

## ORIGINAL ARTICLE

**Clinical Outcome of Fungal Keratitis after Topical use of Injectable Fluconazole**SHAHBAZ ASLAM<sup>1</sup>, NAUSHERWAN AADIL<sup>2</sup>, WAMIQ MEHMOOD<sup>3</sup><sup>1</sup>Associate Professor, NMU & Hospital Multan.<sup>2</sup>Senior Registrar, NMU & Hospital Multan<sup>3</sup>Resident Ophthalmologist, NMU & Hospital MultanCorresponding author: Wamiq Mehmood, Email: [Wamiqhassan312@gmail.com](mailto:Wamiqhassan312@gmail.com), Cell: 03467003338**ABSTRACT****Objectives:** To evaluate the clinical outcome of fungal keratitis after topical use of injectable Fluconazole.**Materials and Methods:** This cross sectional study was conducted in the Department of ophthalmology in Nishtar Medical University, Multan and the duration of this study were from January 2022 to June 2022. Totally 100 patients who were suffering from fungal keratitis were enrolled. The enrolled patients were given topical 2% Fluconazole using Injectable fluconazole 2mg/ml and making it to 2% topical solution. They were also added topical 1% Atropine, lubricant and Cyclosporin A 0.05% was used for corneal melting. Patients were followed after 1 week and 1 month. A predesign questionnaire was used to collect data.**Results:** Out of total 100 patients, 79 were male and 21 were female with mean age of 38.70 ±9.41 years. The most common age group was 20-35 years and 36-50 years, followed by >50 years of age group. Out of total patients, 69 (69.0%) patients had full recovery of appreciable vision, quality of life and pain related complaints. 30 (30%) patients had no improvement in vision. 1 (1%) patient had worsening of keratitis.**Practical implication:** This study suggest that topical use of injectable fluconazole is a safe and effective antifungal drug for the treatment of fungal keratitis. So this study will help the ophthalmologist to select better treatment option in order to recover the patients at time.**Conclusion:** It is concluded that Fluconazole in the form of injection can be a very useful treatment for severe fungal keratitis.**Keywords:** Fluconazole, Fungal Keratitis, Topical, Injectable, Ophthalmology, Sight-Threatening,**INTRODUCTION**

Fungal keratitis is a rare but a serious cause of sight-threatening disorder in both children and adults in the modern world.<sup>(1, 2)</sup> Different factors such as corneal scarring, perforation, and loss of visual function are responsible for such disorder.<sup>(3)</sup> Trauma by organic and plant-based material is one of the risk factor for a fungal infection of the cornea.<sup>(4)</sup> It is caused by infection of the cornea by filamentous fungi or yeasts. Fungi can be classified into yeast or filamentous.<sup>(5)</sup> In low income countries, it accounts for most of cases of microbial keratitis.<sup>(6)</sup>

It is a male predominant disorder, as compared to female, the male were mostly affected.<sup>(7)</sup> In 2020, the incidence of FK was approximately >1 million cases in a year, depending upon the area. Less than 1% of microbial keratitis cases were found in European countries and about over 80% cases were found in south and south-east Asia. However, globally, majority of cases is attributable to the filamentous fungi and these infections predominantly affect the poorest patients in warm, humid, tropical climatic regions.

A large number of infectious diseases exists in Pakistan but the exact and true burden of fungal infection is not known. Fungal infections have been termed as 'hidden killers'. Fungal keratitis is considered as the most common cause of unocular blindness globally. Fungal keratitis also cause severe sight problem in Pakistani population, with an estimated rate of 44/ 100,000.<sup>(8)</sup> Pakistan probably has a high rate of sight-threatening due to fungal infections. So we are conducting this study to evaluate the clinical outcome of fungal keratitis after topical use of injectable Fluconazole. Keratitis can be caused by various organisms including bacteria, fungi, viruses and parasites. Variation is found in the etiology and epidemiology of infectious keratitis from place to place and time to time, so research are essential to have local data. Infectious keratitis is an economic and social problem, mostly poor and middle age peoples are affected.

This study will show that topical use of injectable fluconazole is either effective antifungal drug or it shows no effectiveness for the treatment of fungal keratitis. So this study will help the ophthalmologist to select better treatment option in order to recover the patients at time.

**Objective:** To evaluate the clinical outcome of fungal keratitis after topical use of injectable Fluconazole.**MATERIALS AND METHODS****Study Design and setting:** This Cross-sectional Study was conducted at the Department of ophthalmology in Nishtar Medical University, Multan.**Duration of the study:** Duration of the study was 6 months (January 2022 – June 2022).**Sampling Technique:** Consecutive nonprobability sampling technique was used for the recruitment of patients.**Inclusion Criteria:**

- Patients suffering from fungal keratitis.
- Patients having history of vegetative trauma.
- Patients with satellite lesions on cornea.
- Involvement of corneal stroma.
- Both genders.

**Exclusion Criteria:**

- History of corneal insult other than vegetative trauma.
- Corneal ulcer not definite of fungal keratitis.
- Fungal keratitis extending beyond stroma and anterior chamber.

**METHODS**

Totally 100 patients with fungal keratitis were enrolled in this study. Approval was obtained from hospitals ethical committee. Informed consents were obtained which were duly signed by the patients or their guardian. The purpose of the study was explained to the patients. For the collection of data, a predesign questionnaire were used to collect data after clinical examination of the patients. Demographic data were also noted. The enrolled patients were given topical 2% Fluconazole using Injectable fluconazole 2mg/ml and making it to 2% topical solution. They were also added topical 1% Atropine, lubricant and Cyclosporin A 0.05% was used for corneal melting. Patients were followed after 1 week and 1 month. The follow up of clinical picture and quality of life of the patient were recorded.

**Statistical Analysis:** The SPSS version 25.0 was used for the analysis of collected data. All the collected data were analyzed by using the software SPSS version 25.0.**RESULTS**

In this study a total of 100 patient's fungal keratitis were enrolled. Out of total 46% were male and 54% were female with mean age

of 38.70±9.41 years (Table 1, Fig 1-0). The most common age group was 21-35 years and 36-50 years in which the same number of (46.0%) of patients fall, followed by >50 years in which there is only 8 (8.0%) patients (Table 2, Fig 2-0).

Table 1: Distribution of patients according to gender (n=100)

Variable	Frequency	Percentage
Gender		
Male	79	79.0
Female	21	21.0
	Mean	SD
Age (Years)	38.70	9.41

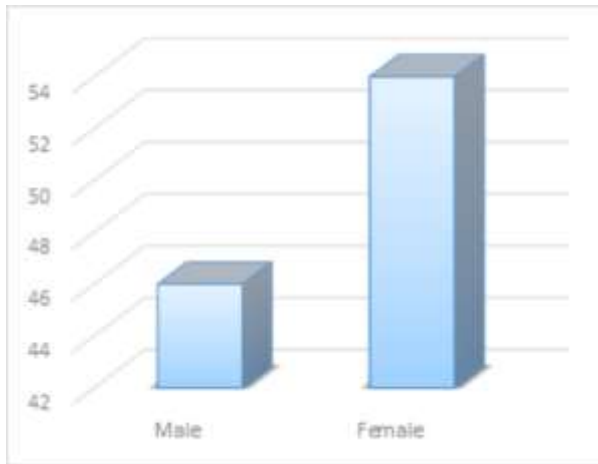


Figure 1: Graphical Representation of gender

Table 2: Distribution of patients according to age group (n=100)

Age Group (Years)	Frequency	Percentage
21-35	46	46.0
36-50	46	46.0
> 50	8	8.0
Total	100	100.0

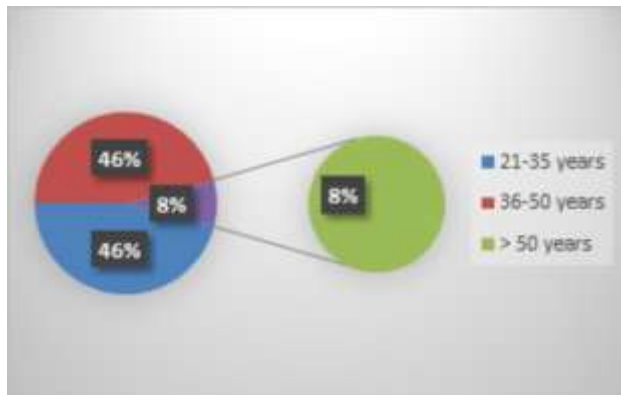


Figure 2: Graphical Representation of distribution of patients according to age group (n=100)

Out of total patients, 69 (69.0%) patients had recovery of appreciable vision, quality of life and pain related complaints. 30 patients had no improvement in vision. 1 patient had worsening of keratitis. (Table 2-0)

Table 3: Distribution of patients according to Vision Recovery (n=100)

Vision Recovery	Frequency	Percentage
Yes	69	69.0
No	30	30.0
Worsening of keratitis	1	1.0
Total	100	100.0

Table 4: Stratification of age group and gender with respect to vision recovery (n=100)

Age group (years)	Vision Recovery			P-Value
	Yes	No	Worsening of keratitis	
21-35	32	14	0	0.86
36-50	31	14	1	
> 50	6	2	0	
Gender	Yes	No	Worsening of keratitis	P-Value
Male	55	23	1	0.82
Female	14	7	0	

## DISCUSSION

Globally, the prevalence of fungal keratitis is high in tropical and subtropical region.<sup>(9)</sup> It can lead to severe ocular morbidity and cause blindness.<sup>(10)</sup> The treatment of fungal keratitis is a challenge for ophthalmologists because the antifungal agents are not always easily available in many countries. Antifungal medications commonly used in ophthalmologic department include polyene, ketoconazole, fluconazole, itraconazole, and miconazole.<sup>(11)</sup> For the 1<sup>st</sup> time Fungus was documented in 1879 and accounts for 40 to 50% of all cases of keratitis.<sup>(12)</sup> There are about seventy types of fungi but two are more relevant in ophthalmology which are yeast and filamentous fungi. In this study we used fluconazole in the form of injection to see its effect. A number of risk factors are responsible for the development of fungal keratitis, these factors includes age, gender, pre-existing ophthalmic, income status, occupation, contact-lens use and region. In a study conducted in Larkana Sindh, the reported incidence of fungal keratitis patients in Pakistani population was 38.45%.<sup>(13)</sup> This study was conducted in order to evaluate the clinical outcome of fungal keratitis after topical use of injectable Fluconazole. In our study majority of peoples got improved form fungal keratitis. These results are similar to that of natamycin 5% for the treatment of fungal keratitis.<sup>(14)</sup> In our study only 1% patients got worsening of keratitis. Fluconazole in the form of injection can be a very useful treatment for severe fungal keratitis. In case of failure of the treatment the patients often leads to call for early surgical intervention like penetrating keratoplasty. In this study most of the patients were improved by topical use of Injectable Fluconazole. In another study it is also stated that Topical fluconazole 0.2% is a safe and effective antifungal drug for the management of filamentous mycotic keratitis.<sup>(15)</sup>

In our study most of the patients were male. Similar results were also given by some other epidemiologic studies.<sup>(15-17)</sup> Ashok Kumar Narsani stated in his study that 62.1% male were affected. In the entire world .males engaged more in outdoor activities as compared to females.<sup>(18)</sup> So in Pakistani population male were dominant in outdoor activities so the chances of this disease is also high. Age is also one of the risk factor as it is stated that trauma is common in the lower age groups peoples.<sup>(19)</sup> In our study most of the patients were fall in 21-35 years and 36-50 years of age group. Both factors age and gender are not considered as an independent risk factors for fungal keratitis, they both affect other risk factors such as trauma, which is more common in younger men. Most studies shows that patients of age group of 20–40 years were very prone to disease.<sup>(20, 21)</sup> Ashok Kumar Narsani et al.<sup>(22)</sup> also stated that 68.97% patients were between the 3<sup>rd</sup> and 5<sup>th</sup> decade of life.

The prevalence of fungal keratitis is more in warm climate. This study was conducted in Multan, Pakistan which is warm climate area. A Saad-Hussein et al<sup>(23)</sup> stated that hot and windy climate makes fungal keratitis. Multan is among fast-growing cities in Punjab, Pakistan. From 1960–2013, an average increase of 1.9 °C in the mean lowest temperature has been observed in Punjab province, with a projected increase of 1.4 °C in the following 30 years<sup>(24)</sup>.

## CONCLUSION

It is concluded that Fluconazole is a good antifungal though not available in topical form. But still further data is required.

## REFERENCES

1. Al-Falki YH, Alshehri MA, Joseph MR, Hamid ME. Fungal keratitis caused by a rare ocular pathogen, *Gjaerumia* minor: A case report. *Saudi Journal of Ophthalmology*. 2018;32(2):160-3.
2. Gopinathan U, Garg P, Fernandes M, Sharma S, Athmanathan S, Rao GN. The epidemiological features and laboratory results of fungal keratitis: a 10-year review at a referral eye care center in South India. *Cornea*. 2002;21(6):555-9.
3. Mravičić I, Dekaris I, Gabrić N, Romac I, Glavota V, Mlinarić-Missoni E. An overview of fungal keratitis and case report on trichophyton keratitis. *Keratitis*. 2012:1-14.
4. Hoffman JJ, Burton MJ, Leck A. Mycotic keratitis—A global threat from the filamentous fungi. *Journal of Fungi*. 2021;7(4):273.
5. Smedsgaard J, Nielsen J. Metabolite profiling of fungi and yeast: from phenotype to metabolome by MS and informatics. *Journal of experimental botany*. 2005;56(410):273-86.
6. Schaefer F, Bruttin O, Zografos L, Guex-Crosier Y. Bacterial keratitis: a prospective clinical and microbiological study. *British Journal of Ophthalmology*. 2001;85(7):842-7.
7. Punia RS, Kundu R, Chander J, Arya SK, Handa U, Mohan H. Spectrum of fungal keratitis: clinicopathologic study of 44 cases. *International journal of ophthalmology*. 2014;7(1):114.
8. Denning D, Zafar A. K. Jabeen, J. Farooqi, S. Mirza.
9. Brown L, Leck AK, Gichangi M, Burton MJ, Denning DW. The global incidence and diagnosis of fungal keratitis. *The Lancet Infectious Diseases*. 2021;21(3):e49-e57.
10. Tilak R, Singh A, Maurya OPS, Chandra A, Tilak V, Gulati AK. Mycotic keratitis in India: a five-year retrospective study. *The Journal of Infection in Developing Countries*. 2010;4(03):171-4.
11. Xie L, Zhai H, Zhao J, Sun S, Shi W, Dong X. Antifungal susceptibility for common pathogens of fungal keratitis in Shandong Province, China. *American journal of ophthalmology*. 2008;146(2):260-5. e1.
12. Tena D, Rodríguez N, Toribio L, González-Praetorius A. Infectious keratitis: microbiological review of 297 cases. *Japanese journal of infectious diseases*. 2019;72(2):121-3.
13. Shah SIA, Shah SA, Abbasi PRSA, Fatima H, Soomro AA. Etiology of infectious keratitis as seen at a tertiary care center in Larkana, Pakistan. *Pakistan Journal of Ophthalmology*. 2016;32(1).
14. Tanure MAG, Cohen EJ, Sudesh S, Rapuano CJ, Laibson PR. Spectrum of fungal keratitis at Wills eye hospital, Philadelphia, Pennsylvania. *Cornea*. 2000;19(3):307-12.
15. Sonogo-Krone S, Martino S-D, Ayala-Lugo R, Torres-Alvariza G, Ta CN, Barbosa L, et al. Clinical results of topical fluconazole for the treatment of filamentous fungal keratitis. *Graefes Archive for Clinical and Experimental Ophthalmology*. 2006;244(7):782-7.
16. Iyer SA, Tuli SS, Wagoner RC. Fungal keratitis: emerging trends and treatment outcomes. *Eye & contact lens*. 2006;32(6):267-71.
17. Tuft S, Tullo A. Fungal keratitis in the United Kingdom 2003–2005. *Eye*. 2009;23(6):1308-13.
18. Tucker P. The physical activity levels of preschool-aged children: A systematic review. *Early childhood research quarterly*. 2008;23(4):547-58.
19. Arunga S, Kintoki GM, Gichuhi S, Onyango J, Ayebazibwe B, Newton R, et al. Risk factors of microbial keratitis in Uganda: a case control study. *Ophthalmic epidemiology*. 2020;27(2):98-104.
20. Deorukhkar S, Katiyar R, Saini S. Epidemiological features and laboratory results of bacterial and fungal keratitis: A five-year study at a rural tertiary-care hospital in western Maharashtra, India. *Singapore medical journal*. 2012;53(4):264.
21. Ong HS, Fung SS, Macleod D, Dart JK, Tuft SJ, Burton MJ. Altered patterns of fungal keratitis at a London ophthalmic referral hospital: an eight-year retrospective observational study. *American journal of ophthalmology*. 2016;168:227-36.
22. Narsani AK, Nangdev PR, Surhio SA, Kumar M, Jatoi SM. Demographic pattern, risk factors, clinical and microbiological characteristics of fungal keratitis. *JLUMHS*. 2012;11(01):42.
23. Saad-Hussein A, El-Mofty H, Hassanien M. Climate change and predicted trend of fungal keratitis in Egypt. *East Mediterr Health J*. 2011;17(6):468-73.
24. Deng J-L, Shen S-L, Xu Y-S. Investigation into pluvial flooding hazards caused by heavy rain and protection measures in Shanghai, China. *Natural Hazards*. 2016;83(2):1301-20.