Original Article

Epidemiologic and Microbiologic profile of Fungal keratitis in Rohilkhand region

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ABSTRACT

Purpose: To report epidemiologic and microbiologic profile of 106 culture positive cases of fungal keratitis at a teritary centre in Rohilkhand region of Western Uttar Pradesh.

Methods: Clinical and microbiological records of 106 culture positive cases of fungal keratitis reported over a period of 2 years between June 2012 and May 2014 were analyzed. Review of demographic features , clinical course , risk factors and laboratory findings were done retrospectively.

Results: Of the 106 patients, 68 (64%) were males (male:female ratio 1.79:1), 77 (72.6%) were in age group between 20 and 45 (mean age 37.6), 83(78%) were rural based agriculture workers. Ocular trauma was reported in 83 (78.3%) cases. Time of reporting following advent of symptoms ranged from 1.3 to 6.8 weeks (avg. 2.4 weeks). 89 Patients (83.96%) were already on multidrug therapy including steroids and antibiotics at the time of presentation.

Microbiologically, Fusarium species were the predominant isolates in 58 cases (54.7%) followed by Aspergillus in 28(26.4%), Candida in 12(11.3%), 02 cases of Alternaria and Curvularia and solitary cases of Nocardia & Scedosporium .02 strains remained unidentified. Mode of injury had a causal relationship with etiologic agent ; Fusarium with vegetative injuries 36 (62.06%) , Aspergillus with exposure to soil/dust, 17 (60.71%)and candida with prolonged antibiotic and steroid use in 8 (66.6%) eyes. Coexisting ocular surface disorders & systemic diseases were present in 9 (8.4%) & 7 (6.6%) of the fungal keratitis cases , respectively.

Conclusion: Epidemiologic and Microbiologic profile of fungal keratitis has revealed variation inter regionally even in subtropical zone. The study aims at providing epidemiologic and microbiologic data on fungal keratitis in Rohilkhand region of Northern India.

Key Words: Fungal Keratitis, Epidemiology, Etiology

INTRODUCTION

Fungal Keratitis (Keratomycosis or Mycotic Keratitis) refers to a suppurative usually ulcerative mycotic infection of cornea.[2]Accounting for nearly 50% of all cases of suppurative keratitis in the tropical and it poses a major public health challenge. The severity of these infections , late detection, limited treatment options together with a confounding etiological spectrum results in an invariable poor prognosis.

The first reported case of fungal keratitis was by'Leber' in 1879. [10] Since then nearly 105 fungal species classed in 56 genera have been reported to cause keratitis and Oculomycosis.[12] Two basic forms have been recognized due to Filamentous fungi (especially Fusarium and Aspergillus) which commonly occur in tropical and subtropical zone , and due to yeast like and related fungi (particularly Candida) which are the predominant isolates in temperate climates.[25]

Ocular trauma is the key predisposing factor for filamentous fungal infections.[11,13] The usual sufferers are healthy young males engaged in agricultural or outdoor activities. Traumatizing agents of plant or animal origin as even dust particles either directly implant fungal conidia in the corneal stroma or abrade corneal epithelium permitting invasion of exogenous fungi.[25] Environmental factors like temperature, humidity, wind, influence occurrence of fungal keratitis as

also the type and frequency of fungal isolate. Less frequent predisposing factors include immunological incompetence , prior administration of steroids or antibiotics , Ocular surface disorders , systemic diseases like diabetes and use of hydrophilic contact lenses.[11,24] The latter factors are particularly important in keratitis due to Candida albicans and related fungi.

Although specific clinical features are documented for corneal infections due to bacterial, fungal or parasitic agents, accurate diagnosis is commonly elusive due to prolonged use of wrongly administered antimicrobials, steroids or propensity for mixed infections. Delay in accurate diagnosis forestalls a favorable outcome in majority of patients. Information about epidemiological and etiological features of a large series of fungal keratitis from representative geographical region is limited.

This review analyzes epidemiological record and laboratory findings of 106 culture proven cases of fungal keratitis diagnosed at a tertiary care hospital of Rohilkhand region in Northern India over a 2 year period (june2012 to may2014).

MATERIALS AND METHODS

All cases of fungal keratitis identified from the clinical & microbiological records at Rohilkhand Medical College & Hospital between 01 June 2012 and May 31 2014 were retrospectively analyzed. Medical records of patients were reviewed for age, sex, occupational background, mode and month of onset of infection, predisposing risk factors, prior medications, associated systemic illness , clinical course and duration of active disease.

A uniform protocol for laboratory diagnosis comprised of subjecting corneal scrapings taken from the base and advancing edge of the ulcer using a kimura spatula, to Gram stain and 10% potassium hydroxide wet mount (Figures-7). Scraped material was further inoculated on Blood Agar, McConkey's Agar and Sabouraud's Dextrose Agar (SDA) supplemented with 50microgram/ml gentamicin. SDA was kept at ambient temperature and other media were incubated at 370°C. Fungal cultures were followed for 2 weeks before a negative result was declared. Patients with a negative culture from initial specimen or insufficient inoculums underwent repeat scraping/corneal biopsy at a later date if the disease progression so warranted.

A positive culture was defined by (i) a positive smear with fungal elements substantiated by a confirmatory growth of fungus in a culture media (ii) growth of the same fungus on two or more culture media (iii) growth of fungus on at least one medium followed with growth of the same fungus on at least one medium at a subsequent date (Figures-5, 6).

RESULTS

The study included 106 eyes (106 patients). Of these 68(64%) were males and 38(36%) females; Male : female ratio was 1.79:1. Age of patients ranged from 14 to 76 years . Mean Age was 37.6 years. Majority of patients 77(72.6%) were in the productive age group between 20 and 45 years. Occupationally, 83(78%) patients were rural based, agricultural workers of low socio-economic group.

The chief predisposing factor was Trauma, observed in 83(78.3%)patients particularly caused by vegetative matter 42(39.6%), (Table-1). Of particular note was the inadvertent injury caused by sugarcane leaf(12 cases).

The time duration between advent of symptoms / injury and the reporting at our centre varied substantially from 1.3 to 7.4 weeks. Mean reporting time was 2.4 weeks. Majority of patients, i.e. 89 cases (83.96%) were under an empirical multidrug treatment that included broad spectrum antibiotics, steroids, antivirals and unconventional domestic drugs at the time of reporting.

The filamentous fungi dominated the etiological spectrum 92 cases (86.79%)as shown in Table-2.

Of these the majority comprised of Fusarium species, 58 cases (54.72%) followed by Aspergillus, 28 cases (26.41%) and two cases each of Alternaria and Curvularia. Candida infections accounted for 12 cases (11.32%), 9 cases had a history of ocular surface disorders, 7 had coexisting systemic disease including 4 diabetics (Table-1). 13 were on pre-infection long term topical antibiotics and steroids therapy.

Mode of injury had an interesting etiological relationship with vegetative injuries accounting for 36(62.06%) of total 58 Fusarium infections, Soil and dust exposure eyes leading to 17 (60.71%) of 28 Aspergillus infections and long term steroids use in 8 (66.6%) of 12 Candida infections.

Seasonal variation as shown in Figure-1 was more marked with Aspergillus infections, with the majority i.e. 22 cases (78.57%) reported in the warm and humid months of June to September. Infections due to Fusarium and Candida were uniformily distributed throughout the year. This was a statistically significant variation as per chi-square test ($p<0.005$). Diagnostically, the simple test of KOH wet mount was most effective in diagnosing fungal keratitis in the majority, 96(90.56%).

DISCUSSION

Incidence of fungal keratitis may have increased in recent decades as a result of improved clinical awareness, better diagnostic techniques an increased use of topical broad spectrum antibiotics and corticosteroids and cosmetic contact lens wear.Three genera (Fusarium, Aspergillus and Candida) have emerged as important pathogens that cause fungal keratitis world wide.[12]

Successful management of this blinding disorder relates to its early and accurate etiological identification. This is especially so as the prevailing antifungal drugs vary in their clinical efficacy and in- vitro sensitivity depending on the causative fungal strain.

Epidemiological and microbiological data reveals disparagingly dissimilar results not only between temperate and tropical territories but also inter regionally in the same climatic zone.

Isolated case reports even through useful are ineffective in portraying the realistic clinical scenario of a particular region. The present case series of 106 culture proven cases of fungal keratitis reported from Rohilkhand region of western Uttar Pradesh is a pilot effort in reflecting the epidemio-microbiological status of fungal keratitis in this agro-dominated state.

Notable findings of the study include a high risk factor for males ($p<0.0001$); a greater incidence in younger age group of 20-45 years i.e. 77 cases; (72.6%), a greater preponderance for filamentous fungal infections i.e. 92 cases (86.79%) and with vegetative trauma, 36 cases (33.96%) as the commonest mode. A significant association with direct vegetative trauma was noted for Fusarium infections while falling of dust or soil in eyes particularly in hot and humid weather contributed towards corneal infections with aspergillus. Role of pre existing 'Ocular surface disorder', systemic illness and immune suppression was more evident in yeast category of infections.

The largest case series of fungal keratitis are reported from southern India.[13,1]The primacy of Fusarium as the primary etiological agent and trauma as the chief predisposing factor is corroborated by both these studies as well as studies from Ghana, Florida, Paraguay,Nigeria and China.[3,4,5,7,8,9,11,18] A much higher incidence of Aspergillus is reported, however in similar studies in Indian subcontinent, [19], neighboring countries like Srilanka, Bangladesh , Nepal, [15,16,21] and worldover.[2,23] A solitary study in northern India on Pediatric Fungal Keratitis. [14] sites a much higher incidence of Aspergillus (40%) as opposed to Fusarium (10.7%) which shares near equal pathogenecity with Alternaria (10.2%), Curvularia (7.4%) and

Penicillium (7%). A recent study on Fungal Keratitis at Moorfield Hospital, London [22] implicated Candida as the major fungal etiological isolate (60.6%) as compared to the filamentous fungi which accounted for the remaining. Even though Aspergillus is accorded an ubiquitous status with continued detection in cooler climates, unlike Fusarium, [20]. Our study has noted a marked predilection of this isolate for the hot and humid months. The seasonal preponderance of Aspergillus in hot and humid months, while a seemingly constant incidence of Fusarium suggests a variation in etiopathogenesis of these two important genera of filamentous fungi. Equally pertinent is the role of immunosuppressions and ocular surface disorders in Candida infections. A significant number of Candida infections (11.6%) were noted in our case series, is in contra diction to similar studies in South India[13], where the role of Candida as an etiologic agent is reported to be minimal (0.7%). Yeast infections are rarely reported in tropical climates but are common in temperate zones [20,22]. The role of contact lenses as an important cause of fungal keratitis is not substantiated by our study, largely due to a lower socioeconomic group of study population with insignificant contact lens usage. The role of 'trauma' as the primary risk factor for fungal keratitis as reported in many studies,[1,11,13] is well substantiated in our review(Table-1). The high association of Fusarium infections with direct invasive plant trauma is well explained by the fact that Fusarium species constitute important plant pathogens with wide range of plant diseases like 'Crown rot' ,'Head blight' in cereal grains and 'Pokkah boeng' on sugarcane.[24] All 12 cases reported with trauma due to sugarcane leaves , grew Fusarium in culture suggesting high etiological association. The wide spread distribution of Fusarium in tropical regions along with their ability to grow on a wide range of substrates probably explains their high prevalence as causative agents.

The delay in seeking medical help at a tertiary centre(avg. duration 2.4 weeks) and multidrug empirical regime followed by majority of patients(83.9%) at the time of presentation explains poor clinical outcome.

In this report , an attempt has been made to enlist key epidemiological and microbiological features of fungal keratitis in the region to arouse high index of suspicion among treating physicians andenable early initiation of treatment on the basis of established regional epidemio-etiological data. The authors believe that a larger case series encompassing extensive areas of rural and urban India , would be more representative of a factual profile of fungal keratitis.

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Table 1: Predisposing Factors of Fungal Keratitis

Risk Factor	No. of Eyes (%)
Trauma	83 (78.3%)
Vegetative matter	42(39.62%)
Industrial	04(3.77%)
Domestic	24(22.64%)
Animal related	13(12.26%)
Severe systemic illness	07(6.60%)
Ocular surgery	02(1.89%)
Dry eye	05(4.71%)
Contact Lens	Nil
Use of Steroids	13(12.26%)
Others	03(2.83%)

Table 2: Organisms Isolated in Fungal Keratitis

Organisms	No of Isolates(%)
Fusarium	58(54.72%)
Aspergillus	28(26.41%)
Candida	12(11.32%)
Alternaria	2(1.88%)
Curvularia	2(1.88%)
Nocardia	01(0.94%)
Scedosporium	01(0.94%)
Others (Not Identified)	02(1.88%)

Figure 1: Seasonal Distribution of fungal isolates

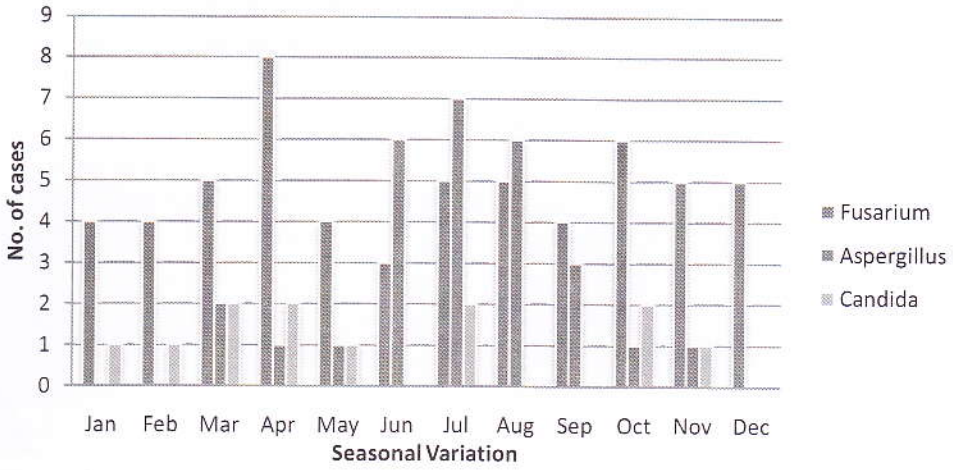

Fig 2 : Aspergillus fungal keratitis

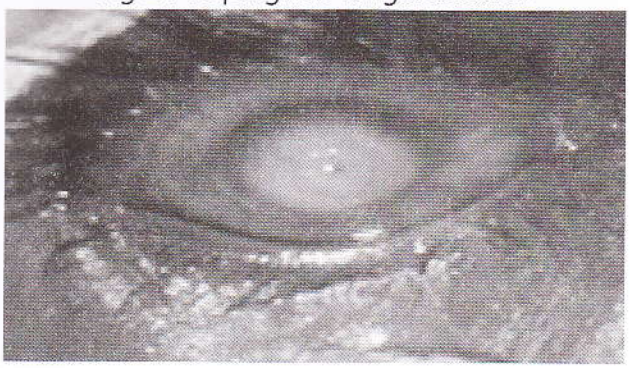

Fig 3: Fungal keratitis due to Fusarium sp.

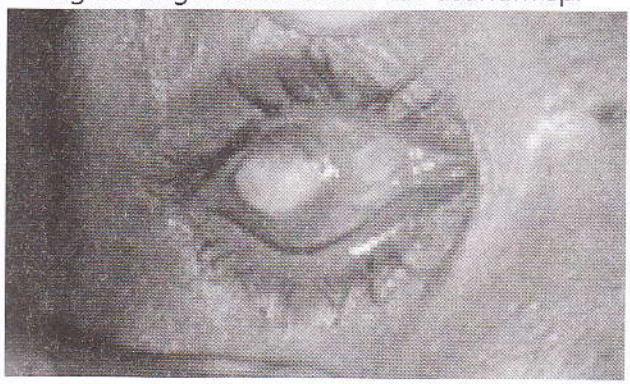

Fig 4:Fungal keratitis by Candida sp.

Fig 5: SD Agar showing Aspergillus growth

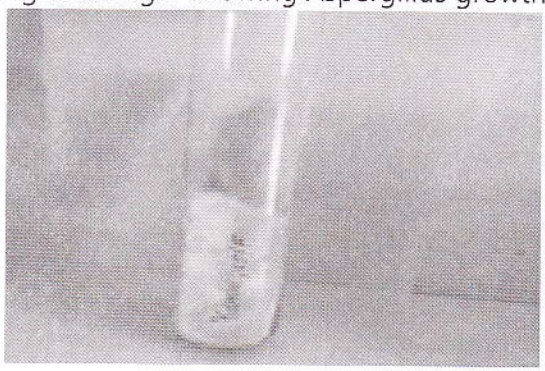

Fig 6: SD Agar showing Fusarium growth

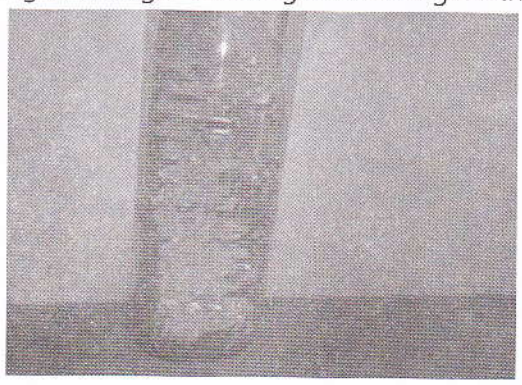

Fig 7: KOH Smear showing Fungal Hyphae