

Fungal keratitis among inpatients with corneal ulcers in Thai Binh, Vietnam: A retrospective observational study



Nguyen Thi Anh Van¹, Pham Ngoc Bich², Bui Thi Ngoc Ha³, Nguyen Thu Huong⁴

¹Principal Investigator, ⁴Associate Professor, Faculty of Basic Medicine, Hanoi University of Public Health, Viet Nam, ²Research Associate, Laboratory Center, Hanoi University of Public Health, Viet Nam, ³Research Associate, Department of Cornea, Ophthalmology Hospital, Thai Binh, Viet Nam

Submission: 24-04-2024

Revision: 03-06-2024

Publication: 01-08-2024

ABSTRACT

Background: Infectious keratitis can be caused by bacteria, fungi, and viruses. Fungi are a common pathogen, especially in developing countries like India, Nepal, and Bangladesh where the prevalence ranges from 20% to 60%. In Vietnam, fungal keratitis accounted for the highest number of keratitis cases in a study conducted at the central eye hospital over a 5-year period (57%). Therefore, it is necessary to collect specific background information connected to the types of fungal keratitis in corneal ulcer cases in this region.

Aims and Objectives: The aim of this study was to investigate the prevalence of fungal keratitis and the epidemiological features in 216 cases of fungal keratitis out of a total of 240 cases of infectious keratitis. **Materials and Methods:** This retrospective study collected secondary data from medical records of 240 inpatients with infectious keratitis who were treated at the ophthalmology hospital in Thai Binh, Vietnam, from January 01st, 2021 to June 30th, 2022. Patients with a positive fungal-directed smear were analyzed in detail for the type of fungus isolated, sociodemographic data, predisposing risk factors, prior treatment modalities, and laboratory results for the distribution pattern of fungus species.

Results: Among the 240 cases, 126 (52.5%) were diagnosed with fungal keratitis by direct microscopic examination. Culture results showed the highest rate of *Fusarium* spp. (43.3%). The age group of 41–60 years was most commonly involved (40.5%). Males were more affected by fungal keratitis than females, (53.2% compared to 46.8%), with farmers being the most common occupation correlated with fungal keratitis (55.6%). The rate of fungal keratitis patients due to agricultural injuries was the highest compared to other risks (47.6%) and most patients self-medicated before going to the hospital, with many not knowing or remembering what medications they had taken (52.4%). **Conclusion:** The study revealed a high rate of fungal keratitis among the total of infectious keratitis cases in Thai Binh, Vietnam. *Fusarium* spp. was the most commonly isolated fungi. The study also highlighted the impact of agricultural injuries on fungal keratitis, especially in regions like Thai Binh.

Key words: Fungal keratitis; *Fusarium* spp.; Keratitis

Access this article online

Website:

<http://hepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v15i8.65103

E-ISSN: 2091-0576

P-ISSN: 2467-9100

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INTRODUCTION

Infectious keratitis can be caused by bacteria, fungi, and viruses. Fungi are a common pathogen, especially in developing countries like India, Nepal, and Bangladesh where the prevalence ranges from 20% to 60%.¹⁻³ In Vietnam, fungal keratitis accounted for the highest number of keratitis cases in a study conducted at the central eye

hospital over a 5 year period (57%).⁴ The most common fungi causing keratitis include *Fusarium*, *Aspergillus*, *Candida*, *Curvularia*, and *Penicillium*.^{5,6} Agricultural injuries, particularly from plant-based agents, often lead to a higher risk of fungal corneal ulcers due to the tropical climate and environmental conditions in places like Thai Binh, Vietnam. The Thai Binh Ophthalmology Hospital receives many patients for fungal keratitis treatment every year. Therefore,

Address for Correspondence:

Dr. Nguyen Thi Anh Van, Principal Investigator, Faculty of Basic Medicine, Hanoi University of Public Health, Thai Binh, Viet Nam.

Mobile: +84.973984783. **E-mail:** ntav@huph.edu.vn

it is necessary to collect specific background information connected to the types of fungal keratitis in corneal ulcer cases in this region.

Aims and objectives

The current study is done to report the prevalence of fungal keratitis and the epidemiological features of fungal keratitis.

MATERIALS AND METHODS

This retrospective cross-sectional study collected medical records of patients with fungi identified by microscopic examination with the direct method and gram stain or positive corneal cultures for fungus. Information on fungal keratitis was gathered from a total of 240 qualified patients' medical records with infectious keratitis diagnosed on admission at the corneal and conjunctival department, Ophthalmology Hospital in Thai Binh, Vietnam, from January 01, 2021, to June 30, 2022.

Data on demographic information, medical history, medication use, eye disease information, and microbiological data were collected. Evaluation standards for test results were in accordance with decision No. 26/QD-BYT dated January 03, 2013, by the Ministry of Health, which promulgates "guidelines for technical processes in medical microbiology."

Data management and analysis

Data were entered using Excel and analyzed using SPSS 20.0 software. Descriptive analysis included frequencies and rates of variables related to the general information of the research subjects.

Ethical considerations

The study was approved by the Scientific and Ethics Council at Hanoi University of Public Health in accordance with to decision No. 022-177/DD-YTCC dated May 31, 2022.

RESULTS

Out of 240 cases, 126 were diagnosed with fungal keratitis, representing 52.5% of the total cases, as confirmed by direct microscopy examination. Among these 126 cases, 60 showed positive results only through culture testing. On analyzing the 126 cases, it was found that 67 (53.2%) were male and 59 (46.8%) were female. The age group with the highest number of recorded keratitis cases was 41–60, accounting for 51 cases (40.5%). More than half of the study participants (55.6%) were farmers and the majority (90.5%) resided in rural areas (Table 1).

Table 1: Demographic parameters of patients with fungal keratitis

Characteristics	Frequency	Percentage
Age group		
<18 years old	4	3.2
18–40 years old	38	30.2
41–60 years old	51	40.5
>60 years old	33	26.2
Gender		
Male	67	53.2
Female	59	46.8
Location		
Rural area	114	90.5
Urban area	12	9.5
Occupation		
Farmer	70	55.6
Worker	4	3.2
Students	2	1.6
Government employee	4	3.2
Retiree	44	34.9
Others	2	1.6
Total	126	100

Table 2: Results of fungal culture and identification

Fungus species	Total	Percentage
<i>Aspergillus fumigatus</i>	12	20
<i>Cephalosporium</i>	2	3.3
<i>Curvularia</i>	4	6.67
<i>Fusarium</i> spp.*	26	43.3
<i>Penicillium</i>	2	3.43
Unspecified hyaline	14	23.3
Total	60	100

**Fusarium* species

Table 3: Risk factors of fungal keratitis

Risk factors	No. of cases	Percentage
Agricultural injuries	60	47.6
Industrial injuries	14	11.1
Surgery in the ocular surface	2	1.6
Cleft eyelid, entropion	4	3.2
Using contact lenses	0	0
Diabetes	0	0
Unknown	46	36.5
Total	126	100

Table 4: Initial medications on detecting the signs/symptoms

Initial medications	No. of cases	Percentage
Not remember/not know	66	52.4
Antibiotic eye drops	24	19.0
Antifungal eye drops	6	4.8
Eye drops containing corticoid	8	6.3
Others	18	14.3
No treatment yet	4	3.2
Total	126	100

The rate of fungal keratitis patients with positive culture results was 60 cases out of 126 cases, accounting for 47.6%,

and 66 culture cases did not grow. The culture results in the medical records showed that keratitis caused by *Fusarium* spp. was the most common (43.3%) (Table 2).

The rate of fungal keratitis patients due to agricultural injuries is highest compared to other risks (47.6%) (Table 3).

Most patients self-medicate before going to the hospital, and the majority do not know or remember which medications they have taken (52.4%). There are a small number of patients who did not take any medications before going to the hospital for examination and treatment (3.2%) (Table 4).

DISCUSSION

Among 240 medical records studied in this research, the most common pathogens causing keratitis were fungi, accounting for 52.5%. Our study is consistent with similar studies on keratitis pathogens in Vietnam. A study by Dong et al., at the Vietnam National Eye Hospital based on the results of 1706 samples, found that fungal keratitis accounted for 57% (n=1115).⁴ This prevalence in Asia, in general, was 32.7% of a total of 6626 eyes in a prospective multicenter study of infectious keratitis in Asia.³ Vietnam is in tropical zones with a warm and wet climate, creating favorable conditions for fungal growth, which explains the high prevalence of fungal keratitis.

The positive results of fungal culture were only 47.6%, quite similar to the results of other studies, such as the study by Dong et al., where 426 of 838 fungal cultures were positive (50.8%).⁴ This is often due to the long onset period and patients often misuse medication before detection or diagnosis. In addition, the amount of specimen collected in fungal keratitis is also less than in other infections. Research by Ferrer and Alió shows that taking specimens using the corneal biopsy method produces a higher positive rate than conventional methods.⁷ Collecting sufficient specimens in terms of both quantity and depth in the corneal stroma affects microbiological results, especially for cases where fungi migrate into the deep stroma. For a successful culture, the fungi in the specimen must be alive; meanwhile for staining, both living and inactivated fungi can be seen. Furthermore, fungal culture also depends on other conditions such as temperature, humidity, and nutrients. Culture results showed that *Fusarium* spp. was the most common, accounting for 43.3%, followed by unidentified filamentous fungi accounting for 23.3%. Yeast-associated keratitis was not isolated in our study. Filamentous fungi such as *Fusarium* and *Aspergillus* thrive in tropical regions like Vietnam. Other researchers also suggest that *Fusarium* spp. is the main species causing fungal keratitis,¹⁻³ in Nepal, it was 31.9%,² and in China, it was 73.3%.⁸

Fungal keratitis can occur in patients of any age (from 2 to 95 years old). However, in young and old age groups, the cause is often due to trauma or injuries in daily life or sequelae of other eye diseases. In this study, patients with fungal keratitis were mainly in the age group from 18 to 60 years old, accounting for 74.6%. The results of our study are consistent with national and international studies.^{3,4,9} A study in Nepal showed that corneal ulcers were highest (84%) between 21 and 60 years of age.⁹ Hoffman's research in Southern India showed that patients (from 21 to 50 years old) often suffer from fungal keratitis.¹⁰ It is interesting to note that farmers make up the majority (55.6%), this group being at high risk for eye injuries due to their occupational hazards. The agricultural injuries from tree branches, grains, and rice leaves are also related to this group of diseases (47.6%). Reflecting the actual situation in the Thai Binh province of Vietnam, where agriculture is the main occupation for working-age people. Of the total 126 medical records, 90.5% of patients lived in rural areas where unsanitary living and working environments have created conditions for bacteria, viruses, fungi, etc. to grow and cause diseases. This fact aligns with studies in Vietnam where agriculture-related injuries accounted for 53.3%,⁴ in Nepal where 75% were farmers and 84.7% of trauma was due to vegetative matter and in China, especially injuries from plants accounted for 25.7% in all patients.⁸ In countries where agriculture is the main industry, the prevalence of fungal keratitis is high. The study by Chidambaram et al., in India, shows a rate of 63%, while research by Leck et al., in Ghana shows a rate of 72%.^{11,12}

This study found that the majority of patients visited other medical facilities for examination and treatment before going to the hospital with 52.4% not remembering or knowing the initial medications used. This rate is similar to studies conducted at the central eye hospital (46%).⁴ In summary, most patients in this study still obtained medication over the counter at pharmacies, which is a factor that delays the treatment process, especially in the early stages. We found that 6.3% of patients used eye drops containing corticosteroids, which are contraindicated in this case. Fungal infections are due to increased toxicity and decreased immunity of the eye to infections, and overuse of antibiotics can also be a factor in the development of fungi. Research records show that 19% of patients used antibiotics before going to the hospital, similar to Dong et al., research which also showed that 27.4% of patients with fungal keratitis used medicines containing antibiotics, and 2.5% containing corticosteroids before coming to the hospital.⁴ In India, a rate of 29.2% use topical corticosteroids in patients with fungal keratitis.¹

Limitations of the study

Due to limited time and resources, the study only evaluated and analyzed the prevalence of fungal keratitis from January 01, 2021, to June 30, 2022 in a province in Vietnam.

Keratitis is a common disease with pathogens other than fungi such as bacteria and viruses. Therefore, it is necessary to conduct more studies on keratitis caused by non-fungal pathogens to provide comprehensive evaluations.

The study did not show an association between fungal keratitis and patients' eye hygiene habits because the research data were extracted from medical records. Prospective studies with questionnaires about patients' eye hygiene habits will help overcome this limitation.

CONCLUSION AND RECOMMENDATION

In this study, the rate of fungal keratitis is high, accounting for 52.5% of the total number of keratitis cases. The culture results show that keratitis caused by *Fusarium* spp. is the highest at 43.3%. The study is based on the results of two staining and culture methods with a sensitivity of only 52.4% culture positive. It is recommended that more molecular biology tests, pathology, histopathological cells, etc. should be developed for fungal keratitis diagnosis at Thai Binh Provincial Ophthalmology Hospital so that the disease can be detected quickly, accurately, and promptly.

Moreover, it is necessary to seek examination and treatment at medical facilities. People should not self-medicate or buy medications over the counter and should not delay seeking medical attention. Farmers working in agriculture are the most common population affected by fungal keratitis (55.6%). Therefore, it is recommended that people of working age in rural areas take measures to prevent agricultural injuries at work such as wearing protective glasses and helmets.

ACKNOWLEDGMENT

The authors would like to acknowledge the Ophthalmology Hospital Thai Binh staff for their assistance.

REFERENCES

- Kusumesh R, Ambastha A, Arya LK, Kumari A, Kumari N, Sinha BP, et al. Epidemiological and microbiological profiles of microbial keratitis in a tertiary eye center in Eastern India (Bihar). *Indian J Ophthalmol.* 2003;71(11):3506-3512.
- Bajracharya L, Bade AR and Gurung R. Demography, clinical features, and outcome of fungal keratitis presenting in tertiary eye care in Nepal. *Asian J Med Sci.* 2023;14(9):145-151. https://doi.org/10.4103/IJO.IJO_1605_23
- Khor WB, Prajna VN, Garg P, Mehta JS, Xie L, Liu Z, et al. The Asia cornea society infectious keratitis study: A prospective multicenter study of infectious keratitis in Asia. *Am J Ophthalmol.* 2018;195:161-170. <https://doi.org/10.1016/j.ajo.2018.07.040>
- Dong PN, Hang DT, Duong NT, Lien MT, Chen AC and Aldave AJ. Infectious keratitis in Vietnam: Etiology, organisms, and management at Vietnam National Eye Hospital. *Int J Ophthalmol.* 2022;15(1):128-134. <https://doi.org/10.18240/ijo.2022.01.19>
- Ansari Z, Miller D and Galor A. Current thoughts in fungal keratitis: Diagnosis and treatment. *Curr Fungal Infect Rep.* 2013;7(3):209-218. <https://doi.org/10.1007/s12281-013-0150-110.1007/s12281-013-0150-1>
- Mahmoudi S, Masoomi A, Ahmadikia K, Tabatabaei SA, Soleimani M, Rezaie S, et al. Fungal keratitis: An overview of clinical and laboratory aspects. *Mycoses.* 2018;61(12):916-930. <https://doi.org/10.1111/myc.12822>
- Ferrer C and Alió JL. Evaluation of molecular diagnosis in fungal keratitis. Ten years of experience. *J Ophthalmic Inflamm Infection.* 2011;1(1):15-22. <https://doi.org/10.1007/s12348-011-0019-9>
- Xie L, Zhong W, Shi W and Sun S. Spectrum of fungal keratitis in North China. *Ophthalmology.* 2006;113(11):1943-1948. <https://doi.org/10.1016/j.optha.2006.05.035>
- Ganguly S, Salma KC, Kansakar I, Sharma M, Bastola P and Pradhan R. Pattern of fungal isolates in cases of corneal ulcer in the Western periphery of Nepal. *Nepal J Ophthalmol.* 2011;3(2):118-122. <https://doi.org/10.3126/nepjoph.v3i2.5262>
- Hoffman JJ, Burton MJ and Leck A. Mycotic keratitis-a global threat from the filamentous fungi. *J Fungi (Basel).* 2021;7(4):273. <https://doi.org/10.3390/jof7040273>
- 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. <https://doi.org/10.1080/09286586.2018.1454964>
- 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):1211-1215. <https://doi.org/10.1136/bjo.86.11.1211>

Authors' Contributions:

NTAV – Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, manuscript preparation, and submission of article; **NTH** – Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **BTNH** – Statistical analysis and editing of the article; and **PNB** – Data collection and data analysis.

Work attributed to:

Hanoi University of Public Health, Viet Nam; Ophthalmology Hospital, Thai Binh, Viet Nam.

Orcid ID:

Nguyen Thi Anh Van - <https://orcid.org/0000-0001-9694-7191>
Pham Ngoc Bich - <https://orcid.org/0009-0009-4841-0328>
Bui Thi Ngoc Ha - <https://orcid.org/0009-0003-7415-3229>
Nguyen Thu Huong - <https://orcid.org/0000-0001-6910-5677>

Source of Support: Nil, **Conflicts of Interest:** None declared.