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Trends and Clinical Outcomes of Fungal Keratitis in Canada: a 20-year Retrospective Multicentre Study

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Abstract

Purpose: An increase in fungal and particularly filamentous keratitis has been observed in many geographic areas, mostly in contact lens wearers. This study seeks to characterize long-term trends in fungal keratitis in a continental climate area to provide guidance for diagnosis and treatment.

Design: Retrospective multicentric case series.

Methods: Cases of microbiology-confirmed fungal keratitis from 2003 to 2022 presenting to tertiary care centers across Canada were included. Charts were reviewed for patient demographics, risk factors, visual acuity, and treatments undertaken.

Results: A total of 138 patients were identified: 75 had yeast keratitis while 63 had filamentous keratitis. Patients with yeast keratitis had more ocular surface disease (79% vs 28%) while patients with filamentous keratitis wore more refractive contact lenses (78% vs 19%). *Candida* species accounted for 96% of all yeast identified, while *Aspergillus* (32%) and *Fusarium* (26%) were the most common filamentous fungi species. The mean duration of treatment was 81 ± 96 days. Patients with yeast keratitis did not have significantly improved visual acuity with medical treatment (1.8 ± 1 LogMAR to 1.9 ± 1.5

LogMAR, $p = 0.9980$), in contrast to patients with filamentous keratitis (1.4 ± 1.2 LogMAR to 1.1 ± 1.3 LogMAR, $p = 0.0093$).

Conclusions: Fungal keratitis is increasing in incidence, with contact lenses emerging as one of the leading risk factors. Significant differences in the risk factors and visual outcomes exist between yeast keratitis and filamentous keratitis which may guide diagnosis and treatment.

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Introduction

Fungal keratitis has historically been an uncommon cause of infectious keratitis in non-tropical geographic areas, with poor visual outcomes despite extensive medical and surgical treatment^{1,2}. Patients with fungal keratitis are five times more likely to experience corneal perforation requiring therapeutic penetrating keratoplasty (TPK) and have larger corneal scars following prolonged treatment³. In similar temperate climates, such as Northern Europe, an incidence of 0.02 per 100, 000 people has been reported⁴. Given its low prevalence, there are often significant diagnostic challenges starting from delayed recognition by the clinician to prolonged time until positive fungal culture and susceptibility testing results are available.

An increase in incidence of fungal keratitis has been noted over the last decade in tropical and non-tropical climates^{4,5}. This appears to be at least in part attributable to the increase of contact lens (CL) use as a risk factor for fungal keratitis⁵⁻⁷. While historically yeast keratitis has typically been more common in temperate areas, a proportional increase in filamentous fungi has also been described lately^{2,7}.

This large retrospective study provides an update on the epidemiology, patient demographics, risk factors for infection, and clinical outcomes of fungal keratitis in a large temperate and continental climate geographical area from 2003 to 2022.

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Methods

This is a multicentre retrospective observational case series reviewing microbiologically confirmed cases of fungal keratitis in Canada. The study was approved by the institutional clinical research ethics boards of all participating centers (University of British Columbia Clinical Research Ethics Board; University of Toronto Health Sciences Research Ethics Board; Centre Hospitalier de l'Université de Montréal Research Ethics Board; McMaster University – McMaster Research Ethics Board; Université Laval Comités d'éthique de la recherche avec des êtres humains de l'Université Laval). Informed consent was not required by any ethics boards list previously due to the retrospective nature of this study. This study adheres to the tenets of the Declaration of Helsinki and applicable governmental laws of Canada. The microbiological laboratory specimen database at participating centers was searched for corneal scrapings culture positive for fungi from January 1, 2003 to January 1, 2022. Clinical records of identified cases were reviewed for demographic information, risk factors (including CL use, ocular injury, pre-existing ocular surface disease (OSD), ocular surgery, systemic disease, healthcare contact), corrected distance visual acuity (CDVA; Snellen and LogMAR), and medical or surgical management. Ocular surface disease was defined as any disease involving the ocular surface requiring prescription medications. Initial visual acuity was recorded from the first clinical encounter describing a corneal ulcer; final visual acuity was recorded from the earliest clinical encounter in which clinical resolution was deemed by the clinician, or the final visual acuity noted in the chart. The data was collated by the leading center (University of British Columbia).

Antifungal susceptibility testing was performed according to institutional protocols. In brief, corneal scrapings were taken using a surgical blade (Bard-Parker, Caledonia, MI) and plated onto Sabouraud dextrose agar, blood agar and chocolate agar plates, as well as glass slides for Gram stain and Giemsa stain, and thioglycolate broth. The agar plates were incubated at 35°C for at least 24 hours. Antifungals tested include fluconazole (0.12 – 256 µg/ml), itraconazole (0.015-16 µg/ml), voriconazole (0.008-8 µg/ml), 5-fluorocytosine (0.06-64 µg/ml), amphotericin B (0.12- 8 µg/ml), and caspofungin (0.008-µg/ml). Susceptibilities based on the minimal inhibitory concentration (MIC) were interpreted according to the Clinical and Laboratory Standards Institute M27-S3 and M27-S4 guidelines⁸.

Statistical analysis was performed using Prism GraphPad software. The mean, standard deviation, and descriptive statistics were calculated. Student's t-test and chi-squared tests were used. $P < 0.05$ was considered significant.

Results

A total of 138 patients/138 eyes with microbiologically confirmed fungal keratitis were included in the study: 69 males and 69 females, from 2003 to 2022. There were 68 right eyes and 70 left eyes involved. The average age of these patients was 59 ± 20 years (range 19 to 92 years). Most patients presented with central ulcers (73%) and the first corneal scrapings were taken at 21 ± 37 days from symptom onset. Seventy-five (54%) patients had yeast keratitis while 63 had filamentous fungal keratitis (46%). A significant rise in the incidence of fungal keratitis was noted when comparing the first half of the study period to the second half (0.01 cases/100 000 people from 2003 to 2012 vs. 0.03 cases/100 000 people from 2013 to 2022, $p = 0.034$). With the COVID-19 pandemic beginning at the end of 2019, the number of cases fell over the last four years. There were no significant changes over time in the proportion of fungal keratitis that was attributed to yeast versus filamentous fungi. Only two centres (Vancouver, BC and Toronto, ON) had data for all years of the study period (**FIGURE 1**).

1.1 Risk Factors

Of the 138 patients with fungal keratitis, OSD was identified in 74 cases (54%), including herpes simplex virus (HSV) keratitis ($n=16$), previous corneal abrasion/ulcer ($n=6$), ocular graft-versus-host disease (oGvHD, $n=6$), varicella zoster virus (VZV) keratitis ($n=5$), pseudophakic bullous keratopathy (PBK, $n=4$), neurotrophic ulcer ($n=4$), alkali burn ($n=3$), dry eye ($n=3$), limbal stem cell deficiency (LSCD, $n=3$), Steven-Johnson syndrome (SJS, $n=3$), exposure keratopathy ($n=3$), trachoma ($n=2$),

decompensated Fuchs' endothelial dystrophy (n=2), blepharitis (n=1), keratouveitis (n=1), radiation keratopathy (n=1), scleritis (n=1), keratoconus (KC, n=1), ocular rosacea (n=1), recurrent corneal erosion syndrome (RCES, n=1), and Sjogren syndrome (SS, n=1).

Sixty patients were CL wearers (45%). Cases with CL use as a risk factor were most common during the years with the highest incidence of fungal keratitis, from 2016 to 2019. Thirty patients (50%) wore bandage contact lenses (BCLs) while 24 patients wore refractive CL (40%), and it is unclear what type of CLs the remaining 6 patients wore (10%). Of the refractive CLs used, 1 case was cosmetic, 2 cases were 2-week duration soft CLs, 1 case was monthly soft CLs, and the rest were soft CLs of unspecified duration. One case of *C. krusei* involved the use of the recalled-product AMO Complete Moisture Plus Solution. Twenty-nine of these patients (25%) slept while using their CLs, and 20 patients (17%) also engaged in water-contact with CLs in (including swimming, showering, hot tub use, etc). Interestingly, refractive CL was significantly more common in cases of *Fusarium* keratitis (47% vs 17%, $p = 0.0124$). No increase in CL-related cases overall and refractive CL-cases were observed over the study period.

Ocular injury was implicated in 35 cases (28%), including insect in fornix for days (1), hit with hard object (1), BCL accidentally removed during separate medical procedure (1), tetracaine abuse following corneal abrasion with nonhealing epithelial defect (1), wood injury (2), metallic foreign body (1), unknown foreign body (1), soil/vegetation injury (2); the mechanisms in the rest of the cases were not specified. Ten cases were acquired from international locations with tropical climates (4 in India, 2 in Southern United States

of America [California, Florida], 2 in the Caribbean [Trinidad and Tobago, Jamaica], and 1 in Ghana).

Fifty-seven patients (41%) had previous ocular surgery, and 13 of these post-surgical patients (27%) self-reported manipulating their BCL. Of the post-surgical patients, many had undergone anterior segment surgery: PK (therapeutic or optical; n=32), cataract surgery (CS, n=18), amniotic membrane transplant (AMT, n=11), Keratoprosthesis (n=11; all Boston K-Pro), lamellar keratoplasty (Descemet stripping automated endothelial keratoplasty [DSAEK]: n=2, Descemet membrane endothelial keratoplasty [DMEK]: n=1), laser-assisted in situ keratomileusis (LASIK, n=1), photorefractive keratectomy (PRK, n=1), corneal cross linking (CXL, n=1), pterygium excision (n=1), globe rupture repair (n=1), and limbal stem cell transplant (LSCT) procedures (Cincinnati procedure: n=2, keratolimbal allograft: n=3, LSCT: n=2, conjunctival limbal autografting: n=1).

1.2 Microbiological Diagnosis

Seventy-five samples of yeast and 64 samples of filamentous fungi were identified. One sample in the filamentous group grew both *Scedosporium apiospermum* and *Pseudoallescheria boydii*. *C. albicans* and *C. parapsilosis* accounted for 89% of all yeast identified, while *Aspergillus* (32%) and *Fusarium* (26%) predominated the filamentous fungi group (**FIGURE 2**). Prior to 2018, *C. albicans* and *C. parapsilosis* were pan-sensitive to Amphotericin B, Fluconazole, and Voriconazole, but more recently, three new cases of *C. albicans* (1/9 samples) and *C. parapsilosis* (2/12 samples) subjected to susceptibility testing were only intermediately susceptible to Amphotericin

B. *C. guilliermondii* was sensitive to fluconazole (1/1 sample) but intermediately susceptible to Amphotericin B (1/1 sample), while the one sample of *C. krusei* isolated was resistant to Fluconazole as expected. Overall, 97% (32/33 samples) of *Candida* identified were sensitive to fluconazole (**SUPPLEMENTAL TABLE 1**). Half of the *Fusarium* species isolated were susceptible to Amphotericin B and were all resistant to Fluconazole. Voriconazole sensitivity was not tested for *Fusarium*. *Penicillium* mold was susceptible to Fluconazole and Voriconazole.

1.3 Clinical Course and Treatment

Patients presented with LogMAR 1.7 ± 1.2 CDVA on average, which did not change significantly following treatment (final CDVA LogMAR 1.6 ± 1.5). On average, patients were started on antifungal treatment 31 ± 44 days after symptom onset. Patients were treated for an average of 81 ± 96 days, which was similar between patients with yeast and filamentous keratitis. Most patients were treated with topical 0.15% Amphotericin B (29%), 1% Voriconazole (25%), or both (11%). A minority of patients additionally received 2% Fluconazole (3.6%), 0.5% Caspofungin (0.7%), or 2% Ketoconazole (1.4%) either as single agents or in combination with other antifungals. Eight patients were able to access and use topical 5% Natamycin which is currently not commercially available in Canada. One patient with yeast keratitis and one patient with *Fusarium* keratitis received intrastromal antifungal injections: one patient received eight injections of intrastromal amphotericin B for *C. parapsilosis* and an optical penetrating keratoplasty (OPK), and the final CDVA was 0.6 LogMAR, while the other case resulted in corneal perforation and underwent emergent TPK. Twenty-six patients (19%) also received oral

antifungal therapy, which was most commonly Voriconazole (58% of all patients that received oral antifungals). A total of 42 patients (30%) received 48 PKs amongst them: 36 were TPK (6 of which were repeat transplants) and 12 were TPK. By the end of the study period, nine patients (6.5%) underwent either enucleation or evisceration of the infected eye. Of these, 2 were due to *C. albicans*, 3 due to *C. parapsilosis* and 1 due to *Cryptococcus* in the yeast group, and 2 due to *A. fumigatus*, 1 due to filamentous fungi, and 1 due to *Penicillium* in the filamentous fungi group.

1.4 Differences between Yeast and Filamentous Keratitis

Patients with yeast or filamentous keratitis had similar demographics with respect to their age, sex, and eye involved (**Table 1**). Before being diagnosed with fungal keratitis, patients with yeast keratitis were more likely to be on topical steroids (45% vs 25%, $p = 0.0152$), and more likely to be on topical antibiotics (64% vs 46%, $p = 0.0343$); a high proportion of yeast keratitis patients were on both (52% vs 16%, $p < 0.0001$). In contrast, more filamentous keratitis cases were on antibiotics only (30% vs 12%, $p = 0.0082$). Few patients in either group were on steroids alone (4% vs 5%, $p = 0.82$). Though there was no significant difference in the proportion of CL use between these two groups, patients with filamentous keratitis wore more refractive CL (78% vs 19%, $p = 0.0001$). Patients with yeast keratitis were also more likely to have OSD (79% vs 28%, $p = 0.0001$), have previous anterior segment surgery (61% vs 27%, $p = 0.0001$), have had healthcare contact within the past year (13% vs 0%, $p = 0.0240$). When examining systemic risk factors, patients with yeast keratitis were more likely to be

immunosuppressed than patients with filamentous keratitis (32% vs 9%, respectively, $p = 0.0040$).

Both groups presented with similar CDVA: yeast keratitis patients had on average 1.8 ± 1 LogMAR while filamentous keratitis patients had 1.4 ± 1.2 LogMAR. CDVA improved significantly in patients with filamentous keratitis (final visual acuity = 1.1 ± 1.3 LogMAR, $p = 0.0093$), but not patients with yeast keratitis (final visual acuity = 1.9 ± 1.5 LogMAR, $p = 0.9980$) (**FIGURE 3**). Ulcer size at the time of diagnosis was not significantly different between the two groups (17 ± 17 mm² in yeast keratitis, 13 ± 15 mm² in filamentous keratitis; $p = 0.2$). Initiation of anti-fungal treatment was more delayed in yeast keratitis patients (39 ± 51 days) when compared to filamentous keratitis patients (19 ± 26 days, $p = 0.011$). Nine cases of yeast keratitis (11%) and 10 cases of fungal keratitis (17%) had bacterial co-infection; there was no significant difference between the proportion of patients with polymicrobial infections between the two groups ($p = 0.3101$). Most patients with yeast keratitis were treated with Amphotericin B initially (60%), followed by Voriconazole (30%). On the other hand, patients with filamentous keratitis were mostly treated with Voriconazole (52%) rather than Amphotericin B (40%). Fewer cases of yeast keratitis achieved clinical resolution with medical treatment (47% vs 73%, $p = 0.0018$), and thus required more surgical intervention (64% vs 46%, $p = 0.0343$). In the yeast group, 27 patients received 24 TPKs (4 repeat transplants) and 8 OPKs. In the filamentous fungi group, 14 patients received 12 TPKs (2 repeat transplant) and 4 OPKs. Of the patients that underwent enucleation/evisceration surgery: 6 patients had yeast keratitis and 3 patients had filamentous keratitis.

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DISCUSSION

This study reports the largest series of fungal keratitis in Canada to date and one of the largest and longest series in North America to analyze shifting trends in fungal keratitis over a 20 year-period. The incidence of fungal keratitis increased over the past decade, though this trend was not sustained during the years of the COVID-19 pandemic. CL use was recognised as a common risk factor for fungal keratitis, particularly in patients with filamentous keratitis wearing refractive CL. In patients that had yeast as the causative organism, topical antibiotic and steroid use, recent healthcare contact, and immunosuppression were additional risk factors as compared to patients with filamentous keratitis. Final visual acuity was significantly improved from initial visual acuity only in patients with filamentous keratitis, while patients with yeast keratitis required more surgical intervention.

Fungal keratitis is a relatively uncommon diagnosis in temperate and continental climates in comparison to tropical climates, though its incidence appears to be increasing in several geographic areas including the United Kingdom, Switzerland, and Spain^{5,9-11}. The observed increase in incidence of fungal keratitis in temperate climates was often observed to be non-significant, largely due to insufficient follow-up time and reduced sample size^{9,10}. This study found a significant increase in the incidence of fungal keratitis over the past two decades. The number of cases of fungal keratitis declined during the COVID-19 pandemic. This finding is likely multifactorial in etiology, from decreased trauma and CL use to decreased access to and use of health care

during this time¹². Reduced travel during the pandemic, particularly to tropical climates, may also have contributed to reduced cases.

Classically, yeast keratitis is more frequent in temperate climates whereas filamentous fungi more commonly cause infectious keratitis in tropical climates, often resulting from injuries with organic materials¹³. The increased incidence in fungal keratitis reported over the recent years in non-tropical climates seems to be largely attributable to a rise in filamentous keratitis in temperate climates, approaching parity with yeast keratitis in some studies¹. This was not observed in our study, where both yeasts and molds seemed to increase over time at the same rate.

The most common risk factors identified for fungal keratitis in this study were CL use, topical steroid use, topical antibiotic use, previous ocular surgery and OSD. Previous studies have substantiated the increased incidence of filamentous keratitis in the emergence of molds as CL-related pathogens^{10,11,14}. CL use is a well-established risk factor for bacterial keratitis¹⁵, though there is increasing evidence for its role in fungal keratitis, particularly filamentous keratitis. In a previous multicentre study conducted in USA from 2001 to 2007 by one of the authors, refractive CL use was identified in 37% of fungal keratitis cases, 86% of which were attributable to filamentous fungi. In that study, the rise in number of *Fusarium* cases in CL wearers between 2004 and 2006 was largely associated with the period that ReNu with MoistureLoc (Bausch & Lomb, Rochester, NY) was available. There was a subsequent steep return to previous incidence after the product was pulled from the market. Nonetheless, persistence of a

higher number of fungal keratitis cases after the *Fusarium* outbreak has been reported¹⁶. An association between the use of soft refractive CLs and *Fusarium* keratitis was also noted in this study, but there is a paucity of national data regarding trends in CL use. In the UK, the incidence of CL wear as a risk factor in the fungal keratitis population rose from 12% in the 1994-2006 series to 57% in the 2016 series^{5,17}. The predilection of filamentous fungi for CLs is postulated to be due to the formation of biofilms on CL and storage cases¹⁸. Some studies report CL use to be the predominant risk factor in young, healthy patients without significant ocular disease^{14,19}. Though CL use was not significantly different between yeast and filamentous keratitis groups, this study found refractive CL use more common in filamentous keratitis while bandage CL use was more common in yeast keratitis. This is in line with previous evidence that yeasts are associated with therapeutic CL use while refractive CL use is more closely associated with filamentous keratitis²⁰.

This study further confirms our previous findings that topical steroid use and OSD were particularly significant risk factors for the development of yeast keratitis²¹. The widespread prophylactic and pre/post-operative use of topical corticosteroids and antibiotics may alter the conjunctival microbiome and hamper local immunity, allowing fungi to proliferate and infect susceptible corneal tissue²². Topical antibiotics may cause iatrogenic corneal toxicity, allowing fungal infection to worsen and delaying appropriate diagnosis^{23,24}. Patients with fungal keratitis have decreased and altered bacterial diversity in both their affected and unaffected eyes, which may play a role in their risk of

infection²³. A similar mechanism may play a role in patients under systemic immunosuppression, an additional risk factor for fungal keratitis¹⁷.

This study reports worse overall outcomes for yeast keratitis vs filamentous, with no improvement in average final visual acuity and more patients needing surgical intervention and resulting in enucleation. This could be in part attributable to the reported ocular and systemic comorbidities in patients with yeast keratitis. In fact, the observed diagnostic delay for yeast keratitis in patients using topical steroids may be attributable to decreased intensity of pain and better visual acuity initially²⁵, masquerading clinical signs in an infection that usually presents with more severe keratitis²⁶. The presentation of yeast keratitis may also more closely resemble bacterial keratitis in comparison to filamentous fungal keratitis, which could contribute to the delay in its diagnosis²⁷. Additionally, in the above-mentioned study by Keay et al surgical intervention appeared to be more common in filamentous keratitis but was also highest in the sub-group of patients with OSD²⁰.

In patients that developed keratitis from filamentous fungi, relatively rapid detection and treatment with antifungals improved their vision significantly. This has been seen previously in studies from tropical climates such as Florida⁶, where over 70% of patients achieved 20/40 or better vision.

Antifungal medications of choice in this series were Amphotericin B initially (60%), followed by Voriconazole (30%) in yeast keratitis and Voriconazole (52%) followed by

Amphotericin B (40%) in filamentous keratitis. While the Mycotic Ulcer Treatment Trial (MUTT) 1 trial demonstrated the superiority of topical Natamycin when compared to Voriconazole in filamentous fungal keratitis²⁸, Natamycin is presently not commercially available in Canada and only 8 patients in our series could access this medication (via out-of-country purchase or special access programs). Clinical outcomes in patients treated with Natamycin did not seem to differ from the rest of our cohort.

Only two patients in this series received intrastromal antifungal injections treatment and had opposing outcomes. Previous evidence regarding the benefit of intrastromal injection in fungal keratitis has been conflicting²⁹. Konar et al found that intrastromal voriconazole hastens the resolution of filamentous keratitis with poor response to topical therapy in small corneal ulcers without a hypopyon³⁰, while others showed a similar rate of resolution when comparing topical antifungals alone versus additional intrastromal injections^{31,32}. A large randomized control trial recently showed no benefit and increased complications when intrastromal injections were added to topical natamycin³³. Further research is needed to better define the role of intrastromal antifungal injections for patients with fungal keratitis.

Half of the *Fusarium* species included in this study were sensitive to Amphotericin B. There is a body of previous evidence showing the superiority of Amphotericin B to newer azoles in *Fusarium* spp in terms of MIC^{34–36}. Although Natamycin remains the drug of choice for filamentous keratitis cases as per the results of MUTT I³⁷, our findings corroborate the use of Amphotericin B as a suitable alternative in countries where

Natamycin is not available, or as an appropriate second-line treatment in high endemic areas where Natamycin and Voriconazole resistance has been increasing over time³⁸.

An interesting element in our study was the high sensitivity to Fluconazole reported for *Candida*, which would make this agent a suitable first line treatment for *Candida* keratitis in our geographic area. Sensitivity to Fluconazole 0.2% in *Candida* keratitis isolates was reported to be minimal by Spierer et al³⁹, to the point that Fluconazole was not recommended as the drug of choice for either *albicans* or non-*albicans* subspecies. Effectiveness of Fluconazole treatment was described in earlier series of *Candida* keratitis^{40,41}. This inconsistency may reflect local microbiological patterns, as resistance has been observed to be high in countries with widespread use of Fluconazole³⁴.

There are several limitations to this study given its retrospective nature. A multi-decade study time may not have included all cases that occurred during this period. A standardized data recording process was not in place across the diverse study sites. Though an increase in incidence was observed, it is possible this was the result of improved fungal detection methods and centralized referral patterns. All cases were detected by culture of corneal scrapings which adds validity to the diagnosis of fungal keratitis, but other methods for diagnosis such as confocal microscopy (only available in one of the centers involved in the study) and corneal biopsy were not explored in this study. There were no cases that utilized these techniques in this study, and these techniques are rarely utilized in Canada due to limited equipment and slow turnaround times for pathology analysis.

In summary, this multicentre series reports an overall increase in incidence of fungal keratitis at 5 Canadian tertiary cornea centres over a 20-year period. This study also identified the relative rise in filamentous fungi and the emergence of CL wear as a risk factor for fungal infections. Given that these observations have occurred in a geographic area characterised by temperate and continental climate, the ophthalmological community should maintain a high level of suspicion for fungal keratitis in patients with CL-related infections not responding to standard empirical treatment. Further research would be needed to elucidate the mechanisms underlying this long-term shift in fungal ecology and risk factors, and to possibly define preventative public health strategies.

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FIGURES

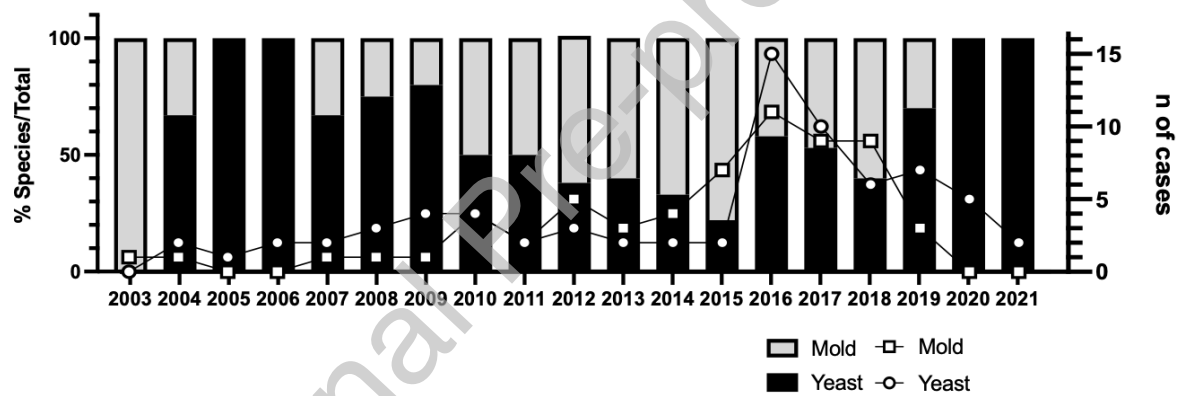


Figure 1: Number of cases and proportion of yeast versus filamentous keratitis in

Canada from 2003 to 2021. Centers with data points for all years were included.

The proportion of a given species with respect to the total case number per year is represented by the grey and black bars (mold and yeast, respectively). The number of cases of a given species per year is represented by boxes and circles markers (mold and yeast, respectively).

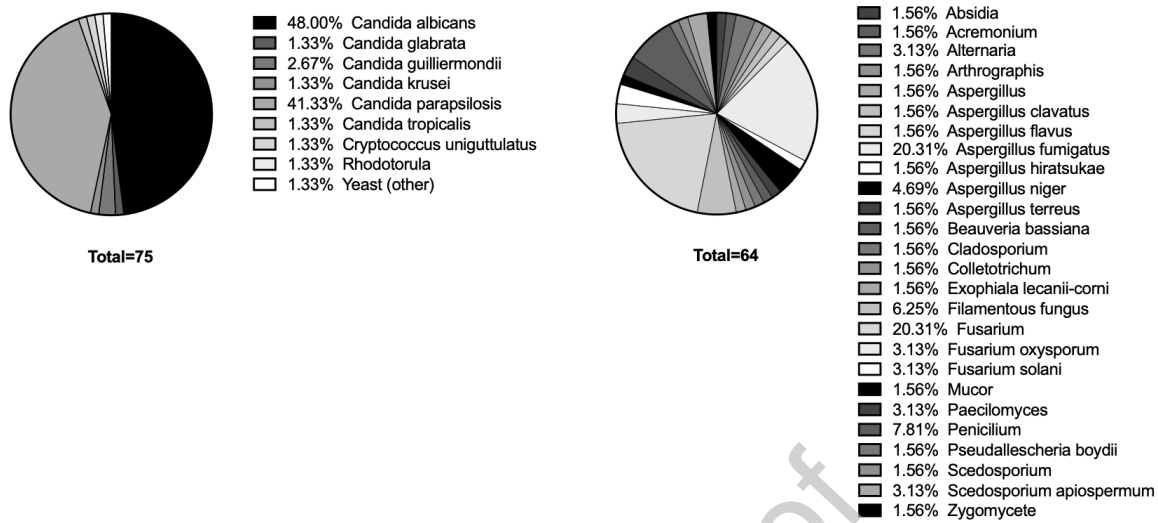


Figure 2: Species of fungi identified by microbiological analysis. Percentages of total samples identified is indicated. Total = number of samples.

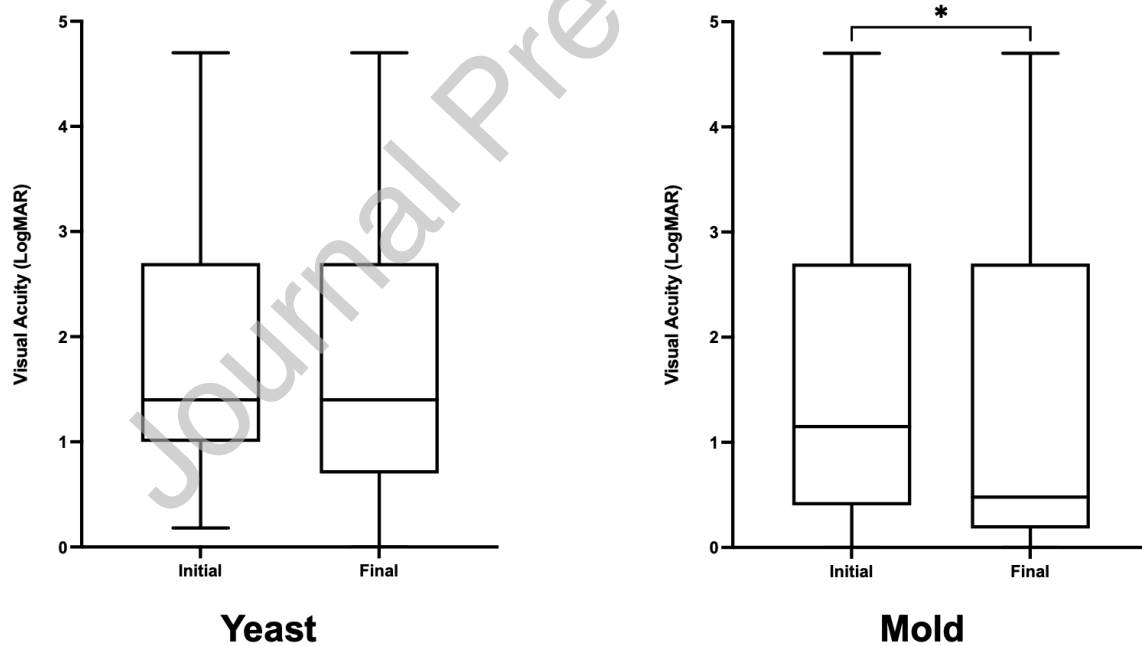


Figure 3: Mean corrected distance visual acuity at initial diagnosis versus final encounter in patients with yeast versus filamentous keratitis. Visual acuity is represented in LogMAR. ** indicates $p < 0.05$.

Table 1: Demographics, risk factors, and outcomes of patients with fungal keratitis. age is described as mean \pm standard deviation. $p < 0.05$ was deemed statistically significant.

		Yeast n= 75	Mold n = 63	p
Sex	69 M, 69 F	40F, 35M	29F, 34M	0.39
Age	59 \pm 20y	61 \pm 20y	56 \pm 20y	0.12
Eye	68 OD, 70 OS	42 OD, 33 OS	26 OD, 37 OS	0.08
Risk Factors				
Ocular Surface Disease	74 yes, 64 no (54% yes)	57 yes, 18 no (79% yes)	13 yes, 45 no (28% yes)	<0.05
Topical Steroids	50 yes, 22 no (69% yes)	34 yes, 7 no (83% yes)	16 yes, 15 no (52% yes)	<0.05
Immunosuppression	25 yes, 85 no (23% yes)	22 yes, 45 no (33%)	3 yes, 40 no (7%)	<0.05
Diabetes mellitus	9 yes, 95 no (8.7% yes)	6 yes, 60 no (9%)	3 yes, 35 no (8%)	0.8345
Contact Lens Use	60 yes, 72 no (45% yes)	33 yes, 40 no (45% yes)	27 yes, 32 no (46% yes)	0.9
Water Contact with Contact Lenses	20 yes, 95 no (17% yes)	9 yes, 60 no (13% yes)	11 yes, 35 no (24% yes)	0.1319
Sleeping in Contact Lenses	29 yes, 96 no (25% yes)	21 yes, 48 no (30% yes)	8 yes, 38 no (17% yes)	0.1146
Ocular Injury	35 yes, 90 no (28% yes)	17 yes, 53 no (24% yes)	17 yes, 37 no (31% yes)	0.3732
Previous Ocular Surgery	57 yes, 18 no (77% yes)	46 yes, 7 no (87% yes)	16 yes, 2 no (89% yes)	0.74
Manipulation of Bandage Contact Lens	13 yes, 36 no (27% yes)	12 yes, 21 no (36% yes)	1 yes, 15 no (6.25% yes)	<0.05
Healthcare Contact within 1 Year	8 yes, 89 no (7% yes)	8 yes, 55 no (13% yes)	34 no (0% yes)	<0.05
Recent Travel	9 yes, 76 no (11% yes)	6 yes, 44 no (12% yes)	3 yes, 32 no (9% yes)	0.6131
Polymicrobial Infection	19 yes, 119 no (14%)	9 yes, 66 no (12% yes)	10 yes, 53 no (16%)	0.31
Treatment				
Medical Treatment Only	82 yes, 56 no (59% yes)	35 yes, 39 no (47% yes)	47 yes, 17 no (73% yes)	<0.05
Surgical Intervention	77 yes, 61 no (56% yes)	48 yes, 27 no (64% yes)	29 yes, 34 no (46% yes)	<0.05

Trends and Clinical Outcomes of Fungal Keratitis in Canada: a 20-year Retrospective Multicentre Study

Table of Contents

Fungal keratitis in temperate climates has increased in incidence over the past few decades.

Yeast keratitis was slightly more common than filamentous keratitis (64% vs 46%). Common risk factors include ocular surface disease, contact lens use, prior anterior segment surgery and ocular injury. *Candida*, *Aspergillus*, and *Fusarium* were the most common organisms.

Filamentous keratitis cases had significantly different risk factors, improved final visual acuities and decreased need for surgical intervention, as compared to yeast keratitis.

Word count: 75/75