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Original Article

Ophthalmology Section

Clinical Characteristics and Outcome Predictors in Microbiologically Proven Mycotic Keratitis

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ABSTRACT

Introduction: Mycotic keratitis is a major cause of monocular blindness in tropical and subtropical climates. The difficulty to differentiate mycotic keratitis (fungal keratitis) from other causes, limited availability of antifungal agents, their poor ocular penetration and indolent course of the disease lead to significant ocular complications and vision loss.

Aim: To analyse the typical presenting clinical characteristics which predict the final visual outcome in microbiologically proven mycotic keratitis over two years in a tertiary eye care centre of South Kerala, India.

Materials and Methods: The present study was a retrospective study, conducted on 165 eyes of 165 patients treated for culture proven mycotic keratitis in the Regional Institute of Ophthalmology, South Kerala, India, from August 2018 to July 2020. Best Corrected Visual Acuity (BCVA), detailed history including history of injury and systemic diseases were noted. Treatment outcome was measured as BCVA at the end of three months. The association between age, sex, presenting features like size, depth, margins and colour of the keratitis and the final BCVA were assessed by linear regression analysis.

Results: Among 165 eyes, 90 (54.6%) had a history of injury in the affected eye. The majority of the keratitis had a size of 2-6 mm in 150 (90.9%), peripheral in location in 107 (64.8%) and involvement up to anterior 2/3rd of the stroma in 93 (56.4%). Of 165, 112 (67.9%) of the ulcers had a greyish white or pigmented colour, 118 (71.5%) had dry texture and 115 (69.7%) had feathery margins. Raised exudates were present in 99 (60%) patients, satellite lesions in 29 (17.6%), immune ring in 6 (3.6%), endothelial plaque in 20 (12.1%) and hypopyon in 40 (24.2%) at the time of diagnosis. The important predictors of final BCVA at three months were the larger size of the ulcer, increase in depth, central location, presence of hypopyon and poor vision at presentation.

Conclusion: Small superficial keratitis with good vision at presentation had a better final BCVA. Dry texture and feathery edges were seen more frequently in fungal keratitis. Large, deep, central keratitis and poor vision at presentation are associated with worse final visual outcome after treatment.

Keywords: Corneal, Fungus, Fusarium, Ulcer, Vision

INTRODUCTION

Microbial keratitis has a significant impact on the vision and quality of life of the affected people [1]. Keratitis caused by fungi is the major cause in tropical counties with a warm and humid climate. The epidemiological features of mycotic keratitis vary by geographical locations [2-4]. Mycotic keratitis or fungal keratitis is most prevalent in tropical and subtropical countries and accounts for 20-60% of all culture positive corneal infections in these regions [5]. Typical characteristics signs of fungal keratitis like feathery margins, dry texture, satellite lesion, immune ring and hypopyon help in the early diagnosis in cases with negative culture reports or in centres without microbiological facilities [6]. The difficulty to differentiate mycotic keratitis from bacterial and protozoal keratitis are- limited availability of antifungal agents and its ocular antifungal activity and indolent course of the disease which can lead to significant ocular complications and vision loss [7]. Information about the typical clinical features and risk factors for poor prognosis can help the ophthalmologist to start appropriate antifungal therapy early and reduce the possibility of vision threatening complications.

The present study was conducted to identify clinical features of mycotic keratitis and the factors associated with visual prognosis in subjects with mycotic keratitis seeking care at a tertiary care Institute in Regional Institute of Ophthalmology, South Kerala, India.

MATERIALS AND METHODS

This retrospective study was conducted on 165 eyes of 165 patients treated for culture proven mycotic keratitis in Regional Institute of Ophthalmology, South Kerala, from August 2018 to July 2020. The analysis of the study was done from April to June 2021. The study was approved by the Institutional Ethics Committee (IEC) (No:060/HEC/RIO/TVM/2021).

Inclusion and Exclusion criteria: Records of 225 culture proven mycotic keratitis were retrieved, among which 165 patients had the details of follow-up and were included in the study. Corneal ulcers that were attributed to causes other than fungi including mixed keratitis, culture negative keratitis or cases where culture was not done, and patients who did not have at least three months follow-up were excluded from the study.

Study Procedure

Demographic data, detailed history including history of injury, systemic diseases, treatment history and history of pre-existing ocular surface disease were retrieved from the medical records. The BCVA recorded at the time of presentation by Snellen's visual acuity chart was documented. Details of slit lamp biomicroscopy including size, depth and location of the infiltrate were noted from the records. The size of the infiltrate was recorded in millimetres. The mean of the measurement was estimated from its longest diameter and the maximum width perpendicular to this diameter. The depth of infiltrates was classified as less than 1/3rd, 1/3rd to 2/3rd, and more than 2/3rd of the involvement of stromal thickness.

Details of documented clinical examinations like colour, texture, location and margins of the ulcer were noted. The colour of the ulcer was recorded as white or pigmented and colour other than white or and pigmented, the texture was classified as dry or wet, margins were recorded as round or feathery. The location of the ulcer was considered as central if the whole or part of the infiltrate was covering the central 4 mm of the cornea and non central ulcers were considered

as peripheral. The presence or absence of satellite lesions, immune ring, endothelial plaque or hypopyon were also noted.

The results of the microbiological analysis were noted including the direct microscopy in 10% potassium hydroxide (KOH) mount for presence or absence of fungal hyphae. The type of fungus isolated from Sabouraud Dextrose Agar (SDA) was noted from the documents. Only culture proven fungal keratitis with the records of three months follow-up were included for analysis.

Details of treatment with one or more topical antifungal eye drops which included 5% natamycin, 0.15% amphotericin B and 1% voriconazole along with other supportive medications and systemic antifungals were noted. Surgical procedures for non healing keratitis or perforation like therapeutic keratoplasty or eviscerations and complications like perforation were taken from the records. The patients who underwent therapeutic keratoplasty, evisceration and perforation were considered as primary treatment failure as the ulcers progressed even after maximum possible medical therapy and ended up in surgical treatment.

The outcome of treatment was taken as final visual acuity after treatment. Final visual acuity was recorded using Snellen's Visual acuity chart at the end of three months, converted into LogMAR were classified into categories according to World Health Organisation (WHO) classification for blindness [8], for analysis. Patients who underwent evisceration were considered as NoPL (no perception of light) and the final visual acuity of patients who underwent therapeutic keratoplasty was recorded as the visual acuity just before the surgical procedure.

STATISTICAL ANALYSIS

Frequencies and proportions were used to calculate binary and categorical variables like the presence or absence of various clinical features like hypopyon and satellite lesions. Mean and standard deviation was used to summarise continuous variables like age and visual acuity. Comparison of visual acuity at different time intervals was carried out using the McNemar test. Linear regression analysis was done to assess the association between baseline clinical characteristics and the final visual acuity. For all statistical interpretations, $p<0.05$ was considered the threshold for statistical significance. Statistical analysis were performed by using a statistical software package Statistical Package for the Social Sciences (SPSS) version 20.0.

RESULTS

Males (68.5%) were affected more than that of females (31.5%). The age group ranged from 7 to 88 years, the commonest age group was 40-59 years (44.2%). Right eyes (56.4%) were more involved than left (43.6%). Only 8.5% of the patients were agricultural workers, 41.8% were manual labourers and the rest of the patients 49.7% were not belonging to these two groups. Most of the patients were from rural areas (75.2%) and (24.8%) from urban areas. About 54.6% sustained some form of injury or foreign body fall in the affected eye before the onset of disease. While 45.5% had no history of injury to the same eye. Only 16.4% (27) had an injury with the vegetative matter. Only 16 patients had a history of pre-existing ocular surface diseases like dry eyes and Meibomian gland disease. Thirty eight patients had a history of systemic diseases altering the immune system, among these most common was diabetes mellitus.

The majority of the patients received some form of topical medications prior to the presentation [Table/Fig-1]. Thirty three patients were on topical antifungal agents at the time of presentation, only 12 patients had no history of any topical or systemic medications.

Most of the keratitis 150 (90.9%) had a size between 2-6 mm, 1 (0.6%) patient had less than 2 mm size and 14 (8.5%) had more than 6 mm. Majority of the ulcers were peripheral in location 107 (64.8%), rest 58 (35.2%) were involving the whole or part of the central 3 mm of the cornea. About 22 (13.3%) patients had involvement up to anterior 1/3rd of the depth of the stroma, 93 (56.4%) had up to 2/3rd of the stroma and in 50 (30.3%) posterior 2/3rd also involved.

Drug history	Number	%
No medication	12	7.3
Topical antifungals and antibiotics	33	20
Topical antibiotics only	110	66.7
Topical and systemic antifungals	5	3
Topical steroids	5	3
Total	165	100

[Table/Fig-1]: Percentage distribution of sample according to the history of previous medications.

A 112 (67.9%) of the ulcers had a greyish white or pigmented colour those were typical of fungal keratitis and 118 (71.5%) had dry texture in the whole area of the ulcer or at the prominent leading edges. The margins were irregular or feathery at any part of the ulcer in 115 (69.7%) of the patients. Raised exudates were present in 99 (60%) patients, satellite lesions in 29 (17.6%), immune ring in 6 (3.6%), endothelial plaque in 20 (12.1%) and hypopyon in 40 (24.2%) at the time of diagnosis. These results indicate that the presence of greyish white colour, dry texture and feathery or serrated margins are more in favour of fungal keratitis.

Among 165 patients, in 141 (85.5%) fungal filaments were detected in the wet mount by KOH which indicates the importance of this test as it is a rapid method to detect fungal keratitis, otherwise one has to wait one or two weeks for the fungal growth in culture media [Table/Fig-2]. *Fusarium* was the most common fungi isolated from the keratitis, followed by *Aspergillus*.

Culture	Number	%
Fusarium	79	47.9
Aspergillus	74	44.9
Penicillium	6	3.6
Curvularia	2	1.2
Candida	1	0.6
Drechslera	1	0.6
Sporothrix	1	0.6
Alternaria	1	0.6
Total	165	100

[Table/Fig-2]: Percentage distribution of sample according to the type of fungus isolated.

About 58 (35.2%) patients were treated with both topical and systemic antifungal drugs and the rest of the patients 107 (64.8%) were treated with topical antifungals alone, along with other medications like topical and systemic antibiotics, cycloplegics and non steroidal anti-inflammatory drugs as and when indicated.

The BCVA were classified into categories according to WHO classification for blindness, for analysis. Median BCVA at presentation was 1.08 and at the end of three months, it was 0.80. The comparison between the initial BCVA and final BCVA after three months of treatment was assessed by the McNemar test [Table/Fig-3]. Vision improved after treatment in 103 (62.4%) patients, 23 (13.9%) maintained the same vision, 39 (23.7%) had a decrease in vision after treatment.

Patients who had not responded to medical therapy underwent therapeutic keratoplasty, evisceration or perforation within three months period were considered as primary medical treatment failure. Among 165 patients 15 (9.1%) patients underwent therapeutic keratoplasty, 7 (4.2%) patients underwent evisceration and 10 (6.1%) patients had perforation, healed by itself or by application of cyanoacrylate glue.

McNemar test	Initial visual acuity		Final visual acuity		p-value
	Count	%	Count	%	
0.00-0.50	23	13.9	79	47.9	<0.001
0.52-1.0	56	33.9	34	20.6	
1.02-1.30	32	19.4	8	4.8	
>1.32	54	32.8	44	26.7	

[Table/Fig-3]: Comparison of initial and final BCVA (Log MAR) and categories of visual impairment according to world health organisation criteria by McNemar test.

Poor vision at presentation, larger size, greater in depth, central location of the ulcer, presence of hypopyon, feathery edges and dry texture had more chance of poor final visual outcome and primary treatment failure (p-value <0.05) compared to those who do not have those features, as assessed by Chi-square test [Table/Fig-4]. The initial vision at presentation is significantly associated with the final visual outcome and treatment failure. Patients with good vision at presentation had a better chance for healing of the ulcer and good final BCVA.

Linear regression analysis [Table/Fig-5] revealed important predictors causing poor outcome in terms of visual acuity were the larger size of the ulcer, increase in depth, central location and presence of hypopyon. In patients with those clinical signs had a poor final BCVA at the end of three months.

Variables	Final acuity				p-value	Total	Primary treatment failure (n=32)	p-value*
	0.00-0.50	0.52-1.0	1.02-1.30	>1.32				
Age group (in years)								
<50	50 (54.9)	18 (19.8)	2 (2.2)	21 (23.1)	0.107	91 (100.0)	15 (16.5)	0.197
≥50	29 (39.2)	16 (21.6)	6 (8.1)	23 (31.1)		74 (100.0)	17 (23.0)	
Sex								
Male	59 (52.2)	26 (23.1)	4 (3.5)	24 (21.2)	0.050	113 (100.0)	16 (14.2)	0.012
Female	20 (38.5)	8 (15.4)	4 (7.7)	20 (38.4)		52 (100.0)	16 (30.8)	
Initial visual acuity								
0.00-0.50	20 (87.0)	3 (13.0)	0	0	<0.001	23 (100.0)	0 (0.0)	<0.001
0.52-1.0	40 (71.4)	12 (21.4)	1 (1.8)	3 (5.4)		56 (100.0)	1 (1.8)	
1.02-1.30	14 (43.8)	12 (37.5)	1 (3.1)	5 (15.6)		32 (100.0)	0 (0.0)	
>1.32	5 (9.2)	7 (13.0)	6 (11.1)	36 (66.7)		54 (100.0)	31 (57.4)	
History of trauma								
Yes	48 (53.3)	13 (14.4)	4 (4.5)	25 (27.8)	0.169	90 (100.0)	18 (20.0)	0.494
No	31 (41.3)	21 (28.0)	4 (5.3)	19 (25.4)		75 (100.0)	14 (18.7)	
Trauma with vegetative matter								
Yes	12 (44.4)	4 (14.9)	1 (3.7)	10 (37.0)	0.574	27 (100.0)	7 (25.9)	0.424
No	67 (48.6)	30 (21.7)	7 (5.1)	34 (24.6)		138 (100.0)	25 (18.1)	
Occupation as agricultural work								
Yes	5 (35.7)	4 (28.6)	0	5 (35.7)	0.541	14 (100.0)	4 (28.6)	0.276
No	74 (49.0)	30 (19.9)	8 (5.3)	39 (25.8)		151 (100.0)	28 (18.5)	
Size of the ulcer at presentation (mm)								
<2	1 (100.0)	0	0	0	<0.001	1 (100.0)	0	<0.001
2-6	78 (52.0)	33 (22.0)	8 (5.3)	31 (20.7)		150 (100.0)	20 (13.3)	
>6	0	1 (7.1)	0	13 (92.9)		14 (100.0)	12 (85.7)	
Depth of the ulcer at presentation								
<1/3	16 (72.8)	3 (13.6)	0	3 (13.6)	<0.001	22 (100.0)	2 (9.1)	<0.001
1/3-2/3	55 (59.0)	19 (20.4)	3 (3.2)	16 (17.2)		93 (100.0)	9 (9.7)	
>2/3	8 (16.0)	12 (24.0)	5 (10.0)	25 (50.0)		50 (100.0)	21 (42.0)	
Location of the ulcer								
Central	3 (5.2)	7 (12.1)	6 (10.3)	42 (72.4)	<0.001	58 (100.0)	31 (53.4)	<0.001
Peripheral	76 (71.0)	27 (25.2)	2 (1.9)	2 (1.9)		107 (100.0)	1 (0.9)	
Texture								
Dry	68 (57.6)	28 (23.7)	4 (3.4)	18 (15.3)	<0.001	118 (100.0)	11 (9.3)	<0.001
Wet	11 (23.4)	6 (12.8)	4 (8.5)	26 (55.3)		47 (100.0)	21 (44.7)	
Feathery edges								
Present	65 (56.5)	27 (23.5)	4 (3.5)	19 (16.5)	<0.001	115 (100.0)	13 (11.3)	<0.001
Absent	14 (28.0)	7 (14.0)	4 (8.0)	25 (50.0)		50 (100.0)	19 (38.0)	
Endothelial plaque								
Present	4 (20.0)	7 (35.0)	1 (5.0)	8 (40.0)	0.058	20 (100.0)	5 (25.0)	0.339
Absent	75 (51.7)	27 (18.6)	7 (4.8)	36 (24.9)		145 (100.0)	27 (18.6)	
Hypopyon								
Present	5 (12.5)	5 (12.5)	3 (7.5)	27 (67.5)	<0.001	40 (100.0)	25 (62.5)	<0.001
Absent	74 (59.2)	29 (23.2)	5 (4.0)	17 (13.6)		125 (100.0)	7 (5.6)	

Satellite lesions								
Present	16 (55.2)	8 (27.6)	0	5 (17.2)	0.251	29 (100.0)	3 (10.3)	0.134
Absent	63 (46.3)	26 (19.1)	8 (5.9)	39 (28.7)		136 (100.0)	29 (21.3)	

[Table/Fig-4]: Analysis of variables which affect final BCVA (LogMAR) and primary treatment failure by chi-square test.
*A p-value <0.05 was considered to be statistically significant

Characteristics	Coefficient (95% CI)	p-value
Age	1.662 (-0.001-0.010)	0.099
Sex	0.743 (-0.112-0.248)	0.459
Size of the ulcer	4.156 (0.076-0.213)	<0.001
Location	-8.401 (-1.175-0.728)	<0.001
Depth of the ulcer	3.095 (0.098-0.444)	0.002
Raised exudates	-0.143 (-0.182-0.157)	0.887
Texture	1.263 (-0.077-0.350)	0.209
Satellite lesions	-1.632 (-0.388-0.037)	0.105
Hypopyon	-3.593 (-0.636-0.185	<0.001
Injury with vegetative matter	0.288 (-0.187-0.251)	0.774

[Table/Fig-5]: Linear Regression analysis results of the primary outcome variable (BCVA in LogMAR) with presenting clinical characteristics.

DISCUSSION

Climate and the natural environment plays an important role in the development of fungal keratitis [9,10]. The study was done in a region of tropical climate where the fungus is an important cause of keratitis. Present study showed a male preponderance and middle age, related to more outdoor activities or occupation of these age group, similar to other study [11].

There are reports of the association between ocular trauma with vegetative matter [12,13] and fungal keratitis in which epithelial defects act as a route of entry of pathogenic fungi causing keratitis. In present study, trauma due to vegetative matter was less (16.4) probably the agricultural work was not a predominated occupation in the area where the study was conducted. Most of the patients were from rural areas and the injuries could be related to agricultural and other occupations or domestic injuries. This indicates the need for early treatment of corneal injuries follow-up of such patients for the development of keratitis and the timely diagnosis, if the causative organism is fungi.

The risk factors and microbiological profile show variations from region to region which mostly depends on climate and environment [14-19]. In this study, the most common risk factor was ocular trauma 54.6%, pre-existing ocular risk factors were dry eye and meibomian gland disease which were less (9.7%) in number. The most common systemic condition present in these patients was diabetes mellitus.

Only 12 (7.3%) patients did not use any topical medications before the presentation and 23% of the patients were on topical antifungals. This indicates the need for awareness about the possible correct clinical diagnosis of fungal keratitis from referring hospitals and initiation of antifungal therapy based on only clinical signs, where microbiological investigations are not possible. Only five patients were using topical steroids before the presentation which was less than the previous studies [20]. This indicates increased awareness among people about eye diseases and complications of self-medications. No patient was microbiologically diagnosed with fungal keratitis before the presentation. None of the patients was using any form of traditional eye medications even though it was a common practice earlier.

According to Dalmon C et al., the cornea specialists were able to correctly differentiate fungal keratitis from bacterial keratitis in only 66% of the time [21]. The clinical diagnosis of fungal keratitis is difficult as it may mimic bacterial, acanthamoebic and other causes of keratitis at presentation, but some clinical characteristics may help in the diagnosis [22,23]. In this study, those clinical characteristics previously reported as fungal, were studied in detail. Authors observed the leading or progressive part of the ulcer along with its centre for more accurate results. The central part of the ulcer may not show these typical characteristics features because of superadded infection or due to already established necrosis of the stroma.

In the present study, most of the ulcers were less than 6 mm in size, not involving the posterior one third of the corneal stroma and peripheral in location. This type of keratitis has a good final visual outcome because after healing the scar may not affect the central 3 mm of the cornea. Irregular or feathery margins (69.7%), raised exudates (60%), greyish white or pigmented colour (67.9%) and dry texture (71.5%) were observed more commonly among these patients. The presence of all these clinical features in an ulcer indicates the possibility of fungal keratitis. These clinical characteristics help the ophthalmologists to diagnose fungus as the cause when the microbiological diagnosis is not possible or in patients who are not cooperative to take a smear, especially small children. The presence of satellite lesions, endothelial plaque and hypopyon were less in present study, than previously those were reported more in fungal keratitis [24-26]. It is not always possible to diagnose fungal keratitis with characteristic clinical features like white, dry, feathery margins and hypopyon because bacterial and acanthamoebic keratitis can also present with these clinical signs. Microbiological investigations are required to confirm the diagnosis.

In centres, where a microbiological facility is available KOH mount is a rapid method of confirmation. Among 165 patients, in 85.5% of all culture positive cases revealed fungal hyphae in wet mount. Antifungal treatment could be started at presentation without any delay as the fungal culture may need one or two weeks to show a positive result. *Fusarium* and *Aspergillus* were the most common organisms isolated similar to another south Indian report [27].

Even small ulcers can progress and cause loss of vision due to lack of response to medical treatment [28-30]. Some large ulcers show a good response to treatment but leave a scar of large size after the reparative process which decreases the final visual outcome.

A 19.4%(32) of patients in the treatment failure group underwent therapeutic keratoplasty, perforation or evisceration. Among this 4.2%(7) patients ended up in evisceration and lost the affected eye. In this study, the rate of primary treatment failure was significantly less than those reported previously for fungal keratitis [31]. Majority of the lesions in present study had a size of less than 6 mm and had a good response to medical treatment because of early presentation. The reason for this can be an increase in awareness about eye diseases and the availability of eye care facilities.

In majority of the patients (62.4%) vision improved after treatment, but in 13.9% maintained the same vision and in 23.6% patients vision decreased despite maximum medical therapy. Even if the ulcer heals well, in some of them it leaves a central scar which leads to visual impairment. A 4.8% patients had severe visual impairment and 26.7% had blindness according to WHO classification of visual impairment at the end of three months which indicate the need for very early diagnosis and aggressive treatment for fungal keratitis. Most of these patients may require optical keratoplasty later and need long term follow-up and treatment, again it will be a financial burden for the patient.

In the present study, authors assessed the association between various presenting clinical features and the final visual outcome. Poor vision at presentation, larger size, greater depth, central location of the ulcer, presence of hypopyon, feathery edges and dry texture showed an association with a worse final visual outcome and treatment failure.

Linear regression analysis revealed the size, depth and location of the keratitis and the presence of hypopyon were the major factors predicting the final visual acuity at three months which was comparable with a previous report [32]. According to the study by Cho CH and Lee SB et al., hypopyon was the only significant risk factor for evisceration or enucleation [33]. In contrast to previous reports [34-36] age and gender differences were not significant predictors, as found in the present study.

Ulcers with large size and depth progress to perforate and fail to respond to medical treatment or may cause a greater reduction in visual acuity due to large scars after healing. The central location of the ulcer causes a greater reduction in visual acuity after treatment even if the ulcer heals well.

Limitation(s)

The time lag between the onset of symptoms and presentation at the hospital was not studied here and could not be assessed how early they had taken the treatment. The type of fungus isolated and the difference in clinical characteristics among them were also not studied here. Further investigations are needed to find out the causes of non healing and progression of keratitis in some cases even after maximum possible medical therapy.

CONCLUSION(S)

Patients with a history of ocular injury need frequent follow-up, to assess the development of keratitis. In some cases of mycotic keratitis, the course of the disease cannot be changed with topical medications and can progress even after maximum possible medical therapy and may end up in complications. The knowledge about the characteristic clinical features helps in the early diagnosis of mycotic keratitis. Large, deep, central keratitis and patients with poor vision at presentation need aggressive therapy from the early stage to prevent the progression of keratitis and the development of complications causing visual impairment.

REFERENCES

[1] Whitcher JP, Srinivasan M. Corneal ulceration in the developing world- A silent epidemic. Br J Ophthalmol. 1997;81:622-23.
[2] Varaprasathan G, Miller K, Lietman T, Whitcher JP, Cevallos V, Okumoto M, et al. Trends in the etiology of infectious corneal ulcers at the F. I. Proctor Foundation. Cornea. 2004;23(4):360.
[3] Tanure MA, Cohen EJ, Sudesh S, Rapuano CJ, Laibson PR. Spectrum of fungal keratitis at Wills Eye Hospital, Philadelphia, Pennsylvania. Cornea. 2000;19(3):307-12.
[4] Leck AK, Thomas PA, Hagan M, Kaliamurthy J, Ackuaku E, John M, et al. Aetiology of suppurative corneal ulcers in Ghana and south India, and epidemiology of fungal keratitis. Br J Ophthalmol. 2002;86(11):1211-15.
[5] Bongomin F, Gago S, Oladele RO, Denning DW. Global and multinational prevalence of fungal diseases-estimate precision. J Fungi. 2017;3:57.
[6] Thomas P A, Leck,A K, Myatt M, Characteristic clinical features as an aid to the diagnosis of suppurative keratitis caused by filamentous fungi. Br J Ophthalmol. 2005;89(12):1554-58.
[7] Maharana PK, Sharma N, Nagpal R, Jhanji V, Das S, Vajpayee RB. Recent advances in diagnosis and management of mycotic keratitis. Indian J Ophthalmol. 2016;64(5):346-57.
[8] Word Health Organization. Universal eye health: A global action plan 2014-2019. Spain: WHO Press 2013: Pp. 7.
[9] Gonzales CA, Srinivasan M, Whitcher JP, Smolin G. Incidence of corneal ulceration in Madurai district, South India. Ophthalmic Epidemiol. 1996;3(3):159-66.
[10] Bharathi MJ, Ramakrishnan R, Vasu S, Meenakshi R, Palaniappan R. Epidemiological characteristics and laboratory diagnosis of fungal keratitis. A three-year study. Indian J Ophthalmol. 2003;51(4):315-21.
[11] Chowdhary A, Singh K. Spectrum of fungal keratitis in North India. Cornea. 2005;24(1):08-15.
[12] Bharathi MJ, Ramakrishnan R, Meenakshi R, Padmavathy S, Shivakumar C, Srinivasan M, et al. Microbial keratitis in South India: Influence of risk factors, climate, and geographical variation. Ophthalmic Epidemiol. 2007;14(2):61-69.
[13] Srinivasan M, Gonzales 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(11):965-71.
[14] 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 J Ophthalmol. 2009;57(4):273-79.
[15] Garg P, Gopinathan U, Choudhary K, Rao GN. Keratomycosis: Clinical and microbiologic experience with dematiaceous fungi. Ophthalmology. 2000;107(3):574-80.
[16] Pérez-Balbuena AL, Vanzzini-Rosano V, Valadéz-Virgen Jde J, Campos-Möller X. Fusarium keratitis in Mexico. Cornea. 2009;28(6):626-30.
[17] Srinivasan M. Fungal keratitis. Curr Opin Ophthalmol. 2004;15(4):321-27.
[18] Jurkunas U, Behlau I, Colby K. Fungal keratitis: Changing pathogens and risk factors. Cornea. 2009;28(6):638-43.
[19] Laspina F, Samudio M, Cibils D, Ta CN, Fariña N, Sanabria R, et al. Epidemiological characteristics of microbiological results on patients with infectious corneal ulcers: A 13-year survey in Paraguay. Graefes Arch Clin Exp Ophthalmol. 2004;242(3):204-09.
[20] Lalitha P, Risk factors for treatment outcome in fungal keratitis. Ophthalmology. 2006. PMID: 16581414.
[21] Dalmon C, Porco TC, Lietman TM, Prajna NV, Prajna L, Das MR, et al. The clinical differentiation of bacterial and fungal keratitis: A photographic survey. Invest Ophthalmol Vis Sci. 2012;53(4):1787-91.
[22] Norina TJ, Raihan S, Bakiah S, Ezanee M, Liza-Sharmini AT, Wan Hazzabah WH, et al. Microbial keratitis: Aetiological diagnosis and clinical features of patients admitted to Hospital Universiti Sains Malaysia. Singapore Med J. 2008;49:67-71.
[23] Bourcier T, Thomas F, Borderie V, Chaumeil C, Laroche L. Bacterial keratitis: Predisposing factors, clinical and microbiological review of 300 cases. Br J Ophthalmol. 2003;87:834-38.
[24] Thomas PA, Kaliamurthy J. Mycotic keratitis: Epidemiology, diagnosis and management. Clin Microbiol Infect. 2013;19(3):210-20.
[25] Chidambaram JD, Venkatesh Prajna N, Srikanthi P, Lanjewar S, Shah M, Elakkiya S, et al. Epidemiology, risk factors, and clinical outcomes in severe microbial keratitis in South India. Ophthalmic Epidemiol. 2018;25(4):297-305.
[26] Alfonso EC, Miller D, Cantu-Dibildox J, O'brien TP, Schein OD. Fungal keratitis associated with non therapeutic soft contact lenses. Am J Ophthalmol. 2006;142(1):154-55.
[27] Prajna NV. Lalitha P. Srinivasan M. Fungal keratitis: The Aravind experience. Indian J Ophthalmol. 2017;65(10):912. 1114-17.
[28] Gudmundsson OG, Ormerod LD, Kenyon KR, Glynn RJ, Baker AS, Haaf J, et al. Factors influencing predilection and outcome in bacterial keratitis. Cornea. 1989;8(2):115-21.
[29] McLeod SD, LaBree LD, Tayyanipour R, Flowers CW, Lee PP, McDonnell PJ, et al. The importance of initial management in the treatment of severe infectious corneal ulcers. Ophthalmology. 1995;102(12):1943-48.
[30] Poole TR, Hunter DL, Maliwa EM, Ramsay AR. Aetiology of microbial keratitis in northern Tanzania. Br J Ophthalmol. 2002;86(8):941-42.
[31] Ibrahim YW, Boase DL, Cree IA. Epidemiological characteristics, predisposing factors and microbiological profiles of infectious corneal ulcers: The Portsmouth corneal ulcer study. Br J Ophthalmol. 2009;93:1319-24.
[32] Miedziak A, Miller M, Rapuano C, Laibson P, Cohen E. Risk factors in microbial keratitis leading to penetrating keratoplasty. Ophthalmology. 1999;106:1166-71.
[33] Cho CH, Lee SB. Clinical analysis of microbiologically proven fungal keratitis according to prior topical steroid use: A retrospective study in South Korea. BMC Ophthalmol. 2019;19:207.
[34] Prajna NV, Krishnan T, Mascarenhas J, Srinivasan M, Oldenburg CE, Toutain-Kidd CM, et al. Mycotic ulcer treatment trial group. Predictors of outcome in fungal keratitis. Eye. 2012;26:1226-31.
[35] Das S, Sharma S, Mahapatra S, Sahu SK. Fusarium keratitis at a tertiary eye care centre in India. Int Ophthalmol. 2015;35(3):387-93.
[36] Rautaraya B, Sharma S, Ali MH, Kar S, Das S, Sahu SK. A 3 (1/2)-year study of bacterial keratitis from Odisha, India. Asia Pac J Ophthalmol (Phila). 2014;3:146-50.

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