Title

Characterization of Polymicrobial and Antibiotic-Resistant Infectious Keratitis in a County Hospital Setting.

Journal

Cornea Open, 2(3)

ISSN

2833-6992

Authors

Chan, Lawrence
Lopez, Jacqueline B
Saifee, Murtaza
et al.

Publication Date

2023-09-01

DOI

10.1097/coa.0000000000000016

Peer reviewed

HHS Public Access

Author manuscript

Cornea Open. Author manuscript; available in PMC 2024 March 21.

Published in final edited form as:

Cornea Open. 2023 September ; 2(3): . doi:10.1097/coa.0000000000000016.

Characterization of Polymicrobial and Antibiotic-Resistant Infectious Keratitis in a County Hospital Setting

Lawrence Chan, MD[1], **Jacqueline B. Lopez, BS**[1], **Murtaza Saifee, MD**[1], **Sriranjani Padmanabhan, MD**[1,2], **Matilda F. Chan, MD, PhD**[1,2,3], **Madeline Yung, MD**[1,2]

[1]University of California, San Francisco, Department of Ophthalmology, San Francisco, CA, USA

[2]Zuckerberg San Francisco General Hospital and Trauma Center, Department of Ophthalmology, San Francisco, CA, USA

[3]Francis I. Proctor Foundation, University of California, San Francisco, San Francisco, CA, USA

Abstract

Purpose: Infectious keratitis is a serious cause of visual impairment, particularly in low-income communities. This study examines the associations between social risk factors and polymicrobial keratitis, multidrug resistance, pathogen spectrum, and outcomes at a county hospital.

Methods: We performed a retrospective study of Zuckerberg San Francisco General Hospital patients treated for infectious keratitis from 2010–2021. Multivariable regression was performed to analyze the relationships between social, medical, and psychiatric risk factors with polymicrobial growth, multidrug resistance, and clinical outcomes.

Results: Of 174 patients with infectious keratitis, 44 (25%) had polymicrobial growth. Six patients (14%) with polymicrobial growth had multidrug-resistant organisms. Homeless patients were more likely to present with polymicrobial infection (OR 3.4, $p = 0.023$), and polymicrobial infections were associated with multidrug-resistant organisms ($p = 0.018$). Smoking, drug use, HIV positivity, prior corneal pathology, and contact lens use were not associated with an increased risk of polymicrobial infection. Eleven patients (6.3%) were started on topical antibiotics prior to presentation; of these, none developed polymicrobial infections or multidrug-resistant organisms. Polymicrobial infections increased the likelihood to initiation of fortified antibiotics (OR 2.9, $p = 0.011$) but did not impact ulcer size, final visual acuity, time to resolution, or likelihood of emergent procedures.

Conclusions: Homelessness correlates with an increased risk of polymicrobial keratitis and subsequent multidrug resistance, supporting initiation of broad antibiotic coverage in this population. Prior topical antibiotics did not increase risk of polymicrobial infection. Polymicrobial infection did not significantly worsen clinical outcomes.

Corresponding author: Madeline Yung MD, University of California, San Francisco, Department of Ophthalmology, 490 Illinois Street, Floor 5, San Francisco, CA 94143-4081, Telephone: 415-514-6853, Madeline.Yung@ucsf.edu.

Conflicts of Interest:

M.F.C. has consulted for Surrozen, Inc. and XCaliber Biotechnology, Inc. and is currently receiving a grant (R01EY032161) from the NIH/NEI. M.Y. has consulted for Iota Biosciences, Inc and is currently receiving a grant from Carl Zeiss Meditec, Inc. For the remaining authors none were declared.

Keywords

infectious keratitis; county hospital; antibiotic resistance; polymicrobial

Introduction

Infectious keratitis is an important cause of visual disability worldwide. Proper diagnosis and aggressive therapy are key to preventing poor clinical outcomes.[1] Knowledge of the spectrum of pathogens and antibiotic susceptibilities allow for providers to effectively deliver targeted antibiotic therapy. Differences in the microbial profiles of infectious keratitis have been demonstrated across geographic regions, types of care centers, and time.[2–5] Infectious keratitis is more severe in at-risk patient populations and disproportionately affects those with low socioeconomic status and barriers to care.[6–8] However, there is a paucity of data on the microbial spectrum and antibiotic resistance patterns in this population.

Polymicrobial keratitis, defined as keratitis caused by more than one bacterium or a combination of bacterial, fungal, and/or parasitic agents, has an incidence of 1.9–15%.[9–11] Polymicrobial keratitis is more challenging to treat and has worse visual outcomes compared to monomicrobial keratitis.[9,12,13] To our knowledge, there have been no studies examining polymicrobial infections in county hospital or low socioeconomic patient populations. The purpose of our study is to identify the incidence and risk factors associated with polymicrobial keratitis, as well as elucidate the microbial spectrum, multidrug resistance patterns, and treatment outcomes in a San Francisco county hospital.

Materials and Methods

A retrospective study at the Zuckerberg San Francisco General Hospital (ZSFGH) was conducted with the approval of the Institutional Review Board of the University of California, San Francisco (IRB# 19–28768). Records were reviewed for all patients who had corneal cultures obtained for suspected infectious bacterial or fungal keratitis between 2010 and 2021. Exclusion criteria included patients with a documented absence of epithelial defect on presentation, and patients with solely viral keratitis without suspected bacterial or fungal keratitis.

The following demographic data were collected from each medical record where available: age, gender, race/ethnicity (Native American, Asian/Pacific Islander, Black/African American, Hispanic/Latino(a), White, and Other), preferred language, employment status, and housing status. Patients were defined as unemployed if documented as being unemployed, disabled, or incarcerated. Retired patients were not classified as unemployed. Unhoused status was determined if the patient address was documented as “homeless” or if an unhoused status was specifically mentioned in the clinical notes. Pertinent medical history data included smoking history, recreational drug use, diabetes, human immunodeficiency virus (HIV) seropositivity, psychiatric comorbidities, prior corneal pathology (e.g., ulcers, abrasions, corneal surgeries), and contact lens use. Documented clinical data pertinent to presentation included duration of symptoms prior to presentation,

initial Snellen best-corrected visual acuity (BCVA), initial size and location of ulcer, organisms isolated from corneal cultures, and antibiotic susceptibilities. Ulcer size was determined by approximating the ulcer shape as an ellipse, using documented measurements as the horizontal and vertical diameters. For ulcers whose epithelial defect dimensions were documented, areas in mm^2 were calculated using the equation $A = \pi \cdot a \cdot b$, where a and b are the major and minor radii. Snellen visual acuity was converted to approximate logMAR equivalent values using the formula

$$\text{logMAR} = \log_{10}(\textit{Snellen denominator} / \textit{Snellen numerator})$$

with numerical imputations for low vision states (count fingers [CF] 1.9, hand motion [HM] 2.3, light perception [LP] 2.7, no light perception [NLP] 3.0) as proposed by Bach et al.[14] Collected treatment data included use of topical antibiotics (e.g., fortified vancomycin and tobramycin), use of subconjunctival antibiotics, need for emergent tectonic keratoplasty or corneal gluing, and need for delayed optical penetrating keratoplasty. Clinical outcome measures included final BCVA and time to ulcer clearance (i.e., time in days between initial presentation and documented resolution of epithelial defect). Final BCVA was defined as the visual acuity measured when the epithelial defect was first noted to be healed, or during the last documented visit if the patient was lost to follow-up before the epithelial defect was healed.

Statistical analyses were conducted using the chi-square test and 2-sided Fisher's exact test, as well as univariable and multivariable logistic and linear regressions with Stata version 16.0 (StataCorp LP, College Station, Texas). Statistical significance was defined as $p < 0.05$.

Results

A total of 237 corneal cultures were identified from the microbiology laboratory database from 2010 to 2021. Of these cultures, 174 fulfilled the inclusion criteria. Reasons for excluding 63 corneal cultures included repeat cultures from the same patient, absence of an initial epithelial defect, herpes simplex viral keratitis, and insufficient information from the records to make a definitive diagnosis of infectious keratitis.

Of the 174 patients with corneal cultures obtained for suspected bacterial or fungal keratitis, 65 (37%) had no growth on corneal cultures, 65 (37%) had monomicrobial growth, and 44 (25%) had polymicrobial growth. Ages ranged from 14 to 83 years (mean 46 years, standard deviation [SD] 14 years). By gender, the majority of patients were male (63% male and 37% female). Table 1 summarizes the demographic and relevant clinical parameters of the patients stratified by microbial growth profile. The age and gender distributions were consistent across no growth, monomicrobial, and polymicrobial culture growth profiles.

Of the patients with polymicrobial growth, 48% were unhoused, compared to 25% of monomicrobial and 11% of no growth ($p = 0.00007$, Table 1). There were no significant differences in rates of smoking history, recreational drug use, psychiatric history, HIV positivity, contact lens use, prior corneal history, and multiple corneal cultures between

culture growth profiles. When stratified by housing status, there were no differences in culture profiles for each of the above risk factors, including contact lens use.

A history of antibiotic eye drop use was documented in 11% of cases with no culture growth, 6.2% of monomicrobial cases, and 0% of polymicrobial cases. Prior antibiotic use trended toward absent culture growth, although this difference was not significant ($p = 0.11$). However, none of the patients with a prior history of antibiotic eye drop use were found to have multidrug-resistant organisms (MDRO) on culture, defined as any organism with documented resistance to two or more antibiotics on susceptibility testing. On the other hand, polymicrobial infections demonstrated an increased risk for MDRO at a rate of 14%, compared to 6.2% of monomicrobial cases ($p = 0.018$, Table 2). 14% of homeless patients had MDRO on culture, compared to 2.8% of housed patients with MDRO ($p = 0.019$). 83% of MDRO polymicrobial cases were homeless, while 25% of MDRO non-polymicrobial cases were homeless ($p = 0.19$, Table 2).

The organisms isolated in polymicrobial corneal ulcers are listed in Table 3. The five most common organisms were coagulase negative staphylococcus (64%), *Corynebacterium* spp (48%), *Moraxella* spp (30%), *Streptococcus viridans* (25%), and *Staphyloccocus aureus* (23%). Only three patients with polymicrobial infections had a fungal component. Six of 44 patients with polymicrobial infections grew MDRO. Of these six patients, five were homeless and one patient had unknown housing status. MDRO included: *Morganella morganii* resistant to ampicillin, cefazolin, and trimethoprim/sulfamethoxazole; *Staphylococcus aureus* resistant to penicillin and tetracycline; methicillin-resistant *Staphylococcus aureus* resistant to clindamycin, erythromycin, nafcillin, penicillin, and tetracycline; methicillin-resistant *Staphylococcus aureus* resistant to ciprofloxacin, clindamycin, erythromycin, levofloxacin, nafcillin, and penicillin; *Corynebacterium* spp resistant to clindamycin and erythromycin; and coagulase negative staphylococcus resistant to clindamycin, erythromycin, nafcillin, penicillin, and trimethoprim/sulfamethoxazole.

A logistic multivariable regression was performed to determine the risk factors for polymicrobial growth (Table 4). Homeless patients had a 3.4 times odds ratio of presenting with polymicrobial infection (95% CI = 1.2 – 9.9, $p = 0.023$). Smoking, recreational drug use, HIV positivity, prior corneal history, and contact lens use were not associated with an increased risk of polymicrobial infection.

The impact of polymicrobial infection on clinical measures and outcomes was assessed. Univariate logistic and linear regression analyses did not show any significant impact of polymicrobial infection on initial epithelial defect size, final logMAR visual acuity, likelihood of emergent tectonic keratoplasty/gluing, and time to epithelial defect resolution (Figure 1). The presence of polymicrobial infection was associated with an increased likelihood of initiating fortified topical antibiotics (OR 2.9, 95% CI = 1.3 – 6.4, $p = 0.011$). However, no association was seen between polymicrobial infection and initiation of subconjunctival antibiotics. No patient required a change in antibiotics as a result of their culture data; of the patients who were not started on fortified antibiotics (n = 67), only one patient had growth of an MDRO on culture (*Serratia marcescens* resistant to ampicillin and cefazolin). Receiving fortified antibiotic treatment was significantly associated with a larger

initial ulcer size (9.8 mm^2 for fortified vs 2.7 mm^2 for non-fortified, $p = 0.001$), worse initial logMAR visual acuity (1.7 for fortified vs 0.61 for non-fortified, $p < 0.001$), worse final logMAR visual acuity (1.3 for fortified vs 0.63 non-fortified, $p < 0.001$), and an increased time to epithelial defect resolution (28 days for fortified vs 13 days for non-fortified, $p = 0.008$). There was no significant difference in likelihood of emergent tectonic keratoplasty/gluing between the fortified and non-fortified groups ($p = 0.96$).

Discussion

In this study, we examined cases of infectious keratitis at a county hospital in San Francisco and report the incidence, risk factors, microbial spectrum, drug-resistance patterns, and outcomes associated with polymicrobial keratitis. The mean ages of patients were similar across the no growth, monomicrobial, and polymicrobial infection groups. All three groups also showed a male predominance, which is consistent with previous studies of infectious keratitis showing a predilection for male gender.[15,16]

There was a higher percentage of homeless patients in the polymicrobial group compared to the no growth and monomicrobial groups, and homelessness was associated with increased risk for polymicrobial infection on multivariate regression, with an odds ratio of 3.4. Polymicrobial infection was also associated with an increased risk for multidrug resistance. Possible mechanisms for the association between homelessness and increased risk of polymicrobial infection include exposure to a greater diversity of microbes in the community,[17] crowded living conditions with limited access to sanitation facilities, increased risk of trauma,[18] diminished immunity from malnutrition,[19,20] and poor contact lens hygiene. There was no association between contact lens use and polymicrobial infection in our subjects, but we did not examine their contact lens hygiene patterns. We did not find a significant association between contact lens use and housing status. Homelessness is also a risk factor for loss to follow-up and incomplete antibiotic treatment,[21] which may contribute to polymicrobial infection and multidrug resistance. Despite this association, we did not find any adverse impact of polymicrobial growth on clinical outcomes, likely due to our institutional protocol to admit unhoused patients for frequent fortified antibiotics and close monitoring. Research on the impact of social determinants on infectious keratitis outcomes is lacking relative to other ophthalmic conditions such as glaucoma, cataracts, and diabetic retinopathy.[6,22,23] One study from Aravind Eye Hospital in India found that socioeconomic barriers such as lack of access to local care contributed to delayed presentation for infectious keratitis and increased healthcare costs.[6] In the United States, patients with poor housing conditions – a known precursor to homelessness – have worse adherence to diabetic retinopathy screenings.[24] Our results suggest that homelessness is an independent risk factor for polymicrobial keratitis and subsequently MDRO, supporting the initiation of broad antibiotic coverage in this population.

Although homelessness was found to be a significant risk factor for polymicrobial infection, we found that smoking history, recreational drug use, HIV positivity, prior corneal history, and contact lens use were not significantly associated with polymicrobial infection in the multivariable regression models in this study. Interestingly, there was not a high degree of multicollinearity among these predictor variables that precluded our drawing conclusions

for the impact of each individual predictor variable on polymicrobial infection (i.e., not all patients with a history of smoking, recreational drug use, HIV positivity, etc. were homeless).

The incidence of polymicrobial infections in our study population was 25%, which is higher than previously cited rates of 1.9% to 15%.[9] One recent study from a tertiary referral center in Mexico City found a similarly high incidence of polymicrobial keratitis (32%).[25] Aside from a relatively low sample size, geographic and socioeconomic variation may contribute to this discrepancy. For example, a significant proportion of our patients is unhoused, which may result in a higher incidence of polymicrobial infection.

The most common bacterial isolates seen in polymicrobial infections were coagulase negative staphylococcus (64%), *Corynebacterium* spp (48%), *Moraxella* spp (30%), *Streptococcus viridans* (25%), and *Staphyloccocus aureus* (23%). Prior studies found similar results with *Staphylococcus* spp and *Streptococcus* spp as common bacterial isolates in polymicrobial keratitis.[11,26] *Moraxella* keratitis is relatively rare, accounting for 2–3% of all bacterial keratitis cases,[27] yet it was one of the more commonly seen organisms in our study population. It classically affects patients who have alcohol use disorder or are immunocompromised and is known to cause a wide spectrum of pathology from blepharoconjunctivitis to corneal perforation.[28] Other studies have shown that *Moraxella* infections were more severe on presentation, slower to respond to antibiotic therapy, characterized by marked inflammation requiring concurrent steroids, and had worse visual outcomes.[29,30] Hence, it is important for providers to have an increased index of suspicion for *Moraxella* keratitis in socioeconomically disadvantaged communities given the high rates in our county population.

Antibiotic resistance has become an important issue in healthcare and in ophthalmology, where resistance to moxifloxacin has been increasing over time in Northern California.[3] This knowledge affects the choice of empiric treatment in infectious keratitis cases in which culture and susceptibility data have not yet resulted. At our institution, empiric fortified antibiotics are favored over initial fluoroquinolone monotherapy. We looked at whether initiation of antibiotic eye drops by a non-ophthalmology or outside providers prior to presentation to ophthalmology at our institution impacted infection and culture data. None of the patients on prior antibiotic eye drops developed MDRO. Initiation of topical antibiotics by non-ophthalmology providers for the treatment of infectious keratitis does not appear to increase risk for multidrug resistance, although further investigation of prior antibiotic agent selection and duration of use is required. Use of topical antibiotics prior to culture trended towards decreased growth on cultures, suggesting that this practice may decrease culture yield and prevent identification of the infectious agent and precise targeting of antibiotic therapy.

Polymicrobial infection has been theorized to have worse outcomes compared to monomicrobial infections, underscoring the need to accurately identify all causative organisms to avoid complications. Microbial synergism through reduction in host resistance, increase in virulence of other microbes, and production of essential growth elements for other organisms have been postulated as mechanisms behind enhanced virulence

in infectious keratitis.[11] However, in our study, polymicrobial growth did not impact clinical outcomes on regression analyses, including final logMAR visual acuity, likelihood of emergent tectonic keratoplasty/gluing, and time to epithelial defect resolution. The presence of polymicrobial infection was associated with an increased likelihood of initiating fortified topical antibiotic treatment (OR 2.9, $p = 0.011$). We also found that receiving fortified antibiotic treatment was significantly associated with a larger initial ulcer size, worse initial and final logMAR visual acuity, and an increased time to epithelial defect resolution. However, there was no significant difference in likelihood of emergent tectonic keratoplasty/gluing between the fortified and non-fortified groups. Our outcome data may reflect institutional protocols for management of infections keratitis. Polymicrobial patients were more likely to be homeless and thus admitted to the hospital, placed on fortified antibiotics, and closely monitored to prevent medication non-compliance. The association of homelessness with polymicrobial infections and multidrug resistance supports the aggressive initiation of fortified antibiotics for unhoused patients with infectious keratitis. Our data suggest that appropriate management of polymicrobial infections may prevent worsened outcomes, though the benefits of aggressive fortified antibiotic treatment may be attenuated by the more severe initial clinical presentations of patients who receive them.

Limitations of our study include the heterogeneity of data collection; a transition from paper-based to electronic medical records during the study period resulted in incomplete records for some of the study patients. As a single-center study in a public county hospital setting, these results may not be generalizable to other locations and patient populations. The retrospective nature of the study makes it susceptible to confounders and biases such as information and selection bias. Moreover, clinical data was derived from a clinic with rotating ophthalmologists, which may lead to variable treatment regimens. We did not distinguish between contaminant and true pathogenic microbes within the culture data. Our regression models had low R^2 values, which means our variables explain a small portion of the variability in the response variable; however, significant p values still suggest a true relationship between the predictor variables, and the purpose of our models is to test for significant associations rather than to make predictions. Finally, best-corrected visual acuities were not measured with logMAR charts but rather converted from Snellen measurements with numerical imputations for low vision states.[14]

In conclusion, polymicrobial keratitis is a vision-threatening condition that can be challenging to manage. Our retrospective study of infectious keratitis cases at a San Francisco county hospital demonstrates that homelessness correlates with an increased risk of polymicrobial infection and multidrug resistance. Initial broad antibiotic coverage is warranted in this population, which aligns with conventional practice patterns among clinicians to treat corneal ulcers aggressively in homeless patients using fortified antibiotics. Prior antibiotic eye drop therapy by non-ophthalmology providers did not increase risk of polymicrobial infections or MDRO, although this practice may decrease culture yields and prevent targeted therapy. Polymicrobial infection did not significantly worsen clinical outcomes, demonstrating that successful management of these cases with appropriate triage and consideration of socioeconomic risk factors is possible.

Acknowledgments

Funding:

This study was supported by grants from the National Institutes of Health (R01 R01EY032161 [M.F.C.] and NIH-NEI P30 EY002162 – Core Grant for Vision Research), Research to Prevent Blindness (unrestricted grant to the UCSF Department of Ophthalmology), and All May See Foundation.

References

1. McLeod SD, Kolahdouz-Isfahani A, Rostamian K, Flowers CW, Lee PP, McDonnell PJ. The role of smears, cultures, and antibiotic sensitivity testing in the management of suspected infectious keratitis. Ophthalmology. 1996;103(1):23–28. doi:10.1016/s0161-6420(96)30738-0 [PubMed: 8628555]
2. Jeng BH, Gritz DC, Kumar AB, et al. Epidemiology of ulcerative keratitis in Northern California. Arch Ophthalmol Chic Ill 1960. 2010;128(8):1022–1028. doi:10.1001/archophthalmol.2010.144
3. Peng MY, Cevallos V, McLeod SD, Lietman TM, Rose-Nussbaumer J. Bacterial Keratitis: Isolated Organisms and Antibiotic Resistance Patterns in San Francisco. Cornea. 2018;37(1):84–87. doi:10.1097/ICO.0000000000001417 [PubMed: 29053557]
4. Alexandrakis G, Alfonso EC, Miller D. Shifting trends in bacterial keratitis in south Florida and emerging resistance to fluoroquinolones. Ophthalmology. 2000;107(8):1497–1502. doi:10.1016/s0161-6420(00)00179-2 [PubMed: 10919897]
5. Truong DT, Bui MT, Cavanagh HD. Epidemiology and Outcome of Microbial Keratitis: Private University Versus Urban Public Hospital Care. Eye Contact Lens. 2018;44 Suppl 1:S82–S86. doi:10.1097/ICL.0000000000000334 [PubMed: 27755163]
6. Shah H, Radhakrishnan N, Ramsewak S, et al. Demographic and socioeconomic barriers and treatment seeking behaviors of patients with infectious keratitis requiring therapeutic penetrating keratoplasty. Indian J Ophthalmol. 2019;67(10):1593–1598. doi:10.4103/ijo.IJO_1821_18 [PubMed: 31546487]
7. Song X, Xie L, Tan X, et al. A multi-center, cross-sectional study on the burden of infectious keratitis in China. PloS One. 2014;9(12):e113843. doi:10.1371/journal.pone.0113843 [PubMed: 25438169]
8. Vajpayee RB, Ray M, Panda A, et al. Risk factors for pediatric presumed microbial keratitis: a case-control study. Cornea. 1999;18(5):565–569. [PubMed: 10487431]
9. Fernandes M, Vira D, Dey M, Tanzin T, Kumar N, Sharma S. Comparison Between Polymicrobial and Fungal Keratitis: Clinical Features, Risk Factors, and Outcome. Am J Ophthalmol. 2015;160(5):873–881.e2. doi:10.1016/j.ajo.2015.07.028 [PubMed: 26210867]
10. Ray M, Nigel LCS, Tan AM. Triple infection keratitis. Eye Contact Lens. 2014;40(3):123–126. doi:10.1097/ICL.0000000000000022 [PubMed: 24681610]
11. Jones DB. Polymicrobial keratitis. Trans Am Ophthalmol Soc. 1981;79:153–167. [PubMed: 7342399]
12. Lim NCS, Lim DKA, Ray M. Polymicrobial versus monomicrobial keratitis: a retrospective comparative study. Eye Contact Lens. 2013;39(5):348–354. doi:10.1097/ICL.0b013e3182a3024e [PubMed: 23945525]
13. Khoo P, Cabrera-Aguas MP, Nguyen V, Lahra MM, Watson SL. Microbial keratitis in Sydney, Australia: risk factors, patient outcomes, and seasonal variation. Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol. 2020;258(8):1745–1755. doi:10.1007/s00417-020-04681-0
14. Bach M, Schulze-Bonsel K, Feltgen N, Burau H, Hansen L. Author Response: Numerical Imputation for Low Vision States. (eLetter). Published online January 1, 2007.
15. Sirikul T, Prabriputaloong T, Smathivat A, Chuck RS, Vongthongsri A. Predisposing factors and etiologic diagnosis of ulcerative keratitis. Cornea. 2008;27(3):283–287. doi:10.1097/ICO.0b013e31815ca0bb [PubMed: 18362653]
16. Panda A, Satpathy G, Nayak N, Kumar S, Kumar A. Demographic pattern, predisposing factors and management of ulcerative keratitis: evaluation of one thousand unilateral

cases at a tertiary care centre. Clin Experiment Ophthalmol. 2007;35(1):44–50. doi:10.1111/j.1442-9071.2007.01417.x [PubMed: 17300570]

17. Pan ES, Diep BA, Charlebois ED, et al. Population dynamics of nasal strains of methicillin-resistant Staphylococcus aureus--and their relation to community-associated disease activity. J Infect Dis. 2005;192(5):811–818. doi:10.1086/432072 [PubMed: 16088830]
18. Fleisch SB, Nash R. Medical Care of the Homeless: An American and International Issue. Prim Care. 2017;44(1):57–65. doi:10.1016/j.pop.2016.09.009 [PubMed: 28164820]
19. Thorndike AL, Yetman HE, Thorndike AN, Jeffrys M, Rowe M. Unmet health needs and barriers to health care among people experiencing homelessness in San Francisco's Mission District: a qualitative study. BMC Public Health. 2022;22(1):1071. doi:10.1186/s12889-022-13499-w [PubMed: 35637496]
20. Schaible UE, Kaufmann SHE. Malnutrition and infection: complex mechanisms and global impacts. PLoS Med. 2007;4(5):e115. doi:10.1371/journal.pmed.0040115 [PubMed: 17472433]
21. Lopez JB, Chan L, Saifee M, Padmanabhan S, Yung M, Chan MF. Risk Factors Predicting Loss to Follow-Up, Medication Noncompliance, and Poor Visual Outcomes Among Patients With Infectious Keratitis at a Public County Hospital. Cornea. Published online August 25, 2022. doi:10.1097/ICO.0000000000003121
22. Nirmalan PK, Katz J, Robin AL, et al. Utilisation of eye care services in rural south India: the Aravind Comprehensive Eye Survey. Br J Ophthalmol. 2004;88(10):1237–1241. doi:10.1136/bjo.2004.042606 [PubMed: 15377541]
23. Sleath BL, Krishnadas R, Cho M, et al. Patient-reported barriers to glaucoma medication access, use, and adherence in southern India. Indian J Ophthalmol. 2009;57(1):63–68. doi:10.4103/0301-4738.44495 [PubMed: 19075417]
24. Cai CX, Li Y, Zeger SL, McCarthy ML. Social determinants of health impacting adherence to diabetic retinopathy examinations. BMJ Open Diabetes Res Care. 2021;9(1):e002374. doi:10.1136/bmjdrc-2021-002374
25. González-Dibildox LA, Oyervidez-Alvarad JA, Vazquez-Romo KA, et al. Polymicrobial Keratitis: Risk Factors, Clinical Characteristics, Bacterial Profile, and Antimicrobial Resistance. Eye Contact Lens. 2021;47(8):465–470. doi:10.1097/ICL.0000000000000777 [PubMed: 33625061]
26. Pate JC, Jones DB, Wilhelmus KR. Prevalence and spectrum of bacterial co-infection during fungal keratitis. Br J Ophthalmol. 2006;90(3):289–292. doi:10.1136/bjo.2005.081869 [PubMed: 16488946]
27. Hoarau G, Merabet L, Brignole-Baudouin F, Mizrahi A, Borderie V, Bouheraoua N. Moraxella keratitis: epidemiology and outcomes. Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol. 2020;39(12):2317–2325. doi:10.1007/s10096-020-03985-7
28. Stern GA. Moraxella corneal ulcers: poor response to medical treatment. Ann Ophthalmol. 1982;14(3):295–298. [PubMed: 7046594]
29. McSwiney TJ, Knowles SJ, Murphy CC. Clinical and microbiological characteristics of Moraxella keratitis. Br J Ophthalmol. 2019;103(12):1704–1709. doi:10.1136/bjophthalmol-2018-313557 [PubMed: 30709811]
30. Marioneaux SJ, Cohen EJ, Arentsen JJ, Laibson PR. Moraxella keratitis. Cornea. 1991;10(1):21–24. [PubMed: 2019103]

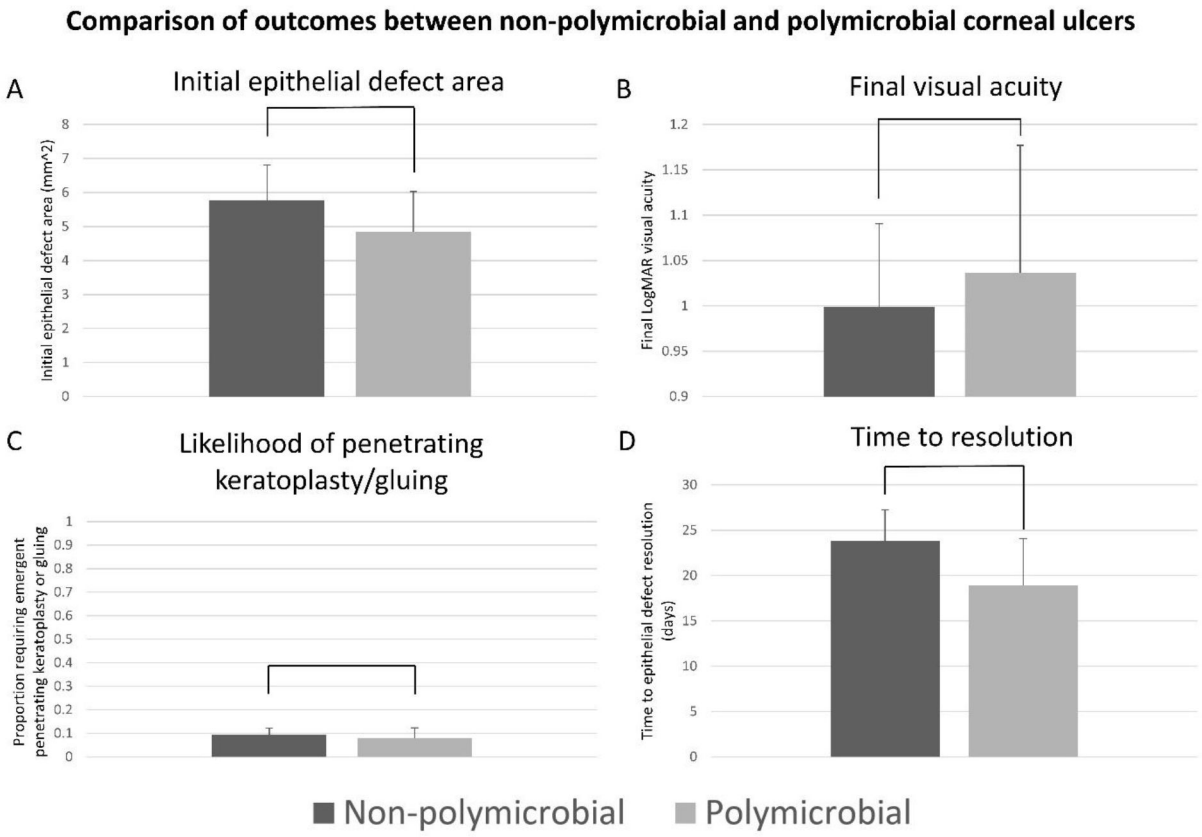

FIGURE 1. Comparison of outcomes between non-polymicrobial and polymicrobial corneal ulcers.

The presence of a polymicrobial infection did not significantly impact epithelial defect size (A, $p = 0.39$), final LogMAR visual acuity (B, $p = 0.91$), need for emergent tectonic keratoplasty/gluing (C, $p = 0.63$), or time to epithelial defect resolution (D, $p = 0.74$).

TABLE 1.

Demographic and clinical parameters of infectious keratitis stratified by microbial growth profile

Variable	No growth (N = 65)	Monomicrobial (N = 65)	Polymicrobial (N = 44)
Age			
Mean ± SD	45 ± 14	47 ± 15	46 ± 12
Median (min-max)	46 (16–80)	48 (14–77)	47 (21–83)
Gender			
Male	42 (65%)	41 (63%)	27 (61%)
Female	23 (35%)	24 (37%)	17 (39%)
Housing status			
Housed	48 (74%)	40 (62%)	19 (43%)
Unhoused *	**7 (11%)**	**16 (25%)**	**21 (48%)**
Unknown	10 (15%)	9 (14%)	4 (9.1%)
Smoking history	25 (39%)	25 (39%)	22 (50%)
Recreational drug use	20 (31%)	31 (48%)	27 (61%)
Psychiatric history	12 (19%)	12 (19%)	11 (25%)
HIV positivity	6 (9.2%)	5 (7.7%)	10 (23%)
Contact lens use	22 (34%)	20 (31%)	15 (34%)
Prior corneal history	14 (22%)	15 (23%)	7 (16%)
Multiple corneal cultures obtained	14 (22%)	15 (23%)	13 (30%)

* Significant association between homelessness and polymicrobial infection ($p < 0.0001$, Pearson chi-square = 15.70, 1 degree of freedom)

TABLE 2.

Relationship between culture growth profile, multidrug resistance, and housing status

Growth profile (total cases)	Number of MDRO cases by housing status			
	Housed (107)	Unhoused (44)	Unknown (23)	# MDRO/total cases
No growth (65)	0	0	0	0/65 (0%)
Monomicrobial (65)	3/107 (2.8%)	1/44 (2.3%)‡	0	4/65 (6.2%)†
Polymicrobial (44)	0	5/44 (11%)‡	1/23 (4.3%)	**6/44 (14%)*†**

*Significant association between multidrug resistant organisms and polymicrobial keratitis ($p = 0.018$)

†None of the monomicrobial or polymicrobial cases with multidrug-resistant organisms had a history of prior antibiotic eye drop use

‡No significant association between housing status and polymicrobial growth among MDRO cases ($p = 0.19$)

MDRO: multidrug-resistant organisms

TABLE 3.

Organisms isolated in polymicrobial corneal ulcers

Organism	Number of patients	Percentage of total (N = 44)
Gram positive cocci		
Coagulase negative staphylococcus (not specified)	28	64%
Streptococcus viridans	11	25%
Staphylococcus aureus	10	23%
Staphylococcus epidermidis	1	2.3%
Streptococcus pneumoniae	1	2.3%
Micrococcus spp	1	2.3%
Gemella spp	1	2.3%
Gram positive bacilli		
Corynebacterium spp	21	48%
Bacillus spp (not *anthracis*)	3	6.8%
Lactobacillus spp	1	2.3%
Gram negative cocci		
Moraxella spp	13	30%
Neisseria spp	2	4.5%
Gram negative bacilli		
Haemophilus spp	5	11%
Pseudomonas aeruginosa	4	9.1%
Gram negative rods (not specified)	2	4.5%
Burkholderia cepacia	1	2.3%
Morganella morganii	1	2.3%
Fungi		
Aspergillus spp	2	4.5%
Penicillium spp	1	2.3%

TABLE 4.

Logistic regression of potential predictors for polymicrobial infection

Variable	Odds ratio	95% confidence interval
Homelessness	**3.4***	**(1.2, 9.9)**
Smoking history	1.3	(0.49, 3.4)
Recreational drug use	1.6	(0.57, 4.5)
HIV positivity	2.9	(0.98, 8.8)
Prior corneal history	1.5	(0.46, 4.9)
Contact lens use	1.0	(0.40, 2.6)

* $p = 0.023$, $R^2 = 0.12$