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Mucormycosis (Black fungus): An Emerging Fatal Mycosis of 21st Century- An Overview of History, Epidemiology, Clinical Spectrum, Diagnostic Approaches and Treatment

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ABSTRACT

Mucormycosis (zygomycosis, black fungus), is an emerging, noncontagious, opportunistic, life-threatening disease of sinuses, lungs, skin and brain of immunocompromised individuals, caused by the mucoraceous fungi. Friedrich Küchenmeister, a German physician, discovered the first case of mucormycosis in 1855. The fungal infections of humans, called mycoses, are a growing global health concern affecting more than one billion people causing over 3.75 million deaths each year. Due to the global surge in mucormycosis incidence with a marked increase in India and China especially among patients with uncontrolled diabetes mellitus (DM), it is designed as an emerging fatal mycosis of the 21st century. Globally, 39 fungal species belonging to 11 genera of Mucoromycetes (Mucoromycota) are involved in mucormycosis. Seventy-five percent incidences of mucormycosis are caused by the 3 genera Rhizopus, Mucor, Lichtheimia, and Rhizopus arrhizus (R. oryzae) alone is the main causative agent involved in 50 % of all cases of mucormycosis globally. The mortality rate is much higher in mucormycosis, considered to be an emerging mycosis, compared to aspergillosis and candidiasis, the two other fatal emerging mycoses. The infection mainly occurs when the fungal spores (sporangiospores) are inhaled by humans from the environment of the saprophytic mucoraceous fungi occurring in soil and decomposing plant residues. The inhalation is the most common mode of transmission compared to inoculation and ingestion. The epidemiology and mortality, despite antifungal therapy, has shown an exponential rise, the disease named as "black fungus" in 2021 following the second wave of COVID-19 pandemic. Prevalence of mucormycosis in India is nearly 80 times higher than global picture. Histopathological microscopic examination of stained biopsy samples for nonseptate wide hyphae and identification of fungi based on fungal culturing are often used in diagnosing mucormycosis. Molecular (PCR- based fungal DNA), qPCR kits, protein homolog in spore coating, serology, and imaging techniques are the other diagnostic techniques. Early diagnosis and prompt initiation of antifungal therapy along with surgery and control of risk factors are needed for successful management of mucormycosis. Antifungal drugs to treat mucormycosis include: amphotericin B, Isavuconazole, posaconazole and itraconazole, the former two recommended by the USFDA for the primary therapy. Amphotericin B, preferably liposomal amphotericin B (L- AMB), is the drug of choice globally for managing mucormycosis of various types: rhino-orbital-cerebral, pulmonary, gastrointestinal, cutaneous, renal, disseminated and COVID-19-associated mucormycosis.

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Introduction

Mucormycosis (previously called zygomycosis) described in 1855 by Friedrich Küchenmeister, a German physician, is a noncontagious opportunistic, life- threatening mycosis coenocytic filamentous fungi belonging to the class Mucoromycetes.The Fungal infections of humans, called mycoses, are common affecting more than one billion people annually. They posed a significant global health burden with an annual incidence of 6.5 million life- threatening mycoses leading to mortality ranging between 2.5 and 3.8 million [1]. The mortality rate is much more in mucormycosis (90% or even more) than the two other fatal mycoses namely aspergillosis and candidiasis during and after the COVID-19 pandemic. The burden of mucormycosis is grossly under reported because fungal cultures are so often negative due to problems associated with identification [2]. The prevalence of mucormycosis has doubled in the pandemic era, especially India which is estimated as 140 per million population, which exceeds 80 times more than the prevalence in developed countries [2]. The disease had been named as COVID-associated mucormycosis (CAM) and black fungus among hospitalized, recovering and recovered COVID-19 patients. The WHO declared black fungus disease as an emerging disease during the second wave of COVID-19 pandemic and has put Mucorales, the causative agents of mucormycosis, in the "First Fungal Priority Pathogens List" which are critical or highly important to human health [3-5].

Not much emphasis has been given to the fungal diseases worldwide and mycoses are considered as neglected human pathogens [6]. There are several problems associated with the management of mucormycosis, including limited knowledge on the taxonomy and biology of Mucorales, poor estimation of incidence, multiple manifestations, similarities in symptoms with viral and bacterial pathogens, delayed and imprecise diagnosis, resistance to antifungal drugs, diagnosis requiring longer duration of time and difficulty in drug sensitivity testing due to several fungal causative agents involved in infection and the harmful side effects of antifungal drugs due to the similarity of eukaryotic cell biology in the fungal causative agents as well as human host.

History

Friedrich Küchenmeister, a German physician, was the first scientist to discover the first case of mucormycosis in 1855 following its second report in 1876 by Fürbringer, another German scientist, from the lungs of a cancer patient who suffered a haemorrhagic infarct with fungal hyphae and sporangia in the right lung [7]. Ludwig Lichtheim, a German physician and microbiologist, was one of the first scientist to isolate and identify two causative agents of mucormycosis *Mucor corymbifera* and *M rhizopodiformis*, and were later reclassified as *Lichtheimia corymbifera* and *Rhizopus rhizopodiformis* which are still recognized as the common causative agents of mucormycosis. *Lichtheim* in 1884 carried out detailed experimental work and successfully induced mucormycosis in rabbits through inoculation, and established a foundational animal model for studying mucormycosis, in order words, proving the Koch's postulates, using fungal pathogens, instead of bacteria. He demonstrated that fungi invaded blood vessels in rabbits causing infarction (tissue death from loss of blood supply) and necrosis, resulting to lesion development [8]. Mucor spp. were later on found related to humans with poorly controlled diabetes in three cases with severe sinus, brain, and eye involvement. isolated Saksenaea vasiformis, from Indian forest soil of Sagar (M.P) which was later on discovered as causative agent in several cases of mucormycosis. Misra in 1979 examined soil from an Indian mango orchard from where he isolated Apophysomyces elegans, to be a major fungus causing mucormycosis, ranging from localized cutaneous infections to aggressive disseminated disease involving vital organs [9-11]. Several mucoraceous fungi have since been described as causative agents of mucormycosis, worldwide.

The term "mucormycosis" had its origin from the word *mucor* = mouldy + *mycosis* = fungal infection, often used interchangeably with "zygomycosis". It was coined by Arnold Paltauf in 1885, after describing a case with systemic symptoms involving the sinus, brain, and gastrointestinal tract.

Epidemiology and Incidence

The incidence rate of mucormycosis globally varies from 0.005 to1.7/ million population. In India, it is estimated as 140 / million population, which is about 80 times higher than the prevalence in developed countries (WHO, 2025). The incidence of mucormycosis earlier to COVID-19 pandemic (2000-2017) was found to be most prevalent in Europe where maximum cases had been reported (34%) followed by Asia (31%), and North and South America (28%), while lower in Africa, Australia and New Zealand (3%) [12].

Due to the global surge in mucormycosis incidence, with a marked increase in India and China, especially among patients with uncontrolled diabetes mellitus (DM), it is designed as an emerging fatal mycosis of the 21st century. Increase in CAM cases (41000) especially during the 2nd wave of COVID-19 pandemic in India, resulted in 3200 deaths by the end of June 2021, making it the most important outbreak of mucormycosis [13]. The mortality rate of mucormycosis is quite higher varying from 50 to 100%, compared to two other fatal mycoses, candidiasis and aspergillosis that cause mortality from 20-50% and 35-45%, respectively [14]. Based upon the rate of mortality, the World Health Organization has put Mucorales in its "First Fungal Priority Pathogens List" which are critical or highly important to human health [4].

The Causative Agents

Globally, a total of 39 fungal species belonging to 11 genera of Mucoromycetes are identified as causative agents of mucormycosis varying depending on the geographical area. These include: *Rhizopus arrhizus* (formerly *R oryzae*), *R. rhizopodiformis R. microsporus*, *Mucor circinelloides, Lichtheimia (Absidia) corymbifera, Rhizomucor (Mucor) pusillus, Cunninghamella bertholletiae, Saksenaea vasiformis, Apophysomyces elegans, Cokeromyces, Actinomucor and Syncephalastrum*. Species of Rhizopus, Lichtheimia and Mucor accounted for 75% of all cases globally, R. arrhizus being the most important and involved in most of the mucormycosis infections [15,16].

Morphologically mucoromycetes are characterized by their fast-growing colonies, large-diameter, coenocytic (non-septate), rhizoidal and non-rhizoidal hyphae, producing aerial sporangiophores, columellate and non-columellate sporangia, producing globose, nonmotile asexual spores (sporangiospores/ aplanospores), and the sexual spores (zygospores) produced in zygosporangia. The members are either homothallic or heterothallic [17].

Distinguishing features, such as colonial growth, hyphae, sporulating structures (sporangiophores, sporangia, columella, sporangiospores) of the four mucoraceous genera, often involved in various types of mucormycosis globally are shown in figures 1 to 4: *Rhizopus* (Figure 1), Mucor (Figure 2), *Rhizomucor* (Figure 3) and *Lichtheimia* (Figure 4).

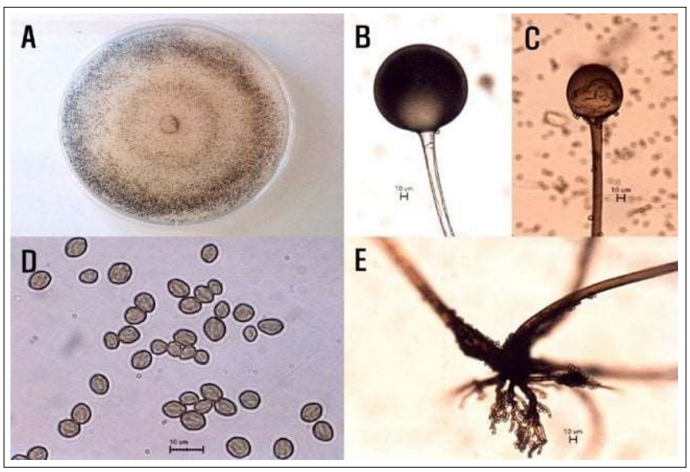

Figure 1: *Rhizopus arrhizus* (*R. oryzae*) showing colonial growth on PDA (A), columellate sporangium with sporangiophore(B), columella (C), unicellular sporangiospores (D), and rhizoids arising opposite to a sporangiophore (E)

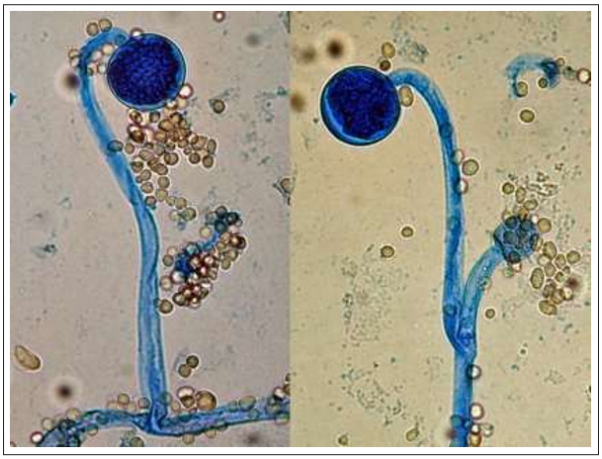

Figure 2: Mucor circinelloides showing circinate, branched sporangiophores, brown columellate sporangia with brown single-celled sporangiospores.

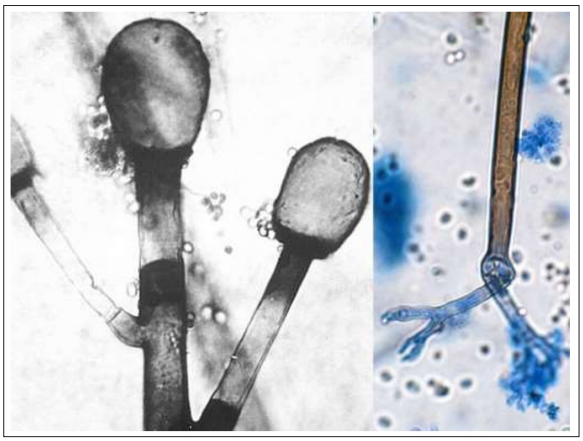

Figure 3: Rhizomucor (Mucor) pusillus showing sympodially branched sporangiophores, bearing columellae, hyaline, smooth -walled, globose sporangiospores, and a sporangiophore with primitive rhizoids

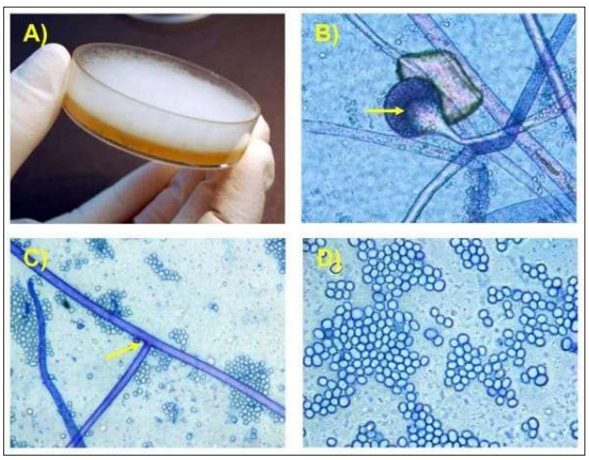

Figure 4: *Lichtheimia (Absidia) corymbifera* showing woolly or cottony growth (A), sporangium with a conical columella (B), non-septate hypha branching at right angle (C), and ellipsoid sporangiospores (D).

The causative agents of mucormycosis were formerly classified in the order Mucorales and the class Zygomycetes (=*Phycomycetes*) [18]. Phylogenetically, these are now classified as follows: *Mucorales* (order), *Mucoromycetes* (class), *Mucoromycotina* (subphylum), *Mucoromycota* (phylum), *Mucoromycete* (subkingdom), and *Fungi* (kingdom) [19-21].

Pathogenesis And Transmission

Mucormycosis is a noncontagious disease and does not spread from person-to- person through direct contact. Infection occurs when a person inhales, ingests or come in contact with spores of the mucoraceous saprophytic fungi, occurring in soil, air, compost, decomposing plant materials, mouldy bread, decaying fruits and vegetables. Occasional outbreaks occur in communities from natural disasters. Flooding and damp conditions promote growth of molds and enhance sporulating structures, resulting to the abundance of spores in the air / environment. Mucormycosis outbreaks in hospitals can also occur due to mold contamination occurring through adhesive bandages and hospital linens, tongue suppressors, water leaks, poor air filtration, dust carrying molds from nearby construction and contaminated linens. The modes of transmission include inhalation, inoculation and ingestion of fungal spores from the environment. Inhalation is the most common mode for getting infection of mucormycosis [14-24].

Inhalation: The breathing of fungal spores from air of the mucoraceous agents commonly found in the environment causing systemic (deep) mycosis, leading to infection of lungs, sinuses, and extending into the brain and eyes.

Inoculation: In inoculation, the fungal infection of susceptible individuals can occur through cuts, abrasions, wounds, burns or any other type of skin injury, leading to cutaneous mucormycosis. Ingestion: The spores, including mycelia of fungi, can be ingested through contaminated foods and water, leading to the infection of the intestinal tract and resulting to gastrointestinal mucormycosis.

Clinical Manifestations

Based upon the organ/tissue involvement, mucormycosis is categorized into six clinical types (Figure 5), producing different types of symptoms. Based upon the association of mucormycosis with COVID-19 disease due to infection of SARS- CoV-2 virus, has been named as COVID-associated mucormycosis (CAM), popularly famous as “black fungus”, is considered as the 7th type of mucormycosis.

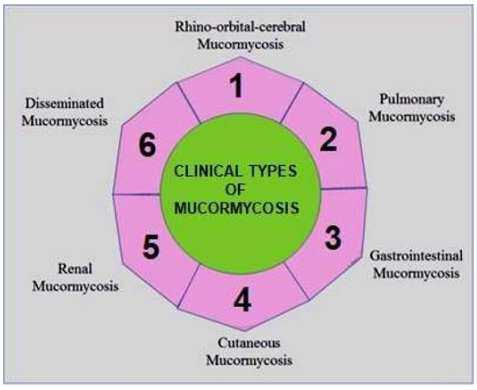

Figure 5: Six Manifestations/Clinical Types of Mucormycosis

Rhino-orbital-cerebral (sinus, eyes and brain) mucormycosis (ROCM): ROCM is the most common and severe clinical manifestation which isranked number one globally. It primarily affects the nasal and orbital regions, and is mainly associated with diabetic ketoacidosis or with uncontrolled diabetes mellitus. Infection occurs in the nose, orbit of eye/ eye socket, oral cavity and even spread to the brain, and resulting to life-threatening

complication. The most common symptoms are fever, one-sided facial swelling, headache, nasal or sinus congestion, vision changes, proptosis (i.e., forward displacement of the eye), and black eschar (necrotic black coloured tissue) on nasal bridge or upper inside of mouth that quickly becomes more severe [22-24].

Five species of *Rhizopus* cause ROCM. Maximum cases of infection occur due to *R. arrhizus* (Figure 1), followed by *R. arrhizus*. Sporadic infections occur due [26]. Infections in India are caused by *R. homothallicus* and *R. homothallicus* [27,28].

Pulmonary (lung) Mucormycosis: It is the 2nd most prevalent mucormycosis worldwide and predominantly occurs in patients with haematological malignancy, neutropenia and transplantation. The major symptoms include fever, cough, chest pain, shortness of breath and haemoptysis (coughing up blood). The infection from lungs rapidly disseminates to other organs resulting in death of the patient [29]. Species of *Cunninghamella*, *Rhizopus* and *Mucor* are responsible for causing this mycosis.

Cutaneous (skin) Mucormycosis: This mycosis is ranked as the 3rd in frequency of occurrence worldwide. In addition to the skin infection, involvement of subcutaneous tissues also occurs. It is caused by various species of Mucor, *Lichtheimia, Apophysomyces* and *Saksenaea*, species of the latter two genera mainly cause this mycosis. The fungi frequently attack immunocompetent patients and associated with trauma and burns. It causes an acute inflammatory response with pus, blisters or ulcers, and the injected area may turn from red to black eschar at the site of infection. Additional symptoms include pain, warmth, redness, or swelling around the wound. The lesions progress rapidly leading to destruction of tissue and possible dissemination to deeper tissues leading to subcutaneous mucormycosis [12-30].

Gastrointestinal (stomach and intestine) Mucormycosis: This mycosis results by consuming contaminated foods, especially fermented food products (e.g., yogurt, fermented milk and porridge), dried bread products, spores-contaminated herbal and homeopath drugs, dietary supplements (e.g., ABC Dophilus powder) [31]. These foods affect the gastrointestinal tract, especially among patients who have undergone gastrointestinal surgery, and in neonates. The symptoms include abdominal pain, nausea, vomiting, gastrointestinal bleeding (either upper or lower) and intestinal perforation [33-34]. It is mainly caused by species of *Mucor, Rhizopus* and Rhizomuco [35].

Disseminated Mucormycosis: In this mycosis, the causative fungi, spreads through the bloodstream from its initial site to invade multiple organs and tissues, most commonly brain, in addition to spleen, heart, skin, and other organs. It is the most severe form of mycosis resulting in mortality ranging from 63.9 to 96% [36]. The infection is more common in immunocompromised individuals with conditions like HIV, leukaemia, or who had undergone transplants. Major symptoms include: fever and chills [37].

Renal (kidney) Mucormycosis (RM)
RM is a dangerous but rare infection of the kidneys often occurring in immunocompromised individuals like those with uncontrolled diabetes, undergoing transplants, and patients with COVID-19 infection. The symptoms include: fever, flank pain (either one or both sides) and acute kidney injuries due to tissue damage. The pathogenesis involves retrograde spread from lower urinary tract infection and via bloodstream (hematogenous spread) to the kidneys. The species of Rhizopus, especially R. oryzae and R. microsporus, are the main causative agents. In addition to Rhizopus, other fungal pathogens involved are Apophysomyces elegans, Rhizomucor spp., Lichtheimia corymbifera, L. ramosa, Cunninghamella spp. and Mycocladus corymbifer [38].

COVID-19-Associated Mucormycosis (CAM): It is often called "black fungus" has its origin from India during the second wave of COVID-19 pandemic in 2021. CAM is linked to the SARS-CoV-2 virus itself, causing an overstimulated immune response in the patient, due to the use of corticosteroids to manage COVID-19 which suppressed the immune system and increased blood sugar levels, making a person diabetic, and create opportunities for fungi to attack resulting to mucormycosis. CAM occurred on an average of 22 days after COVID-19 and 8 days after hospitalization. Mortality of CAM reported to be high, especially in low 'or middle- income countries. The CAM patients showed one-sided facial swelling, headaches, nasal or sinus congestion, black lesions on the face, bridge of the nose or upper inside of mouth, fever, lethargy, slurred speech or partial paralysis, which are similar to COVID-19, making a patient very serious, and resulting to mortality. Mode of infection of the SARS-CoV-2 virus and through the spores of mucoraceous fungi, and various sites of infection among CAM patients are diagrammatically shown in Figure 6. The most common site of infection in CAM is rhino-orbital followed by rhino-orbital-cerebral and pulmonary mucormycosis. More deaths are caused by the rhino-orbital-cerebral, pulmonary, gastrointestinal and disseminated mucormycosis, as compared to the rhino- orbital, facial, and rhino sinusoidal infections which are less fatal (Figure 7). *Rhizopus* is the most commonly identified taxon from all locations except cutaneous and facial where *Mucor* is the predominant genus [39].

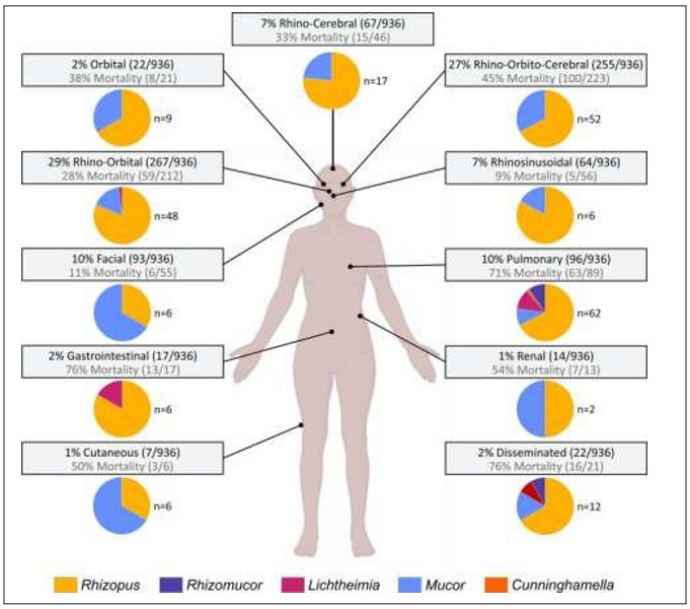

Figure 6: Mode of infection of a fungus and a virus through inhalation and clinical depiction of black fungus on SARS-CoV-2 infected CAM patients [39].

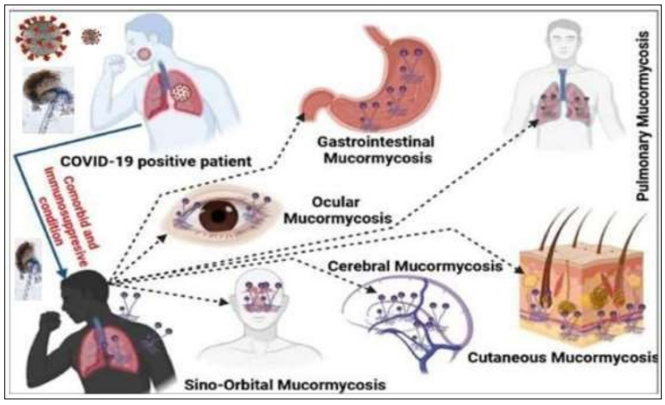

Figure 7: Mortality rates and distribution of isolated mucoraceous fungal pathogens for various sites of mucormycosis

Diagnosis

The diagnosis of mucormycosis involves identifying mucoraceous fungi, the causative agents of mucormycosis through laboratory methods, such as histopathology (observing broad, ribbon-like, non-septate hyphae in tissue samples), fungal culturing from affected tissues, supported with imaging techniques (e.g., CT scan of lungs, sinuses or other suspected body parts). PCR- based molecular techniques to detect fungal DNA are used for rapid, non - invasive detection from blood, urine, and bronchoalveolar lavage (BAL) samples which provide more accurate and fast results for early diagnosis and treatment, especially for immunocompromised patients. Histopathology (biopsy and fungal staining with KOH) and identification of a fungus based on cultural and microscopic characteristics, are considered as the gold standard to diagnose mucormycosis [40-41] The laboratory-based assays, techniques and characteristics used in the identification of fungi for diagnosing mucormycosis are summarized in Table 1.

Table 1: Laboratory-Based and Clinical Assays for Diagnosis of Mucormycosis

Diagnostic techniques		Techniques for a mucoraceous fungus identification	
1.	**Microscopic viewing (histopathological)** ➢ Simple KOH staining (10-20% w/v). ➢ Calcofluor white fluorescent stain. ➢ Periodic acid-Schiff (PAS) stain. ➢ Grocott methenamine silver (GMS) stain. ➢ Fluorescent in situ hybridization (FISH).	1.	**Culturing on agar media for macroscopic and microscopic morphology** ➢ Sabouraud's dextrose chloramphenicol agar (SDCA). ➢ Potato dextrose agar (PDA).
2.	**Molecular-based techniques (Biopsy samples)** ➢ Conventional PCR. ➢ Restriction fragment length polymorphism (RFLP). ➢ DNA sequencing. ➢ Real-time PCR.	2.	**Molecular (DNA)** ➢ DNA sequencing. ➢ Conventional PCR. ➢ Restriction fragment length polymorphism (RFLP). ➢ Real-time PCR. ➢ Matrix-assisted laser desorption ionization-time of flight (MALDI-TOF).
3.	**Commercial qPCR kits for serum**, BAL and biopsies ➢ Mucor Genius. ➢ Myco GENIE. ➢ Fungiplex.	3.	**Sporulating features** ➢ Colony: Color, growth. ➢ Hyphae: Non-septate, wide. ➢ Rhizoids: Presence, absence. ➢ Stolon: Organization and branching. ➢ Sporangiophores: Aerial, nonseptate. ➢ Sporangia: Columellate, noncolumellate (multi-spored), mero-sporangia (spores in rows) sporangiola (single/few spored). ➢ Shape of columella. ➢ Apophysis: Presence, absence. ➢ Sporangiospores: Shape, size, and color. ➢ Nature: Homothallic or heterothallic. ➢ Zygospores: Presence, absence, structure (shape and size) and its suspensory cells. Important facts/issues should always be kept in mind: ➢ Some clinical isolates fail to sporulate and cultures missing characteristic structures. ➢ Antifungal drugs show morphological abnormalities in pathogenic organisms that sometimes makes their correct identification difficult.
4.	**Sporangiospore coating protein homolog** ➢ cotH genes.		
5.	**Serology** ➢ Antigen from saliva.		

Collection of samples: Samples are collected, according to the site/ type of mucormycosis, through biopsy, and of exudates/ scraping/ pus, sputum, and used for diagnosis by using various techniques:

Histopathological microscopic examination of stained biopsy samples: for the presence of characteristic wide (5-20 μm), thin walled, ribbon-like hyphae, without septa (non-septate) or with minimal septations (pauci-septations), and having right-angel branching.

Molecular methods: For identifying causative organisms from the sample, ideally serum with PCR standing out as the most reliable and user- friendly approach. Quantitative PCR (qPCR) methods for serum, tissue, and BAL offers rapid results within around three hours. qPCR assays are mainly based on detecting ITS1 and ITS2 ribosomal regions or the 18S region of rDNA [42-46].
Commercial qPCR kits: For early and easy diagnosis 3 qPCR kits are commercially available.
Muco Genius (from Patho Nosttics)
Myco GENIE (from Ademtech)
FuGueganngiplex (from Bruker).
These kits facilitate testing of mucormycosis in serum, BAL, and biopsies, with a sensitivity ranging between 75 and 95 % [47-50].

Fungus culture: Culturing of fungi is made on agar media (e.g., SCDA, PDA) often incubated at 37°C (human body temperature) for 48 to 72 hours, for colony formation (since they are fast growing), to identify up to generic/ species level (Table 1) based on colonial growth, nature of hyphae and sporulating structures (sporangiophores, sporangia, mero-sporangia, sporangiospores and zygospores), and molecular (DNA), as well as susceptibility testing for proper treatment. ***Rhizopus*** and Lichtheimia are thermotolerant which grew best at 37 °C, *Rhizomucor* is thermophilic and can grew up to 55°C, and Mucor spp. are commonly mesophilic and unable to grow at temperatures exceeding 34°C hence needs to be incubated at various temperatures (30, 37 & 55°C), depending upon the sites of infection, for detecting almost all the fungal organisms involved in infection [51].

Differential thermotolerance of causative agents can be used as an important criterion to diagnose the mucormycosis type: Mucor spp. are typically restricted to cutaneous infections while *Rhizopus, Lichtheimia,* and *Rhizomucor* cause pulmonary, ROCM, gastrointestinal and disseminated infections [52-53].

Rapid antigen testing: Saliva can be used as a non-invasive biofluid for point-of-care detection of an infectious disease. Identification of *Rhizopus arrhizus* from the patient's saliva through rapid point-of-care detection of the signature 15-kDa biomarker can be used to get accurate result in a short time for ROCM detection among CAM patients.

Imaging tests: CT scan of lungs, sinuses and other suspected parts of the body, depending upon the location of the infection, a clinical test, can be used to support the diagnosis.

Treatment

Early diagnosis of mucormycosis based on clinical, histopathological, cultural or radiological features, in addition to controlling the underlying features, is key for successful management. Treatment includes prolonged antifungal therapy, controlling the risk factor/s and a surgical debridement, especially in individuals with severe complications, for the best outcome.

Antifungal Therapy

Amphotericin B, isavuconazole, posaconazole and itraconazole, the four antifungal drugs, are currently available for treating mucormycosis. Amphotericin B and isavuconazole are licenced by the US Food and Drug Administration (FDA) for the primary therapy of mucormycosis. Amphotericin B, especially L- Amb, is most effective and considered the drug of choice which is administered intravenously to target the fungal infection systemically. Duration of therapy is decided based on radiological and clinical resolution of disease in individuals. Positron emission tomography (PET) is a good tool to monitor disease assessment response and treatment [54]. Administration of amphotericin B involves: initially, 1mg dose is injected slowly over 10-15 minutes into a vein, followed by a daily dose (3-5 mg/ kg/day) according to the body weight for the next 14 days or longer, in severe cases. Isavuconazole and posaconazole are the two alternative medicines. Isavuconazole (both oral and IV) is given 200 mg every 8 hours (q8h) for initial 2 days followed by 200 mg once a day. Posaconazole is given as suspension- 200 mg q6h or 400mg q12h; IV and tablets-300 mg q12h for 2 doses, then 300 mg q24h.

Control of Risk Factors

The second important step to manage mucormycosis, after initiation of antifungal drug, amphotericin B is to identify the reversal of the risk factor. For example, control of diabetes (a reversal of diabetic ketoacidosis if present), reduction in immunosuppression, especially reduction in steroids in patients receiving triple drug immunosuppression for an organ transplant, granulocyte-stimulating factor or granulocyte transfusion for patients with prolonged and severe neutropenia. These two steps will limit the local and distant spread of mucormycosis. Distant spread to the other vital organs will increase morbidity with reduced chances of survival. Dexamethasone (DM), the most common corticosteroid, which is an anti-inflammatory drug, administered to treat the CAM serious patients, since it has been found to be effective against both COVID-19 and pneumonia infections. Lower doses of DM decreased mortality and gave significant results in individuals with swear COVID-19 symptoms.

Surgical Debridement

Surgical debridement/debulking of necrotic lesion is a critical and often lifesaving treatment for mucormycosis. It involves the aggressive removal of infected and necrotic (dead tissue) to inhibit the fungal spread in the deeper tissues (e.g., skin, muscle, bone, sinuses, skull base and brain), and improving the drug penetration to the infected site. In severe cases of rhino-orbital mucormycosis (ROM), the removal affected eye may be a life-saving measure to prevent intracranial extension [55-76].

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