

## Background

Once overlooked, invasive fungal infections such as mucormycosis have been thrust into the spotlight after a growing incidence of the disease in COVID-19 patients. Also known as "black fungus," mucormycosis (or zygomycosis) is caused by molds of the order Mucorales and can present itself in multiple locations in the human body, including the sinuses, brain, lungs, and skin<sup>1</sup>. While Mucorales fungal spores can be frequently encountered in the surrounding environment, mucormycosis mainly only develops in the immunocompromised. Therefore, although its severity is well documented, there still has not been a concerted effort to epidemiologically map the incidence and prevalence of the disease globally, especially in developing countries such as India, China, and Brazil. This information will be invaluable for healthcare professionals to properly identify and mitigate the underlying factors causing mucormycosis and effectively treat patients with the disease<sup>2</sup>.

## Methodology

- Systematic literature review was undertaken using the PubMed database to compile information on mucormycosis epidemiology on a worldwide scale.
- Only articles specifically mentioning epidemiological data related to Mucorales fungi (including case reports) and published after January 1, 2000 were included in the final review.
- Sample search: ((Burden) OR (Prevalence) OR (Incidence) OR (Epidemiology)) AND (("Black fungus") OR (Mucormycosis) OR (Zygomycosis) OR ("Mucormycete mold") OR ("Mucormycete mould") OR ("Rhizopus oryzae") OR (Mucor\*)) AND ((France)) AND (["2000/01/01"[Date - MeSH] : "2020/12/31"[Date - MeSH]]) - a new search was done for every country.
- Data and estimates of prevalence/incidence were recorded in a spreadsheet, along with underlying conditions or predisposing factors mentioned in the articles.
- Spatial mapping of the number of hits/included articles per country was conducted for qualitative analysis.

## Results

Qualitatively, the mapping of search "hits" from the literature review shown in Fig 1 clearly shows the skewed nature of epidemiological knowledge on mucormycosis – while most of the world has minimal articles/studies reporting mucormycosis, there is a **large clustering of literature on mucormycosis from India, the United States, and France**. What is especially evident is the miniscule, or absolute lack thereof, of research into mucormycosis from most developing countries located in South America, Africa, and Asia; in comparison, simply looking at Fig 1, there seems to be a profusion of at least 1 research article reporting on mucormycosis in most European countries, while much of the vast regions of Africa and Asia remain "empty." In fact, **22 out of the 64 (34%) total countries for which at least 1 research article was found in the literature search were from Europe**, representing an outsize proportion of the available literature on the burden of mucormycosis globally.



*Fig 1 Global visualization of the number of "hits"/articles per country*

Another trend that presented itself in the master spreadsheet of literature search results was specifically related to the underlying conditions among mucormycosis patients – while most patients from countries in the US and Europe had underlying hematological malignancies or traumatic accidents/burns that made them vulnerable to fungal colonization, the **majority of patients from Asian countries, especially India, had uncontrolled diabetes mellitus** as their primary predisposing factor for developing mucormycosis infection. Additionally, many "hits" (articles) from countries such as China, India, Iran, and Brazil only encompassed singular case reports; on the other hand, **research articles from the US and France frequently included multicenter prospective or retrospective studies** following thousands of patients over many years.

## Conclusion

- Clear disparity in available literature on mucormycosis epidemiology – the majority of articles from developed countries in Europe and North America (besides outliers like India and China)
- Additional disparity in the quality/depth of studies conducted – well funded, multicenter studies more often seen from developed countries rather than more narrative style case reports
- Large number of mucormycosis patients with diabetes from developing countries such as India points to intersection of public health knowledge with infectious disease epidemiology
  - Only patients with uncontrolled diabetes (i.e. they are unaware of being diabetic) are vulnerable to mucormycosis
- Even estimations of mucormycosis burden in the minimal number of articles from developing countries used statistical data pulled from previously conducted studies in developed countries to extrapolate these approximations
- **Future directions:** Initial, in-depth review into the current state of mucormycosis burden around the globe exposes need for further research/funding into the unique conditions impacting patients in developing countries
  - Increasing incidence of diabetes in developing countries also indicates possible increase in mucormycosis cases seen in upcoming years

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<sup>1</sup><https://www.cdc.gov/fungal/diseases/mucormycosis/definition.html>

<sup>2</sup> Cornely et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. *Lancet Infect Dis.* 2019 Dec;19(12):e405-e421 doi: 10.1016/S1473-3099(19)30312-3.