains a challenge. Treatment was beneficial in both the groups which was statistically significant $P<0.001$.

Visual acuity	Fungus				Bacteria			
	Vision improvement	Vision deterioration	No change in vision	Lost to followup	Vision improvement	Vision deterioration	No change in vision	Lost to followup
> 6/18	11(12.36%)	13(14.60%)	07(7.86%)	0(0%)	04(8.51%)	06(12.77%)	04(8.51)	02(4.25%)
6/18-6/60	24(26.97%)	06(6.74%)	06(6.74%)	00(0.00)	15(31.91%)	04(8.51%)	04(8.51)	0(0%)
<6/60	11(12.36%)	01(1.12%)	06(6.74)%	04(4.49)	05(10.64%)	01(2.13%)	0(0%)	02(4.25%)

Table 4: Visual outcome

	< 3 days (n=67)	4-7 days (n=13)	> 1 week (n=9)
Visual improvement	56(83.58%)	7(53.84%)	2(22.22%)
Decrease in vision	10(14.92%)	4 (30.76%)	6(66.66%)
Lost to followup	1(1.49%)	2 (15.38%)	1(11.11%)

Visual outcome according to the duration of presentation of symptoms (Fungal keratitis, n=89)

	< 3 days (n=34)	4-7 days (n=8)	> 1 week (n=5)
Visual improvement	29(85.29%)	2(25%)	1(20%)
Decrease in vision	4(11.76%)	5(62.5%)	2(45%)
Lost follow-up	1(2.945%)	1(12.50%)	2(40%)

(Bacterial keratitis, n=47)

	Fungus	Bacteria
Healed scars	66(74.15%)	37(78.72%)
Adherent leucoma	7(7.86%)	2(8.51%)
Penetrating keratoplasty	3(3.37%)	2(4.25%)
No response/worsening	5(5.61%)	2(4.25%)
Evisceration	3(3.37%)	1(2.12%)
Phthisis bulbi	3(3.37%)	1(2.12%)
Lost follow up	2(2.24%)	2(4.25%)

Table 5: Clinical outcome

The treatment protocol followed in patients with fungal keratitis included topical natamycin 5% eye drops instilled half hourly till the ulcer responds to treatment, followed by hourly instillation till the ulcer starts regressing and topical atropine 1% instilled 6th hourly. Topical fortified Amphotericin B 0.05% eye drops was added in unresponsive cases. Systemic fluconazole 150 mg daily was given to patients with ulcers situated near the limbus and in patients with history of trauma for about 3 weeks along with systemic analgesics.

In patients with bacterial keratitis, the treatment included moxifloxacin 0.5% eye drops instilled half hourly for 6 hours and then hourly for three days and atropine 1% eye drops instilled 6th hourly. Once the keratitis is responding to therapy, topical moxifloxacin dosage was reduced to 6 times a day until the ulcer resolves totally with no positive staining. For all the ulcers situated closer to limbus and secondary to trauma, oral Ciprofloxacin 750 mg BID was given until the ulcer was responsive to treatment. Fortified topical therapy with cefuroxime 5% or vancomycin 5% was given in cases unresponsive to monotherapy. In patients in whom the cultures were negative, depending upon the history, occupation and clinical appearance of the ulcer, we decided the treatment. In most of the patients, we treated them as fungal ulcers. In patients with mixed cultures obtained from the ulcer, we empirically treated the patient with both antifungal and antibacterial drugs.

The patients on treatment reviewed were as follows: 1st day, after 3 days, after 1 week, after 15 days, 1 month and 2 months. The positive response to the treatment is assessed by symptomatic improvement of the patient, reduction in circumciliary congestion, well-defined ulcer margins, reduction in fluorescein staining and reduction in anterior chamber reaction.

DISCUSSION: Microbial keratitis is a leading cause of avoidable blindness in developing nations. It is second to cataract as the commonest cause of visual debility in the world today.

In our study, the incidence of fungal keratitis (65.44%) was more common than bacterial keratitis which was comparable to studies done by Basak et al[11] (49.7%), Krishna et al[12] in Bellary district (63.2%). Incidence of bacterial and fungal keratitis was almost equal in study by Bharathi et al[13] (32.4% bacterial, 34.5% fungal). In other studies by Amrutha et al[14] (67.17% bacterial, 23.57% fungal); Tasanee et al [15] (60% bacterial, 38% fungal) Pervez et al[16] (52% bacterial; 36% fungal); Usha et al[17] (51.9% bacterial, 2% fungal) there was preponderance of bacterial keratitis. The reason for the disparity with other studies could be that our hospital is rurally located and 90% of our patients were from agricultural background. A review of literature shows that there are distinct patterns of geographical variation in the aetiology of suppurative keratitis, the proportion of corneal ulcers increase towards tropical latitude. In tropical countries like South Florida[6] (37%), Bangladesh.[7]

(36%-49%) and South India[8] (31-34%), the incidence of fungal keratitis was reported to be up to 40%. In

temperate countries like UK[9] & US,[10] bacteria were responsible for larger proportion of suppurative keratitis.

In our study in 72 patients (80.98%), trauma was the major predisposing factor for fungal keratitis. This correlates with all the other studies where trauma was the main predisposing factor for fungal keratitis in studies by Bharathi et al[13] (71.5%), Basak et al[11] 82.9%, Tasanee et al[15] 45%, Amrutha et al[14] 77.4%. The most commonly isolated fungus was Fusarium in 21 cases (44.65%), followed by Aspergillus in 13 cases (27.65%). It was similar to the pattern of fungal pathogens reported in other studies like Bharathi et al[13] in Madurai, Amrutha et al[14] and Tasanee et al.[15] This was the common pathogen reported from other tropical countries of South Florida,[16] Ghana, Peruguay, Hongkong[18] and Singapore[19] whereas in the temperate regions of subtropical countries like Nepal,[5] North India and Bangladesh,[6] Aspergillus species was identified. In more temperate climates, corneal ulcers are more frequently associated with Candida species than filamentous fungi. This difference in the prevalence of fungal pathogens can be explained by differences in climate and environment. There was not any climatic influence in the prevalence of bacterial pathogen causing corneal ulcers, whereas geographic variation was seen.

In contrast, the most common risk factor identified for the causation of bacterial keratitis in our study was co-existing ocular disease accounting for 53.19% (25) patients which was similar to other studies by Bharathi et al[13] 68%, Basak et al[11] 82.9%, Pervez et al[16] 44%, Tasanee et al[15] 45%, Amrutha et al[14] 77.14%. The common pre-existing ocular diseases like corneal degeneration, lid disorders, dry eye, conjunctivitis accounted to a major extent in (53.19%) of cases for causation of bacterial keratitis.

Staphylococcus aureus was identified as the predominant bacterial organism in 36.56% of cases. This was the similar to the studies by Krishna et al[12] and Amrutha et al[14] and Basak et al.[11] In a study done by Bharathi et al[13,20] the organism identified was S. pneumoniae. However, in a study by Usha et al,[17] and other studies from USA,[6] Australia[21] S. epidermidis was commonest, S. epidermidis being the commonest commensal of the extraocular surface reported. It is probable that these organisms invade corneal tissues when compromised by antimicrobial or steroid therapy or trauma.

In our study, the incidence of complications in fungal keratitis (34.83%) was higher as compared to bacterial keratitis, the treatment phase was prolonged and the requirement for surgical intervention was higher in fungal keratitis. This correlates with studying done by Usha et al.[17] This study reiterates the fact although both bacterial and fungal keratitis can be treated effectively; the treatment of fungal keratitis definitely poses a challenge.

CONCLUSION: Corneal diseases are an important cause of blindness after cataract and glaucoma in developing countries. Infective keratitis constitutes a very important cause of avoidable blindness; it is essential to impart education to the public regarding importance of eye care.

Misuse of antibiotics and steroids should be avoided. In a country with limited resources and vast population, optimisation of available facilities and prioritisation of health care commitments need to be proportioned rationally. Addressing this problem from the country level is essential. Involving the eye care personnel available in public health centres to identify the disease and timely referral to an ophthalmologist is to be stressed upon to avoid the complication due to delay in treatment and aim for best possible visual and clinical outcome.

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