

Bacterial Profile and Antibiotic Susceptibility Pattern of Bacterial Keratitis at a Tertiary Hospital in Riyadh

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Background: The most common cause of ocular infections worldwide is bacteria; therefore, bacterial keratitis requires rapid and proper intervention because it is a major cause of loss of vision and ocular morbidity. Resistance studies have found increases in the resistance to ciprofloxacin, ceftazolin, and gentamicin in bacterial keratitis cases that are caused by gram-positive organisms.

Aim: To identify the common predisposing factors, causative organisms, and antibiotic profile of bacterial keratitis (BK) in a tertiary care hospital in Riyadh, Saudi Arabia.

Method: This is a retrospective study of the microbiological record of all patients diagnosed with BK at KAUH. From the first of May 2015 until the first of January 2018. Demographic data, diabetes mellitus, contact lens use, history of eye trauma, ocular surface disorders, recent ocular surgeries, current and recent medications, initial and final visual acuity, and location and size of the infiltrate were all used in the study. VA was converted to the logarithm of the minimum angle of resolution (LogMAR) for statistical analysis.

Results: 177 cases positive for BK were included. 100 (56.5%) were males, and 77 (43.5%) were females. The mean age was 43.15. Trauma was the most common predisposing factor, which was observed in 68 (38.4%) cases, followed by Ocular surface disease [52 (29.4%)]. *Staphylococcus epidermidis* was the most commonly isolated organism [61 (34.5%)], followed by *Streptococcus pneumoniae* [23 (13%)], and *Staphylococcus aureus* [18 (10.2%)]. All gram-positive cases were Vancomycin sensitive. *Staphylococcus epidermidis* showed only 4 resistant cases to chloramphenicol (7.27%), and resistance to penicillin and ampicillin was found in 55 (90%) and 53 (89.83%) cases, respectively. All *Streptococcus pneumoniae* cases were resistant to gentamicin (100%). *Staphylococcus aureus* showed high sensitivity for erythromycin [18 (100%)].

Conclusion: The most common cause of bacterial keratitis was *Staphylococcus epidermidis* (N=61), followed by *Streptococcus pneumoniae* (N=23). Trauma was the most common predisposing factor (38.4%), while contact lens use was only identified in 14 cases (7.9%). All organisms tested were sensitive to vancomycin, and there was high resistance toward penicillin (90%).

Keywords: keratitis, antibiotic, infection

Introduction

Bacterial keratitis is an infectious disease caused by a variety of bacterial strains that lead to inflammation of the cornea. It is a serious, sight-threatening condition that requires immediate intervention and proper treatment to prevent corneal scarring, perforation, and even blindness.¹ It is reported that some highly virulent organisms showed corneal destruction at the first 24–48 hrs.² Bacterial keratitis is one of the most important causes of corneal opacification, which is the second most common cause of legal blindness worldwide.³

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Staphylococcus aureus, *Streptococcus pneumoniae*, and *Pseudomonas aeruginosa* have been reported to be the leading etiological causes of bacterial keratitis.⁴ Coagulase-Negative *Staphylococci* (CoNS) have been increasingly documented as the cause of many ocular infections.⁵ Some of the common risk factors predisposing the cornea to infection are contact lens use, ocular surface disease, ocular trauma, and prior ocular surgery.^{6,7} Diagnosis of bacterial keratitis requires scraping of the cornea and culture growth to look for antibiotic sensitivity. While waiting for microbiological results, empirical therapy must be started immediately according to the clinical setting and the present microbiological spectrum and antibiotic sensitivity from the local data.⁸

Resistance studies have found increases in the resistance to ciprofloxacin, cefazolin, and gentamicin in bacterial keratitis cases that are caused by gram-positive organisms.⁸ Recent data are lacking regarding the bacterial profile and its antibiotic susceptibility pattern of bacterial keratitis in Saudi Arabia. Hence, this study aims to identify the causative organisms, predisposing factors, and antibiotic profile of bacterial keratitis in a tertiary care hospital in Riyadh, Saudi Arabia.

Methodology

Sampling

We reviewed all cases diagnosed with bacterial keratitis from May 1, 2015, until January 1, 2018, at King Abdulaziz University Hospital. By using a computer-based diagnosis code of corneal scraping, all culture-positive cases of bacterial keratitis were selected. We excluded all subjects with non-bacterial, multiple isolate cultures.

Data Collection

177 cases with a positive culture were extracted from the microbiological records and reviewed. The following data were collected from the patient's medical records: age, gender, diabetes mellitus, contact lens use, history of eye trauma, ocular diseases, recent ocular surgeries, current and recent medications, initial and final visual acuity (VA) (final VA was based on the last follow up), location and size of the infiltrate, presence of hypopyon, and complications. Details of the corneal cultures were collected, including the name of the organism and the suitability of the antibiotics used. VA was converted to the logarithm of

the minimum angle of resolution (LogMAR) for statistical analysis.

Statistical Analysis

Categorical variables were summarized as numbers and percentages, and continuous variables were summarized with mean values. Paired t-tests were used to study the association between organisms and visual acuity as well as risk factors and visual acuity, where the mean visual acuity score was compared at the first and last visits. The analysis was performed using SAS/STAT software, version 9.2 (SAS Institute Inc., Cary, NC, USA.) and R foundation for statistical computing (Vienna, Austria). A 2-sided p value < 0.05 was considered statistically significant.

Results

A total of 177 bacterial keratitis cases were included. Of the 177 cases, 100 (56.5%) were males, and 77 (43.5%) were females. The mean age of all included subjects was 43.15 years. The results of the cultures showed that the most common organisms were *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Staphylococcus hominis*, representing 61 (34.5%), 23 (13%), 18 (10.2%), 16 (9.04%), and 15 (8.48%), respectively. Risk factors for bacterial keratitis were identified and are shown in Table 1. The most common predisposing factors for bacterial keratitis were trauma, ocular surface disease (OSD), diabetes mellitus (DM), surgery, and contact lens use with a total number of 68 (38.4%), 52 (29.4%), 40 (22.6%), 39 (22%), and 14 (7.9%) cases, respectively. *Moraxella* sp commonly occurs after trauma and was observed in 7 (87.5%) cases. Moreover, *Moraxella* sp was the most commonly isolated organism after recent ocular surgery in 4 cases (50%). Methicillin-resistant *Staphylococcus aureus* (MRSA) was the most frequently isolated organism with DM and OSD in 3 patients (75%) and 2 patients (50%), respectively (Table 1). Initial and final VAs in association with organisms are summarized in Table 2. We found that 55 out of 61 cases of *Staphylococcus epidermidis* were resistant to penicillin, while 53 were resistant to ampicillin. 19 out of 23 cases of *Streptococcus pneumoniae* were tested for gentamicin and were all resistant, while 12 cases (54.55%) were resistant to penicillin (Table 3). The association between the risk factors and the visual outcomes is shown in Table 4.

Table 1 Associations Between Organisms and Risk Factors of Bacterial Keratitis

Risk Factors	Organism							
	<i>Pseudomonas aeruginosa</i> N=16	<i>Staphylococcus Epidermidis</i> N=61	<i>Staphylococcus aureus</i> N=18	<i>Streptococcus pneumoniae</i> N=23	<i>Moraxella</i> sp N=8	<i>Staphylococcus hominis</i> N=15	MRSA N=4	Others N=32
Contact lens	3 (18.75)	6 (9.84)	3 (16.67)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6.25)
Ocular surface disease	1 (6.25)	18 (29.51)	6 (33.33)	10 (43.48)	0 (0)	6 (40)	2 (50)	9 (28.13)
Recent ocular surgery	2 (12.5)	10 (16.39)	3 (16.67)	9 (39.13)	4 (50)	1 (6.67)	1 (25)	9 (28.13)
Trauma	4 (25)	17 (27.87)	7 (38.89)	10 (43.48)	7 (87.5)	3 (20)	1 (25)	19 (59.38)
Diabetes mellitus	0 (0)	13 (21.31)	3 (16.67)	8 (34.78)	3 (37.5)	2 (13.33)	3 (75)	8 (25)
Topical steroid	0 (0)	3 (4.92)	2 (11.11)	3 (13.04)	0 (0)	3 (20)	0 (0)	2 (6.25)
Systemic immunosuppression	1 (6.25)	0 (0)	1 (5.56)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Discussion

The most common cause of ocular infections worldwide is bacteria;⁹ therefore, bacterial keratitis requires rapid and proper intervention because it is a major cause of loss of vision and ocular morbidity.¹ There is a broad discrepancy in the literature about the predisposing factors, visual outcomes, and resistance patterns of bacterial keratitis; therefore, recurrent studies are required to renew the present practice and guidelines.

Table 2 Associations Between Organisms and Visual Acuity (VA)

Organism	Number	VA First Visit	VA Last Visit	P-value
<i>Pseudomonas aeruginosa</i>	3	0.45	0.10	0.500
<i>Staphylococcus epidermidis</i>	22	1.50	1.47	0.907
<i>Staphylococcus aureus</i>	7	1.76	0.94	0.093
<i>Streptococcus pneumoniae</i>	12	1.85	1.81	0.718
<i>Moraxella</i> sp	5	2.28	1.54	0.250
<i>Staphylococcus hominis</i>	4	2.75	2.50	0.915
MRSA	2	3.50	3.50	–
Others	21	1.81	1.66	0.641
Overall	76	1.78	1.58	0.076

Our study revealed that bacterial keratitis is more common in males (57%) than in their female counterparts with a mean age of 41 years. Conversely, a 2017 study conducted in Iran found that females are more susceptible to bacterial keratitis with a mean age of 22 years. This variation in results could be due to the high prevalence of contact lens use in their study, which are more widely used by the younger population.¹⁰ Our results show that the most commonly associated predisposing factor for bacterial keratitis was ocular trauma (38.4%), which is consistent with previous studies done in a neighboring country.^{10,11} Moreover, ocular trauma has been the most common cause of corneal ulcer in low-income countries (77.5%).¹² Conversely, ocular trauma was found to be less common in some studies conducted in France and the UAE,^{12,13} which could be due to the difference in the socio-economic status. OSD was the second most commonly associated factor leading to bacterial keratitis (29.4%), which seems to be high compared to other studies. However, this could be attributed to the high prevalence of OSD in Saudi Arabia, which was reported before by Bukhari A and colleagues.¹⁴ Contact lens usage was not a common cause of bacterial keratitis in our sample, which is similar to a previous study conducted in Egypt,³ however, other studies in Al-Qassim, Saudi Arabia,⁶ and Jordan¹⁵ demonstrated that contact lens use is a common cause.

According to a study that was published in 2016 in Riyadh, Saudi Arabia, the most common causative organism of bacterial keratitis was *Staphylococcus epidermidis*, followed by *Staphylococcus aureus* and *Streptococcus pneumoniae*.¹⁶ Our study reveals similar findings with

Table 3 Sensitivity and Resistance Against Most Common Causative Organisms of Bacterial Keratitis

Antibiotics	Level	Organism								
		Ps N=16	Se N=61	Sa N=18	Sp N=23	Mx N=8	Sh N=15	MRSA N=4	Gp N=20	Gn N=12
Penicillin	R	3 (100%)	55 (90.16%)	15 (83.33%)	12 (54.55%)	1 (50%)	13 (86.67%)	4 (100%)	9 (47.37%)	5 (71.43%)
Tobramycin	R	0 (0%)	1 (100%)	–	–	–	–	–	–	–
Ceftazidime	R	1 (7.69%)	–	–	0 (0%)	0 (0%)	–	–	0 (0%)	0 (0%)
Ofloxacin	R	0 (0%)	7 (13.46%)	1 (7.14%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (33.33%)
Gentamicin	R	0 (0%)	10 (16.39%)	1 (5.56%)	19 (100%)	0 (0%)	0 (0%)	0 (0%)	3 (20%)	2 (18.18%)
Ciprofloxacin	R	0 (0%)	8 (15.09%)	2 (11.11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (36.36%)
AMPICILLIN	R	4 (100%)	53 (89.83%)	14 (87.5%)	10 (47.62%)	4 (57.14%)	12 (80%)	4 (100%)	9 (45%)	6 (60%)
Erythromycin	R	2 (66.67%)	29 (48.33%)	0 (0%)	11 (47.83%)	0 (0%)	8 (57.14%)	3 (75%)	9 (45%)	4 (66.67%)
Piperacillin/ Tazobactam	R	1 (8.33%)	0 (0%)	0 (0%)	–	0 (0%)	–	–	–	1 (25%)
Amikacin	R	0 (0%)	–	–	1 (100)	0 (0%)	–	–	–	0 (0%)
Chloramphenicol	R	4 (40%)	4 (7.27%)	0 (0%)	0 (0%)	1 (16.67%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Amox/Cla	R	1 (33.33%)	26 (44.07%)	1 (5.56%)	6 (30%)	2 (25%)	8 (53.33%)	4 (100%)	3 (15.79%)	4 (40%)
Tetracycline	R	1 (50%)	19 (44.19%)	2 (11.76%)	6 (30%)	0 (0%)	3 (27.27%)	1 (25%)	3 (21.43%)	1 (50%)
Cefalexin	R	2 (50%)	26 (42.62%)	2 (11.76%)	10 (50%)	1 (20%)	8 (53.33%)	4 (100%)	6 (31.58%)	5 (62.5%)
Cefuroxime	R	2 (50%)	26 (42.62%)	1 (5.56%)	1 (5%)	1 (20%)	8 (53.33%)	4 (100%)	3 (16.67%)	5 (55.56%)
Ceftriaxone	R	2 (40%)	23 (43.4%)	0 (0%)	0 (0%)	0 (0%)	6 (50%)	3 (100%)	2 (11.76%)	1 (11.11%)
Imipenem	R	0 (0%)	–	–	–	0 (0%)	–	–	–	0(0%)
Vancomycin	R	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: Pa, *Pseudomonas aeruginosa*; Se, *staphylococcus epidermidis*; Sa, *Staphylococcus aureus*; Sp, *Streptococcus pneumoniae*; Mx, *Moraxella sp*; Sh, *Staphylococcus hominis*; MRSA, Methicillin-resistant *Staphylococcus aureus*; Gp, Gram Positive; Gn, Gram Negative; R, Resistant.

Staphylococcus epidermidis as the most common cause, while *Streptococcus pneumoniae* is the second, followed by *Staphylococcus aureus*. These results differ with one study carried out in the UAE that found *Pseudomonas*

aeruginosa to be the most common causative organism.¹³ This discrepancy in the prevalence of the causative organism could be explained due to the low number of contact lens usage in our sample, which is known to be associated

Table 4 Associations Between Risk Factors and Visual Acuity

Risk Factors	Number	VA First Visit	VA Last Visit	P-value
Contact lens	7	0.56	0.01	0.062
Osd	18	1.67	0.97	0.033
Recent ocular surgery	24	2.43	2.38	0.483
Trauma	41	2.16	2.01	0.389
Diabetes mellitus	24	2.50	2.49	0.954
Topical steroid	11	2.69	2.25	0.093

with *Pseudomonas aeruginosa*.^{17,18} Our study shows that the most common site of bacterial infiltration is paracentral (45.9%), Although another study showed that the most common infiltration site was central (51.1%).¹⁶ Our study illustrates that the paracentral infiltration is most common for all organisms except for *Staphylococcus hominis*. All causative organisms of microbial keratitis are not often associated with the presence of hypopyon except in *Streptococcus pneumoniae* where hypopyon presence is estimated to be 52.94%.

Visual outcomes after bacterial keratitis depend on several factors, such as the location, size, predisposing factors, and the causative organism.¹⁹ In our study, we looked at the effect of different predisposing factors on the visual outcomes, and we found that the presence of systemic diseases such as diabetes mellitus is associated with poor outcomes as well as a recent ocular surgery. This might be related to the fact that those patients tend to have poor visual baseline compared to normal individuals. Moreover, final VA improved for all cases except in cases caused by MRSA. This result is similar to a recent study conducted in Spain in which MRSA cases were associated with the worst prognosis.²⁰ All isolates tested for vancomycin were sensitive, including 4 cases of MRSA. Other regional data offer the same result—that is, no organism showed resistance to vancomycin.¹⁶

Staphylococcus epidermidis is the most commonly isolated organism (n=61) and showed a high sensitivity rate for vancomycin [61 (100%)], chloramphenicol [51 (92.73%)], ofloxacin [45 (86.54%)], ciprofloxacin [45 (84.91%)], and gentamicin [51 (83.61%)]. On the other hand, resistance to penicillin and ampicillin was found in 55 (90%) and 53 (89.83) cases, respectively.

The resistance pattern of *Streptococcus pneumoniae* to penicillin is higher in our study (54.55%) compared to a previous study conducted in Riyadh (31.9%).¹⁶ However, a study conducted in the USA showed a higher resistance to penicillin (64%).²¹ Two previous studies were performed in Saudi Arabia and Australia and showed no resistance cases to ofloxacin; on the other hand, one case of *Streptococcus pneumoniae* was resistant to ofloxacin. Moreover, all cases tested for gentamicin were resistant. Similar to other previous studies, no cases were resistant to vancomycin, ceftriaxone, ciprofloxacin, and chloramphenicol.^{20,22}

In our study, all cases of *Staphylococcus aureus* tested for erythromycin were sensitive (100%), which is in contrast to studies done in the USA, Saudi Arabia, and Taiwan that found the resistance to erythromycin to be 67%, 18.6%, and 88%, respectively.^{20,21,23} None of *Staphylococcus aureus* cases were resistant to chloramphenicol, which contrasts with the results from a previous study conducted in Australia that found a higher resistance rate (21%).²² All cases of *Staphylococcus aureus* were tested for ceftriaxone, and they were all found to be sensitive to cefoxitin. While comparing the resistance pattern of *Pseudomonas aeruginosa* to ceftazidime, it was found to be 7.69% in our study, while it was around 5.6% in a previous national study.¹⁶ *Pseudomonas aeruginosa* is sensitive to several antibiotics such as tobramycin, ofloxacin, gentamicin, ciprofloxacin, amikacin, imipenem, and meropenem. This is in contrast to the result of another study that showed resistance patterns for gentamicin, ceftazidime, and ciprofloxacin to be 4.9%, 5.6%, and 4.9%, respectively.¹⁶ Moreover, a previous study conducted in Australia predicted the resistance for ciprofloxacin to be 7%.²²

Conclusion

This work showed the common causative organisms, risk factors, and antibiotic profile of patients with bacterial keratitis in a tertiary hospital in Riyadh, Saudi Arabia. We found that the most common etiological organism of bacterial keratitis is *staphylococcus epidermidis*.

The results of our study might be helpful in clinical practice by aiding appropriate diagnosis and accurate management through the selection of the proper empirical therapy. For an accurate assessment of visual outcome, we recommend conducting a prospective study with a larger sample size. Choosing vancomycin empirically for Gram-positive organisms with Tobramycin or Ceftazidime for the coverage of gram-negative organisms is recommended followed by modifying this regimen after the culture result.

Ethical Approval and Informed Consent

This retrospective study was reviewed and approved by the institutional review board of King Saud University Hospital. The study adhered to the tenets of the Declaration of Helsinki. Since the data were anonymous and all patients had been told about possible research use of their data, informed consent had not been taken. All data were coded before analysis to ensure patient confidentiality. Only assigned staff had access to patient's information.

Disclosure

The authors report no conflicts of interest in this work.

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