

## Recent Advancement in Diabetes ,Mellitus , Ketoacidosis & Mucormycosis

Dhanashree Bajarang Sastare <sup>1</sup>, Hemantkumar Bhosale <sup>2</sup>

Institute of Pharmaceutical Science & Research (for girls ), Swami –Chincholi, Dund ,Pune – 413130

### ABSTRACT

Mucormycosis is an angioinvasive fungal infection. . The prevalence of mucormycosis in India is about 80 times the prevalence in developed countries, being approximately 0.14 cases per 1000 population. Diabetes mellitus is the main underlying disease globally, especially in low and middle-income countries. In developed countries the most common underlying diseases are hematological malignancies and transplantation. India has a very high incidence of mucormycosis cases when compared to other countries even prior to Covid. The incidence of mucormycosis in India is around 14/100,000 population while that in Australia is 0.06/100,000 population. The reason behind this is India's hot humid climate where the spores of mucor survive for a longer time.

**KEYWORDS:** Black fungus , Symptoms , Diabetes, immunity, Mucormycosis, etc.

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### I. INTRODUCTION

Mucormycosis is a infection which is caused by exposure to mucor mould (a fungus) which is commonly found in soil , plant , manure , and decaying fruit and vegetables . Mucor is a fungal infection caused due to mucormycetes , a group of fungi . These fungi are ubiquitous in soil , fallen leaves , compact , and air . current nomenclature of medically important mucoralean species according to updated taxonomy Current Species Names

1. Lichtheimia corymbifera
2. Lichtheimia ornata
3. Lichtheimia ramosa
4. Mucor circinelloides Mucor janssenii
5. Mucor lusitanicus
6. Rhizopus arrhizus (incl. var. delemar)
7. Rhizopus microsporus

What is Black fungus infection(mucormycosis)?



Black fungus, also known as Mucormycosis, is a rare but dangerous infection. Black fungus is caused by getting into contact with fungus spores in the environment. It can also form in the skin after the fungus enters through a cut, scrape, burn, or another type of skin trauma. Fungi live in the environment, particularly in soil and decaying organic matter such as leaves, compost piles, rotten wood, and so on. This fungal infection is caused by a type of mould known as 'mucromycetes'. It should be noted that this rare fungal infection affects persons who have health issues or who use drugs that weaken the body's ability to fight the infections.

**Causes of Black Fungus :**

Mucormycetes are a type of mould that causes fungal infections. These moulds can be found everywhere in the environment, including soil, air, and food. They enter the body via the nose, mouth, or eyes and can have an impact on the brain if it is not treated on time. According to medical experts, the main cause of black fungus (mucormycosis) is steroid misuse during COVID treatment.

Black fungus (mucormycosis) primarily affects people who have health problems or who take medications that reduce the body's ability to fight germs and illness. The person's immunity is low after covid treatment, which makes them vulnerable to black fungus infection. People with diabetes and COVID-19 patients are at greater risk of developing an infection.

**Symptoms:**

The symptoms of black fungus will vary depending on where the fungus is growing in your body. They may include the following:

- 1) Fever
- 2) Cough
- 3) Chest pain
- 4) Shortness of breath
- 5) Swelling on one side of your face
- 6) Headache
- 7) Sinus congestion
- 8) Black lesions on the top of the nose or the inside of the mouth
- 9) Belly pain
- 10) Nausea and vomiting
- 11) Gastrointestinal bleeding
- 12) Blood in your stool
- 13) Diarrhea

**Prevention of Black Fungus**

Since the primary cause noted for black fungal infection is unhygienic health conditions, it is important to maintain a strict level of cleanliness, especially if you are a person suffering from health comorbidities. Nasal care and good hygiene are the only ways by which you can keep the infection at bay. India witnesses a large population of diabetic patients, and studies claim that black fungal infection can severely and promptly attack those who have high sugar levels. Thus, it is advised to maintain your sugar levels and be aware of the symptoms, in order to start immediate treatment in case of infection.

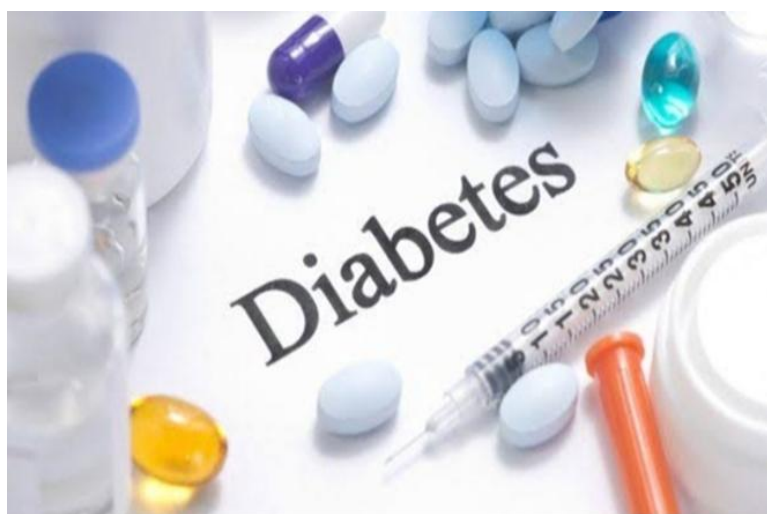
**Black Fungus Risks:**

People who fall into the following categories are more likely to develop black fungus:

Uncontrolled diabetes, diabetic ketoacidosis, and diabetics taking steroids or tocilizumab.

Patients taking immunosuppressants or receiving anticancer treatment, as well as those suffering from a chronic debilitating illness.

## **Diabetes Mellitus**



Diabetes mellitus, commonly known as diabetes, is a metabolic disease that causes high blood sugar. The hormone insulin moves sugar from the blood into your cells to be stored or used for energy. With diabetes, your body either doesn't make enough insulin or can't effectively use the insulin it does make. Untreated high blood sugar from diabetes can damage your nerves, eyes, kidneys, and other organs.

### **•Moving toward improved Diabetesmellitus mucormycosis understanding**

Diabetic patients who have recently recovered from Covid-19 infection after being treated with steroids especially remain at risk of contracting Mucormycosis or Black Fungus infection. Reports have quoted unpublished medical studies reporting over 80 per cent of Black Fungus infections only among the diabetic Covid survivors.

Black fungus infection after Covid had diabetes and 67 per cent of them had uncontrolled sugars. When the sugars are not controlled, the increased level of sugar in blood provides acidic media which is a favourable environment for the growth of black fungus. Thus, the reason behind increased black fungus cases now can be attributed to uncontrolled diabetes and the use of drugs, which causes further decrease in immunity.

Fungal infections are most often caused by a yeast-like fungus called *Candida albicans*. This fungus is actually naturally found on our GI tracts and mouth, but diabetes patients are prone to develop an overabundance, which can lead to a fungal infection. Since *Candida albicans* is so prevalent, it's the leading cause of fungal infections for both those with diabetes and those without diabetes.

### **Diabetes Mellitus and Ketoacidosis**

Diabetes mellitus is the leading underlying disease in patients with mucormycosis globally .

According to the World Health Organization (WHO) "the global prevalence (age-standardized) of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population. Globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. The number of people aged 20–79 years with diabetes in 2011 was 61.3 million in India, and it is estimated to rise to 101.2 million in 2030 . A great rise in the diabetic population is also predicted for China, Brazil, Japan, Mexico, Egypt and Indonesia . Accordingly, the cases of mucormycosis are expected to increase. In the latest review by Jeong et al. diabetes mellitus was the most common underlying condition in 40% of cases and 20% had documented ketoacidosis . Uncontrolled, type II, diabetes is the most common type in diabetic patients with mucormycosis. In a recent study comparing North and South India, diabetic ketoacidosis was found in 90% of cases from North India and 10% of cases from South India . Diabetes has been reported as a risk factor for mucormycosis in 73.5% of cases in India , 75% in Iran and 72% in Mexico. In contrast, the percentages from the European ECMM study were 17% from Italy 18% from France 23% and from Lebanon 35% . In the Indian publications, mucormycosis was the unmasking disease for diabetes mellitus in 12–31% of patients.

### **Altered immunity in DM and mucormycosis**

There are several different aspects of DM that create an ideal environment for Mucorales fungi. First and foremost, patients with DM often exhibit impaired innate and adaptive immunity, which increases their susceptibility to any type of infection, particularly mucormycosis, as this infection is rarely seen in non-immunocompromised hosts. Upon exposure to Mucorales spores, a competent immune system will send

macrophages to engulf spores and prevent their germination. Comparatively, DM patients often have altered phagocytic pathways, thus rendering macrophages unable to phagocytize these spores. As a result, the free spores swell and form buds throughout the blood vessels of the respiratory tract. Although polymorphonuclear (PMN) cells are recruited to these areas, these cells often exhibit an impaired function in DM patients, which limits their ability to prevent the proliferation of Mucorales. As a result, the fungal spores are able to extensively invade tissues and large blood vessels.

### The role of iron and pH

In addition to the altered immune system in DM patients that allows for the proliferation of Mucorales fungi, both the iron and pH levels of DM patients can also contribute to the development of mucormycosis. When cultured in vitro, the *R. oryzae* Mucorales species cannot survive in human serum due to the sequestration of iron by iron proteins. Comparatively, when present in iron-limited environments, the high-affinity iron permease allows *R. oryzae* to acquire iron and thrive in these environments.

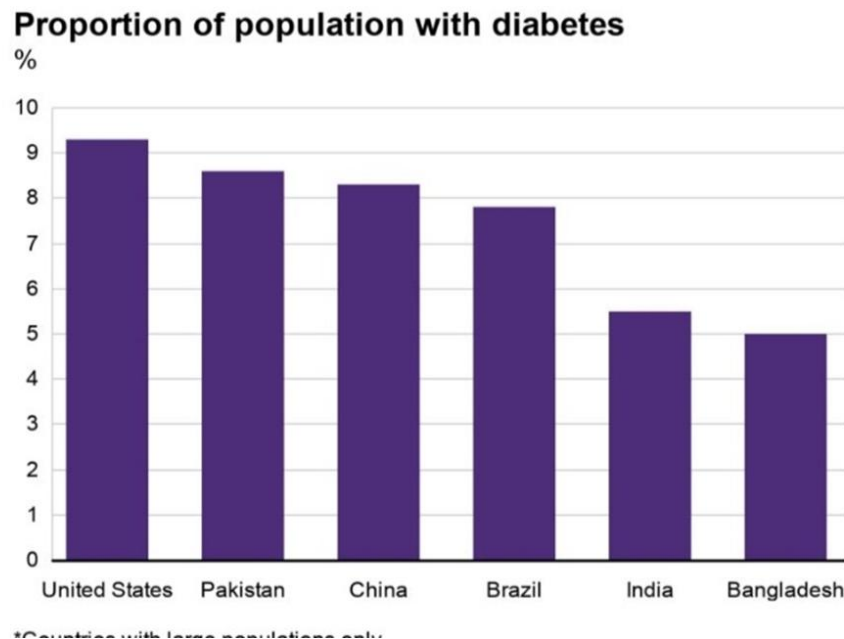
When the pH of human serum is reduced, which often occurs in ketoacidosis, *R. oryzae* can disrupt the iron-binding capacity of transferrin. This disrupted function in transferrin, therefore, allows for free iron to be released into the serum, which can be readily used by the Mucorales spore to thrive in these environments.

### Which countries have got black fungus?

Prior to the Covid pandemic, at least 38 countries around the world had reported cases of mucormycosis, more commonly known as black fungus. India and Pakistan had the highest rates with around 140 cases per million annually, according to Leading International Fungal Education.

### Is a link to diabetes seen in other countries?

Top of the countries with a high per-capita prevalence of diabetes, others (apart from India) have reported cases of mucormycosis



India's neighbours, Pakistan and Bangladesh, both have a high prevalence of diabetes in their populations, and have had mucormycosis cases - but not in especially large numbers. In Bangladesh, doctors have been treating one confirmed case of mucormycosis and are awaiting test results for another suspected case. Doctors told the BBC that both patients also had diabetes. Pakistan has also reported five cases of mucormycosis in recent weeks and four had died as of 12 May, according to media reports. Brazil has reported 29 cases so far, but it's not yet clear how many of these had Covid and/or were diabetic. Russia has also reported "isolated" cases of mucormycosis in Covid patients recently - but it is unclear how many have been detected so far. The US has a very high prevalence of diabetes - 9.3% of the population is estimated to have the condition. It also has the highest number of Covid cases globally. But mucormycosis is very rare - diabetes cases there are largely managed with only 3% going undiagnosed, according to the US Centers for Disease Control.

### Undiagnosed diabetes globally

Region	% undiagnosed
Africa	59.7
South-East Asia (includes India)	56.7
Western Pacific	55.8
Middle East and North Africa	44.7
South and Central America	41.9
Europe	40.7
North America and Caribbean	37.8

The IDF estimates that about 57% of those with diabetes in India, Nepal, Bangladesh, Sri Lanka are undiagnosed cases - and nearly all of these are found in India.

Pakistan is also estimated to have a high proportion of undiagnosed diabetes.

"There's a lot of uncontrolled diabetes in India because people don't do regular health check-ups," says Dr Hariprasath Prakash at the International School of Medicine in Kyrgyzstan.

He says a large majority of diabetes cases are "discovered through other health complications" and remain untreated.

Poorly controlled diabetes puts you at higher risk of certain infections, including some fungal ones.

The Africa region also has a high proportion of undiagnosed diabetes at nearly 60%, but estimates show the incidence of mucormycosis there is low - only 3%.

Dr Denning points out that "it could be because [mucormycosis] cases might be going undiagnosed... it is not the easiest thing to diagnose."

Studies have suggested that cases of black fungus go undiagnosed because of the difficulty in tissue sample collection and the lack of sensitivity of the diagnostic tests.

## II. CONCLUSIONS:

Epidemiology of mucormycosis is evolving. In light of new evidence, diabetes mellitus remains the main underlying disease globally. As diabetes is rising, especially in low and middle-income countries, a rise in mucormycosis cases is expected and this should be alarming. In developed countries.

New emerging species

include *Rhizopus homothallicus*, *Thamnostylum lucknowense*, *Mucor irregularis* and *Saksenaea erythrospora*.

Diagnosis of mucormycosis remains challenging. Histopathology, direct examination and culture remain essential tools, although the molecular methods are improving. New molecular platforms are being investigated and new fungal genetic targets are being explored. Molecular-based methods have been used for confirmation of the infection when applied to tissues. Methods on detection of Mucorales DNA in blood have shown promising results for earlier and rapid diagnosis and could be used as screening tests in high-risk patients, but have to be validated in clinical studies.

More, much needed, rapid methods that do not require invasive procedures, such as serology-based point-of-care, or metabolomics-based breath tests, are being developed and hopefully will be evaluated in the near future.

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