

Journal of Pharmaceutical Advanced Research**(An International Multidisciplinary Peer Review Open Access monthly Journal)**Available online at: www.jparonline.com**Current Scenario and the way to protect us from Black Fungus: A review****Selvaraj Selvamurugan**

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ABSTRACT: As the human-to-human transmitted disease, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARSCoV-2), has been an emergency global public health event. Those patients were easily affected by means of mucormycete. Mucormycosis, commonly called black fungus, is a rare but serious fungal infection caused by a kind of fungus called mucormycetes, which is abundant in the environment. It mainly affects people who have health problems or take medicines that lower the body's ability to fight germs and sickness. It is being detected relatively frequently among COVID-19 patients in some states of India. While there is no major outbreak, the national COVID task force has issued an advisory regarding this disease. This entity needs to be picked up early by spreading awareness among the family physicians, internists, otolaryngologists, ophthalmologists, neurosurgeons, pulmonary physicians, critical care specialists so that an early management can be initiated to achieve better control over the disease. This review is an attempt to initiate an interdisciplinary approach to achieve a better outcome.

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INTRODUCTION:

Coronavirus disease 2019 (COVID-19) is an infection caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Since the first case was detected, in December 2019 in Wuhan, China, there have been various turns and twists in terms of its pathophysiology, diagnosis, management, sequelae and complications^[1]. The Covid-19 symptom spectrum has expanded since the first days of the disease's presentation, which initially included only a dry cough and high grade fever, to additionally include various multisystem problems such as shortness of breath, anosmia, ageusia, diarrhoea, generalised malaise, acute cardiac injury and secondary infections. Early identification of these high-morbidity conditions is

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crucial for optimal treatment and improved outcomes. Recently observed another association between ENT and coronavirus, a more dangerous and potentially deadly one: that of invasive fungal sinusitis resulting from mucormycosis. The western state of Maharashtra, home to Mumbai, has recorded about 2,000 cases and eight fatalities due to mucormycosis disease. The incidence of mucormycosis has risen more rapidly during the second wave compared with the first wave of COVID-19 in India, with at least 14 872 cases as of May 28, 2021. The state of Gujarat alone contributed to the highest number of cases, with at least 3726 cases of mucormycosis in patients with active and recovered COVID-19, followed by the state of Maharashtra. Since the communication from the Health Minister of Maharashtra on May 19, 2021, there have been 90 deaths attributable to mucormycosis. Other states such as Rajasthan, Andhra Pradesh, Karnataka, Haryana, Madhya Pradesh, Uttarakhand, and Delhi have also shown a steady rise in the number of mucormycosis cases and deaths related to it [2].

As the second wave of COVID-19 continues to rage across India, some parts of the country have begun witnessing the resurgence of COVID-19-induced black fungus cases. This fungal infection, which caused many patients to lose their eyesight last year, has emerged in several hospitals in Delhi and Gujarat this week. The second wave of COVID-19 has affected India substantially, with the highest number of daily reported cases being slightly more than 0.4 million on May 7, 2021, and has declined since. Even though the number of new reported cases has reduced, India still contributed to approximately 45 % of the new cases detected globally and nearly 34% of the deaths globally during the third week of May, 2021 [3]. Though *Aspergillus* and *Candida* are more common fungi, this fungus is particularly harmful because it affects the sinuses and the brain, and it appears in immunocompromised patients and/or those taking steroids, available information from [4]. Mucormycosis cases have a 54 percent all-cause mortality rate, according to the Centres for Disease Control and Prevention (CDC). Mucormycosis cases have a 54 percent all-cause mortality rate, according to the Centre for Disease Control and Prevention (CDC). This rate, however, varies depending on the underlying medical condition, fungus type, and infected body location. The black fungus has moved many COVID-recovered patients back into ICUs since the onset of the

pandemic [5,6]. This article intended to explore the disease, symptoms and treatment strategy of Black fungus' in Covid-19 patients.

BACKGROUND:

Mucormycosis is an angioinvasive disease caused by fungi of the order Mucorales like *Rhizopus*, *Mucor*, *Rhizomucor*, *Cunninghamella* and *Absidia*. The prevalence of mucormycosis in India is approximately 0.14 cases per 1000 population, about 80 times the prevalence in developed countries [7]. COVID-19 infection has been associated with fungal infections. Mucormycosis is more often seen in immunocompromised individuals, and complications of orbital and cerebral involvement are likely in diabetic ketoacidosis and with concomitant use of steroids. The most common risk factor associated with mucormycosis is diabetes mellitus in India [8]. In the background of the COVID-19 pandemic, only a limited number of cases of mucormycosis have been reported, but there are no known documented cases of sudden-onset visual loss with incidental COVID-19 infection in a newly detected young non-ketotic diabetic [9].

MUCORMYCOSIS:

Black fungus, also known as mucormycosis (previously called zygomycosis), is a serious but rare fungal infection. Mucormycosis is a very rare infection. It is caused by exposure to mucor mould which is commonly found in soil, plants, manure, and decaying fruits and vegetables. It is ubiquitous and found in soil and air and even in the nose and mucus of healthy people [6].

Diversity of fungi caused mucormycosis:

Mucormycosis is a fungal infection that is angioinvasive and is associated with a high rate of morbidity and mortality. This is caused by a number of fungi. Mucormycetes are fungi belonging to the Mucorales scientific order. Mucormycosis is caused by *Rhizopus* and *Mucor* species, which are the most widespread. Other examples include *Rhizopus arrhizus*, *Rhizopus homothallicus*, *Mucor irregularis*, *Syncephalastrum* species, *Cunninghamella bertholletiae*, *Apophysomyces variabilis*, *Thamnostylum lucknowense*, *Lichtheimia (formerly Absidia) and Saksena* [8,10].

EPIDEMIOLOGY OF MUCORMYCOSIS:

Most of the data regarding the epidemiology of mucormycosis originate from case reports and case series. The first extensive review of the literature was

made by the Roden team^[11]. The analysis comprised 929 cases published from 1940 to 2003, providing useful information about the disease, but it also included cases of entomophthoromycosis. More recently, Jeong's team analyzed 851 cases published from 2000 to 2017. In this study, the review was undertaken and reported using the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines and it included only cases caused by Mucorales^[12]. Other relatively large case series were collected either on a national level or in patients with selected underlying diseases, for example, hematopoietic stem cell transplantation^[13,14]. Registries are another source of valuable information, despite their inherent limitations. The Working Group on Zygomycosis of the European Confederation of Medical Mycology (ECMM) and the International Society of Human and Animal Mycology (ISHAM) constructed such a registry in 2004 (www.zygomycosis.net) and published 230 cases from Europe in 2011^[15]. Mucormycosis is contracted as people encounter fungal spores in the atmosphere. With the increase in prevalence, new causative agents, and a vulnerable population, the epidemiology of mucormycosis has changed in recent years. The rising has been seen all over the world, but it is especially noticeable on the Asian continent. After inhaling spores, for example, the virus may manifest itself in the lungs or sinuses. This type of mucormycosis is most common in individuals that have health issues or who take medications that reduce the body's capacity to combat germs and illness. After the fungus reaches the skin through a slash, scratch, burn or other form of skin trauma, mucormycosis may develop^[16,17].

How does the fungal infection spread?

Mucormycosis is not contagious, and therefore, it cannot transmit between people and animals. Individuals contract this infection by coming in contact with the fungal spores in their environment. If inhaled, the spores can infect the lungs or sinus. If the fungus enters the skin through a cut, scrape, burn, or other types of skin trauma, mucormycosis can also develop on the skin. The infection can subsequently spread to the bloodstream, and reach organs like the brain, heart and spleen as well^[18]. While most cases of mucormycosis are sporadic, outbreaks of mucormycosis have occurred in the past. In healthcare settings, healthcare-associated mucormycosis outbreaks have been linked to adhesive bandages, wooden tongue depressors, hospital linens,

negative pressure rooms, water leaks, poor air filtration, non-sterile medical devices, and building construction. Community-onset outbreaks have also been associated with trauma sustained during natural disasters. The fungal disease, called mucormycosis, has a 50 % mortality rate. It affects patients initially in the nose but the fungus can then spread into the brain, and can often only be treated by major surgery removing the eye or part of skull and jaw. The disease is caused by fungal spores found in soil and organic matter, usually inhaled by humans from the air. The mould enters the body and then manifests around the nose and eye sockets, causing the nose to blacken, and if not stopped will move fatally into the brain. Healthy individuals will usually fight off the fungus but it can spread fast in those with compromised immunity. It is usually a rare disease, but more than 7,200 people in India have now been reported with mucormycosis and 219 have lost their lives. The rise in black fungus infections, mostly in patients who had severe cases of COVID-19, has been linked to an overuse of steroids in the treatment of the coronavirus, which can acutely compromise the immune system if taken over a prolonged period. The high incidence of diabetes in India has also been blamed, with high blood sugar levels linked to susceptibility. India has the second highest rate of diabetes in the world^[19].

So five states, Tamil Nadu, Odisha, Gujarat, Rajasthan and Telangana, have declared black fungus to be an epidemic, and more states are expected to follow. The Indian Council of Medical Research has issued an advisory on the diagnosis and treatment of the disease. Maharashtra, the first state to be hit hard by India's second COVID-19 wave, has already reported upwards of 1,500 cases and 90 deaths, the highest in the country. Hospitals in Delhi have also begun reporting an unprecedented rise in cases – as many as 15 to 20 new cases a day in some hospitals, compared with previous rates of one or two cases a month. In Delhi and Bangalore, there are now waiting lists for beds for treatment for the disease.

SYMPTOMS OF MUCORMYCOSIS:

The symptoms of mucormycosis depend on where the fungus is growing in the body. For rhinocerebral (sinus and brain) mucormycosis, the symptoms are one-sided facial swelling, headache, nasal or sinus congestion, fever, and black lesions on the nasal bridge or upper inside of the mouth that quickly become more severe. For pulmonary (lung) mucormycosis, the symptoms

include fever, cough, chest pain, and shortness of breath [20].

DIAGNOSIS:

Physical examination, swab test, tissue biopsy, imaging tests like CT or MRI scans to understand about the severity [21].

How can we protect ourselves from black fungus [22]?

- The most effective way to prevent the black fungus is to wear a mask while venturing out, especially to gardens, dusty areas, where there is garbage bumping or food rotting.
- Wear long clothes and have less exposure to skin.
- Most importantly for diabetic and other immune-compromised people, controlling sugar levels and blood glucose is a must.
- People who are prescribed steroids should be constantly monitored and the dosage should be reduced in consultation with your doctor.
- Importantly, steroids must only be taken after consulting with your doctor – do not self medicate.

How can black fungus be treated?

As per the CDC, this serious infection needs to be treated with prescription antifungal medicine, usually Amphotericin B, Posaconazole, or Isavuconazole. These medicines can be taken orally or through intravenously. The infection often requires surgery to cut away the infected tissue [23].

CONCLUSION

In this situation, a novel Coronavirus causes a global pandemic that affects nearly the whole world, resulting in a deadly condition. As of now no major outbreak of mucormycosis, a lethal black fungal infection, have been seen in COVID-19 patients.

The scientific community has an immediate focus on developing antivirals and vaccines for the treatment and prevention of COVID-19. However, this new emerging serious disease puts many patients at risk for opportunistic microbial infections, including fungal ones.

This fact highlights the importance of the continued commitment to developing novel promising effective (and safe) antifungal drugs to combat invasive aspergillosis and other resistant fungal infections. Infection is most likely in patients on steroids, diabetics, or others who have had a transplant. As a result, early diagnosis, antifungal therapy, and prevention steps can be used to cure the infection.

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REFERENCES:

1. Wuhan City Health Committee. Wuhan Municipal Health and Health Commission's briefing on the current pneumonia epidemic situation in our city 2019. <http://wjw.wuhan.gov.cn/front/web/showDetail/2019123108989> (Accessed January 14, 2020).
2. Akshay raut, Nguyen Tien Huy. Rising incidence of mucormycosis in patients with COVID-19: another challenge for India amidst the second wave? *Lancet Respir Med*, 2021; 256(4): 1-2.
3. World Health Organisation. COVID-19 Weekly Epidemiological Update. https://www.who.int/docs/defaultsource/coronavirus/situationreports/20210525_weekly_epi_update_41 (Accessed May 25, 2021).
4. Biswas S. Mucormycosis: The black fungus maiming Covid patients in India. <https://www.bbc.com/news/world-asia-india-57027829> (Accessed May 9, 2021).
5. Varun Rai. COVID-19 Triggering Rare, Deadly Fungal Infection, Claims Delhi's Ganga Ram Hospital. <https://www.news18.com/news/india/covid-19-triggering-rare-deadly-fungal-infection-claims-delhis-ganga-ram-hospital-3177929.html> (Accessed December 14, 2020).
6. Swathymoorthy M, Manigandan ACV. Mucormycosis an emerging Fungal Infection. *Indian J Appl Res*, 2015; 5(8): 661-664.
7. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: an update. *J Fungi*, 2020; 6(4): 265-280.
8. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. *J Fungi*, 2019; 5(1): 26-44.
9. Gangneux JP, Bougnoux ME, Dannaoui E, Cornet M, Zahar JR. Invasive fungal diseases during COVID-19: we should be prepared. *J Mycol Med*, 2020; 30(2): 100971.
10. Al-ajam MR, Bizri AR, Mokhbat J. Mucormycosis in the Eastern Mediterranean: a seasonal disease. *Epidemiol Infect*, 2006, 134(2): 341–346.
11. Jeong W, Keighley C, Wolfe R, Lee WL, Slavin MA, Kong DC, *et al*. The epidemiology and clinical manifestations of mucormycosis: A systematic

- review and meta-analysis of case reports. Clin Microbiol Infect, 2009; 25: 26-34.
12. Corzo-Leon DE, Chora-Hernandez, LD, Rodríguez-Zulueta AP, Walsh TJ. Diabetes mellitus as the major risk factor for mucormycosis in Mexico: Epidemiology, diagnosis, and outcomes of reported cases. Med Mycol, 2018, 56: 29-43.
 13. Lanternier F, Dannaoui E, Morizot G, Elie C, Garcia-Hermoso D, Huerre M, *et al.* The French Mycosis Study Group. A Global Analysis of Mucormycosis in France: The RetroZygo Study (2005–2007). Clin Infect Dis, 2012; 54: S35–S43.
 14. Skiada A, Pagano L, Groll A, Zimmerli S, Dupont B, Lagrou K, Lass-Flörl C, Bouza E, Klimko N, Gaustad P. Zygomycosis in Europe: Analysis of 230 cases accrued by the registry of the European Confederation of Medical Mycology (ECMM) Working Group on Zygomycosis between 2005 and 2007. Clin Microbiol Infect, 2011; 17: 1859–1867.
 15. Petrikos G, Skiada A, Lortholary O. Epidemiology and clinical manifestations of mucormycosis. Clin Infect Dis, 2012; 54(1): S23-S34.
 16. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. Clin Microbiol Rev, 2000; 13(2): 236-301.
 17. Namdeo P. A Review on Herbal Immunity Booster and Nutrition – To Fight against COVID-19. J Pharm Adv Res, 2021; 4(5): 1226- 1237.
 18. Van Arkel ALE, Rijpstra TA, Belderbos HNA, van Wijngaarden P, Verweij PE, Bentvelsen RG. COVID-19 associated pulmonary aspergillosis. Am J Respir Crit Care Med, 2020; 202(1): 132-135.
 19. Bhat I, Beg MA, Athar FA. Contemporary intimidation for COVID-19 patients coinfecting with mucormycosis in India. J Bacteriol Mycol Open Access, 2021; 9(2): 69–71.
 20. Petrikos G, Skiada A, Lortholary O. Epidemiology and clinical manifestations of mucormycosis. Clin Infect Dis, 2012; 54(1): S23-S34.
 21. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. Clin Microbiol Rev, 2000; 13(2): 236-301.
 22. KR Kumar P. Mucormycosis: A Black Fungus- Post Covid Complications. J Regen Biol Med, 2021; 3(4): 1-8.
 23. Kontoyiannis DP, Azie N, Franks B, Horn DL. Prospective Antifungal Therapy (PATH) Alliance®: Focus on mucormycosis. Mycoses, 2014; 57: 240–246.

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