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Original Research Article

Bacterial Corneal Ulcer and Drug Sensitivity

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Abstract

Aim: The aim of the present study was to determine predisposing factors, common bacterial causes, and antibiotic sensitivity of corneal ulcers

Material & Methods: A cross-sectional observational study was carried out on 100 at Patna Medical College & Hospital, Patna, during the period of 2 years from 2012-2014. Ethical approval was obtained from the Ethical Committee of Institution. The study adhered to the tenets of the Helsinki Declaration. Consecutive patients who consented and satisfied the inclusion criteria for corneal ulcer were recruited till the required sample size was obtained.

Results: In the present study, 75% were male as compared to females. Most of the patients belonged to 31-40 years age group. 55% were having agriculture occupation and 75% were illiterate. 30% had corneal infection due to trauma. The main symptoms associated with corneal ulcer were pain (91%), red eye (81%), and decreased vision (65%). All patients had stromal infiltrate and 41% had hypopyon at presentation. Of the 100 samples investigated, 50% (50/100) were positive for etiology in both microscopy and culture, indicating that smear microscopy was highly predictive of culture positivity. Among the 50 (50%) positive samples, bacterial isolates were recovered in 60% and fungal isolates in 40% of the cases. S. pneumoniae (15/50) was the most commonly isolated bacteria followed by viridians group streptococci. Nocardia species and Bacillus species was also detected. Fusarium species were the most commonly isolated fungus followed by Aspergillus flavus and unidentified dematiaceous fungus, Curvularia, Bipolaris species and Exserohilum species.

Conclusion: Bacterial corneal ulcer is showing an increasing trend in our society. Causative bacteria are showing resistance to the available drugs. Farm workers are found to be more prone to corneal ulcer development. Besides this, children from rural background are also susceptible to corneal ulcer development. Radical environmental changes and indiscriminate use of drugs have been linked to the occurrence of resistance among bacteria.

Keywords: Antibiotic Sensitivity, Bacterial Organism, Corneal Ulcer.

Introduction

Corneal ulcer is a serious vision threatening inflammation of the cornea involving disruption of its epithelium layers along with involvement of the stroma of corneal, is one of the main causes of monocular blindness after cataract in several of the developing countries in Africa, Asia and the Middle East. [1,2,3] It can be caused by several bacteria agglutinating to the corneal epithelium that has lost its integrity after trauma. Very few bacteria (listeria, haemophilus, neisseria, gonorrhea and corynebacterium diphtheriae) may in grow the intact corneal epithelium and cause an infective ulcer. [4,5,6,7] The annual incidence of corneal ulcers is estimated to be 10 more times in developing countries compared with developed countries. [8,9] It is a sight threatening disorder that affects both males and females across all age groups worldwide. Inappropriate contact lens use is often incriminated, as 62,7% of the young corneal ulcer patients are contact lens users. Other factors that may favor the creation of an ulcer include: older age, generally pathologic ophthalmic surface, chronic steroid use (28,6%), systemic disease (36.4%), chronic blepharitis (20,8%), previous ophthalmic surgery (33,8%)and herpetic keratitis (28,85%). Prognosis is worse in older patients, in diabetic patients and in Gram-bacterial infection. [10]

Antibiotics are preferentially used in cases of bacterial corneal ulcers, but in most of the instances, it is used empirically which may lead to resistant mutants with consequent treatment failure. [11] The common management approach if bacterial infection is suspected is to collect specimen of corneal tissue for culture and subsequently to initiate antibiotics therapeutic

options empirically. [12] The clinical outcome in corneal ulcer is possible to be dependent on the infecting bacteria virulence, host factors including the host's immune system or the presence of ocular surface disorder, as well as the minimum inhibitory concentration (MIC) of the antibiotic against the bacteria. [13] Drug resistance poses a major challenge to the management of various infection disease, and corneal ulcer is not an exception. [14] Corneal ulcer is an ophthalmic condition requiring prompt medical attention. Thus, precise knowledge of the causative agents and their susceptibility patterns is important for deciding the proper course of treatment.

Hence the aim of study was to determine predisposing factors, common bacterial causes, and antibiotic sensitivity of corneal ulcers in bihar region.

Material & Methods

A cross-sectional observational study was carried out on 100 at Patna Medical College & Hospital, Patna, during the period of 2 years from 2012-2014. Ethical approval was obtained from the Ethical Committee of Institution. The study adhered to the tenets of the Helsinki Declaration. Consecutive patients who consented and satisfied the inclusion criteria for corneal ulcer were recruited till the required sample size was obtained.

Inclusion Criteria

- Patients with corneal ulcers in one or both eyes aged 12 years and above who would cooperate in obtaining corneal scrapping met the inclusion criteria.

Exclusion Criteria

- Patients with chemical burns-related corneal ulcers, suspected viral ulcers, noninfective traumatic corneal ulcers that presented <12 h and aged younger than 12 years were excluded from the study.

Methodology

Written informed consent/assent was obtained from each participant. Necessary information was obtained from each participant using interviewer-administered structured questionnaire. This consists of interview section to obtain information on relevant clinical, sociodemographic data, duration of symptoms, risk factors, and drug history. History of symptoms such as ocular pain, sensitivity to light, decrease vision, redness, tearing, eye discharge, and ocular discomfort among others. Examination of the patient includes visual acuity test with Snellen's acuity chart, or E-chart, as the case may be. The eye was stained with rose Bengal strip (1.5 mg) and examined with slit lamp (Keeler SL 16, Manufactured by CSO Italy), followed by fluorescein strip (1 mg) stain. Slit-lamp bio-microscopical examination was performed on every patient to characterize the ulcer such as the location of ulcer, presence of satellite lesions, margins of the ulcer, presence of foreign body on the ulcer, presence of pigments, stromal infiltrations, and surrounding inflammation with or without hypopyon.

The procedure was performed under slit-lamp magnification with aseptic precautions. Lid speculum (Barraquer) was used to expose the globe after instillation of preservative containing amethocaine eye drop (0.5%). Using a sterile 23-gauge bent needle, three corneal scrapings and in some cases corneal swabs were obtained gently from the base and peripheral margins of the ulcer with great care avoiding contamination from lashes or the eyelid.

Corneal scrapings from the ulcer were directly and immediately inoculated onto separate solid culture media plates including blood agar, MacConkey agar, and chocolate agar. The inoculation was done in C-shaped streaks pattern ensuring localization of inoculation site of the scraped material on the culture medium.

Inoculated culture medium plates were taken to the microbiology laboratory within 30 min, for Gram staining and microscopy (LEICA Microscope, Model DM 500), culture, and sensitivity test. Samples were incubated in Chocolate agar plate at 35°C–37°C in carbon dioxide atmosphere. Blood agar and MacConkey's agar were incubated aerobically. Culture was examined after 18–24 h. Isolated colonies were identified macroscopically to describe colony appearance. A part of the colonies were used to make smears, which were air-dried, fixed, and Gram stained for microscopic examination. The result is considered positive when an organism is isolated on culture media. Culture plates were discarded after 48 h in the absence of any growth.

Antibiotic sensitivity test on different antibiograms was done using modified Kirby–Bauer technique by disc diffusion method for the bacterial isolates determining its sensitivity or resistance to relevant antibiotics. Results were interpreted based on the Clinical and Laboratory Standard Institute guidelines.

Statistic Al Analysis

Data analysis was done using a computer-based Statistical Package for the Social Sciences version 16.0 (SPSS Inc, Chicago, IL). The qualitative variables were presented as bar charts, pie charts, and percentages. The nonparametric test Chi-square was used appropriately to compare proportions. A

confidence interval of 95% was used and a $P \leq 0.05$ was considered statistically significant

Results

Table 1: Demographic factors and clinical presentations of corneal ulcers

Variables	N	%
Gender		
Male	75	75
Female	25	25
Age in years		
<10	5	5
11-20	4	4
21-30	12	12
31-40	20	20
41-50	12	12
51-60	25	25
61-70	15	15
71-80	4	4
>80	3	3
Occupation		
Agriculture	55	55
Others	45	45
Trauma		
Yes	30	30
No	70	70
Education Level		
Literate	25	25
Illiterate	75	75

In the present study, 75% were male as compared to females. Most of the patients belonged to 31-40 years age group. 55% were having agriculture occupation and 75% were illiterate. 30% had corneal infection due to trauma.

Table 2: Symptoms and Signs

Symptoms	N	%
Pain	91	91
Red eye	81	81
Decreased vision	65	65
Foreign body sensation	34	34
Discharge	24	24
Tearing	15	15
Photophobia/ sensitive to light	7	7
Swelling	5	5
Whitish discoloration of the eye	3	3
Signs Stromal infiltrate		
Epithelial defect	78	78
Hypopyon	41	41
Anterior chamber inflammation	15	15
Foreign body	3	3
Corneal rupture	3	3
Hyphema	3	3
Descemetocele	2	2

The main symptoms associated with corneal ulcer were pain (91%), red eye (81%), and decreased vision (65%). All patients had stromal infiltrate and 41% had hypopyon at presentation.

Table 3: Corneal ulcer microbial isolates

		N
Bacterial corneal ulcer N=30	Bacillus species	3
	Nocardia species	3
	Enterobacter cloacae	1
	Pseudomonas aeruginosa	1
	Staphylococcus aureus	4
	Streptococcus pneumonia	15
	Viridians group of streptococci	3
Fungal corneal ulcer N=20	Aspergillus flavus	5
	Bipolaris species	1
	Curvularia species	2
	Exserohilum species	1
	Fusarium species	6
	Unidentified dematiaceous fungi	5

Of the 100 samples investigated, 50% (50/100) were positive for etiology in both microscopy and culture, indicating that smear microscopy was highly predictive of culture positivity. Among the 50 (50%) positive samples, bacterial isolates were recovered in 60% and fungal isolates in 40% of the cases. S. pneumoniae (15/50) was the most commonly isolated bacteria followed by viridians group streptococci. Nocardia species and Bacillus species was also detected. Fusarium species were the most commonly isolated fungus followed by Aspergillus flavus and unidentified dematiaceous fungus, Curvularia, Bipolaris species and Exserohilum species.

Table 4: Antibiotic susceptibility pattern of bacterial isolates

Organisms	**Antibiotics Used**	**Susceptible Patterns**		
		Susceptible	**Intermediate**	**Resistant**
Streptococcus pneumoniae N=15	Azithromycin	15	0	0
	Ceftazidime	15	0	0
	Chloramphenicol	15	0	0
	Ciprofloxacin	15	0	0
	Moxifloxacin	15	0	0
	Ofloxacin	15	0	0
Viridians group of streptococci N=3	Azithromycin	3	0	0
	Ceftazidime	3	0	0
	Chloramphenicol	3	0	0
	Ciprofloxacin	3	0	0
	Moxifloxacin	3	0	0
	Ofloxacin	3	0	0
Staphylococcus aureus N=4	Amikacin	4	0	0
	Ceftazidime	4	0	0
	Chloramphenicol	0	0	4
	Ciprofloxacin	0	4	0
	Moxifloxacin	4	0	0
	Ofloxacin	4	0	0
Bacillus species N=3	Amikacin	3	0	0
	Azithromycin	1	0	2
	Chloramphenicol	1	0	2
	Ciprofloxacin	3	0	0
	Moxifloxacin	3	0	0
	Ofloxacin	3	0	0
Nocardia species N=3	Amikacin	3	0	0
	Azithromycin	1	0	2
	Chloramphenicol	3	0	0
	Ciprofloxacin	1	0	2
	Moxifloxacin	3	0	0

	Ofloxacin	1	0	2
Pseudomonas aeruginosa N=1	Amikacin	1	0	0
	Ceftazidime	0	0	1
	Chloramphenicol	0	0	1
	Ciprofloxacin	1	0	0
	Moxifloxacin	1	0	0
	Ofloxacin	1	0	0

Among the eight different antibiotics used against the bacterial isolates, moxifloxacin showed 100% susceptibility followed by ofloxacin 92% and ciprofloxacin 88%. Both S. pneumoniae and viridians group of streptococci were 100% susceptible to all of the antibiotics used. Nocardia species were 66.67% resistant to azithromycin, ciprofloxacin and ofloxacin but 100% susceptible to amikacin, chloramphenicol and moxifloxacin. Although P. aeruginosa were sensitive to amikacin, ciprofloxacin, moxifloxacin and ofloxacin, they were resistant against ceftazidime, chloramphenicol and tetracycline.

Discussion

Bacterial keratitis is a potentially devastating corneal infection due to the possibility of rapid progression; corneal destruction may be complete in 24–48 hours with some of the more virulent bacterial aetiological agents. The spectrum of bacterial corneal pathogens is largely dictated by the local microbial flora and also by geographic and climatic factors; these probably account for disparate rates of various pathogens reported in

series from different localities. [15,16] Species of high virulence, such as Staphylococcus aureus, Streptococcus pneumoniae, Pseudomonas aeruginosa, and even Neisseria meningitidis, have been reported. [17]

In the present study, 75% were male as compared to females. Most of the patients belonged to 31-40 years age group. 55% were having agriculture occupation and 75% were illiterate. 30% had corneal infection due to trauma. Similar to other studies [18,19] infected corneal ulcers were more common in males and trauma was the most common risk factor. The main symptoms associated with corneal ulcer were pain (91%), red eye (81%), and decreased vision (65%). All patients had stromal infiltrate and 41% had hypopyon at presentation. 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. Nonetheless, the inconsistency in prevalence and causes of corneal blindness across geography and ethnic groups make it challenging to administer a standard set of protocols in order to lower the incidence of corneal ulcer. [20]

Of the 100 samples investigated, 50% (50/100) were positive for etiology in both microscopy and culture, indicating that smear microscopy was highly predictive of culture positivity. Among the 50 (50%) positive samples, bacterial isolates were recovered in 60% and fungal isolates in 40% of the cases. S. pneumoniae (15/50) was the most commonly isolated bacteria followed by viridians group streptococci which were in harmony with the findings of similar studies conducted. [15,21] Nocardia species and Bacillus species was also detected. Fusarium species were the most commonly isolated fungus followed by Aspergillus flavus and unidentified dematiaceous fungus, Curvularia, Bipolaris species and Exserohilum species.

In the view of frequent reports of changing pattern of susceptibility among the bacteria, testing of clinical isolates for their susceptibility to antimicrobial drugs is necessary for selection of appropriate antibiotics or for changing an already administered drug. In this study, the isolated bacteria were tested against eight different antibiotics in the laboratory as recommended by CLSI. [22] All the bacterial isolates (Gram positive and negative) were 100% susceptible to fourth generation quinolone antibiotic moxifloxacin, the drug of choice for bacteria incriminated with ophthalmic problems. Among the eight different antibiotics used against the bacterial isolates, moxifloxacin showed 100% susceptibility followed by ofloxacin 92% and ciprofloxacin 88%. Both S. pneumoniae and viridians group of streptococci were 100% susceptible to all of the antibiotics used. Nocardia species were 66.67% resistant to azithromycin, ciprofloxacin and ofloxacin but 100% susceptible to amikacin, chloramphenicol and moxifloxacin. Although P. aeruginosa were sensitive to amikacin, ciprofloxacin, moxifloxacin and ofloxacin, they were resistant against ceftazidime, chloramphenicol and tetracycline.

Conclusion

Bacterial corneal ulcer is showing an increasing trend in our society. Causative bacteria are showing resistance to the available drugs. Farm workers are found to be more prone to corneal ulcer development. Besides this, children from rural background are also susceptible to corneal ulcer development. Radical environmental changes and indiscriminate use of drugs have been linked to the

occurrence of resistance among bacteria. Hence, a further study with larger sample size to look at the predictability of predisposing factors as well as the determination of susceptibility pattern of antifungal agents would be clinically valuable.

References

1. Green M, Apel A, Stapleton F. Risk factors and causative organisms in microbial keratitis. Cornea. 2008 Jan 1;27(1):22-7.
2. Jp W. Corneal blindness: a grobal perspective. Bull World Health Organ. 2001;79:214-21.
3. Bhadange Y, Sharma S, Das S, Sahu SK. Role of liquid culture media in the laboratory diagnosis of microbial keratitis. American Journal of Ophthalmology. 2013 Oct 1;156(4): 745-51.
4. Ly CN, Pham JN, Badenoch PR, Bell SM, Hawkins G, Rafferty DL, McClellan KA. Bacteria commonly isolated from keratitis specimens retain antibiotic susceptibility to fluoroquinolones and gentamicin plus cephalothin. Clinical & experimental ophthalmology. 2006 Jan;34(1):44-50.
5. Mah-Sadorra JH, Yavuz SG, Najjar DM, Laibson PR, Rapuano CJ, Cohen EJ. Trends in contact lens–related corneal ulcers. Cornea. 20 05 Jan 1;24(1):51-8.
6. Bourcier T, Thomas F, Borderie V, Chaumeil C, Laroche L. Bacterial keratitis: predisposing factors, clinical and microbiological review of 300 cases. British Journal of Ophthalmology. 2003 Jul 1;87(7):834-8.
7. Ibrahim YW, Boase DL, Cree IA. Epidemiological characteristics, predisposing factors and microbiological profiles of infectious corneal ulcers: the Portsmouth corneal ulcer study. British Journal of Ophthalmology. 2009 Oct 1;93(10):1319-24.
8. Erie JC, Nevitt MP, Hodge DO, et al. Incidence of ulcerative keratitis in a defined population from 1950 through 1988. Arch Ophthalmol Chic Ill 1960 1993; 111:1665–71.
9. Gonzales CA, Srinivasan M, Whitcher JP, et al. Incidence of corneal ulceration in Madurai district, South India. Ophthalmic Epidemiol 1996; 3:159–66.
10. Terzidou C, Dalianis G, Brozou CG, Marmaras N, Golegou S. Corneal Ulcer: Analysis of Isolated Bacteria and Antibiotics Sensitivity in the Urban Region of Attica, Greece. Adv Ophthalmol Vis Syst. 2016;5(3):00155.
11. Akter L, Salam MA, Hasan B, Begum N, Ahmed I. Etiological agents of suppurative corneal ulcer: Study of 56 cases. Bangladesh Journal of Medical Microbiology. 2009;3(2): 33-6.
12. Rodman RC, Spisak S, Sugar A, Meyer RF, Soong HK, Musch DC. The utility of culturing corneal ulcers in a tertiary referral center versus a general ophthalmology clinic. Oph - thalmology. 1997 Nov 1;104(11):1897-901.
13. Kaye S, Tuft S, Neal T, Tole D, Leeming J, Figueiredo F, Armstrong M, McDonnell P, Tullo A, Parry C. Bacterial susceptibility to topical antimicrobials and clinical outcome in bacterial keratitis. Investigative ophthalmology & visual science. 2010 Jan 1;51(1):362-8.
14. Al-Dhaheri HS, Al-Tamimi MD, Khandekar RB, Khan M, Stone DU. Ocular pathogens and antibiotic sensitivity in bacterial keratitis isolates at King Khaled Eye Specialist Hospital, 2011 to 2014. Cornea. 2016 Jun 1;35(6):789-94.
15. Leck AK, Thomas PA, Hagan M, Kaliamurthy J, Ackuaku E, John M, Newman MJ, Codjoe FS, Opintan JA, Kalavathy CM, Essuman V. Aetiology of suppurative corneal ulcers in Ghana and south India, and epidemiology of fungal keratitis. British Journal of Ophthalmology. 2002 Nov 1;86(11):1211-5.
16. Bharathi MJ, Ramakrishnan R, Vasu S, Meenakshi R, Palaniappan R. In-vitro efficacy of antibacterials against bacterial isolates from corneal ulcers. Indian Journal of Ophthalmology. 2002 Apr 1;50(2):109-14.
17. Schaefer F, Bruttin O, Zografos L, Guex-Crosier Y. Bacterial keratitis: a prospective clinical and microbiological study. British Journal of Ophthalmology. 2001 Jul 1;85(7): 842-7.
18. Keshav BR, Zacheria G, Ideculla T, Bhat V, Joseph M. Epidemiological characteristics of corneal ulcers in South Sharqiya Region. Oman medical journal. 2008 Jan;23(1):34.
19. Lavaju P, Arya SK, Khanal B, Amatya R, Patel S. Demograhic pattern, clinical features and treatment outcome of patients with infective keratitis in the eastern region of Nepal. Nepalese Journal of Ophthalmology: a Biannual Peer-reviewed Academic Journal of the Nepal Ophthalmic Society: NEPJOPH. 20 09 Jul 1;1(2):101-6.
20. Whitcher JP, Srinivasan M, Upadhyay MP. Corneal blindness: A global perspective. Bull World Health Organ. 2001;79(3):214–21.
21. Feilmeier MR, Sivaraman KR, Oliva M, Tabin GC, Gurung R. Etiologic diagnosis of corneal ulceration at a tertiary eye center in Kathmandu, Nepal. Cornea. 2010;29(12):138 0–5.
22. Testing S. M100-S25 Performance Standards for Antimicrobial [Internet]. Wayne: Clinical Laboratory Standard Institute; 2015.