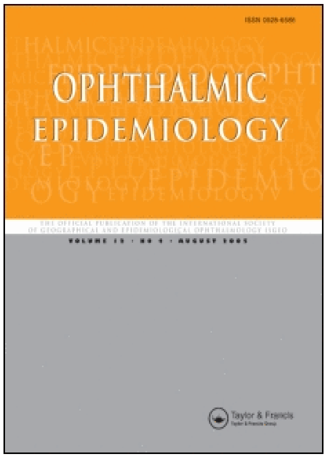

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Microbial Keratitis in South India: Influence of Risk Factors, Climate, and Geographical Variation

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ABSTRACT

Purpose: **To determine the influence of risk factors, climate, and geographical variation on the microbial keratitis in South India.** ***Methods:*** **A retrospective analysis of all clinically diagnosed infective keratitis presenting between September 1999 and August 2002 was performed. A standardised form was filled out for each patient, documenting sociodemographic features and information pertaining to risk factors. Corneal scrapes were collected and subjected to culture and microscopy.** ***Results:*** **A total of 3,183 consecutive patients with infective keratitis were evaluated, of which 1,043 (32.77%) were found to be of bacterial aetiology, 1,095 (34.4%) were fungal, 33 (1.04%) were** ***Acanthamoeba*****, 76 (2.39%) were both fungal and bacterial, and the remaining 936 (29.41%) were found to be culture negative. The predominant bacterial and fungal pathogens isolated were** ***Streptococcus pneumoniae*** **(35.95%) and** ***Fusarium*** **spp. (41.92%), respectively. Most of the patients (66.84%) with fungal keratitis were between 21 and 50 years old, and 60.21% of the patients with bacterial keratitis were older than 50 ($p < 0.0001$) (95% CI: 5.19–7.19). A majority of patients (64.75%) with fungal keratitis were agricultural workers ($p < 0.0001$) [odds ratio (OR): 1.4; 95% CI: 1.19–1.61], whereas bacterial keratitis occurred more commonly (57.62%) in nonagricultural workers ($p < 0.0001$) (OR: 2.88; 95% CI: 2.47–3.36). Corneal injury was identified in 2,256 (70.88%) patients, and it accounted for 92.15% in fungal keratitis ($p < 0.0001$) (OR: 7.7; 95% CI: 6.12–9.85) and 100% in** ***Acanthamoeba*** **keratitis. Injuries due to vegetative matter (61.28%) were identified as a significant cause for fungal keratitis ($p < 0.0001$) (OR: 23.6; 95% CI: 19.07–29.3) and due to mud (84.85%) for** ***Acanthamoeba*** **keratitis ($p < 0.0001$) (OR: 26.01; 95% CI: 3.3–6.7). Coexisting ocular diseases predisposing to bacterial keratitis accounted for 68.17% ($p < 0.0001$) (OR: 33.99; 95% CI: 27.37–42.21). The incidence of fungal keratitis was higher between June and September, and bacterial keratitis was less during this period.** ***Conclusion:*** **The risk of agricultural predominance and vegetative corneal injury in fungal keratitis and associated ocular diseases in bacterial keratitis increase susceptibility to corneal infection. A hot, windy climate makes fungal keratitis more frequent in tropical zones, whereas bacterial keratitis is independent of seasonal variation and frequent in temperate zones. Microbial pathogens show geographical variation in their prevalence. Thus, the spectrum of microbial keratitis varies with geographical location influenced by the local climate and occupational risk factors.**

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INTRODUCTION

Corneal blindness is a major public health problem worldwide, and infectious keratitis is one of the predominant causes.[1] There have been increasing reports from different parts of the world.[1–9] Ulcerative keratitis due to infection with a wide range of organisms such as viruses, bacteria, fungi or protozoa has been reported.[1] There are regional variations in the predominance of different microbes, reflecting different patient populations and climatic effects. Fungal keratitis is relatively rare in temperate climates. However, in the tropical regions of the world, fungal keratitis is a common and important cause of corneal morbidity.[8–11] Bacterial keratitis typically occurs in eyes having some predisposing risk factors, and its predominance has been reported in temperate climatic zones.[12–15] *Acanthamoeba*, free-living protozoa that cause a serious troublesome keratitis, has frequently been reported among contact lens wearers in many parts of the world.[16] In addition to regional differences, there was a seasonal variation in the pattern of microbial keratitis.[10,17] Thus, a periodic regionwide review on microbial keratitis in terms of aetiology and epidemiology must be updated for comprehensive strategy for diagnosis and management of this disease.

The following study was conducted to evaluate all microbial keratitis treated at a tertiary eye care referral centre in South India. The aim of this investigation was to determine the influence of risk factors, climate, and geographical variation on the incidence of microbial keratitis, and the prevalence of microbial pathogens causing keratitis in South India.

MATERIALS AND METHODS

This retrospective study included all patients with clinically diagnosed microbial keratitis treated at Aravind Eye Hospital and Postgraduate Institute of Ophthalmology, Tirunelveli, South India, over a 3-year period from September 1999 to August 2002. Corneal ulceration was defined as a loss of the corneal epithelium with underlying stromal infiltration and suppuration associated with signs of inflammation with or without hypopyon.[2] A standardised form was filled out for each patient, documenting sociodemographic features, predisposing factors, history of corneal trauma, traumatic agents, associated ocular conditions, and other systemic diseases. All patients were examined on the slit-lamp biomicroscope. After a detailed ocular examination using standard techniques,[2] corneal scrapes were performed under aseptic conditions from each ulcer by an ophthalmologist using a flame-sterilized Kimura's spatula or sterile Bard-Parker blade (No 15) after instillation of 0.5% proparacaine hydrochloride. The scraped material was initially smeared onto clean sterile labeled glass slides for 10% potassium hydroxide wet mounting, Gram-staining, and Giemsa-staining procedures.[18,19] The material obtained by next scrapes were directly inoculated onto the surface of solid media such as sheep's blood agar, chocolate agar, Sabouraud's dextrose agar, and non-nutrient agar in a row of C-shaped streaks and also in liquid media such as brain heart infusion broth and thioglycollate medium.[18,19] All laboratory methods were performed under standard protocols, which have been discussed in detail in the previous studies.[2,10,17] Pearson's chi-square test was used to carry out the statistical analysis whenever required and $p < 0.05$ was considered to be statistically significant.

RESULTS

Microbiological profile

From September 1999 to August 2002, there were 3,183 patients with clinical diagnosis of corneal ulceration who were evaluated. Of 3,183, one eye was infected in 3,180 (99.91%) patients, and both eyes were infected in 3 (0.09%) patients; thus, a total of 3,186 eyes with corneal ulcers were studied. A total of 3,183 patients; corneas were scraped; 2,247 (70.59%) had positive microbial growth, and the remaining 936 (29.41%) negative growth. Bacteria alone were recovered in culture from the corneal scrapes of 1,043 (32.77%) patients, fungi alone from 1,095 (34.4%), *Acanthamoeba* alone from 33 (1.04%), and both bacteria and fungi from 76 (2.39%) patients. Of the 1,043 culture-positive bacterial keratitis cases, one eye was infected in 1,040 (99.71%) patients, and both eyes were infected in 3 (0.29%) patients. A total of 1,185 bacterial pathogens were isolated from the 1,122 keratitis eyes. Of 1,122, 1,046 eyes yielded only bacterial growth, and the remaining 76 eyes yielded both bacterial and fungal growth. Of 1,122 keratitis eyes, 1,059 eyes had single species of bacterial growth, and 63 eyes had two species of bacterial growth. The predominant bacterial species isolated were *Streptococcus pneumoniae* (426 of 1,185; 35.95%), followed by *Pseudomonas aeruginosa* (236 of 1,185; 19.92%) (Table 1); 1,176 fungal isolates were recovered from 1,171 keratitis eyes. Of 1,171, 1,095 eyes yielded only fungal growth and the remaining 76 eyes yielded both bacterial and fungal growth; 1,166 cases had single species of isolates, and the remaining 5 cases had two species of fungal isolates. The predominant fungal species isolated was *Fusarium* spp. (493 of 1,176; 41.92%) followed by *Aspergillus* spp. (294 of 1,176; 25%) (Table 2). Among the 3,186 corneal ulcers cultured, only 33 (1.03%) eyes were found to be culture-positive for *Acanthamoeba* species.

Demographics

The demographic features of 3,183 patients with microbial keratitis are documented in Table 3. Of 3,183 patients, 1,879 (59.03%) were males and 1,304 (40.97%) were females; the male to female ratio was 1.44 to 1. Males (712 of 1,095; 65.02%) were affected more often in fungal keratitis ($p < 0.0001$) (odds ratio [OR]: 1.47; 95% CI: 1.26–1.71). A major group of patients (51.81%; 1,649 of 3,183) were between the age of 21 and 50 years. However, patients above the age of 50 years (628 of 1,043; 60.2%) were significantly ($p < 0.0001$) (OR: 6.11; 95% CI: 5.19–7.19) more than patients below 50 years (415 of 1,043; 39.8%) in bacterial keratitis, whereas a larger group of patients with fungal keratitis (732 of 1,095, 66.85%) were between the age 21 and 50 years ($p < 0.0001$). Significantly more patients (879 of 1,095; 80.27%) with fungal keratitis ($p < 0.0001$) (OR: 2.2; 95% CI: 1.87–2.65) and with *Acanthamoeba* keratitis (100%) were rural population ($p < 0.0001$) (95% CI: 1.0–2.0), whereas patients with bacterial keratitis were more often among urban population (479 of 1,043; 45.93%), and it was statistically significant ($p < 0.0001$) (95% CI: 2.54–3.4). Non-agricultural workers were significantly ($p < 0.0001$) (OR: 2.88; 95% CI: 2.47–3.36) more in number than agricultural workers (44 of 1,043; 42.38%) among patients with bacterial keratitis, whereas agricultural workers were significantly more in number among patients with fungal keratitis (709 of 1,095; 64.75%) ($p < 0.0001$) (OR: 1.4; 95% CI: 1.19–1.61) and *Acanthamoeba*

Table 1. Bacterial pathogens isolated from 1,122 eyes with microbial keratitis (nonviral) treated at tertiary eye care referral centre in South India

S. no.	Name of the bacterial isolates	Pure isolates no.	Mixed with other bacteria no.	Mixed with fungal species	Total bacterial isolates no. (%)
1	Total gram positive cocci	659	63	35	757 (63.88)
	S. pneumoniae	411	5	10	426
	S. epidermidis	150	43	23	216
	S. aureus	33	10	0	43
	Miccrococcus spp.	6	0	0	6
	Alphahaemolytic streptococci	44	5	2	51
	Beta haemolytic streptococci	6		0	6
	Nonhaemolytic streptococci	9		0	9
2	Total gram-positive bacilli	33	22	2	57 (4.81)
	Bacillus spp.	12	15	0	27
	Corynebacterium spp.	21	7	2	30
3	Total gram-negative cocci and cocco bacilli	12			12 (1.01)
	Moraxella spp.	9			9
	Neisseria spp.	3			3
4	Total aerobic actinomycetes	39	7		46 (3.88)
	Nocardia spp.	39	7		46
5	Total gram-negative bacilli	240	34	39	313 (26.41)
	Pseudomonas spp.	173	27	36	236
	Enterobacter spp.	24	5	3	32
	Klebsiella spp.	10	2		12
	Proteus spp.	6			6
	Alkaligens spp.	6			6
	Haemophilus spp.	6			6
	Acinetobacter spp.	6			6
	E. coli	4			4
	Serratia spp.	3			3
	Citrobacter spp.	2			2
	Total no. of isolates (% of isolates)	983 (82.95)	126 (10.63)	76 (6.41)	1,185 (100)

keratitis (26 of 33; 78.79%) ($p < 031$) (OR: 2.54; 95% CI: 0.9–2.0).

The risk factors predisposing to corneal ulceration identified are summarised in Table 4. A history of recent injury to the cornea predisposing to corneal ulceration was identified in 2,256 (70.88%) patients compared to other predisposing risk factors in 927 (29.12%) patients. Corneal injury was identified as the predominant predisposing factor (1,009 of 1,095; 92.15%) for fungal keratitis, and the correlation between trauma and fungal keratitis was highly significant ($p < 0.0001$) (OR: 7.7; 95% CI: 6.12–9.85) (Table 4). Of 1,009, 671 (61.28% of 1,095) had corneal injury with vegetative matter, and this correlation was highly significant ($p < 0.0001$) (OR: 23.6; 95% CI: 19.07–29.3). Coexisting ocular diseases predisposing to bacterial corneal

Table 2. Fungal pathogens isolated from 1,171 eyes with microbial keratitis (nonviral) treated at tertiary eye care referral centre in South India

S. no.	Name of the fungal isolates	Pure isolates no.	Mixed with other fungal species no.	Mixed with bacterial species	Total fungal isolates no. (%)
1	Hyaline fungi	814	8	38	860 (73.13)
	Fusarium spp.	469	2	22	493
	Aspergillus spp.	282	4	8	294
	Mucor spp.	6			6
	Rhizopus spp.	4			4
	Penicillium spp.	4			4
	Unidentified hyaline fungal species	49	2	8	59
2	Dematiaceous fungi	276	2	38	316 (26.87)
	Cladosporium spp.	73		7	80
	Botryodiploidia spp.	53		4	57
	Curvularia spp.	29		9	38
	Biopolaris spp.	26		3	29
	Exserohilum spp.	21		3	24
	Alternaria spp.	11		2	13
	Unidentified dematiacious fungal species	63	2	10	75
	Total no. of isolates (%)	1,090 (92.69)	10 (0.85)	76 (6.46)	1,176 (100)

Table 3. Demographic characteristics and microbial growth pattern of 3,183 patients with microbial keratitis (nonviral) treated at tertiary eye care referral centre in South India

S. no.	Demographic characters	Total number of cases (%)	Bacterial growth (%)	Fungal growth (%)	*Acanthamoeba* growth (%)	Bacterial & fungal (%)	No growth (%)
	Total no. of cases	3,183 (100)	1043 (100)	1095 (100)	33 (100)	76 (100)	936 (100)
1	Gender						
	Male	1879 (59.03)	592 (56.76)	712 (65.02)	22 (66.67)	47 (61.84)	506 (54.06)
	Female	1304 (40.97)	451 (43.24)	383 (34.98)	11 (33.33)	29 (38.16)	430 (45.94)
2	Age in years						
	< 21	481 (15.11)	171 (16.4)	161 (14.7)	0	3 (3.95)	146 (15.6)
	21–30'	464 (14.58)	82 (7.86)	229 (20.91)	2 (6.06)	9 (11.84)	142 (15.17)
	31–40'	596 (18.72)	67 (6.42)	267 (24.38)	9 (27.27)	19 (25)	234 (25)
	41–50'	589 (18.5)	95 (9.11)	236 (21.55)	13 (39.39)	25 (32.89)	220 (23.5)
	> 50	1053 (33.08)	628 (60.21)	202 (18.45)	9 (27.27)	20 (26.34)	194 (20.73)
3	Residence						
	Rural	2229 (70.03)	564 (54.07)	879 (80.27)	33 (100)	60 (78.95)	693 (74.04)
	Urban	954 (29.97)	479 (45.93)	216 (19.73)	0	16 (21.05)	243 (25.96)
4	Occupation						
	Agricultural workers	1879 (59.03)	442 (42.38)	709 (64.75)	26 (78.79)	52 (68.42)	650 (69.44)
	Nonagricultural workers	1304 (40.97)	601 (57.62)	386 (35.25)	7 (12.21)	24 (31.58)	286 (30.56)

ulceration were identified in 711 (68.17%) patients, compared to other predisposing risk factors in 332 (31.83%) patients ($p < 0.0001$) (OR: 33.99; 95% CI: 27.37–42.21). A history of definite corneal injury was recorded in all 33 (100%) patients with *Acanthamoeba* keratitis, of which 28 (84.85%) had corneal injury with mud, compared to 5 (15.15%) who had corneal injury due to other materials, and this difference was statistically significant ($p < 0.0001$) (OR: 26.01; 95% CI: 3.3–6.7).

The monthly distribution in the occurrence of microbial keratitis analysed over a 3-year period and the seasonal observation

Table 4. Association between the identified predisposing risk factors and the causative microorganisms isolated from corneal scrapes obtained from 3,183 patients with microbial keratitis (nonviral) treated at a tertiary eye care referral centre in South India

S. no.	Predisposing risk factors	Total no. of cases (%)	Bacterial growth (%)	Fungal growth (%)	*Acanthamoeba* growth (%)	Bacterial & fungal (%)	No growth (%)
1	Ocular injuries	2,256 (70.88)	292 (28.01)	1,009 (92.15)	33 (100)	76 (100)	846 (90.38)
	Vegetative matters	802 (25.2)	26 (2.5)	671 (61.28)	3 (9.09)	17 (22.37)	85 (9.08)
	Dirt	561 (17.62)	26 (2.5)	163 (14.88)	0	2 (2.63)	370 (39.53)
	Soil/sand/stone	586 (18.41)	177 (16.97)	79 (7.21)	28 (84.85)	24 (31.58)	278 (29.7)
	Animal matters	164 (5.15)	42 (4.03)	62 (5.66)	1 (3.03)	33 (43.42)	26 (2.78)
	Miscellaneous items:	143 (4.49)	21 (2.01)	34 (3.11)	1 (3.03)	0	87 (9.29)
2	Coexisting ocular diseases	874	711 (68.17)	73 (6.67)	0	0	90 (9.62)
	Chronic dacryocystitis	242 (7.6)	242 (23.20)	0	0	0	0
	Spheroidal degeneration	284 (8.92)	242 (23.20)	26 (2.37)	0	0	16 (1.71)
	Blepharitis	97 (3.05)	74 (7.09)	0	0	0	23 (2.46)
	Suture infiltration	49 (1.54)	30 (2.88)	16 (1.46)	0	0	3 (0.32)
	Dry eye syndrome	40 (1.26)	24 (2.3)	0	0	0	16 (1.71)
	Preexisting viral keratitis	35 (1.1)	13 (1.25)	14 (1.28)	0	0	8 (0.85)
	Conjunctivitis	30 (0.94)	26 (2.5)	0	0	0	4 (0.43)
	Bullous keratopathy	26 (0.82)	19 (1.82)	0	0	0	7 (0.75)
	Lid abnormalities	23 (0.72)	12 (1.15)	7 (0.64)	0	0	4 (0.43)
	Lagophthalmos	17 (0.53)	8 (0.77)	8 (0.73)	0	0	1 (0.11)
	Bell's palsy	12 (0.38)	10 (0.96)	0	0	0	2 (0.21)
	Trichiasis	10 (0.31)	6 (0.58)	0	0	0	4 (0.43)
	Adherent leucoma	9 (0.28)	5 (0.48)	2 (0.18)	0	0	2 (0.21)
3	Contact lens usage	33 (1.04)	33 (3.16)	0	0	0	0
4	Usage of steroides (topical)	20 (0.63)	7 (0.67)	13 (1.19)	0	0	0
5	Systemic diseases	224 (7.04)	38 (3.64)	176 (16.07)	0	0	10 (1.07)
	Diabetes mellitus	211 (6.63)	30 (2.88)	172 (15.71)	0	0	9 (0.96)
	Leprosy	9 (0.28)	6 (0.57)	2 (0.18)	0	0	1 (0.04)
	Tuberculosis	2 (0.06)	0	2 (0.18)	0	0	0
	Stevens-Johnson syndrome	2 (0.06)	2 (0.19)	0	0	0	0
	Total	3183 (100)	1043 (100)	1095 (100)	33 (100)	76 (100)	936 (100)

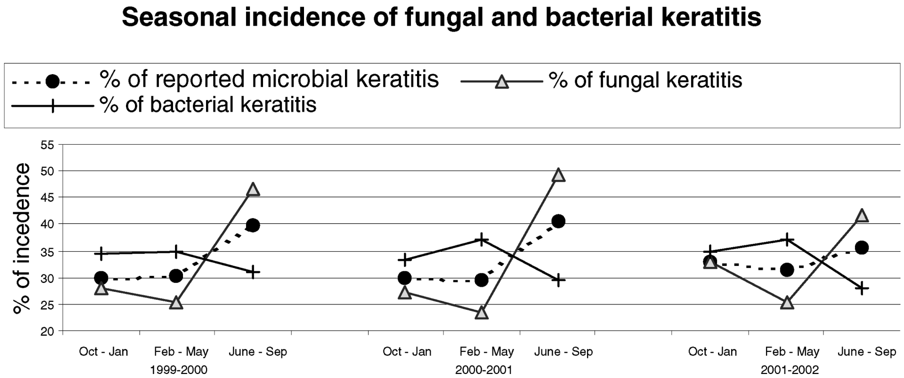

Figure 1. Comparison of seasonal incidence of fungal and bacterial keratitis seen at tertiary eye care referral centre in South India from September 1999 to August 2002.

of 3,183 patients with microbial keratitis are depicted in Figure 1. In our study, the fungal keratitis was seen more often between June and September, although this was not statistically significant, and there was lower incidence of bacterial keratitis from June to September than in other months.

DISCUSSION

Microbial keratitis is suppurative inflammation of the cornea produced by replicating microorganisms.[1,18,19] Microbial keratitis from either bacterial or fungal or parasitic infection exists in all geographic regions of the world.[1] The entire population is at risk of developing corneal infection, but some are at greater risk than others. The incidence of microbial keratitis varies from 11 per 100,000 persons per year in the United States[1] to 799 per 100,000 persons per year in Nepal.[7] At this centre, the incidence of culture-proven microbial keratitis between September 1999 and September 2002 was observed to be 70.59%. A similar rate of incidence was reported in Madurai (68.4%)[2] and in South Africa (65%[3] to 68%[4]), whereas in Nepal (80%)[20] and Bangladesh (82%)[21] it was reported to be higher. In contrast, very low recovery rate was reported in Taiwan (40%).[22] A review of literature shows that the reported culture-positivity ranges from 34.52% to 82% and was influenced by previous empirical treatment with antimicrobials before referral, use of topical anesthetic agents,[23] and corneal scrapes. In addition to these factors, the use of transporting media instead of direct inoculation for recovery of microbial pathogens is still in controversy.[24] Therefore, these factors may have false-negative culture results.

The proportion of fungal and bacterial keratitis in this study accounted for 34.4% and 32.77%, respectively, and this proportion is nearly equal. Similarly, Srinivasan et al. reported equal proportion of fungal (32%) and bacterial (32.3%) corneal infection in Madurai.[2] A review of literature shows that there are distinct patterns of geographical variation in the aetiology of suppurative keratitis, and the proportion of corneal ulcers caused by filamentous fungi increases toward tropical latitudes (Table 5). In tropical countries like South Florida (35%),[8] Bangladesh (36%–40%),[9] and South India (32–34%)[2,10] the incidence of fungal keratitis was reported to be up to 40%. In temperate countries like Britan[12] and United States,[13] the proportion of fungi causing suppurative keratitis is very low, whereas bacteria were responsible for larger proportion of corneal ulceration in these temperate regions.[8] Areas where the climate is warm and humid, especially near the equator, appear to have more cases of fungal keratitis, and in all of these areas filamentous fungi are the dominant fungal corneal pathogen. Thus, the temperature and humidity have a major role in determining the microorganisms found in the environment.

The most commonly isolated fungal pathogen in the study, *Fusarium* spp., is similar to the pattern of fungal pathogens reported from tropical areas of South Florida,[8] Ghana,[25] Paraguay,[26] Nigeria,[27] Tanzania,[28] Hong Kong,[14] and Singapore,[29] whereas in the temperate regions of subtropical countries of Nepal,[7] North India,[30] and Bangladesh[9] *Aspergillus* spp. was found to be predominant. In more temperate climates, fungal corneal ulcers are more frequently associated with *Candida* spp. than filamentous fungi. This difference in the prevalence of fungal pathogens may be explained by differences in climate and the environment. There was no climatic influence in the prevalence of bacterial pathogens causing corneal ulcers, whereas geographic variation was seen. *Streptococcus pneumoniae* was found to be the predominant bacterial species isolated in this study. Similarly, *Streptococcus pneumoniae* was reported to be the predominant bacterial pathogen in Madurai[2] and Nepal.[20] *Pseudomonas* spp. were identified as the most common bacterial species in the studies of Bangladesh,[21] Hong Kong,[14] and Paraguay.[26] A predominance of *Staphylococcus* spp. has been reported in South Florida,[8] Switzerland,[31] and Hyderabad.[32] These reports show that there is distinct pattern of geographical variation in the prevalence of bacterial pathogens.

In this investigation, males predominated females in all forms of keratitis. Corneal infection among males could be attributed to their greater involvment in outdoor activities, thus being prone to corneal injury with external agents. Younger age groups in both sexes are more physically active and are at a risk for corneal injury. Similarly, in this report, the higher incidence

Table 5. Geographic comparison of the incidence of microbial keratitis (nonviral)

Place	Author	Year	Total no. of the patients studied	Culture positivity (%)	Bacterial aetiology % of incidence	Bacterial aetiology Predominant pathogen	Fungal aetiology % of incidence	Fungal aetiology Predominant pathogen	Culture negativity (%)
USA	Liesegang et al.	1977	663	56'	35.59'%	*Pseudomonas* spp.,*S. aureus*	20.06	*Fusarium* spp.	44.04
Africa	Carmichael et al.	1985	283	44.88	42.76	*Str. pneumoniae, Pseudomonas spp.*	2.12	*Curvularia* spp.	55.12
California	Ormerod et al.	1987	227	82	76.21'	Coagulase negative staphylococci	5.73	*Candida* spp.	15
South Africa	Ormerod et al.	1987	120	75.22	96	*Staphyloccus* spp.	4	24.78	
Nepal	Upadhyay et al.	1991	405	80	79	*Stre. penumoniae, Staphylococcus* spp.	21	*Aspergillus* spp.,*Candida* spp.	20
Bangladesh	Dunlop et al.	1994	142	82	59	*Pseudomonas* spp., *Stre. pneumoniae*	41	*Aspergillus* spp., *Fusarium* spp.	
West Africa	Hangan et al.	1995	199	57.3	49	*Staphyloccus* spp., *Pseudomonas* spp.	51	*Fusarium* spp.	
South India (Madurai)	Srinivasan et al.	1997	434	68.4	32.3	*Str.pneumoniae, Pseudomonas* spp.	32	*Fusarium* spp., *Aspergillus* spp.	31.6
Hong Kong	Houang et al.	2001	223	34.52	95.07	*Pseudomonas* spp., Coagulase negative staphylococci	2.24	*Fusarium* spp.	65.48
Ghana	Leck et al.	2002	290	50.34	12.4	*Staphylococcus* spp., *Pseudomonas* spp.	36.2	*Fusarium* spp., *Aspergillus* spp.	49.76
South India (Trichi)	Leck et al.	2002	800	68.87	23.9	*Str. pneumoniae*, Coagulase negative staphylococci	38.6	*Fusarium* spp., *Aspergillus* spp.	31.1
South India (Tirunelveli)	Bharathi et al.	2002	1618	69.54	34.98	*Str.pneumoniae, Pseudomonas* spp.	32.26	*Fusarium* spp., *Aspergillus* spp.	30.41
Taiwan	Fong et al.	2003	455 eyes	49	81.18	*Pseudomonas spp.*	13.5	*Fusarium spp.*	51
Sydney	Butter et al.	2004	190	62.8'	94.44'	*Staphylococcus spp.*	3.7	0	37.2
Eastern India	Basak et al.	2005	1198	67.7	15.3	*S. aureus, Pseudomonas spp.*	42.5	*Aspergillus spp., Fusarium spp.*	32.3
Present study	Bharathi et al.	2005	3183	70.59	32.77	*Str. pneumoniae, Pseudomonas* spp.	34.4	*Fusarium* spp., *Aspergillus* spp.	29.38

of fungal (66.85%) and *Acanthamoeba* keratitis (72.72%) is documented among the age group between 21 and 50 years; in marked contrast, bacterial keratitis is more frequent among patients older than 50 years. A very high percentage of the patients with history of corneal injury were recorded in fungal keratitis (92%) and in *Acanthamoeba* keratitis (100%), whereas in bacterial keratitis corneal injury was found to be very low (28%). Because the history of corneal injury is more frequent in the younger age group than in elderly patients, the rate of incidence of fungal keratitis and *Acanthamoeba* keratitis was more frequent in the younger age group. The majority of the patients with fungal keratitis and *Acanthamoeba* keratitis were agricultural workers, whereas nonagricultural workers had more in bacterial keratitis; this contrast is due to the difference in the predominance of risk factors.

On a global level, predisposing risk factors for microbial keratitis vary tremendously between developing and developed countries.[1] Corneal trauma is the leading cause for microbial keratitis in South India.[1,2,10] Similarly, in this study, a history of recent injury to cornea (70.88%) was identified as the principal predisposing factor for the development of corneal ulcers. The incidence of microbial keratitis due to corneal injury was reported to be higher in India (65.4% in South India;[2] 82.9% in East India;[33] and 55% in North India[30]), Nepal (52.8%),[20] Ghana (39.2%),[25] and Taiwan (23.8%),[22] whereas in the United States (8.33% in Philadephia),[34] New Zealand (23.5%)[35] and Australia (15% in Perth[36] and 3.7% in Sydney[37]), it was reported to be infrequent. This difference in the pattern of risk factors is due to the variation in the occupation profile of the patients who live in those regions. Agricultural-related works are common in developing countries, whereas nonagricultural jobs are predominant in developed nations. A retrospective study in Singapore reported that a mechanical corneal injury is the most common risk factor (55%) for corneal ulcer,[29] whereas in Philadelphia, chronic ocular surface diseases, contact lens wear, and use of topical corticosteroides were common risk factors.[37] Contact lens wear appeared to be the predominant risk factor in Taiwan (44.3%),[22] Hong Kong (36%),[14] and prior ocular surgery in New Zealand (29.6%),[35] and Australia (43.4% in Perth[36] and 46.3% in Sydney[37]).

In this report, corneal trauma (92%) was identified as the major risk factor for fungal keratitis. Similarly, fungal keratitis was frequently reported among patients with corneal injury in Hyderabad (54.4%),[38] Calcutta (72.2%),[39] Sri Lanka (55%),[40] Florida (44%),[41] Bangladesh (35%),[21] and Singapore (55%).[29] In marked contrast, the most common risk factor identified for the development of bacterial keratitis (68%) was coexisting ocular diseases. Bourcier et al.[42] documented that 50.3% of the patients with bacterial keratitis were contact lens wearers, and 21.3% had nontraumatic ocular surface diseases in Paris. Schaefer et al.[31] identified coexisting ocular diseases and contact lens wear as the cause for the development of bacterial keratitis in 80% of the patients in Switzerland. Corneal trauma (52%) was reported to be the risk for bacterial keratitis in Bangladesh,[21] and preexisting ocular diseases (41%) and contact lens wear (31%) in Singapore.[29] In this study, chronic dacryocystitis (23%) and spheroidal degeneration (22%) were frequently noted among the patients with bacterial keratitis, and the use of contact lens was documented in 3% of the patients. Predominance of contact-lens-related bacterial keratitis was reported by Houang et al. in Hong Kong.[14]

In South India, paddy or rice stalks in the fields, thorns, and tree branches were the most common cause of corneal injury. In this study, corneal injury with vegetative matter predisposing to corneal infection was found to be higher (25.2%) than other agents. It was reported to be 38.7% in Madurai,[2] whereas in West Bengal it was reported to be higher (59.6%).[33] Vegetative matter as cause for corneal trauma resulting in fungal keratitis was found to be higher (61.28%) than bacterial keratitis (2.5%) and *Acanthamoeba* keratitis (9%), whereas corneal injury with mud responsible for *Acanthamoeba* keratitis (85%). *Acanthamoeba* is ubiquitous free-living protozoa; because of the widespread distribution, human contact with this organism is inevitable and frequent.[16,43] Ocular infection by *Acanthamoeba* is rare but has been reported in almost all parts of the world.[43] Several important risk factors are associated with *Acanthamoeba* keratitis, of which contact lens wear is the predominant risk factor in the developed world; however, in developing countries it is usually associated with trauma or exposure to contaminated water.[16,43]

Like fungal keratitis and unlike bacterial keratitis, corneal injury was identified as the leading risk factor for the development of *Acanthamoeba* keratitis in this series. In contrast with the present study, contact lens wear was the most widely recognised risk factor for occurrence of *Acanthamoeba* keratitis in developed countries,[1] but in developing countries like India, contact lens wear does not emerge as an important risk factor for *Acanthamoeba* keratitis.[43] This can probably be attributed to the relatively few lens wearers in this country. The occurrence of *Acanthamoeba* keratitis has also been associated with flooding, tank-fed water in the home, warmer weather, and poor socioeconomic conditions.[16,43] *Acathamoeba* keratitis after penetrating keratoplasty and radial keratotomy has been reported.[16,43] The use of contact lenses as the cause for microbial keratitis was identified in very low proportion (1.04%) in this study, and all of these were found to be of gram-negative bacterial aetiology, mainly *Pseudomonas aerugionsa*. The increased incidence of Pseudomonas infection in contact lens wearers by formation of slimy biofilm on contact lenses due to poor lens hygiene was well described.[1] Prolonged use of topical corticosteroids predisposing to corneal ulcers was minimal (0.63%), of which fungal infection was more frequent (65%) than bacterial (35%), especially *Streptococcus pneumoniae*. The use of topical corticosteriods can create localised immunosuppression and prevent neutrophil migration in response to chemotatic factors released during microbial infection.[44] They appear to activate and increase the virulence of fungi by suppressing host immune response, and impairment in opsonisation predisposes to infection with encapsulated bacteria, including *S. pneumoniae*.[44] The analysis on the risk factors identified and microorganisms recovered in this study indicate that the predisposing factors influence the type of infection that develop.

In this study, there was an increase in the number of reported cases of microbial keratitis between June and September. The incidence of fungal keratitis was higher during paddy harvesting and also during the time of year when agricultural activity was higher. In our study, it was more prevalent between June and September. The peak incidence correlates with windy and dry weather between June and September. However, the proportion of corneal ulcers due to bacteria remained consistently the same throughout the year except from June to September, and the incidence of bacterial keratitis was less than fungal keratitis during the same period. In coastal Karnataka,[45] higher incidence is reported during the winter (from October to January) and monsoon (from June to September) seasons. Nigeria experiences a climate similar to that of South India and has reported a higher incidence of fungal keratitis during the hot and humid season,[27] and in Hyderabad,[38] a higher incidence of fungal keratitis was reported during the winter (from October to January) and monsoon (from June to September) seasons. A hot, humid, windy climate and an agriculture-based occupation of a large population make fungal keratitis more frequent in tropical zones.

In conclusion, climate and the environment in which the person lives influences the type of infection that develops. Filamentous fungal keratitis are common in tropical climates, whereas bacteria are more common in temperate climates. The microbial causes of infective keratitis vary according to the risk factors for infection, and their prevalence shows geographical variation. Corneal injury is the principal risk factor for the development of fungal keratitis, but coexisting ocular diseases are the main risk factors for bacterial keratitis. There was a seasonal increase in the incidence of fungal keratitis and the reported cases of microbial keratitis during windy and dry weather, whereas the incidence of bacterial keratitis is consistently the same throughout the year. Thus, the spectrum of the microbial keratitis varies with geographical location, influenced by the local climate and occupational risk factors.

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