

## Let's talk about mucormycosis emergency with COVID-19: Invest in future

Kamlesh Malik<sup>1</sup>, Jyoti Arora<sup>1</sup>, Parvin K. Yadav<sup>2</sup>, Kusum K. Rohilla<sup>3</sup>

<sup>1</sup>College of Nursing, Postgraduate Institute of Medical Sciences, Rohtak, Haryana, <sup>2</sup>M.Ch. Student, Department of Ophthalmology, Postgraduate Institute of Medical Education and Research, Chandigarh, <sup>3</sup>PhD Scholar, College of Nursing, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India

### ABSTRACT

Despite recent breakthroughs in the detection and treatment during the COVID-19 pandemic, mucormycosis is a serious infection with a high death rate. It is a filamentous fungal infection from the zygomycetes class of order mucorales. It is a fatal fungal infection with a 50% or higher overall fatality rate. Mucormycosis is a fungal infection caused by mucor, which is a mold that can be found in soil, rotting fruits, and vegetables. It can primarily affect the brain, lungs, and sinuses. It is very much fatal in patients with diabetes or who are highly immunocompromised such as patients with cancer. In addition to more than 50% mortality rate, surgical intervention may require necrotic tissue removal, which leads to severely disfiguring surgery.

**Keywords:** Black fungus, COVID-19, mucormycosis

### Introduction

Mucormycosis, also known as black fungus, has sparked public alarm during the COVID-19 pandemic,<sup>[1]</sup> but the disease is not all that frequent.<sup>[2]</sup> Mucormycosis is primarily a fungal infection, which mainly occurs in post-COVID-19 patients who are also suffering from uncontrolled diabetes (56%). A recent study from India also reported 388 mucormycosis cases, nearly 56% of whom were suffering from uncontrolled diabetes.<sup>[3,4]</sup> Another study from Chandigarh also discovered a higher prevalence of fungal infection in north India, as well as a higher mortality rate after infection with COVID-19.<sup>[5]</sup>

According to World Health Organization (WHO), India is the new diabetes capital of the world, with the highest diabetes prevalence rates in the world, with 9% of India's adult population

suffering from diabetes.<sup>[6,7]</sup> Although mucormycosis is a typically opportunistic infection among post-COVID-19 patients that primarily affects the person who is already suffering from diabetes mellitus (DM), acquired immunodeficiency syndrome (AIDS), cancer, chronic renal disease, neutropenic, and who underwent organ or hematopoietic stem cell transplants.<sup>[8,9]</sup>

Mucormycosis is a fungal infection caused by mucorales fungi belonging to the zygomycetes class.<sup>[10]</sup> These fungi are usually found in organic waste, i.e., fruits, vegetables, and soil.<sup>[11]</sup> The member of this family that most usually causes mucormycosis infection is *Rhizopus oryzae*.<sup>[12,13]</sup> Another member of the Apophysomyces family, which thrives in tropical and subtropical climes, is common in India as well. Other species, i.e., *Rhizopus arrhizus*, *Rhizopus microsporus*, *Apophysomyces variabilis*, and *Rhizopus homothallicus* were the most commonly recognized fungi for mucormycosis.<sup>[12]</sup>

### Classifications of Mucormycosis

1. Rhinocerebral mucormycosis: Rhinocerebral mucormycosis is a fungal infection that affects the brain and sinuses.

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**Address for correspondence:** Ms. Kusum K Rohilla, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.

E-mail: kus2211@gmail.com

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Patients with poorly controlled diabetes and those on immunosuppressive medicines, such as kidney transplant recipients are at risk

2. Pulmonary mucormycosis: It is a fungal infection that mostly affects the lungs. Mucormycosis is a kind of mucormycosis that is common among cancer patients as well as individuals who have had an organ or stem cell transplant
3. Gastrointestinal mucormycosis: The gastrointestinal system is most affected by gastrointestinal mucormycosis. Premature and low-birth-weight newborns with weakened immunity to infection are particularly vulnerable
4. Cutaneous mucormycosis: Cutaneous mucormycosis mainly affects the skin. Common among patients with leukemia, diabetes mellitus, graft versus host disease, HIV, and intravenous drug use following burn/skin injury
5. Disseminated mucormycosis: When mucor infection spreads through the bloodstream to other organs, it is said to be widespread and known as disseminated mucormycosis
6. Miscellaneous mucormycosis: In miscellaneous mucormycosis, other sites may be affected, although these are less prevalent.<sup>[14,15]</sup>

## Pathophysiology of Mucormycosis

When a person's immune system is weakened or compromised, i.e., in patients with diabetes and cancer, who are depleted of white blood cells (WBCs) due to their any therapy, such as in transplant recipients to prevent organ rejection.<sup>[10]</sup> Because of its propensity to quickly enter tissues and cause severe tissue necrosis.<sup>[16]</sup> Steroids, i.e., dexamethasone cause a decrease in the deadly overexuberant inflammatory response, which is again emerged as a viable therapeutic during the COVID-19 phase.<sup>[17]</sup> A reduced inflammatory response affects the body's ability to fight opportunistic fungal infections such as mucormycosis.

Mucormycosis is particularly common in these patients according to recent studies.<sup>[18]</sup> Poorly controlled sugar and steroid treatment predispose patients to higher risk for mucormycosis. Using corticosteroids in diabetes patients with uncontrolled diabetes is a perfect storm for fungal infections like mucormycosis.<sup>[19]</sup> Patients with mucormycosis have the following signs and symptoms: facial/periorbital swelling (34%), ophthalmoplegia (29%), fever (44%), nasal ulceration/necrosis (38%), reduced vision (30%), sinusitis (26%), and headache (25%).

## Risk Factors and Route of Transmission

In patients with moderate or severe COVID-19, cytokine storm develops among patients who are taking frequent steroids to calm the immune system and reduce the inflammatory response, which is often very fatal.<sup>[20]</sup> Steroids eventually raise blood glucose levels and weaken the immune system and expose the body to other opportunistic infections like bacterial and fungal infections.<sup>[21]</sup> Fungal sporangiospores are transmitted to the body via the inhalation route when spore ingested by direct implanted into wounded skin, trauma to body with contaminated soil,

and intravenous drug users transmission,<sup>[22]</sup> and following nasal inoculation it spreads swiftly to surrounding tissues, including the eye orbits, sinuses and occasionally to the brain.<sup>[23]</sup>

## Burden of Mucormycosis

*Indian Journal of Medical Research*, in March, quantified the prevalence of mucormycosis and identified the burden of undiagnosed fungal illness.<sup>[24]</sup> Mucormycosis is significantly underreported since cultures are frequently negative and the first polymerase chain reaction (PCR) diagnostic was just recently commercialized. Because of these reasons, including lack of awareness of the disease, i.e., even qualified physicians had no information and lack of standardized diagnostic procedures to estimate conditions of patients, incidence, and prevalence is also a challenge.<sup>[25]</sup> Research estimates the overall prevalence of mucormycosis in India to be 0.14 instances per 1,000 people or around 187,460 patients.<sup>[24]</sup> When mucormycosis is treated properly the overall death rate ranges from 30% to 46.7%. If these figures were extended to the WHO Southeast Asian Region (SEAR), about 105,000 individuals could die from these illnesses each year.<sup>[25]</sup>

## Treatment of Mucormycosis

Surgical debridement and antifungal medication are two important treatment modalities used to treat mucormycosis. Hyperglycemia, neutropenia, metabolic acidosis, immunosuppressive medicines, and deferoxamine administration are all key predisposing factors for infection.

**1. Surgery:** Surgical debridement of affected tissues should be explored when mucormycosis is discovered. Recent studies stated that proper clinical assessments of rhino-cerebral and pulmonary infection followed by surgical intervention with removal of necrotic tissue and debulking infection helps to enhance survival among mucormycosis patients.<sup>[26]</sup>

**2. Antifungal therapy:** Intravenous liposomal amphotericin-B is the important drug of choice for the first treatment. During step-down therapy, patients who received liposomal amphotericin-B will be given posaconazole or isavuconazole. Studies stated that patients who do not respond to or are unable to take amphotericin-B might be treated with posaconazole or isavuconazole. The choice of posaconazole or isavuconazole for salvage therapy is determined by the severity of the patient's sickness. The usual starting dose of liposomal amphotericin-B or amphotericin-B lipid complex is 5–10 mg/kg per day.<sup>[27]</sup> Amphotericin-B is a common antifungal drug used in the treatment, but supplies are running out due to rising demand.

## Conclusion

Mucormycosis is a life-threatening infection that mainly affects immunocompromised people, those who have taken too many steroids, and people who have had post-COVID-19

opportunistic infections, and it has a high fatality rate despite aggressive multimodal treatment. To begin the right diagnostic workup and treatment, a strong index of suspicion is essential. In post-COVID-19 patients, mucormycosis was most common in the rhino-orbital-cerebral cavities, with diabetes mellitus being the most common underlying illness. Because liposomal amphotericin B is often prohibitive in third-world countries due to financial constraints, our patients were given conventional amphotericin B instead. There must be further evidence supports are required to examine in view of suggesting that early and aggressive delivery of liposomal amphotericin-B for treatment of mucormycosis.

Mucormycosis knowledge aids physicians in providing better patient care by enhancing inter-professional care coordination. Nurses and clinicians who work together will achieve the best results. The prognosis remains grim, even with early, adequate inspection, and treatment by the inter-professional team.

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### Conflicts of interest

There are no conflicts of interest.

### References

1. Rohilla K KV. COVID-19 Emergency in India. *Natl J Community Med* 2021;12:120-1.
2. Mucormycosis: The 'black fungus' maiming Covid patients in India [press release]. 2021. [Last accessed on 2021 May 05].
3. Mucormycosis not uncommon in India: Studies [press release]. 2021. [Last accessed on 2021 May 21].
4. Furman D, Campisi J, Verdin E, Carrera-Bastos P, Targ S, Franceschi C, *et al.* Chronic inflammation in the etiology of disease across the life span. *Nat Med* 2019;25:1822-32.
5. Gow NA, Netea MG. Medical mycology and fungal immunology: New research perspectives addressing a major world health challenge. *Philos Trans R Soc Lond B Biol Sci* 2016;371:20150462.
6. Nagarathna R, Bali P, Anand A, Srivastava V, Patil S, Sharma G, *et al.* Prevalence of diabetes and its determinants in the young adults indian population-call for yoga intervention. *Front Endocrinol (Lausanne)*. 2020;11:507064. doi: 10.3389/fendo.2020.507064.
7. Sharma R, Rohilla K, Chadha L, Malhotra P, Sharmila S, Jelly P. Strategy to prevent infection from Covid-19 among security officers of tertiary care centre: A preexperimental study. *J Family Med Prim Care* 2021;10:3257-61.
8. Vasantha Kalyani C, P M, Kusum K Rohilla. Immunity boosting measures: A gateway toward preventive measure for coronavirus disease 2019. *Natl J Physiol Phar Pharmacol* 2021;11:1-6.
9. Al-Anazi KA, Al-Jasser AM, Al-Anazi KA, Al-Jasser AM. Brucellosis in Immunocompromised hosts. *J Arch Organ Transplant* 2017;1:1-21.
10. Ibrahim AS, Spellberg B, Walsh TJ, Kontoyiannis DP. Pathogenesis of mucormycosis. *Clin Infect Dis* 2012;54(Suppl 1):S16-22.
11. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. *Clin Microbiol Rev* 2000;13:236-301.
12. Hibbett DS, Binder M, Bischoff JF, Blackwell M, Cannon PF, Eriksson OE. A higher-level phylogenetic classification of the Fungi. *Mycol Res* 2007;111:509-47.
13. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, *et al.* Epidemiology and outcome of zygomycosis: A review of 929 reported cases. *Clin Infect Dis* 2005;41:634-53.
14. Kwon-Chung KJ. Taxonomy of fungi causing mucormycosis and entomophthoromycosis (zygomycosis) and nomenclature of the disease: Molecular mycologic perspectives. *Clin Infect Dis* 2012;54:S8-15.
15. Petrikos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. *Clin Infect Dis* 2012;54:S23-34.
16. McDonald PJ. What is the pathophysiology of mucormycosis (zygomycosis). Available from: <https://www.medscape.com/answers/222551-121797/what-is-the-pathophysiology-of-mucormycosis-zygomycosis>. [Last accessed on 06/07/2021].
17. Ahmed MH, Hassan A. Dexamethasone for the Treatment of Coronavirus Disease (COVID-19): A Review. *SN Compr Clin Med* 2020;1-10. doi: 10.1007/s42399-020-00610-8.
18. Noreen S, Maqbool I, Madni A. Dexamethasone: Therapeutic potential, risks, and future projection during COVID-19 pandemic. *Eur J Pharmacol* 2021;894:173854.
19. Report on new treatment for mucormycosis, the deadly 'black fungus'. *J Medical Xpress* [press release]. 2021/05/17 2021.
20. Singh AK, Majumdar S, Singh R, Misra A. Role of corticosteroid in the management of COVID-19: A systemic review and a Clinician's perspective. *Diabetes Metab Syndr* 2020;14:971-8.
21. Perico L, Benigni A, Casiraghi F, Ng LFP, Renia L, Remuzzi G. Immunity, endothelial injury and complement-induced coagulopathy in COVID-19. *Nat Rev Nephrol* 2021;17:46-64.
22. Muszewska A, Pawłowska J, Krzyściak P. Biology, systematics, and clinical manifestations of Zygomycota infections. *Eur J Clin Microbiol Infect Dis* 2014;33:1273-87.
23. Spellberg B, Edwards J, Jr., Ibrahim A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. *Clin Microbiol Rev* 2005;18:556-69.
24. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. *J Fungi (Basel)* 2019;5:26.
25. Black fungusinfection: Are men more susceptible to mucormycosis? Here is what a study suggests [press release]. 2021. [Last accessed on 2021 May 22].
26. Spellberg B, Ibrahim AS. Recent advances in the treatment of mucormycosis. *Curr Infect Dis Rep* 2010;12:423-9.
27. Cox GM. Mucormycosis (zygomycosis). 2021. [Last accessed on 2021 April 21].