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Laboratory Results, Epidemiological Features, and Outcome Analyses of Microbial Keratitis: A 15-Year Review from Saint Louis

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Abstract

Purpose: To evaluate the laboratory results and prognostic factors of poor clinical outcomes in microbial keratitis cases over 15 years at Saint Louis University.

Design: Retrospective cohort and trend study.

Methods: Microbiological and clinical information from culture-positive cases seen at Saint Louis University from 1999–2013 were reviewed retrospectively. Statistical analyses were used to determine microbiological and antibiotic susceptibility trends. Prognostic factors of poor clinical outcome from the literature were used to create multivariate regression models to describe our cohort.

Results: Gram-positive organisms predominated (48%), followed by Gram-negative organisms (34%) and fungi (16%). The most commonly isolated organism was *Pseudomonas aeruginosa* (21%). Oxacillin-resistant rates of *Staphylococcus aureus* and Coagulase-negative *Staphylococci* were 45% and 43%, respectively. Only the proportion of *Pseudomonas* changed significantly over time (p=0.02). The only antibiotic found to lose efficacy over time was gentamicin for Gram-positive organisms (p=0.005). Multivariate logistic regression analyses revealed that major complications were associated with large ulcers (p<0.006), fungal cases (p<0.001), and co-morbid ophthalmic conditions (p<0.001). Poor healing was associated with large ulcers (p<0.001) and fungal cases (p<0.001). Lastly, poor visual outcome was associated with large ulcers (p<0.01) and age > 60 years (p<0.02).

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Table of contents statement:

This 15-year retrospective review of microbial keratitis in Saint Louis found a high percentage of *Pseudomonas,* fungi, and oxacillin-resistant organisms. Gentamicin efficacy against Gram-positive organisms decreased over time. Multivariate logistic regression found that a large ulcer was a universal predictor of poor outcomes while fungal infections, co-morbid ophthalmic conditions, and age ≥ 60 years were also contributory factors.

Conclusions: In the Saint Louis area, oxacillin-resistant organisms, *Pseudomonas aeruginosa,* and fungi are commonly recovered from microbial keratitis cases with a disproportionally high incidence. Hence, empiric antibiotic choice should reflect these trends. Special care needs to be taken for patients with large ulcers and fungal infections as well as elderly patients with co-morbid ophthalmic conditions, as these patients have worse clinical outcomes.

Introduction:

Of the 71000 or higher cases per year of microbial keratitis in the United States, the vast majority are treated empirically without culture or attempts to identify the causative agent.[1–4] It is the understanding of the potential infectious agents in a particular geographic region and the expected antimicrobial response derived from surveillance studies that informs a clinician's initial choice in empiric therapy.[5,6] Despite various single-center and nation-wide surveys, pockets of geography and patient population are not sampled and represented.[5,7,8] The Saint Louis region in the Midwestern portion of the United States is one such area.

Even fewer than surveillance studies are studies that evaluate risks factors or prognostic factors for microbial keratitis and patient outcomes. Nonetheless, various factors have been put forth as potentially associated with poor outcomes.[9–12]

Hence, we undertook the current retrospective review of microbial keratitis cases at Saint Louis University's Department of Ophthalmology, which is an inner-city, university-based practice, with two purposes in mind. First, we wish to establish the incidence and spectrum of causative organisms and their antibiotic susceptibility profiles in the Saint Louis Area along with any changes over time that might impact clinical practice and antibiotic selection. Second, we wish to examine the relationship between various prognostic factors established in the ophthalmic literature and clinical outcomes observed in our cohort as a way of validating these prognostic factors.

Methods:

This retrospective cohort and trend study was approved by the Institutional Review Board of Saint Louis University and conforms to the Declaration of Helsinki. We were approved by the IRB to retrospectively search the database of the microbiology department and the diagnosis database of the ophthalmology department at Saint Louis University to identify cases of microbial keratitis from 1999–2013. Clinical records of identified cases were reviewed retrospectively to verify the diagnosis of microbial keratitis. Microbial keratitis cases were then extracted and studied to determine the organism(s) isolated and their antibiotic susceptibility profiles. The corresponding clinical data on culture-positive cases were also collected, including demographic information, clinical history and characteristics, case history, and various outcome measures. Subject informed consent was not required for this study.

Microbiology studies were conducted at the Saint Louis University microbiology laboratory. Clinically, scrapings from infected corneas were submitted for staining and were directly inoculated onto solid (blood, chocolate, and Sabouraud's agar) and liquid media (thioglycolate broth) except for cases of suspected mycobacterium/nocardia or

acanthamoeba which were submitted in Lowenstein-Jensen agar or in saline (which was then shipped to a reference laboratory) respectively. For this study, after reviewing both the general microbiological and clinical results and information, identified cultures were considered positive based on described criteria for ocular microbiology.[13,14] Essentially, moderate to heavy growth in any media, including thioglycolate broth, was considered a positive culture as well as concordant very-light to light growth on two solid media and very-light to light growth from one media, including thioglycolate broth, that match the Gram stain result. Contaminant isolates were removed from the study. Antibiotic susceptibility profiles were determined by the microbiology laboratory of Saint Louis University, per their laboratory protocol.

The prevalence of various risk factors as determined by previous literature was calculated. Also, based on prior reports in the literature, the following potential prognostic factors were chosen for analyses: age ≥ 60 years; large ulcers (defined in the current study as > 5 mm in any extent), the recovery of *Pseudomonas;* the recovery of either acanthamoeba or fungi; referred cases (defined as cases that were treated elsewhere before referral to our center); prior ophthalmic steroid use either as treatment for other ophthalmic conditions or added to the treatment of the keratitis prior to presentation or referral; and the existence of other ocular co-morbid conditions (including prior ophthalmic surgery and pre-existing ocular surface disease).[9–12] The following three results were chosen as dependent outcome variables which were then analyzed: 1) major complications (such as descemetocele, perforation, and endophthalmitis); 2) treatment time to heal > 29 days; and 3) visual outcomes in the absence of optical keratoplasty or other vision-limiting conditions (e.g. macular degeneration) of worse than or equal to 20/200.[9–12] Time to heal for this study is defined as the duration of time from the initiation of treatment to full epithelialization of the ulcer. If the exact date of full epithelialization is not known, the date is calculated as the mid time-point between the first clinical visit with full epithelialization and the preceding clinic visit before full epithelialization. Since fungal and acanthamoeba cases are typically expected to have a greater chance of developing major complications, take a long time to resolve, and have poorer visual outcomes, in addition to analyzing the entire cohort, bacteria-only cases were also analyzed separately.[15–17]

Descriptive statistics were calculated. Fisher’s exact test was used to calculated differences between two groups. Logistic regression modeling with time as a covariate was used to evaluate changes in the proportions of organisms recovered over time as well as changes in antibiotic susceptibility rates over time. Univariate logistic regression with Bonferroni correction for multiple comparisons was performed to ascertain the relationship between the prognostic factors and outcome variables. Additionally, multivariate logistic regression with backwards step-wise regression was performed to build statistical models for the data. For the multivariate analyses, we adopted a theoretic approach and included all prognostic variables as they were all derived from published literature, and a data-drive approach was relied upon to derive the final model. Statistical significance was set at 0.05. Statistical analyses were performed using Prism 6 (GraphPad Software Inc., La Jolla, CA) and SPSS (Version 24.0, IBM Corp. Armonk, N.Y.).

Results:

Microbial and antibiotic-susceptibility results

For the 15-year period, 610 cases of microbial keratitis were identified of which 416 (68%) were cultured and for 231 cases (38%) a scraping was submitted for staining from the department of ophthalmology. The overall positive culture-growth rate was 74%. The overall contaminant rate was 19% of positive cultures. Special staining of scrapings identified organisms 33% of the time.

From the 251 culture-positive, non-contaminant cases, 286 isolates were identified. Ten percent of these cases were polymicrobial. Overall, Gram-positive organisms were the most commonly isolated (48%) followed by Gram-negative organisms (34%). Fungi represented 16% of the overall isolates (Table 1).

Pseudomonas aeruginosa was the most commonly isolated organism overall (21%) followed by Coagulase-negative *Staphylococci* (CNS, 16%), *Staphylococcus aureus* (14%) and *Streptococcus* species (13%). The only organism whose proportion increased significantly over the 15 years was *Pseudomonas aeruginosa* ($p = 0.023$). An increase in the number of fungal cases was observed in the mid-2000's, but overall, fungal cases did not increase in a statistically-significant manner ($p = 0.69$). Among the filamentous fungi, *Fusarium* species were the most commonly encountered (35%) followed by *Aspergillus* species (23%) and *Curvularia* species (13%).

The overall proportion of *Staphylococcus aureus* isolates that were oxacillin-resistant (ORSA) was 45%, and there was not a statistically-significant annual trend ($p = 0.25$). The overall proportion of CNS isolates there was oxacillin-resistant (ORCNS) was 43%; again, there was not a significant annual trend ($p = 0.71$).

Gram-positive isolates' antibiotic susceptibility—Table 2 lists the antibiotic susceptibility of Gram-positive isolates recovered over time. All tested organisms remained 100% susceptible to vancomycin over time. Collectively, the Gram-positive organisms were fairly susceptible to gentamicin (81%), tetracycline (83%), and trimethoprim-sulfamethoxazole (82%). To cefazolin, erythromycin, and the fluoroquinolones (ciprofloxacin and levofloxacin), the overall Gram-positive susceptibilities hovered around 50%. As a group, Gram-positive organisms' susceptibility to levofloxacin reduced over time in a statistically-suggestive manner ($p = 0.054$), while the group's susceptibility to gentamicin decreased significantly over time ($p = 0.005$). However, when analyzed as individual Gram-positive species or strain, there was no statistically-significant reduction of susceptibility to any of the aforementioned antibiotics with the statistically-suggestive exception of CNS and ORCNS susceptibility to gentamicin ($p = 0.111$ and $p= 0.069$ respectively).

For Gram-positive, species-specific susceptibility results, we found that, as expected, susceptibility was lower for the oxacillin-resistant *Staphylococci* strains. ORSA was susceptible to gentamicin, trimethroprim, and levofloxacin 76, 94, and 6% of the time respectively while their oxacilin-sensitive counterparts were susceptible 89, 100, and 50% of

the time respectively to the same antibiotics. The pattern was similar for the CNS strains. ORCNS was susceptible to gentamicin, trimethroprim, and levofloxacin 60, 63, and 29% of the time respectively versus 100, 89, and 83% of the time respectively for oxacillin-sensitive CNS. *Streptococcus pneumoniae* was universally susceptible to levofloxacin (100%) but less to erythromycin (62%) and trimethroprim (65%).

Gram-negative isolates' antibiotic susceptibility—Gram-negative isolates' susceptibility to antibiotics over time is listed in Table 3. The Gram-negatives were near-universally susceptible to ceftazidime, aminoglycosides, and fluoroquinolones, and like the Gram-positive isolates, over time, there were no significant changes of Gram-negative isolates' susceptibility to antibiotics. Of more specific interest, *Pseudomonas aeruginosa* isolates remained 100% susceptible to aminoglycosides and fluoroquinolones.

Risk factors, prognostic factors, and outcome measure analyses

Demographics and Risk factors—Of the 251 culture-positive cases, clinical information was complete for 240. The mean age of this cohort was 49 ± 2.9 years, and 56% of the cases were female. Potential risk factors for microbial keratitis were identified in 93.3% of the cases. 34% had two or more risk factors. Pre-existing ocular surface disease or reasons to have a compromised ocular surface was found in 44% of cases, including, but not limited to, bullous keratopathy, various causes of neurotrophic keratopathy, exposure keratopathy, persistent epithelial defect, and keratoconjunctivitis sicca. Patient-reported contact-lens use was found in 43% of cases. 34% of cases had prior ophthalmic surgeries, and ophthalmic trauma was associated in 13% of cases.

Prognostic factors—As mentioned above, seven prognostic factors were analyzed. Among the 240 cases with complete clinical data, 36% were ≥ 60 years of age. Large ulcers (>5 mm) represented 27% of the cases. 25% of the cases were infected with *Pseudomonas* while 17% were either fungal or acanthamoeba cases. 33% were referred cases to our center, and also about a third (30%) were on topical steroids at the time of the keratitis or were treated with topical steroids prior to referral to our center. Lastly, over half of our cases (57%) had other pre-existing ophthalmic co-morbid conditions.

Major complications—Overall, forty of 233 cases (17.2%) with complete outcome data presented with or developed major complications. 12 of 40 (30%) fungal/acanthamoeba cases had major complications, versus 28 of 193 (14.5%) of bacteria cases ($p = 0.035$). Examples of these complications included descemetoceles, frank corneal perforations, endophthalmitis, need for therapeutic or tectonic keratoplasty, phthisis bulbi, and eyes that were enucleated or eviscerated. Table 4 contains the logistic regression analyses results with major complications as the outcome measure. For all cases, using univariate logistic regression with Bonferroni correction for multiple comparisons, 2 out of the 7 prognostic factors were statistically associated with major complications: age ≥ 60 ($p = 0.007$) and having other ocular co-morbid condition ($p = 0.007$). Large ulcers > 5 mm was an additional clinically-suggestive prognostic factor ($p = 0.056$). The multivariate logistic regression model included age ($p = 0.051$), large ulcers ($p = 0.006$), fungi or acanthamoeba cases ($p =$

0.001), and ocular co-morbid conditions (p = 0.011) with an overall model significance of p < 0.001 and a Hosmer-Lemeshow p-value of 0.518.

When analyzing the bacteria-only cases using univariate logistic regression, age ≥ 60, large ulcers, and having co-morbid conditions remained statistically-significant predictors of a major complication. The final multivariate statistical model included large ulcers and co-morbid conditions as significant prognostic factors. This overall model was significant (p < 0.001) with a Hosmer-Lemeshow p-value of 0.443.

Slow healing (> 29 days)—As healing is defined as the sterilization and epithelialization of the ulcer from medical therapy, eyes that were enucleated or needed therapeutic or tectonic keratoplasty were removed from analysis. Subsequently, 183 culture-positive cases had complete follow-up to determine eventual healing from their infectious keratitis episode. Overall, seventy-two cases (39.3%) took longer than 29 days to heal. 70% (21 of 30) of fungal/acanthamoeba and 33.3% (51 of 153) of bacterial cases took more than 29 days to heal (p < 0.001). Table 5 details the logistic regression analyses results for all cases as well as for the bacteria-only cases. For all cases, large ulcers (p < 0.01), infection by fungal or acanthamoeba organisms (p < 0.01), and referred cases (p = 0.028), were significant prognostic factors under univariate analysis with Bonferroni correction. Of note, having co-morbid conditions was statistically suggestive (p = 0.098) as “protective” against delayed healing with a negative coefficient. Multivariate logistic regression result included large ulcers, fungal or acanthamoeba cases, and co-morbid conditions in the statistical model with an overall model significance of p < 0.001 and a Hosmer- Lemeshow p-value of 0.944.

Amongst bacteria-only cases, the univariate logistic regression analyses with Bonferroni correction identified large ulcers (p < 0.01) as the sole factor statistically associated with slow healing. Being infected with Pseudomonas species was a suggestive factor (p = 0.102). The multivariate logistic regression analysis created a statistical model containing large ulcers as a positively-correlated variable (p < 0.001) and having co-morbid conditions as a significant but negatively correlated variable (p = 0.033). The overall statistical model was significant (p < 0.001; Hosmer-Lemeshow p-value = 0.703).

Poor visual outcome (worse than 20/200)—Seventy-three eyes that had other pre-existing, vision-limiting conditions were excluded from the analyses. Examples of these included amblyopia, end-stage glaucoma, central retinal vein occlusion, proliferative diabetic retinopathy, retinal detachment, and macular degeneration. Since poor vision as a dependent variable is defined as the visual outcome from successful medical treatment, eyes that suffered major complications which were analyzed separately above were also excluded from the analyses, including eyes that received successful therapeutic or tectonic keratoplasty grafts. In contrast, patients that went on to have optical keratoplasty were included in the current analyses, utilizing their final, pre-keratoplasty visual outcome to again reflect the visual outcome of successful medical therapy.

For all cases, 31 of 140 cases (22%) had visual outcomes worse than or equal to 20/200 after successful medical treatment of their infectious keratitis which included 5 of 23 (22%) fungal or acanthamoeba cases and 26 of 117 (22%) bacterial cases. For these eyes, 61% of

the visual acuities were determined by contact-lens over-refraction, 25% were best spectacle- correction, and 13% were uncorrected. Those eyes with spectacle correction or were uncorrected were all offered, scheduled, or subsequently had optical keratoplasties performed. By comparison, 48 (34%) of cases had worse than or equal to 20/60 visual acuity, including 7 of 23 (30%) fungal/acanthamoeba cases and 41 of 117 (35%) bacterial cases ($p = 0.81$). Table 6 contains the logistic regression analyses results for visual outcome worse than or equal to 20/200. For all cases, none of the tested variables were statistically significantly related to visual outcomes ≤ 20/200 under univariate analyses with Bonferroni correction. Age ≥ 60 ($p = 0.098$), large ulcers ($p = 0.098$), and having co-morbid ophthalmic conditions ($p = 0.07$) were suggestive variable. However, backwards stepwise multivariate logistic regression did generate a statistical model that included age ≥ 60 and large ulcers as statistically-significant variables and prior steroid use as a statistically-suggestive variable ($p = 0.072$). The overall statistical significance of this model had a p-value of 0.001 and a Hosmer-Lemeshow p-value of 0.926.

The univariate logistic regression analyses with Bonferroni correction of the bacteria- only cohort likewise did not find a statistically-significant factor. Again, age ≥ 60 ($p = 0.09$), large ulcers ($p = 0.066$), and co-morbid conditions ($p = 0.066$) were statistically-suggestive factors associated with a visual outcome worse than or equal to 20/200. Multivariate logistic regression analysis of the bacteria-only cohort found age ≥ 60 and large ulcers as the two variables in a statistically-significant model ($p = 0.001$; Hosmer-Lemeshow $p = 0.631$).

Discussion:

This is the first report in many decades to document the spectrum of organisms involved in microbial keratitis in the St. Louis area with associated antibiotic susceptibilities. We find that the only statistically significant change over the fifteen years of this review is the relatively high and steady increase in the incidence of *Pseudomonas aeruginosa* recovered from cultured cases. While there is no significant trend in the incidence of fungal cases, we are surprised at the disproportionately high incidence of fungal keratitis at our center, particularly filamentous fungi. In comparison to contemporaneous reports from other centers in North America, our series from St. Louis differed with respect to the relative proportions of infectious microbes isolated.[18–23] The proportion of *Pseudomonas aeruginosa* recovered in St. Louis is high at 21% which is in contrast to most other centers at approximately 10% except for the recent report out of Houston (34%).[24] Our proportion of fungi is likewise relatively high at 16% whereas most centers report 10% or less fungi except Dallas at 14 to 15%.[21] We excluded the contaminant isolates, hence, it is unclear the degree of impact this has on our reporting versus those from other centers some of which did not report the removal of contaminant isolates.

When comparing the antibiotic susceptibility profiles of common organisms to commonly used antibiotics in this report to other contemporaneous studies from North America that include comparable data, a few noteworthy observations can be made. 1) *Pseudomonas* organisms are near universally susceptible to aminoglycosides and fluoroquinolones—more so in the United States. 2) *Staphylococcus* species in Saint Louis are more resistant to fluoroquinolones than the United States aggregate data, as reported by the ARMOR study.[5]

This resistance amongst the *Staphylococcus aureus* and CNS organisms in Saint Louis as well as elsewhere is driven by the respective oxacillin-resistant sub-groups. In Saint Louis, the overall rate of ORSA is 45%, but for the period 2009–2013, it is 50%. For ORCNS, the overall rate is 43%, and for the period 2009–2013, it is 46%.

From our cohort, the only significant reduction in susceptibility is that of the Gram-positive group of organisms to gentamicin which is 81%. However, we are unable to attribute this change to any specific species or strain of Gram-positive organisms. This is likely due to our numbers not being adequately powered to determine that change.

While reports such as this from a tertiary, referral center have built-in selection bias in the types of cases seen and hence reported, taken together, these microbiological data are important in guiding and informing initial empiric therapy. The differences between geographic areas with the high incidence of *Pseudomonas aeruginosa* and fungal keratitis reported herein deserve the attention of eye-care professionals in the St. Louis area.

The high incidence and increasing trend of *Pseudomonas aeruginosa* keratitis at our institution appear to be related to the increase in the number of contact lens-related keratitis. We hypothesize that we are seeing more contact lens-related cases due to the presence of a growing population in the St. Louis area that use and abuse contact lenses. An epidemiological analysis of our contact lens-related cases mirror the findings of a Centers for Disease Control and Prevention report regarding the relative young age and female preponderance of contact lens wearer and their high prevalence of reported misuse of contact lenses which predisposes them to eye infections.[25]

The high rate of filamentous fungi seen at St. Louis University is likely multifactorial, and we believe it is due to the regional climate and the type of patients seen. Filamentous fungi cases are reportedly more common in warm climates, and in the United States, Miami in South Florida has the highest reported rates of fungal keratitis.[26] Climate-wise, the St. Louis area is classified as having a humid, sub-tropical climate comparable to northern and central Florida and has an average July temperature only one degree Fahrenheit less than that in Miami. Next, the St. Louis University department of ophthalmology draws many of its patients from the rural, agrarian population of Southern Illinois where environmental exposure to fungi is high analogous to other areas with frequent filamentous fungal cases due to farm or environmental ocular exposure.[26] Additionally the department also draws many patients from the inner city residents of metropolitan St. Louis. Many of these patients reside in very old buildings with reportedly high mold exposure in a region that is known to be an epicenter for excessive mold counts perennially, and we believe these environmental exposures also predispose the development of filamentous fungal keratitis.

Based on the microbiological results, we conclude that for the Saint Louis area, fluoroquinolones should predictably cover gram-negative organisms but without reliable grampositive coverage. Due to the high percentage of oxacillin-resistant organisms, when desiring additional gram-positive coverage, aminoglycosides such as gentamicin should be considered. Also, given the high percentage of oxacillin-resistance, vancomycin should be

used instead of cephalosporins for those cases in which compounded medications are chosen.

Adverse outcomes analyses in our cohort included the occurrence of a major complication, delayed healing of > 29 days, and poor visual outcome of < 20/200 vision after medical treatment. As expected, we find that fungal/acanthamoeba cases have statistically- greater chances of developing major complications and are slower to heal. However, we are surprised to find that the visual outcomes at both the 20/200 and 20/60 levels are not statistically different between fungal/acanthamoeba and bacterial cases treated medically alone.

With regard to prognostic factors, we find that among the seven risks factors previously identified in the literature, several are statistically associated with the three adverse outcomes in our cohort utilizing univariate models with Bonferroni correction · However given the high degree of variable correlation, multivariate logistic regression models identify fewer significant prognostic factors. Large ulcers, defined herein as ulcers > 5 mm in any dimension, are universally a poor prognostic factor for all adverse outcomes regardless of the infectious agent. Fungal/acanthamoeba cases are statistically associated with major complications and delayed healing as noted. Patient factors associated with a poor visual outcome include age ≥ 60 years, and having co-morbid ophthalmic conditions is associated with developing major complications. In multivariate statistical models, *Pseudomonas aeruginosa,* referred cases, and prior steroid use are not associated with poor outcomes. The latter two findings from our cohort stand in contrast to other reports in the literature.[11,12]

Our study has several weaknesses and limitation, including the relative small sample size of isolates, despite the long duration of time studied. Consequently, our findings and conclusions need to be taken with a grain of salt as the small database limits the power of this study so we may not be able to detect actual trends and changes. Additionally, the sample size limits how finely we care parse the data for analyses. Like other similar studies, we can only comment on those cases that were cultured and which yielded positive growth. In addition, we removed contaminant organisms in our study. Over the time period of the study, nearly a third of presumed microbial keratitis cases seen at our center were not cultured and were treated empirically, so it is not known what caused those infections. Lastly, in this study and others from academic/tertiary/referral centers, more virulent and recalcitrant cases such as fungal cases are over-represented relative to what likely occurs in the community. Nonetheless, from a surveillance perspective, our results can still be understood and evaluated in the context of results from other similar centers.

Limitations and caveats aside, the information in the current study is the first of its kind from the Saint Louis area of Midwestern United States which is important to practicing ophthalmologists in the Saint Louis area. For treating eye-care providers in the area, we recommend a low threshold to consider *Pseudomonas aeruginosa,* oxacillin-resistant organisms, and fungi as causative infectious pathogens. Additionally, we recommend considering the use of aminoglycosides for empiric therapy. Analyses of our database revealed that older patients with large ulcers and other ophthalmic co-morbid conditions, particularly involving the cornea and ocular surface, are more likely to have poor outcomes.

Hence we suggest appropriate microbiological work-up, potentially more aggressive treatment, and closer monitoring and care of these patients.

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Table 1:

15-years (1999–2013) of microbial isolates in Saint Louis

	Total	
Isolates	**N**	**%**
Gram-positive	137	48%
*Staphylococcus aureus (*ORSA*)*	40(18)	
CNS (ORCNS)	47(20)	
Streptococcus species	38	
Other Gram-positive	12	
Gram-neaative	96	34%
Pseudomonas aeruginosa	60	
Moraxella catarrhalis	9	
Serratia marcescens	9	
Other Gram-negative	18	
Fungi	45	16%
Filamentous	31	
Yeast	14	
Others[*]	8	3%
Total	286	

ORSA = Oxacilli-resistant *Staphylococcus aureus*

CNS = Coagulase-negative *Staphylococcus*

ORCNS = Oxacillin-resistnat Coagulase-negative *Staphylococcus*

[*] All Acanthamoeba except for a single isolate of *Mycobacterium chelonae* in 2009–2013

Table 2:

Percentage (%) Antibiotic Susceptibility of Gram-Positive Organisms Isolated from Saint Louis (1999–2013)

Organism	**Cefazolin**	**Erythromycin**	**Vancomycin**	**Gentamicin**
All Gram-positive, N=116	31/53 (58%)	55/113 (49%)	112/112 (100%)	61/75 (81%)
OSSA, N=22	20/20 (100%)	14/22 (64%)	22/22 (100%)	17/19 (89%)
ORSA, N=18	0/8 (0%)	2/18 (11%)	17/17 (100%)	13/17 (76%)
OSCNS, N=19	10/10 (100%)	10/19 (53%)	19/19 (100%)	19/19 (100%)
ORCNS, N=20	0/14 (0%)	7/20 (35%)	20/20 (100%)	12/20 (60%)
Strep pneumoniae, N=21	NT	13/21 (62%)	21/21 (100%)	NT
Other Strep, N=13	NT	9/13 (69%)	13/13 (100%)	NT
Organism	Tetracycline	Trimethroprim / Sulfa	Ciprofloxacin	Levofloxacin
All Gram-positive (N=116)	66/80 (83%)	82/100 (82%)	6/11 (55%)	52/90 (58%)
OSSA, N=22	20/22 (91%)	22/22 (100%)	2/5 (40%)	8/16 (50%)
ORSA, N=18	15/18 (83%)	17/18 (94%)	*	1/16 (6%)
OSCNS, N=19	16/19 (84%)	17/19 (89%)	NT	15/18 (83%)
ORCNS, N=20	12/18 (67%)	12/19 (63%)	NT	5/17 (29%)
Strep pneumoniae, N=21	NT	13/20 (65%)	NT	19/19 (100%)
Other Strep, N=13	NT	NT	NT	3/3 (100%)

OSSA = Oxacillin-susceptible *Staphylococcus aureus*

ORSA = Oxacillin-resistant *Staphylococcus aureus*

OSCNS = Oxacillin-susceptible Coagulase-negative *Staphylococcus*

OSCNS = Oxacillin-resistant Coagulase-negative *Staphylococcus*

Strep = *Streptococcus*

*: ≤ 2 isolates were tested against this antibiotic

NT: not tested

Table 3:

Percentage (%) Antibiotic Susceptibility of Gram-Negative Isolated Organisms from Saint Louis (1999–2013)

Organism	Ampicillin	Ceftazidime	Gentamicin	Tobramycin	Amikacin
All Gramnegative, N=81	9/20 (45%)	74/74 (100%)	77/78 (99%)	74/76 (97%)	74/75 (99%)
Pseudomonas aeruginosa, N=56	NT	55/55 (100%)	56/56 (100%)	55/55 (100%)	55/55 (100%)
Serratia marcescens, N=9	3/7 (43%)	9/9 (100%)	9/9 (100%)	7/8 (88%)	9/9 (100%)
Other Gramnegative, N=16	6/12 (50%)	10/10 (100%)	12/13 (92%)	12/13 (92%)	10/11 (91%)

Organism	Trimethoprim / Sulfa	Ciprofloxacin	Levofloxacin
All Gram-negative, N=81	17/19 (89%)	70/71 (99%)	34/34 (100%)
Pseudomonas aeruginosa, N=56	NT	56/56 (100%)	18/18 (100%)
Serratia marcescens, N=9	7/7 (100%)	5/5 (100%)	7/7 (100%)
Other Gramnegative, N=16	9/9 (100%)	9/10 (90%)	9/9 (100%)

NT = not tested

Table 4:

Prognostic factors of major complication* outcomes of microbial keratitis cases from Saint Louis (1999–2013)

All Cases (N=233)	Univariate logistic regression			Multivariate logistic regression		
Prognostic factors	**OR**	**95% CI**	**p-value#**	**OR**	**95% CI**	**p-value**
Age ≥ 60 years	3.41	1.69—6.88	***.007***	2.26	1.00—5.14	.051
Large ulcers > 5 mm	2.62	1.29—5.29	.056	2.94	1.36—6.37	***.006***
Pseudomonas sp.	0.56	0.23—1.34	1			
Fungi/acanthamoeba	2.53	1.15—5.54	.147	4.80	1.88—12.31	***.001***
Tertiary referred cases	1.11	0.54—2.27	1			
Prior ophthalmic steroid use	2.16	1.08—4.35	.217			
Co-morbid ocular conditions§	3.96	1.74—9.03	***.007***	3.66	1.88—12.31	***.001***
Bacteria-only cases (N=193)						
Age ≥ 60 years	3.27	1.43—7.46	***.030***			
Large ulcers > 5 mm	4.17	1.82—9.54	***.006***	4.26	1.78—10.19	***.001***
Pseudomonas sp.	0.70	0.28—1.76	1			
Tertiary referred cases	1.23	0.52—2.91	1			
Prior ophthalmic steroid use	2.01	0.91—4.70	1			
Co-morbid ocular conditions§	11.10	2.55—48.3	***.006***	11.30	2.55—50.12	***.001***

*Including descemetocele, perforation, and endophthalmitis

#Bonferroni corrected p-values

OR = odds ratio

CI = confidence interval

§Including prior ophthalmic surgery and pre-existing ocular surface disease

Table 5:

Prognostic factors of slow healing (> 29 days) of microbial keratitis cases from Saint Louis (1999–2013)

All Cases (N=183)	**Univariate logistic regression**			**Mutivariate logistic regression**		
Prognostic factors	**OR**	**95% CI**	**p-value[#]**	**OR**	**95% CI**	**p-value**
Age ≥ 60 years	0.85	0.45–1.60	1			
Large ulcers > 5 mm	4.95	2.38–10.27	< ***.01***	6.38	2.90–14.06	< ***.001***
Pseudomonas sp.	1.48	0.77–2.84	1			
Fungi/acanthamoeba	4.67	1.99–10.92	< ***.01***	5.05	2.03–12.55	< ***.001***
Tertiary referred cases	2.51	1.33–4.72	***.028***			
Prior ophthalmic steroid use	0.77	0.40–1.47	1			
Co-morbid ocular conditions[§]	0.47	0.26–0.86	.098	0.44	0.22–0.87	***.018****
Bacteria-only cases (N=153)						
Age ≥ 60 years	1.04	0.52–2.11	1			
Large ulcers > 5 mm	6.09	2.73–13.55	< ***.01***	6.76	2.95–15.51	< ***.001***
Pseudomonas sp.	2.35	1.17–4.74	.102			
Tertiary referred cases	1.83	0.89–3.78	.618			
Prior ophthalmic steroid use	0.49	0.22–1.09	.48			
Co-morbid ocular conditions[§]	0.53	0.27–1.05	.408	0.44	0.21–0.93	***.033****

OR = odds ratio

CI = confidence interval

[#] Bonferroni corrected p-values

[§] Including prior ophthalmic surgery and pre-existing ocular surface disease

[*] co-morbid ocular conditions are statistically correlated in a negative fashion

Table 6:

Prognostic factors of visual outcome ≤ 20/200 of microbial keratitis cases from Saint Louis (1999–2013)

All Cases (N=140)	Univariate logistic regression			Multivariate logistic regression		
Prognostic factors	**OR**	**95% CI**	**p-value[#]**	**OR**	**95% CI**	**p-value**
Age ≥ 60 years	2.99	1.25–7.18	.098	3.11	1.23–7.89	***.017***
Large ulcers > 5 mm	2.99	1.25–7.18	.098	3.63	1.42–9.26	***.007***
Pseudomonas sp.	0.80	0.33–1.90	1			
Fungi/acanthamoeba	0.97	0.33–2.87	1			
Tertiary referred cases	0.73	0.32–1.66	1			
Prior ophthalmic steroid use	2.41	0.97–5.96	.406	2.44	0.92–6.49	.072
Co-morbid ocular conditions[§]	2.94	1.29–6.70	.070			
Bacteria-only cases (N=117)						
Age ≥ 60 years	3.19	1.25–8.17	.09	3.63	1.35–9.78	***.011***
Large ulcers > 5 mm	3.44	1.33–8.86	.066	3.89	1.44–10.53	***.008***
Pseudomonas ps.	0.77	0.31–1.92	1			
Tertiary referred cases	0.59	0.23–1.55	1			
Prior ophthalmic steroid use	2.44	0.89–6.70	.492			
Co-morbid ocular conditions[§]	3.23	1.32–7.94	.066			

OR = odds ratio

CI = confidence interval

[#]Bonferroni corrected p-values

[§]Including prior ophthalmic surgery and pre-existing ocular surface disease