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UNMASKING MUCORMYCOSIS: A POST-COVID-19 PUBLIC HEALTH EMERGENCY IN INDIA

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Abstract

Mucormycosis, often dubbed the "black fungus," rose to national and international attention during India's second wave of COVID-19. What was once a rare, opportunistic fungal infection suddenly turned into a parallel crisis, affecting thousands of patients recovering from COVID-19—many of whom had diabetes and had received corticosteroids. This review takes a closer look at how mucormycosis evolved into a post-pandemic emergency, exploring its causes, risk factors, clinical manifestations, diagnostic hurdles, and treatment strategies. The disease is caused by fungi of the Mucorales order, which normally exist harmlessly in the environment but can become lethal when the immune system is compromised. Rhino-orbito-cerebral mucormycosis (ROCM) emerged as the most common and destructive form, often leading to facial disfigurement, vision loss, or worse, death. With timely diagnosis, surgical intervention, and antifungal therapy—especially liposomal amphotericin B—patients can be saved, but delays in diagnosis often mean grim outcomes. India's public health response included declaring the disease notifiable, launching awareness campaigns, and improving drug access, though challenges in rural healthcare access, drug shortages, and lack of early warning systems persist. This review aims not only to map the medical landscape of mucormycosis during the COVID era but also to underscore the importance of preparedness, multidisciplinary collaboration, and public education in tackling such emerging threats. Understanding this deadly yet preventable fungal disease is a crucial step in strengthening our healthcare response for future pandemics and opportunistic infections.

Keywords: Mucormycosis, Black fungus, COVID-19, Rhino-orbito-cerebral, Amphotericin B, Diabetes, Fungal infections, India outbreak, Immunosuppression, Public health response

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Introduction

Mucormycosis, often feared for its rapid and destructive course, is a rare but serious fungal infection caused by molds belonging to the *Mucorales* order. These fungi are typically harmless to most people and are found all around us—in soil, plants, decaying fruits, and even in the air. However, in individuals whose immune defenses are weakened—such as those with uncontrolled diabetes, cancer, or those on immunosuppressive drugs—this infection can turn deadly. Depending on where it strikes in the body, mucormycosis can take several forms, the most common being rhino-orbito-cerebral, which begins in the sinuses and can spread rapidly to the eyes and brain. Other forms include pulmonary, cutaneous, gastrointestinal, and disseminated types [1].

The term "black fungus," though medically inaccurate, gained widespread attention during the COVID-19 pandemic. It refers to the blackish discoloration seen in infected tissues due to tissue death, especially around the nose and palate. This stark visual made a strong impression during news coverage, creating public concern and a sense of urgency around the infection. During the second wave of COVID-19 in India in 2021, mucormycosis emerged as a devastating secondary infection, affecting thousands of recovering COVID patients. This sudden explosion of cases was unlike anything seen before and overwhelmed hospitals already struggling with oxygen shortages and ICU demands. Many of those affected had underlying diabetes and had been treated with steroids to manage severe COVID-19 symptoms—creating a perfect storm for fungal infection. As cases surged, mucormycosis was declared a notifiable disease in India, triggering focused health interventions and emergency responses [2,3].

This review aims to shed light on how mucormycosis became one of the most feared complications during the pandemic in India. By exploring its causes, clinical features, diagnostic challenges, and treatment approaches, we hope to provide a clear understanding of this deadly

fungus and its link to COVID-19. The goal is not only to inform healthcare professionals but also to support the development of more effective strategies to manage and prevent such infections in future health emergencies.

Epidemiology & Outbreak Patterns

Before COVID-19 shook the world, India was already quietly battling a different invisible enemy—mucormycosis. This rare but dangerous fungal infection was far more common in India than in most countries, largely due to the high number of people living with uncontrolled diabetes and widespread exposure to fungal spores in the environment. While the global incidence of mucormycosis hovered around 1.7 cases per million, India reported a staggering 140 cases per million, making it a global hotspot even before the pandemic began [4].

Then came the second wave of COVID-19 in 2021, which pushed India's healthcare system to its limits. Hospitals were overflowing, oxygen supplies were strained, and doctors were doing everything possible to save lives—including prescribing corticosteroids to reduce inflammation in severe COVID-19 patients. But this lifesaving treatment came with a hidden risk. In the weeks following recovery, thousands of patients began reporting symptoms like facial swelling, nasal congestion, vision problems, and black lesions in the mouth or nose. These weren't lingering signs of COVID—they were symptoms of mucormycosis, now turning into a full-blown epidemic within a pandemic [5].

By May 2021, the Indian government was compelled to act swiftly, declaring mucormycosis a notifiable disease under the Epidemic Diseases Act. This meant that all hospitals and clinics had to report suspected or confirmed cases to health authorities, allowing for better surveillance, drug supply coordination (especially liposomal amphotericin B), and awareness campaigns. States like Gujarat, Maharashtra, Rajasthan, Telangana, and Andhra Pradesh emerged as epicenters of this outbreak. Several regional factors contributed to the concentrated surge in these states—high diabetes prevalence, over-the-counter access to steroids, humid climate, and possibly the use of contaminated oxygen or poorly maintained ventilators. Although some of these connections are still being studied, what became clear is that COVID-19 plus uncontrolled diabetes plus steroid use created the perfect storm for mucormycosis to thrive [6].

This outbreak not only exposed gaps in our healthcare preparedness but also reminded us how quickly a secondary infection can escalate when primary disease management is not carefully balanced. It highlighted the need for responsible prescribing, early screening, and most importantly, public awareness—because the earlier this deadly fungus is caught, the better the chances of survival [7].

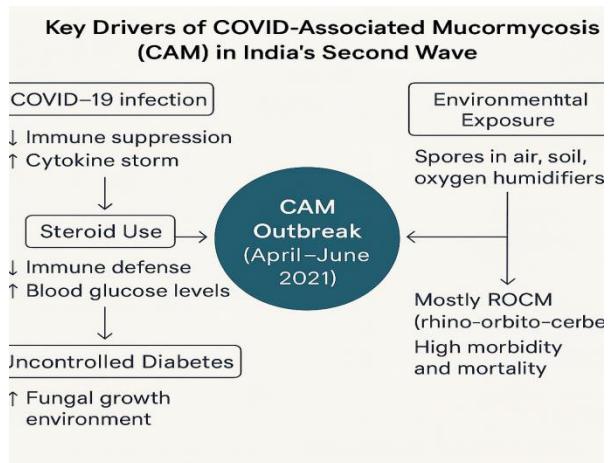


Figure 01: Key drivers of COVID

Etiology and Pathogenesis of Mucormycosis

Mucormycosis is caused by a group of filamentous fungi belonging to the order *Mucorales*, with the most frequently encountered species being *Rhizopus oryzae*, followed by *Mucor*, *Lichtheimia*, and *Rhizomucor*. These fungi are not foreign to our environment—they live naturally in soil, decaying organic matter like leaves, compost, and even in the air we breathe. In most healthy individuals, inhaling these spores doesn't lead to illness, thanks to the immune system acting as a natural barrier. However, in people with weakened immunity or underlying health issues, these otherwise harmless spores can become deadly [8]. The infection typically begins when a person inhales the fungal spores into their sinuses or lungs, but they can also enter the body through cuts, burns, or contaminated medical tools. In patients suffering from diabetes, especially those in diabetic ketoacidosis, or those receiving immunosuppressive treatments like steroids or chemotherapy, these fungi find a perfect breeding ground. Once inside, the spores germinate into long, branching structures called hyphae that invade and grow rapidly through blood vessels—a process known as angioinvasion. This leads to the formation of blood clots, cuts off oxygen supply to tissues, and results in the characteristic black, dead tissue (necrosis) often seen in affected areas, such as the nose or palate [9].

What makes mucormycosis particularly dangerous is how quickly it spreads and how stealthily it invades. In rhino-orbital-cerebral mucormycosis, for instance, the infection can begin in the sinuses and within days involve the eyes and brain. The fungus damages the inner lining of blood vessels, leading to severe inflammation and tissue destruction. The immune system, already weakened or overwhelmed, fails to contain the spread. In the context of COVID-19, many patients received high doses of steroids to control inflammation, unknowingly suppressing their immune defenses. Combined with oxygen therapy and prolonged hospital stays, this created an unfortunate window for the fungus to strike. In essence, mucormycosis is not merely an opportunistic infection—it is an aggressive invader that exploits every weak link in the

body's defense. Its pathogenesis is a chilling reminder of how quickly an environmental organism can turn into a life-threatening adversary, especially in the presence of underlying health conditions or compromised immunity [10,11].

Risk Factors for Mucormycosis

Mucormycosis doesn't strike without warning—it preys on vulnerability. One of the strongest and most consistent risk factors is uncontrolled diabetes mellitus, particularly in patients experiencing diabetic ketoacidosis. In such cases, high blood sugar levels, a drop in blood pH, and weakened immunity come together to create a perfect storm. This acidic, glucose-rich environment gives the fungal spores an open invitation to grow and spread. In India, where diabetes is already prevalent, this became a major underlying condition in a large number of cases during the pandemic [12].

Then came corticosteroids—drugs used widely during COVID-19 to tame inflammation and manage severe cases. While they helped in saving lives, they also suppressed the immune system and elevated blood sugar levels, even in non-diabetics. It's this unintended consequence that opened the door for mucormycosis. Add to this the prolonged ICU stays, mechanical ventilation, and oxygen therapy—especially when administered through contaminated or non-sterile humidifiers—and you get a scenario where fungal spores can easily enter the body and begin to germinate in the sinuses or lungs. These hospital environments, strained by the overwhelming patient load, sometimes became inadvertent breeding grounds for infection [13].

The use of immunomodulatory drugs like *tocilizumab* added another layer of risk. Though vital in managing the hyper-inflammatory state known as the cytokine storm in COVID-19 patients, these agents further blunted the immune response. Additionally, iron overload—whether from certain medications or frequent transfusions—provided a nutritional edge to the fungus, as it thrives on free iron in the bloodstream. Acidosis from various metabolic disturbances further tilted the balance in favor of infection [13]. And finally, environmental factors—something many overlooked—played a surprisingly big role. Spores are present in soil, construction debris, and even in hospital dust. During the pandemic, many hospitals underwent rapid expansions or makeshift construction. This, along with the use of unclean humidifiers and poor air filtration systems, especially in rural or overburdened hospitals, contributed to rising case numbers. In essence, mucormycosis is not just a medical complication—it's a social, systemic, and environmental outcome. It reveals the cracks in both public health and personal health management, teaching us that even a tiny fungal spore can become lethal when the body's defenses are down and our systems are overwhelmed [14].

Clinical Spectrum

This table 1 categorizes mucormycosis based on anatomical involvement—such as rhino-orbito-cerebral, pulmonary, cutaneous, gastrointestinal, and disseminated forms—highlighting their key clinical features and most affected patient populations. It helps clinicians quickly identify the likely presentation based on site and risk profile [15-18].

Table 01: Clinical Spectrum of Mucormycosis

| Type | Primary Site Involved | Common Clinical Features | High-Risk Groups |
|---|--|---|---|
| Rhino - orbit o-cerebral (ROC M) | Nasal cavity, sinuses, orbit, brain | Nasal congestion, facial pain, orbital swelling, black eschar, vision loss, cranial nerve palsy | Uncontrolled diabetes, post-COVID-19 patients |
| Pulmonary | Lungs, bronchi | Fever, cough, hemoptysis, pleuritic chest pain, worsening respiratory distress | Hematologic malignancies, transplant recipients |
| Cutaneous | Skin, subcutaneous tissue | Necrotic lesions, cellulitis, black eschars, wound infection | Trauma, burns, catheter sites |
| Gastrointestinal | Stomach, colon, small intestine | Abdominal pain, GI bleeding, perforation, sepsis | Neonates, malnourished, ICU patients |
| Disseminated | Multiple organs (brain, kidneys, etc.) | Multi-organ failure, altered mental status, systemic signs of sepsis | Severely immunocompromised |

Diagnosis

This table 2 outlines essential diagnostic tools ranging from clinical suspicion to advanced molecular methods like PCR and MALDI-TOF. It compares their utility, advantages, and limitations to guide timely and accurate diagnosis while differentiating mucormycosis from other infections [19-21].

Table 02: Diagnostic Modalities for Mucormycosis

| Diagnostic Method | Principle/Utility | Advantages | Limitations |
|-------------------------------|--|---|--|
| Clinical Suspicion | Early symptom recognition based on history and risk factors | Critical for early intervention | Non-specific; overlaps with other infections |
| CT Scan / MRI | Imaging for extent of tissue involvement (sinuses, brain, lungs) | Non-invasive, useful in surgical planning | Cannot confirm fungal type |
| KOH Mount (Direct Microscopy) | Identifies broad aseptate hyphae in tissue/scrappings | Rapid, inexpensive | Requires skilled interpretation |
| Histopathology | Demonstrates tissue invasion by fungal hyphae | Confirms angioinvasion, guides management | Time-consuming, invasive biopsy needed |
| Fungal Culture | Grows specific species of Mucorales | Helps in species identification and sensitivity testing | Slow; often yields false negatives |
| PCR / Molecular Methods | Detects fungal DNA from tissue or blood | High sensitivity, rapid | Not widely available; expensive |
| MALDI-TOF | Protein-based fungal identification from cultures | Accurate and fast | Requires established fungal libraries |
| Differential Diagnosis | Rule out aspergillosis, bacterial infections, neoplasms | Prevents misdiagnosis | May require combined clinical and lab inputs |

Treatment Modalities

The treatment of mucormycosis demands a swift, aggressive, and multidisciplinary approach. At the forefront is surgical debridement, which involves the physical removal of all necrotic and infected tissue. This is not a one-time procedure—patients often require multiple surgeries to halt the spread of the fungus. Especially in cases like rhino-orbito-cerebral mucormycosis (ROCM), timely surgical intervention can be the difference between life and death, or vision loss and preservation. While

distressing, such radical surgeries—sometimes including orbital exenteration or partial brain resection—are often life-saving [22].

Equally critical is the prompt initiation of antifungal therapy, with Liposomal Amphotericin B being the gold standard due to its potent activity and improved safety profile compared to conventional Amphotericin B. Alternatives or step-down therapies include Posaconazole and Isavuconazole, which are effective azoles with oral availability and better tolerability. These antifungals are usually administered for prolonged durations, often for weeks to months, depending on the extent of disease resolution. However, high costs and limited availability in resource-constrained settings pose serious treatment challenges [23].

Another pillar of management is addressing underlying risk factors—especially uncontrolled diabetes and immunosuppression. Tight glycemic control and tapering of corticosteroids, whenever possible, are essential to halt further fungal progression. Patients with hematological malignancies or transplant recipients may require dose adjustments in their immunosuppressive regimens to improve immune reconstitution [24].

Adjunctive therapies, such as hyperbaric oxygen therapy (HBOT) and iron chelation with deferasirox, have been explored to enhance outcomes. HBOT may help improve oxygenation and healing in ischemic tissues, while iron chelation theoretically starves the fungus of essential nutrients. However, the use of such therapies remains controversial and not routinely recommended due to limited evidence and accessibility issues [25]. Ultimately, delays in diagnosis, limited drug availability, lack of surgical infrastructure, and socioeconomic disparities significantly impact outcomes, particularly in low-resource settings. Mucormycosis care isn't just about medical protocols—it reflects broader healthcare system strengths and gaps. Successful treatment depends as much on timely access and coordinated care as it does on the right antifungal [25].

Public Health Response in India

The sudden surge of mucormycosis cases in India during the second wave of the COVID-19 pandemic caught the healthcare system off guard. As the black fungus crisis deepened, the Government of India responded swiftly, recognizing mucormycosis as a notifiable disease under the Epidemic Diseases Act, 1897 in May 2021. This critical step mandated the reporting of all suspected and confirmed cases, enabling better surveillance, data collection, and allocation of healthcare resources. Simultaneously, the Ministry of Health and Family Welfare (MoHFW) issued national guidelines for screening, diagnosis, and management of mucormycosis, which were regularly updated to reflect evolving clinical insights. To coordinate efforts across states, several expert task forces and clinical advisory groups were formed, comprising infectious disease specialists, ENT surgeons, endocrinologists, and intensivists. These bodies not only

standardized treatment protocols but also advised on drug procurement strategies and surgical triaging. Recognizing the urgency of drug availability, the government facilitated emergency import and distribution of Liposomal Amphotericin B, which was in short supply due to global demand [26].

At the state level, the response varied based on the intensity of outbreaks. Maharashtra, Gujarat, Rajasthan, and Andhra Pradesh were among the worst-affected states, prompting them to set up dedicated mucormycosis wards, surgical units, and referral centers. State governments collaborated with medical colleges and tertiary hospitals to ensure round-the-clock care for critical patients. Special registries were also created to track mucormycosis cases, aiding in epidemiological mapping and resource planning.

Public health awareness became another cornerstone of the response. Recognizing that many cases stemmed from unmonitored steroid use, especially in home-treated COVID-19 patients, the government and professional bodies like ICMR and AIIMS launched campaigns on rational steroid use and the importance of monitoring blood glucose levels. Posters, infographics, and social media outreach in multiple regional languages were used to educate both healthcare professionals and the public. Television, radio, and newspapers ran awareness drives urging people to report early symptoms like nasal congestion, facial swelling, or blackish discharge—critical signs of mucormycosis. Despite these efforts, challenges persisted—particularly in rural areas where specialist care, imaging facilities, and antifungal availability remained limited. The crisis highlighted the need for a stronger healthcare infrastructure, better drug supply chains, and robust public-private collaboration in emergency responses[27].

India's response to mucormycosis stands as a lesson in crisis-driven mobilization. It reflects how a proactive, multi-tiered public health strategy—spanning from policy to grassroots education—can help tackle even rare but devastating outbreaks when backed by coordinated effort and scientific guidance.

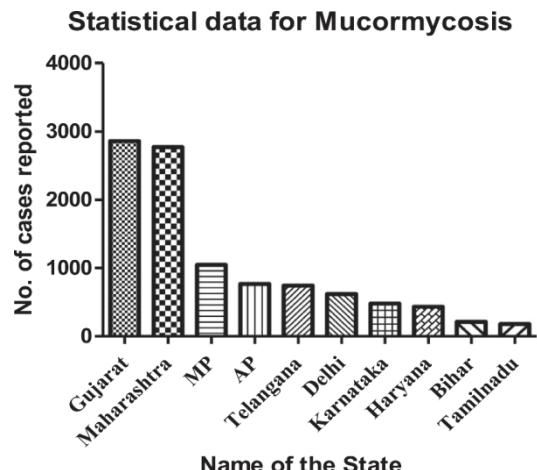


Figure 02: Statistical data for Mucormycosis

Outcomes and Prognosis

Mucormycosis is a high-stakes infection where time and timely intervention can often determine whether a patient survives or succumbs. The overall survival rates vary widely depending on the form of the disease, underlying conditions, and how early the infection is detected and treated. With aggressive surgical debridement, proper antifungal therapy, and good glycemic control, survival in rhino-orbito-cerebral mucormycosis (ROCM) can reach up to 60–70%, particularly when diagnosed early. However, delayed diagnosis, especially after brain involvement, drastically reduces survival, sometimes to below 30%[28].

The timing of diagnosis and intervention is perhaps the single most important prognostic factor. Patients who receive treatment within 5–7 days of symptom onset show markedly better outcomes compared to those treated later. Unfortunately, many cases are diagnosed only after necrosis or eye involvement, by which time the fungal spread is advanced and often life-threatening. In pulmonary or disseminated mucormycosis, especially in patients with hematologic malignancies or transplant recipients, mortality rates can exceed 70–80% due to the aggressive and invasive nature of the infection[29].

Even in survivors, the morbidity is often devastating. Orbital exenteration—a disfiguring procedure to remove the eye and surrounding tissues—is frequently necessary in ROCM to stop the spread. Neurological complications such as cranial nerve palsies, stroke, hemiparesis, or cognitive deficits may persist in patients where the infection reaches the brain. Long hospital stays, high emotional distress, and the financial burden of prolonged antifungal therapy further worsen the quality of life. In India, where a majority of cases were reported during the second COVID wave, multiple case series and hospital audits documented high mortality rates ranging from 30% to 60% in ROCM and over 70% in pulmonary/disseminated forms. The lack of access to timely diagnostics, antifungals, and surgical infrastructure in many regions contributed significantly to these outcomes[30].

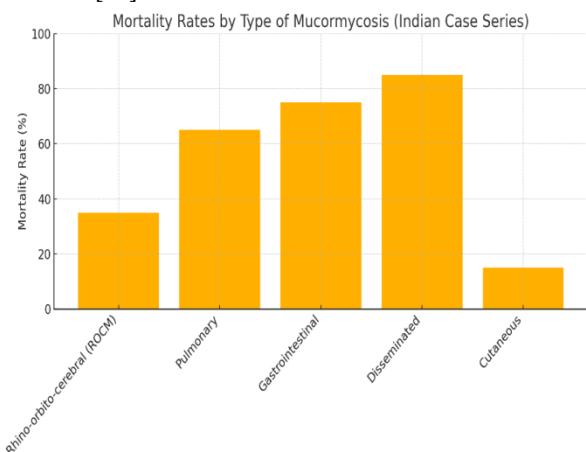


Figure 03: Mortality Rates by Type of Mucormycosis

Conclusion

Mucormycosis has re-emerged as a major health threat, particularly in India during the COVID-19 pandemic, where the confluence of diabetes, corticosteroid use, and overwhelmed healthcare systems created an ideal setting for this invasive fungal disease. Despite being a rare infection globally, India witnessed an unprecedented surge, exposing systemic vulnerabilities in disease detection, clinical preparedness, and drug accessibility. Early recognition, prompt antifungal therapy, and aggressive surgical intervention are vital for improving outcomes, especially in rhino-orbito-cerebral forms. However, high mortality in pulmonary and disseminated mucormycosis reflects the need for faster diagnostics, better antifungal stewardship, and public health awareness. The Indian government's rapid response—including notification policies, awareness drives, and task forces—offers a blueprint for future outbreak responses. As we move forward, interdisciplinary collaboration, robust surveillance, and research into novel antifungal therapies will be key in managing mucormycosis and similar opportunistic infections in immunocompromised populations.

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Conflict Of Interest

Authors are declared that no conflict of interest.

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Author Contributions

N. S. L. Devi, R. Saranya, and O. Meghana contributed to data collection, literature review, and writing of the manuscript. A. Suneetha assisted in content structuring and critical revisions. Patibandla Jahnavi conceptualized, supervised, and approved the final manuscript.

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