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Original Research Article

Retrospective Clinico-Pathological Associations of Fungal Keratitis in Series of Patients: An Observational Study

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Abstract

Aim: The aim of the present study was to analyse the causes, presentation, and clinico-pathological associations of fungal keratitis in a retrospective series of patients.

Material & methods: A retrospective analysis was conducted in the Department of Ophthalmology for the duration of 1 year. The outpatient department saw a total of 850 patients, of whom 100 cases (11.76%) of microbial keratitis and 10 cases (10%) of keratomycosis were observed. The study was performed in compliance with the Declaration of Helsinki. Patients with fungal keratitis were identified by reviewing medical records in between the duration of 1 year. Risk factors, clinical manifestation and outcome were recorded.

Results: The age incidence of keratomycosis in the current study showed that the age range of 51 to 60 years has the highest incidence (4), followed by 21 to 30 years (2), 41 to 50 years (1), 31 to 40 years (3), 11 to 20 years (0) and 0 to 10 years (0). In this study, there were 6 affected males (60%) and 4 affected females (40%). In the current study, agricultural labourers have the highest incidence of fungal ulcers [8], i.e. 80%, others (20%, or 2 cases) (Rickshaw drivers, students, and business people). In the present study, aspergillus fungi were found in 5 cases. The current investigation revealed that Fluconazole is effective against Candida Albicans and Natamycin 5% eye drops are effective against Aspergillus species. All of the straightforward fungal corneal ulcers, or those lacking hypopyon, responded well to natamycin eye drops.

Conclusion: Natamycin was the better option for the treatment of fungal keratitis. Filamentous fungi (Aspergillus species, fusarium, and curvularia) responded effectively to Natamycin 5% eye drops. Cases that responded well later left a corneal opacity.

Keywords: Keratomycosis, Fungal Culture, Corneal Scraping, Pathogenic Fungi.

Introduction

Infective keratitis is the inflammation of cornea due to infection. It can be caused by bacteria, viruses, fungi or parasites. Compared to other infective corneal ulcers, fungal corneal ulcers are most challenging to diagnose, treat and are more likely to get perforated and lead to irreversible changes in the cornea. [1] Mycotic keratitis is an infection caused by fungus that leads to inflammation and ulceration, usually following trauma. [2] Invasion of fungi into corneal layers followed by the subsequent tissue damage that follows is particularly devastating as it can disrupt the visual axis. [1]

The ocular surface is constantly exposed to a large number of infectious agents; however, only a few pathogens can cause a corneal infections. Filamentous fungi are frequent causes of fungal corneal ulcers in humans. More than 105 species of fungi, classified in 56 genera, have been identified as the aetiological agents of fungal keratitis. Fungal keratitis can cause a deep and severe corneal ulcer. It is caused by Aspergillus spp., Fusarium spp., Candida spp., Rhizopus, Mucor, and other fungi. [3] The highest prevalence of fungal keratitis is shown in hot and humid climate zones, where it may constitute 30–62% of all cases of keratitis. [4,5,6,7,8,9] Traditionally, fungal keratitis is a

suppurative lesion with a dry, raised ulcer with crenate, speculated or pseudohyphate borders, satellite lesions and hypopyon; associated with failure to respond to antibacterial treatment.

Both filamentous fungi and yeasts are implicated as causative agents of fungal keratitis. Symptoms are usually nonspecific, although possibly more prolonged in duration (5–10 days) than in bacterial corneal ulcers. [3,10] Early and accurate diagnosis allowing timely specific treatment remains the corner stone of vision saving management; however, appropriate empirical treatment needs to be started till the time a microbiological diagnosis is made. [11] Natamycin, voriconazole, and amphotericin B are topical medications used to treat fungal keratitis. [12] Fungal keratitis poses a significant diagnostic and therapeutic challenge, due to limited diagnostic options, microbial isolation, poor penetration of drug in deeper corneal layers, and the limited number of therapeutic agents available.

Hence the aim of study was to analyse the causes, presentation, and clinico-pathological associations of fungal keratitis in a retrospective series of patients.

Material & Methods

A retrospective analysis was conducted in the Department of Ophthalmology, Nalanda Medical College and Hospital, Patna, Bihar, India for the duration the duration of 1 year. The outpatient department saw a total of 850 patients, of whom 100 cases (11.76%) of microbial keratitis and 10 cases (10%) of keratomycosis were observed. The study was performed in compliance with the Declaration of Helsinki. Patients with fungal keratitis were identified by reviewing medical records in between the duration of 1 year. Risk factors, clinical manifestation and outcome were recorded.

Methodology

All subjects underwent a comprehensive assessment which included medical history, risk factor identification for fungal keratitis, slit lamp examination, confocal microscopy with Rostock Corneal Module on HRT3 (Heidelberg Engineering, Germany), and corneal scrapings (using 23G needle) or conjunctival smear for microbial testing. Depending on lesion location, limbal involvement and the presence of hypopon, a dedicated treatment algorithm was followed involving systemic and topical antifungal agents, subconjunctival, intracorneal, intracameral injections and cross-linking. Corneal graft was performed in eyes not responding to antifungal treatments and those with corneal perforation. The factors affecting the development of infection, visual acuity at baseline and at the end of treatment as well as treatment method selection were analysed.

Statistical Analysis

To assess the normality of distribution for the available data, the Shapiro-Wilk's test was used. Excel (Office 365). Normally distributed variables were reported as a mean and standard deviation (SD). The unpaired student's t-test was used for comparisons between patients with yeast versus filamentous keratitis. Visual acuity was presented as a logMAR scale, assuming a 95% confidence interval (95% CI). Due to the normal distribution of visual acuity on the logMAR scale, the Wilcoxon test was used for the analysis of BCVA values at baseline and at the end of treatment. Pearson's chi-squared test was used for comparing categorical variables between patients with yeast versus filamentous keratitis.

Results

Table 1: Incidence of corneal ulcers in our OPD

Census	No. of cases	Percentage (%)
OPD patients	850	100%
Corneal microbial keratitis	100	11.76%
Keratomycosis	10	10%

Table 2: Demographic details

Age group	No. of cases	Percentage (%)
0-10 years	0	0%
11-20 years	0	0%
21-30 years	2	20%
31-40 years	3	30%
41-50 years	1	10%
51-60 years	4	40%
Sex		
Male	6	60%
Female	4	40%
Occupation		
Agricultural Labourers	8	80%
Others	2	20%

The age incidence of keratomycosis in the current study showed that the age range of 51 to 60 years has the highest incidence (4), followed by 21 to 30 years (2), 41 to 50 years (1), 31 to 40 years (3), 11 to 20 years (0) and 0 to 10 years (0). In this study, there were 6 affected males (60%) and 4 affected females (40%). In the current study, agricultural labourers have the highest incidence of fungal ulcers [8], i.e. 80%, others (20%, or 2 cases) (Rickshaw drivers, students, and business people).

Table 3: Types of fungi isolated in the present series and effect of antifungal agents against various fungal species

Fungi isolated	No of cases	Percentage (%)
Aspergillus	5	50%
Fusarium	3	30%
Curvularia	1	20%
Candida	1	20%
S.NO	**Anti-Fungal agent**	**Targeted Species**
1	5% Natamycin	Aspergillus, Fusarium, Curvularia.
2	0.3% Fluconazole	Candida

In the present study, aspergillus fungi were found in 5 cases. The current investigation revealed that Fluconazole is effective against Candida Albicans and Natamycin 5% eye drops are effective against Aspergillus species. All of the straightforward fungal corneal ulcers, or those lacking hypopyon, responded well to natamycin eye drops.

Discussion

Corneal infection is a leading cause of ocular morbidity and blindness worldwide. Early diagnosis and treatment are important in preventing further complications such as hypopyon formation, endopthalamitis, or loss of vision. [13-15] Many micro-organisms can cause infectious corneal ulcers. Among them are bacteria, fungi, viruses, protozoa and Chlamydia. Mycotic keratitis is an infection caused by fungus that leads to inflammation and ulceration, usually following trauma or treatment for a bacterial infection with steroids or antibiotics. [16] The ocular surface is constantly exposed to a large number of infectious agents; however, only a few pathogens can cause a corneal infection. Several mechanisms play a major role in the protection of the surface of the eye from infectious agents Filamentous fungi are frequent causes of fungal corneal ulcers in humans. More than 105 species of fungi, classified in 56 genera, have been identified as the aetiological agents of fungal keratitis. Fungal keratitis can cause a deep and severe corneal ulcer. It is caused by Aspergillus spp., Fusarium spp., Candida spp., Rhizopus, Mucor, and other fungi. [17]

10% of the corneal ulcers in our study were mycotic, out of the total. Today's indiscriminate topical steroid use and increased antibiotic use as a result of agricultural eye injury during cultivation are to blame for the increased occurrence of fungal corneal ulcers. [18] Keratomycoses and systemic mycoses are becoming more common everywhere in the world. The crowded continents of Asia and Africa are seeing an increase in the occurrence of fungal keratitis. One of the main causes of vision loss and blindness, according to the World Health Organization, is corneal illness. [19] The age incidence of keratomycosis in the current study showed that the age range of 51 to 60 years has the highest incidence (4), followed by 21 to 30 years (2), 41 to 50 years (1), 31 to 40 years (3), 11 to 20 years (0) and 0 to 10 years (0). In this study, there were 6 affected males (60%) and 4 affected females (40%). In the current study, agricultural labourers have the highest incidence of fungal ulcers (8), i.e. 80%, others (20%, or 2 cases) (Rickshaw drivers, students, and business people). In the present study, aspergillus fungi were found in 5 cases. According to Badiee P, et al. economic and climatic factors are associated to the epidemiological variance and vast geographic distributions. Mycotic keratitis involving the cornea can cause significant visual damage or perhaps blindness and is challenging to treat. [20] Although, it is widespread throughout the planet, the tropics and subtropics are where it is most prevalent. [21]

Some of the fungi enter the corneal stroma. [22] In conditions like herpes keratitis, even minor damage to any vegetative material can quickly lead to a subsequent fungal infection. [23] Additionally, diabetes mellitus is the primary risk factor, and corticosteroid users are more susceptible to a fungal infection. [24] In this group of patients, it was thought that a special risk factor for a fungal infection of the cornea was trauma from plant material. Fungi that have been contaminated with them can enter the anterior chamber or the posterior section and damage the tissue using specialised mechanisms including proteolytic enzymes and mycotoxins. The current investigation revealed that Fluconazole is effective against Candida Albicans and Natamycin 5% eye drops are effective against Aspergillus species. All of the straightforward fungal corneal ulcers, or those lacking hypopyon, responded well to natamycin eye drops. When treating fungal keratitis, natamycin was a better option, particularly in the early stages of Fusarium infections. [25] The most effective medication for fungal keratitis involves topical antifungal drops like Natamycin and topical amphotericin B. [26]

The gold standard for the treatment of fungal keratitis has not yet been identified. [27] The most crucial agent in the treatment of fungal keratitis is thought to be the tetraene polyene 5% natamycin. Due to the easy and ready availability of natamycin, it has been chosen in this study. It works by forming a bond with ergosterol, a crucial element of the fungal cell wall and inhibiting microbial development. [28]

Conclusion

Natamycin was the better option for the treatment of fungal keratitis. Filamentous fungi (Aspergillus species, fusarium, and curvularia) responded effectively to Natamycin 5% eye drops. Cases that received good responses revealed corneal opacity. The medications utilised in the current RCTs differed from one another, and the small sample size made it difficult to determine which agent was more successful for treating fungal keratitis.

References

1. Ansari Z, Miller D, Galor A. Current thoughts in fungal keratitis: diagnosis and treatment. Curr Fungal Infect Rep 2013;7(3):209–18.
2. P Siva Reddy, OM Satyendran, M Satapathy, H Vijaya Kumar, P Ranga Reddy (1972) Mycotic keratitis. Invest Ophthal 20: 101-108
3. Thomas PA, Geraldine P. Infectious keratitis. CurrOpin Infect Dis 2007;20:129–41.
4. Chang HY, Chodosh J. Diagnostic and therapeutic considerations in fungal keratitis. Int Ophthalmol Clin. 2011; 51: 33–42.
5. Gopinathan U, Sharma S, Garg P, Rao GN. Review of epidemiological features, microbiological diagnosis and treatment outcome of microbial keratitis: experience of over a decade. Indian journal of ophthalmology. 2009 Jul;57(4):273.
6. Lam DS, Houang E, Fan DS, Lyon D, Seal D, Wong E. Incidence and risk factors for microbial keratitis in Hong Kong: comparison with Europe and North America. Eye. 2002 Sep;16(5):608-18.
7. Keay LJ, Gower EW, Iovieno A, Oechsler RA, Alfonso EC, Matoba A, Colby K, Tuli SS, Hammersmith K, Cavanagh D, Lee SM. Clinical and microbiological characteristics of fungal keratitis in the United States, 2001–2007: a multicenter study. Ophthalmology. 2011 May 1;118(5):920-6.
8. Leck AK, Thomas PA, Hagan M, Kaliamurthy J, Ackuaku E, John M, Newman MJ, Codjoe FS, Opintan JA, Kalavathy CM, Essuman V. Aetiology of suppurative corneal ulcers in Ghana and south India, and epidemiology of fungal keratitis. British Journal of Ophthalmology. 2002 Nov 1;86(11):1211-5.
9. Tilak R, Singh A, Maurya OP, Chandra A, Tilak V, Gulati AK. Mycotic keratitis in India: a five-year retrospective study. The Journal of Infection in Developing Countries. 2010 Mar 23;4(03):171-4.
10. Thomas PA (1994) Mycotic keratitis: an underestimated mycosis. J Med Vet Mycol 32: 235–254.
11. Sharma S. Diagnosis of infectious diseases of the eye. Eye 2012;26:177–84.
12. Medical treatments for fungus keratitis. Florcruz NV, Peczon I, Jr. 2008;CD004241 Cochrane Database Syst Rev.
13. Vemuganti GK, Garg P, Gopinathan U, Naduvilath TJ, John RK, Buddi R, Rao GN. Evaluation of agent and host factors in progression of mycotic keratitis: a histologic and microbiologic study of 167 corneal buttons. Ophthalmology. 2002 Aug 1;109(8): 1538-46.
14. Poria VC, Bharad VR, Dongre DS, Kulkarni MV (1985) Study of mycotic keratitis. Ind J Opththalmol 33: 229-231.
15. Sharma S, Srinivasan M, George C. The current status of Fusarium species in mycotic keratitis in South India. Indian J Med Microbiol. 1993;11(2):140-47.
16. P Siva Reddy, OM Satyendran, M Satapathy, H Vijaya Kumar, P Ranga Reddy (1972) Mycotic keratitis. Invest Ophthal 20: 101-108.
17. Thomas PA. Fungal infections of the cornea. Eye. 2003 Nov;17(8):852-62.
18. Srinivasan R, Kanungo R, Goyal JL. Spectrum of oculomycosis in South India. Acta Ophthalmol (Copenh). 1991 Dec;69(6):744-9.
19. Ibrahim MM, Vanini R, Ibrahim FM, Fioriti LS, Furlan EM, Provinzano LM, De Castro RS, Sousa SJ, Rocha EM. Epidemiologic aspects and clinical outcome of fungal keratitis in southeastern Brazil. Eur J Ophthalmol. 2009 May-Jun;19(3):355-61.
20. Lai J, Pandya V, McDonald R, Sutton G. Voriconazole and amphotericin B are administered intracamerally to treat the concomitant fungal iris nodule and fusarium keratitis. Clin Exp Opthalmol; 2014; 97(2): 181– 183;
21. Florcruz NV, Peczon I Jr. Medical interventions for fungal keratitis. Cochrane Database Syst Rev. 2008 Jan 23;(1): CD00 4241.
22. Basak SK, Basak S, Mohantha A, Diagnoses of suppurative keratitis in Gangetic West Bengal, East India, based on epidemiology and microbiology. Indian Journal of Ophthal mology. 2005; 53(1):17–22.
23. Bhartiya P, Daniell M, Constantinou M, Islam FMA, Taylor HR. Melbourne keratitis caused by fungi. Clin Experiment Ophthalmol. 2007; 35(2): 124–130.
24. Gopinathan U, Garg P, Fernandes M. A 10-year assessment at a referral eye care centre in

South India of the epidemiological characteristics and laboratory findings of fungal keratitis. Cornea. 2002; 21: 555-559.
25. Lalitha P, Vijaykumar R, Prajna NV, Fothergill AW. In vitro natamycin susceptibility of ocular isolates of Fusarium and Aspergillus species: comparison of commercially formulated natamycin eye drops to pharmaceutical-grade powder. J Clin Microbiol. 2008 Oct;46(10):3477- 8. doi: 10.1128/JCM.00610-08. Epub 2008 Aug 13. PMID: 18701666; PMCID: PMC2566114.
26. Vemuganti GK, Garg P, Gopinathan U, Naduvilath TJ, John RK, Buddi R, Rao GN. Evaluation of agent and host factors in progression of mycotic keratitis: A histologic and microbiologic study of 167 corneal buttons. Ophthalmology. 2002 Aug; 109(8): 1538-46. doi: 10.1016/ s0161-6420(02)01088-6. PMID: 12153808.
27. Arora R, Gupta D, Goyal J, Kaur R. Voriconazole versus natamycin as primary treatment in fungal corneal ulcers. Clin Exp Ophthalmol. 2011 Jul;39(5):434-40.
28. Rasool BK, Salmo HM. For the treatment of fungal keratitis, clotrimazolebeta-cyclodextrin eyedrops were created and clinically tested. AAPS Pharm Sci Tech; 2012; 13(3):883-889.