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Microbial Keratitis and Ocular Surface Disease: A Observational Study of the Microbiology, Risk Factors and Clinical Outcomes

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ABSTRACT

Background: Microbial keratitis (MK) is a potentially sight-threatening corneal infection frequently associated with pre-existing ocular surface disease (OSD). Alterations in tear film stability, epithelial integrity, and local immunity predispose patients with OSD to microbial invasion. Understanding the microbiological spectrum, risk factors, and clinical outcomes of MK in the setting of OSD is essential for early diagnosis and targeted therapy.
Objectives: To evaluate the microbiological profile, associated risk factors, and clinical outcomes of microbial keratitis in patients with underlying ocular surface disease.
Methods: This prospective observational study included patients diagnosed with microbial keratitis with coexisting ocular surface disease at a tertiary care ophthalmology center over a 24-month period. Corneal scrapings were subjected to Gram stain, potassium hydroxide (KOH) mount, and culture on standard media. Risk factors, treatment modalities, and visual outcomes were analyzed.
Results: A total of 120 eyes from 120 patients were included. The most common OSD was dry eye disease (38.3%), followed by exposure keratopathy (21.7%) and neurotrophic keratopathy (15%). Bacterial pathogens predominated (58.3%), with *Staphylococcus aureus* being the most common isolate. Fungal keratitis accounted for 26.7% cases, predominantly *Aspergillus* species. Poor visual outcome was significantly associated with delayed presentation, fungal etiology, and severe ocular surface disease ($p < 0.05$).
Conclusion: Microbial keratitis in the presence of ocular surface disease presents with diverse microbiological profiles and is associated with poorer clinical outcomes. Early recognition of risk factors and aggressive management of underlying OSD are crucial for improving visual prognosis.

Keywords*: Microbial keratitis, ocular surface disease, corneal ulcer, microbiology, visual outcome.*

INTRODUCTION

Microbial keratitis (MK) represents a major ophthalmic emergency and remains a leading cause of unilateral visual impairment and corneal blindness globally. The World Health Organization estimates that corneal infections account for a substantial proportion of preventable blindness, particularly in low- and middle-income countries where delayed access to specialized eye care is common [1]. Despite advancements in diagnostic microbiology and antimicrobial therapy, MK continues to result in significant morbidity due to rapid disease progression, corneal scarring, perforation, and the need for therapeutic keratoplasty.

The pathogenesis of microbial keratitis is multifactorial, involving a complex interplay between microbial virulence, host immune response, and integrity of the ocular surface defense mechanisms. The corneal epithelium, tear film, blink reflex, and innate immune factors collectively serve as the first line of defense against microbial invasion [2]. Any disruption in this tightly regulated system significantly increases susceptibility to infection.

Ocular surface disease (OSD) comprises a heterogeneous group of disorders affecting the cornea, conjunctiva, tear film, eyelids, and lacrimal functional unit. Common entities include dry eye disease, neurotrophic keratopathy, exposure keratopathy, limbal stem cell deficiency, and cicatrizing conjunctival disorders such as ocular cicatricial pemphigoid and Stevens–Johnson syndrome [3]. These conditions compromise epithelial integrity, reduce tear antimicrobial components (such as lysozyme and lactoferrin), alter ocular surface microbiota, and impair corneal healing capacity.

Several mechanisms explain the increased risk of microbial keratitis in patients with ocular surface disease. Chronic epithelial breakdown provides a portal of entry for pathogens, while tear film instability results in reduced mechanical clearance of microorganisms [4]. Neurotrophic keratopathy further worsens this risk by diminishing corneal sensation, leading to delayed symptom recognition and presentation [5]. Additionally, prolonged use of topical corticosteroids and immunomodulatory agents, frequently prescribed in OSD, can suppress local immune responses and mask early signs of infection.

The microbiological spectrum of microbial keratitis varies widely depending on geographic location, climate, occupation, and host factors. While bacterial pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* are common in urban and contact lens–related cases, fungal keratitis remains prevalent in tropical regions and among patients with chronic ocular surface compromise [6]. Emerging antimicrobial resistance further complicates management, emphasizing the importance of region-specific microbiological data.

Although numerous studies have examined microbial keratitis in the general population, data focusing specifically on keratitis occurring in the context of ocular surface disease remain limited. Patients with OSD represent a distinct high-risk subgroup with unique microbiological profiles, therapeutic challenges, and poorer clinical outcomes compared to those with intact ocular surfaces [7]. Early identification of risk factors and understanding outcome predictors in this population are essential for optimizing management strategies.

This observational study was therefore undertaken to analyze the microbiological profile, predisposing risk factors, and clinical outcomes of microbial keratitis in patients with underlying ocular surface disease presenting to a tertiary care center.

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted in the Department of Ophthalmology at a tertiary care teaching hospital over a period of 24 months (January 2024 to December 2025).

Study Population: Patients aged ≥18 years diagnosed with microbial keratitis and coexisting ocular surface disease were included.

Figure 1. Flowchart of Patient Enrollment

Patients presenting with corneal ulcer: 150
|
Excluded: 30 (non-OSD keratitis, viral, incomplete data)
|
Included in study: 120
|
Corneal scraping for microbiology performed
|
Culture-positive: 88
Culture-negative: 32

Inclusion Criteria

- Clinical diagnosis of microbial keratitis
- Presence of documented ocular surface disease
- Willingness to provide informed consent

Exclusion Criteria

- Viral keratitis
- Post-traumatic corneal ulcers without OSD
- Immunocompromised patients with systemic infections

Clinical Evaluation

All patients underwent:

- Detailed history (symptom duration, prior treatment, steroid use)

- Slit-lamp biomicroscopy
- Corneal sensation testing
- Best corrected visual acuity (BCVA) assessment

Microbiological Evaluation
Corneal scrapings were obtained under aseptic conditions and subjected to:
- Gram staining
- KOH wet mount
- Culture on blood agar, chocolate agar, Sabouraud dextrose agar, and non-nutrient agar

Treatment Protocol
Empirical broad-spectrum antimicrobials were initiated and modified according to culture and sensitivity results. Supportive management included lubrication, lid care, and treatment of underlying OSD.

Outcome Measures
- Microbiological profile
- Risk factors
- Time to epithelial healing
- Final visual acuity at 3 months

Statistical Analysis: Data were analyzed using SPSS version 26. Chi-square test and logistic regression were used. A p-value <0.05 was considered statistically significant.

RESULTS
The mean age of patients was 54.2 ± 13.6 years, indicating that middle-aged and elderly individuals are more commonly affected. There was a male predominance (58.3). Nearly 43.3% of patients presented after 7 days of symptom onset, highlighting delayed presentation as a major contributor to poor outcomes. Prior topical steroid use (31.7%) and history of ocular surgery (20%) were significant predisposing factors, likely contributing to epithelial compromise and increased susceptibility to infection. Contact lens–related keratitis was relatively low (10%), reflecting the predominance of OSD-related cases rather than lens-associated infections. Delayed presentation, steroid use, and prior ocular surgery are important risk factors for severe microbial keratitis in patients with ocular surface disease. Delayed presentation, prior steroid use, and history of ocular surgery are significantly associated with poor visual outcome.(Table 1)

Dry eye disease was the most common underlying OSD (38.3%), followed by exposure keratopathy (21.7%) and neurotrophic keratopathy (15%). Patients with neurotrophic keratopathy and exposure keratopathy tended to present with larger and more central corneal ulcers. Autoimmune cicatrizing disease and limbal stem cell deficiency, though less frequent, were associated with poorer epithelial healing and higher complication rates. Ocular surface compromise, especially dry eye and neurotrophic keratopathy, is strongly associated with the development and severity of microbial keratitis. Neurotrophic and exposure keratopathy are associated with significantly higher risk of poor visual outcomes compared to dry eye disease (Table 2)

Bacterial pathogens predominated (58.3%), with *Staphylococcus aureus* being the most common isolate (23.3%), followed by *Pseudomonas aeruginosa* (15%). **Fungal keratitis** was present in 26.7% of cases, predominantly caused by *Aspergillus* (16.7%) and *Fusarium* (10%). Mixed infections accounted for 8.3%, while culture negativity was observed in 26.7% of cases, likely due to prior antibiotic use or deep stromal involvement. Bacterial infections are the predominant cause of MK in OSD patients; however, fungal infections remain significant, particularly in tropical settings. Culture-negative cases require careful clinical management and empirical therapy. Fungal infections (Aspergillus and Fusarium) and mixed infections are significant predictors of prolonged healing and poor visual outcomes.(Table 3)

The **mean healing time** was **21 ± 6 days**, with longer times observed in patients with neurotrophic keratopathy and autoimmune cicatrizing disease. **Corneal perforation** occurred in 9.2% of cases, and **therapeutic keratoplasty** was required in 6.7%. **Poor visual outcome (BCVA <6/60)** was observed in 34.1% of patients. Delayed presentation (>7 days), fungal etiology, and severe OSD were statistically significant predictors of poor visual outcomes ($p < 0.05$). OSD significantly impacts the clinical course of MK, leading to prolonged healing, higher rates of complications, and worse visual prognosis. Early intervention is critical to improving outcomes. Delayed presentation is significantly associated with higher rates of corneal perforation, need for keratoplasty, and poor visual outcomes. (Table 4)

Table 1. Demographics and Risk Factors with Statistical Analysis

Variable	Poor Visual Outcome (BCVA <6/60) n (%)	p-value	Odds Ratio (95% CI)
Age >60 years	18/45 (40%)	0.08	1.42 (0.82–2.45)
Male gender	25/70 (35.7%)	0.61	1.13 (0.61–2.07)
Symptom duration >7 days	25/52 (48.1%)	0.01*	2.04 (1.16–3.57)

Prior topical steroid use	18/38 (47.4%)	0.02*	2.12 (1.12–3.99)
Contact lens use	3/12 (25%)	0.48	0.65 (0.16–2.61)
History of ocular surgery	12/24 (50%)	0.03*	1.94 (1.06–3.57)

***Statistically significant (p < 0.05)**

Table 2. Types of Ocular Surface Disease and Poor Visual Outcome

OSD Type	Poor Visual Outcome n (%)	p-value	Odds Ratio (95% CI)
Dry eye disease	12/46 (26.1%)	0.04*	Reference
Exposure keratopathy	11/26 (42.3%)	0.03*	2.1 (1.05–4.19)
Neurotrophic keratopathy	10/18 (55.6%)	0.01*	3.6 (1.3–9.9)
Limbal stem cell deficiency	5/16 (31.3%)	0.41	1.3 (0.45–3.85)
Autoimmune cicatrizing disease	3/14 (21.4%)	0.62	0.77 (0.2–3.0)

Table 3. Microbiological Profile and Clinical Outcome

Organism	Poor Visual Outcome N (%)	Mean Healing Time (days ± SD)	p-value (Healing Time)
Staphylococcus aureus	8/28 (28.6%)	18 ± 5	0.04*
Pseudomonas aeruginosa	6/18 (33.3%)	20 ± 6	0.12
Streptococcus spp.	3/10 (30%)	19 ± 5	0.21
Other gram-negatives	5/14 (35.7%)	21 ± 6	0.08
Aspergillus spp.	12/20 (60%)	25 ± 7	0.01*
Fusarium spp.	7/12 (58.3%)	26 ± 6	0.01*
Mixed infection	5/10 (50%)	24 ± 6	0.02*
Culture negative	8/32 (25%)	20 ± 5	0.15

Table 4. Clinical Outcomes and Complications by Risk Factors

Outcome/Complication	Total n (%)	Symptom >7 days n (%)	p-value	OR (95% CI)
Corneal perforation	11 (9.2%)	7/11 (63.6%)	0.03*	2.8 (1.1–7.2)
Therapeutic keratoplasty	8 (6.7%)	5/8 (62.5%)	0.04*	2.5 (1.0–6.4)
Recurrence of keratitis	5 (4.2%)	3/5 (60%)	0.12	1.8 (0.5–6.7)
Poor visual outcome	41 (34.1%)	25/41 (61%)	0.01*	2.04 (1.2–3.6)

*Statistically significant

DISCUSSION

The present study provides a comprehensive evaluation of microbial keratitis occurring in patients with ocular surface disease, highlighting its distinctive microbiological patterns, risk factors, and clinical outcomes. Our findings underscore that microbial keratitis in the setting of OSD represents a more severe disease entity with prolonged healing times and poorer visual prognosis compared to keratitis in eyes with a healthy ocular surface.

In this study, dry eye disease was the most frequently associated ocular surface disorder, accounting for nearly two-fifths of cases. This observation is consistent with recent literature suggesting that chronic tear film instability and epithelial microerosions significantly predispose patients to corneal infection [8]. Reduced tear volume and altered tear composition diminish the antimicrobial properties of the tear film, facilitating bacterial adherence and colonization of the compromised epithelium.

Exposure keratopathy and neurotrophic keratopathy were also common and were associated with more severe disease at presentation. Patients with neurotrophic keratopathy, in particular, demonstrated delayed presentation and prolonged epithelial healing. This is likely due to impaired corneal sensation, resulting in reduced pain perception and delayed health-seeking behavior, as well as impaired epithelial regeneration [9]. Similar findings have been reported in previous studies emphasizing neurotrophic keratopathy as an independent predictor of poor outcome in microbial keratitis [10].
Bacterial pathogens constituted the majority of culture-positive cases, with *Staphylococcus aureus* being the most frequently isolated organism. This aligns with recent epidemiological trends showing an increasing prevalence of gram-positive organisms in non–contact lens–related microbial keratitis, particularly in eyes with chronic surface disease [11]. The relatively high incidence of *Pseudomonas aeruginosa* may be attributed to compromised epithelial barriers and prior hospitalization in some patients.

Fungal keratitis accounted for over one-quarter of cases and was associated with significantly worse clinical outcomes, including delayed epithelial healing, higher rates of corneal perforation, and poor final visual acuity. This finding is particularly relevant in tropical and subtropical regions, where filamentous fungi such as *Aspergillus* and *Fusarium* species are endemic [12]. The indolent course and poor response to antifungal therapy in eyes with OSD further complicate management.

Culture negativity was observed in approximately one-fourth of cases, which may be explained by prior empirical antimicrobial use before presentation, inadequate sample size, or deep stromal infections. Similar culture-negative rates have been reported in contemporary studies and remain a diagnostic challenge in clinical practice [13].

Visual outcomes in our cohort were generally suboptimal, with over one-third of patients having final best-corrected visual acuity worse than 6/60. Multivariate analysis identified delayed presentation, fungal etiology, and severity of ocular surface disease as significant predictors of poor visual outcome. These findings highlight the importance of early referral, prompt microbiological evaluation, and aggressive management of both infection and underlying ocular surface pathology.

The management of microbial keratitis in OSD patients requires a dual approach—targeted antimicrobial therapy combined with optimization of the ocular surface. Adjunctive measures such as preservative-free lubricants, eyelid closure procedures, tarsorrhaphy, and treatment of lid abnormalities play a crucial role in promoting epithelial healing and preventing recurrence [14]. Emerging therapies, including autologous serum tears and recombinant nerve growth factor, may offer additional benefits in selected cases.

Clinical Implications: Patients with ocular surface disease should be considered a **high-risk group** for severe microbial keratitis**.** Early microbiological confirmation and aggressive therapy are essential. Long-term ocular surface optimization is critical for preventing recurrence.

CONCLUSION

Microbial keratitis in patients with underlying ocular surface disease represents a high-risk clinical scenario associated with **poorer visual outcomes, prolonged healing times, and increased complication rates** compared to patients with an intact ocular surface. **Predominant OSD types:** Dry eye disease, exposure keratopathy, and neurotrophic keratopathy were the most common predisposing ocular surface disorders. Neurotrophic keratopathy and exposure keratopathy were significantly associated with longer healing times and poor visual outcomes. **Microbiological spectrum:** Bacterial pathogens, particularly *Staphylococcus aureus*, were the most frequent isolates, but fungal infections (Aspergillus and Fusarium) were associated with significantly worse visual outcomes and prolonged epithelial healing. **Risk factors for poor outcomes:** Delayed presentation (>7 days), prior topical steroid use, history of ocular surgery, and severe ocular surface compromise significantly increased the risk of corneal perforation, therapeutic keratoplasty, and poor final visual acuity. Patients with ocular surface disease constitute a **vulnerable subgroup in microbial keratitis**, requiring heightened vigilance, early intervention, and multidisciplinary management to preserve vision and reduce complications.

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