

Research Paper

## A Comparative Study Of Diabetic And Non-Diabetic With Covid-19 Associated Mucormycosis

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### ABSTRACT

**Aim:** The COVID-19 global pandemic had resulted in a rise in a spike of Mucormycosis (black fungus) in COVID-19 individuals and diabetes is a standalone risk factor for both severe COVID-19 and black fungus, especially in India. We sought to find out how often CAM (Covid 19-associated Mucormycosis) was among both diabetes and non-diabetic individuals.

**Method:** The data was gathered from Kaushik pathology Lab, Barara, Ambala, Haryana. The study includes 300 patients divided into 2 groups. Both the groups comprise of 150 patients each. Group 1 consist of patients with diabetes whereas group 2 comprise of non-diabetic patients. Prevalence of CAM was then noted in both the groups.

**Result:** The study showed that in group 1, 74.4% cases were reported as CAM and 25.6% cases were identified as non-CAM whereas in group 2, only 38.4% CAM cases were reported in non-diabetic patients and majority of them (61.6%) were evaluated as non-CAM. A significant difference was also observed between the prevalence rate of both the groups ( $P < 0.05$ ).

**Conclusion:** A significant difference in the CAM cases of both the groups was observed. Interestingly diabetic patients were found to be more prevalent to be infected with CAM. Further, it was concluded that New-onset diabetes was the predominant risk factor for CAM in our study. COVID-19 being other important ones for Mucormycosis in COVID-19 patients.

**Keywords:** Black Fungus, CAM, Covid 19, Diabetes, Mucormycosis.

### INTRODUCTION

The world is being devastated by the COVID-19, which has now become a worldwide danger [1]. Even though the preponderance of COVID-19 patients has low to mild lung diseases and recover without the requirement for specific treatments, elderly people and those with acute systemic disorders are more likely to encounter the severe form of the disease [2-5]. Acute respiratory distress syndrome (ARDS) may result from the illness in the individuals, which is progressing quickly and causing respiratory impairment [6]. Therapeutic trials and observational research have shown poor outcomes and several risk factors for severe COVID-19. DM (Diabetes mellitus), among the most prevalent illnesses in the globe with an estimated incidence of 9.3 percent and is a well-known risk factor. It is usually co-found with other comorbidities in the form of metabolic syndrome and mucormycosis [7].

Diabetes was significantly linked to death and morbidity both in COVID-19 individuals [8]. The WHO [9] estimates that diabetes is responsible for around 1.5 million deaths worldwide, and its incidence is rising quickly in low- and middle-income nations. The incidence of diabetes is rapidly increasing in India, which is habitat to over seventy-seven million diabetics and has the 2nd highest number of diabetics in the globe after China [10,11].

Numerous risk variables have been linked to COVID-19-related death in T1DM and T2DM patients in England, according to a population-based cohort research by Holman et al., [12] Individuals with T1DM and T2DM, respectively, had an elevated incidence of COVID-19-related mortality of 113 percent and 61 percent compared to patients with HbA1C of 48 to 53 mmol/mol (6.5 to 7.0 percent) and HbA1C of  $\geq 86$  mmol/mol (10.0 percent). Patients under the age of seventy were also shown to be at an increased risk.

Despite the fact that Covid instances are presently under control, mucormycosis, sometimes known as "black fungus," is an uncommon but very dangerous fungi ailment that is recently causing a healthcare disaster in India. *Mucor* and *Rhizopus* are among the most prevalent species in the group of moulds known as mucormycetes, which are the source of black fungus [13]. Angio invasive black fungus is a fungus infection that is linked with a significant death rate, particularly in individuals who are immuno – compromised [14]. The main reason that seems to be facilitating spores of Mucorales to develop in individual with COVID-19 is an perfect environment with high glucose concentrations (steroid-induced hyperglycemia, diabetes, new-onset hyperglycemia), high iron levels (increased ferritins), hypoxia, an acidic medium (DKA [diabetic ketoacidosis], metabolic acidosis), and decreased activity of WBC (white blood cells) phagocytes due to immunosuppression (steroid-mediated or background comorbidities, SARS-CoV-2 mediated) coupled with many other shared risk variables such as prolonged hospitalisation with ventilators or without mechanical ventilators. The most common underlying condition connected to black fungus is diabetes. Furthermore, diabetes is another significant illness that makes managing COVID-19 more difficult [15].

Eighty instances of black fungus linked to COVID-19 were examined by Hoenigl et al., Systemic corticosteroid therapy, as well as uncontrolled hyperglycemia were present across most individuals with ROCM (rhino-orbital cerebral mucormycosis), and COVID-19- related black fungus was the most prevalent illness [16].

Meher et al., (2022) discovered the potential influence of COVID 19 infection and other diseases on the development of ROCM and illustrated the results based on surgical and therapeutic therapies. One people's condition deteriorated, six people passed away, and one hundred individuals made a full recovery. Three of the 101 known diabetics died, while ninety-eight made a full recovery. There was no sign of steroid use, diabetes, or any other complication in Seven people who had a history of COVID contamination [17].

Between March to May 2021, Chouhan et al., (2021) identified forty-one Covid19 individuals with ROCM from a tertiary care facility for their investigation. The average age of the group of thirteen female and twenty-eight male was 48.2 years (range, 21 to 68 years). 12 people had diabetes for a long time, whereas twenty-eight had just received a diagnosis. At the most recent checkup, thirty-seven individuals (90.24 percent) were receiving antifungal treatment, however 4 (9.75 percent) failed to survive [18].

By unpublished instances and examining known of COVID-19-associated black fungus in diabetic and without diabetes individuals, the purpose of this study was to explain risk factors, the prevalence, outcome, and therapy of this condition in both diabetes and non-diabetes individuals.

## Methodology

In the current research, the samples were collected from Kaushik pathology Lab, Barara, Ambala, Haryana. With a focus on Covid-19 linked black fungus, we observed the incidence of superinfection and co-infection in this observational research in both diabetes and non-diabetes individuals. All instances of proven black fungus among Covid-19-positive diabetes and non-diabetic individuals recorded in 2020-21 were compiled. The ethics committees of each centre gave their approval to the study protocol. Between May 21 to June 30 (2021), a total of 300 individuals records were assessed and placed into 2 distinct groups for the research. Out of 300 individuals, 150 were in group 1 and had diabetes in addition to CAM. Rest 150 individuals who had CAM but did not have diabetes were included in group 2.

- **Inclusion and Exclusion criteria**

The research examined individuals with and without diabetes who had verified CAM. Exclusion criteria for the research were individuals with black fungus related with Covid-19 who also had other concomitant conditions such as mental illness, hypertension, cardiovascular disease, ketoacidosis, etc. and whose postoperative histology did not demonstrate aggressive fungal infection.

- **Data collection**

The data was collected from Kaushik pathology Lab, Barara, Ambala, Haryana. The mentioned information was taken from the clinical documentation: demographics, underlying conditions including DM, organ transplantation, haematological malignancy, and others, days between the period of COVID-19 diagnosis and the duration of the black fungus diagnosis, the anatomic site that the ailment has influenced, the disease's diagnostic techniques, such as culture, histopathology or microscopy, and the specifics of the diagnosis, such like antifungal medication, surgical therapy, regarded hematologic malignancy as the main risk factor. Multiple endpoints and results were used to collect and evaluate each individual's characteristics. Careful investigation has gone into the case studies of individuals with Covid-19 and black fungus. The data was gathered and examined for any components that may be dangerous.

- **Statistical analysis**

With SPSS 25.0, statistical analysis was performed. The mean and standard deviations were calculated. Results were deemed significant if the two-sided P value was less than 0.05. A 2-tailed independent sample t-test was used to determine if there was a distinction between the 2 groups.

## Result

The demographic characteristics of diabetic and non-diabetic individuals are shown in Table 1.

Variables		Diabetic	Non-Diabetic
<b>Gender</b>	<b>Male</b>	86 (57.3%)	94 (62.7%)
	<b>Female</b>	64 (42.7%)	56 (37.3%)
<b>Age Group</b>	<b>20-30</b>	46 (30.7%)	45 (30%)
	<b>31-40</b>	34 (22.7%)	42 (28%)
	<b>41-50</b>	37 (24.7%)	29 (19.3%)
	<b>51-60</b>	33 (22%)	34 (22.7%)
<b>Education</b>	<b>Below High School</b>	13 (8.7%)	36 (24%)

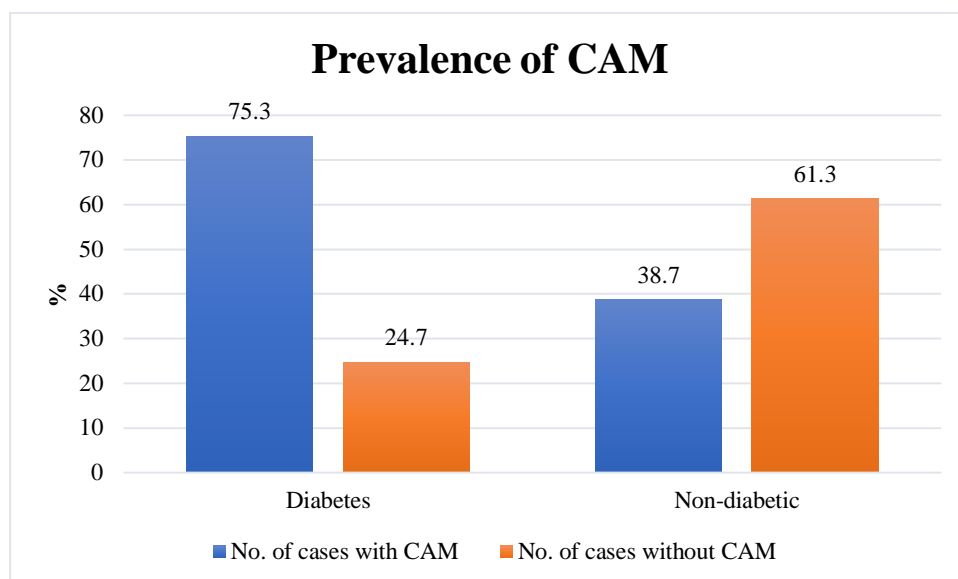
	<b>High School</b>	46 (30.7%)	14 (9.3%)
	<b>Intermediate</b>	37 (24.7%)	44 (29.3%)
	<b>Undergraduate</b>	33 (22%)	25 (16.7%)
	<b>Postgraduate</b>	21 (14%)	31 (20.7%)
<b>Marital Status</b>	<b>Married</b>	81 (54%)	112 (74.7%)
	<b>Unmarried</b>	48 (32%)	38 (25.3%)
	<b>Widow</b>	21 (14%)	00
<b>Locality</b>	<b>Rural</b>	72 (42%)	47 (31.3%)
	<b>Urban</b>	78 (52%)	103 (68.7%)
<b>Occupation</b>	<b>Unemployed</b>	41 (27.3%)	18 (12%)
	<b>Private</b>	31 (20.7%)	43 (28.7%)
	<b>Business</b>	26 (17.3%)	32 (21.3%)
	<b>Government</b>	52 (34.7%)	57 (38%)

In diabetes individuals, there were 57.3% males and 42.7% females, compared to 62.7% males and 37.3% females in non-diabetic individuals. Out of them, 74.7% of non-diabetic individuals were married, 25.3% were single, and no widows were there, only 54% of diabetes individuals were married, 32% were not and 14% were widows. In diabetic individuals, 30.7% individuals were between the ages of 20 and 30, 22.7% were between 31 and 40, 24.7% were between 41 and 50, and 22% were between the ages group of 51 to 60. In contrast, in non-diabetic individuals, 30% were between the age group of 20 to 30, 28% were between 31 and 40, 19.3% were between 41 and 50, and 22.7% were between the age group of 51 to 60. In terms of education, diabetic individuals had completion rates of 30.7%, 24.7%, 22% and 14% for high school, intermediate, undergraduate, and post-graduate studies, respectively, while non-diabetic individual had completion rates of 9.3%, 29.3%, 16.7% and 20.7% for high school, intermediate, undergraduate, and post-graduate studies, respectively. Among diabetes individuals, 52% and 42% were from urban and rural areas, respectively, but among non-diabetic individuals, 31.3% were from rural and 68.7% were from urban areas. In diabetic and non-diabetic patients, majority of them were in government sector.

#### Prevalence of CAM cases among diabetic and non-diabetic patients

<b>Variables</b>	<b>Diabetes</b>	<b>Non-diabetic</b>
<b>No. of cases with CAM</b>	113 (75.3%)	58 (38.7%)
<b>No. of cases without CAM</b>	37 (24.7%)	92 (61.3%)

The table 2 represents the total number of non-CAM and CAM cases in diabetic and non-diabetic patients. There were 150 patients in each group. In which 75.3% cases in group 1 were reported as CAM whereas only 24.7% cases were identified as non-CAM along with diabetes. In group 2, about 38.7% cases were reported as CAM whereas 61.3% cases were evaluated as non-CAM in non-diabetic patients indicating that patients with diabetes were more prevalent to CAM as compared to the non-diabetic patients.



**Figure.1** Prevalence of CAM in diabetic and non-diabetic patients

	Mean Difference	Std. Error Difference	t	df	Sig. (2-tailed)
<b>Equal variances assumed</b>	-.366	.054	-6.705	298.00	.000
<b>Equal variances not assumed</b>	-.366	.054	-6.705	295.059	.000

Table 3 represents the independent sample test between CAM and non-CAM cases included in the study. Between CAM and non-CAM cases, statistically a highly significant difference was observed between the two groups ( $P < 0.05$ ). It was observed that CAM cases were more prevalent in diabetic patients as compared to the non-diabetic patient.

### Discussion

Due to SARS-CoV-2, the world is now dealing with a common disease COVID-19. Shocking reports of secondary invasive fungal infections have been made since the COVID-19 pandemic started [19]. A rising number of instances of black fungus among COVID-19 carriers have been documented worldwide, particularly in India. Uncontrolled diabetes is one of the risk factors that predisposes people to black fungus. The demography and prevalence of CAM individuals with and without diabetes are summarised in this research.

In the research mentioned above, we compared the incidence of CAM in diabetic and non-diabetic individuals. The results showed that diabetes was a significant risk factor for those who had black fungus related with Covid 19. 75.3% of the individuals had CAM in group 1, while 24.7% did not have it. Similarly, among the non-diabetic individuals, 38.7% had CAM, while rest 61.3% did not. In related research by Selarka et al., (2021) 47 (1.8%) out of a total of 2567 COVID-19 individuals hospitalised to 3 tertiary centres were found to have black fungus. The majority ( $n = 36$ , 76.6%) of participants had diabetes, with an average age of 55 12.8 years. Most ( $n = 31$ , 66.0%) did not get a COVID-19 vaccination, and the majority ( $n = 43$ , 91.5%) had moderate-to-severe pneumonia, with 20 (42.6%) requiring invasive ventilation. However, their results were inconsistent [20].

However, after a recent COVID-19 infection, Meher et al., (2022) identified the individuals as having acute invasive fungal rhinosinusitis. A positive RT-PCR result indicated that 111 of the 131 patients had a background of SARS COVID 19 contamination, whereas the other twenty individuals had no such past. 67 individuals with COVID 19 infection got therapy with steroids. According to their research, 131 patients had 124 recoveries, 1 worsening, and 6 deaths. Out of 101 known diabetes, 98 made a full recovery, while three died. Seven individuals who had previously had COVID did not show signs of diabetes, steroid use, or any other disease [21].

23 individuals with black fungus participated in research by Sharma et al., (2021), all of them also had Covid19 illness. The most often impacted sinuses were the ethmoids (100 percent) and frontal sinuses. While intra-orbital extension was observed in 43.47 percent of cases, and intracranial extension was only detected in 8.69 percent of instances. In 21 out of 23 individuals, diabetes was diagnosed, and it was uncontrolled in Twelve instances. All of the individuals had previously used steroids for Covid19 therapy [22].

Nair et al., (2021) conducted the research in which 127 individuals with CAM were investigated at 4 centres in India, which is contrary to our results. In addition to receiving systemic amphotericin-B treatment, all individuals had endoscopic sinus debridement operations. After release, there was an average follow-up duration of 9.2 weeks (within a ranging from 3 to 18 weeks). In every instance, it was feasible to save a life. Globe preservation was achievable in 4/5 of the individuals who had retrobulbar amphotericin-B injections, even if total world salvage was only achieved in 42.8 percent (6/14 eyes) [23].

### Conclusion

Since the development of COVID-19 over a year ago, it has been shown that diabetes, a known risk factor for black fungus, is substantially related with death and morbidity in COVID-19 individuals. Critical sections have aggressively intervened in diabetic individual since the CAM epidemic. In this research, we observed that patients with diabetes had a higher prevalence of CAM than individuals without diabetes. The primary reason for the CAM to worsen is uncontrolled diabetes, which has to be thoroughly examined. If infected, early surgical intravenous and intervention anti-fungal medication should be considered for care, as instances of post-coronavirus black fungus may be managed with a favourable prognosis and a less fulminant illness state. As a result, it is advised to have an early diagnosis, a high index of suspicion, stop using steroids, maintain strict glycemic control. The current gold standard of therapy is posaconazole, liposomal amphotericin B, prompt radical surgical debridement. As an additional metric, the function of dietary nutraceuticals may be assessed.

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