

Fungal keratitis in Saudi Arabia

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Abstract. We studied a total of 27 cases of fungal keratitis in Saudi Arabia. History of trauma was found in 9 patients, and previous use of topical steroids in 6 patients. In the majority of patients the onset of the disease was in fall and spring. The most frequent cause of fungal keratitis was found to be *Aspergillus* spp., and these were isolated from 11 cases (41%). Eight of the 11 isolates were *Aspergillus flavus*. Other causes of keratomycosis included: *Fusarium*, *Candida*, and *Mycelia sterilia*. All patients were treated with antifungal therapy and 18 patients required surgical intervention. Vision improved among 11 patients, remained the same in 4 patients, and deteriorated after treatment in 6 patients. (6 patients failed to return for follow-up.) Four of the 27 patients developed fungal endophthalmitis. The high prevalence of *Aspergillus* spp. may be due to the fact that spores of *Aspergillus* can survive the hot and dry weather of Saudi Arabia.

Introduction

The incidence of fungal keratitis (keratomycosis) has increased in the last two decades [1]. This has been attributed to the use and abuse of topical corticosteroids [2, 3], to contact lens wear, and to the use of broad-spectrum antibiotics [2, 4]. Contaminated donor corneas have been implicated in certain cases of fungal keratitis with disastrous consequences [5, 6]. Furthermore, our understanding of fungi has improved [7, 8], as well as laboratory methods for the diagnosis, and hence the early detection and management of such infections. The main objective of this study is to assess the causes and predisposing factors among 27 cases of keratomycosis in Saudi Arabia.

Patients and methods

Patients. We studied a total of 27 patients with fungal keratitis at the King Khaled Eye Specialist Hospital in Riyadh, Saudi Arabia. The history of each patient was recorded, including the patient's age, sex, occupation, place of residence, history of ocular trauma, use of topical steroids or other medica-

tion, and previous surgical treatment for the current ocular condition. All patients underwent a complete ophthalmic evaluation and each patient was given a general medical examination on admission.

Laboratory investigation. Corneal scrapings were subjected to Giemsa and Gram staining, and were cultured. Corneal scraping specimens were spread out onto two clean slides. These were stained by Gram stain and Giemsa stain, and examined by light microscopy using 400x and 1000x magnification. If hyphae were present or suspected, another smear, or one previously stained by Gram or Giemsa was stained by the Grocott-Gomori methenamine silver (GMS) stain. Scraped corneal specimens were directly inoculated in multiple C-shaped streaks onto Sabouraud's dextrose agar without cyclohexamide but containing 50 µg/ml of gentamicin to inhibit bacterial contamination. The pH of the Sabouraud's agar was between 6.8 to 7.4 (Emmon's modification) [9]. Sabouraud's dextrose agar plates were incubated in a non-CO₂ atmosphere at 27 °C to 30 °C and observed daily under 10x magnification for seven days, after which they were inspected every four days during a period of 21 days before being reported as negative. Scrapings were also inoculated onto other media, including 5% sheep's blood agar, incubated at room temperature (25 °C) and also at 37 °C on chocolate agar, brain/heart infusion medium, and on thioglycolate liquid medium. A sterile dacron swab moistened in sterile broth was sometimes used to obtain conjunctival and lid specimens. These were inoculated onto blood and chocolate agars.

Results

Patients. Out of 191 patients with microbial keratitis seen in the period of 30 September 1984 to 30 September 1987, 27 (14%) were caused by fungi. The age of patients with fungal keratitis ranged from 2–83 years with a mean age of 65 years. Twenty three patients were males and four were females.

Causes of fungal keratitis. Eleven out of the 27 cases of fungal keratitis (41%) were caused by *Aspergillus* species. *Aspergillus flavus* accounted for keratomycosis in 8 patients, *Aspergillus fumigatus* in 2, and *Aspergillus terreus* in 1 patient. Less commonly encountered organisms were *Fusarium* spp., *Candida albicans*, *Mycelia sterilia* and others. Fourteen patients with keratomycosis (52%) resided in the central region of Saudi Arabia. Seven (50%) of these 14 patients from the central region and keratomycosis caused by *Aspergillus* spp. Eight patients (30%) were from the western region of Saudi Arabia, and *Aspergillus* spp. were recovered from three of them (37.5%) (see also Fig. 1).

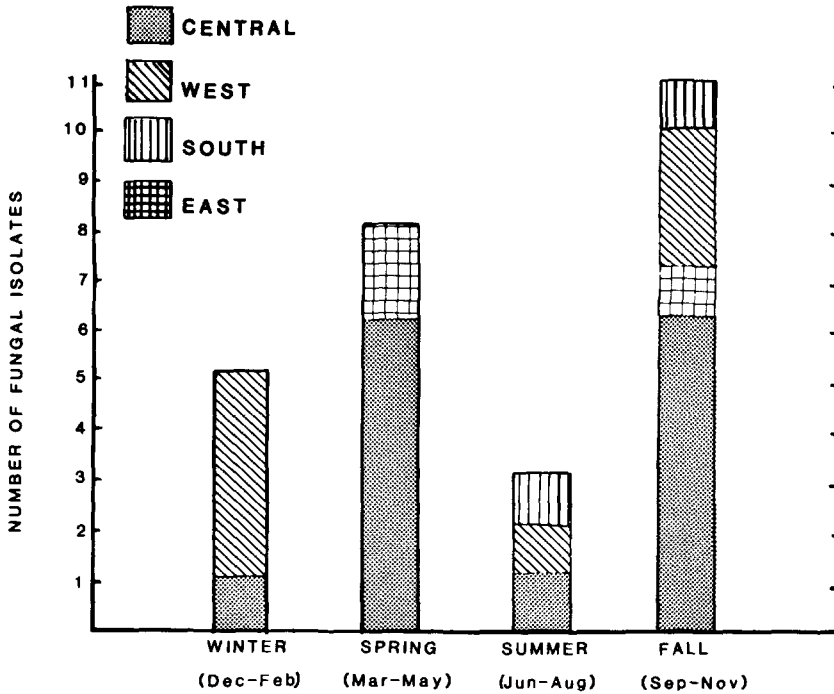
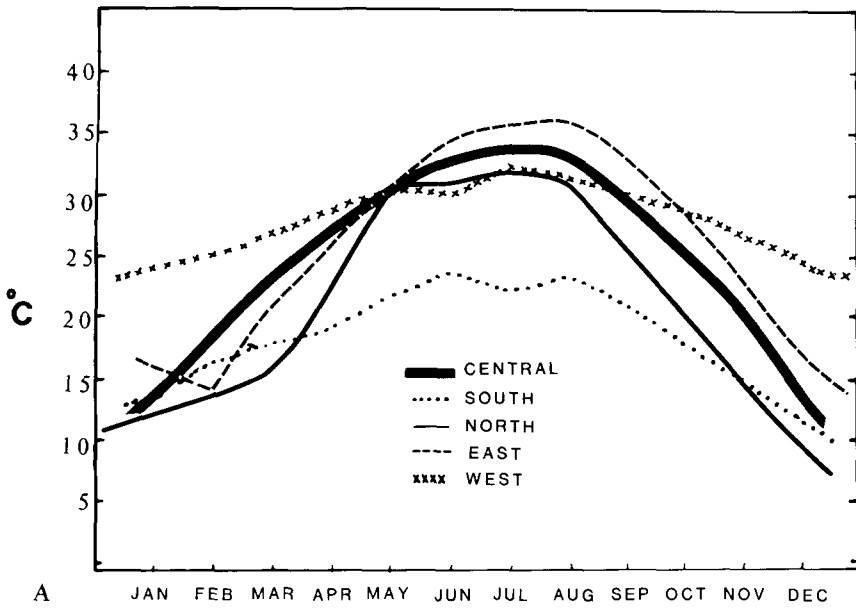


Fig. 1. Outline of the seasonal prevalence of fungal keratitis, and breakdown according to the geographical regions of Saudi Arabia.

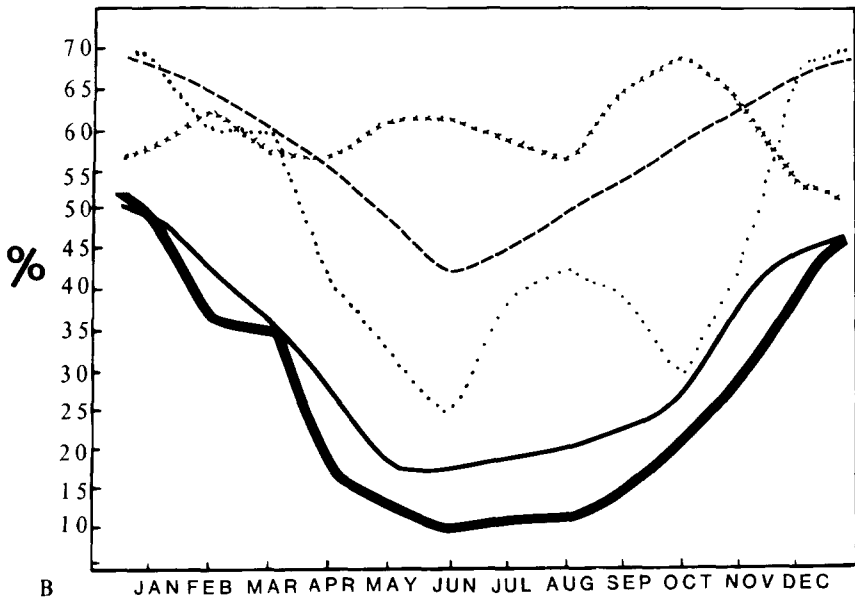
Predisposing factors. There was clear male preponderance, which may be due to their outdoor activities and exposure to vegetation in farming. Nine (33%) out of the 27 patients gave a history of ocular trauma. Six patients (22%) used topical steroids prior to presentation to us. On the other hand, four patients (15%) had used topical drops but failed to bring their medications. Two patients had adult onset diabetes mellitus and one patient was on renal dialysis.

Analysis of the time of onset of the keratomycosis revealed that the highest prevalence (11 cases) of the disease occurred during the months of September to November (fall) and eight cases occurred between March and May (spring) (Fig. 1). Temperatures during fall and spring ranged from 13 °C to 38 °C, with an average temperature of 25.5 °C. In addition there was low degree of relative humidity, and occasional rain and wind [10, 11]. The average monthly temperature and relative humidity levels are depicted in Figs. 2 and 3.

Laboratory findings. Fungal isolated from corneal scraping specimens was possible in 24 patients (89%). Hyphal elements were seen by histopathology



A
 Fig. 2. Average temperatures during the year in various regions of Saudi Arabia.



B
 Fig. 3. Average relative humidity during the year in various regions of Saudi Arabia.

in the deep stromal layer of the corneal button in one patient. In two patients, no fungal growth was documented, but GMS-stained corneal scrapings showed fungal elements, and these two patients improved clinically on antifungal treatment alone. Corneal scrapings of 16 patients with fungal keratitis were stained with GMS and 12 of them (75%) showed fungal elements. Hyphae could be detected in 15 out of the 27 cases (55.5%) by Giemsa staining of corneal scrapings, and in 11 (41%) by Gram stain.

Management. the main antifungal agent used in the initial treatment among 23 patients (85%) was topical natamycin (primaricin) 5% suspension. Topical and/or subconjunctival miconazole was used in 18 patients (67%). Amphotericin B was used in 6 patients (22%) as an additive treatment regimen. Tissue adhesive was used for sealing of corneal perforation among 5 patients (18%). Therapeutic penetrating keratoplasty was performed on 10 patients (37%). Three eyes (11%) required enucleation/evisceration because of uncontrolled keratomycosis leading to fungal endophthalmitis.

Outcome. The final visual acuity improved by one to two lines from that taken at presentation in 11 patients (41%), remained the same in 4 patients (15%), worsened to no light perception in 6 patients (22%), and remained unknown in 6 patients (22%), who failed to come for follow-up examination.

Discussion

The most common organism causing keratomycosis in this study was found to be *Aspergillus* spp., and specifically *Aspergillus flavus*. This could be related to many factors, including the fact that *Aspergillus* spp. are ubiquitous, saprophytic fungi related to the class ascomycetes, which are characterized by their light-weight spores (conidia), necessary to their sexual reproduction [12–14]. Sterigma (spore-producing organs), which are characteristic of *Aspergillus* spp., contain hundreds of spores at the end parts of the fungus, which can be widely disseminated by air and wind [12–14]. *Aspergillus* spp. are able to grow on several types of substrates. *A. flavus* in particular is regularly isolated from soil, especially in tropical and subtropical areas, from forage, decaying vegetation, stored seeds and grains, and from various types of food products including damp bread, spoiled food, and from damp clothing, especially shoes during summer in the tropics [15]. *Aspergillus* can grow anywhere under a wide range of environmental conditions [12]; it is thermophilic, growing well at 37 °C [13], but can tolerate and grow at 50 °C [16].

In this study, *Aspergillus* spp. appeared to be common in the central

Table 1. Worldwide frequency of *Aspergillus* isolates reported to cause keratomycosis

Geographic area	No. of isolates	All types <i>Aspergillus</i> %	Percent <i>A. flavus</i> %	Author(s)/Year
Saudi Arabia	35	43	23	Byrne 1987
East Nepal	57	49	12.3	Upadhyay 1987 [19], personal communication with K.A.B.
Bangladesh	12	75	not reported	Katz et al. 1983 [20]
Singapore	22	*	not reported	Lim 1976 [21]
India (total)	160	59	9.2	Puttana 1969 [22], Prasad et al. 1982 [23], Koul et al. 1975 [24], Dutta et al. 1981 [25], Sandhy et al. 1980 [26], Sharma 1981 [27]
U.S.A.	193	7.8	2	Doughman et al. 1982 [17], Chin et al. 1975 [28], Polack et al. 1971 [29], Liesegang et al. 1980 [30]
U.K.	—	*	—	Jones 1975 [1]
France	—	*	—	Blank et al. 1975 [31], Verin et al. 1984 [32]
Japan	—	*	—	Matsumoto 1976 [33]

* No figures given, report only that majority were *Aspergillus* and *Candida*.

province of Saudi Arabia. This is a relatively high plateau, where the climate is quite dry and the temperatures are higher than on the coastal plains. During summer the average temperature may reach up to 42.4 °C, and sandstorms occur during certain months of the year. *Aspergillus* spp. with its thermotolerant character can survive in this environment and become pathogenic to humans causing keratomycosis particularly under the more favorable conditions during spring and fall when the climate is optimal for its growth. Spring and fall in the Kingdom of Saudi Arabia, in general, are characterized by an average temperature of 25 °C, accompanied by a low degree of relative humidity (15%) and occasional rain and wind [10, 11] (see also Figs. 2 and 3).

Aspergillus spp. are ubiquitous organisms. Several reports appeared in the literature worldwide reporting its frequency, especially in the eastern parts of the world in comparison to western parts (Table 1).

Aspergillus spp., and *A. flavus* in particular, produce diastatic and proteolytic enzymes [12], such as phospholipase, protease, and pseudo-collagenase, causing coagulative necrosis of invaded corneal tissues [7]. These toxins produced by *Aspergillus* spp. may help its pathogenicity [1, 7], and probably are the reason for loss of the eyes when the infection extends to the posterior chamber, causing 'fungal malignant glaucoma' [1].

Fungi are generally saprophytic, and their presence in the conjunctival sac varies from 2 or 3%, to 80% in people working in harvesting fields in autumn [4]. Fungal keratitis occurs almost always in eyes with a history of trauma or other predisposing factors such as dry eye syndrome and lid abnormalities [1], or in association with systemic disorders such as diabetes, neoplasms, chronic alcoholism [4], immune suppressed patients, or in patients using topical corticosteroids [1, 4, 17]. In this study, a history of trauma was found in 9 patients (33%). A history of use of topical steroids before presenting to the hospital was found in 6 patients (22%), while two patients had adult onset diabetes mellitus and one patient was on renal dialysis.

Fungal keratitis should be suspected in patients with indolent corneal ulceration in Saudi Arabia. Early diagnosis and prompt treatment is mandatory in all cases of keratomycosis [1, 18].

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