

Study of epidemiological characters, predisposing factors and treatment outcome of corneal ulcer patients

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Abstract

Introduction: Corneal ulcer is one of the common reasons for ophthalmic OPD and IPD visit. It is responsible for vision loss in large number of patients. We have conducted this study to evaluate epidemiological characteristics, predisposing factors and treatment outcome of corneal ulcer patients in tertiary care teaching hospital. **Method:** A prospective study of corneal ulcer patients from Dec 2009 to Nov 2013 was done. Data related to socio-demography, predisposing factors, prior treatment and duration of symptoms were recorded. Ulcer was evaluated by slit lamp examination. Corneal scrapings were subjected to Gram's stain and 10% KOH wet mount. **Results:** 432 eyes were evaluated. 53.9% were between 26-45 yrs. 71.06% eyes presented with vision <3/60. Trauma was commonest factor found in 53.93% patients. On staining 22.9% were having fungal and 64.12% mixed bacterial and fungal infection. Anatomically 34.7% completely recovered leaving scar. 3 eyes were eviscerated, rest not completed treatment. **Conclusion:** Corneal ulcer is common eye problem in developing countries. Most of ulcers were moderate to severe grade. Treatment given on the basis of basic laboratory investigations and clinical features was effective in about 84% of patients. Severe consequences can be prevented by community based awareness.

Keywords – corneal ulcer, evisceration, fungal, scraping, snellen acuity, staining

Introduction

Corneal infection is a major public health problem worldwide & most common cause of monocular corneal blindness.¹ The incidence of ulcerative keratitis varies from 11 per 100000/yr in USA² to 799 per 100000/yr in developing countries.³ Condition is even worse in developing countries not only due to high incidences but also due to late presentation to an ophthalmologist. Availability of investigations like microbiological evaluation and culture sensitivity, necessary for proper management is limited in rural areas. Early diagnosis & rational therapy reduces the dreaded complications of ulcer. Most patients belong to rural areas in developing countries, as agriculture trauma is a leading cause of ulcer. Lack of knowledge of proper use of steroids makes condition even worse.

Purpose of this study is to evaluate the efficacy of management of ulcer on the basis of clinical features and corneal scraping results. It will help medical and

paramedical staff working at rural places to treat ulcer more effectively. Bundelkhand Medical College is situated in central part of Madhya Pradesh serving large rural population surrounding Sagar division and adjacent areas. Most of the patients are from rural areas. In the present study, we have highlighted the demographic pattern, predisposing factors, and status of ulcer at the time of presentation with result of management in uncomplicated cases on the basis of basic laboratory investigation and clinical findings.

Material and Methods

This study was conducted in ophthalmology department of Bundelkhand Medical College Sagar from December 2009 to November 2013. During these four years about 80,000 patients were seen in our department out of which 693 were recorded ulcer patients. We included 432 eyes of 432 patients in our study. Patients with presumed microbial keratitis were included in this study with exclusion criteria of

1. Those with viral keratitis
2. Ulcer with impending or actual perforation
3. Ulcer with near total corneal melting

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4. Ulcer in healing stage with prior treatment
5. Patients not certain of regular follow up
6. Small children in whom proper examination and scraping was not possible without GA.

Study was conducted with the approval of hospital management. Data related to socio demographic features were recorded. History was taken to find out predisposing factors, previous treatment, and duration of symptoms. Presenting visual acuity was recorded at the time of presentation. Patients were evaluated on slit lamp biomicroscope to record size, depth and location of ulcer along with examination of margins, floor and infiltrations. Presence or absence of hypopyon was noted. Examination of ocular adnexa including lids, eyelashes and lacrimal sac area was done. Patency of lacrimal system was checked by syringing. Blood sugar was done to screen diabetes mellitus in every patient.

The scraping of corneal ulcer was then performed and subjected to Gram's stain and 10% KOH wet mount to identify fungus or bacteria.⁵ Pre disposing factors if more than one were included separately. Ulcer was graded as per our criteria in to mild, moderate & severe form.⁶

The therapy was started on the basis of clinical examination & laboratory staining results. For suspected bacterial ulcer, therapy given was ciprofloxacin 0.3% eye drop alone. Combination of fortified cefazoline 5% & gentamicin 1.4% was given in non-responding cases. Oral Ciprofloxacin was added in patients with ulcer near limbus. In the fungal corneal ulcers initial therapy was Natamycin 5% eye drop alone, in ulcers not more than 50% of corneal thickness. Oral ketoconazole tablets 3.3-6.6mg/kg body weight daily were added if deeper infection was present. Fluconazole eye drops were added in to the therapy in non responding cases. Combination therapy including both antibacterial and antifungal were

Results

234(54.2%) patients presenting to our hospital were male with male female ratio of 1.18.

Table No 1: Distribution of patients according to age

Age group of the patient	No. of patients
< 15 yrs	18
16-25 yrs	50
26-35 yrs	123
36-45 yrs	110
46-55 yrs	74
56-65 yrs	41
>65 yrs	16

As per the table depicted 233 (53.9%) patients were in between 26 to 45 years of age. Only 18(4.16%) patients were of pediatric age group (<15years).

given in ulcers with suspected mixed infection, either clinically or on scrapings.

Patients were seen again after 48 hours & response was evaluated on the basis of signs of inflammation & symptomatic relief to the patient. Atropine 1% eye drop three-time daily was given in all patients as supportive therapy. Systemic carbonic anhydrase inhibitor (Acetazolamide) 1.5mg/kg body weight was given to the patients with ulcer extending to the limbus or those in which secondary glaucoma was suspected.

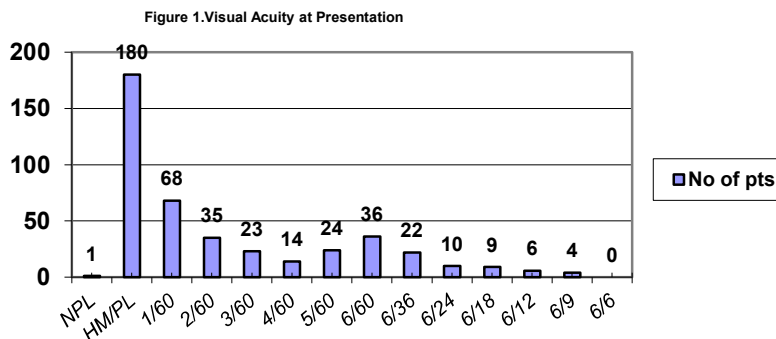
Patients showing improvements were reevaluated after seven days & those who were not showing improvement were admitted to see compliance, re-scraping was done & therapy modified accordingly. Those who came with perforation or impending perforation were treated either by cyanoacrylate glue application or tarsorrhaphy or conjunctival grafting as per indication. We had to eviscerate 3 eyes because of severe progression of ulcer.

First follow up in our study means follow up after one week of initiation of therapy & second follow up was in 2-3 weeks. Status of ulcer was evaluated on each follow up, on the basis of clinical features as whether healing or deteriorated. Visual acuity was recorded & change in visual acuity was noted.

Patients were kept on follow up till complete resolution of ulcer. Antimicrobials were prescribed four times a day after complete healing for one week in bacterial and for two weeks in fungal corneal ulcer to prevent recurrences.

Treatment was considered as successful if final outcome was an inactive corneal opacity and was recorded as complete recovery. Patients, in whom anatomical integrity couldn't be saved, like those who were eviscerated or perforated, were categorized as deteriorated.

307(71.06%) eyes were blind (<3/60) at the time of presentation & 19 (4.39%) had visual acuity more than or equal to 6/18. (Figure 1)



Trauma was the most common predisposing factor, found in 233(53.93%) patients but cause was not identified in 188(43.51%).

Table No 2: Location and size of Ulcer

Location Of Ulcer	No. of patients	Size of Ulcer	No of Patients
Central	90	< 2 mm	22
Paracentral	57	2-5 mm	322
Peripheral	09	> 5 mm	88
Central+ Paracentral	182		
Central+ Paracentral+ Pericentral	76		
Paracentral+Pericentral	18		

On slit lamp biomicroscopy, ulcers were found to be in central & Para central region of cornea in 329(76.15%) patients while in 9(2.1%) patients only peripheral part was involved. In 76 (17.6%) cases ulcer was large enough to involve central, paracentral and peripheral part. 322 (74.53%) ulcers were of size 2-5 mm, 88(20.37%) were of size >5mm and only 22 (5.1%) patients were mild type involving <2mm of cornea (Table No.2)

Table No 3: Depth of Ulcer and Microbial agent

Depth of Ulcer	No. of Patients	Microbial agent	
<20 % of corneal thickness	1	Fungal	99 (22.91%)
20-50%	352	mixed	277 (64.12%)
>50%	79	bacterial	36(8.3%)
		Not known	20(4.6%)

79(18.28%) ulcers were involving more than 50% of corneal thickness, 352(81.48%) involving superficial stroma & only 1 was epithelial ulcer. On corneal scraping, 99 (22.91%) were pure fungal ulcers & 277 (64.12%) were fungal ulcers having co-infection with bacteria while only bacteria was identified in 36(8.3%) patients. (Table 3)

Table No 4: Status of Ulcer on follow-up

Status of Ulcer	First follow-up	Second follow-up
Healing	281	195
No change	48	16
Progressed	8	14
Perforated	2	10
No follow-up	93	104

339(78.47%) patients came for 1st follow up. 281(82.9%) were in healing stage. 10(2.94%) were deteriorating out of which 2 cases i.e. 0.59% were perforated.

Table No 5: Change in visual acuity on follow-up

Change in visual acuity	First follow-up	Second follow-up
Improved	118	155
Deteriorated	17	28
No change	204	52
No follow-up	93	104

118(34.8%) had shown improvement on snellen acuity, while 17(5.01%) patient's visual acuity decreased compared to their acuity at the time of presentation. In rest of the 204(47.22%) patients there was no change in visual acuity.

Out of 339 patients who came for 1st follow up, 235 (69.3%) came for subsequent follow-ups. In these patients 195(82.97 %) were healing and 24(10.2%) were deteriorating clinically in which 10(4.2%) were perforated.

Anatomically, 150(34.7%) patients recovered completely leaving a corneal scar only. 3 (0.6%) eyes were eviscerated. Rest of the patients stopped follow ups before completion of treatment.

Discussion

Infective keratitis is a major public health problem in developing countries.^{7,8} If not diagnosed early and treated effectively may lead to loss of not only sight but even eye too. The spectrum of corneal ulcer presentation worldwide has large variations & this is especially due to difference in geographical & socio economic structures. Occurrence of corneal ulcer is significantly associated with lower socio economic status.⁹

Highest number of patients presenting to our hospital were between 26 to 45 years of age.

This is socio economically active age group. Morbidity of these people affects whole of the family. Most of them are agriculture worker as this is the commonest occupation of rural population in developing countries. This explains why agriculture trauma is the leading predisposing factor of corneal ulcer in developing countries.¹⁰

This is in concurrence with that of Panda et al¹⁰ and other studies^{3, 4, 11} where non-surgical trauma is found to be the leading cause of corneal ulcer. We had 43.5% patients in which cause was unidentified. This is a large number and certainly needs improvement in our work-up system.

Schaefer et al have identified co existing ocular diseases as a major pre disposing factor¹² but in our study only one percent ulcers had concurrent ocular diseases. Bourcier et al found contact lenses as major risk factor, which is less in this part of world.¹³

Male preponderance is 1.18 that of female. Male predominance is found in many studies^{4,14}, some has found it in ratio as high as 1.6. This may be because males are more involved in outdoor activities and also males are preferred over females to seek medical advice.

Most of the ulcer presenting to us are of severe grade and late presentation is mainly responsible for this. Majority of patients coming to our hospital are from nearby rural places. Most of them take initial treatment from local practitioner including paramedical and medical personnel, relatives, traditional healer and even directly from drug stores. Patient's accessibility to eye care services is the main barrier for early consultation followed by cost, social belief, and ignorance about the disease. 23.8% patients were on steroid therapy at initial presentation. Topical steroids could have suppressed the inflammation so that patient might have been less symptomatic¹⁵ & thus presenting late to the ophthalmologist. Steroids also predispose to fungal keratitis. More than 2/3rd of the patients had vision <3/60 in affected eye at initial presentation. Similar results were noted in other studies¹⁰

Large numbers of fungal infection were found in our hospital, which was higher than that found in other studies.^{4, 16, 17} Agriculture trauma is responsible in our study. Similar results are also seen in other studies^{3, 4,11}. Many of the patients were using either corticosteroid (23.8%) or some unidentified drops (40.3%) before coming to this hospital and association of fungal keratitis with use of corticosteroid and diabetes mellitus has been reported earlier.^{18, 19}

Percentage of mixed bacterial and fungal infection is also high. About 65% of fungal infections are having co-infection with the bacteria. Recent studies found bacteria in 5% to 25% of keratomycosis.^{4, 20-23} But other laboratories in Asia and South America have isolated bacteria in approximately 30% to 60% of corneal specimen during fungal keratitis.^{3, 24, 25} This diverse prevalence estimate may indicate non-conformity in distinguishing microbial co-infection, and dual infections,

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but could be due to differences in risk factors, climate & access to care also. The detection of fungal filaments in 10% KOH mount has 90-99% sensitivity.^{16, 26} While sensitivity & specificity of bacterial detection in Gram's stain is inferior to that of culture method.²⁷ Sensitivity of Gram stain in detection of bacteria was 36.0% in early and 40.9% in advanced keratitis cases, however specificity is higher (84.9% and 87.1% respectively).⁵ This could also be a reason for less bacterial detection in our series.

Microbiological work-up is now recommended in all suspected cases of microbial keratitis and its importance is proved in many studies, but most general ophthalmologists do not practice the recommendations.²⁸ In a study only 10% ophthalmologists were found to have the facility of Gram stain and only 14.5% of all ulcers were examined with scraping for Gram stain and culture.²⁸ A survey in United States had revealed that commonly practitioners start empirical treatment with antimicrobials for ulcers and microbiological evaluation is done only in non-responding cases.²⁸

This practice can be applied if bacterial infection is the dominating cause of ulcer but places like India and other countries where fungal ulcers are more common^{4,16,17} this approach is not recommended. Jones DB's suggestions of initial therapeutic treatment on the basis of corneal smear, clinical features and severity of keratitis²⁹ are very much applicable in areas with high prevalence of fungal corneal infections.

To grade the ulcer prior to its management is an important parameter, as severe ulcer requires closer observation. 20.4% ulcers were more than 5mm size and, 18.3% were having ulcer of depth more than 50%. 76% of ulcer were involving central part of cornea. Other studies¹⁰ have found a large percentage of severe grades of ulcer.

Treatment was given as Netamycin³⁰ drops & systemic ketoconazole in deeper penetration of suspected fungal corneal ulcers. Suspected bacterial ulcers were treated with either ciprofloxacin eye drops or combination fortified cefazoline & gentamicin eye drops³¹⁻³³.

We had 12 perforations during our study, reasons could be poor patient compliance or resistant cases, but possibility of prolong use of topical fluoroquinolones being responsible for this hazard cannot be ruled out and causes other than fungal and bacteria can also be responsible for non healing ulcers

Major limitation of this study is that we had to exclude large number of patients attending the OPD. About 40%

of total ulcer patients were excluded. Follow up rate was also not encouraging as only 2/3rd patients came for follow-up, but 82% follow up were clinically in healing stage. Though 34.1% were still with poor vision but 65.9% had improvement in snellen's acuity. Less follow up may be because most patients coming to our hospital are poor and coming from far places. That's why only 35.4% had actually completed the therapy; rest had stopped follow-ups before completion of therapy.

Conclusion

In summary our study highlights that corneal ulcer in this part of the world is a major eye problem. Incidence can be reduced, if the predisposing factors can be controlled³⁴. If treatment starts at early stage then basic laboratory investigations & knowledge of clinical features is very helpful in effective management of corneal ulcers.

Topical fluoroquinolones & Natamycin supported with fortified cefazoline & gentamicin & Fluconazole are effective in uncomplicated cases. So the prevention of predisposing factors, appropriated diagnosis at early stage & proper medical management can help greatly in handling microbial keratitis properly.

Local paramedical and medical people if trained to manage ulcer with the use of this knowledge than we can manage them effectively at an early stage. A community based awareness program regarding risk factors like trauma to eye and use of medications without proper prescription may create a difference in over all scenario of ulcer presentation.

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References

1. Chirambo MC, Tielsch JM, West KP, Katz J. Blindness and visual impairment in southern malwai. WHO bull 1986; 64(4); 576-82.
2. Erie JC, Nevitt MP, Hodge DO, Ballard DJ. Incidence of ulcerative keratitis in a defined population from 1950 through 1988. Arch ophthalmol 1993, 111(12); 1665-71.
3. Upadhyay M, Karmacharya PC, Koirala S, Shah DN, Shakya S, Shrestha JK, Bajracharya H, Gurung CK, Whitcher JP. The Bhaktapur eye study: ocular trauma and antibiotic prophylaxis for prevention of corneal ulceration in Nepal. Br J Ophthalmol 2001;85(4);388-92.

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4. Srinivasan M, Gonzales CA, George C, Cevallos V, Mascarenhas JM, Asokan B. Epidemiology & aetiological diagnosis of corneal ulceration in madurai. *Br J ophthalmol* 1997; 81(11):965-71.
5. Sharma S, Kunimoto DY, Gopinathan U, Athmanathan S, Garg P, Rao GN. Evaluation of corneal scraping smear examination methods in diagnosis of bacterial and fungal keratitis :A survey of eight year of laboratory experience. *Cornea* 2002;21(7):643-7.
6. Gregory S, Ogawa & Rober A, Hyndiuk in "The Cornea" by Smolin & Theoft, 3rd edition; 128
7. Bharathi M, Ramakrishnan R, Vasu S. Epidemiology of bacterial keratitis in a referral centre in south India. *Indian J Ophthalmol.* 2003;21(4):239-245.
8. Goonawardana S, Ranasinghe K, Arseculeretnae S, et al. Survey of mycotic and bacterial keratitis in Sri Lanka. *Mycopathologia* 1994; 127:77-81
9. Vajpayee RB, Ray M, Panda A, Sharma N, Taylor HR, Murthy GV, Satpathy G, Pandey RM. Risk factors for paediatric presumed microbial keratitis: a case control study. *Cornea* 1999;18(5):565-9.
10. Panda A, Satpathy G, Nayak N, Kumar S, Kumar A. Demographic pattern, predisposing factors and management of ulcerative keratitis: evaluation of thousand cases at a tertiary care centre. *Clinical and experimental ophthalmol* 2007;35(1):44-49.
11. Thylefors B. Epidemiological pattern of ocular of ocular trauma. *Aust NZ J ophthalmol* 1992(2); 20:95-98
12. Schaefer F, Bruttin O, Zografos L, Guex-Crosier Y. Bacterial keratitis: A prospective clinical and microbiological study. *Br J Ophthalmol* 2001;85:842-47.
13. Boucier T, Thomas F, Borderie V, Chaumeil C, Laroche L. Bacterial Keratitis :Predisposing factors, clinical and Microbiological review of 300 cases. *Br J Ophthalmol* 2003; 87(7):430-6.
14. Gonxales CA, Srinivasan M, Whitcher JP, Smolin G. Incidence of corneal ulceration in maduari. *Ophthalmic epidemiol* 1996; 3(3):159-66.
15. Wilhelmus KR. Indecision about corticosteroids for bacterial keratitis; an evidence-based update. *Ophthalmology* 2002; 109(5):835-42.
16. Bharathi M, Ramakrishnan R, Vasu S, Meenakshi R, Palaniappan R. Epidemiological characteristics and laboratory diagnosis of fungal keratitis: A three year study 2003; *IJO* : 51(4), 315-321.
17. Chander J, Sharma A. Prevalence of fungal corneal ulcer in northern India. *Infection* 1994; 22(3):207-209.
18. Gopinathan U, Garg P, Fernandes M, Sharma S, Atmanathan S, Rao GN. The epidemiological features and laboratory results of fungal keratitis: a ten year review in a referral eye care centre in south India. *Cornea* 2002;21(6) :555-59.
19. Agrawal PK, Roy P, Das A, Banerjee A, Maity PK, Banerjee AR; Efficacy of systemic and topical Itraconazole as a broad spectrum anti fungal agent in mycotic corneal ulcer. A preliminary study. *Indian J Ophthalmol.* 2001; 49(3):173-76.
20. Leck AK, Thomas PA, Hagan M, Kalamurthy J, Ackuaku E, John M, et al. Etiology of suppurative corneal ulcer in Ghana and South India, and epidemiology of fungal keratitis. *Br J Ophthalmol* 2002;88(11):1211-15.
21. Satpathy G, Vishalakshi P. Ulcerative keratitis: Microbial profile and sensitivity pattern-a five year study. *Ann Ophthalmol* 1995:27;301-6.
22. Basak SK, Bask S, Mohanta A, Bhowmick A. Epidemiological and microbiological diagnosis of suppurative keratitis in Gangetic West Bengal, eastern India. *Indian J ophthalmol* 2005:53(1);17-22.
23. Choudhary A, Singh K. Spectrum of fungal keratitis in northern India. *Cornea* 2005:24(1);8-15.
24. Laspina F, Samudio M, Cibils D, TaCN, Farina N, Sanabria R, Klauss V, Mino de Kaspar H. Epidemiological Characteristic of microbiological results on patients with infectious corneal ulcer: a 13 years survey in Paraguay; *Grafes Arch clin exp ophthalmol* 2004;242 (3) :204-9.
25. Khanal B, Deb M, Panda A, Sethi HS. Laboratory diagnosis in ulcerative keratitis; *Ophthalmic Ref* 2005; 37(3):123-7.

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26. Vajpayee RB, Angra SK, Sandramouli S, Honavar SG, Chhabra VK. Laboratory diagnosis of keratomycosis: Comparative evaluation of direct Microscopy and culture results. *Ann Ophthalmol* 1993;25(2):68-71
27. Wahl J, Katz, H and Abrams D. Infectious Keratitis in Baltimore. *Ann Ophthalmol*, 23(6):234, 1991.
28. McDonnell P, Nobel J, Gauderman W, Lee P, Aiello A, Trousdale M. Community care of corneal ulcers. *Am J Ophthalmol* 1992;114(5):531-8.
29. Jones DB. Decision-making in the Management of microbial keratitis. *Ophthalmology* 1981; 88(8):814-20
30. O'Day D. Selection of appropriate antifungal therapy. *Cornea* 1987;6(4); 238-45.
31. O'Brien TP, Maguire MG, Fink NE, Alfonso E, McDonnell P. Efficacy of Ofloxacin vs Cefazoline and tobramycin in the therapy of bacterial keratitis report from the bacterial keratitis study group. *Arch Ophthalmol*. 1995; 113(10):1257-1265.
32. Prajna NV, George C, Selvaraj S, Lu KL, McDonnell PJ, Srinivasan M. Bacteriological and clinical efficacy, Ofloxacin 0.3% versus Ciprofloxacin 0.3% ophthalmic solution in treatment of patients with culture positive Bacterial keratitis. *Cornea* 2001;20(2); 175-8.
33. Morlet N, Daniell M. Microbial keratitis: What the preferred initial therapy? View- 2: Empirical fluoroquinolone therapy is sufficient initial treatment. *Br J Ophthalmol* 2003;87(9);1169-72.
34. Getshen K, Srinivasan M, Upadhyay M, Priyadarsini B, Mahalaksmi R, Whitcher JP. Corneal ulceration in South East Asia. A model for the prevention of bacterial ulcers at the village level in rural Bhutan. *Br J Ophthalmol* 2006; 90(3):276-8.

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