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Fungal keratitis culture results from a major commercial laboratory

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Introduction

In the United States, nearly 1 million healthcare visits for keratitis (inflammation of the cornea) occur each year, and an estimated 6% of suspected microbial keratitis cases are caused by fungi.(1, 2) However, data on the causative species of fungal keratitis primarily come from decades-old single-center studies.(3) To better characterize the burden of fungal keratitis and help inform treatment practices, we used data from a major national commercial laboratory to describe testing patterns and causative species.

Methods

We analyzed nationwide Labcorp data sent to the Centers for Disease Control and Prevention's National Syndromic Surveillance Program (<https://www.cdc.gov/nssp/index.html>). We identified results of fungal cultures ordered during March 1, 2019–October 1, 2023 and selected patients with International Classification of Diseases, 10th Revision code H16 (keratitis) listed as a reason for testing.

Results

Among 1,160,133 fungal culture results, 5,104 had keratitis listed as a reason for testing; 182 were excluded from the analysis because of missing or non-fungal results. Among the 4,922 remaining results, 774 (15.7%) were positive (Table 1). Percent positivity was highest among patients aged 45–64 years (19.2%), males (17.0%), and those in the South (19.0%).

Positive results (>40 different species) were 76.6% molds and 21.8% yeasts (Table 2).

Among molds, 63.1% were hyaline (mainly *Fusarium* [36.2%] and *Aspergillus* [35.4%]),

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This activity was reviewed by the CDC and was conducted consistent with applicable federal law and CDC policy (e.g., 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.). The data are fully de-identified, so this analysis was not subject to review by the Centers for Disease Control and Prevention institutional review board.

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and 35.9% were dematiaceous (most frequently *Bipolaris* (now *Curvularia*) [30.8%] and *Curvularia* [27.6%]). *Candida albicans* was the most common yeast (49.1%). Mold results were more common among patients in the South (86.9% vs 74.6% of yeasts, $p < 0.001$).

Discussion

Our study provides updated epidemiologic data and highlights the fungal diversity implicated in keratitis throughout the United States. Consistent with previous literature, males, middle-aged adults, and residents of the South appeared to be disproportionately affected, possibly because of increased risk for occupational ocular trauma.(3, 4) The predominance of molds in the South is also similar to results from single-center studies and is likely related to the warmer climate.(3) The potential for climate-related geographic expansion of pathogenic fungi and antifungal resistance warrants increased attention to timely diagnosis and treatment of fungal keratitis.

Worldwide, most fungal keratitis cases are caused by *Fusarium* and *Aspergillus*.(4) the most common molds identified in this analysis. These fungi have demonstrated decreased susceptibility to natamycin and voriconazole in keratitis in India.(5) Species-level information was unavailable for most *Fusarium* results in this analysis; however, studies have shown that *F. solani* in particular appears to have higher in-vitro minimum inhibitory concentrations to multiple antifungals.(6) Dematiaceous molds, isolated in over a quarter of results in this analysis, are also notable causes of fungal keratitis worldwide.(2, 4) The clinical differences between keratitis caused by dematiaceous and hyaline fungi, along with patient risk factors and geographic location, may help guide initial treatment decisions.(4)

Limitations include the inability to identify contaminants or multiple results per patient. Furthermore, data about risk factors, clinical features, treatment, antifungal resistance, or outcomes were unavailable, and the dataset may not be nationally representative. Nonetheless, our study provides updated causative species data, which may inform future surveillance efforts and guide treatment practices.

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Disclaimer:

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Data availability statement:

This study used third-party data that we cannot legally distribute. All relevant summary data are within the manuscript and the supporting files.

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Table 1.

Fungal culture results^a from patients with keratitis listed as a reason for testing in a large national commercial laboratory, by result, March 2019–October 2023, United States

| | All results (n=4,922) | | Mold (n=596) | | Yeast (n=169) | | p-value |
|---|-----------------------|------------|--------------|----------|---------------|----------|---------|
| | n positive/n tested | % positive | n | Column % | n | Column % | |
| Age group, years (n=4,812) | | | | | | | <0.001 |
| 0 to 17 | 10/88 | 11.4% | 10 | 1.7% | 0 | 0.0% | |
| 18 to 44 | 164/1,152 | 14.2% | 142 | 24.6% | 20 | 12.0% | |
| 45 to 64 | 340/1,769 | 19.2% | 270 | 46.8% | 65 | 39.2% | |
| 65+ | 238/1,803 | 13.2% | 155 | 26.9% | 81 | 48.8% | |
| Sex (n=4,822) | | | | | | | 0.003 |
| Male | 381/2,247 | 17.0% | 322 | 55.5% | 57 | 34.5% | |
| Female | 373/2,575 | 14.5% | 258 | 44.5% | 108 | 65.5% | |
| U.S. census region (n=4,921) | | | | | | | <0.001 |
| South | 648/3,410 | 19.0% | 518 | 86.9% | 126 | 74.6% | |
| Northeast | 15/157 | 9.6% | <i>b</i> | <i>b</i> | <i>b</i> | <i>b</i> | |
| West | 69/996 | 6.9% | 38 | 6.4% | 28 | 16.6% | |
| Midwest | 42/358 | 11.7% | <i>b</i> | <i>b</i> | <i>b</i> | <i>b</i> | |
| Provider type (n=4,490) | | | | | | | 0.024 |
| Ophthalmologist | 562/3,175 | 17.7% | 451 | 80.4% | 106 | 69.7% | |
| Optometrist | 38/338 | 11.2% | <i>b</i> | <i>b</i> | <i>b</i> | <i>b</i> | |
| Family, general practice, internal medicine | 25/133 | 18.8% | <i>b</i> | <i>b</i> | <i>b</i> | <i>b</i> | |
| Hospital | 25/124 | 20.2% | 15 | 2.7% | 10 | 6.6% | |
| Other | 72/720 | 10.0% | 52 | 9.3% | 18 | 11.8% | |
| Total | 774/4,922 | 15.7% | 596 | 77.9% | 169 | 22.1% | |

^aLogical Observation Identifiers Names and Codes (LOINC[®]) result codes 580-1, 17947-3, 17948-1, 17949-9, 18482-0, 42804-5, 42805-2, 51723-5, 88143-3

^bnumber <10 or number that would enable calculation of another cell <10.

Table 2.

Fungal culture results from patients with keratitis listed as a reason for testing in a large national commercial laboratory, March 2019–October 2023, United States

| Culture result | n=744 | % |
|--|----------|----------|
| Hyaline mold | 376 | 48.6% |
| <i>Fusarium</i> | 136 | 17.6% |
| <i>Aspergillus</i> | 133 | 17.2% |
| <i>A. fumigatus</i> | 44 | 5.7% |
| <i>A. niger</i> | 43 | 5.6% |
| Unspecified <i>Aspergillus</i> | 28 | 3.6% |
| Other specified <i>Aspergillus</i> | 17 | 2.3% |
| <i>Penicillium</i> | 18 | 2.4% |
| Non-sporulating hyaline mold | 21 | 2.7% |
| <i>Scedosporium</i> | 18 | 2.4% |
| <i>Purpureocillium</i> | 13 | 1.7% |
| <i>Acremonium/Sarcocladium</i> | 11 | 1.4% |
| Other specified hyaline mold ^a | 26 | 3.5% |
| Dematiaceous mold | 213 | 27.5% |
| <i>Bipolaris</i> | 66 | 8.5% |
| <i>Curvularia</i> | 59 | 7.6% |
| <i>Alternaria</i> | 44 | 5.7% |
| <i>Cladosporium</i> | 21 | 2.7% |
| Other specified dematiaceous mold ^b | 13 | 1.7% |
| Unspecified dematiaceous mold | 10 | 1.3% |
| Mucormycete mold | <i>c</i> | <i>c</i> |
| Unspecified mold | <i>c</i> | <i>c</i> |
| Yeast | 169 | 21.8% |
| <i>Candida</i> | 158 | 20.4% |
| <i>C. albicans</i> | 83 | 10.7% |
| <i>C. parapsilosis</i> | 44 | 5.7% |
| <i>C. tropicalis</i> | 11 | 1.4% |
| Other <i>Candida</i> species ^d | 20 | 2.7% |
| Other ^e or unspecified yeast | 11 | 1.4% |
| Unspecified fungus | <i>c</i> | <i>c</i> |

^a*Paecilomyces*, *Beauveria*, *Trametes versicolor*, *Chrysosporium*, *Geotrichum*, *Scopulariopsis*, *Bjerkandera adusta*, *Verticillium*, *Trichoderma*, *Trichophyton*, *Irpex lacteus*, *Sepedonium*.

^bEpicoccum, Exserohilum, Chaetomium, Exophiala, Pithomyces, Phoma.

^cnumber <10 or number that would enable calculation of another cell <10.

^d*C. glabrata*, *C. dubliniensis*, *C. guilliermondii*, *C. pelliculosa*, *C. orthopsilosis*, *C. sake*, *C. lipolytica*.

^eRhodotorula, Trichosporon.

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