

Mucormycosis (A Black Fungus): An Association with COVID-19

Shivani Sanjay Ingole, Pradnya Dandekar*

Department of Kriyasharir, Mahatma Gandhi Ayurvedic College Hospital and Research Center, Wardha, Maharashtra, India

ABSTRACT

The Corona virus COVID19 is severe respiratory disorder which is caused due to infection of corona virus previously known as 2019-nCoV the infection is caused due to contagious virus which leads to severe respiratory disease known as COVID-19. COVID-19 infection can be related with a wide range of bacterial and fungal infections, which are most commonly encountered in people with pre-existing conditions such as diabetes mellitus and lung illness. Mucormycosis, a black fungus can be diagnosed during the course treatment of COVID-19 infection. During treatment of COVID-19 patient may developed orbital cellulitis. Soft tissue of brain orbits and paranasal sinuses shows swelling in MRI (Magnetic Resonance Imaging) the use of a lot of steroids and broad-spectrum antibiotics can cause fungal infections. Broad aseptate filamentous fungal hyphae suggestive of mucormycosis revealed in nasal biopsy which get confirmed in culture. Due to immunological dysregulation, COVID-19 is linked to a high prevalence of secondary infections, both bacterial and fungal. COVID-19 is linked to a high prevalence of secondary infections, both bacterial and fungal. Diabetes mellitus is the most risk factor in COVID-19 patients can develop Mucormycosis. An invasive black fungus may affect to nose and sinus this could be because respiratory system affect the most.

Keywords: COVID-19; Cellulites; Fungal infection; Mucormycosis; Immune deregulation; Diabetes mellitus; Black fungus

INTRODUCTION

Aim

To establish mucormycosis (a black fungus) association with COVID-19 disease.

Objectives

- To assess the causes of mucormycosis a black fungus in Covid patients. And it's association with COVID-19.
- To establish mucormycosis association with COVID-19.
- To analyze it's association in preexisting diseases like diabetes mellitus.

This study is done on basis of different research articles of COVID -19. Online research was done using the keywords mucormycosis and its association with COVID -19. The textbook of Harrison was screened to learn about mucormycosis.

Different research articles were studied to find about the association of mucormycosis and preexisting diseases like diabetes .Google scholar and Pubmed articles were screened to establish mucormycosis and COVID-19 association.

The pandemic Corona virus is continuing spreading worldwide while it is having several treatment options. Systemic glucocorticoid plays an important role in treatment of covid19. Glucocorticoid improves the survival in COVID-19 patients. But the widespread use of glucocorticoid may lead to secondary bacterial and fungal infection.

Corona virus damages the lungs of patients. Mucormycosis can affect the lungs but the most common site for mucormycosis if nose and sinuses and then it spread to eyes and brains showing various symptoms like blindness , headache and seizures.[1] The patient who are suffering from diabetic ketoacidosis are at high risk in developing mucormycosis [2]. Acidity in diabetic ketoacidosis increase iron and hyperglycaemia promotes

Correspondence to: Dr. Pradnya Dandekar, Department of Kriyasharir, Mahatma Gandhi Ayurvedic College Hospital and Research Center, Wardha, Maharashtra, India, E-mail: drpddandekar@gmail.com

Received: 07-Jan-2022, Manuscript No. FGB-22-44877; **Editor assigned:** 10-Jan-2022, PreQC No. FGB-22-44877 (PQ); **Reviewed:** 24-Jan-2022, QC No. FGB-22-44877; **Revised:** 28-Jan-2022, Manuscript No. FGB-22-44877 (R); **Published:** 04-Feb-2022, DOI: 10.35841/2165-8056.22.12.178

Citation: Ingole SS, Dandekar P (2022) Mucormycosis (A Black Fungus): An Association with COVID-19. Fungal Genom Biol.12: 178.

Copyright: © 2022 Ingole SS, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

organism growth, it increases fungal and host receptors leading to adherence and penetrations into tissue developing mucormycosis [3]. Mucormycosis shows mainly 5 clinical syndromes they are Rhino orbital cerebral disease, pulmonary disease, cutaneous disease, gastrointestinal disease and miscellaneous disorders [4]. According to a recent study, 62/806 (8 percent) of patients got secondary bacterial or fungal illnesses while in the hospital. Broad-spectrum antibiotics were widely used, with 1450/2010 (72 percent) of patients receiving them, often without any underlying signs of infection [5]. In India, the prevalence of mucormycosis is about 0.14 instances per 1000 people, which is roughly 80 times higher than the global prevalence in developed countries. [5,6]. Mucormycosis is an immunocompromised condition, and consequences of ocular and cerebral involvement are more common in immunocompromised patients with diabetic ketoacidosis and concomitant steroid use. [7]. Among *Mucoraceae*, *Rhizopusoryzae* is the most common cause of infection [8]. Phagocytes are the major host defense mechanism against mucormycosis. [2,3]. Additionally, corticosteroid treatment affects the [9]. The isolated renal mucormycosis is the unique clinical presentation [10].

MATERIALS AND METHODS

Clinical forms of mucormycosis

The clinical features of mucormycosis is different according to anatomical view 1) ROCM mucormycosis is the commonest form among all (45%-75%), another common clinical features is cutaneous (10%-15%) and others are pulmonary and renal mucormycosis (Table 1).

Clinical forms of mucormycosis	Prevalence rate
Rhino-orbital-cerebral	45%-75%
Cutaneous	10%-15%
Pulmonary	3%-22%
Renal	0.5%-9%
Gastrointestinal	2%-8%
Disseminated	0.5%-9%

Table 1: Clinical forms of mucormycosis and their prevalence rate

Causative forms of mucormycosis

Thermotolerant saprophytic fungi found in decaying organic matter and soil samples are Mucorales. The pathogenic species found in Indian soils are *Rhizopus*, *Lichtheimia*, *Cunninghamella*, *Rhizomucor* (Table 2).

Pathogen	Mortality
<i>Rhizopusoryzae</i>	60% of all cases or 90% of rhinocerebral cases
<i>Rhizopus spp</i>	46% mortality
<i>Lichtheimia spp</i>	~40%

Table 2: Major pathogenic species causing mucormycosis.

The treatment of mucormycosis is the early detection of disease, antifungal therapy and surgical removal of infected tissue cells. Amphotericin is the first choice of drug in invasive black fungal disease Mucormycosis. The comparable efficacy with amphotericin in new mucormycosis is drug isavuconazole, this too shows the salvage therapy in Mucormycosis patients with diabetes mellitus associated with COVID-19.

Mucormycosis prevalence and incidence in India: The data indicates that the estimated prevalence of mucormycosis in India is nearly 70 times higher than the global data, which were estimated to be at 0.02 to 9.5 cases (with a median of 0.2 cases) per 100,000 persons.

Hyperglycaemia in diabetic patients shows favorable environment for the growth of fungal infection. prolonged corticosteroids therapy for COVID-19 patients and immunosuppressant patients have more risk factor for Mucormycosis. While treatment the patient with COVID-19, patient suffer from fungal infections due to damaged lungs and suppression of immune system. This spores of Mucormycosis spread to air spaces in sinuses and started growth of invasive filamentous fungi and developed different symptoms involving nose, eyes and brain.

The pattern of COVID-19 disease is from mild case to severe patients; patients suffer from ever pneumonia associated with bacterial and fungal infections. The black fungal infection (Mucormycosis) is manifest in COVID-19 patients with prolonged disease history like diabetes mellitus or uncontrolled diabetes. Patients with severe influenza bad pulmonary manifestation leads to the development of Mucormycosis. After CT scan patients with COVID-19 revealed the ground glass opacities in lungs. A fungal pathogens known as aspergillus develops devastating disease like Mucormycosis in COVID-19 patients with diabetes mellitus.

Infections from Mucorales are usually rapid, they were initially reported in farmers from China. Some reports show they are opportunistic fungus like *Mucor irregularis*, that has completely different epidemiology. Their infections are highly chronic but without any risk factors effecting only skin and tissue cells. Drugs such as corticosteroids should help in early diagnosis such as to stop tissue invasion. Mucormycosis has characteristics to invade vessel that leads to thrombosis and tissue necrosis.

The use of Positron Emission Tomography-Computed Tomography (PET/CT) with fluorodeoxyglucose is another aggressive lab technique for detecting mucormycosis (FDG). The best and most useful diagnostic tool for mucormycosis is endobrochial ultrasonography guided injection. After extensive search and study on mucormycosis and with little or no result of journals on this deadly fungus, one search result lead to another researcher, Yang et al. found a little higher percentage of people affected by this disease. Clinically many patients are subjected to fungal testing attributing to severe respiratory symptoms. Some diagnosis like antibiotics has delayed this fungus. It is critical to pay attention to this mucormycosis in current COVID-19 patients.

RESULTS

According to our study it is observed that the patient suffering from COVID-19 with preexisting diseases like diabetes mellitus having more chances of developing mucormycosis. The

prevalence of the disease in diabetic patients is 0.15% however the high mortality rate for this disease is 30 to 60 % still exists with diabetes mellitus. Mucormycosis is a fungus that causes blackening or colouring of the nose, impaired or double vision, chest pain, breathing problems, and blood in the cough. Uncontrolled diabetic mellitus in ketoacidosis, various kinds of metabolic acidosis, and treatment with corticosteroids in COVID-19 patients are all substantial risk factors for mucormycosis. Mucormycosis is contracted when mould spores are breathed or, less usually, when spores enter the body through a cut or other skin breach. The Mucormycosis infection mostly affect the sinus cavities and most common in COVID-19 patient and mostly in those who are suffering from diabetes mellitus . Patients with hyperglycaemia and taking treatment of COVID-19 with corticosteroids have feasible environment for the growth of black fungus. Mucormycosis shows the different type of fungal infections like black fungus, white fungus and rare yellow fungus. The COVID-19 patients have low immunity and diabetes mellitus patients are more prone to any infection like bacterial and fungal infection. Immunosuppressant patients with COVID-19 having preexisting diseases like diabetes mellitus having weakens immunity and unable to fight against bacterial and fungal infections, so they could suffer from black fungus Mucormycosis.

DISCUSSION

The primary goal of this research was to learn more about the relationship between mucormycosis, a black fungus, and COVID-19. An active search of literature reviewed few mucormycosis a black fungus cases associated with COVID-19. Diabetes mellitus is an independent risk factor for mucormycosis, and the most prevalent species isolated was *Rhizopus* species, which had a 46 percent overall fatality rate. COVID-19 with fungal infections cases, cell count revealed there was progressive increase in white blood cells and neutrophils while lymphocytes progressively decreased. specific T cells shows only by invasive mucormycosis patients and this T cells helps as a marker for diagnostic method in mucormycosis. Elevated glucose level may suppress the antiviral activity. Dysregulation immune response and increased level of glucose in diabetic patients increases the severity of mucormycosis. The use of corticosteroids and a history of pulmonary disease were linked to a higher risk of invasive fungal infection. The sign of orbital infection or Mucormycosis can develop after 10 days of Covid infection, during which time the patient was given corticosteroids and broad-spectrum antibiotics. All of these elements contribute to the development of a fungal co infection in the COVID-19 illness. In some situations, a previously undiagnosed *mucor* infection can be worsened, or a new one can develop. Studies on mucormycosis were reported. COVID-19 is a pandemic disease as a doctor we must treat the patient without taking risk. The decreased ability of neutrophils to phagocytose In diabetes patients may adhere to endothelial wall, Neutrophils' phagocytosis capacity has deteriorated. Patients with diabetes may attach to the endothelium wall, and acidosis and

hyperglycemia create an excitant environment for fungal development, resulting in the invasive fungal infection mucormycosis. *Rhizopusoryzae* is the most common pathogen, accounting for 60 percent to 90 percent of all rhinocerebral cases. Mucormycosis is a fungal infection that can affect the nose, sinuses, orbit, central nervous system, lungs, gastrointestinal tract, skin, jaw bones, joints, heart, and kidneys. Mucorales spores are spreading COVID-19 patients in a perfect environment of low oxygen (hypoxia), high glucose, acidic medium, and diminished white blood cell activity owing to immunosuppressant treatment. It said that while global prevalence of this fungal infection ranges from 0.005 to 1.7 per million people in the United States, but it is 80 times greater in India due to a bigger diabetic population Cerebro-Rhino-Orbital Phycomycosis (CROP), which was primarily caused by *Rhizopus* spp, was found in diabetic ketoacidosis patients. Because of the brain involvement, CROP causes proptosis, vision loss, ophthalmoplegia, and death. The most pathogenic species of the family, *Mucoraceae* is *Rhizopus*. *Rhizopus* is the most pathogenic species in the *Mucoraceae* family. *Rhizopusoryzae* is the most common pathogen, accounting for 60 percent of all cases and 90% of rhinocerebral cases. Despite breakthroughs in diagnosis and therapy, this disease still has a significant fatality rate of 30-70 percent. Untreated or unsuccessfully treated individuals may die within two weeks. It's an acute opportunistic infection caused by a saprophytic, broad-spectrum fungus found in soil, air, bread mould, and rotten fruits and vegetables. Tissue necrosis is the benchmark for mucormycosis. Mucormycosis is a disease that is rare but poses an important burden on immune compromised patients. Newly developed medications have several pathogenesis but cure to mucormycosis is still a challenge. Several methods have delayed the mortality but still possess a challenge in curing Mucorales.

We conclude that coronavirus disease and mucormycosis may be associated with each other. As the COVID-19 infection is immunosuppressant and mucormycosis may developed in patients having less immunity. The invasive fungal infection is associated with increased level of glucose and treatment like steroids and broad spectrum antibiotics having higher risk. COVID-19 is associated with significant infections like bacterial and fungal both probably due to immune dysregulation. Mucormycosis may be developed in those cases who are having preexisting diseases like diabetes. There is need of monitoring the glucose level and therapeutic treatment with steroids with lowest dose and shortest duration. In the absence of infection, wide spectrum antibiotics should not be used. Physicians should be aware of secondary invasive fungal infections and therapeutic effects of COVID-19. The high mortality rate in mucormycosis with severe infection of COVID-19 in association with preexisting disease diabetes. Clinical diagnosis may be delayed in some cases due to delayed symptoms. The physician should pay attention towards COVID-19 patients with diabetes mellitus having any facial symptoms especially which do not respond to antibiotics therapy. Histicmicrobial studies are required to diagnose the disease. To improve the disease outcome, early diagnosis with combined surgical and medical treatment is needed. It has been understood that a black fungus called

mucormycosis is complicating the treatment and recovery of COVID-19 patients.

CONCLUSION

There were several reports of patients with invasive aspergillosis and positive growth of *Aspergillus fumigatus* and *Aspergillus-ag* in endotracheal aspirate. Many patients tested has a two-week history of COVID-19 before and after admission in ICU, a CT scan a valuable tool for corona patients revealed, slight mold infections in the chest region, but slight reversible halo, ground-glass opacities also observed in some. Patients with severe influenza or halo or reversible halo show pulmonary mold leading to mucormycosis. Direct examination of culture, molecular diagnostic techniques, PCR and situ hybridization offer an alternate to initiation the treatment. The management of mucormycosis depends on underlying factors such as injection of antifungal agents, surgical intervention and timely dosage of antifungal therapy. Immunologic and metabolic profiling is the way to approach this black fungus i.e. mucormycosis.

ACKNOWLEDGMENT

I would like to thanks my guide teacher Dr. Pradhnya Dandekar as well as our principle Dr. Vaishali Kuchewar, who gave us Golden opportunity to do this wonderful work on the topic- Mucormycosis (black fungus)-An association with COVID-19.

FUNDING SUPPORT

There is No funding support

INTEREST CONFLICT

There is no conflict of interest.

REFERENCES

1. Afroze SN, Korlepara R, Rao GV, Madala J. Mucormycosis in a diabetic patient: a case report with an insight into its pathophysiology. *Contemp Clin Dent.* 2017;8(4):662.
2. Rawson TM, Moore LS, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis.* 2020;71(9): 2459-68.
3. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: an update. *J Fungi.* 2020(4);6: 265.
4. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. *J Fungi.* 2019;5(1):26.
5. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. *Clinical Microbiol Rev.* 2000;13(2):236-301.
6. Waldorf AR. Pulmonary defense mechanisms against opportunistic fungal pathogens. *Immunol Ser.* 1989;47:243-271.
7. Chakrabarti A, Dhaliwal M. Epidemiology of mucormycosis in India. *Curr Fungal Infect Rep* 2013;7(4):287-292.
8. Kataria SP, Sharma J, Singh G, Kumar S, Malik S, Kumar V. Primary breast mucormycosis: FNAC diagnosis of a rare entity. *Diagn Cytopathol.* 2016;44(9):761-3.
9. Prakash H, Singh S, Rudramurthy SM, Singh P, Mehta N, Shaw D, et al. An aero mycological analysis of Mucormycetes in indoor and outdoor environments of northern India. *Med Mycol.* 2020;58(1): 118-23.
10. Walther G, Pawłowska J, Alastruey-Izquierdo A, Wrzosek M, Rodriguez-Tudela JL, Dolatabadi S, et al. DNA barcoding in Mucorales: an inventory of biodiversity. *Persoonia Mol Phylogeny Evol Fungi.* 2013;30:11-47.