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Management of infective corneal ulcers in a high-income developing country

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Abstract

Microbial keratitis is a major risk for corneal blindness worldwide. We aimed to study the clinical presentation and outcome of hospitalized patients having infective corneal ulcers.

All patients who were diagnosed as microbial keratitis and were admitted to Al-Ain Hospital during the period July 2011-Dec 2016 were retrospectively studied. Patients' demography, predisposing factors, symptoms and signs at presentation, time to presentation after onset of symptoms, microbial isolates, hospital stay, and visual acuity (VA) outcome were studied.

74 patients with corneal ulcers were hospitalized. 79.7% were males. The median (range) age was 44 years (1–91). 36.5% had trauma as a risk factor. The main presenting symptoms were pain (90.5%), red eye (79.7%), and decreased vision (63.5%). All patients had stromal infiltrate while 39.2% had hypopyon at presentation. The average time from the start of the symptoms to hospital presentation was 11 (1–90) days. The mean (range) hospital stay was 10.6 (1–60) days. Forty eyes were culture positive. Bacteria were identified in 27 eyes and fungus in 16. *Pseudomonas aeruginosa* (9 eyes) and *Staphylococcus epidermis* (5 eyes) were the most common bacterial islolates. *Aspergillus* (6 eyes) was the most common fungus species. 95.2% of the bacterial isolates were susceptible to the quinolone antibiotics group. Twenty eight (51.9%) patients had a vision worse than 6/60 in the affected eye.

Corneal ulcer poses a significant threat to the sight of an affected eye. Trauma was the most common risk factor for corneal ulcers. Usage of eyes personal protective equipment for high risk occupations and earlier accessibility to health care may reduce the impact of corneal ulcers in our community.

Abbreviations: AAHEC = Al-Ain Hospital Research Ethics Committee, KOH = Potassium hydroxide, UAE = United Arab Emirates, VA = visual acuity.

Keywords: antibiotics, corneal ulcer, microbial keratitis, microbiology, vision

1. Introduction

Infectious corneal ulcer is a major risk for corneal blindness.[1,2] The most common cause for endophthalmitis with subsequent enucleation is an infected corneal ulcer.[3] Furthermore, traumatic corneal ulcer, especially by organic substances is the most common cause for evisceration or enucleation as a result of corneal ulcer.[4]

The annual incidence of corneal ulcers is estimated to be 10 more times in developing countries compared with developed countries.[5,6] Around 2 million new corneal ulcers occur annually only in Asia and Africa.[1] The annual cost for corneal ulcers and keratitis is estimated to be $175 million in USA alone.[7] In contrast, the economic cost of corneal ulcers in developing countries is not known but expected to be high.[8] There are limited studies on the outcome of corneal ulcers in the Gulf region.[9–12] Al-Ain City is the fourth largest city in the United Arab Emirates (UAE). Al-Ain City is famous for its agricultural activities. It has an estimated population of 767,000 which is predominately expatriate workers.[13]

To the best of our knowledge, no data concerning corneal ulcers is available from UAE; hence, we aimed to study the clinical presentation, management and clinical outcome of hospitalized corneal ulcers at our setting.

2. Patients and methods

This study was approved by Al-Ain Hospital Research Ethics Committee (AAHEC-09-17-071). Al-Ain Hospital has a capacity of 402 beds, annually treats about 20,000 inpatients, and has around 320,000 outpatient visits.[14] Al-Ain Hospital is the main health care center for corneal ulcers admission and treatment in Al-Ain City. The medical records of patients admitted to Al-Ain hospital with infectious keratitis during the period January 2011- December 2016 were studied. We admit patients who have corneal ulcers that are sight-threating, those who are

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non-compliant to frequent drops administration, those with transportation difficulties, and those with suspected fungal corneal ulcers because of limited outpatient access to Natamycin eye drops.

A specific protocol was developed for data collection. The studied variables included age, gender, nationality, place of injury, eye scraping microbiology cultures, medications, hospital stay and visual outcome.

Patients presenting to Al-Ain Hospital with corneal epithelial defect and underlying stromal infiltrates routinely undergo corneal scrapings for infiltrates larger than 1 mm, sight-threatening, non-satisfactory response to previous treatment or when suspecting an unusual microorganism. Patients presenting to Al-Ain Hospital with corneal epithelial defect and underlying stromal infiltrates routinely undergo corneal scrapings for infiltrates larger than 1 mm, sight-threatening, non-satisfactory response to previous treatment or when suspecting an unusual microorganism. All patients in our study were admitted to the hospital and all had corneal scraping for culture and sensitivity. Thioglycolate broth, Blood agar, Sabouraud dextrose, and Chocolate agar are the standard media for culture. Smears are used for gram stain and a potassium hydroxide (KOH) preparation. Admitted patients typically receive gentamicin (15 mg/mL) and moxifloxacin 0.5% eye drops every 30 minutes. Natamycin 5% eye drop is used for most of fungus cases and if not available then amphotericin B 0.15% drops or voriconazole 0.5 mg/mL are the other alternatives.

3. Statistical analysis

The data were collected as hard copy, entered into Microsoft Office Excel 2007, and analyzed using PASW Statistics (Version 25, SPSS Inc, Chicago, IL). Data were presented as median (range) or number (%) as appropriate. The Snellen visual acuity, which is the method for vision documentation, was converted into logMAR unit for the statistical analysis. Wilcoxon signed rank test was used to compare the continuous data of two related groups while McNemar test was used to compare the categorical data of two related groups. A P value of less than .05 was accepted as statistically significant.

4. Results

Seventy-four patients (77 eyes, 3 patients had bilateral ulcers) were hospitalized for corneal ulcer treatment during the study period. Majority were males (79.7%), mostly (54.9%) from the Indian subcontinents (Table 1). The median (range) age was 44 (1–91) years. Thirty-six of the involved eyes were right and 41 were left.

Twenty-seven (36.5%) patients had trauma as a risk factor for corneal ulcer development, followed by contact lens usage in 9 patients (12.2%), ocular surface disease in five (6.8%), corneal surgery in 3 (4.1%), and corneal suture removal in one patient. Ocular surface disease included one patient with blepharitis, 2 with exposure keratitis, 1 with band keratopathy and 1 with vernal keratoconjunctivitis. Ten patients recorded vegetable matter; mainly from date palm tree; as the source of trauma, 6 had injury by stone/concrete, 7 with others objects. The source of trauma was unknown in 4 patients. The main symptoms associated with corneal ulcer were pain (90.5%), red eye (79.7%), and decreased vision (63.5%). All patients had stromal infiltrate and 39.2% had hypopyon at presentation (Table 2).

Table 1

Demography of 74 patients admitted to Al-Ain Hospital with corneal ulcers during the period of January 2011 to December 2016.

Variable	Number (%)
Gender	
Male	59 (79.7)
Female	15 (20.3)
Age	44 (1–91 years)
Nationality	
Bangladeshi	19 (25.7)
Pakistani	15 (20.3)
Emirati	12 (16)
Indian	5 (6.8)
Egyptian	4 (5)
Omani	4 (5)
Others	15 (20.3)

Data are presented as median (range) or number (%) as appropriate.

The average (range) time between symptoms and hospital presentation was 11 (1–90) days. The mean (range) hospital stay (excluding chronic patients admitted for comorbid disease) was 10.6 (1–60) days. Imaging is not performed routinely for corneal ulcer patients in our hospital.

Six (10.7%) potassium hydroxide (KOH) and 10 (17%) gram stains of ulcer samples were positive. Forty eyes had a positive culture (54%). 27 eyes showed bacterial isolates and 16 eyes grew fungus. Five eyes had multiple organism growth, 2 of which was mixed fungus and bacterial growth. Among bacteria, *Pseudomonas aeruginosa* (9 eyes) was the highest followed by *Staphylococcus epidermis* (5 eyes). *Aspergillus* (6 eyes) was the most common fungus species cultured (Table 3). All bacterial organisms (21 isolates) that were tested for sensitivity to fluoroquinolone group of antibiotics (ciprofloxacin, levofloxacin or moxifloxacin) were found to be susceptible except one

Table 2

Presenting symptoms and signs for 74 patients admitted with corneal ulcers to Al-Ain Hospital during the period of January 2011 to December 2016.

Symptoms and signs	Number (%)
Symptoms	
Pain	67(90.5)
Red eye	59 (79.7)
Decreased vision	47 (63.5)
Foreign body sensation	25 (33.8)
Discharge	17 (23)
Tearing	11 (14.9)
Photophobia/ sensitive to light	5 (6.8)
Swelling	4 (5.4)
Whitish discoloration of the eye	2 (2.7)
Signs	
Stromal infiltrate	74 (100)
Epithelial defect	57 (77)
Hypopyon	29 (39.2)
Anterior chamber inflammation	11 (14.9)
Foreign body	2 (2.7)
Corneal rupture	2 (2.7)
Hyphema	2 (2.7)
Descemetocele	1 (1.3)

Data are presented as number (%).

Table 3

Corneal ulcer microbial isolates of 40* eyes with positive corneal scraping culture admitted to Al-Ain Hospital during the period of January 2011 to December 2016.

Etiologies	Number (%)
Gram negative bacterial	
Pseudomonas aeruginosa	9 (22.5)
Serratia marcescens	1 (2.5)
Enterobacter cloacae	1 (2.5)
Klebsiella oxytoca	1 (2.5)
Neisseria elongate	1 (2.5)
Stenotrophomonas maltophilia	1 (2.5)
Achromobacter xylosoxidans	1 (2.5)
Gram positive bacterial	
Staphylococcus epidermis	5 (12.5)
Staphylococcus warneri	2 (5)
Staphylococcus aureus	2 (5)
Streptococcus viridans	2 (5)
Streptococcus pneumoniae	2 (5)
Streptococcus mitis	1 (2.5)
Staphylococcus huminis	1 (2.5)
Staphylococcus capitis	1 (2.5)
Fungus	
Aspergillus	6 (15)
Fusarium	4 (10)
Other Fungus	5 (12.5)

* Five eyes had multiple organisms' isolates.

Achromobacter xylosoxidans isolate (95.2%). Two *S epidermis* isolates were Oxacillin-resistant, however all Coagulase-Negative Staphylococci were sensitive to vancomycin. The *P aeruginosa* isolates were ciprofloxacin, ceftazidime and gentamicin sensitive.

Two patients had eye perforations, 2 eyes ended up with evisceration, 1 had corneal graft and another vitrectomy. The latter was a 39-year old patient who developed corneal ulcer with no history of trauma. His corneal scraping grew *Fusarium*. He developed corneal perforation with vitreous prolapse in the anterior chamber that required anterior vitrectomy. The patient was referred to another facility for tectonic corneal graft. There was significant vision improvement following treatment ($P < .05$, Wilcoxon signed rank test) (Fig. 1). Nevertheless, 49 patients out of 63 (77.8%) with recorded visual acuity were at the level of counting finger or worse at presentation. Twenty-six out of 54 patients (48%) with recorded visual acuity at last follow up retained vision at level of counting finger or worse and 28 (51.9%) had a vision worse than 6/60. The visual acuity was reported both at presentation and at last follow up in only 50 patients. There was no significant difference in vision outcome for patients with counting fingers or worse ($P=.72$, McNemar test). Only 5 patients out of 28 (17.6%) showed some improvement from the baseline of counting fingers or worse. Twenty-three patients vision remained the same, while vision deteriorated to counting fingers or worse in 3 patients. The main reason for vison limitation was corneal pathology (74 eyes, 96.1%), lens (five eyes, 6.7%), and retina (1 eye, 1.3%). Five patients had cataract; 3 were age-related, 1 congenital and 1 traumatic.

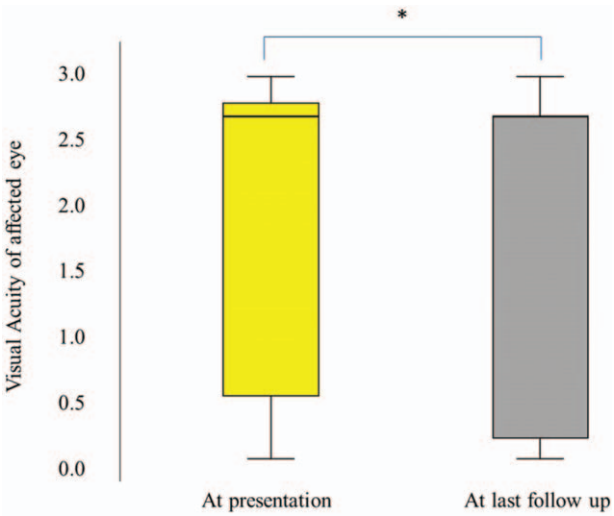

Figure 1. Box-and-whiskers plot of visual acuity (VA) at presentation and follow up. The box resembles the 25th to 75th Interquartile Range (IQR). The horizontal line within the box represents the median. Those values that are not outliers lie within the whiskers lines. $P < .05$, Wilcoxon signed rank test.

5. Discussion

Our study has shown that corneal trauma is the major predisposing factor for corneal ulcers. Majority of patients were young males. Most of isolates were bacterial and were found to be susceptible to the quinolone antibiotic group. Our cohort of microbial keratitis had poor visual acuity outcome with more than 50% of patients ending up with poor visual outcome.

Similar to other studies[12,15] infected corneal ulcers were more common in males and trauma was the most common risk factor. Trauma was responsible for 50% to 80% of corneal ulcers in other studies[16,17] These findings are higher compared with our study (36.5%). Farming is a high risk occupation for corneal ulcers.[16,18–20] The impact of ocular trauma can be catastrophic and preventive measures are essential.[21]

Consistent with other studies, bacterial isolates were common in corneal ulcers.[9,19] Among the bacteria, *P aeruginosa* and Staphylococci species were the most common isolates.[11,12,16,22] There are geographical variations of corneal ulcers isolates. Staphylococci were dominate isolates in India,[23] Paraguay,[24] France,[25] and New Zealand.[26] On the other hand, *Pseudomonas* comprised the predominant bacterial isolates in Malaysia,[27] Singapore,[28] Kingdom of Bahrain,[11] Bangladesh[29] and Hong Kong.[30] The reason for this variation is not completely understood. This may be attributed to economic status of patients, contact lens usage or other various predisposing factors.[27,30,31] Furthermore, geographical location, climate, occupational hazards, corneal scraping methods and interpretation of cultures might affect the reported variation of corneal ulcers.[31,32]

Etiology of fungal corneal ulcers vary between countries; *Aspergillus*[20,29,33–37] was the main fungi causing corneal ulcer in our setting while *Fusarium* were the predominant etiological factors of fungal corneal ulcers in many other studies.[19,32,38–43] Agricultural outdoor workers of developing countries who are exposed to trauma by organic objects, and those in tropical and subtropical areas are at risk for Aspergillus keratitis.[44] UAE is located in southwestern Asia. Al- Ain City has a hot, dry and often windy weather with high agricultural activities which may contribute to this observation. Dunlop et al[29] stated that

microorganisms may be introduced during eye washing with contaminated water. This could be another source for corneal ulcer infection in low income farm workers.

Positive corneal ulcer cultures range between 43% and 77%.[9,12,23] We had 54% positive culture samples. The variations between centers could be attributed to differences in the methods used to ascertain positivity, or in methods of sample collection. Consistent with other studies,[19] all bacterial isolates were found to be susceptible to the quinolone group of antibiotics except *A xylosoxidans* (1 case). All Staphylococci species were sensitive to vancomycin, gentamicin, linezolid and rifampin. Streptococci species were sensitive to the entire panel of antibiotics. *P aeruginosa* was 100% susceptible to gentamicin, ciprofloxacin, ceftazidime, amikacin, tobramycin and piperacillin/tazobzctam.

The delay in presentation of corneal ulcers ranged between 1 to 30 days.[27,45] This can be attributed to lack of pain or absence of vision deterioration at the beginning, lack of availability of an escort, travel costs, involvement with other commitments, and poor knowledge of local eye care services.[45] Our patients presented after a median of 11 days of the start of their symptoms. Eighteen patients reported using some topical medications prior to hospital presentation. So it is possible that they had sought help from other healthcare providers or used over-the-counter medications prior to presentation similar to other studies.[24,45]

Despite improvements in eye care services at our facility, visual outcome was unfavorable in our study with almost 52% of patients showed vision worse than 6/60. Chidambaram et al[45] reported 34% severe visual impairment in their series. Keshav reported that 88% of their patients were blind or had no perception of light.[12] This can be due to delayed presentation. Hooi and Hooi[27] found that the time to presentation after the onset of ocular symptoms is affecting visual outcome. Laspina et al[24] speculated that severe keratitis is an ultimate outcome for delayed presentation to the hospital. Furthermore, hypopyon at presentation and *aspergillus* species isolates are associated with poorer outcome.[45]

Agriculture-related superficial corneal trauma with subsequent corneal ulcer development is a worldwide cause of monocular corneal blindness.[21] As such, antibiotic prophylaxes for superficial corneal trauma causing corneal abrasions is recommended to be started by community physicians in high risk occupations and in remote places.[1]

There are no published data concerning management of corneal ulcers in UAE. Our present study highlights an important eye health problem. However, there are certain limitations in this study. Our data are from a single hospital and cannot be generalized for all UAE. The outcome may differ in other settings having other treatment modalities such as corneal cross-linking for refractory cases.[46] In addition, corneal transplantation service is not provided at our hospital. Accordingly, we speculate that workers prefered to return to their home countries for further management. Villarejo reported that most of the workers went back to Mexico for treatment because of the barriers they encountered in accessing health care in the United States.[47] The retrospective nature of our study limited the amount of data collected including reasons for delayed hospital presentation. Besides, we have looked at hospitalized patients who have more severe pathology with virulent organism's over-representation. Finally, there is a selection bias as we studied hospitalized patients and not those who were treated as outpatients or at the Emergency Department. This study represents the tip of an iceberg of the corneal ulcer problem in our setting and a more detailed prospective study on corneal ulcers in our setting is needed.

6. Conclusions

Corneal ulcers pose a significant threat to the sight among young people in our setting. Trauma is a significant predisposing factor. Usage of eyes personal protective equipment for high risk occupations and earlier accessibility to health care may reduce the impact of corneal ulcers in our community.

Author contributions

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