Spectrum of Fungal Keratitis in North China

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Purpose: To report the epidemiological features, laboratory findings, and treatment outcomes in patients with fungal keratitis in north China.

Design: Retrospective hospital-based study.

Participants: A total of 654 patients diagnosed with fungal keratitis at the Shandong Eye Institute from January 1999 to December 2004.

Methods: The medical records of 654 inpatients (654 eyes) with fungal keratitis were reviewed retrospectively for demographic features, risk factors, seasonal variation, clinical characteristics, laboratory findings, and treatment strategy.

Main Outcome Measures: Patient history, ocular examination findings by slit-lamp biomicroscopy, laboratory findings from direct smear examination and fungal culture, and treatment protocol.

Results: Fungal keratitis constituted 61.9% of cases of severe infective keratitis among the inpatients at the Shandong Eye Institute during the 6 years. Males (60.6%) were more likely to be affected by fungal keratitis than females (39.4%). Almost one third of the patients (203) were middle aged (41–50 years old). Corneal trauma (51.4%), especially injury from plants (25.7% in all patients), was the most commonly associated risk factor. The incidence of fungal keratitis was higher in harvest seasons, including summer and autumn. An increasing tendency of incidence was noted in more recent years. Direct microscopic examination of the corneal scraping samples stained with potassium hydroxide showed positivity in 88.7% of the eyes. The fungal isolates were of *Fusarium* species in 437 eyes (73.3%) and *Aspergillus* species in 72 eyes (12.1%). Surgical interventions were performed in 604 eyes (92.4%), including therapeutic penetrating keratoplasty in 399 eyes (66.0%) and therapeutic lamellar keratoplasty (LK) in 177 eyes (29.3%). Globe integrity was preserved in 626 eyes (95.7%).

Conclusions: With *Fusarium* species being the most commonly isolated pathogens, fungal keratitis is the leading cause of severe infective corneal ulcers in north China. Direct microscopic examination with potassium hydroxide wet mounts proves to be a rapid, simple, inexpensive diagnostic means. Corneal transplantation continues to be the most effective approach for the treatment of severe fungal keratitis. Early surgery, especially LK, can be considered if aggressive topical therapy does not achieve early disease control. *Ophthalmology 2006;113:1943–1948 © 2006 by the American Academy of Ophthalmology.*

Corneal diseases, especially infective corneal diseases, are major causes of blindness worldwide, second only to cataract in overall importance.[1] Among severe infective corneal ulcers, fungal keratitis is most common in many developing countries like China, India, Ghana, and Nepal.[2–6] The incidence of fungal keratitis is increasing on the Chinese mainland.[2,7] Factors that have been correlated with this increasing incidence include the growing number of trauma cases, widespread abuse of broad-spectrum antibiotics and steroids, and increasing use of corneal contact lenses. Meanwhile, improvement of the health care system, increasing awareness of this disease by ophthalmologists, and popularization of the diagnostic methods and instruments also help to identify patients who otherwise might have been undetected previously.[8,9]

The epidemiological features of fungal keratitis vary among different geographic regions and climate conditions.[5] To improve the management of patients with fungal keratitis, it is important for ophthalmologists to gain information about the etiology of fungal keratitis. The action plan enumerated in the initiative Vision 2020: The Right to Sight also suggests that we obtain a more clear and concise understanding of this disease in each country. However, such information from China is limited. Our study analyzed the epidemiologic features, laboratory findings, and treatment outcomes of fungal keratitis in north China to provide a useful guide for both practicing ophthalmologists and vision scientists.

Patients and Methods

In this hospital-based retrospective study, we reviewed the medical history data of 1056 patients (1056 eyes) with infective corneal ulcers (excluding 461 inpatients with viral keratitis during the corresponding period) hospitalized at the Shandong Eye Institute

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from January 1999 to December 2004. As one of the largest tertiary referral eye centers in north China, this institution caters to a great proportion of patients with eye diseases in Shandong Province and neighboring provinces.

Detailed information from each patient was recorded, including (1) patient history (demographic features, onset time of symptoms, risk factors, and previous therapy); (2) ocular examination findings by slit-lamp biomicroscopy; (3) laboratory findings from direct smear examination and culture of corneal scrapings and culture and histopathological examination findings of diseased corneal tissues obtained at surgery, if done; and (4) treatment received at our institution.

Corneal scrapings were obtained aseptically from the base and edges of each ulcer, except those with corneal perforation, using a disposible microblade. The operated eyes were anesthetized topically with 0.5% proparacaine hydrochloride. A portion of each scraping was examined for the presence of fungi, bacteria, or *Acanthamoeba* by using 10% potassium hydroxide wet mounts, smears stained with Gram's stain, and saline wet mounts, respectively. Another portion was inoculated onto Sabouraud glucose agar, brain–heart infusion broth, and chocolate agar, respectively, and cultured for potential growth of fungi, bacteria, or *Acanthamoeba.* Sabouraud glucose agar slants were incubated at 28° C, while others at 37° C. All media were cultured for a period of 14 days and observed daily. The diseased corneal tissue removed during surgery was cut aseptically into 3 equal parts, 1 of which was prepared for histopathologic examination by periodic acid–Schiff staining and 2 of which were cultured for fungi and bacteria, respectively.

A diagnosis of fungal keratitis was made when at least one of the following was confirmed: (1) corneal scraping examination revealed fungal presence in smears, (2) the same fungal pathogens grew in ≥2 culture media, (3) fungus grew confluently at the inoculated site on a single solid medium, and (4) histopathologic examination revealed fungal presence. Confocal microscopy also was used to assist diagnosis in many patients but not taken as singular proof of final diagnosis.[10]

The patients who were diagnosed with fungal keratitis were treated following the antifungal protocol used in our previous studies.[2,11] The fungal lesions in all eyes except those with corneal perforation were scraped and curetted to eliminate superficial necrotic tissues. All patients were treated with hourly 0.5% fluconazole combined with 5% natamycin or hourly 0.5% fluconazole combined with 0.25% amphotericin B so that a drop was received every 30 minutes while awake. Antifungal ointments of 1% fluconazole and 1% amphotericin B were used before bedtime. All patients also received 200 mg of fluconazole orally per day. Patients with hypopyon were given 100 mg of fluconazole IV twice a day. If the status of corneal ulcers deteriorated or did not improve after 5 to 7 days of antifungal therapy, surgical interventions were recommended, including therapeutic penetrating keratoplasty (PK), therapeutic lamellar keratoplasty (LK), and keratectomy in combination with a conjunctival flap.

Immediately after surgery, 2×10^4 U of tobramycin and 1 mg of fluconazole were injected subconjunctivally. Antifungal eyedrops were continued for 2 weeks postoperatively and tapered thereafter. Some patients with severe inflammatory reaction in the anterior chamber (AC) were given nonsteroidal antiinflammatory eyedrops 4 times daily and atropine ointment at night until the inflammatory reaction resolved. Oral fluconazole was prescribed for all cases for a total of 3 weeks after surgery. Systemic and topical steroids and topical 0.5% cyclosporine A were given from 2 weeks after surgery if the fungal infection did not recur. The systemic steroids were tapered off within 2 months, but topical steroids and 0.5% cyclosporine A were used for 1 year in the patients undergoing LK with donor grafts smaller than 8.5 mm in diameter and for at least 2 years in the other patients undergoing PK or LK. All patients were hospitalized for the first 7 to 10 days after surgery and followed up weekly for the first month, every 2 weeks for 2 months, monthly for a minimum of 6 months, and then at varying intervals thereafter.

The surgical intervention was regarded as a success if fungal infection was under control with globe integrity after only one surgery. When the fungal infection recurred after PK or LK, an attempt was made to control it by antifungal therapy and even repeat surgery.

Results

Epidemiologic Features

Of the 1056 eyes with infective corneal ulcers, 654 (61.9%) were diagnosed as fungal keratitis, 129 (12.2%) as bacterial keratitis, and 15 (1.4%) as *Acanthamoeba* keratitis, whereas no pathogens could be isolated in the other 258 eyes (24.5%).

Of the 654 patients with fungal keratitis, 396 (60.6%) were male, and 258 (39.4%) were female. The male-to-female ratio was 1.5:1. The age of patients ranged from 7 to 80 years (mean, 44.9±12.5). Patients ages 41 to 50 were most frequent (203 [31.0%]), followed by those 31 to 40 (173 [26.5%]), 51 to 60 (138 [21.1%]), 61 to 70 (61 [9.3%]), 21 to 30 (43 [6.6%]), 11 to 20 (26 [4.0%]), 71 to 80 (9 [1.4%]), and 0 to 10 (1 [0.2%]). Of these patients, 588 (89.9%) were farm workers, 27 (4.1%) were physical laborers, 18 (2.8%) were nonmanual employees, 14 (2.1%) were students and children, and 7 (1.1%) were temporary employees.

When the potential risk factors were reviewed, an explicit history of antecedent trauma to the cornea was obtained in 336 eyes (51.4%), with plants (168 [25.7%]) being the major traumatic agents involved. The other agents are listed in Table 1. Other risk factors included ocular or systemic diseases that compromised the cornea or lowered corneal resistance to infection. Topical glucocorticoid use before or after the onset of keratitis was noted in 46 eyes (7.0%). Nine eyes (1.4%) had a prior herpes simplex keratitis. Two eyes (0.3%) had exposure keratitis. Two eyes (0.3%) received ocular surgery not long before presentation. Eleven patients (1.7%) had diabetes mellitus.

The duration from the onset of symptoms to presentation to our institution ranged from 3 to 150 days (mean, 26.6±19.0). Forty-one percent of the patients were seen at our institution within 16 to 30 days (Table 2). Concerning seasonal variation in the incidence, the peak occurred in the months of October to December, followed by July to September. The number of cases increased in more recent years (Fig 1).

Before their initial visit to our institution, 650 patients (99.4%) had received topical antibiotics, antivirals, antifungals, and/or glu-

Table 1. Traumatic Agents in Fungal Keratitis Patients

Traumatic Agents	No. of Patients	Percentage
Plants/agriculture	168	25.7
Dust, soil, or stone	59	9.0
Unidentified foreign body	48	7.3
Physical violence	35	5.4
Metallic foreign body	8	1.2
Small winged insect	5	0.8
Animal hair	3	0.5
Electric welding light	3	0.5
Sewage	3	0.5
Heat injury	2	0.3
Chemical gas	2	0.3
Total	336	51.4

Table 2. Duration of Symptoms in Fungal Keratitis Patients

Duration (Days)	No. of Patients	Percentage
0–7	51	7.8
8–15	179	27.4
16–30	268	41.0
31–90	151	23.1
>90	5	0.7

cocorticoids, either alone (404) or in combination (209), but there were 37 patients whose antecedent topical medications were not defined. Of those 404 patients who had not received combined medications, antifungals had been used in 118 eyes, glucocorticoids in 15, antibiotics in 218, and antivirals in 53. Of the 209 patients who had received combined topical medications, antifungals had been used in 84 eyes, glucocorticoids in 31, antibiotics in 89, and antivirals in 57.

The diameter of corneal ulcers in our 654 eyes ranged from 3.5 to 11 mm (mean, 6.2±2.9). Three hundred thirty-seven eyes (51.5%) had larger ulcers (diameter > 6 mm). The depth was from one third of corneal thickness to full thickness, and corneal perforation occurred in some cases. Three hundred three eyes (46.3%) had hypopyon, 46 (7.0%) had corneal perforation, 44 (6.7%) had elevated intraocular pressure, 36 (5.5%) had endophthalmitis, and 6 (0.9%) had complicated cataract.

Laboratory Findings

Of the 654 eyes with fungal keratitis, fungi alone were the etiological agents in 622 (95.1%), and bacteria were identified with fungi in 32 (4.9%). Corneal scrapings obtained from 626 eyes were examined by direct microscopy with potassium hydroxide wet mounts and inoculated for culture. The diseased corneal tissues obtained at surgery from 604 eyes were processed for microbial culture and histopathologic examination. Three hundred twelve eyes were examined by confocal microscopy. The results are shown in Table 3.

Of the 596 fungal culture-positive eyes, *Fusarium* species were the most frequent isolates (437 [73.3%]), followed by *Aspergillus* species (72 [12.1%]). Among the *Fusarium* species, *F. solani* was isolated most frequently (173 [29.0%]). Other fungi isolated were, in decreasing order, *Alternaria* species, *Penicillium* species, *Candida albicans, Pseudallescheria boydii, Acremonium, Microsporum, Monilia, Mucor racemosus,* and *Sporothrix schenckii.* There were also 27 unidentified cultured specimens (Table 4). Fungi were isolated from all the 46 patients receiving topical corticosteriod administration, including *F. oxysporum* (26), *F. moniliforme* (8), *F. solani* (5), *Aspergillus flavus* (5), *Alternaria* species (1), and *S. schenckii* (1). Fungi also were isolated from all the 11 patients with diabetes mellitus, including *F. oxysporum* (3), *F. moniliforme* (2), *F. solani* (1), *Alternaria* species (1), *Aspergillus flavus* (1), *Microsporum* (1), other *Fusarium* species (1), and unidentified species (1).

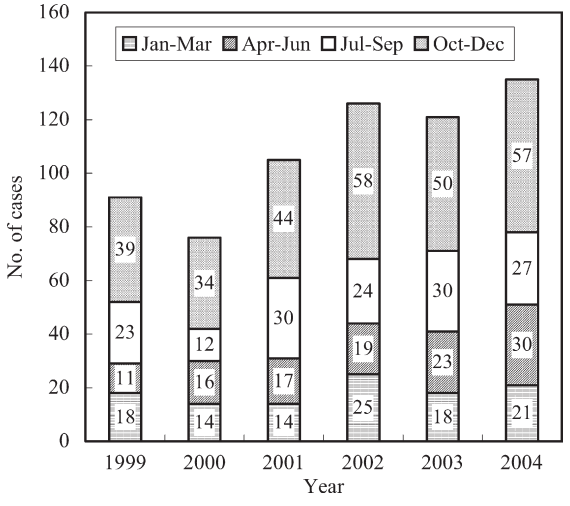

Figure 1. Distribution of fungal keratitis over time.

Table 3. Laboratory Findings

Methods	No. of Examined Cases	No. of Positive Cases (%)
Potassium hydroxide wet mounts	626	555 (88.7)
Fungal culture	654	596 (91.1)
Of corneal scrapings	626	387 (61.8)
Of diseased cornea	604	581 (96.2)
Histopathologic examination	604	593 (98.2)
Confocal microscopy	312	239 (76.6)

Treatment Outcome

Surgeries were performed in 604 eyes (92.4%), including therapeutic PK in 399 (66.0%), therapeutic LK in 177 (29.3%), keratectomy in combination with a conjunctival flap in 4 (0.7%), evisceration in 18 (3.0%), and enucleation in 6 (1.0%). Of the 399 eyes receiving PK, fungal infection recurred in 14 (3.5%), in which most of the pathogens were *Fusarium* species (13), including *F. solani* (5), *F. oxysporum* (3), and *F. moniliforme* (2), and the other one was *Aspergillus flavus.* Ten of the 14 recurrent infections were controlled with antifungal injection into the AC and/or vitreous cavity, with repeat PK, and/or with vitrectomy; 2 had evisceration; and 2 had enucleation for uncontrolled endophthalmitis. Fungal

Table 4. Spectrum of Fungal Species in North China (n = 596)

Species	No. of Isolates	Percentage
Fusarium species	437	73.3
F. solani	173	29.0
F. moniliforme	116	19.5
F. oxysporum	113	19.0
F. nivale	11	1.8
F. subglutinans	3	0.5
Others	21	3.5
Aspergillus species	72	12.1
A. flavus	41	6.9
A. fumigatus	18	3.0
A. terreus	4	0.7
A. niger	3	0.5
A. oryzae	2	0.3
A. nidulans	2	0.3
A. versicolor	2	0.3
Alternaria species	19	3.2
Penicillium species	15	2.5
Candida albicans	12	2.0
Pseudallescheria boydii	5	0.8
Acremonium	3	0.5
Microsporum	2	0.3
Monilia	2	0.3
Mucor racemosus	1	0.2
Sporothrix schenckii	1	0.2
Unidentified	27	4.5
Total	596	100

infection recurred in 7.3% of eyes (13/177) after LK, and most of the pathogens were also *Fusarium* species (8), including *F. oxysporum* (3), *F. solani* (2), and *F. moniliforme* (1). The pathogens in the other 5 eyes were *Aspergillus flavus* (2), *Aspergillus terreus* (1), *Penicillium* species (1), and unidentified species (1). All recurrent keratitis after LK was controlled with intensive topical antifungal therapy or repeat LK (2) or PK (8). Of the above 27 recurrent cases, the recurrence time of 26 patients was within 1 week, including 21 patients within 3 days. Fungal keratitis recurred in 1 eye at 9 days after surgery. All recurrences after PK or LK were apparent within 2 weeks, so if a graft remained clear till that time, the surgical intervention was successful.

Globe integrity and useful visual acuity (VA) were preserved in 626 eyes (95.7%). Twenty-eight patients (4.3%) lost their eyes (via evisceration in 20 and enucleation in 8), in which the *Fusarium* species were isolated from 24, including *F. solani* (11), *F. oxysporum* (6), and *F. moniliforme* (4). In addition, *A. flavus* was isolated from 1 eye, and the other 3 species were unidentified. The duration from the onset of symptoms to presentation to our institution ranged from 7 to 85 days in those lost eyes (mean, 28.4±17.9 days). There was no significant difference between the lost eyes and the other 626 preserved eyes (mean, 26.6±19.1 days) in the duration of symptoms.

During the follow-up of 6 to 51 months (mean, 15.6±9.2), all eyes receiving LK retained clear grafts. Fifty-three eyes (13.2%) after PK experienced an immune rejection, and 47 grafts became clear after systemic and topical antirejection therapy. The other eyes receiving PK without immune rejection retained clear grafts. At last follow-up, the best-corrected VA (BCVA) of 403 patients after PK (including 8 recurrent patients after LK who received PK) was 20/40 or better in 191 eyes (47.4%), between 20/100 and 20/50 in 121 (30.0%), 20/200 in 57 (14.1%), and <20/200 in 24 (3.5%). One hundred sixty-nine eyes after LK had BCVA of 20/200 or better, including 20/40 or better in 79 (46.7%) and 20/100 to 20/50 in 67 (39.6%).

Discussion

Due to high incidence and poor responses to antifungal agents, fungal keratitis has become an important cause of visual loss in many developing countries, where a large number of the population are farm workers. Moreover, the climate is mild and humid, and malnutrition is common. All these factors predispose people to the development of fungal keratitis from minor eye trauma. Fungi reside as commensals in flora of the conjunctival sac in 3% to 28% of healthy eyes[12–14] and may invade the cornea if the eyes are injured, particularly when topical corticosteroids are administered, or if patients have chronic ocular surface disorders. For more effective prevention and treatment of fungal keratitis, it is important for ophthalmologists to be aware of regional epidemiologic features, risk factors, and etiologic data concerning this disease.

Of the 1056 inpatients with infective keratitis from January 1999 to December 2004 at our institution, fungal keratitis was diagnosed in 654 eyes (61.9%). This figure, though not a real incidence rate, shows that fungal keratitis is the leading cause of severe infective corneal ulcers in north China. It is quite different in a Taiwanese hospital in the southeast of China, where fungal pathogens were isolated from only 13.5% of 476 eyes (453 patients) with microbial keratitis.[15] This further confirms that there is regional difference in the incidence of fungal keratitis.

In line with other studies,[3,4,16,17] males (60.6%) predominated in our series. This is usually attributed to the fact that men are more actively involved in outdoor activities, which subsequently increases their vulnerability to this disease. We found that the largest proportion of the patients were 41 to 50 years old (31.0%), followed by 31 to 40 years (26.5%), which differs from many reports noting that fungal keratitis was most common during 51 to 60 years[17–19] or 31 to 40 years.[4] This also may be explained by the fact that the subjects ages 41 to 50 in this study are the main force of manual work, especially farm work, and more involved in outdoor activities in China. Farm worker usually is the most common occupation in patients with fungal keratitis, the percentage being as high as 89.9% in the current study.

As in previous studies,[3,4,20,21] corneal injury was identified as a major risk factor, with agricultural plants being the most common agents (25.7%) in the present series. Topical corticosteroid use has been correlated with the incidence of fungal keratitis.[3,4,19,22] In the current study, glucocorticoids were topically administered in 7.0% of the patients, and globe integrity was not preserved in 2 of them.

Diabetes mellitus was reported in 11 patients (1.7%), and the percentage is lower than that in other studies.[3,4] We found that the responses to antifungal agents in patients with diabetes were poor. When the levels of blood sugar were controlled, their responses to antifungal agents improved. Contact lens wear was reported a major risk factor in many studies,[4,18,19] but there was no case of contact lens wear in our series. Very few farmers wear contact lenses in China.

A majority of patients (41.0%) visited our institution between 16 and 30 days after the onset of symptoms. We found that the longer the duration of symptoms, the worse the response of patients to antifungal agents, and the more likely that patients underwent corneal transplantation. Two hundred eighty-two patients (43.3%) visited our institution in the months of October to December. We assume that the shift from harvest season (August to November) in this area to the leisure season contributes to the sharp increase in the number of cases.

Before their initial visit to our institution, 650 patients (99.4%) had received medical therapy. Among them, 209 (32.2%) had received combined antifungals, antibiotics, antivirals, or steroids. This indicates that the general practitioners and ophthalmologists at the primary clinics or secondary medical facilities in China like to prescribe a cocktail of drugs at the very beginning and refer patients to professional tertiary eye hospitals only when their empirical treatment fails. In the 118 patients (18.2%) who had been treated only with antifungal agents, it was common that the dosage had been insufficient or in an incorrect frequency. It has been reported that glucocorticoids can weaken the defense mechanism of the cornea, thereby favoring the fungal growth and progression of the disease.[22–24] In our series, 46 patients (7.0%) had received topical corticosteroids before they visited us, and 2 of them had their diseased eyes removed eventually. Long-term use of antibiotics also is believed to compromise the cornea.[22] Therefore, it is very important to reach a definite diagnosis and start proper

antifungal therapy for fungal keratitis patients when the disease is diagnosed.

In the clinical examination, hypopyon was observed in 303 eyes (46.3%), which is similar to several Indian studies.[4,21,25] Viscous hypopyon is thought to be a major sign of fungal keratitis, but it does not reliably reflect the severity of the disease. The presence of hypopyon does not give a clue as to whether fungal filaments have penetrated the cornea and into the AC. In a previous study,[26] we noted that 17 (65.4%) of 26 mycotic eyes without corneal perforation had negative results when the hypopyon was cultured. In the 34 eyes with hypopyon treated by LK in this study, fungal infection recurred in 5, 1 of which was controlled by repeat LK, whereas the other 4 were controlled by PK.

In the current study, the positive rate of direct microscopic examination of corneal scraping samples with potassium hydroxide wet mounts was 88.7%, which is similar to the findings of Gopinathan et al[3] (91%) and Panda et al (90%).[16] Chowdhary and Singh[4] reported a lower rate, 62%, whereas Bharathi et al[27] reported as high as 99.2% in a retrospective study. According to Sharma et al,[8] specificities of potassium hydroxide with calcofluor white staining in early and advanced fungal keratitis were 99.0% and 83.7%, respectively. In another report,[4] the specificity of potassium hydroxide wet mounts was 97.0%. Therefore, considering its low cost, convenience, speediness, and high sensitivity and specificity, direct microscopic examination with potassium hydroxide wet mounts continues to be an ideal technique to assist the diagnosis of fungal keratitis. The positive rate of culture of corneal scrapings was 61.8% in this study, which tallies with previous studies.[5,21,27] However, the positive rate of culture of diseased corneal tissues obtained at surgery reached 96.2%. Although it is still helpful to establish an accurate diagnosis of fungal keratitis, fungal culture may not be valuable for early identification of the disease because it usually requires several days or weeks for the process. The histopathologic examination of the diseased corneal tissues showed the highest positive rate (98.2%), which is in accordance with our previous reports.[2,11] However, the samples for histopathologic examination were obtained at surgery, which does not make it helpful for early diagnosis of the disease. Although corneal biopsy can be obtained for histopathologic examination at the early stage of disease, it is difficult to adopt in clinical practice. The reason is that patients are usually reluctant to undergo even minor diagnostic surgical procedures because debriding corneal ulcers may be followed by enlargement of the confined lesion or perforation. Also, the samples obtained are sometimes difficult to spread on slides.

In this study, *Fusarium* species (73.3%) predominated in the fungal pathogens isolated, followed by *Aspergillus* species (12.1%). This is in accordance with the finding in a retrospective study[7] in this region. *Fusarium* species were found to be the most commonly isolated pathogens of fungal keratitis by many investigations in both north and south China during the past 2 decades.[28,29] Similar findings were seen in south India,[3,5] but in north India, *Aspergillus* species were the most frequent cause of fungal keratitis.[4] Generally, although *Candida* species were reported most common in a few developed countries,[19,30,31] *Fusarium* species and *Aspergillus* species were the most common pathogens for fungal keratitis in other parts of the world.[2,3,5,7,8,11,21,22]

Currently, the medical therapy of fungal keratitis appears unsatisfactory,[18,31,32] which is further confirmed by this study. In the 654 fungal keratitis eyes, the infection was controlled by medical therapy in only 50 eyes (7.6%). Surgical interventions were required in 92.4% of the eyes. This may be related to the long delay in presentation and incorrect use or abuse of drugs that the patients previously received. We recommend early surgery if the initial response to treatment is unsatisfactory after 5 to 7 days of intensive antifungal therapy. Recall that most of our patients had a long duration of symptoms, with a history of topical medical therapy and severe corneal lesions. Early surgery may not be needed as often if the correct diagnosis is made promptly, followed by appropriate therapy. As for the patients who visited our institution directly after the onset of infection, antifungal therapy was prescribed routinely at the outpatient department. They were admitted in hospital only when the medical treatment was ineffective. In this study, 399 eyes (66.0%) had therapeutic PK, with a success rate of 96.5%. The recurrence rate (3.5%) is far lower than that reported in another study.[4] Moreover, 177 eyes (29.3%) underwent therapeutic LK, with a success rate of 92.7%, which indicates that satisfactory results could be achieved by therapeutic LK for treatment of fungal keratitis.[11] Although the recurrence rate (7.3%) after LK is twice that after PK, the results of LK are still favorable and may permit a lower rate of postoperative immune rejection. As for the surgical timing of LK, we recommend performing this surgery when 5 to 7 days of intensive antifungal therapy fails, with the corneal lesions at anterior or middle stroma. Globe integrity and useful VA were preserved in 626 eyes (95.7%). The rate is similar to that in Yao et al's report (2/45 [4.4%])[33] and lower than that reported by Chowdhary and Singh (8/119 [6.7%]).[4] Most of the pathogens in the patients with eye loss and recurrent infections after keratoplasty were *Fusarium* species. This might be related to the high percentage (73.3%) of *Fusarium* species isolated. Our study design does not allow us to know if *Fusarium* species are more invasive. No obvious relation between eye loss and duration of the symptoms was observed.

In conclusion, *Fusarium* species are the most commonly isolated pathogens, and fungal keratitis is the leading cause of severe infective corneal ulcers in north China. The incidence of fungal keratitis, closely related to seasonal variation, shows an increasing tendency in more recent years. In our patients who tend to be diagnosed late, corneal transplantation remains most effective for the treatment of severe fungal keratitis. We hope that by sharing our data we may help our colleagues learn to diagnose and treat this disease earlier, so as to achieve a better outcome. Adequate protection during outdoor activities and minimization of topical glucocorticoid use are practical means that may reduce or prevent the incidence of this disease. We advocate using direct microscopic examination with potassium hydroxide wet mounts as a rapid, simple, inexpensive approach to assist early diagnosis of fungal keratitis. We also consider that corneal transplantation at an early stage, especially

therapeutic LK under suitable conditions, may improve the prognosis for patients with fungal keratitis.

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