EPIDEMIOLOGY AND OUTCOME OF CORNEAL ULCER IN YAZD SHAHID SADOUGHI HOSPITAL

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Abstract- The objectives of this study were to define the clinical risk factors, microbiological spectrum, and visual outcome of bacterial keratitis at Shahid Sadoughi Hospital (Yazd, Iran). A cross-sectional prospective study, identified 80 cases of microbial keratitis from March 1999 to March 2001. Inclusion criteria were presence of corneal stromal infiltrate in slit lamp examination, and microbiologic evaluation of corneal scrapings. Clinical features, risk factors, VA were analyzed. The mean (±SD) age of patients was 45.3 years (±18.50) with a range of 3 to 79 years. Forty-six (57.5%) patients were male and (42.5%) female. The predominant predisposing factors were corneal trauma (39%), ocular diseases (34.1%), previous ocular surgery (10%) and use of contact lens (9.8%). Forty percent of cases were culture- positive. *Staphylococcus epidermis* (21.9%), *Staphylococcus aureus* (18.8%) and *Streptococcus pneumonia* (15.6%) were the most common isolates. Fungi were isolated in five eyes. Twenty-nine patients (36.2%) achieved VA of 20/120 or better at the final follow-up. Fourteen eyes (17.5%) required surgery and 4 eyes (5%) eventually needed evisceration. Microbial keratitis resulting in loss of the eye occurred typically in elderly patients, with pre-existing poor VA and delayed treatment. This study illustrated that the epidemiology of corneal ulcer in this area is different from what is observed in other parts of the world.
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INTRODUCTION

Because of its high incidence worldwide, and its complications, bacterial keratitis is considered to be an important cause of blindness (1). Trachoma keratitis is one of the common causes of blindness in the third world (2).

Infectious keratitis is an ocular emergency caused by bacteria, fungi, protozoa or viruses, and presents with pain, photophobia and redness. Clinically, it presents with infiltration and corneal edema and anterior chamber reaction. If left untreated, apart from scar formation, it can lead to endophthalmitis and even corneal perforation and blindness. Corneal

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perforation due to pseudomonas keratitis can occur in less than 24 hours after onset. Identification of pathogens, selection of fortified antibiotics, and their early administration is the mainstay of management (3). According to different studies, prevalence of keratitis in different parts of the world differs with geographical area, occupation, age and even different seasons (4,5). Despite this, the epidemiology and risk factors of corneal ulcer have not been determined in our province. Various studies have been performed in different parts of the world, including the study of Derek in Heidarabad, India (5), Upadahay in Nepal (6) and also a prospective study by Schafer in Switzerland (7). Similar studies have been performed by Forootan (8) and Sadeghi in Tehran (9) and Behboodi in Rasht (10). The first step in the prevention of corneal ulcer, is the determination of its epidemiology in different parts of the country, by which risk factors can be identified and preventive

measures implemented as necessary. This study was conducted to determine the epidemiology of corneal ulcer, risk factors, and visual outcome of patients referred to Yazd Raah Ahan Eye Hospital.

MATERIALS AND METHODS

A cross-sectional descriptive study was conducted on patients with infectious keratitis admitted to this referral center, in the period between March 1999 to March 2001. Age, sex, laterality of the involved eye, place of living (rural or urban), level of education were recorded. The patients who met the following criteria were included in the study: presence of corneal infiltrate upon slit lamp examination, and microbiological evaluation of corneal scrapings for microbial keratitis. Patients with keratitis of more than 3 weeks duration (chronic), and viral acanthamoeba keratitis were excluded. After instillation of topical anesthetic drops, samples were taken from the corneal ulcer with a number 15 surgical knife, and from the cul de sac and lid margin of both eyes with a sterile applicator, and transferred to media cultures (blood, chocolate and Sabouraud's agar). Giemsa and Gram's staining were then performed. If the patient had received antibiotics before admission, they were discontinued, and samples were taken 24 hours later. Infectious keratitis was diagnosed based on ulceration of epithelium and supportive presence of either focal or diffuse inflammation. Risk factors, VA (VA) and response to therapy were analyzed. The patients were all visited and followed by one ophthalmologist.

Treatment protocol

The standard treatment included: 1) cefazolin forte 50 mg/ml and gentamicin forte 13 mg/ml every 0.5 hour in first 24-48 hours and then administered alternately, with subsequent tapering according to clinical response; 2) ciprofloxacin 0.3%, every 1 hour and subsequent tapering according to clinical response. The following parameters were considered: history of risk factors like trauma, contact lens, lid lesions, previous ocular surgeries and dry eye. The time interval between developing ulcer and referral to this center was recorded. VA was checked with

Snellen charts on admission and at the time of discharge and also on the final follow-up visit.

The location, size and thickness of keratitis, and the presence of cell and flare in the anterior chamber were determined with Haagstreit 900 slit lamp. Patients were followed up for at least 6 months, and results were analyzed with SPSS software.

RESULTS

Demographics

Eighty patients were studied during 24 consecutive months. Forty-six (57.5%) patients were male and 34 (42.5%) female. Forty-six percent had right eye and 54% left eye involvement. Sixty-five percent were of urban and 35% from rural areas. Most patients were farmer or manual worker (33.3% and 21.2%, respectively). Thirty-five percent of patients were illiterate or had only primary school education. The mean age was 45.3 ± 18.5 years (range 1-79 years), (table 1);the highest frequency (mode) belongs to the 40 to 50 age group, and 70% of the cases were under 60.

Predisposing factors

In this study, the predominant predisposing factor for corneal ulcer was trauma, which was present in 39% of cases, followed by ocular disease (35%), together comprising three-fourths of all cases. Ocular disease included dry eye syndrome, blepharitis, lid disorders, and bullous keratopathy. Previous ocular surgery on the same eye included corneal grafts and trabeculectomy (9.8%).

Table 1. Distribution of patients with corneal ulcer according to age groups

Age groups (years)	Number of patients	Percent	Cumulative percentage
0-10	8	10	10
10-20	9	11.3	21.3
20-30	6	7.5	28.8
30-40	9	11.2	40
40-50	14	17.5	57.5
50-60	10	12.5	70
60-70	12	15	80
70-80	12	15	100
Total	80	100	

Table 2. Distribution of the patients according to age and predisposing factors*

| Age groups | Predisposing factors | | | | | |
	Trauma	Ocular disease	Previous ocular surgery	Contact lens	Systemic disease	Total
0-20	12 (66.7)	3 (16.7)	1 (5.5)	2 (11.1)	0 (-)	18
20-50	11 (40.8)	7 (25.9)	3 (11.1)	6 (22.2)	0 (-)	27
50-80	9 (25.7)	18 (51.5)	4 (11.4)	0 (-)	4 (11.4)	35

* Data are given as number (percentage)

Patients who developed corneal ulcer after corneal graft were all from rural areas, with no follow-up, aged over 50, and had a history of long-term topical corticosteroid use. Advance age (P< 0.001), delay in referral to the corneal specialist (P<0.02) were statistically significant factors associated with the need for penetrating keratoplasty. In addition, ulcers extending to the limbus, contact lens-induced ulcers, and ulcers on donor …, needed keratoplasty.

The fourth leading predisposing factor was the use of contact lens (9.8%). Keratitis induced by contact lens was more common in 20 to 49 years age group (table 2); 7 of the 8 cases were due to soft contact lens. Most ulcers had a large diameter. Three of the 8 keratitis cases were due to pseudomonas and all led to keratoplasty. Risk factors for contact lens-induced keratitis were overnight wearing, low socioeconomic situation and male gender. Two cases of diabetes mellitus, one case of rheumatoid arthritis and one case of Stevens-Johnson syndrome suffered keratitis, all were over 50 years of age.

Under 50 years of age, the most common predisposing factor was trauma, and over 50 years, the predisposing factor was ocular disease in more than 50% of the cases (Table 2).

Clinical examination

Central ulcer was seen in 58.5% of the eyes, peripheral ulcer (within 4 mm of the limbus), in 16.2%, the ulcer was between periphery and the center in 25%.

Central ulcer was more common in contact lens wearers. The area of infiltrate was small (largest diameter < 2 mm) in 30 cases, medium (2-6 mm) in 42 eyes, and large (>6 mm) in 8 eyes. In 9.3% of cases with small-sized ulcers, the final vision was worse than prior to the development of ulcer, but in the large-sized group it was worse in 30%. Ulceration depth was less than 30% in 45% of the cases, between 30% and 60% in 36.4%, and more than 60% in 18.8%.

Microbiology

ln this study, 32 patients (40%) had positive cultures, 22 of which were gram-positive. The most common strains were *Staphylococcus epidermidis*, S*taphylococcus aureus* and *Streptococcus pneumonia* and in the gram-negative group, pseudomonas was the most common isolate. In 21% of gram-negative and 13% of gram-positive cultures, the patients had used one or more topical antibiotics before admission. Keratitis caused by pseudomonas strain (10 cases) had the largest diameter, the highest mean number of days of hospital stay, and the poorest final VA. Two of the 5 patients with fungal keratitis, developed corneal perforation.

Treatment and outcome

In all patients, medical management was initiated; in 14 cases surgical management became necessary. Five patients underwent penetrating keratoplasty (PK), 4 enucleation, 3 conjunctival flap and 2 underwent tarsorrhaphy. All 4 cases who ultimately underwent enucleation presented with no light perception (NLP), were aged over 50, and had a delay of more than 48 hours in the initiation of medical management. Of the 5 cases undergoing PK, 2 cases presented with primary graft failure, and 2 with graft rejection in the first 3 months. Table 3 shows the interval between the development of corneal ulcer and referral time to the hospital according to residential area (rural vs. urban). An interval of more than 24 hours was observed in 21.1% and 50% of cases in urban and rural areas, respectively; the difference in frequency was statistically significant (P<0.01, Chi-square test). The predominant outcome was a corneal scar, with or without vascularization. VA at the final follow-up is demonstrated in figure 1, most (30%) cases were in the range of 20/200 to 20/120. Overall, 36.2% of patients had a VA of over 20/120, and 7.5% over 20/60. Visual outcome had a significant relation with age (P<0.001) and delay in starting of medical therapy (Fig. 1).
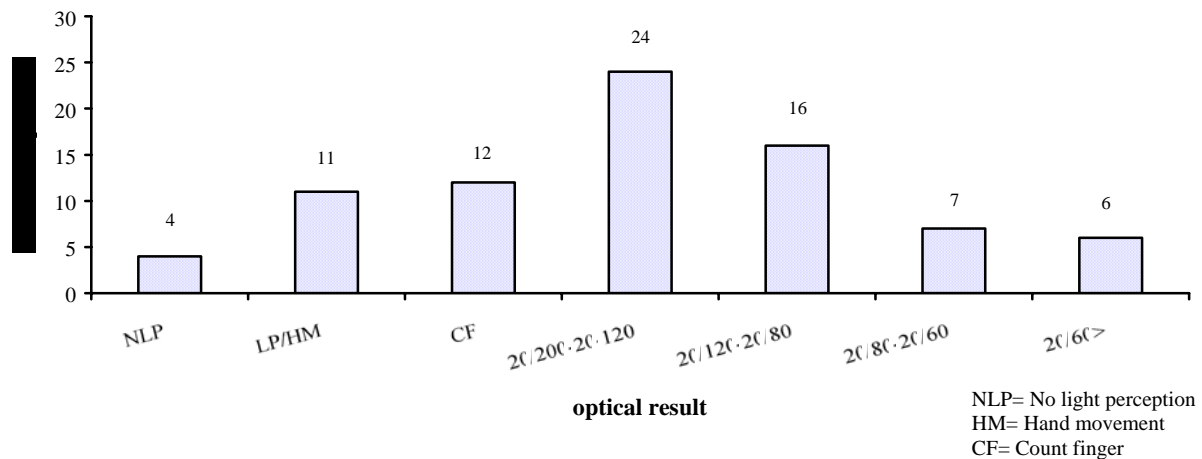
Fig. 1. Outcome at final follow-up visit in patients with corneal ulcer

NLP= No light perception
HM= Hand movement
CF= Count finger

Table 3. Distribution of patients with corneal ulcer according to referral time and residential area *

| | Referral time (h) | | | |
	< 12	12-24	24 >	Total
Urban	16 (3.8)	25 (48.1)	11 (21.1)	52
Rural	4 (14.3)	10 (35.7)	14 (50)	28
total	20 (25)	35 (43.7)	25 (31.3)	80

* Data are given as number (percentage)

DISCUSSION

In our study 57.5% of cases, in Behboody's study (10) 64.2%, and in Ormerds' series(11) 71% of the cases were male. In observations made by Srinivasan (l2), this frequency was 61.3%. The result of this study shows the highest frequency for corneal ulcer belonging to age group of 40-50 years, that is similar to the observations made by Upadahyay, in Nepal (6), as well as in others series (5-8). In Sadeghi's study (7) housekeepers, in Behboodi's report (10), farmers (66%) and in our study farmers (33.3%) and workers(21.2%) were most frequently affected. In this study, as in others (4,7), trauma was the leading predisposing factor (39%). Trauma is the most common predisposing factor of bacterial keratitis in poor countries, reaching 77.5% (13) in some areas (13). The second common risk factor in our study was ocular disease(34.1%), similar to the study made in Heidarabad, India (35.5%). In this study, trauma was the most common cause of corneal ulcer under the age of 50, and ocular disease beyond the age of 50. In a study on bacterial keratitis in the elderly,

ocular diseases and trauma played the first and second roles, respectively (14). Within the category of ocular diseases, the most frequent were dry eye syndrome, chronic blepharitis, eyelid lesions and bullous keratopathy, respectively. In our series, previous keratoplasty was the most common surgical factor predisposing to corneal ulcer, which is similar to the observations made by Vajpayee (15).

In our study contact lenses were responsible for 9.8% of the cases of keratitis , but in Schaefer's (7) study the leading risk factor was contact lens (36%) followed by trauma (20%). this difference may be attributed to low prevalence of contact lens usage in Iran. Ninety percent of the cases of contact lens-induced keratitis were caused by extended-wear lenses, that is in agreement with our data (16,17). Similar to the observations made by Tabara (18) and Liesegang (19), in our study the most common pathogen was pseudomonas. In Derek's study, extended-wear contact lenses were a associated with a five-fold increased risk of keratitis compared to daily-wear ones, and the prevalence of keratitis was significantly higher with extended-wear soft contact

lenses (19). The largest-diameter ulcers and the poorest prognosis were seen in this group. Positive cultures were observed in 40% of our cases, 49% in Behboodi's study (10), 71% in Forootan's series (9), 72.5% in Derek's, and 86% in Derek and in Schaefer's study (7). These studies are not compatible with ours, probably because of laboratory problems and the frequent use of antibiotics prior to culture in our study. In positive cultures, *Staphylococcus epidermidis* (21.9%) was the most common pathogen, which is similar to the results of several other studies (5,7), followed by *Staphylococcus aureus* (18.8%) and *Streptococcus pneumoniae* (15.6%). In Behboodi's (10) series, fungi caused 20.75% of the cases of keratitis, whereas 6.2% of our cases were caused by fungi. This difference could be due to the exposure of farmers to the stalk of rice in northern Iran where the former study was performed. Also, in a study in Bangladesh, the most common strain was fungus (35.9%). These differences are due to the differences in epidemiologic factors.

All of the patients were started on antimicrobial treatment. Fourteen patients (17.5%) needed surgical intervention, and 4 (17.5%) underwent evisceration. In Derek's study (5), 11.8% of the cases needed surgical intervention, and 14.7% underwent evisceration. In our study, old age, delay in referral, previous ocular surgeries, were risk factors for keratoplasty as the final treatment. In the present study, patients using ciprofloxacin had less itching and irritation than standard treatment; the same observation was reported by Cutareli (20) and Shoja (21).

According to this study, the final best VA's were 20/200 to 20/120. Overall, visual prognosis in our study was related to the size of the ulcer, predisposing factors, and the pathogen isolated in culture, similar to Miedzia's study (22). In conclusion, the principal risk factor for bacterial keratitis in this study was trauma. Contact lens-wearers, especially those using soft- and extended-wear lenses, should be warned against the risk of bacterial keratitis. Patients with chronic eye disorders such as dry eye syndrome, lid lesions and bullous keratopathy should closely be followed and warned of the risk of developing corneal ulcers.

REFERENCES

1. Burd EM, Ogawa GSH, Hyndiu RA. Bacterial keratitis and conjunctiva, Smolin thoft RA The cornea 1994; 115-167.

2. Adela Hs. Organization of a Trachoma- control program in Africa. In: Kupfer C. Gillen T, editors. World blindness and its prevention. Vol 4. International Agency for the prevention of blindness: 1990. p.193-197. 1990.

3. Ostler HB, Mitchell CW. Disease of the external eye and adnex. Baltimore: Williams and Wilkins 1995. p.137-252.

4. Matthews TD, Frazer DD,Minassian DC. Risks factors of keratitis and patterns of disposable contact lenses. Arch Ophthalmol 1992; 110: 1559-1562.

5. Derek Y, Kunimoto S Sh, Prashant Gary, Usha G,et al. Corneal ulceration in the elderly in Hyderabad South India. Br J ophthalmol 2000; 84: 54-59.

6. Upadahyay Murthy GV. Epidemiologic characterestics , predisposing factors and etiologic diagnosis of corneal ulceration in Nepal. A J O 1991; 111: 92-99.

7. Schaefer Frederic, Olivier Bruttin, Zagrafos, Bacterial keratitis: A prospective clinical and microbiological study. B J Ophthalmology 2001; 85: 842-847.

8. Sadeghi A. Evaluation of Bacterial Keratitis in F arabi Eye hospital Tehran ,Iran. The Journal of the Iranian Society of Ophthalmology 1992; 4(1): 18-20.

9. Fourotan A, Joshegahni M. Epidemiology and Predisposing Factors of Bacterial Keratitis in Ras Akram hospital Tehran, Iranian. Journal of Ophthalmology Bina 1997; 3(3): 213-215.

10. Behboody H, Mohammadi MJ. Epidemiology of Bacterial Keratitis in Toetoonkaran hospital Rasht, Iranian Journal of Ophlhalmology Bina 2001;7(1): 3-90.

11. Ormerod LD, Hertzmark E. Epidemiology of microbial keratitis In southern california A multivarate analysis. Ophthalmology 1987; 94: 1322-1333.

12. Srinivasan M, Gonzales CA, Gerge CA. Epidemiology and etiological diagnosis of corneal ulceration in Medurai south India Br J Opht 1997; 81: 965-971.

13. Vaj payee RB, Dada T Saxen R. Study of the first contact management profile of cases of infectious keratitis a hospital-. based study. Cornea 2000; 52-56 (Medline).

14. Ormerod LD, Lazarus HM. Causes and management of bacterial keratitis in the elderly, Can ophthalmol 1989; 24:112-116.

15. Vajpayee RB,adat, Murthy GV, Pandey, Boral SK. Risk factors for graft infection in India. A case -contiol study. Br J Ophthalmol Mar 2002; 86(3): 261-265.

16. Radford CF, Minassian DC. Disposable contact lens use as a risk factor for microbial keratitis. Br J Ophthalmol 1998; 1272-1275.

17. Schein OD Glynn RJ. The relative risk of ulcerative keratitis among users of daily- wear and extended- wear soft contact lenses. N Engl J Med 1989; 773-778.

18. Tabbara, Kholid F. EL-Sheikh,Hishamf, Aabed Bassan Extended wear contact lenz related bacterial keratitis. B J O

2000; 84(3) 327-328.

19. Liesegang, TJ,Lamd ,F Contact lenz- related microbial keratitis Cornea May 1997; 16(3): 265-273.

20. Cutarelli PE, Lass JH, Lazarus HM, et al. Topical fluoroquinolones antimicrobial activity and invitro corneal epithelial toxity. Currewt Eye Research 1999; 106. 1441-1446.

21. Shoja MR ,Miratashi .AM,Comparison of ciprofloxacin 0.3% with standard drops In Bacterial Keratitis ,Journal of Shahid Sadoughi University of Medical Sciences and Health Services 1996; 7(3): 11-17.

22. Miedzia R AL Miller MR, Rapuanocy, Laibsonpr,et al Risk factors in microbia keratitis leading to penetrating keratoplasty. Ophthalmology 1999; 100: 1166-1171.