

To Describe the Epidemiology, Management and Outcome of Black Fungus and To Minimize the Risk Factor Associated with Black Fungus Disease: A Review

Dhananjay Patel ¹, Diksha Dilliwar ¹, Jagriti ¹, Monika Dewangan ¹, Chandraprabha Dewangan ², Rajesh Kumar Nema ¹, Harish Sharma ², Gyanesh Kumar Sahu ²

¹Rungta Institute of Pharmaceutical Sciences, Bhilai, India. ²Rungta Institute of Pharmaceutical Sciences and Research, Bhilai, India. Corresponding Author: Chandra.prabha@rungtacolleges.com

Abstract: - The disorder Mucorales, a type of filamentous moulds, is what causes the disease known as mucormycosis. Infections may be brought on by contaminated food, spore inhalation into the nose or lungs, or injection into open wounds or damaged skin. In industrialised countries, mucormycosis primarily affects hosts who are severely immunocompromised (such as those who have haematological malignancies, organ transplants, neutropenia, autoimmune diseases, or other immune system deficits). The estimated prevalence of mucormycosis in India is over 70 times higher than it is worldwide. Diabetes mellitus is the most frequent risk factor, followed by solid-organ transplant and haematological cancer. In this country, people with postpulmonary TB and chronic renal disease are more likely to develop mucormycosis. Trauma is a risk factor for cutaneous mucormycosis. renalmucormycosis in one occurrence. An immunocompetent host is a distinct species in India. Even though Rhizopusarrhizus is the most common etiological agent of mucormycosis in this country, Rhizopushomothallicus, Rhizopusmicrosporus, and Apophysomycesvariabilis infections are on the rise. Despite being a long-standing disease, mucormycosis has recently attracted attention because to its widespread occurrence in COVID-19 patients in India. Disposable face masks constructed of polymer materials have been widely used by the public as effective and reasonably priced personal protective equipment (PPE) to halt the spread of infectious diseases. A N95 respirator js a type of respiratory protective equipment that is designed to fit the user's face tightly and to filter airborne particles very efficiently. Be mindful that the corners of the respirator are designed to shut out the nose and mouth. surgical N95.

Key Words: - Mucormycosis, Covid19, N95 Mask.

I. INTRODUCTION

It is a dangerous fungal illness that falls under fulminant fungal sinusitis and is also referred to as black fungus and zygomycosis.

Manuscript revised May 20, 2023; accepted May 21, 2023. Date of publication May 22, 2023.

This paper available online at <u>www.ijprse.com</u> ISSN (Online): 2582-7898; SJIF: 5.59 It is caused by a mould that develops on rotting and decaying organic waste. These fungi are widespread in soils, rotting organic materials (such fruit and vegetables), and animal dung, yet they typically have no negative effects on humans.[1] It is caused by members of the filamentous mold fungus, the

Mucorales (ranging from 3 to 11 μ m in diameter and are easily aerosolized) such as Apophysomyces, Cokeromyces, Cunninghamella, Lichtheimia, Mortierella, Mucor, Rhizopus, Rhizomucor, Saksenaea, Syncephalastrum, Thamnostylum and Mucormycetes that causes the infection and affects peoples.[2] It most commonly infects thenose, sinuses, brain (rhinocerebral mucormycosis), and eyes resulting in arunny nose, one-sided facial swelling and pain, headache, fever, blurred vision,

DHANANJAY PATEL., et.al.: TO DESCRIBE THE EPIDEMIOLOGY, MANAGEMENT AND OUTCOME OF BLACK FUNGUS AND TO MINIMIZE THE RISK FACTOR ASSOCIATED WITH BLACK FUNGUS DISEASE: A REVIEW



bulging or displacement of the eye (proptosis), and tissue death Other forms of disease may infect thelungs(pulmonary mucormycosis), stomach and intestines(gastrointestinal mucormycosis), and skin(cutaneous mucormycosis).[3]

"Black Fungus" is applied to human pathogenic Mucorales species due to the formation of black-colored sporangium and these spores are airborne and found in indoor and outdoor air, and in dust and also found in hospital environments such as hospital bed sheets, negative-pressure rooms, water leaks, contaminated medical equipment, and building works. [4].

1.1 Case Report

		GLOBAL		INDIAN			
YEAR	TP	TP	%TP	CITATIONS	СРР	%ICI ICP	Р
1998	104	11	10.5	148	13.4	0	0
1999	121	12	9.9	175	14.5	1	8.3
2000	99	7	7	54	7.7	2	28.5
2001	121	10	8.2	193	19.3	0	0
2002	115	10	8.7	80	8	0	0
2003	119	13	10.9	373	28.7	0	0
2004	161	15	9.3	261	17.4	1	606
2005	191	19	0.9	682	35.9	2	10.5
2006	219	27	12.3	592	21.9	2	7.4
2007	223	33	14.8	527	15.9	0	0
2008	252	24	9.5	316	13.1	1	4.1
2009	277	32	11.5	737	23	5	15.6
2010	276	38	13.7	453	11.9	5	13.1
2011	273	38	13.9	374	9.8	4	10.5
2012	317	47	14.8	299	6.3	7	14.9
2013	296	48	16.2	239	4.9	3	6.2
2014	347	52	14.9	662	12.7	2	3.8
2015	305	57	18.7	326	5.7	6	10.5
2016	300	52	17.6	506	9.7	6	11.5
2017	304	40	13.1	152	3.8	2	5

2018	326	49	15	160	3.2	6	12.2
2019	392	66	16.8	333	5	5	7.5
2020	355	60	16.9	57	0.9	6	10
2021	165	39	23.6	12	0.3	4	10.2

ABBREVIATION:	TP	=Total	publications;	CPP	=Citations	per			
publications; ICP=International collaborative publications									

II. TYPES OF MUCORMYCOSIS

ROCM (rhino-orbital-cerebral mucormycosis): The most prevalent type of mucormycosis is which affects 45-74% of people.

GASTROINTESTINAL (0.8%): Young children are more likely to experience it than adults. Infants who are premature or low birth weight and are younger than one month of age are at risk if they have undergone surgery, received antibiotics, or are taking drugs that impair the body's defences against infection.

CUTANEOUS [Skin] (6.1%): It happens once the fungi get inside the body through a skin breach. After a burn, scrape, cut, surgery, or other sort of skin trauma, this kind of infection may develop. Among those who do not have compromised immune systems, this is the most prevalent type of mucormycosis.

RHINOCEREBRAL (Sinus and Brain) (3.5%): It is an infection in the sinuses that can spread to the brain. This is most common in people with uncontrolled diabetes and in people who have had a kidney transplant.

DISSEMINATED FORM (1.4%): It happens when the illness travels to another area of the body through the bloodstream. The infection typically affects the brain, but it can also harm the spleen, heart, and skin, among other organs.

PULMONARY [Lung] (3-22%): It is the most prevalent kind of mucormycosis in cancer patients, transplant recipients, and stem cell recipients.

OTHER INFECTIONS: such as Bone, Beat, Spine, And Heart Infections.

SYMPTOMS [7]:

Symptoms mainly depend on the location in the body of the infection. The Infection usually begins in the mouth or nose and enters the central nervous system via the eyes.

- Stuffy (Nasal and blood vesels become swollen with excess fluids) and bleeding nose;
- Swelling of and pain in the eye;
- Drooping of eyelids (excess sagging of upper eyelids)
- Blurred or loss of vision.



- Change in Mental status
- Lapse into coma



Fig.1. Signs and Symptoms

III. RISK FACTORS

DIABETES MELLITUS: Diabetes mellitus leads to tremendous health problem Excess glucose in blood impairs the defence mechanism by suppressing cytokine (IL – 6) production and phagocytises which is responsible for antibiotics production. High level of glucose level causes disfunction and Fc- γ receptors present on monocyts resulting in suppression of cytokine. (8)

DIABETIC KETOACIDSIS: Excess ketones make our blood more acidic which decreases the binding of iron to the transferritin, these free iron ions in blood increase the growth of black fungus. (8)

EXCESS IRON: Peoples with Thalassemia and Leukaemia are more prone to develop iron overload. Black fungus absorbs iron in the form of haem and free iron ions for cellular process and produce energy for their growth. High amount of free iron leads to destruction of heamostasis.(9)

KAWASAKI DISEASE (KD): People with KD disease has low level of T cells and B cells which triggers prolong self-directed immune response. (10)

STEROIDS: Prolonged use of steroids causes excess stimulation of glucocorticoid and mineralocorticoid receptors, which suppresses the immune by segregating CD4+ T-lymphocytes, resulting mucormycosis. (11)

UNSTERILIZED MEDICAL DEVICES: Unsterilized medical devices, contaminated equipment's and impure water increases

the growth of infections. Dry nose with oxygen therapy leads to invasion of black fungus in the body. (12)



Fig.2. Mucormycosis Risk Factors

3.1 Mode of Action of Black Fungus

Mucormycetesmould can invade in the susceptible host through nose, mouth or burned /disrupted skin which results in rhinogastrointestinal or orbito-cerebral, cutaneous wound that cerebral infections[13].Studies proposed Rhino Mucormycosis is most common among all other cases progression of this rhino-cerebral Mucormycosis may leads to central nervous systemand it becomes dangerous, the second most preferred site of infection are lungs and sinuses[14]. Physicians suggested that immuunosuppresed patients are more likely to be affected with Mucormycosis or Black fungus. Patients with hyperglycemia(High Blood Glucose) and ketoacidosis(Lack of Insulin level) are more susceptible to get attacked by Mucormycosis moulds[15]. Covid-19 patients developes dysfunction of immune system with decrease in lymphocyte counts and increament in inflammatory cytokines such as IL-6, IL-1 β , IFN- γ etc. and Tumor necrosis factor(TNF) that leads to hyperinflammation in the lungs[16]. Covid-19 patient with immunosuppressant may leads to dysfunctional phagocytes causes impaired intracellular killing by oxidative and nonoxidative mechanism. [17]



INTERNATIONAL JOURNAL OF PROGRESSIVE RESEARCH IN SCIENCE AND ENGINEERING, VOL.4, NO.05, MAY 2023.



3.2 Co-Relation Between Covid and Black Fungus

A lack of oxygen (hypoxia), an increase in glucose (diabetes, new-onset hyperglycemia, and steroid-induced hyperglycemia), an acidic environment (metabolic acidosis, diabetic ketoacidosis (DKA)), and a higher level of iron (high ferritins) are among the conditions that have recently been linked to mucormycos is in COVID-19 patients. Low white blood cell phagocytic activity (WBC) in COVID-19-infected individuals appears to aid Mucorales spore germination [18].



Fig.4. Mucormycosis

These infections could be caused by fungi, bacteria, viruses, parasites, or even bacteria. COVID - 19 Patients with SARS-CoV-2 infection are more susceptible to develop opportunistic infections.

3.3 Protective Methods for Black Fungus

Patients must bear in mind the following behaviours to prevent contracting mucormycosis; some of these activities are unique to COVID patients, while others are general advice to prevent the COVID symptoms of mucormycosis.

- Wear a face mask when visiting dusty locations or construction sites to lessen mucus production and prevent mistakenly breathing in fungi that could cause symptoms of mucormycosis.
- Mucormycosis is brought on by a substance called mucor, which is found in rotting plants, fruits, and vegetables as well as in gardens that are exposed to dirt, manure, and plants. When outdoors or working with dirt and manure, put on the proper footwear, long trousers, full-sleeved shirts and gardening gloves to stay safe and avoid the symptoms of black fungus.
- Consistently exercise proper hygiene and take full baths.

3.4 Use of Fack Mask

They are used in community and clinical settings as source control to reduce viral spread and for individual safety to avoid infection. Masks that are worn properly both reduce the number of respiratory droplets and aerosols that are transferred by infected people and aid in preventing infection in healthy people. [20]

A face mask acts as a shield to shield the respiratory tract from airborne droplets and particles. One may trace the development of mouth and nose covering to the turn of the 20th century. Examples include mouth guards, face veils, face masks, and mouth bandages.

By lowering the rates of infection by airborne transmission, face mask use has been crucial in protecting both HCWs (Healthcare Workers) and the general public. A patient's face mask might lower not only the release of virus carrying droplets into the open air but both the intake of virus-carrying droplets from the open air as well as the discharge of virus-carrying droplets into the open environment. The wearing of a mask can protect an infected but asymptomatic healthcare provider from dispersing viruses into the open air. The mask can also shield users from airborne infections at the same time. Wearing a mask in a clinical setting can help lower the risk of infection spread via airborne contact between patients and medical personnel. [21]



INTERNATIONAL JOURNAL OF PROGRESSIVE RESEARCH IN SCIENCE AND ENGINEERING, VOL.4, NO.05, MAY 2023.



Fig.5. Multifunctional Masks

CHOICE OF MASK [22]



Fig.6. Different types Masks



Fig.7. Different types Masks

3.5 N 95 Mask [23,24,25]

Peter Tsai, a Taiwanese-American, and his colleagues created the N95 mask filter, which was granted a U.S. patent in 1995.A particulate-filtering facepiece respirator that filters at least 95% of airborne particles is known as a N95 filtering facepiece respirator, or simply a N95 respirator. It serves as an illustration of a mechanical filter respirator, which offers protection from particulates but not from gases or vapours.

The words "NIOSH" or the NIOSH emblem, as well as the filter class, are stamped on an official N95 respirator ("N95"). A tiny mesh of synthetic polymer fibres, specifically a nonwoven polypropylene fabric, is necessary for the N95 respirator. It is created by melt blowing and serves as the primary filter for dangerous particles.





3.6 Misinformation's about Mucormycosis: [32]

- Mucorales are not a type of dark fungi. They are many fungal species where melanin is found in the cell walls.
- Mucormycosis is not a dangerous condition. No body can catch it from another person.
- Water, humidifiers, and oxygenation do not spread micorycosis. Both the indoor and outdoor environments still contain the fungi. The respiratory system is exposed to the spores through the air.
- It is not advised to use antifungal prophylaxis because the incidence is not more than.

IV. DISCUSSION

Mucormycosis is an uncommon condition that almost exclusively affects patients with compromised immune systems.8 Following the COVID-19 pandemic, there has been a sharp rise in CAM cases, which suggests the possibility that COVID-19 infection is already a risk factor for mucormycosis. This may occur directly as a result of its immune systemdamaging effects or indirectly as a result of COVID-19 prevention and control measures. Even before the COVID-19 period, India had the highest prevalence of mucormycosis in the world, at nearly 70 times the average.2 This disproportionate burden has been associated with the high prevalence of both patient variables (diabetes) and environmental factors (hot, humid environment).9 Due to a bias in referrals for a difficult disease, CAM patients were more likely to live in rural areas to treat the conditions.

The disease reportedly struck three weeks after the onset of COVID-19 symptoms and primarily impacted the rhino-orbital regions.1 Poor glycemic control, systemic steroid therapy, and the presence of diabetes all increase the risk of CAM..The Occupational Safety and Health Administration (OSHA) mandates that healthcare workers in the US wear respiratory protection, such as a N95 respirator, when performing patient activities with people who are known or suspected to be COVID-19 infected. The CDC (Centres for Disease Control and Prevention) suggests using respirators with at least N95 certification to shield the wearer from inhaling infectious particles such as Mycobacterium tuberculosis, avian influenza, severe acute respiratory syndrome (SARS), pandemic influenza, and Ebola virus.

V. RESULTS AND CONCLUSION

Because with COVID-19, the entire world's population is now in risk. Lack of a specific cure for the lethal viral infection and the arrival of the second wave in India caused the situation to spiral out of control. With their limited access to medical resources, frontline health professionals and paramedical staff were unable to contain the pandemic because the infection rate was increasing everyday. The management problem during the handling of COVID-19 has been made worse by the frequent use of steroids, antibiotics, and supportive therapy (supportive oxygen and ventilators) for patients with known comorbidities such diabetes and cardiovascular problems. Patients with comorbid illnesses are more likely to get later coinfections such mucormycosis. Due to their weakened systems, people with a history of comorbidities are more likely to contract a virus that might cause a potentially fatal fungal infection. An N-95 mask or respirator provides additional protection since it fits the face securely and more effectively filters airborne germs. It filters at least 95% of airborne pollutants. The N-95 mask comes in a variety of varieties. A one with valves is widely used. There is a one-way filtering mechanism in these masks.

REFERENCES

- Sagar GR, Jha BC, Meghanadh KR. A study of anatomy of frontal recess in patients suffering from 'chronic frontal sinus disease'. Indian J Otolaryngol Head Neck Surg. 2013 Aug;65(Suppl 2):435-9.
- [2]. Grossman, M.E.; Fox, L.P.; Kovarik, C.; Rosenbach, M. Subcutaneous and Deep Mycoses: Zygomucosis/Mucormycosis. Cutaneous Manifestations of Infection in the Immunocompromised Host, 2nd ed.; Springer: New York, NY, USA, 2012; pp. 51–58.
- [3]. Surkis A, Spore S. The relative citation ratio: what is it and why should medical librarians care? J Med Libr Assoc. 2018;106(4):508-13.
- [4]. Richardson, M. The ecology of the Zygomycetes and impact on environmental exposure. Clin. Microbiol. Infect. 2009, 15, 2–9.
- [5]. Lim S, Bae JH. COVID-19 and diabetes mellitus: from pathophysiology to clinical management. Nat Rev Endocrinol. 2021; 17: 11-30.
- [6]. Carlo Perricone, Elena Bartoloni. COVID-19 as a part of the hyper ferritinemic syndromes: The role of iron depletion therapy. Immunol Res. 2020; 68: 213-24.
- [7]. Suriya Rehman, Tariq Majeed. Syndrome resembling Kawasaki Disease in Covid-19 asymptomatic Children. J Infect Public Health. 2020; 13(12): 1830-32.
- [8]. Vamsi Krishna VN, Siva Ramesh C. Rational use of corticosteroids in Covid-19- A Review. Asian Jour Hosp Phar. 2021; 2(2): 38-39.
- [9]. Josie moriera et.al. Cutaneous mucormycosis in advanced HIV disease. The Braz jour of Inf dis. 2016; 20(6): 637-40.
- [10].S. Mohindra, S. Mohindra, R. Gupta, J. Bakshi, S.K. Gupta Rhinocerebral mucormycosis: the disease spectrum in 27 patients Mycoses, 50 (2007), pp. 290-296.
- [11].B. Spellberg, J. Edwards Jr., A. IbrahimNovel perspectives on mucormycosis: pathophysiology, presentation, and management Clin Microbiol Rev, 18 (3) (2005), pp. 556-569.
- [12]. JMaertens, H. Demuynck, E.K. Verbeken, et alMucormycosis in allogeneic bone marrow transplant recipients: report of five cases and review of the role of iron overload in the pathogenesis Bone Marrow Transplant, 24 (1999), pp. 307-312.
- [13].Q. Zhou, V. Chen, C.P. Shannon, et al.Interferon-α2b treatment for COVID-19 Front. Immunol, 11 (2020 May 15), p. 1061.
- [14].K. Ahmadikia, S.J. Hashemi, S. Khodavaisy, et al. The double-edged sword of systemic corticosteroid therapy in viral pneumonia: a case report and comparative review of influenza-associated mucormycosis versus COVID-19 associated Mucormycosis Mycoses (2021), pp. 1-11.
- [15]. Singh A.K., Singh R., Joshi S.R., Misra A., Mucormycosis in COVID-19: A systematic review of cases reported



worldwide and in India. Diabetes & Metabolic Syndrome. 2021; 15 (4): 102146.

- [16]. Sugar AM. Agents of mucormycosis and related species. In: GI Mandell, JE Bennett, Dolin R, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 5th edn. New York: Churchill Livingstone, 2000; 2685–95.
- [17].Bourouiba L (July 2021). "Fluid Dynamics of Respiratory Infectious Diseases". Annual Review of Biomedical Engineering. 23 (1): 547–577.
- [18].X. Wang, E.G. Ferro, G. Zhou, D. Hashimoto, D.L. Bhatt Association between universal masking in a health care system and SARS-CoV-2 positivity among health care workers J Am Med Assoc, 324 (2020), pp. 703-704.
- [19].Brosseau LM. Are Powered Air Purifying respirators a solution for protecting healthcare workers from emerging aerosol-transmissible diseases? Ann Work Expo Heal. 2020; 64 (4), 339-41.
- [20]. "Meet the U.S. scientist who invented the N95 mask filter". U.S. Embassy in Georgia. August 12, 2020. Retrieved June 12, 2022.
- [21]. "Personal Protective Equipment: Questions and Answers". Centers for Disease Control and Prevention. February 11, 2020. Retrieved October 25, 2020.
- [22]. "Comparison of FFP2, KN95, and N95 and Other Filtering Facepiece Respirator Classes" (PDF). 3M Technical Data Bulletin. January 1, 2020. Retrieved March 28, 2020.
- [23].K.C. Dantas, T. Mauad, C.D.S. deAndré, A.L. Bierrenbach, P.H.N. Saldiva A single-centre, retrospective study of the incidence of invasive fungal infections during 85 years of autopsy service in BraziLSci. Rep., 11 (2021), pp. 1-10.
- [24]. Iyer Mahalaxmi, Mucormycosis. An Oppurtunistics pathogen during COVID 19, Revised 1 July 2021, Accepted 1 July 2021, Volume 201, October 2021, 111643.
- [25].S. Schmidt, L. Tramsen, S. Perkhofer, C. Lass Flörl, M. Hanisch, F. Röger, T. Klingebiel, U. Koehl, T. LehrnbecherRhizopus oryzae hyphae are damaged by human natural killer (NK) cells, but suppress NK cell mediated immunity Immunobiology, 218 (2013), pp. 939-943.
- [26]. A. Khatri, K.-M. Chang, I. Berlinrut, F. Wallach Mucormycosis after Coronavirus disease 2019 infection in a heart transplant recipient–case report and review of literature, J. Med. Mycol., 101125 (2021).
- [27]. "Recommended Guidance for Extended Use and Limited Reuse of N95 Filtering Facepiece Respirators in Healthcare Settings". cdc.gov. NIOSH Workplace Safety and Health Topic. CDC. 27 March 2020.
- [28].Brosseau LM. Are Powered Air Purifying respirators a solution for protecting healthcare workers from emerging aerosol-transmissible diseases? Ann Work Expo Heal. 2020; 64 (4), 339-41.

- [29].Global guideline for diagnosis & management of mucormycosis. Lancet infect Dis 2019; e405-e421.
- [30]. Honavar SG. Rhino-orbital-cerebral mucormycosis Guidelines for diagnosis, staging, and management, India J Ophthalmol 2021;69.