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REVIEW ARTICLE

The Spectrum of Microbial Keratitis: An Updated Review

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Abstract:

Background:

In microbial keratitis, infection of the cornea can threaten vision through permanent corneal scarring and even perforation resulting in the loss of the eye. A literature review was conducted by Karsten, Watson and Foster (2012) to determine the spectrum of microbial keratitis. Since this publication, there have been over 2600 articles published investigating the causative pathogens of microbial keratitis.

Objective:

To determine the current spectrum of possible pathogens implicated in microbial keratitis relative to the 2012 study.

Methods:

An exhaustive literature review was conducted of all the peer-reviewed articles reporting on microbial pathogens implicated in keratitis. Databases including MEDLINE, EMBASE, Scopus and Web of Science were searched utilising their entire year limits (1950-2019).

Results:

Six-hundred and eighty-eight species representing 271 genera from 145 families were implicated in microbial keratitis. Fungal pathogens, though less frequent than bacteria, demonstrated the greatest diversity with 393 species from 169 genera that were found to cause microbial keratitis. There were 254 species of bacteria from 82 genera, 27 species of amoeba from 11 genera, and 14 species of virus from 9 genera, which were also identified as pathogens of microbial keratitis.

Conclusion:

The spectrum of pathogens implicated in microbial keratitis is extremely diverse. Bacteria were most commonly encountered and in comparison, to the review published in 2012, further 456 pathogens have been identified as causative pathogens of microbial keratitis. Therefore, the current review provides an important update on the potential spectrum of microbes, to assist clinicians in the diagnosis and treatment of microbial keratitis.

Keywords: Microbial keratitis, *Staphylococcus*, Bacterial keratitis, *Acanthamoeba*, Mycotic keratitis, *Pseudomonas*, Herpetic keratitis.

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1. INTRODUCTION

Microbial keratitis is a common infectious disease of the cornea that, if untreated, can have severe consequences [1 - 3]. Consequently, keratitis is considered an ophthalmic emergency requiring immediate and appropriate anti-microbial treatment to prevent permanent vision loss [4]. Current practice is to combat infection through the application of empiric broad-spectrum anti-microbial therapy, which is instituted immediately after corneal scrapings to combat the infection while cultures are processed [3, 5, 6]. Complications, however, may arise due to misidentification of the microbial cause and subsequent inadequate and/or inappropriate treatment [7, 8]. With definitive identification and treatment, the significant morbidity associated with severe microbial keratitis may be avoided.

In 2012, Karsten, Watson & Foster conducted a literature review investigating the spectrum of pathogens implicated in microbial keratitis. According to their review of the literature, 232 species from 142 genera representing 80 families were implicated in microbial keratitis, with bacterial keratitis, the

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most common. Since this publication, however, there have been over 2700 articles published investigating the identity and aetiology of causative pathogens of microbial keratitis. Therefore, an updated review is required to provide clinicians with current data on causative pathogens and management of microbial keratitis.

The aim of this study was to determine the current spectrum of possible pathogens implicated in microbial keratitis relative to the 2012 study, as well as the aetiological factors and treatment of this eye-threatening disease.

2. MATERIALS AND METHODS

A review of peer-reviewed articles, case reports and conference submissions reporting microbial keratitis pathogens was conducted. The search strategy; 'keratitis', 'microbial keratitis', 'bacterial keratitis', 'viral keratitis', 'fungal keratitis', 'amoebic keratitis' OR 'parasitic keratitis' was used in MEDLINE, EMBASE, Scopus and Web of Science databases within the year limits of each of the databases. Searches were restricted to the English language. The most recent search was conducted in August 2019.

The search strategy generated over 12600 articles, case reports and conference submissions to be reviewed. Publications were reviewed and information reporting the identification of organisms that were implicated in microbial keratitis were abstracted on the basis of (a) organism identity, (b) aetiology and (c) treatment. Pathogens were included in the review only if the method of the article outlined that the pathogen was retrieved from a corneal biopsy or scraping and cultured appropriately. The review objective was restricted to species diversity and did not aim to compile any incidence data.

3. RESULTS AND DISCUSSION

In microbial keratitis, a range of microorganisms, including fungi, bacteria, protozoa, and viruses, have been identified as infectious agents. A comprehensive review of the current literature identified 688 species representing 271 genera from 145 families reported to cause microbial keratitis. According to the literature, fungal keratitis, although less common than bacterial keratitis, demonstrated the greatest diversity of pathogens with 393 species from 169 genera being implicated in causing keratitis. Moreover, 254 species of bacteria from 82 genera, 27 species of amoeba from 11 genera, and 14 species of virus from 9 genera were found to be pathogens of microbial keratitis (Fig **1**).

In total, 49 bacterial families were identified; 22 were Gram-positive and 27 Gram-negative with *Proteobacteria* phylum being the most common (Table **1**). Eighty-two fungal families were identified, the most common were filamentous fungi (76 families, Table **2**). In viral keratitis, 5 families were reported with the majority of the species belonging to the *Herpesviridae* family. In amoebic keratitis, 8 families were identified to cause microbial keratitis, the most common was *Acanthamoeba* species.

The presentation of keratitis is often similar between the pathogens, with photophobia, pain, lacrimation and foreign body sensation all common presenting symptoms [9]. The clinical appearance of the cornea, however, may differ depending on the cause of the keratitis [7, 10].

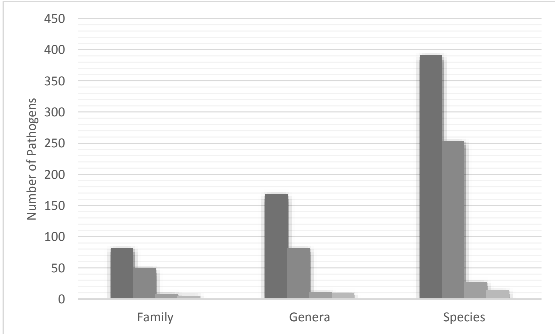

Fig. (1). Distribution of microbial pathogens implicated in keratitis Fungal, Bacterial, Amoeba, Viral.

Table 1. Number of identified families in bacterial.

	Phylum	Number of Identified Families
Gram Positive	Actinobacteria	10
	Firmicutes	12
Gram Negative	Bacteriodetes	5
	Fusobacteria	1
	Proteobacteria	20
	Spirochaetae	1

Table 2. Number of identified families in fungal keratitis.

	Phylum	Number of Identified Families
Mycota	Ascomycota	59
	Basiiomycota	16
	Zygomycota	5
Slime Mold	Myoxmycota	1
Straminipila	Oomycota	2

3.1. Bacterial Keratitis

Bacterial pathogens described in the literature were responsible for a greater proportion of keratitis than mycotic pathogens throughout various populations [11 - 13]. Bacterial keratitis often occurs in patients with inherent ocular risk factors, such as ocular trauma, contact lens use, or corneal disease [4]. Moreover, with the subsequent increased use of prescription and aesthetic contact lenses, there has been an increased prevalence of bacterial keratitis [14].

In this review of the literature, the Gram-positive bacteria identified were almost equally spread between the phylum *Actinobacteria* and *Firmicutes*. However, consistent with Karsten, Watson & Foster (2012), the Gram-negative bacteria identified were largely from the phylum *Proteobacteria* (Table **1**). The most diverse species of bacteria were *Nocardia*, *Staphylococcus,* and *Streptococcus* with 24, 19 and 14 species, respectively (Appendix 1). Gram-positive bacteria such as coagulase-negative *Staphylococcal* (CoNS) species were more common [4] than Gram-negative bacteria as a cause of bacterial keratitis [3, 15]. Although, in contact lens wearers *Pseudomonas aeruginosa* was the most common cause [4, 14] (Table **3**).

Table 3. Families implicated in bacterial keratitis, new families in bold.

Family	References	Family	References
Acetobacteraceae	[25]	*Listeriaceae*	[26]
Actinomycetaceae	[27, 28]	*Microbacteriaceae*	[29, 30]
Aerococcaceae	[31 - 33]	*Micrococcaceae*	[10, 30, 34 - 40]
Aeromonadaceae	[15, 41, 42]	*Moraxellaceae*	[30, 43 - 50]
Alcaligenaceae	[12, 33, 42, 51, 52]	*Mycobacteriaceae*	[47, 53 - 59]
Bacillaceae	[60 - 64]	*Neisseriaceae*	[13, 51, 65 - 67]
Bacteroidaceae	[68]	*Nocardiaceae*	[44, 69 - 86]
Bartonellaceae	[87]	*Pasteurellaceae*	[41, 44, 46, 88 - 91]
Brevibacteriaceae	[12]	*Peptococcaceae*	[92]
Brucellaceae	[49, 93, 94]	***Porphyromonadaceae***	[95]
Burkholderiaceae	[47, 96, 97]	*Propionibacteriaceae*	[1, 68, 98, 99]
Cardiobacteriaceae	[34]	***Prevotellaceae***	[68, 100]
Carnobacteriaceae	[101]	*Pseudomonadaceae*	[30, 33, 38, 52, 102 - 107]
Caulobacteraceae	[108]	***Rhizobiaceae***	[109]
Clostridiaceae	[60, 68, 110 - 112]	***Rhodobacteraceae***	[113]
Comamonadaceae	[55, 98]	***Rickettsiaceae***	[114]
Corynebacteriaceae	[15, 44, 62, 105, 115 - 121]	***Sphingobacteriaceae***	[30]
Enterobacteriaceae	[33, 34, 43, 52, 61, 65, 102, 104, 105, 117, 122 - 136]	***Spirochaetaceae***	[136, 137]
Enterococcaceae	[33, 39, 138]	*Staphylococcaceae*	[10, 15, 23, 33, 34, 36, 39, 43, 46, 52, 60, 138 - 142]
Eubacteriaceae	[143]	*Streptococcaceae*	[33, 41, 46, 47, 49, 60, 64, 65, 117, 126, 144 - 146]
Flavobacteriaceae	[34, 52, 147 - 155]	*Streptomycetaceae*	[131, 156]
Fusobacteriaceae	[157]	***Tsukamurellaceae***	[158, 159]
Intrasporangiaceae	[160]	*Vibrionaceae*	[43, 161]
Lactobacillaceae	[162]	*Xanthomonadaceae*	[46, 98, 163]
Leuconostocaceae	[10]	***Yersiniaceae***	[43, 164]

Table 4. Families implicated in fungal keratitis, new families in bold.

Family	References	Family	References
Ajellomycetaceae	[171, 180, 181]	*Hypocreales Incertae sedis*	[102, 146, 175]
Amphisphaeriaceae	[182]	*Hyponectriaceae*	[12]
Arthrodermataceae	[171, 181, 183 - 188]	*Glomerellaceae*	[41, 78, 169, 189 - 195]
Ascodesmiaceae	[186, 196]	*Gymnoascaceae*	[197]
Basidiobolaceae	[187]	***Lagenidiaceae***	[198]
Bionectriaceae	[186]	*Lasiosphaeriaceae*	[169, 173, 186, 193, 199, 200]
Botryosphaeriaceae	[11, 169, 175, 176, 188, 191, 196, 201 - 209]	***Lichtheimiaceae***	[193, 204]
Cephalothecaceae	[202, 210]	*Lophiostomataceae*	[211]
Ceratobsidiaceae	[169, 175]	***Malasseziaceae***	[175, 212, 213]
Chaetomiaceae	[12, 47, 168, 169, 191, 204, 205, 214]	***Massarinaceae***	[10, 90]
Chaetosphaerellaceae	[175]	*Metacapnodiaceae*	[186]
Chaetosphaeriaceae	[186, 206]	*Microascaceae*	[28, 29, 47, 174, 175, 186, 189, 191, 196, 212, 215 - 221]
Clavicipitaceae	[222 - 224]	*Montagnulaceae*	[225]
Coniochaetaceae	[28, 175, 210]	*Mucoraceae*	[10, 28, 29, 173, 175, 186, 191, 193, 219, 226 - 228]
Cordycipitaceae	[47, 175, 191, 229, 230]	*Mycosphaerellaceae*	[186, 227, 231, 232]
Corticiaceae	[28, 233]	*Nectriaceae*	[8, 11, 28, 112, 127, 146, 172, 173, 175, 186, 191, 193, 199, 204, 234-250]
Corynesporascaceae	[251]	*Niessliaceae*	[186]
Cryptococcaceae	[212, 222, 252, 253]	*Onygenaceae*	[29, 47, 171, 175]
Cunninghamellaceae	[186, 254]	***Ophiocordycipitaceae***	[255]

(Table 4) contd.....

Family	References	Family	References
Cystofilobasidiaceae	[222]	*Ophiostomataceae*	[228, 256]
Davidiellaceae	[115, 204, 247, 257]	*Orbiliaceae*	[258]
Debaryomycetaceae	[259]	***Phaeosphaeriaceae***	[260]
Dermateaceae	[261]	*Phycomycetaceae*	[28]
Diaporthaceae	[262, 263]	***Plectosphaerellaceae***	[175, 264, 265]
Didymellaceae	[12, 92, 175, 191, 266]	*Pleosporaceae*	[34, 111, 115, 169, 171, 175, 190, 191, 193, 199, 204, 207, 212, 220, 240, 249, 267-280]
Dipodascaceae	[175, 210, 281, 282]	*Pleurotheciaceae*	[79]
Dothioraceae	[12, 189, 207, 283]	*Polyporaceae*	[80]
Eremomycetaceae	[175, 284]	*Pythiaceae*	[47, 81]
Gjaerumiaceae	[285]	*Saccharomycetaceae*	[9, 18, 48, 53, 61, 82 - 86, 105, 125, 163 - 170, 175, 191, 212, 222, 236, 259, 286]
Helotailes incertae sedis	[187, 287]	***Schizophyllaceae***	[288]
Herpotrichiellaceae	[47, 115, 146, 154, 173, 175, 191, 196, 206, 240, 283, 289 - 295]	***Schizoporaceae***	[201]
Hypocreaceae	[28, 127, 146, 166, 175, 186, 191, 193, 222, 240, 247, 270, 283, 296]	*Sclerotiniaceae*	[28]

Bacterial keratitis often presents within an epithelial defect with surrounding corneal infiltrate and stromal oedema [7]. Inflammation within the anterior chamber associated with the keratitis may include a cellular reaction, flare and/or a hypopyon. Progression of bacterial keratitis and outcome tends to relate to the severity of the presentation as well as the potential risk factors for severe disease such as systemic disease and previous ocular history [4, 16]

The recommendations for empiric therapy for the treatment of bacterial keratitis by the Australian Therapeutic Guidelines are ciprofloxacin 0.3% or ofloxacin 0.3% or fortified cefalotin 5% plus gentamicin 0.9% [17]. Indeed, a Cochrane review found equal efficacy of such available topical antibiotics for bacterial keratitis. However, an increase in the relative risk of minor adverse events, including discomfort or chemical conjunctivitis was found with aminoglycosides and cephalosporins compared with fluoroquinolones, although there was no difference in serious complications [18 - 22]. Yet, the development of bacterial resistance to antibiotics may lead to the ineffective treatment of bacterial keratitis [23, 24]. Since our prior review (2012) the sole use of fluoroquinolones as primary treatment for bacterial keratitis has increased alongside elevation in fluoroquinolone resistance [24]. Moreover, CoNS and *Staphylococcus aureus* have shown resistance to cephalotin and fluoroquinolones with the degree of resistance differing around the world [3]. Watson *et al*. (2018) demonstrated at the Sydney Eye Hospital that CoNS resistance was 9% to ciprofloxacin, cefatolin and gentamicin. Whereas Ni *et al*. (2015) found that resistance at the Wills Eye Hospital in Philadelphia was 32% to fluoroquinolones. Therefore, the inappropriate use of antibiotics may lead to antimicrobial resistance, prolonged recovery and poor outcomes in bacterial keratitis [3, 24]

3.2. Fungal Keratitis

The aetiology of microbial keratitis was found to differ depending on the geographical location of the patient and the infective pathogen [11]. Fungal keratitis is comparatively uncommon in temperate climates, though in tropical areas it can constitute a significant proportion of microbial keratitis [2, 13, 165]. The tropical climate, combined with greater agricultural and vegetation exposure in lower socioeconomic countries causes an increased risk of contracting fungal keratitis in populations [166, 167]. Moreover, similar to Karsten, Watson & Foster (2012), the fungal pathogens published in the literature were more often cultured from patients in these areas where they were more commonly exposed to contaminated soils and decaying vegetation while suffering ocular trauma [36, 168 - 170].

Fungi within the classification *Mycota* were the most common to cause keratitis; of the 83 families identified, only 3 did not belong to this classification (Table **2**). Filamentous fungi, consistent with Karsten, Watson & Foster (2012), were found to be the most common cause of mycotic keratitis with *Fusarium* and *Aspergillus* species being the most prevalent [165, 171 - 173] and diverse genera with 38 and 25 species identified, respectively (Appendix 2).

Mycotic keratitis caused by filamentous fungi can involve any area of the cornea and often exhibits grey or yellow-white stromal infiltrate with indistinct margins [7, 174]. Progressive infiltration with multiple granular satellite stromal infiltrates is common and an immune-mediated ring infiltrate around the ulcer is often seen [7]. Yeasts may have a similar clinical presentation to filamentous fungi, however, yeasts tend to cause keratitis during immunosuppression and with systemic diseases such as diabetes, Human Immunodeficiency Virus (HIV), and corticosteroid therapy [174, 175].

The treatment of fungal keratitis consists of topical and systemic anti-fungal therapies [2, 176]. Natamycin 5% is often first line, although its effectiveness is limited by its poor penetration into the corneal stroma. Amphotericin B 0.3-0.5% is an alternative topical therapy but exhibits ocular toxicity [2]. Voriconazole is a proposed third option, however, the 'Mycotic Ulcer Treatment Trial I' found that voriconazole was inferior to natamycin in the treatment of all fungal keratitis, especially *Fusarium* keratitis [2, 176]. Since our prior review, the Mycotic Ulcer Treatment Trial II demonstrated that there was no therapeutic benefit of adding oral voriconazole to topical antifungal therapy [177]. Specifically, oral voriconazole, in addition to topical natamycin and voriconazole did not decrease the rate of corneal perforation nor the need for therapeutic penetrating keratoplasty. The study was halted due to the comparatively higher rates of corneal perforations in the oral voriconazole arm [177]. Filamentous fungi have been most frequently reported in our review, supporting current antifungal treatment recommendations [2, 178, 179] (Table **4**).

3.3. Viral Keratitis

Viral pathogens are ubiquitous within populations, as evidenced by 90% of adults being seropositive for Herpes Simplex virus HSV antigens. However, as reported in the literature and Karsten, Watson & Foster (2012) only 20-30% of adults develop ocular manifestations from HSV infections [319]. Nonetheless, herpetic eye disease remains a significant cause of blindness worldwide, affecting over 1 million people annually [320].

The clinical features of HSV keratitis depend on the corneal layer affected and can typically include a dendritiform corneal ulcer or significant breakdown of the corneal epithelium with persistent punctate corneal keratopathy and corneal erosions [319]. Following the primary ocular infection, the viral genome may enter the surrounding nerve fibres and travel to the trigeminal nerve ganglion where it will remain in a latent state [319, 321]. Recurrent HSV infection can then occur in times of immunosuppression as the virus travels from the ganglion to infect the innervated tissue [319, 322]. Similar to HSV, the *Varicella Zoster* virus can remain dormant in the nerve ganglion following primary infection. Reactivation of the virus may lead to the development of Herpes Zoster Ophthalmicus [HZO], which presents as painful vesicular rash along the distribution of the innervation of the ophthalmic nerve [322]. Ocular manifestations of HZO can include Herpes Zoster keratitis [323].

From the review of the literature and consistent with Karsten, Watson & Foster (2012), *Herpesviridae* were the most common family implicated in viral keratitis. *Herpes Simplex Virus Type 1* (HSV-1) was commonly responsible for viral keratitis affecting the skin and mucous membranes in the distribution of the trigeminal nerve [321]. *Varicella Zoster* virus, *Cytomegalovirus*, other members of the *Herpesviridae* family, were also implicated in viral keratitis, along with multiple species of *Adenovirus* (Table **5**).

In the treatment of primary HSV epithelial keratitis acyclovir eye drops were the recommended therapy [17]. However, since Karsten, Watson & Foster (2012) publication, the Herpetic Eye Disease study II demonstrated that oral acyclovir may be utilised prophylactically to prevent recurrent herpetic keratitis, especially in patients with previous HSV stromal keratitis [319 - 324]. Furthermore, Bhatt *et al*. [2016], in their Cochrane Systematic review, demonstrated that oral acyclovir was beneficial in the prevention of recurrent herpes simplex keratitis in patients with corneal grafts [321]. Furthermore, the American Academy of Ophthalmology has produced guidelines to aid in the management of HSV Keratitis [325]. Herpes zoster keratitis is treated with oral antivirals, such as acyclovir or valacyclovir, in the first 72 hours to minimise the risk of ocular and other complications [17, 323].

3.4. Amoebic Keratitis

Amoebic pathogens are an uncommon cause of keratitis and typically occur in immunocompetent patients associated with ocular trauma and contact lens use [337]. *Acanthamoeba*, a unicellular protozoan, is a frequent cause of amoebic keratitis [338]. These protozoa exist in polluted soil or contaminated water supplies such as swimming pools, sewage and tap water [337, 339]. *Acanthamoeba* occur in both active trophozoite and dormant cyst forms. In favourable environments, the *Acanthamoeba* trophozoite exhibits high activity, although, in unfavourable environments such as during antibiotic and biocides treatment, *Acanthamoeba* from cysts with low activity but able to powerfully resist the surrounding environment [337, 338, 340].

The use of contact lenses, especially if used beyond recommended duration from the manufacturer and during contact with contaminated water, such as swimming, has been associated with a greater risk of *Acanthamoeba* keratitis [338, 339]. Similarly, ocular trauma with exposure to vegetable matter and contaminated soil heavily contributes to *Acanthamoeba* keratitis leading to a higher incidence in agricultural populations [167].

Similar to the study by Karsten, Watson & Foster (2012), *Acanthamoeba* was found to be the most common amoebic cause of keratitis in the current review [341]. Moreover, it was the most diverse, with 13 species of *Acanthamoeba* implicated as the cause of keratitis. *Acanthamoeba* is the most prevalent pathogenic amoeba, however, other families such as *Vahlkampfia*, *Encephalotozoon*, *Vittaforma* and *Hartmanella* have also been reported to cause amoebic keratitis (Table **6**).

Acanthamoeba keratitis is often misdiagnosed as bacterial or mycotic keratitis, leading to inappropriate treatment and poor outcomes [257, 339]. Patients often present with pain that ranges from minimal to more commonly disproportionate levels for the clinical features shown [338]. Clinical features are often unilateral, including corneal epitheliopathy, stromal infiltrate, punctate keratopathy, ring infiltrate, perineural infiltrates and pseudo-dendrites [257]. As the disease progresses sterile anterior uveitis with a hypopyon may occur [338].

The prevention of *Acanthamoeba* keratitis prioritises the strict and appropriate use of contact lenses. Contact lenses must be cleaned and stored in appropriate disinfecting solutions and avoid exposure to potentially contaminated water supplies [338].

The current management of *Acanthamoeba* keratitis utilises a combination of anti-amoebic therapy, including a biguanide such as polyheramthylen biguanide 0.02%, or chlorhexideine 0.02% and a diamidine such as propamidine isethionate [339, 342]. It is imperative to institute appropriate therapy quickly to prevent *Acanthamoeba* penetrating deep into the cornea [338, 342]. However, due to the ability of *Acanthamoeba* to encyst, *Acanthamoeba* may remain dormant for extended periods before reactivation. Therefore, therapy combinations utilising diamidines are useful as these are effective against trophozoites and cysts [338, 340]. The use of corticosteroid therapy in *Acanthamoeba* keratitis is controversial, emerging evidence supports its use [343, 344], although there is no clear consensus [338, 345]. In cases of severe anterior segment inflammation, corticosteroids may be used, however, they must be used judiciously to prevent exacerbation of the infection and suppression of the host immune response [338].

Table 5. Diversity of Viral Keratitis. (-) Species not identified. New pathogens in bold.

Family	Genus	Species	References
Adenoviridae	***Adenovirus***	**-**	[326, 327]
		Adenovirus-3	
		Adenovirus-8	
		Adenovirus-19	
Herpesviridae	***Cytomegalovirus***	-	[328]
	Lymphocryptovirus	***Human herpesvirus 4***	[329]
	Simplexvirus	*Herpes Simplex Virus-1*	[327, 330]
		Herpes Simplex Virus-2	
	Varicellovirus	*Varicella Zoster Virus*	[331]
Paramyxoviridae	*Morbillivirus*	*Rubeola virus*	[332]
	Rubulavirus	***Mumps rubulavirus***	[333]
Picornaviridae	***Enterovirus***	**-**	[334]
		Enterovirus B	
Poxviridae	*Orthopoxvirus*	*Vaccinia Virus*	[335, 336]

Table 6. Diversity of Amoebic Keratitis. (-) Species not Identified. New Pathogens in Bold.

Family	Genus	Species	References
Acanthamoebidae	*Acanthamoeba*	***Astronyxis***	[341, 346 - 353]
		Castellanii	
		Culbertsoni	
		Griffini	
		Hatchetti	
		Lenticulata	
		Lugdunesis	
		Mauritaniensis	
		Palestinensis	
		Polyphaga	
		Quina	
		Rhysodes	
		Triangularis	
Demodicidae	***Demodex***	***Brevis***	[354]
		Folliculorum	
Hartmannellidae	*Hartmanella*	-	[355, 356]
		Vermiformis	
Nosematidae	*Anncaliia*	*Algerae*	[357]
	Nosema	***Corneum***	[358]
	Vittaforma	***Corneae***	[359]
Onchocercidae	***Onchocerca***	***Volvulus***	[142]
Tarsonemidae	***Tarsonemid***	***Heterostigmae***	[360]
Unikaryonidae	***Encephalitozoon***	***Cuniculi***	[359]
		Hellem	
		Intestinalis	
Valkampfiidae	*Vahlkampfia*	-	[361, 362]
	Paravahlkampfia	-	[363]

CONCLUSION

Microbial keratitis is an ophthalmic emergency as it can lead to irreversible damage to the cornea and loss of vision [1, 3, 5]. To minimise complications, prompt and effective treatment must be instituted to prevent permanent damage to the cornea. For the successful treatment of microbial keratitis, it is vital to correctly identify the causative organism as it enables the use of the most effective treatments to treat the infection [3].

A comprehensive and exhaustive review of the literature yielded 688 species representing 271 genera from 145 families being implicated in microbial keratitis, in contrast to the 232 species from 142 genera representing 80 families found by Karsten, Watson & Foster (2012). Similarly, from the current review of the literature, there were 135 microbial species found to cause keratitis published before 2012 that were not identified by Karsten, Watson & Foster (2012).

Similar to the study by Karsten, Watson & Foster (2012), the current literature demonstrated that bacterial keratitis was the most common and fungal pathogens were the most diverse, with 391 species identified as causative pathogens of microbial keratitis. Comparatively, there were 254 bacterial species, 27 species of amoeba and 14 viral species found to cause microbial keratitis (Fig **1**).

Correspondingly, the geographical variances noted from Karsten, Watson & Foster (2012) were further reinforced from the literature. It was found that bacterial keratitis is relatively common in developed nations, likely due to the use of contact lenses [14]. Similarly, fungal keratitis is more common in tropical environments and the developing world, most likely due to greater exposure to decaying vegetation and soil [165, 167]. Furthermore, many of the pathogens reported in the literature were often from studies and case reports in patients that had been exposed to poor sanitation, greater agricultural exposure and ocular trauma leading to the development of keratitis [170, 182, 251, 265, 311].

Similarly, the treatment of microbial keratitis has remained similar since Karsten, Watson & Foster (2012). Bacterial keratitis treatment commonly consists of topical fluoroquinolones, yet there is an increasing risk of antimicrobial resistance [24], necessitating the need for judicious and appropriate use of antimicrobials [3]. Contrastingly, since Karsten, Watson & Foster (2012), available evidence now suggests that oral antifungals, in addition to topical therapy do not add a therapeutic benefit [177].

This review has demonstrated the great diversity of the pathogens implicated in microbial keratitis. Relative to Karsten, Watson & Foster (2012), further 443 pathogens were identified as causative organisms of microbial keratitis. Additionally, there has been further investigation of antimicrobial resistance in bacterial keratitis and changes in the management of microbial keratitis. Therefore, the current review provides an important update on the spectrum and management of microbial keratitis, to assist clinicians in its diagnosis and treatment and help reduce the associated morbidity. Advancing the literature into the epidemiology and geographical variance of causative organisms will further aid in the identification and treatment of microbial keratitis.

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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APPENDIX

Table 1. Diversity of Fungal Keratitis [1Formerly Wangiella, 2 Formerly Fusarium fujikuroi, 3 Previously Fusarium avenacas, 4Formerly humicola] [-] Species not identified. New pathogens in bold.

Family	Genus	Species	References
Fungal Keratitis			
Ajellomycetaceae	*Blastomyces*	*dermatitidis*	[171]
	Histoplasma	***capsulatum***	[180]
	Paracoccidioides	***brasiliensis***	[175]
Amphisphaeriaceae	***Pestalotiopsis***	***clavispora***	[182]

(Appnedix Table 1) contd.....

Family	Genus	Species	References
Fungal Keratitis			
Arthrodermataceae	***Epidermophyton***	***floccosum***	[181]
	Microsporum	-	[175, 228, 364]
		canis	
		gypseum	
	Trichophyton	**-**	[171, 183 - 185]
		capitatum	
		mentagrophytes	
		schoenleinii	
		verrucosum	
Ascodesmiaceae	***Cephaliophora***	**-**	[186, 196]
		irregularis	
Basidiobolaceae	***Basidiobolus***	***ranarum***	[187]
Bionectriaceae	*Gliocladium*	-	[186]
Botryosphaeriaceae	***Auerswaldia***	***lignicola***	[188]
	Botryosphaeria	**-**	[169, 201]
		dothidea	
		rhodina	
	Diplodia	-	[11]
	Lasiodiplodia	*theobromae*	[196, 207]
	Macrophomina	***phaseolina***	[169, 208]
	Neoscytalidium	***oculus***	[203]
	Neofusicoccum	***mangiferae***	[209]
	Sphaeropsis	***subglobosa***	[175]
Cephalothecaceae	***Phialemonium***	-	[202, 210]
		curvatum	
Ceratobsidiaceae	*Rhizoctonia*	-	[169, 175]
		bataticola	
Chaetomiaceae	*Chaetomium*	*atrobrunneum*	[47, 168, 191, 214]
		globosum	
		strumarium	
	Humicola	**-**	[12]
	Thielavia	***heterothallica***	[169, 204, 205]
		subthermophila	
		tortuosa	
Chaetosphaerellaceae	*Diplosporium*	-	[175]
Chaetosphaeriaceae	*Gongromeriza*	-	[186]
	Trichothecium	-	[186, 206]
Clavicipitaceae	*Metarhizium*	-	[222 - 224]
		anisopliae	
Coniochaetaceae	***Lecythophora***	-	[175, 210]
		mutabilis	
Cordycipitaceae	*Acrostalagmus*	*cinnabarensis*	[28]
	Beauveria	-	[47, 191, 229, 230]
		bassiana	
	Engyodontium	***alba***	[175]
Corticiaceae	*Sporotrichum*	*schenekii*	[28, 233]
Corynesporascaceae	***Corynespora***	***cassiicola***	[251]
Cryptococcaceae	*Cryptococcus*	**-**	[212, 222, 252, 253]
		albidus	
		curvatum	
		laurentii	
		neoformans	

(Appnedix Table 1) contd.....

Family	Genus	Species	References
Fungal Keratitis			
Cunninghamellaceae	*Cunninghamella*	-	[186, 254]
		spinosum	
Cystofilobasidiaceae	*Guehomyces*	*pullulans*	[222]
Davidiellaceae	*Cladosporium*	-	[115, 247, 257]
	Davidiella	***tassiana***	[204]
Debaryomycetaceae	***Meyerozyma***	***caribbica***	[259]
Dermateaceae	*Gloeosporium*	*fructigenum*	[261]
Diaporthaceae	***Phomopsis***	**-**	[262, 263]
		phoenicicola	
Didymellaceae	***Epicoccum***	**-**	[12, 191, 266]
		nigrum	
		sorghi	
	Phoma	**-**	[12, 92, 175]
		eupyrena	
		oculo-hominis	
Dipodascaceae	*Geotrichum*	**-**	[175, 210, 281]
		candidum	
	Magnusiomyces	***capitatus***	[282]
Dothioraceae	*Aureobasidium*	-	[12, 189, 207, 283]
		pullulans	
Eremomycetaceae	*Arthrographis*	*kalrae*	[175, 284]
Gjaerumiaceae	***Gjaerumia***	***minor***	[285]
Helotailes incertae sedis	*Scytalidium*	***dimidiatum***	[187, 287]
		hyalinum	
Herpotrichiellaceae	***Cladophialophora***	***bantiana***	[196, 240, 293]
		cladosporioides	
		carrionii	
	Exophiala[1]	***dermatitidis***	[115, 146, 154, 175, 289 - 292]
		jeanselmei	
		jeanselmei var. dermatitidis	
		jeanselmei var. jeanselmei	
		moniliae	
		phaeomuriformis	
		spinifera	
	Fonsecaea	***compacta***	[47, 115, 191, 294]
		pedrosoi	
	Phialophora	***bubakii***	[173, 175, 283]
		pedrosoi	
		verrucosa	
	Pullularia	-	[206]
	Torula	-	[295]

(Appnedix Table 1) contd.....

Family	Genus	Species	References
Fungal Keratitis			
Hypocreaceae	*Acremonium*	-	[127, 166, 175, 191, 193, 247, 296]
		atrogriseum	
		curvum	
		falciforme	
		kiliense	
		potronii	
		recifei	
		strictum	
	Acrostalagmus	*cinnabarensis*	[28]
	Gliocladium	-	[186]
	Sepedonium	-	[270, 283]
	Trichoderma	-	[28, 146, 193, 222, 240]
		hamatum	
		longibrachiatum	
		koningii	
Hypocreales Incertae sedis	***Cephalosporium***	-	[102, 146]
	Myrothecium	-	[175]
Hyponectriaceae	*Humicola*	-	[12]
Glomerellaceae	*Colletotrichum*	-	[41, 189 - 195]
		atramentum	
		capsici	
		coccodes	
		dematium	
		gleosporiodes	
		graminicola	
		truncatum	
	Glomerella	***cingulata***	[78, 169]
Gymnoascaceae	*Gymnoascus*	**-**	[197]
Lagenidiaceae	***Lagenidium***	-	[198]
Lasiosphaeriaceae	***Arthrinium***	***phaeospermum***	[173, 193]
	Cladorrhinum	***bulbilosum***	[199, 200]
	Monotospora	-	[186]
	Podospora	-	[169]
Lichtheimiaceae	***Lichtheimia***	***corymbifera***	[193, 204]
		ramosa	
Lophiostomataceae	*Tetrapola*	-	[211]
Malasseziaceae	***Malassezia***	-	[175, 212, 213]
		furfur	
		restricta	
Massarinaceae	*Helminthosporium*	-	[10, 90]
		maydis	
Metacapnodiaceae	*Hormiscium*	-	[186]
Microascaceae	*Doratomyces*	-	[186]
	Cephalotrichum	***stemonitis***	[175]
	Graphium	***eumorphum***	[216]
	Lophotrichus	-	[217]
	Microascus	***brevicaulis***	[29, 191, 218]
		gracilis	

(Appnedix Table 1) contd.....

Family	Genus	Species	References
Fungal Keratitis			
	Monosporium	-	[219]
	Pseudallescheria	*boydii*	[47, 191]
	Scedosporium	*apiospermum*	[174, 196, 220, 221]
		boydii	
		prolificans	
	Scopularisopsis	-	[28, 186, 189, 215]
		blochi	
		brevicaulis	
	Wardomyces	-	[212]
Montagnulaceae	***Microsphaeropsis***	***olivacea***	[225]
Mucoraceae	***Chlamydoabsidia***	***padenii***	[175]
	Mucor	-	[10, 28, 226, 228]
		cornealis	
		racemosus	
		ramosissimus	
	Rhizomucor	**-**	[29]
	Rhizopus	***arrhizus***	[28, 173, 191, 193, 219, 226, 227]
		nigricans	
		oryzae	
		parasiticus	
		stolonifer	
	Zygorhynchus	-	[186]
Mycosphaerellaceae	*Cercospora*	-	[186]
	Hormodendrum	-	[227, 231]
	Microcyclosporella	***mali***	[232]
Nectriaceae	*Bactridium*	-	[186]
	Cylindrocarpon	-	[11, 191, 247, 365]
		destructans	
		lichenicola	
	Fusarium	-	[127, 146, 172, 175, 193, 199, 234 - 246]
		aquaeductum	
		asiaticum	
		boothii	
		cerealis	
		chlamydosporum	
		culmorum	
		delphinoides	
		dimerum	
		episphaeria	
		equiseti	
		graminearum	
		incarnatum	
		incarnatum-equiseti	
		keratoplasticum	
		langsethiae	
		lateritium	
		lichenicola	
		moniliforme	
		musae	
		napiforme	
		nivale	
		nygamai	

(Appnedix Table 1) contd.....

Family	Genus	Species	References
Fungal Keratitis			
Nectriaceae	*Fusarium*	*oxysporum*	[127, 146, 172, 175, 193, 199, 234 - 246]
		penzigii	
		poae	
		polyphialidicum	
		proliferatum	
		pseudograminearum	
		roseum	
		sacchari	
		sambucinum	
		solani	
		sporotrichioides	
		subglutinans	
		temperatum	
		tricinctum	
		ventricosum	
		verticilloides	
	Fusidium	*terricola*	[28]
	Fusoma	-	[186]
	Gibberalla	*avenacea* [2]	[173, 186, 193]
		fujikuroi [3]	
	Moniliaceae	-	[238]
Neocosmospora	***keratoplastica***	[204, 248, 249]	
	rubicola		
	vasinfecta		
Sarcopodium	***oculorum***	[250]	
Volutella	-	[112]	
Niessliaceae	*Stachybotrys*	-	[186]
Onygenaceae	*Chrysosporium*	-	[29, 47, 171, 175]
		inops	
		parvum	
	Coccidioides	***immitis***	[175]
Ophiocordycipitaceae	***Purpureocillium***	***lilacinum***	[255]
Ophiostomataceae	*Sporothrix*	***pallida***	[228, 256]
		schenckii	
Orbiliaceae	*Arthrobotrys*	*oligospora*	[258]
Phaeosphaeriaceae	***Tintelnotia***	***destructans***	[260]
Phycomycetaceae	*Periconia*	*keratidis*	[28]
Plectosphaerellaceae	***Plectosporium***	***tabacinum***	[265]
	Verticillium	**-**	[175, 264]
		searrae	
Pleosporaceae	*Alternaria*	*alternata*	[171, 191, 204, 270 - 272]
		chlamydospora	
		fusispora	
		infectoria	
		longipes	
		nees	
		tenuissima	
	Bipolaris	**-**	[146, 196, 257, 273, 274, 283]
		australiensis	
		hawaiiensis	
		oryzae	

(Appnedix Table 1) contd.....

Family	Genus	Species	References
Fungal Keratitis			
Pleosporaceae		***sorokiniana***	
		spicifera	
	Brachysporium	**-**	[275]
	Cochliobolus	**-**	[169, 240]
		heterostrophus	
		spicifer	
	Curvularia	***borreriae***	[34, 111, 115, 171, 175, 191, 249, 267 - 269]
		brachyspora	
		clavata	
		crepinii	
		fallax	
		geniculata	
		lunata	
		pallescens	
		prasadii	
		senegalensis	
		spicifera	
		verruculosa	
	Dichotomophthoropsis	***nymphaearum***	[249]
	Drechslera	**-**	[220, 269]
		halodes	
	Edenia	***gomezpompae***	[193]
Exserohilum	**-**	[175, 190, 199, 207, 276]	
	longirostratum		
	mcginnisii		
	roseum		
	rostratum		
	solani		
Pithomyces	**-**	[34, 212]	
Pleospora	***tarda***	[146, 240]	
Pyrenochaeta	-	[277, 278]	
	keratinophila		
Stemphylium	**-**	[279]	
Ulocladium	***atrum***	[280]	
Pleurotheciaceae	***Phaeoisaria***	***clematidis***	[79]
Polyporaceae	***Trametes***	***betulina***	[80]
Pythiaceae	*Pythium*	*insidiosum*	[47, 81]
Saccharomycetaceae	***Blastoschizomyces***	***capitatus***	[175]
	Candida	*albicans*	[82 - 86, 105, 170, 191, 212, 222, 236, 259, 286]
		ciferrii	
		curvata	
		dubliniensis	
		famata	
		fermentati	
		glabrata	
		guilliermondii	
		krusei[4]	
		lusitaniae	
		lypolytica	
		orthopsilosis	
		parapsilosis	

(Appnedix Table 1) contd.....

Family	Genus	Species	References
Fungal Keratitis			
		pelliculosa	[18, 48, 53, 61, 68, 125, 163 - 169]
		rugosa	
		tropicalis	
		utilis	
		viswanathii	
		zeylanoides	
	Saccharomyces	***cerevisiae***	[9]
Schizophyllaceae	***Schizophyllum***	***commune***	[288]
Schizoporaceae	***Hyphodontia***	**-**	[201]
Sclerotiniaceae	*Botrytis*	**-**	[28]
Sebacinaceae	***Piriformospora***	**-**	[146]
Septobasidiaceae	***Glenospora***	***graphii***	[175]
Sordariales incertae sedis	***Papulaspora***	**-**	[191, 199]
		equi	
Sordariaceae	***Neurospora***	**-**	[47, 146]
		sitophila	
Sporidiobolaceae	*Rhodotorula*	**-**	[270, 283, 308 - 311]
		glutinis	
		minuta	
		mucilaginosa	
Sporocadaceae	***Pseudopestalotiopsis***	***theae***	[313]
Sordariales	***Pleurothecium***	***recurvatum***	[315]
Sympoventuriaceae	***Verruconis***	***gallopava***	[77]
Syncephalastraceae	*Syncephalastrum*	-	[189]
Togniniaceae	***Phaeoacremonium***	**-**	[316, 317]
		parasiticum	
Torulaceae	***Torula***	-	[12]
Tetraplosphaeriaceae	***Tetraploa***	-	[102, 175]
		aristata	
Tremellaceae	***Bulleromyces***	**-**	[212]
Trichocomaceae	*Aspergillus*	*alternata*	[41, 115, 146, 171, 175, 191, 196, 199, 210, 236, 247, 297 - 302]
		brasiliensis	
		cibarius	
		clavatus	
		fischerianus	
		flavipes	
		flavus	
		fumigatus	
		glaucus	
		janus	
		japonicus	
		nidulans	
		niger	
		niveus	
		nominus	
		ochraceus	
		oryzae	
		pseudotamarii	
		sydowii	

(Appnedix Table 1) contd.....

Family	Genus	Species	References
		Fungal Keratitis	
		tamarii	
		terreus	
		tubingensis	
		versicolour	
		viridinutans	
		wentii	
	Neosartorya	***udagawae***	[303]
	Penicillium	***brocae***	[9, 102, 146, 175, 210, 240, 306, 307]
		canescens	
		chrysogenum	
		citrinum	
		crustaceum	
		expansum	
		implicatum	
		marneffei	
		notatum	
		piceum	
		spinulosum	
	Paecilomyces	-	[95, 154, 270, 305]
		farinosus	
		lilacinus	
		variotti	
	Sagenomella	***keratitidis***	[304]
Trichosphaeriaceae	*Khuskia*	-	[312]
	Nigrospora	-	[12, 191, 283]
		sphaerica	
Trichosporonaceae	*Trichosporon*	***anisopliae***	[78, 105, 127, 309, 312, 314]
		asahii	
		beigelii	
		capitatum	
		mucoides	
		rugosum	
Tritirachiaceae	***Tritirachium***	***oryzae***	[175]
Ustilaginaceae	***Rhodosporidium***	***toruloides***	[175]
	Ustilago	**-**	[175]
Venturiaceae	*Fusicladium*	-	[186]
Wickerhamomycetaceae	***Cyberlindnera***	***fabianii***	[259]
	Wickerhamomyces	***anomalus***	[318]
n/a	***Botryodiplodia***	-	[366]
	Dichotomophthoropsis	-	[175, 312]
		nymphearum	
		portulacae	
	Mycelia	-	[314, 367]
		sterilia	
	Ovadendron	***sulphureo-ochraceum***	[175]
	Phaeotrichoconis	***crotalariae***	[175]
		keratinophila	

Table 2. Diversity of Bacterial Keratitis [1 Previously Comamonas] [-] Species not identified, New Pathogens in Bold.

Family	Genus	Species	References
		Bacterial Keratitis	
Acetobacteraceae	***Roseomonas***	**-**	[25]
Actinomycetaceae	*Actinomyces*	*bovis*	[27, 28]
Actinomycetaceae	*Actinomyces*	***israelii***	[27, 28]
Aerococcaceae	***Abiotrophia***	***defectiva***	[31]
Aerococcaceae	***Aerococcus***	**-**	[32, 33]
Aerococcaceae	***Aerococcus***	***viridans***	[32, 33]
Aeromonadaceae	*Aeromonas*	-	[15, 41, 42]
Aeromonadaceae	*Aeromonas*	*hydrophilia*	[15, 41, 42]
Alcaligenaceae	*Achromobacter*	-	[33, 42, 51, 52]
Alcaligenaceae	*Achromobacter*	***denitrificans***	[33, 42, 51, 52]
Alcaligenaceae	*Achromobacter*	***xylosoxidans***	[33, 42, 51, 52]
Alcaligenaceae	*Alcaligenes*	*faecalis*	[12]
Bacillaceae	*Bacillus*	*cefilius*	[60 - 64]
Bacillaceae	*Bacillus*	***cereus***	[60 - 64]
Bacillaceae	*Bacillus*	***circulans***	[60 - 64]
Bacillaceae	*Bacillus*	***coagulans***	[60 - 64]
Bacillaceae	*Bacillus*	***firmus***	[60 - 64]
Bacillaceae	*Bacillus*	***licheniformis***	[60 - 64]
Bacillaceae	*Bacillus*	***megaterium***	[60 - 64]
Bacillaceae	*Bacillus*	***polymyxa***	[60 - 64]
Bacillaceae	*Bacillus*	*subtilis*	[60 - 64]
Bacteroidaceae	***Bacteroides***	***fragilis***	[68]
Bartonellaceae	***Bartonella***	***henselae***	[87]
Brevibacteriaceae	***Brevibacterium***	**-**	[12]
Brucellaceae	***Ochrobactrum***	***anthropi***	[93]
Brucellaceae	***Pasteurella***	***canis***	[49, 94]
Brucellaceae	***Pasteurella***	***multocida***	[49, 94]
Burkholderiaceae	*Burkholderia*	***ambifaria***	[47, 96, 97]
Burkholderiaceae	*Burkholderia*	*cepacia*	[47, 96, 97]
Burkholderiaceae	*Burkholderia*	***gladioli***	[47, 96, 97]
Cardiobacteriaceae	***Suttonella***	***indologenes***	[34]
Carnobacteriaceae	***Dolosigranulum***	***pigrum***	[101]
Caulobacteraceae	***Brevundimonas***	***diminuta***	[108]
Clostridiaceae	***Clostridium***	**-**	[60, 110]
Clostridiaceae	***Clostridium***	***perfringens***	[60, 110]
Clostridiaceae	*Peptostreptococcus*	***anaerobius***	[68, 111]
Clostridiaceae	*Peptostreptococcus*	*micros*	[68, 111]
Clostridiaceae	*Sarcina*	-	[112]
Comamonadaceae	*Delftia*[1]	*acidovorans*	[55, 98]

(Appnedix Table 2) contd.....

Family	Genus	Species	References
Bacterial Keratitis			
Corynebacteriaceae	*Corynebacterium*	***accolens***	[15, 44, 62, 105, 115 - 121]
		bovis	
		diptheriae	
		hofmannii	
		macginleyi	
		matruchotii	
		minutissimum	
		propinquum	
		pseudodiphtheriticum	
		pyogenes	
		striatum	
		urealyticum	
		ureicelerivorans	
		xerosis	
	Arcanobacterium	***haemolyticum***	[117]
Enterobacteriaceae	*Citrobacter*	*diversus*	[43, 105, 122, 123]
		koseri	
		freundii	
	Enterobacter	*aerogenes*	[34, 61, 123, 146]
		cloacae	
		gergoviae	
	Escherichia	*coli*	[52, 124]
	Hafnia	*alvei*	[125]
	Klebsiella	***ornithinolytica***	[105, 117, 126, 127, 146]
		oxygenate	
		oxytoca	
		ozaenae	
		pneumoniae	
	Morganella	*morganii*	[368]
	Pantoea	-	[65, 129]
		agglomerans	
	Proteus	-	[52, 126, 130, 368]
		mirabilis	
		rettgeri	
		vulgaris	
	Providencia	-	[33, 104, 131 - 133]
		alcalifaciens	
		rettgeri	
		stuartii	
	Raoultella	-	[33, 134]
		ornithinolytica	
Salmonella	-	[102]	
Serratia	*liguefaciens*	[52, 135]	
	marcescens		
Shigella	***flexneri***	[52, 136]	
	sonnei		
Enterococcaceae	*Enterococcus*	*faecalis*	[33, 39, 138]
		faecium	
Eubacteriaceae	***Eubacterium***	***aerofaciens***	[143]

(Appnedix Table 2) contd.....

Family	Genus	Species	References
Bacterial Keratitis			
Flavobacteriaceae	*Capnocytophaga*	-	[147 - 151]
		canimorsus	
		cynodegmi	
		ochracea	
		sputigena	
	Chryseobacterium	-	[152 - 154]
		indologenes	
	Elizabethkingia	***meningoseptica***	[34, 155]
	Flavobacterium	-	[52]
Fusobacteriaceae	***Fusobacterium***	**-**	[157]
Intrasporangiaceae	***Ornithinimicrobium***	***pekingense***	[160]
Lactobacillaceae	***Lactobacillus***	**-**	[162]
Leuconostocaceae	***Leuconostoc***	***mesenteroides***	[10]
Listeriaceae	***Listeria***	***monocytogenes***	[26]
Microbacteriaceae	***Microbacterium***	**-**	[29, 30]
		oxydans	
	Micrococcus	-	[10, 30, 38, 39]
		luteus	
Micrococcaceae		***tetragenus***	
	Kocuria	***koreensis***	[10, 34 - 37]
		kristinae	
		palustris	
		rosea	
		varians	
	Rothia	***dentocariosa***	[35, 40]
		mucilaginosa	
Moraxellaceae	*Acinetobacter*	*baumannii*	[43 - 48]
		calcoaceticus	
		calcoaceticus var. antitratus	
		haemolyticus	
		lwoffi	
		junii	
		schindleri	
	Moraxella	*catarrhalis*	[30, 49, 50]
		lacunata	
		nonliquefaciens	
Mycobacteriaceae	*Mycobacterium*	*abscessus*	[47, 53 - 59]
		asiaticum	
		aurum	
		avium	
		chelonae	
		flavescens	
		fotuitum	
		gordonae	
intracellulare			
marinum			
massiliense			
mucogenicum			
nonchromogenicum			
szulgai			
terrae			
triviale			

(Appnedix Table 2) contd.....

Family	Genus	Species	References
Bacterial Keratitis			
Neisseriaceae	*Eikenella*	*corrodens*	[51]
	Kingella	*denitrificans*	[51, 67]
		kingae	
	Neisseria	*gonorrhoea*	[13, 65, 66]
		meningitides	
		mucosa	
Nocardiaceae	*Nocardia*	***abscessus***	[44, 69 - 76]
		actinomycetes	
		amamiensis	
		araoensis	
		arthritidis	
		asiatica	
		asteroides	
		beijingensis	
		blacklockiae	
		brasiliensis	
		carnea	
		caviae	
		cyriacigeorgica	
	Nocardia	***elegans***	[237, 291 - 298]
		farcinica	
		ignorata	
		levis	
		neocaledoniensis	
		nova	
		otitidiscaviarum	
		pneumoniae	
		pseudobrasiliensis	
		puris	
		rhamnosiphila	
		thailandica	
		transvalensis	
		wallacei	
	Rhodococcus	***equi***	[77]
Pasteurellaceae	***Aggregatibacter***	***actinomycetemcomitans***	[88, 89]
		aphrophilus	
	Haemophilus	*aegyticus*	[41, 44, 46, 90, 91]
		haemoglobinophilus	
		influenza	
		parainfluenza	
Peptococcaceae	*Peptococcus*	*prevotii*	[92]
Porphyromonadaceae	***Parabacteroides***	***distasonis***	[95]
Propionibacteriaceae	*Propionibacterium*	-	[1, 68, 98, 99]
		acnes	
		granulosum	
Prevotellaceae	***Prevotella***	**-**	[68, 100]
		intermedia	
		melaninogenica	

(Appnedix Table 2) contd.....

Family	Genus	Species	References
Bacterial Keratitis			
Pseudomonadaceae	***Azotobacter***	***beijerinckii***	[107]
		chroococcum	
		paspali	
		vinelandii	
	Pseudomonas	*acidovorans*	[30, 33, 38, 52, 102 - 106]
		aeruginosa	
		fluorescens	
		luteola	
		mesophilic	
		oryzihabitans	
		putida	
		pyocyaneus	
		stutzeri	
Rhizobiaceae	***Rhizobium***	***radiobacter***	[109]
Rhodobacteraceae	***Paracoccus***	***yeei***	[113]
Rickettsiaceae	***Rickettsia***	***conorii***	[114]
Sphingobacteriaceae	***Sphingobacterium***	***spiritivorum***	[30]
Spirochaetaceae	***Borrelia***	***burgdorferi***	[369]
	Treponema	**pallidum**	[137]
	Gemella	**-**	[33, 38, 370]
		haemolysans	
		morbillorum	
Staphylococcaceae	*Staphylococcus*	***albus***	[10, 15, 23, 34, 39, 43, 46, 52, 60, 139 - 142]
		aureus	
		auricularis	
		capitis	
		caprae	
		cohnii	
		epidermidis	
		haemolyticus	
		hominis	
		hyicus	
Staphylococcaceae	*Staphylococcus*	***intermedius***	[10, 15, 23, 34, 39, 43, 46, 52, 60, 139 - 142]
		lentus	
		lugdunensis	
		MRSA	
		pasteuri	
		saprophyticus	
		simulans	
		warneri	
		xylosus	

(Appnedix Table 2) contd.....

Family	Genus	Species	References
Bacterial Keratitis			
Staphylococcaceae	*Staphylococcus*	***acidominimus***	[33, 41, 46, 47, 49, 60, 64, 65, 117, 126, 144 - 146]
		agalactiae	
		anginosus	
		dysgalactiae	
		intermedius	
		mitis	
		morbillorum	
		oralis	
		parasanguis	
		pneumoniae	
		pyogenes	
		salivarius	
		sanguinis	
		viridans	
Streptomycetaceae	*Streptomyces*	-	[131, 156]
		thermocarboxydus	
Tsukamurellaceae	***Tsukamurella***	***hongkongensis***	[158, 159]
		spumae	
		tyrosinosolvens	
Vibrionaceae	*Vibrio*	*vulnificus*	[43, 161]
		parahaemolyticus	
Xanthomonadaceae	*Stenotrophomonas*	*maltophilia*	[46, 98]
	Xanthomonas	-	[163]
Yersiniaceae	***Yersinia***	-	[43, 164]
		pseudotuberculosis	

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