

Bacterial Keratitis Risk Factors, Pathogens and Antibiotic Susceptibilities: A 5-Year Review of Cases at Dubai hospital, Dubai

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Abstract

Objective: Microbial keratitis is a sight threatening infection of the cornea. Its incidence has been increased in the past few years, with the contact lens wear as the major risk factor. In the past few years other risk factors have also come up in light. We thus aimed to present a 5-year study comprising of 37 patients with microbial keratitis who yielded only positive culture; other cases with negative cultures were excluded.

Methods: Local microbiology database and retrospective audit of patients (who had a corneal scraping for culture over a 5-year period) medical records were used in this study.

Results: We found that in our study also contact lens wear is the major risk factor for microbial keratitis. *Pseudomonas aeruginosa* was the most widely recognized causative organism isolated, present in 37% of the patient's cultures. We found an association between risk factors for keratitis and variables collectively using multivariate analysis (p value <0.001), and an association of age with the risk factor for keratitis on performing separate ANOVA for each variable (p value <0.001).

Conclusion: This study will help the clinical management of patients with keratitis and will raise awareness of sufficient lens care and disinfection practices.

Keywords: Bacterial keratitis; *Pseudomonas aeruginosa*; Antibiotic susceptibilities; Pathogens; risk factor; antibiotic susceptibility; Dubai

Introduction

Bacterial keratitis is a potentially devastating ocular condition. It presents acutely and is characterized by a corneal epithelial defect with an underlying suppurative stromal infiltrate, with some serious visual impairment. Corneal condition and the pathogenicity of the infecting bacteria determine the gravity of the infection [1]. Immediate intensive antibacterial therapy, often in the form of fortified topical antibiotics, is instituted to arrest the disease process and limit the severity of complications. Nevertheless, infectious keratitis may progress to visually debilitating complications, including corneal perforation, endophthalmitis, and loss of the eye [2,3]. A normal eye's cornea has natural resistance to infection, therefore predisposing conditions lead to severe keratitis. Risk factors for bacterial keratitis have been well documented and most commonly include trauma, contact lens use, and preexisting ocular surface disease [4]. Amongst these, contact lens related keratitis is the major cause of bacterial keratitis in developed countries [3,5]. The most common causative organisms are *Pseudomonas aeruginosa*, *Staphylococcus aureus*, coagulase-negative staphylococci, and *Streptococcus pneumoniae* [4,6,7]. Geographic and climatic factors also influence the incidence of keratitis, with more incidences in populations living in rural or in urban areas, in western,

or in developing countries [8-10]. In this study, we will review the epidemiology, risk factors, microbiologic spectrum, and antibiotic susceptibilities for bacterial keratitis (infection of the cornea) which can be caused by non-viral pathogens [11] of patients' cases during a 5-year period at the Dubai hospital in Dubai. We hypothesize that antibiotic resistance, bacterial culture, and corneal scrapings are the important parameters to be critically evaluated for the treatment of bacterial keratitis.

Materials and Methods

Local microbiology database and retrospective audit of patients (who had a corneal scraping for culture over a 5-year period) medical records were used in this study. All the relevant clinical information pertaining to the medical records and database generated between January 2011 and December 2015 were used in this study.

Data on initial diagnosis of corneal ulceration [12] of patients seen consecutively were collected on Excel spreadsheet. Briefly patients' data was screened for loss of corneal epithelium with underlying stromal infiltration and suppuration associated with signs of inflammation with or without hypopyon [13].

Exclusion criteria: Corneal ulcers with negative cultures were excluded. Typical viral ulcers and healing ulcers were excluded. These will include Mooren's ulcers [14], marginal ulcers [15], interstitial

keratitis [16], sterile neurotrophic ulcers [17], and any ulcers associated with autoimmune conditions.

Inclusion criteria: All patients' data with a corneal scraping for culture over a 5-year period were included in this study. It was identified through the local microbiology database generated between January 2011 and December 2014.

For each patient, a standardized form was filled-out documenting the socio-demographic information and clinical information. All clinical information includes duration of symptoms, previous treatment, predisposing ocular conditions and associated risk factors.

Details of clinical information

Patients were examined at the bio-microscope by an ophthalmologist where the size of the epithelial defect after staining with fluorescein was measured with the variable slit and recorded in millimeters on a standardized form. The size and depth of the stromal infiltrate was also recorded. The presence or absence of a hypopyon was recorded along with its height in millimeters. Associated ocular conditions such as blepharitis [18], dacryocystitis [19], dry eyes, corneal anesthesia were noted. Under aseptic conditions and by using a sterile scalpel blade or sterile cotton-tipped applicators corneal scrapings were made on each ulcer by an ophthalmologist, after a detailed ocular examination. Scrapings were made at slit-lamp biomicroscopy after instillation of tetracaine eye drop without preservatives. Material obtained from scraping the leading edge and the base of each ulcer were inoculated directly onto blood agar, chocolate agar, sabouraud agar and non-nutrient agar overlaid with *Escherichia coli*. For gram stain, material obtained from the corneal scraping was smeared on three separate glass slides.

Details laboratory procedures

All laboratory methods followed standard protocols. Bacterial cultures have been incubated aerobically at 37°C. After 24 hours and 48 hours, cultures on blood agar and chocolate agar were evaluated. However, cultures are discarded if there was no growth. Fungal cultures inoculated onto Sabouraud agar should be incubated at 25°C. Fungal cultures are examined on a daily basis and discarded after 1 week if no substantial growth was seen. Bacterial cultures were considered positive only if the growth of the same organism is sustained in two or more solid media. Bacterial cultures were considered positive if there is semi-confluent growth at the site of inoculation on one solid medium. Cultures for *Staphylococcus epidermidis* and diphtheroids were considered positive only if there is moderate growth on at least two solid media. The specific identification of bacterial pathogens was based on microscopic morphology, staining characteristics, and biochemical properties. A standard laboratory criterion had been used for this purpose. Fungi had been identified based on their colony characteristics on Sabouraud agar. Resistance and susceptibility to the antibiotics like penicillin, gentamicin, ciprofloxacin, vancomycin, tobramycin, polymyxin and chloramphenicol had been tested and determined by using the disc diffusion method in addition to measuring the diameter of inhibited growth around an antibiotic disc placed on an inoculated agar plate. These measurements were interpreted by using a standard protocol from the Clinical and Laboratory Standards Institute. Smear, culture, and antibiotic resistance results had been taken from the local microbiology database.

Statistical Analyses

From each patient, scores for the magnitude of the epithelial defect, anterior-chamber reaction and the location of the lesion were obtained and an index of disease severity was calculated. By using analysis of variance and chi tests with appropriate correction for multiple comparisons, associations between risk factors for keratitis and variables (patient demographics, causative organism and antibiotic resistance) was analyzed.

Controls

Either patients with corneal damage not because of keratitis or patients with *Acanthamoeba* keratitis [20] (nonpathogenic) were treated as negative controls.

Results

A total of 37 cases were enrolled for the study, of which 23 were males. Scores for the magnitude of the epithelial defect, anterior-chamber reaction and the location of the lesion were obtained from each patient, and an index of disease severity was calculated. Figure 1 shows that 40% of the patients scored the highest for disease severity, 57% had intermediate severity of the disease whereas only 3% had very low score for disease severity.

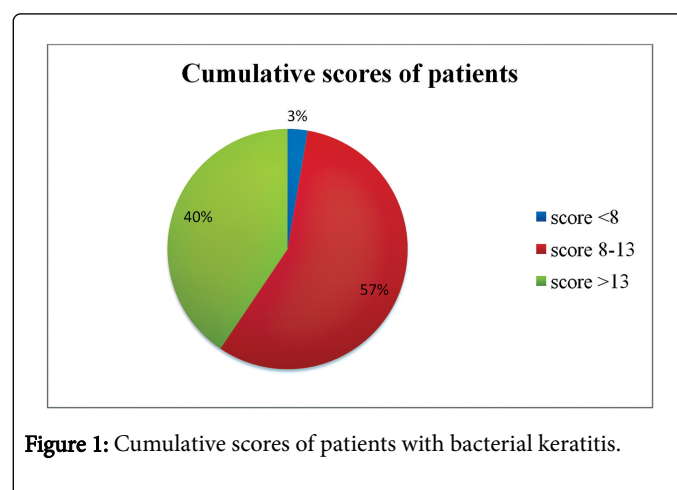


Figure 1: Cumulative scores of patients with bacterial keratitis.

Amongst the four major risk factors related to bacterial keratitis, contact lens use constitutes the maximum number of cases (35%), whereas ocular surgery constitutes the least (16%) (Figure 2).

Antibiotics	<i>Streptococcus pneumoniae</i>	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>	Others
Chloramphenicol	4 (67)	1 (25)	0 (0)	2 (25)
Ciprofloxacin	2 (33)	2 (50)	10 (71)	6 (75)
Gentamycin	0 (0)	2 (50)	9 (64)	5 (62)
Cefazolin	0 (0)	0 (0)	13 (93)	2 (25)
PITA	0 (0)	0 (0)	8 (57)	0 (0)
Tobramycin	0 (0)	2 (50)	9 (64)	3 (37)
CRM	3 (50)	2 (50)	0 (0)	1 (12)

Levofloxacin	4 (67)	0 (0)	0 (0)	0 (0)
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Table 1: Antibiotic sensitivity of microorganisms in patients with bacterial keratitis.

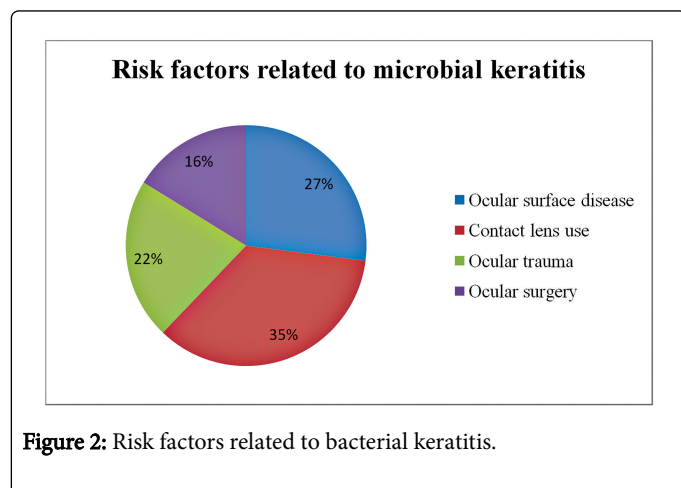


Figure 2: Risk factors related to bacterial keratitis.

From the bacterial cultures, *Pseudomonas aeruginosa* was the most widely recognized causative organism isolated, present in 37% of the patient's cultures. It was mostly sensitive to cefazolin (93%), Ciprofloxacin (71%) and Tobramycin (64%). Amongst other bacterial cultures, *Streptococcus pneumoniae* was mostly sensitive to Chloramphenicol (67%), and *Staphylococcus aureus* was equally sensitive to Ciprofloxacin (50%), Gentamycin (50%), Tobramycin (50%) and CRM (50%) (Table 1).

Multivariate analysis was used to find associations between risk factors for keratitis and the different variables (patient demographics, causative organism and antibiotic resistance). There was a significant

difference between the associated risk factors when considered jointly on the variables (Age, level of anterior chamber reaction, size of epithelial defect, location of lesion and stromal infiltration rate), with Wilk's $\Lambda=0.161$, p value <0.001 and $\eta^2=0.456$.

After performing a separate ANOVA for each of these independent variables, we found that there was a significant difference between age and the associated risk factors for the disease, with p value <0.001 and $\eta^2=0.562$. The other variables were not significantly associated with the risk factors (Table 2).

	Dependent Variable	df	Mean Square	F	Sig.	Partial Eta Squared
Associate Risk Factor	level of anterior chamber reaction	3	0.095	0.099	0.96	0.009
	Size of epithelial defect	3	1.005	1.777	0.171	0.143
	Location of lesion	3	0.066	0.568	0.64	0.051
	Stromal infiltration size and depth	3	0.668	0.783	0.512	0.068

Table 2: ANOVA for each independent variable.

We also performed Chi-square test to find association between the risk factors and causative organisms, and did not find any association between them (p value=0.536) (Table 3). Similarly, no association was found between risk factors and antibiotic resistance after performing Chi test (p value=0.245) (Table 4).

	Value	df	Asymp. Sig.(2-sided)
Pearson Chi-Square	31.626	33	0.536
Likelihood Ratio	30.67	33	0.584
No. of Valid Cases 36 --	36	-	-

Table 3: Chi-square test to find association between risk factors and causative organism.

	Value	df	Asymp. Sig.(2-sided)
Pearson Chi-Square	76.713	69	0.245
Likelihood Ratio	73.212	69	0.342
No. of Valid Cases 36 --	36	-	-

Table 4: Chi-square test to find association between risk factors and antibiotic sensitivity.

Discussion

This case study includes 37 patients (14 females and 23 males) during a 5-year period at the Dubai hospital in Dubai. The epidemiology, risk factors, microbiologic spectrum, and antibiotic susceptibilities for bacterial keratitis were reviewed for each case. Amongst the risk factors related to bacterial keratitis, contact lens use

constitutes the maximum number of cases (35%). Contact lens related keratitis is the major risk factor in patients needing corneal transplantation [21]. Variety of contact lens markets, environmental issues like water storage and disinfection are known to aggravate the contact lens infection [22]. Also, inappropriate lens wear and absence

of awareness of lens usage and care are some other risk factors for corneal ulcer among contact lens wearers [23].

From the bacterial cultures, we found that *Pseudomonas aeruginosa* was the most widely recognized causative organism isolated, present in 37% of the patient's cultures.

Pseudomonas aeruginosa was also found to be a major causative organism in previous studies too [24-29]. It was found that *Pseudomonas aeruginosa* have a tendency to adhere to the contact lens surface and it penetrates the cornea's deeper layers and leading corneal ulcers, which could cause permanent blindness [23]. Also, this higher incidence of keratitis due to contact lens may be due to the tropical climate of Dubai as reported in a study in Brisbane [28]. Similarly, *Pseudomonas aeruginosa* was mostly isolated from tropical places with higher maximum and minimum temperatures [30], whereas lower rates are found in cooler climates [25].

We also found a significant difference between various risk factors for keratitis and the other variables taken collectively. When the significance was checked for individual variables, we found significance between various risk factors for keratitis and age only [30].

Contact lens wear, has been found as a risk factor for bacterial keratitis, and most of the cases were young patients [29]. We also found that contact lens was worn by younger patients and contact lens wear was the most significant risk factor for our study too, hence it is reasonable to assume that amongst the various variables, age has been found to have significant difference with the risk factors. No significance was seen when the risk factors were compared with associated organism or with antibiotic sensitivity.

Conclusion

This case study has defined the common risk factors, causative organisms, antibiotic resistance, and patient demographics, of patients with keratitis in a hospital in Dubai. This study replicates the previous findings that contact lens wear is major risk factor for bacterial keratitis, with *Pseudomonas aeruginosa* found to be major organism associated with the keratitis. This study will help the clinical management of patients with keratitis and will raise awareness of sufficient lens care and disinfection practices. Use of daily-disposable lenses use should be encouraged to prevent the frequent incidences of the disease.

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Conflict of Interest

The authors declare no conflict of interest.

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