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RESEARCH ARTICLE

CLINICAL PATTERN OF INFECTIOUS KERATITIS IN A TERTIARY REFERRAL CENTRE

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ABSTRACT

Background: To determine the clinical pattern of infectious keratitis and to identify the organisms responsible for the infection. **Methods and Materials:** All patients with suspected infectious corneal ulceration presenting to the ophthalmology department, Mamata General Hospital, Khammam, were evaluated. Sociodemographic data and information pertaining to risk factors were recorded, all patients were thoroughly examined. Corneal cultures and scrapings were performed for microbiological examination and appropriate treatment was given. **Results:** Out of 234 patients 152(64.95%) were males and 82(35.04%) were females. Among all the patients, bacterial keratitis was found in 89(38.03%), fungal keratitis was seen in 84(35.89%) and mixed in 15(6.41%). The most common predisposing factor for infectious keratitis was trauma 131(55.98%). Greater risk of infectious keratitis was seen among agricultural workers which constituted 120(51.28%) cases. Most common bacterial isolate was *Streptococcus pneumoniae* 41(46.06%) and most common fungal isolate was *Fusarium* 33(39.28%). Most of the bacteria were sensitive to ceftazidime(92.13%), amikacin(92.13%). **Conclusions:** Corneal ulceration is a common problem in our region and most often occurs after a superficial corneal injury with organic material. The most common bacteria isolated were Gram-positives, and they were less resistant to ceftazidime and amikacin.

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INTRODUCTION

Corneal infections can be considered as one of the most significant visual threatening conditions. Corneal infections are the second most common cause of monocular blindness in developing countries.¹ Infections due to invasive pathogens can cause corneal perforations in <24 h.²

Therefore, early treatment to halt the disease process is warranted. Early treatment may also limit the extent of corneal scarring, which can cause loss of vision. While awaiting culture results, aggressive and broad-spectrum therapy with a combination of fortified antimicrobials is usually initiated.³

Empirical therapy is based on the prevalence of microorganisms in the community. The epidemiologic pattern of microbial species that are responsible for infectious keratitis and their sensitivity to different antibiotics and antifungals varies from one geographic region to another.⁴ In the US, the incidence of corneal ulcer is approximately 11.0/100,000 persons/year.⁵ However, in developing countries the incidence is reported to be approximately 799/100,000 persons/year.⁶ In the northern US, Gram-positive organisms are the most common cause of microbial keratitis.⁴ However, there is a

marked predominance of fungal and Gram-negative organisms in the southern States.⁷ The purpose of the present study was to evaluate all the infectious corneal ulcers seen at Mamata General Hospital, Khammam, India. We documented the antecedent factors predisposing to the onset of corneal ulceration and identified the specific organisms responsible for infection and appropriate treatment was given based on culture and sensitivity.

METHODS AND MATERIALS

All patients with infectious corneal ulcers presenting to the ophthalmology department at Mamata General Hospital, Khammam, India were included in the study. Ulceration was defined as a loss of the corneal epithelium with underlying stromal infiltration and suppuration associated with signs of inflammation with or without hypopyon. Mooren's ulcers, marginal ulcers, interstitial keratitis and any ulcers associated with autoimmune conditions were excluded from the study. A standardized form was filled out on each patient documenting sociodemographic information as well as clinical information including duration of symptoms, previous treatment, predisposing ocular conditions, and associated risk factors.

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We have reviewed demographic characteristics, the time between onset of symptoms and admission, duration of admission, history of trauma, contact lens wear, prior history of corneal surgery, history of ophthalmic disease, antibiotic or corticosteroid consumption prior to admission, location, size and depth of the ulcer, height of the hypopyon, uncorrected visual acuity. The location of corneal ulcer was reported as central, if it was dominant in central 5 mm of the cornea, and peripheral, if it was dominant within 3 mm from the limbus.

Scrapings were performed at an operating microscope after instillation of 4% lignocaine (lidocaine) without preservatives. Material from the corneal scraping was also smeared on three separate glass slides: one for Gram stain, one for Giemsa stain, and the third for microscopic examination in the clinic as a KOH wet mount. All KOH smears were then sent to the laboratory for confirmation. Material was obtained from scraping the leading edge and the base of each ulcer was inoculated directly onto sheep's blood agar, chocolate agar, sabouraud dextrose agar (SDA), and into brain heart infusion broth (BHI) without gentamicin sulphate. The results of the smear and culture of the corneal ulcer, and antibiotic sensitivity of the cultured bacteria were recorded.

RESULTS

Out of 234 patients with corneal ulcer 152 (64.95%) were males and 82 (34.04%) were females. The male to female ratio in the present study was 1.85:1. Most of the patients of infectious keratitis presented during 31 to 60 years of life which constituted for about 69.21%. The patients above 80 years of age were least commonly involved (FIG 1).

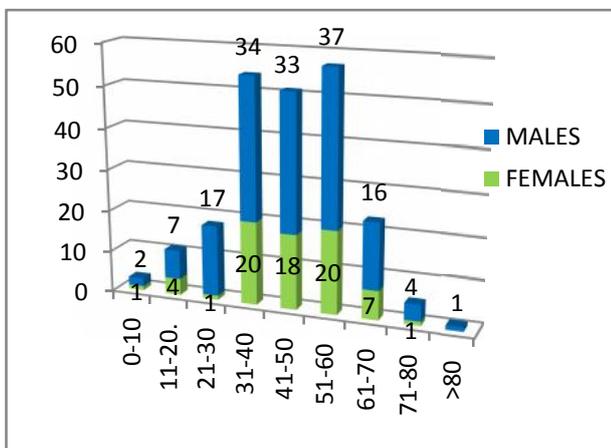


FIG 1 Age And Sex Distribution Of Patients With Corneal Ulcer

In the present study most of the patients with corneal ulcer were agricultural workers, who constituted for 51.10%, followed by housewives 11.53%, labourers 14.10%.

Table 1 Occupation of The Patients With Corneal Ulcer

Occupation	No. Of patients	Percentage
Agricultural workers/farmers	120	51.28%
Housewife	27	11.53%
Labourer	33	14.10%
Tradesman/professionals	22	9.40%
Student	12	5.12%
unemployed	20	8.54%

The students were least affected, who constituted for 5.12% (Table 1). The predominant predisposing factor for infectious keratitis in this study population was trauma which constituted for 55.98%. Other complicating conditions include contact lens wear (5.98%), lagophthalmos (5.12%), diabetes mellitus (3.84%), positive history of herpetic keratitis (3.41%), chronic dacryocystitis (2.56%), dry eye (2.56%), trichiasis (1.70%) and previous corneal scar (1.28%) (Table 2)

Table 2 Predisposing Factors for Corneal Ulcer

Predisposing cause	No. Of patients	Percentage
Trauma	131	55.98%
Foreign body	22	9.40%
Chronic dacryocystitis	06	2.56%
Idiopathic	17	7.26%
Contact lens	14	5.98%
Dry eyes	06	2.56%
Trichiasis	04	1.70%
Lagophthalmos	12	5.12%
Previous history of scar	03	1.28%
Entropion	02	0.85%
Positive H/O herpetic keratitis	08	3.41%
Diabetic mellitus	09	3.84%

Among 153 patients with trauma, paddy or rice stalk was the most common cause which constituted for 26.14%, followed by tree, branch or thorn (18.30%), dust, soil, stone (16.99%), vegetatable matter (15.03%), metallic foreign body (3.92%), animal matter (5.88%), finger nail (3.26%) (Table 3)

Table 3 Nature of Trauma In Patients With Corneal Ulcer

Nature of trauma	No. Of patients	Percentage
Paddy	40	26.14%
Tree, branch or thorn	28	18.30%
Dust, soil, stone	26	16.99%
Vegetative matter*	23	15.03%
Metallic foreign body	06	3.92%
Animal matter ⁺	09	5.88%
Finger nail	05	3.26%
Miscellaneous objects**	06	2.92%
Unknown objects	10	6.53%

*Organic matter, hay, sugar cane, grass, corn stalks, wood, onions, groundnuts, palm leaf

+Cows tail, cow dung, insect

**Metal objects, chemicals, paint, fish nets, broom sticks, cricket balls, cloth etc.

Table 4 Type of Organism Causing Corneal Ulcer

Organism	No of patients	Percentage
No growth	34	14.52%
Bacterial	89	38.03%
Fungal	84	35.89%
Viral	12	05.12%
Mixed*	15	06.41%

*One species of bacteria with one species of fungi

Out of 234 patients with corneal ulcer, cultures were positive in 200 patients. Pure bacterial growth was present in 89 (38.03%), pure fungal growth in 84 (35.89%) and mixed growth was seen in 15 (6.41%)(Table 4). Out of the 89 bacterial organisms cultured 65 (73.03%) were gram positive and 24 (26.96%) were gram negative. Streptococcus pneumoniae was the most commonly isolated bacterial organism representing 41 (46.06%) of all the positive bacterial cultures. The next most commonly isolated gram positive organism was staphylococcus epidermidis with 9 (10.11%) positive cultures. Staphylococcus aureus was cultured from 7 (7.86%) cases and staphylococcus viridians from 4 (4.49%) cases. Pseudomonas spp was isolated from 17 cultures (19.10%) and was the most frequently occurring gram negative organism. Other gram negative organisms cultured included Moroxella spp, Klebsiella spp,

Proteus mirabilis, *Escherichia coli*, *haemophilus influenza* (Table 5).

Table 5 Bacterial Isolates In Patients With Corneal Ulcer

Bacteria	Organism	No. Of patients	Percentage
Gram Positive	<i>Streptococcus pneumoniae</i>	41	46.06%
	<i>Streptococcus epidermidis</i>	09	10.11%
	<i>Streptococcus aureus</i>	07	7.86%
	<i>Streptococcus viridians</i>	04	4.49%
	<i>Bacillus nocardia</i>	01	1.12%
	<i>Pseudomonas</i>	03	3.37%
	<i>Moroxella</i>	17	19.10%
Gram Negative	<i>Proteus</i>	02	2.24%
	<i>Klebsiella</i>	01	1.12%
	<i>Haemophilus influenza</i>	01	1.12%
	<i>Escherichia coli</i>	01	1.12%

Out of the total 84 isolates of fungal organisms, 33 were *Fusarium* spp (39.28%), 23 were *Aspergillus* spp (27.38%). 22 fungal isolates were unidentified. Dematiaceous fungi are pigmented filamentous organisms such as *curvularia* and *cladosporium*. Hyaline fungi, or *moniliaceae*, are non-pigmented filamentous organisms such as *Fusarium* and *Aspergillus* (Table 6).

Table 6 Fungal Isolates In Patients With Corneal Ulcer

Fungal	No. Of patients	Percentage
<i>Aspergillus</i>	23	27.38%
<i>Fusarium</i>	33	39.28%
<i>Curvularia</i>	02	02.38%
<i>Monosporium</i>	01	01.19%
<i>cladosporium</i>	02	02.38%
<i>Candida</i>	01	01.19%
Unidentified	22	26.19%

Bacterial keratitis was treated with fortified cefazolin (5.0%) and gentamicin (1.4%) every minute for 5 minutes and then every 30 minutes for the first day, to be tapered according to clinical response. Once the culture sensitivity reports were obtained, patients were treated based on the antibiotic sensitivity.

Fungal keratitis was treated with one drop natamycin suspension (5%) every 5 minutes for 30 minutes and then every 30 minutes, to be tapered according to clinical response. Epithelium was debrided regularly to increase drug penetration. Oral ketoconazole at a dosage of 200 mg twice daily was added when the ulcer was more than 6 mm in diameter, deeper than the anterior one half of the stroma, or if anterior chamber exudates were present. However, some patients required therapeutic penetrating keratoplasty, cyanoacrylate tissue adhesive and bandage contact lens application, collagen shield or bandage contact lens, tarsorrhaphy and some eventually required evisceration.

In the current study, the antibiogram report indicated that the isolated bacterial species from the corneal ulcers were more sensitive to ceftazidime (92.13%), amikacin (92.13%) followed by cefixime (91.01%). All *P.aeruginosa* isolates were sensitive to ceftazidime (100%) and amikacin (100%). Among the *S. pneumoniae* isolates, 2.44% were resistant to amikacin and cefazolin, all were sensitive to ceftazidime, cefixime and tobramycin (Table 7).

Table 7 Antibiotic resistance of bacterial species isolated from bacterial corneal ulcer

antibiotic	Resistance of all of bacterial species (%)		Resistance to <i>p.aeruginosa</i> (%)		Resistance to <i>s.pneumoniae</i> (%)	
	Positive	Negative	Positive	Negative	Positive	Negative
Cefazolin	37.07%	62.92%	94.11%	5.88%	2.43%	97.56%
Gentamycin	32.58%	67.41%	11.76%	88.23%	73.17%	26.82%
Ciprofloxacin	20.22%	79.77%	5.88%	94.11%	12.19%	87.80%
Vancomycin	13.48%	86.51%	5.88%	94.11%	4.87%	95.12%
Tobramycin	16.85%	83.14%	11.76%	88.23%	-	100%
Cefixime	8.98%	91.01%	11.76%	88.23%	-	100%
amikacin	7.86%	92.13%	-	100%	2.43%	97.56%
ceftazidime	7.86%	92.13%	-	100%	-	100%

DISCUSSION

The prevalence of visual disability from corneal opacity varies from one geographical location to another. The incidence of corneal ulceration in the present study is more than 10 times than that of the population in the USA (11.3 per 10 000) which was similar to the [srinivasan et al study](#)⁸.

In the present study, out of the total 234 patients, 152 (64.95%) were males and 82 (35.04%) were females. The incidence of infectious keratitis in the study was more in males compared to females which was similar to [Srinivasan et al](#)⁸ study which showed male predominance.

The ratio of male to female patients with corneal ulceration is 1.85 to 1, which was in consistent with [Gonzales et al](#) study.⁹ Both sexes tend to develop corneal ulcers in the middle decades of life when presumably they are more physically active and at a higher risk for corneal injury.

Approximately 55.98% of our patients presented with a positive history of ocular trauma. The majority of ulcer patients were agricultural workers, house wives, or labourers (76.96%), an occupation profile similar to Nepal (72%)¹ but in marked contrast with Ghana where only 16.1% of the patients were involved in agricultural activity.¹⁰ Most of the patients in our study were engaged in heavy labour, either in an agricultural setting, in construction, or in physical transport of heavy materials.

Most of the patients in our study were agricultural workers which constituted 51.28% followed by labourers(14.10%), house wives(11.53%), tradesmen(9.40%) which were similar to [srinivasan et al](#) study⁸ where agricultural workers constituted 56.4%. Similar results were seen in [Usha Gopinathan et al](#) study,¹¹ where most of the corneal ulcer patients were agricultural workers.

In the present study, trauma was the most common cause of corneal ulcer (55.98%) followed by corneal foreign body (9.40%), contact lens wearers (5.98%), lagophthalmos(5.12%) and dry eye(2.56%). Similar results were seen in [srinivasan et al](#) study⁸ where corneal ulcer due to trauma was seen in 65.4%. [Di Biseglie et al](#)¹² documented a similar list of predisposing factors in 71 ulcer patients in Africa. Undoubtedly the most common predisposing factor for corneal ulceration in south India was a history of corneal injury. [Thylefors](#)¹³ has observed that in developing countries superficial corneal trauma during agricultural work often leads to rapidly progressing corneal

ulceration and visual loss. In Usha Gopinathan et al study¹¹ trauma constituted for 46.60% of all cases of bacterial corneal ulcer, 81.90% of fungal corneal ulcer and 95.50% of parasitic ulcer. Other important causes for corneal ulcer in Usha Gopinathan et al were prior history of surgery which constituted 22% of cases of bacterial ulcer, 9.5% of fungal corneal ulcer followed by corneal scar and dry eyes.

Trauma was the most common cause of corneal ulcer in the present study, this could be because, that most of the patients attending our hospital were agricultural workers and labourers who work mostly in outdoors, where there are more chances of inflicting trauma. Most of the patients with trauma in the present study developed fungal corneal ulcer which was similar to that of Usha Gopinathan et al study.¹¹ In the present study paddy or rice stalks (26.14%) were the most common cause of trauma followed by tree, branch, thorn or vegetable matter. The results were similar to that of Srinivasan et al study,⁸ where 25% of all patients with a history of trauma implicated paddy as the traumatic object. This was followed by tree branches and thorns, soil and rocks, vegetable matter, animal products, metal objects, and a miscellaneous interesting materials. Paddy is the most common cause of inflicting trauma in the present study, as most of the patients were agricultural workers.

In the present study, culture was negative in 14.52%, whereas culture was positive in 85.45% (bacteria 38.03%, fungi 35.89%, virus 5.12% and mixed 6.41%). Our results were similar to that of Upadhyay et al study¹ where isolation rates were 80% , Dunlop et al study¹⁴ which showed isolation rate of 81.70% and differed from study in Ghana¹⁰ where isolation rates were 57.30% and srinivasan et al study⁸ which showed isolation rates of 68.40%. The higher rates of isolation in our study was due to the fact that most of patients presented directly to the hospital without any prior treatment, because of lack medical facilities in the surrounding area and also due to use of enrichment media for isolation of microbes.

Among all the patients, 89(38.03%) cases showed positive bacterial culture, 84 (35.89%) cases were positive for fungus and 15 cases (6.14%) showed mixed culture. Our results were similar to srinivasan et al study which showed 32.30% positive bacterial culture, 32% positive fungal cultures and 3.40% mixed cultures.

In the present study most common organism causing bacterial corneal ulcer was Streptococcus pneumonia (46.06%). Among the gram negative bacteria causing bacterial corneal ulcer, Pseudomonas aeruginosa was the most common organism isolated (19.10%). Our results were similar to srinivasan et al study⁸, where streptococcus pneumonia was the most common gram positive organism (44.30%) and pseudomonas aeruginosa was the most common gram negative organism (14.40%) isolated whereas in Usha Gopinathan et al study¹¹ staphylococcus epidermidis was the most common organism isolated (32.50%) followed by streptococcus pneumoniae which constituted 13.90% and pseudomonas aeruginosa was the most common gram negative organism (9.70%) isolated. In a recent study conducted by Rahimi et al¹⁵, the most common species isolated was *P. aeruginosa*(24.70%), followed by streptococcus pneumoniae which constituted 20.90%.

Carmichael et al.¹⁶ evaluated a group of African patients and reported *S. pneumonia* was most common and Wong et al.¹⁷ in New Zealand, reported coagulase negative staphylococcus as the most common cause of bacterial corneal ulceration. In the present study *P. aeruginosa* was the most common isolate in patients who were contact lens wearers which was similar to Green et al.study.¹⁸

Among the fungal corneal ulcers, *Fusarium* spp. was the most common organism isolated which constituted (39.28%) followed by *Aspergillus* spp. (27.38%) which was similar to Srinivasan et al study, where *Fusarium* spp. constituted 47.10% of fungal isolates followed by *Aspergillus* spp. (16.10%). This pattern of fungal organisms, dominated by *Fusarium* spp, is similar to the spectrum of microbial keratitis reported from south Florida by Liesegang and Forster¹⁹SRINI and from Ghana by Hagan et al.¹⁰ In south Florida 35% of the isolated organisms were fungi with *Fusarium* spp accounting for 61%. In Ghana fungi alone or in combination with bacteria were isolated from 56% of all culture positive patients. *Fusarium* spp accounted for 52% of all fungal isolates. The climates of south Florida and Ghana are similar in many respects to the climate of south India, which may explain the corresponding pattern of fungal organisms. By contrast, in most of the world *Aspergillus* spp or *Candida* spp are the predominant fungal pathogens responsible for mycotic keratitis.¹⁹ In the temperate climate of Nepal Upadhyay et al¹ found that *Aspergillus* spp accounted for 47% of all fungal pathogens followed by *Candida* spp (13.2%) and *Fusarium* spp (11.7%).

In the current study, the antibiogram report indicated that the isolated bacterial species from the corneal ulcers were more sensitive to ceftazidime (92.13%), amikacin (92.13%) followed by cefixime (91.01%). All *P.aeruginosa* isolates were sensitive to ceftazidime (100%) and amikacin (100%). Among the *S. pneumoniae* isolates, 2.44% were resistant to amikacin and cefazolin, all were sensitive to ceftazidime, cefixime and tobramycin where as in Rahimi et al study¹⁵ the corneal ulcers were less resistant to ceftazidime (6%), amikacin (6%) and all *P.aeruginosa* isolates were sensitive to ceftazidime and amikacin and only 6.7% were resistant to Ciprofloxacin. Among the *S. pneumoniae* isolates, 2.6% were resistant to amikacin, and all were sensitive to cefazolin, ceftazidime, cefixime, and cephalothin.

CONCLUSIONS

This study was developed primarily to determine the specific pathogens responsible for corneal ulceration in Khammam district, India. An attempt was also made to identify the epidemiological characteristics of the population at risk for corneal ulceration as well as those factors which predispose to the development of an ulcer. This knowledge is essential, firstly, to define the magnitude of the problem in terms of health care costs, human costs, and the economic burden of blindness and, secondly, to design an efficient public health programme for the rapid referral, diagnosis, treatment, and ultimately the prevention of corneal ulceration in the population at risk. This approach has important public health implications for the treatment and prevention of corneal ulceration in the developing world.

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