Bacterial Keratitis: A Retrospective Review of 10 Years of Cultures

Queratites Bacterianas: Uma Revisão Retrospectiva de 10 Anos de Culturas

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ABSTRACT

INTRODUCTION: The purpose of this study is to evaluate demographic features, risk factors, bacterial isolates, antibiotic resistance patterns and therapeutic approach of bacterial keratitis over a period of 10 years in a tertiary referral hospital in Lisbon.

METHODS: Retrospective review of all bacterial keratitis diagnosed between 2009 and 2019.

RESULTS: A total of 350 patients were diagnosed with bacterial keratitis between 2009 and 2019. Mean age was 54.77 years and 55% of patients were female. Based on first clinical observation, 72.3% of patients were classified as having serious keratitis and 60.86% were managed as in-patients. Contact lenses were the major risk factor identified (30.3%), followed by previous keratoplasty (11.1%) and ocular trauma (10.9%). Cultures were positive for bacteria in 56.86% of patients, with gram-negative bacteria comprising more than half of the isolates (52.26%). *Pseudomonas aeruginosa* was the most common single isolate (16.3%). Monotherapy with fluoroquinolones was given to 5.7% of patients and 75.4% were treated with fortified drops of ceftazidime and vancomycin. As for outcomes, 41 patients (11.7%) were submitted to a corneal transplant and five patients were eviscerated.

CONCLUSION: Bacterial keratitis is a potentially blinding condition that leads to a great number of emergency department visits and inpatient care. Over the last 10 years, *Pseudomonas aeruginosa* has been the single most common bacterial isolate and contact lens wear the most frequent risk factor for bacterial keratitis in our center. Identifying bacterial isolates and their resistance pattern is of utmost importance for optimal management of patients.

KEYWORDS: Eye Infections, Bacterial/microbiology; Drug Resistance, Bacterial; Keratitis/diagnosis; Keratitis/drug therapy; Pseudomonas Infections; Pseudomonas aeruginosa.

RESUMO

INTRODUÇÃO: O objectivo do estudo foi avaliar as características demográficas, factores de risco, isolados bacterianos, padrões de resistência a antimicrobianos e abordagem terapêutica das queratites bacterianas nos últimos 10 anos num centro de referência terciário em Lisboa.

MÉTODOS: Revisão restrospectiva de todas as queratites bacterianas diagnosticadas entre 2009 e 2019.

RESULTADOS: Um total de 350 doentes foram diagnosticados com queratite bacteriana entre 2009 e 2019. A idade média foi de 54,77 anos e 55% dos doentes eram do sexo feminino. Com base na primeira avaliação clínica, 72,3% das infecções foram classificadas como graves e 60,86% dos doentes foram tratados em regime de internamento. O uso de lentes de contacto foi o factor de risco major identificado (30,3%), seguido de queratoplastia prévia (11,1%) e trauma ocular (10,9%). As culturas foram positivas para bactérias em 56,86% dos doentes, sendo que os gram-negativos representaram mais de metade dos isolados (52,26%). A *Pseudomonas aeruginosa* foi o agente isolado mais frequentemente (16,3%). A monoterapia com fluoroquinolonas foi prescrita a 5,7% dos doentes, enquanto 75,4% dos doentes foram tratados com colírios fortificados de ceftazidima e vancomicina. No que diz respeito a outcomes, 41 doentes (11,7%) foram submetidos a transplante de córnea e cinco foram eviscerados.

CONCLUSÃO: A queratite bacteriana é uma patologia que leva a um grande número de visitas aos serviços de urgência e necessidade de cuidados em regime de internamento. Nos últimos 10 anos, a *Pseudomonas aeruginosa* foi o agente isolado com maior frequência e o uso de lentes de contacto o factor de risco mais importante. A identificação dos isolados bacterianos e dos seus padrões de resistência é fundamental para poder optimizar os cuidados prestados aos doentes.

PALAVRAS-CHAVE: Farmacorresistência Bacteriana; Infecções Oculares Bacterianas/microbiologia; Infecções por Pseudomonas; Pseudomonas aeruginosa; Queratite/diagnóstico; Queratite/tratamento farmacológico.

INTRODUCTION

Bacterial keratitis is a major cause of visual disability.[1] Left untreated it can lead to corneal opacification, perforation, endophthalmitis and eventually blindness.[1] Major risk factors and aetiology are different throughout the globe.[1,2] Even though it is possible for a pathogen to invade a healthy cornea, most cases of bacterial keratitis occur in eyes with predisposing factors.[1] Risk factors include contact lens wear, ocular trauma, ocular surface pathology (OSP), ocular surgery, glaucoma and systemic illnesses such as diabetes mellitus and immunosuppression, amongst many others.[1,3,4] Aetiology is dependent on both environmental factors and patients' occupation, concomitant ocular and systemic diseases and demographic features.[5] Despite these variations worldwide, there appears to be a greater incidence of gram-positive isolates.[5] Predisposing factors and causative pathogens can influence the clinical course and outcome, therefore identifying the culprit microorganism is essential for optimal management and treatment. Most cases of community acquired bacterial keratitis resolve with empirical treatment and can be managed on an outpatient basis.[1] Smears and cultures are essential for cases when there is no response to empirical treatment, the corneal infiltrate is large, central and/or associated with stromal melting, the patient was submitted to corneal surgery or there is a suspected fungal, mycobacterial or amoebic culprit.[1] The gold standard for diagnosis in these cases is gram stain and culture of corneal samples.[2] Several studies have shown similar outcomes with empirical fluoroquinolones or fortified antibiotics but the regimen depends on local prevalence of agents, toxicity, availability and resistance patterns.[2,6,7] There is an emerging concern with the use of empiric broad-spectrum antibiotics and subsequent increase in antimicrobial resistance patterns, therefore frequent updates of microbiologic susceptibilities are central in order to provide best possible treatment to our patients.[8,9]

The main purpose of our study was to analyze demographic features, risk factors, culprit microorganisms and resistance patterns in bacterial keratitis patients in a tertiary referral center in Lisbon, Portugal. To our knowledge this is the first study of this kind conducted in the south of Portugal.

MATERIAL AND METHODS

The authors performed a retrospective review of electronic medical records of all gram stain and culture of corneal samples performed for diagnostic purposes in patients with suspected bacterial keratitis between September 2009 and June 2019 in the Ophthalmology department of Centro Hospitalar Universitário de Lisboa Central, Lisbon, Portugal, a tertiary referral center.

Corneal smears were obtained according to an internal protocol that determines the need for microbiologic diagnosis in patients with large, central corneal infiltrates and/or associated with stromal melting, patients submitted to corneal surgery, chronic infections resistant to broad-spectrum therapy and in suspected cases of fungal, mycobacterial or amoebic aetiology.

Patients were classified has having serious disease according to the "1, 2, 3 Rule" proposed by Vital *et al*[10] that

defines a potentially sight threatening keratitis if any one of the following are present: cells ≥ 1+ in the anterior chamber; dense infiltrate ≥ 2 mm in linear size; edge of the infiltrate ≤ 3 mm from the center of the cornea.

Most frequent risk factors (contact lens wear, keratoplasty, ocular trauma) were analysed individually and least frequent risk factors organized for analysis in four groups: extrinsic factors, ocular surface pathology, epithelial abnormalities and systemic factors.

Scrapes were obtained after instillation of topical anaesthesia from both the base of the ulcer and inferior fornix of the affected eye and inferior fornix of the contralateral eye so as to prevent a contamination bias. The samples were sent to the Microbiology Department for culture and antibiotic sensitivity testing.

The patients were retrospectively evaluated based on demographic characteristics, predisposing factors, clinical features on first visit, need for hospitalization, therapeutic approach, bacterial isolates, antibiotic resistance and final outcome.

RESULTS

A total of three hundred and fifty patients (n=350) were diagnosed with bacterial keratitis with criteria for smears and culture between 2009 and 2019. The mean age was 54.7 years (range, 5 – 95 years) and 54.6% of patients (n=191) were female. Based on first clinical observation, more than two-thirds of patients (72.3%) were classified as having serious keratitis based on the "1, 2, 3 Rule" and this tendency was seen across all subgroups (minimum of 58.5% in the contact lens group and maximum of 89.7% in the keratoplasty group). The rate of hospitalization varied between 48.1% (in the contact lens group) and 79% (in the keratoplasty group), with 60.9% of all patients managed as inpatients (Table 1).

The major risk factor was contact lens wear (30.3%), followed by keratoplasty (11.1%) and ocular trauma (10.9%). Ocular surface pathology, which included lid malposition, trichiasis, lagophthalmos, blepharitis, rheumatoid arthritis, ocular rosacea, was identified as a risk factor in 27 patients (7.7%) and epithelial abnormalities, such as neurotrophic ulcer, persistent epithelial defect, recurrent erosion and previous herpetic keratitis, in another 26 patients (7.4%). Extrinsic factors including ocular medication, previous ocular surgery and intra-corneal ring segment implantation comprised 6.3% of cases and systemic risk factors 6.9%, most frequently diabetes, HIV and other immunosuppressed states. In approximately 19% of cases a risk factor was not identified or elicited by patient history.

Contact lens wear was the major risk factor identified in younger patients and ocular trauma was more frequent in patients with ages comprised between 40 and 70 with a higher prevalence amongst men (86.8%). With increasing age, ocular surface pathology, epithelial abnormalities and previous keratoplasty were identified more frequently as a risk factors.

Cultures were positive for bacteria in 56.9% of patients, with gram-negative bacteria comprising more than half of the isolates (53.3%) and gram-positive bacteria 35.7%. When analysing by risk factor (Fig. 1), in the contact lens group

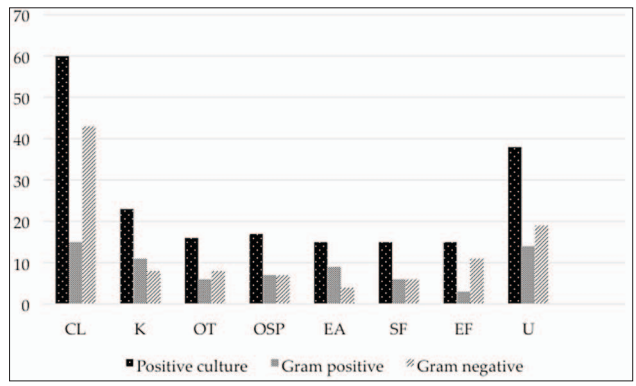

Figure 1. Distribution of positive cultures, gram-negative and gram-positive isolates according to risk factor identified.

CL – contact lens; EA – epithelial abnormalities; EF – extrinsic factor; K – keratoplasty; OSP – ocular surface pathology; OT – ocular trauma; SF – systemic factor; T – total; U – unknown.

Table 1. Distribution of patients, mean age, serious keratitis and hospitalization according to risk factor identified.

Risk Factor	Patients n (%)	Mean age years	Serious keratitis n (%)[a]	Hospitalization n (%)[a]
Contact Lens	106 (30.3)	37.04	62 (58.5)	51 (48.1)
Keratoplasty	39 (11.1)	64.21	35 (89.7)	30 (76.9)
Ocular Trauma	38 (10.9)	55.66	31 (81.6)	30 (79.0)
OSP	27 (7.7)	67.37	19 (70.4)	17 (63.0)
Epithelial abnormalities	26 (7.4)	61.69	18 (69.2)	13 (50.0)
Systemic Factors	24 (6.9)	61.50	17 (70.8)	15 (62.5)
Extrinsic Factors	22 (6.3)	68.14	18 (81.8)	14 (63.6)
Unknown	68 (19.4)	62.18	53 (77.9)	43 (63.2)
Total	350 (100)	54.77	253 (72.3)	213 (60.9)

[a] Percentages were calculated with respect to total number of patients within each risk factor
OSP – ocular surface pathology.

gram-negatives were responsible for the majority of positive cultures (40.6% of all contact lens related cases), as well as in the extrinsic factors group (50%). In the remaining groups gram positive and gram-negative agents were responsible for 15% to 30% of cases each. The rate of polymicrobial keratitis was below 12% in every risk factor group and overall represented 11.1% of all positive cultures.

Pseudomonas aeruginosa was the most common single isolate, identified in 16.3% of all cases, particularly in the contact lens group (34% of all contact lens related cases). *Moraxella* species were responsible for 6.6% and *Serratia* species for 3.4% of cases, being the second and third most frequent gram-negative agents isolated, respectively. Most frequent agents identified in the gram-positive group were *Staphylococcus aureus methicillin-sensitive* (MSSA), responsible for 7.7% of all cases of bacterial keratitis, followed by *Streptococcus pneumoniae* (3.1%), *Streptococcus epidermidis* (2.3%) and *Staphylococcus aureus methicillin-resistant* (MRSA), responsible for 2% of cases (Table 2).

Monotherapy was not the treatment regimen of choice in most cases of bacterial keratitis in our center comprising only 5.7% of cases (Table 3). Less than 10% of cases in each subgroup of risk factors were treated with single agents and most frequent agents prescribed as monotherapy were topical fluoroquinolones namely ofloxacin, ciprofloxacin and moxifloxacin. Almost 76% of patients were initially treated with fortified drops of ceftazidime and vancomycin with more than half of patients in each subgroup being given this treatment regimen. Systemic treatment with the same agents was offered to 40.6% of patients. As an alternative to systemic vancomycin and ceftazidime, 22.6% of patients were given an oral fluoroquinolone, most frequent being oral ciprofloxacin.

With respect to antibiotic resistances, more than half (63.4%) of gram-positive agents isolated demonstrated *in vitro* resistance to at least one antibiotic whilst in the gram-negative group the percentage was much lower (23.6% of isolates) (Table 4). The majority of resistances identified in

Table 2. Distribution of most frequent pathogens according to risk factor identified.

	CL	K	OT	OSP	EA	SF	EF	*U*	T
	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)
P. aeruginosa	36 (34.0)	1 (2.6)	3 (7.9)	2 (7.4)	1 (3.8)	0 (0)	5 (2.7)	9 (13.2)	57 (16.3)
S. aureus MS	4 (3.8)	3 (7.7)	3 (7.9)	1 (3.7)	5 (19.2)	4 (16.7)	2 (9.1)	5 (7.4)	27 (7.7)
Moraxella spp	1 (0.9)	1 (2.6)	4 (10.5)	3 (11.1)	2 (7.7)	3 (12.5)	1 (4.5)	8 (11.8)	23 (6.6)
Serratia spp	3 (2.8)	4 (10.3)	3 (7.9)	2 (7.4)	0 (0)	0 (0)	0 (0)	0 (0)	12 (3.4)
S. pneumoniae	0 (0)	2 (5.1)	2 (5.3)	3 (11.1)	1 (3.8)	0 (0)	1 (4.5)	2 (2.9)	11 (3.1)
S. epidermidis	3 (2.8)	2 (5.1)	0 (0)	1 (3.7)	0 (0)	0 (0)	0 (0)	2 (2.9)	8 (2.3)
S. aureus MR	1 (0.9)	2 (5.1)	0 (0)	0 (0)	1 (3.8)	2 (8.3)	0 (0)	1 (1.5)	7 (2.0)
Other Gram +	7 (6.6)	2 (5.1)	1 (2.6)	2 (7.4)	2 (7.7)	0 (0)	0(0)	4 (5.9)	18 (5.1)
Other Gram -	3 (2.8)	2 (5.1)	1 (2.6)	0 (0)	1 (3.8)	3 (12.5)	2 (9.1)	2 (2.9)	14 (4.0)

[a] Percentages were calculated with respect to total number of patients within each risk factor.

CL – contact lens; EA – epithelial abnormalities; EF – extrinsic factor; K – keratoplasty; OSP – ocular surface pathology; OT – ocular trauma; SF – systemic factor; T – total; U – unknown.

Table 3. Distribution of treatment approach according to risk factor identified.

Risk Factor	Fortified drops	Systemic VAN+CTZ	Oral Quinolone	Monotherapy
	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]
Contact Lens	73 (69.0)	30 (28.3)	20 (18.9)	10 (9.4)
Keratoplasty	32 (82.1)	23 (59.0)	6 (15.4)	1 (2.6)
Ocular Trauma	32 (84.2)	16 (42.1)	15 (39.5)	1 (2.6)
OSP	20 (74.1)	14 (51.9)	6 (22.2)	1 (3.7)
Epithelial abnormalities	16 (61.5)	8 (30.8)	6 (23.1)	1 (3.9)
Systemic Factors	18 (75.0)	9 (37.5)	3 (12.5)	1 (4.2)
Extrinsic Factors	19 (86.4)	11 (50.0)	4 (18.2)	2 (9.1)
Unknown	54 (79.4)	31 (45.6)	19 (27.9)	3 (4.4)
Total	264 (75.4)	142 (40.6)	79 (22.6)	20 (5.7)

[a] Percentages were calculated with respect to total number of patients within each risk factor.

CTZ – ceftazidime; OSP – ocular surface pathology; VAN – vancomycin.

Table 4. In vitro resistances of the most common bacterial isolates to most frequent topical antibiotics prescribed in clinical practice in our center.

	CFX	LFX	OFX	MFX	CTZ	GEN	TOB	*VAN*	ERT	AZT	Total
	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]	n (%)[a]
Gram-positives	4 (5.6)	9 (12.7)	0 (0)	8 (11.3)	0 (0)	5 (7.0)	1 (1.4)	0 (0)	19 (26.8)	0 (0)	45 (63.4)
S. aureus MS	1 (3.7)	2 (7.4)	0 (0)	2 (7.4)	0 (0)	1 (3.7)	0 (0)	0 (0)	4 (14.8)	0 (0)	20 (74.1)
S. pneumoniae	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (18.2)	0 (0)	5 (45.5)
S. epidermidis	2 (25)	2 (25)	0 (0)	2 (25)	0 (0)	2 (25)	0 (0)	0 (0)	7 (87.5)	0 (0)	8 (100)
S. aureus MR	1 (14.3)	4 (57.1)	0 (0)	4 (57.1)	0 (0)	1 (14.3)	1 (14.3)	0 (0)	4 (57.1)	0 (0)	7 (100)
Other gram-positives	0 (0)	1 (5.5)	0 (0)	0 (0)	0 (0)	1 (5.5)	0 (0)	0 (0)	2 (11.1)	0 (0)	5 (27.8)
Gram-negatives	2 (1.9)	2 (1.9)	0 (0)	0 (0)	1 (0.9)	2 (1.9)	1 (0.9)	0 (0)	0 (0)	0 (0)	25 (23.6)
P. aeruginosa	2 (3.5)	2 (3.5)	0 (0)	0 (0)	1 (1.8)	1 (1.8)	1 (1.8)	0 (0)	0 (0)	0 (0)	4 (7.0)
Moraxella spp	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.3)	0 (0)	0 (0)	0 (0)	0 (0)	3 (13.0)
Serratia spp	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	12 (100)
Other gram-negatives	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (42.9)

[a] Percentages were calculated with respect to total number of each agent identified.

AZT – azithromycin; CFX – ciprofloxacin; CTZ – ceftazidime; ERT – erythromycin; GEN – gentamicin; LFX – levofloxacin; MFX – moxifloxacin; MR – methicillin-resistant; MS – methicillin-sensitive; OFX – ofloxacin; TOB – tobramycin; VAN – vancomycin.

the gram-positive group were to penicillin and penicillin derivates not commonly used in clinical practice as topical therapy. With clinical relevance was the resistance to fluoroquinolones in the gram-positive group with *in vitro* resistance to ciprofloxacin in 5.6% of isolates, to levofloxacin in 12.7% of cases and to moxifloxacin in 11.3% of cases. In the gram-negative group we identified two *P. aeruginosa* isolates with in vitro resistance to ciprofloxacin and levofloxacin and one other isolate with resistance to ceftazidime. There were no other clinically relevant resistances in the gram-negative group.

A total of 41 patients (11.7% of all cases) were submitted to a corneal transplant in the sequence of their bacterial keratitis. Sixteen of them where performed in the acute phase due to corneal perforation, 9 of which in the subgroup of patients with previous keratoplasties. The remaining 25 patients were submitted to a penetrating keratoplasty for the management of sequelae, mainly corneal scars and descemetoceles. A total of five patients were eviscerated, three in the acute setting due to resultant endophthalmitis unresponsive to treatment and two latter in the course of their disease.

DISCUSSION

Bacterial keratitis is a sight-threatening condition that leads to a great number of emergency department visits and inpatient care. It requires immediate intervention in order to prevent complications such as corneal scarring, perforation and intra-ocular extension of infection that can ultimately lead to permanent blindness.[1,11]

The literature shows discrepancies worldwide concerning most common risk factors, pathogens and therapeutic approaches. The evolution of the infection is dependent on the causative pathogen with some agents such as *Pseudomonas*, *Streptococcus pneumoniae* and *Neisseria gonorrhoeae* being able to lead to corneal melting within the first 24 to 48 hours.[1,11] Therefore, optimal management depends not only on rapid identification and institution of treatment but also on knowledge of risk factors, microbiologic profile and antibiotic resistance patterns in a given area.

A total of 350 patients with suspected bacterial keratitis and indication for smears and cultures were observed in our hospital center between 2009 and 2019. Patients with small and peripheral corneal ulcers not submitted to prior ocular surgeries or without ocular comorbidities were treated empirically without need for scrapings and thus were not included in this study. We found a slight female preponderance similarly to other results published in literature.[12]

More than half of our patients were hospitalized in contrast with previous studies where 20% to 40% of patients were managed as inpatients.[7,13] We only included patients with criteria for smears and culture in the setting of a suspected bacterial keratitis which can explain the high percentage of serious cases (72.3%) and subsequently high rate of hospitalization (60.9%). This conclusion is in line with the observation that the subgroup of patients with a lower rate of serious infection, namely the contact lens group, showed a lower rate of hospitalization and the subgroup with the highest percentage of serious keratitis, the keratoplasty group, had the highest rate of inpatient care. The fact that our hospital is a tertiary referral center, our cornea department is a tertiary department and the fact that between 2009 and 2019 had a 24-7 emergency department might also explain the high number of severe disease encountered.

Contact lens wear was the major risk factor identified in our population (30.3% of all cases), in line with previous studies and it was as expected more frequent in younger

cohorts.[3,7,13,14] The second most common risk factor was previous keratoplasty (11.1% of all cases) and this might be explained by the high number of keratoplasties performed in our center annually and in particularly complex patients. Microbial keratitis is a major complication in patients submitted to keratoplasties with an estimated incidence of 1.8% – 7.4% in the developed countries.[15] In a study from the United Kingdom[15] gram-positives were responsible for more than half of cases of bacterial keratitis in keratoplasty patients with most frequently involved agents being *S. aureus*, *S. pneumoniae* and *P. aeruginosa.* Similarly, in our study there was a higher number of cases caused by gram-positive bacteria with most frequently isolated organisms being *S. aureus*, *S. pneumoniae*, *S. epidermidis* and *Serratia* species. Ocular trauma, a major risk factor for infectious keratitis and responsible for up to 85% of cases in some regions of the globe, especially in developing countries,[3,8,13] was the third most frequent risk factor identified in our population (10.9%) with a high number of patients referred from rural areas from the south of Portugal.

The yield of positive cultures from the 350 corneal samples collected in our center was 56.9% which contrasts with previous studies where the percentages were much lower.[8,9,12,13] One explanation for this might be the fact that only patients with the criteria presented were cultured as previously explained and similar results were found in a Spanish study[14] that excluded all patient not submitted to corneal scrapings. Truong *el al*[7] also reported a similar strategy where cultures were reserved for severe infections with a yield of positive cultures of 73%. Gram-negative isolates comprised more than half (53.3%), whereas polymicrobial keratitis was responsible for 11.1% of positive cultures. Most studies report gram-positive agents as the most frequently isolated,[5,7,9,14,16,17] including one from the north of Portugal[8] where gram-positive bacteria were responsible for 55.5% of positive cultures. A study conducted in the United Kingdom[12] documented the highest rate of gram-negative isolates (61.1%) highlighting a trend for increasing gram-negative infection due to widespread use of contact lenses, which is in keeping with our results with the most frequent factor being contact lens wear and most frequent agents being gram-negative isolates. *P. aeruginosa* was the most common isolate in our study being responsible for 16.3% of all bacterial keratitis and 28.6% of all positive cultures. Multiple other studies report *P. aeruginosa* as the most frequently isolated gram-negative bacteria.[7,12,17,18] Gram-positive isolates were only responsible for 35.7% of all positive cultures in our study with most frequent isolate being MSSA, responsible for 7.7% of all bacterial keratitis. *S. epidermidis* and MRSA were responsible for 2% of cases each. In a study from Toronto[17] there was a high rate of *coagulase-negative Staphylococcus* (CNS) isolates which accounted for almost 37% of positive cultures, similarly to other studies.[19] CNS are part of the commensal ocular flora and are considered the leading cause of bacterial keratitis in the elderly population according to Manikandan *et al*.[20] The fact that our study cohort had a mean age of 54.7 years might also explain why our data differs from that of other studies.

The preferred treatment approach in our center was fortified drops of ceftazidime and vancomycin with 75.4% of all patients being managed with this combination of antibiotics. Monotherapy with fluoroquinolones was observed in as little as 5.7% of cases, which might be explained by the high rate of serious keratitis at presentation and patient selection for this study. Fluoroquinolone monotherapy is widely used in corneal infections due to its broad-spectrum of action and low toxicity.[12,21] This has led to emerging levels of resistance, particularly among gram-positive bacteria but with some concerns as well in gram-negative isolates.[12] We encountered a higher rate of antimicrobial resistance in gram-positive isolates (63.4%) when compared with gram-negative isolates (23.6%). In the gram-positive group we identified a global 26.8% resistance rate to erythromycin, 12.7% to levofloxacin, 11.3% to moxifloxacin and 5.6% to ciprofloxacin more pronounced amongst *S. aureus* isolates. There is increasing concern with multi-drug resistant MRSA isolates[17] with reports in the United States of isolates of MRSA with 80% of resistance to fluoroquinolones.[2] Even though they were responsible for only 2% of all bacterial keratitis in our study all were resistant to at least one antibiotic with 57.1% resistance documented to levofloxacin, moxifloxacin and erythromycin and 14.3% resistance to ciprofloxacin, gentamicin and tobramycin. In the gram-negative group we identified two *P. aeruginosa* isolates with resistance to ciprofloxacin and levofloxacin, one of which also resistant to gentamicin and tobramycin and the other simultaneously resistant to ceftazidime. Only two other *P. aeruginosa* isolates were resistant to antibiotics not commonly employed in our center with a total of 7% of P. aeruginosa isolates with antimicrobial resistances. With the exception of one *Moraxella* species isolate resistant to gentamicin, we did not find other clinically significant resistances in the gram-negative group.

Unlike previous studies[15,22] we report the rate of keratoplasties as outcome in order to evaluate the burden of bacterial keratitis to our Transplant Department. Almost 12% of our patients were submitted to a corneal transplant in the sequence of their bacterial keratitis either for infection control purposes or management of sequelae. Forty-four percent of cases were regrafts. The severity at presentation is related to the outcome[23] and these numbers highlight the high rate of serious disease encountered in our center and the high demand for corneal tissues.

The authors identify as limitations the retrospective design of the study and the potential for referral bias as the encountered population had a high rate of serious disease at presentation. This was a single center study so results might not be comparable with other countries or different regions in the same country.

The importance of these retrospective reviews resides on providing clinicians evidence-based guidelines with treatment algorithms for management of suspected cases of bacterial keratitis based on local prevalence of agents and antibiotic resistance patterns. Continuous updates on demographic features, risk factors, isolates and resistance patterns are therefore crucial for an optimal standard of care for our patients.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

RSP: Data collection and analysis, conceptualization and original draft creation.

DM, MV: Data collection and analysis.

SC, RA: Methodology, investigation, manuscript revision.

CB, FF, NA, VM, PC, JF: Conceptualization, supervision, manuscript revision.

RSP: Colheita e análise de dados, conceptualização e redação do rascunho.

DM, MV: Colheita e análise de dados.

SC, RA: Metodologia, investigação, revisão do manuscrito.

CB, FF, NA, VM, PC, JF: Conceptualização, supervisão, revisão do manuscrito.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

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