Original Article

Multivariate Analysis of Childhood Microbial Keratitis in South India

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Abstract

Introduction: Corneal infection is the most common cause of profound ocular morbidity leading to blindness worldwide. Corneal infection in children is difficult to diagnose and treat, as they are unwilling and sometimes unable to cooperate during active management. This study analyses the prevalence, microbiology, demography, therapeutic and visual outcome of infectious microbial keratitis in the paediatric age group seen at a tertiary eye care hospital in south India. Materials and Methods: A retrospective review of all cases presenting with keratitis to the ocular microbiology and cornea service at Aravind Eye Hospital, Coimbatore, from February 1997 to January 2004, was done to screen the patients for microbial keratitis. Their records were further analysed for clinical and microbiological details. Cases with culture-proven non-viral keratitis in children ≤15 years were included in the study. Full ophthalmic examination was performed for all cases. Results: Of the 310 patients who attended the cornea clinic, 97 (31.2%) patients were confirmed to be positive for microbial keratitis. 54.6% of cases were male. The most common predisposing cause of ulceration was trauma (69%) with organic matter. Pure bacterial cultures were obtained from 64 (65.9%) eyes, whereas pure fungal cultures were obtained from 37 (38.1%) eyes. Four (4.1%) eyes showed mixed growth. Conclusion: The most commonly isolated organism was *Pseudomonas aeruginosa*. The most common predisposing cause of infectious microbial keratitis was corneal trauma. Early stage of diagnosis and formulation of an uncompromising management protocol can prevent profound visual morbidity.

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Introduction

Corneal infection is the most common cause of profound ocular morbidity leading to blindness worldwide.[1] Corneal infection in children is difficult to diagnose and treat, as they are unwilling and sometimes unable to cooperate during active management. A delay in management may lead not only to blindness but also to secondary amblyopia, especially when severe monocorneal infection occurs in the early years of life. This is more significant and relevant to India, which holds one of the largest blind and at-risk-for-blindness population in the world.

The World Health Organization (WHO) has suggested that there are 1.5 million blind children worldwide and 70,000 children have active corneal involvement.[1] Though various regional studies on microbial keratitis are available, most of them include few children and emphasis is always on adults in these studies, as they constitute the majority of the population. Even treatment protocol is based on adult regimens. Hence this study was planned in Aravind Eye Hospital, Coimbatore, India to describe the spectrum of disease among children in a tropical climate, so that exclusive paediatric management protocols may be formulated.

Materials and Methods

A retrospective review of clinical and microbiological

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records of Aravind Eye Hospital, Coimbatore, India from February 1997 to January 2004 identified 97 culture-positive cases of non-viral microbial keratitis among children <15 years of age. The following inclusion criteria were used for the above cases: presence of corneal infiltration and isolation of microbial organism from the corneal scrapings. All the patients underwent slit lamp examination after their history and general physical examination findings were recorded and the dimensions of the infiltration were noted.

Using standard procedures, corneal scrapings were directly inoculated on blood agar, chocolate agar, potato dextrose agar (PDA), brain-heart infusion broth, thioglycollate broth and non-nutrient agar with *Escherichia coli* overlap for isolation of various bacterial, fungal and protozoan organisms. All were incubated at 37°C except PDA, which was incubated at 25°C. Cultures were confirmed positive whenever growth occurred confluently and in more than one media with consistent microscopic findings or repeat isolation of an organism. Children who were unable to cooperate during slit lamp examination were examined under short general anaesthesia.

All patients were treated as per hospital protocol. Patients with bacterial keratitis were treated with 0.3% ciprofloxacin and tobramycin drops, administered every 30 minutes for the first day and tapered according to clinical response. For mycotic keratitis 5% natamycin, 0.3% fluconozole drops were administered every 30 minutes for first the day and then tapered according to clinical response. There was no documentation of regular debridement of corneal ulcer for enhancing drug penetration. Oral ketoconazole was administered twice daily and liver function tests were done bi-weekly during treatment.

Results

A total number of 97 culture-positive keratitis cases (101 isolates) were reviewed from 1997 to 2003. All of them were <15 years of age and none of them had bilateral ocular involvement. Among these children, 49 (50.5%) cases were from the 10 to 15 age group, the rest were below 10 years of age and the majority of cases (11.3%) were ≥15 years of age (Fig. 1). Fifty-three (54.6%) of them were females and 44 (45.3%) were males. Most of them (69%) had trauma predisposing to corneal ulceration and in 29 (30%) cases, no predisposing factors were found (Table 1). Central corneal ulceration was found in 46 (47.4%) cases followed by paracentral ulceration in 31 (31.9%) and peripheral ulceration in 20 (20.6%) cases. Infiltrations were medium-sized in 56 (57.7%) cases. Large infiltrations were observed in 16 (16.4%) cases. Corneal ulcer was superficial in 39 (40.2%) cases and extended to the mid-stroma in 36 (37.1%) cases. Deep stromal involvement was

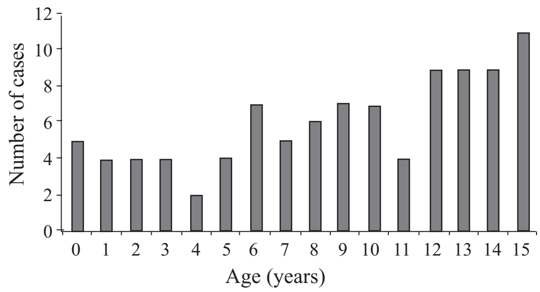

Fig. 1. Age distribution of microbial keratitis in children.

observed in 18 (18.5%) cases and endothelial plaque was noticed in 4 (4%) cases (Table 2). Sixty-six (68%) patients had previous treatment before they were referred to Aravind Eye Hospital. Most of them had been treated with antibiotics (32%) and 11 (11.3%) of them had been treated with antifungals. Surgical intervention was done in the form of therapeutic keratoplasty (TKP) for 4 (4.1%) cases, in which the outcome was not so favourable because of active infection associated with severe inflammation. Penetrating keratoplasty (PKP) was also done for 3 (3%) cases, which had a favourable outcome with medical management and amblyopia therapy. Tarsorraphy was done in 2 (2%) cases. Corneal scarring was observed in 85% of cases, glaucoma in 4 (4.1%) cases, anterior staphyloma in 4 (4.1%) cases and adherent leucoma in 2 (2%) cases. Visual acuity was recorded for 66 (68%) cases during follow-up. A visual acuity of 6/6 to 6/18 was recorded in 32 (32.9%) cases, 6/24 to 6/60 in 20 (20.6%) cases and <6/60 in 14 (14.4%) cases. Follow-up was not available for 20 (21.9%) cases (Table 2).

Table 1. Predisposing Risk Factors for Culture-positive Childhood Microbial Keratitis

Predisposing factors	Number of cases	%
Trauma	67	69.0
Organic		
Stick	23	23.7
Animal	11	11.3
Soil and dust	8	8.2
Stone	5	5.2
Plant leaf and thorn	4	4.1
Insect	4	4.1
Fingernail	3	3.0
Coconut shell	1	1.0
Non-organic		
Metal	6	6.1
Rubber ball	2	2.0
Miscellaneous		
Contact lens	1	1.0
Unknown	29	29.8
Total	97	100

Table 2. Clinical Features in Patients with Culture-positive Childhood Microbial Keratitis

Clinical picture	Number of cases	%
Depth		
Deep stroma	18	18.5
Endothelial plaque	4	4.1
Mid-stroma	36	37.1
Superficial stroma	39	40.2
Infiltration		
Small (<2 mm)	25	25.7
Medium (2-6 mm)	56	57.7
Large (6 mm)	16	16.4
Location		
Central	46	47.4
Paracentral	31	31.9
Peripheral	20	20.6
Visual acuity		
6/6-6/18	32	32.9
6/24-6/60	20	20.6
<6/60	14	14.4
Lost to follow-up	20	20.6
Uncooperative	11	11.3

Bacterial isolates were observed in 64 (65.9%) cases and fungal isolates were observed in 37 (38.1%) cases (Table 3). The commonest gram-positive bacterial cocci isolated were *Staphylococcus epidermidis* (16.4%), followed by *S. aureus* (7.2%) and *Streptococcus pneumoniae* (6.1%). Gram-negative bacilli were isolated in 26 (26.8%) cases. *Pseudomonas aeruginosa* accounted for 18.5% of cases. The other gram-negative bacilli were *Klebsiella* sp. (3%), *Moraxella* sp. (2%), *Enterobacter* sp. (2%) and *Serratia* sp. (1%). Fungi were isolated in 37 (38.1%) culture-positive keratitis cases. *Fusarium* sp. (17.5%) was the commonest fungi isolated, followed by *Aspergillus flavus* (8.2%). The other fungal isolates were *A. fumigatus* (3%), *Bipolaris* sp. (1%) and *Curvularia* sp. (1%). The rest were unidentified.

Table 3. Microbial Aetiology of Keratitis in Children

Organisms	Number of isolates (n = 101)*	%**
Total bacteria	64	63.3
Total gram-positive cocci	32	31.6
Staphylococcus epidermidis	16	15.8
S. aureus	7	6.9
Streptococcus pneumoniae	6	5.9
S. viridans	3	2.9
Total gram-positive bacilli	6	5.9
Corynebacterium species	4	3.9
Bacillus species	2	1.9
Total gram-negative bacilli	26	25.7
Pseudomonas aeruginosa	18	17.8
Klebsiella species	3	2.9
Moraxella species	2	1.9
Enterobacter species	2	1.9
Serratia species	1	1.0
Total fungus	37	36.6
Fusarium species	17	16.8
Aspergillus flavus	8	7.9
Unidentified hyaline fungus	4	3.9
Unidentified dematiaceous fungi	3	2.9
A. fumigatus	3	2.9
Bipolaris species	1	1.0
Curvularia species	1	1.0

* Mixed infections of fungus and bacteria (4 cases)
** Percentage of culture-positive cases

Discussion

The prevalence of various organisms responsible for microbial keratitis differs in different regions of world.[2-12] No age group is spared from microbial keratitis, which is why it is important to analyse the epidemiological parameter of childhood microbial keratitis to find out the differences between this clinical group and age-independent microbial keratitis. In this study, children of all ages were found to be affected by microbial keratitis. Cases have been reported in children from the age of 1 month onwards, by various authors[13-17] and Kunimoto et al[15] reported microbial keratitis in a 20-day-old child. No specific age group was found to be vulnerable for microbial keratitis. The incidence was found to increase with age except during 10 and 11 years, where a lower incidence of microbial keratitis was observed. Other authors have made similar observations.[15-18] However, no reason has been given for this, and studies involving larger populations of children will be required to derive a conclusion. In this study, microbial keratitis was found to occur more commonly in female than male children, in contrast to other studies, which have reported microbial keratitis occurring more often in boys than in girls. The most common predisposing factor being trauma related to agricultural works forms the basis for increased incidence of microbial keratitis in girls. Even now, in many villages, women are denied education and made to do domestic and agricultural work. For boys, injury caused by inanimate playing objects is generally a predisposing factor. Another important observation was the negligible impact of wearing contact lenses in the development of microbial keratitis among these children. Children who used contact lenses were well aware of how to maintain their lenses. This is in sharp contrast to western studies. Clinch et al[17] reported wearing of contact lenses as a predisposing factor in 25% of the cases.

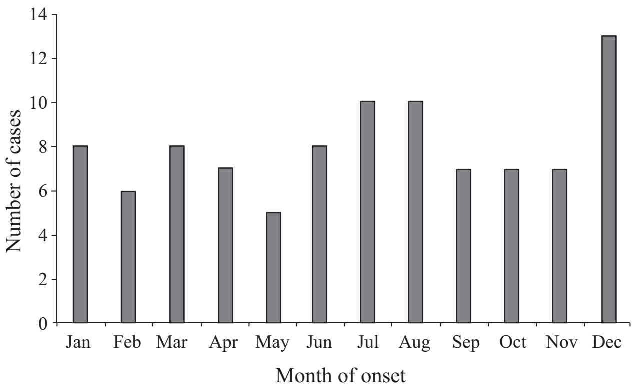

Fig. 2. Seasonal variation in childhood microbial keratitis.

Surprisingly, we have not seen any ocular disease predisposing to microbial keratitis in this study whereas others have described pre-existing ocular disease as a significant predisposing factor. Kunimoto et al[15] and Ormerod et al[18] in their studies reported vitamin A deficiency and acquired external ocular disease as predisposing factors for microbial keratitis. Though prior treatment with antibiotic and antifungals were reported by 60% of the patients, no surgical procedure or debridement was done on them before referring them to this institute. However, Kunimoto et al[15] reported prior penetrating keratoplasty as a predisposing factor. Cruz et al[16] and Clinch et al[17] have also reported similar findings. No seasonal variation was observed in this study except for increased microbial keratitis cases during winter (Fig. 2).

Bacterial keratitis accounted for more cases in this study compared to those conducted by Kunimoto et al[15] and Clinch et al.[17] Among the gram-positive cocci, *S. epidermidis* made up 15.4% of cases. Though the pathogenic potential of coagulase-negative *Staphylococci* and their role in ocular microbiology is being recognised in recent times,[19,20] their role in corneal ulceration is still debated as they can contaminate otherwise sterile corneal scrapings. *S. aureus* and *S. pneumoniae* are the other frequently isolated organisms in microbial keratitis among children. Kunimoto et al[15] reported a similar pattern of microbial isolation from keratitis cases among children in Hyderabad. But Cruz et al[16] had reported *S. aureus* as the commonest gram-positive cocci isolated, followed by *S. pneumoniae* and *S. epidermidis*. Ormerod et al[18] also reported *S. pneumoniae* and *S. aureus* as the most common organisms causing microbial keratitis in children.[18] The isolation of gram-positive bacilli from these cases were less when compared with the results of the study by Kunimoto et al,[15] but significantly more than the western series on microbial keratitis among children.[16,17] The other significant finding in this study was the increased isolation of *P. aeruginosa*, which was isolated in 18.5% of cases, making it the most common organism causing bacterial keratitis in children. Cruz et al[16] reported a similar finding, where *P. aeruginosa* caused 34.1% of bacterial keratitis among children included in the study. In other studies, gram-positive cocci were isolated in more numbers than *P. aeruginosa*. Clinch et al[17] attributed this to the regional prevalence of these micro-organisms. In this study, cases were not inpatient cases as included in the study by Cruz et al[16] and we can be reasonably sure that there was no bias involved to look for more virulent organisms. The other significant observation in this study was the role of fungi in microbial keratitis. In this study, fungi accounted for 38.1% of the cases, or 1/3 of the study group. In this group, *Fusarium* was a much more significant cause of keratitis than *Aspergillus*. Though others have reported *Aspergillus* being isolated more, the total number of fungal isolates were too small to derive any conclusion. According to King et al,[21] increased prevalence of any fungus in a region depends on the prevailing climate in that region. Though we observed no variation in age-dependent microbial keratitis between the prevalence of *Aspergillus* and *Fusarium*, in children *Fusarium* accounted for more keratitis cases. Other complications in the form of corneal scarring (85%), which was managed with refractive error correction and amblyopia therapy if the child was in the amblyogenic age group; glaucoma (4 cases), which was managed medically; anterior staphyloma (4 cases) and adherent leucoma (2 cases). Visual acuity was recorded only in 66 (68%) patients. In the remaining patients, 20 were lost to follow-up and 11 were uncooperative. Thirty-two patients had visual acuity between 6/6 and 6/18, 20 patients had visual acuity between 6/24 and 6/60 and 14 patients had visual acuity <6/60. Early diagnosis and appropriate treatment in the form of antimicrobial therapy and treatment of amblyopia were the probable reasons for the good visual acuity observed in these cases.

Microbial keratitis in children is different from adult keratitis. The predisposing factors, poor compliance during examination and complications with adverse impact on vision collectively make it different from age-independent keratitis. Fortunately, the microbiology of childhood keratitis does not differ markedly from keratitis in adults. It is hence imperative to diagnose them at an early stage and formulate an uncompromising management protocol, so as to prevent profound visual morbidity.

REFERENCES

1. Whitcher JP, Srinivasan M, Upadhyay MP. Corneal blindness: a global perspective. Bull World Health Organ 2001;79:214-21.
2. Kunimoto DY, Sharma S, Garg P, Gopinathan U, Miller D, Rao GN. Corneal ulceration in the elderly in Hyderabad, south India. Br J

Ophthalmol 2000;84:54-9.

3. Srinivasan M, Gonazales CA, George C, Cevallos V, Mascarenhas JM, Asokan B, et al. Epidemiology and aetiological diagnosis of corneal ulceration in Madurai, south India. Br J Ophthalmol 1997;81:965-71.
4. Liesegang TJ, Forster RK. Spectrum of microbial keratitis in South Florida. Am J Ophthalmol 1980;90:38-47.
5. Asbell P, Stenson S. Ulcerative keratitis. Survey of 30 years' laboratory experience. Arch Ophthalmol 1982;100:77-80.
6. Ormerod LD, Hertzmark E, Gomez DS, Stabiner RG, Schanzlin DJ, Smith RE. Epidemiology of microbial keratitis in southern California. A multivariate analysis. Ophthalmology 1987;94:1322-33.
7. Neumann M, Sjostrand J. Central microbial keratitis in a Swedish city population. A three-year prospective study in Gothenburg. Acta Ophthalmol 1993;71:160-4.
8. Williams G, McClellan K, Billson F. Suppurative keratitis in rural Bangladesh: the value of gram stain in planning management. Int Opthalmol 1991;15:131-5.
9. Wahl JC, Katz HR, Abrams DA. Infectious keratitis in Baltimore. Ann Ophthalmol 1991;23:234-7.
10. McClellan KA, Bernard PJ, Billson FA. Microbial investigations in keratitis at the Sydney Eye Hospital. Aust N Z J Ophthalmol 1989;17:413-6.
11. Ormerod LD. Causation and management of microbial keratitis in subtropical Africa. Ophthalmology 1987;94:1662-8.
12. Bharathi MJ, Ramakrishnan R, Vasu S, Meenakshi R, Shivkumar C, Palaniappan R. Epidemiology of bacterial keratitis in a referral centre in south India. Indian J Med Microbiol 2003;21:239-45.
13. Upadhyay MP, Karmacharya PC, Koirala S, Tuladhar NR, Bryan LE, Smolin G, et al. Epidemiologic characteristics, predisposing factors, and etiologic diagnosis of corneal ulceration in Nepal. Am J Ophthalmol 1991;111:92-9.
14. Musch DC, Sugar A, Meyer RF. Demographic and predisposing factors in corneal ulceration. Arch Ophthalmol 1983;101:1545-8.
15. Kunimoto DY, Sharma S, Reddy MK, Gopinathan U, Jyothi J, Miller D, et al. Microbial keratitis in children. Ophthalmology 1998;105:252-7.
16. Cruz OA, Sabir SM, Capo H, Alfonso EC. Microbial keratitis in childhood. Ophthalmology 1993;100:192-6.
17. Clinch TE, Palmon FE, Robinson MJ, Cohen EJ, Barron BA, Laibson PR. Microbial keratitis in children. Am J Ophthalmol 1994;117:65-71.
18. Ormerod LD, Murphree AL, Gomez DS, Schanzlin DJ, Smith RE. Microbial keratitis in children. Ophthalmology 1986;93:449-55.
19. Manikandan P, Bhaskar M, Revathy R, John RK, Narendran K, Narendran V. Speciation of coagulase negative Staphylococcus causing bacterial keratitis. Indian J Ophthalmol 2005;53:59-60.
20. Pinna A, Zanetti S, Sotgiu M, Sechi LA, Fadda G, Carta F. Identification and antibiotic susceptibility of coagulase negative staphylococci isolated in corneal/external infections. Br J Ophthalmol 1999;83:771-3.
21. King AG, Zuravaleff JJ, Yu VL. Fungal infections of the eye. In: Anaissie EJ, McGinnis MR, Pfaller MA, editors. Clinical Mycology. 1st ed. USA: Churchill Livingstone, Elsevier Science, 2003:566-80.