Original Article

Infectious keratitis: Epidemiological profile at Hospital Universitario San Ignacio, Bogotá, DC

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Abstract

Purpose: Describe the population of patients with infectious keratitis during 5 years in a tertiary hospital in Bogotá, Colombia.

Materials and Methods: Retrospective observational cross-sectional study conducted from 2017 to 2021. Clinical records of all patients with infectious keratitis were reviewed, and sex, age, risk factors for keratitis, complications at the moment of initial consultation, and best corrected visual acuity (BCVA) were described, as were clinical and microbiological diagnoses. BCVA discriminated by previous treatment and etiology was evaluated.

Results: Nine hundred and seventy-three cases were reviewed. The mean age was 44.61, and males were slightly more affected. Contact lens use was the most commonly presented risk factor, present in 181 (18.6%). Patients who had received treatment with corticosteroids were more likely to have a BCVA of worse than 20/400 (x^2 test 4.86, $P < 0.05$). BCVA was better than 20/40 in 56.42%, 20/40–20/400 in 26.73%, and worse than 20/400 in 16.86% of patients. Patients with fungal or parasite keratitis were more likely to have a BCVA of worse than 20/400 with an OR if 7.8. 54.16% of patients had bacterial keratitis; the second most frequent etiology was viral, followed by fungal, and lastly, parasites. Cultures were taken in 10.38% of the patients, out of which 54 had positive culture results; the culture positivity proportion was 63.72%.

Conclusions: Infectious keratitis was more common in middle-aged males, and contact lens use was more frequently reported than trauma. Patients were more likely to have a worse BCVA if they had received corticosteroids prior to initial consultation, and patients who presented with fungal or parasitic infections were more likely to have a worse BCVA. Bacterial keratitis followed by viral keratitis was the most commonly clinically diagnosed etiological agent. About 63.72% of cultures were positive, and bacterial infection was the most common microbiological diagnosis with *Pseudomonas aeruginosa* as the most frequently reported germ.

Keywords: Bacterial, culture, epidemiology, infectious keratitis, risk factors

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INTRODUCTION

Infectious keratitis is the main cause of corneal blindness[1] in the US. According to Colier *et al*., infectious keratitis is responsible for one million visits to clinical practitioners and 58.000 emergency departments per year.[2] It is also known that developing countries are more affected by infectious keratitis.[3] However, an early diagnosis and adequate treatment can significantly reduce the risk of long-term sequelae of the infectious process, helping to decrease the burden of disease. Infectious keratitis is caused by microorganisms invading the corneal tissue, such as bacteria, fungi, viruses, or parasites. Incidence varies greatly; in developed countries such as the United States, the incidence is 11 per 100,000 inhabitants,[4] while in developing countries such as Nepal, the incidence is as high as 799 patients per 100,000 inhabitants.[5,6]

Differentiating the cause of each case guarantees targeted treatment with the right antimicrobial agent, improving antimicrobial efficacy and lowering antibiotic resistance, as well as reducing side effects, for example, epithelial toxicity linked to fortified broad-spectrum antibiotics.[7] Similarly, adequately guided antimicrobial therapy results in less corneal scarring, better visual acuity, and a reduced risk of complications such as corneal perforation and endophthalmitis, conditions that can lead to functional or anatomical loss of the eye.[8]

Although corneal cultures remain the gold standard for diagnosis, clinical diagnosis is consistent with culture results,[9] and cultures have the limitation that the criteria on when to take them vary greatly between institutions and are generally based on examiner criteria.

However, there are very few studies conducted in Latin America regarding the epidemiological profile of infectious keratitis in the region. Therefore, we aimed to describe demographic and clinical characteristics as well as etiologic agents and treatments of infectious keratitis in a tertiary hospital. The correlation between clinical diagnosis and best corrected visual acuity (BCVA) and treatment before initial consultation and BCVA is described, as factors that contribute to a worse BCVA at the moment of initial consultation can lead to worse long-term visual outcomes.[10-12]

MATERIALS AND METHODS

This was a retrospective observational cross-sectional study conducted from January 2017 to May 2021, including patients from Hospital Universitario San Ignacio, Bogotá, Colombia. A tertiary hospital that serves as a reference center for patients with ophthalmological diseases, caring for patients from all regions and socioeconomic backgrounds. The study was approved by the Ethics Committee of the Faculty of Medicine, Pontificia Universidad Javeriana. The study was carried out in accordance with the tenets of the Declaration of Helsinki.

Inclusion criteria were a clinical diagnosis of infectious keratitis in patients at least 18 years old. Records were obtained from the hospital's clinical records database. Patient's records with any of the following diagnostic codes H16.0, corneal ulcer, H16.1, other and unspecified superficial keratitis without conjunctivitis, H16.3, interstitial and deep keratitis, H16.8 other keratitis, H16.9 unspecified keratitis, H19.1 conjunctivitis and keratitis in viral diseases, H19.2 keratitis and keratoconjunctivitis in infectious and parasitic diseases and H19.3 keratitis and keratoconjunctivitis in other diseases classified elsewhere. All records were verified for a clinical diagnosis of infectious keratitis.

Records from 6674 patients were obtained, all of them consulted at the emergency department. Out of these, 973 (14.66%) met our inclusion criteria and were included in the analysis. If patients had consulted more than once, only data from their initial consultation was retrieved.

A total of 12 characteristics were measured, including age, gender, laterality of the keratitis, contact lens use, and trauma up to 15 days before consultation (including blunt or penetrating trauma, or corneal foreign body). Treatment before consultation (self-medication or prescribed by non-ophthalmologist medical professionals); complications at the moment of the initial consultation, which included corneal melting, perforation, or endophthalmitis; BCVA measured with the Snell chart, which was divided into three groups: better than 20/40, 20/40–20/400, and worse than 20/400. Clinical diagnosis at the moment of the initial consultation was divided into four groups: bacterial, viral, fungal, or parasitic. Corneal cultures were taken following institutional guidelines when patients presented one or more of the following characteristics: ulcers that were larger than 2 mm, ulcers that compromised the visual axis, or ulcers that were non-responsive to topical medication. Cultures were taken for bacterial, fungal, and parasitic infections. If patients were receiving topical antibiotics at the time of initial consultation, topical treatment was suspended for a minimum of 48 h before cultures were taken.

As previously reported in the literature, we examined with a x^2 test the association between the use of medication

before initial consultation and worse BCVA. And the association between clinical diagnosis of fungal and parasitic keratitis and BCVA worse than 20/400 was analyzed with Fisher's exact test.

RESULTS

In the 973 cases [Supplementary Table 1 for the characteristics of the population], the mean age at diagnosis was 44.51 (standard deviation [SD] = 16.92) years, and there were 511 (52.52%) males. There were 507 (52.11%) keratitis in the right eye and 466 (47.89%) in the left eye.

Contact lens use was present in 181 (18.6%) patients in this group; the most common etiologies were bacterial (93.92%), followed by viral (3.86%), and fungal (1.65%). 106 (10.89%) of patients had a history of trauma. Most patients (513) had received no topical treatment before the initial ophthalmological consultation. Out of the ones who had, the most common medication received was antibiotics, reported in 217 patients, followed by lubricant in 190, corticoids were used by 147 patients, antivirals by 82, 7 had received antifungal therapy, and only 1 received treatment with antiparasitic drops [Supplementary Table 1].

BCVA was better than 20/40 in 549 (56.42%) patients, 20/40–20/400 in 260 (26.73%) patients, and worse than 20/400 in 164 (16.86%) patients [Supplementary Table 1]. Patients who had received topical treatment before consultation (460) had BCVA, [Supplementary Table 2], of better than 20/40 (51.73%), from 20/40 to 20/400 (29.34%), and worse than 20/400 (18.91%). Patients who had received no topical treatment before the initial consultation had BCVA of better than 20/40 (60.62%), from 20/40 to 20/400 (24.36%), and worse than 20/400 (15.00%). Specifically, we tested if the use of corticosteroids before the initial consultation was associated with worse BCVA (X^2 test = 4.86 $P < 0.05$).

At the moment of consultation, 922 (94.75%) patients had no complication; 24 (2.4%) presented with corneal melting, 26 (2.6%) patients presented with corneal perforation, and only 1 patient (0.1%) had endophthalmitis [Supplementary Table 1]. Nonetheless, out of the patients with corneal melting, no patients had BCVA better than 20/40 (0%), 75% had 20/40–20/400, and 20.83% had worse than 20/400. Patients with corneal perforation had a BCVA of better than 20/40 (15.38%), 20/40–20/400 (46.15%), and worse than 20/400 (38.46%). The patient with endophthalmitis had a BCVA of worse than 20/400 (100%).

The most common clinical diagnosis was bacterial in 527 (54.16%) patients, followed by viral in 419 (43.06%), fungal in 24 (2.47%), and parasites, where the least common etiology with only 3 (0.31%) patients [Supplementary Table 1].

In the patients with clinical diagnosis of bacterial keratitis (527), most patients had an initial BCVA of better than 20/40 (57.11%), followed by 20/40–20/400 (23.90%), and the least frequent BCVA was worse than 20/400 (18.97%). In patients that presented with a viral etiology (419), a better than 20/40 BCVA was found in most patients (58.70%); the second most common group was 20/40–20/400 (29.83%), followed by worse than 20/400 (11.45%). In patients with fungal keratitis (24), the most common BCVA was worse than 20/400 (54.16%), followed by 20/40–20/400 (37.5%), and finally, the least common was better than 20/40 (8.3%). In the parasitic group (n = 3), all patients had an initial BCVA of worse than 20/400 (100%) [Supplementary Table 3]. Patients who presented with fungal or parasitic infection were found to have a bigger risk of having a BCVA of worse than 20/400 (odds ratio = 7.8, Fisher's exact test $P < 0.001$). Finally, in patients who used contact lenses, the most common clinical diagnosis was bacterial (93.92%), followed by viral (3.86%), fungal (1.65%), and parasitic 3 (1.10%).

Cultures were taken [Supplementary Table 1] in 101 (10.38%) patients, out of which 54 were positive, making up a positivity of 63.72%. Most cultures were positive for bacterial infection (37, 68.52%), followed by fungal infection (15, 27.78%), and only 1 (1.85%) was positive for parasitic growth.

Of the 37 cultures positive for bacteria, the most frequently cultured bacteria growth, [Supplementary Table 4], was *Pseudomona aeruginosa (*21.62%) and *Staphylococcus epidermidis* (21.62%), with 8 positive cultures each, followed by *Streptococcus pneumoniae* with 6 patients (16.22%), *Staphylococcus aureus* was reported in (n = 5) 13.51%, *Moraxella nonliquefaciens* was reported in (n = 3) 8.11%, *Streptococcus agalactiae* was present in (n = 2) 5.41% of patients. All *Streptococcus sanguis, Stenotrophomonas maltophilia, Serratia marcescens, Moraxella lacunata, Kocuria kristinae*, and *Corynebacterium amycolatum* were only positive in one culture, accounting for 2.7% each.

Fifteen cultures were positive for fungal infections (n = 15) out of which 73.33% (n = 11) were positive for *Fusarium* spp., followed by *Curvularia spicifera* that was positive in (n = 2) 13.33% of patients. *Candida albicans* and *Aspergillus* spp. were positive in 1 culture, accounting for 6.67% of positive fungal cultures each.

DISCUSSION

Infectious keratitis is the leading cause of corneal blindness[1] and can often lead to functional or anatomical loss of the eye,[8] which can have a high burden on morbidity and frequently give rise to the need for expensive visual rehabilitation treatments.[7] However, early diagnosis and adequate treatment can significantly reduce the risk of long-term sequelae of the infectious process.[13] Most infectious keratitis studies are conducted in developed countries; there is a large gap of knowledge in Latin America regarding infectious keratitis, with very few studies that can provide an epidemiological profile in our population. With this study, we aimed to describe the population of patients with infectious keratitis diagnosed during 5 years in a tertiary hospital in Bogotá, Colombia. The present study has a larger population than previous studies in our region,[13-15] and since it was conducted in a tertiary hospital that serves as one of the reference centers for ophthalmological patients all over the country, it provides a broad scope, including patients from different regions and socio-economic backgrounds.

We found that infectious keratitis most commonly presents in middle-aged adults with a mean age of 44.51(SD 16.92), although no patients under 18 year were included in our analysis, a very slight predilection for males (52.52%) was also found, this is similar to what is reported in international literature, for example Bajracharya *et al*., in Nepal reported a mean age of 47.9 years and a similar predilection for males with 53.8% of patients.[16]

The prevalence of contact lens use was (18.6%), was more frequently reported than trauma (10.89%), and patients who had contact lens use were diagnosed with bacterial keratitis more frequently (93.92%) than other infectious keratitis population (54.16%); parasitic keratitis was the least frequent diagnosis, nonetheless, 66% of patients with parasitic keratitis had prior contact lens use. This correlates with the known association between bacterial and parasitic keratitis and contact lens use,[17] which raises questions about whether chair time for contact lens use is effective or if new strategies for ensuring safe contact lens use are needed.

Similarly, patients who had received corticosteroids as topical treatment before initial consultation were more likely to have a BCVA worse than 20/400 compared to patients who had not received them. This could be explained by the well-described association between the use of corticosteroids and progression of infectious keratitis.[10,18] Corticoids were used by 31.95% of patients who had received treatment prior to initial consultation and were the third most commonly reported medication. This highlights the need for education for both the general population and non-ophthalmologist medical professionals on the potential risks of corticoid use without a clear diagnosis.

BCVA varied depending on clinical diagnosis; patients with a clinical diagnosis of both bacterial and viral keratitis were more likely to have an initial BCVA of better than 20/400 than patients who presented with fungal and parasitic keratitis. Considering that worse BCVA at diagnosis directly correlates with worse long-term visual outcomes,[10-12] a follow-up study could be done that could confirm that patients presenting with bacterial or viral keratitis are less likely to have a worse long-term visual outcome than those who presented with fungal or parasitic keratitis.

In our institution, not all cases of infectious keratitis are cultured; only the ones who comply with institutional criteria. Our study showed that bacterial infection is the most common clinical diagnosis (54.16%), and it is also the most common microbiological diagnosis, as cultures were more commonly positive for bacterial infection (68.52%), which is comparable to what is reported in most literature.[8]

In developed countries such as Portugal, Oliveira-Ferreira *et al*. analyzed 1360 corneal cultures over 10 years, obtaining 35.1% of culture positivity.[19] Bacterial infection was the most common etiology, accounting for 76.78% of corneal cultures.[19] In developing countries, Sakr *et al*. carried out a study in Alexandria, Egypt, that included 284 patients in a 5-year retrospective study where viral keratitis was reported as the most frequent etiology, accounting for 41.55% of patients and 76.8% culture positivity.[8]

Farias *et al*. did an 8-year retrospective study in Brazil, analyzing 187 patients with 87.17% culture positivity, with bacteria being the most common etiological agent, accounting for 44.91% of patients.[14] In 2012, Julio C. Hernandez et al. did a 1-year retrospective study in Conde Valenciana, Mexico, that included 120 patients, with a culture positivity proportion of 45.83% with bacteria being the etiological agent in 89.09% of patients.[15]

Even if it could be explained because of large variability in criteria for taking cultures between institutions, with cultures being taken for all patients with a diagnosis of infectious keratitis in some centers, analyzing the previous studies, we can see that there is high variability on both, etiology and culture positivity depending on geographical location, which highlights the need for large studies in Colombia, where the largest study was a 1-year

retrospective study carried out by Serrano-Calderón *et al.* in 2007, which included 86 patients with a reported culture positivity proportion of 88.9%, with bacterial infection accounting for 69% of patients.[13] Although this provides a general idea of our epidemiological profile, reliable data regarding the characteristics of infectious keratitis are barely available at present, particularly in Latin America, and even less so in Colombia.

Even if it was the most common clinical and microbiological diagnosis in our study, the frequency of bacterial keratitis is significantly lower than previously reported in Colombia (69%) and other countries such as Mexico (89.09%),[15,20] and Portugal (76.78%),[19] and is most similar to that reported in Brazil (44.91%).[14]

The most common bacteria reported were *P. aeruginosa* and *S. epidermidis* accounting for 43.22% of all bacterial cultures, Ormerod *et al.* conducted an 11-year retrospective study in California USA analyzing 242 patients, in this study coagulase negative staphylococci were the most frequently reported germs (23%) followed by *S. aureus* (22%) and *P. aeruginosa* (19%).[18] This shows that in culture-positive bacterial keratitis, the causal microbes in our region are similar to those reported in other regions.

The clinical diagnosis of Fungal keratitis was the third most common cause of infectious keratitis in our study, which was expected considering the reported higher prevalence in countries with warm climates.[21] Ahmadikia *et al.* conducted a meta-analysis assessing 169 articles from 36 countries reporting *Fusarium* Species to be the most common etiological agents, followed by *Aspergillus, Candida,* and *Curvularia.*[21,22] In our study, *Fusarium* spp. was by far the most common etiology (73.33%), followed by *Curvularia.* This shows that perhaps, in our region, yeasts still need to be considered a common etiological agent, even if filamentous fungi continue to be the most frequent.

The main limitation with our study is that not all patients had cultures, and using the mentioned criteria for cultures con lead to higher positivity proportions. Strengths include that all of our population was analyzed, and we have a large sample; even if the results are not representative of our population, we did include patients from a wide age range and different sexes.

CONCLUSIONS

Infectious keratitis was more frequent in middle-aged males, although contact lens use was the most frequent risk factor present, trauma was almost as likely to be present. Corticosteroids were the third most frequently reported medication used before consultation, and patients who had used them were more likely to have a worse BCVA.

Most patients had a BCVA of better than 20/40; however, patients who presented with fungal or parasitic infections were more likely to have a worse BCVA. Bacterial keratitis followed by viral keratitis were the most common clinically diagnosed etiological agents for infectious keratitis in our hospital. In addition, 63.72% of the cultures were positive, and bacteria were the most frequent growth, with *Pseudomonas auruginosa* and *Staphylococcus epidermidis* as the most frequently reported germs.

Despite the fact that some results were similar to those most commonly found in the literature, there is high variability between populations that results in differences in culture positivity proportions (although this could be explained by different criteria for taking cultures between institutions) most frequent etiological agents, and risk factors. Therefore, a local epidemiological profile could help guide better treatment in patients with long-standing symptoms, multiple previous treatments, an unclear history, or other conditions that could make clinical diagnosis challenging.

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Conflicts of interest
There are no conflicts of interest.

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Supplementary Table 1: Characteristics of the population

	Mean (*n*=973), *n* (%)
Age (years)	44.51
Sex (male)	511 (52.52)
Laterality (right)	507 (52.11)
Use of contact lenses	181 (18.6)
History of trauma	106 (10.89)
BCVA	
>20/40	549 (56.42)
20/40–20/400	260 (26.73)
<20/400	164 (16.86)
Culture sampling	101 (10.38)
Positive culture results	54 (63.72)
Isolated germ	
Bacterial	37 (68.52)
Fungal	15 (27.78)
Parasite	1 (1.85)
Unreported	1 (1.85)
Complications	
None	922 (94.75)
Melting	24 (2.4)
Perforation	26 (2.6)
Endophthalmitis	1 (0.1)
Treatment initiated prior to the initial consultation	
Antibiotic	217
Antiviral	82
Antiparasitic	1
Antifungal	7
Lubricante	190
Corticosteroid	147
None	513
Primary diagnosis	
Bacterial	527 (54.16)
Viral	419 (43.06)
Fungal	24 (2.47)
Parasite	3 (0.31)

BCVA: Best corrected visual acuity

Supplementary Table 2: Reported bacteria

Identified microorganism (*n*=37)	Percentage
Pseudomona aeruginosa	21.62
Staphylococcus epidermidis	21.62
Streptococcus pneumoniae	16.22
Staphylococcus aureus	13.51
Moraxella nonliquefaciens	8.11
Streptococcus agalactiae	5.41
Streptococcus sanguis	2.7
Stenotrophomonas maltophilia	2.7
Serratia marcescens	2.7
Moraxella lacunata	2.7
Kocuria kristinae	2.7
Corynebacterium amycolatum	2.7

Supplementary Table 3: Reported fungi

Identified microorganism (*n*=15)	Percentage
Fusarium spp	73.33
Curvularia spicifera	13.33
Candida albicans	6.67
Aspergillus sp	6.67

Supplementary Table 4: Treatment before consultation and best corrected visual acuity

Treatment before consultation/BCVA	Better than 20/40 (%)	20/40–20/400 (%)	Worse than 20/400 (%)
Yes	51.73	29.34	18.91
No	60.62	24.36	15.00

BCVA: Best corrected visual acuity