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Original Research Article

Association Between Uncontrolled Diabetes and Development of Mucormycosis in COVID-19 Patients

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Abstract

Introduction: Coronavirus disease 2019 (COVID-19) has been associated with several complications, among which COVID-19-associated mucormycosis is a rare but severe invasive fungal infection. Caused by Mucorales species, it predominantly affects immunocompromised individuals and is associated with high morbidity and mortality, especially when diagnosis and treatment are delayed.

Aims: To evaluate the association between uncontrolled diabetes and the development of mucormycosis in patients with COVID-19, and to assess the role of poor glycaemic control as a major risk factor for COVID-19–associated mucormycosis.

Methods: This was a hospital-based observational study conducted at Dr. VithalraoVikhe Patil's Foundation Medical College and Hospital, Ahilyanagar, Maharashtra, over a one-year period from January 2021 to December 2022. The study included 100 patients diagnosed with COVID-19 who were evaluated for mucormycosis during the study period and fulfilled the inclusion criteria.

Result: Among the 100 study participants, most were aged 41–60 years (46%) and were predominantly male (68%). Uncontrolled diabetes was the most common glycaemic status (62%). Mucormycosis occurred significantly more frequently in patients with uncontrolled diabetes (90.3%) compared to those with controlled diabetes (42.9%) and newly detected diabetes (80%), demonstrating a highly significant association between poor glycaemic control and the development of mucormycosis ($p < 0.001$).

Conclusion: The study demonstrates that poor glycaemic control and steroid use are strongly associated with mucormycosis, with middle-aged and elderly males being most affected. Uncontrolled diabetes was identified as the primary risk factor, highlighting the critical role of chronic hyperglycaemia in the development of the infection.

Keywords: COVID-19, Mucormycosis, Uncontrolled Diabetes, Hyperglycemia, Fungal Infection, SARS-CoV-2.

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Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to numerous direct and indirect complications since its emergence. Among the most devastating secondary complications observed during the pandemic has been COVID-19-associated mucormycosis (CAM), a rare but highly invasive fungal infection caused by Mucorales species. Mucormycosis primarily affects immunocompromised individuals and is associated with high morbidity and mortality, particularly when diagnosis and management are delayed. A striking pattern observed globally—especially in India during the second wave of the pandemic—was the disproportionate number of CAM cases occurring in individuals with diabetes mellitus (DM), and notably among those with poorly controlled glycemia. Epidemiological evidence reveals that pre-existing diabetes is one of the most common risk factors for CAM, with studies reporting that between 62% and 80% of CAM cases have underlying diabetes, and poor glycemic control present in 41%–76% of these cases. [1] COVID-19 itself can exacerbate glucose dysregulation through mechanisms such as stress-induced hyperglycemia, cytokine-mediated insulin resistance, and potential direct viral damage to pancreatic islet cells, further increasing the susceptibility of diabetic patients to opportunistic infections. [2][4] Diabetes, particularly when

uncontrolled, compromises multiple components of host immune defense, including neutrophil chemotaxis and phagocytic function, creating a permissive environment for fungal angioinvasion characteristic of mucormycosis pathogenesis. [1][6] In addition, hyperglycemia and associated metabolic derangements such as diabetic ketoacidosis can elevate the expression of host cell receptors like glucose-regulated protein 78 (GRP78), which facilitates fungal adherence and endothelial invasion, a key step in mucorales pathogenicity. [1][9] The confluence of COVID-19's immune dysregulation and the systemic effects of uncontrolled diabetes creates a "perfect storm" for mucormycosis. SARS-CoV-2 infection induces lymphopenia and neutrophil dysfunction, weakening innate immune defenses that normally curb opportunistic fungi, while the inflammation and cytokine storm can increase insulin resistance and exacerbate hyperglycemia in patients with and without prior diabetes. [2][4] This is reflected in clinical observations where uncontrolled diabetes and diabetic ketoacidosis were significant risk factors for mucormycosis even in the absence of other classic immunosuppressive conditions. [1] Moreover, the use of corticosteroids—a mainstay treatment for severe COVID-19—further aggravates hyperglycemia and suppresses host immunity, synergistically increasing the risk of CAM in diabetic individuals. [3][5] Epidemiological studies have highlighted the prominence of diabetes in CAM cohorts worldwide; for instance, systematic reviews report that over 80% of diagnosed CAM patients had pre-existing diabetes mellitus, and a large proportion of these individuals exhibited poor glucose control at presentation. [7] In several case-control analyses conducted in India, uncontrolled diabetes was significantly more frequent in patients who developed mucormycosis after COVID-19 compared to controls, underscoring its role as a pivotal risk factor. [5] Additional evidence suggests that new-onset diabetes during COVID-19 or undiagnosed cases with suboptimal glycemic status are also over-represented in mucormycosis cohorts, pointing toward a complex interplay between viral infection, metabolic stress, and fungal susceptibility. [6] Beyond direct effects on immunity, chronic hyperglycemia alters iron homeostasis and promotes an environment conducive to fungal growth by increasing free serum iron through acidosis-driven dissociation from binding proteins, further enhancing the likelihood of mucorales proliferation. [5] Importantly, uncontrolled diabetes not only increases the risk of developing mucormycosis but also adversely impacts clinical outcomes, with higher rates of complications and mortality observed in diabetic CAM patients compared with non-diabetic counterparts. [1][7]

This has profound implications for clinical practice, especially in regions with a high prevalence of diabetes, where stringent glycemic monitoring, rational use of corticosteroids, and early screening for mucormycosis symptoms are essential preventive strategies. The global experience of CAM during the COVID-19 pandemic therefore underscores the urgent need for integrated management approaches that prioritize glycemic control as a fundamental component of care in COVID-19 patients with diabetes to reduce the incidence and severity of mucormycosis. [3][7]

Materials and Methods

Study Design: Hospital-based observational study.

Study Setting: Conducted at Dr. VithalraoVikhe Patil's Foundation Medical College & Hospital, Ahilyanagar, Maharashtra.

Study Duration: One year, from January 2021 to December 2022.

Study Population: Patients diagnosed with COVID-19 infection and evaluated for mucormycosis during the study period.

Sample Size: 100 patients fulfilling the inclusion criteria were enrolled in the study.

Sampling Method: Consecutive sampling of eligible patients presenting to the hospital during the study period.

Inclusion Criteria

- Patients aged ≥18 years.
- Laboratory-confirmed COVID-19 positive cases (RT-PCR/rapid antigen test).
- Patients with clinically and/or microbiologically confirmed mucormycosis.
- Patients with a known history of diabetes mellitus or newly detected hyperglycemia.
- Patients who provided informed consent.

Exclusion Criteria

- Patients with mucormycosis not associated with COVID-19.
- Patients with incomplete medical records.
- Patients unwilling to participate in the study.
- Paediatric patients (<18 years).

Table 1: Demographic Profile of Study Participants (N = 100)

Variable	Number (n)	Percentage (%)
Age Group (years)		
18–40	22	22.0
41–60	46	46.0
>60	32	32.0
Gender		
Male	68	68.0
Female	32	32.0

Table 2: Glycaemic Status of Study Participants

Glycaemic Status	Number (n)	Percentage (%)
Controlled diabetes	28	28.0
Uncontrolled diabetes	62	62.0
Newly detected diabetes	10	10.0
Total	**100**	**100**

Table 3: Association Between Glycaemic Control and Development of Mucormycosis

Glycaemic Status	Mucormycosis Present n (%)	Mucormycosis Absent n (%)	Total	p-value
Controlled diabetes	12 (42.9)	16 (57.1)	28	
Uncontrolled diabetes	56 (90.3)	6 (9.7)	62	
Newly detected diabetes	8 (80.0)	2 (20.0)	10	
Total	76	24	100	<0.001

Table 4: Association Between Steroid Use and Mucormycosis

Steroid Use	Mucormycosis Present n (%)	Mucormycosis Absent n (%)	Total	p-value
Yes	58 (85.3)	10 (14.7)	68	
No	18 (56.3)	14 (43.7)	32	
Total	76	24	100	0.002

Table 5: Mean Glycaemic Parameters in Patients With and Without Mucormycosis

Parameter	Mucormycosis Present (Mean ± SD)	Mucormycosis Absent (Mean ± SD)	p-value
FBS (mg/dL)	198 ± 42	136 ± 28	<0.001
PPBS (mg/dL)	276 ± 56	182 ± 34	<0.001
HbA1c (%)	9.1 ± 1.4	6.8 ± 0.9	<0.001

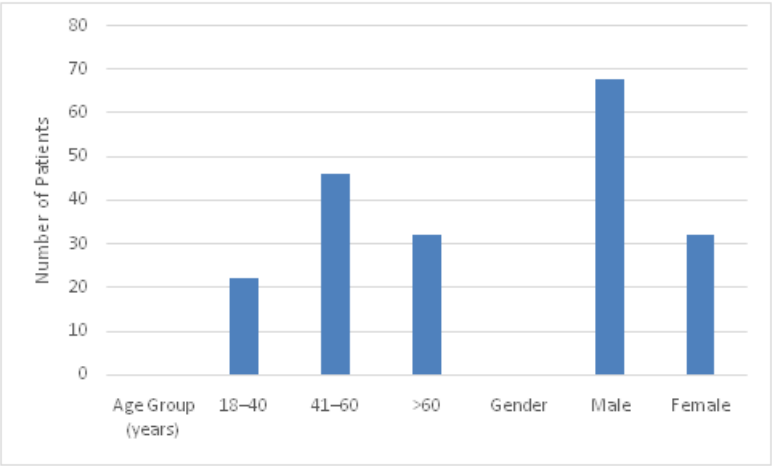

Figure 1: Demographic Profile of Study Participants (N = 100)

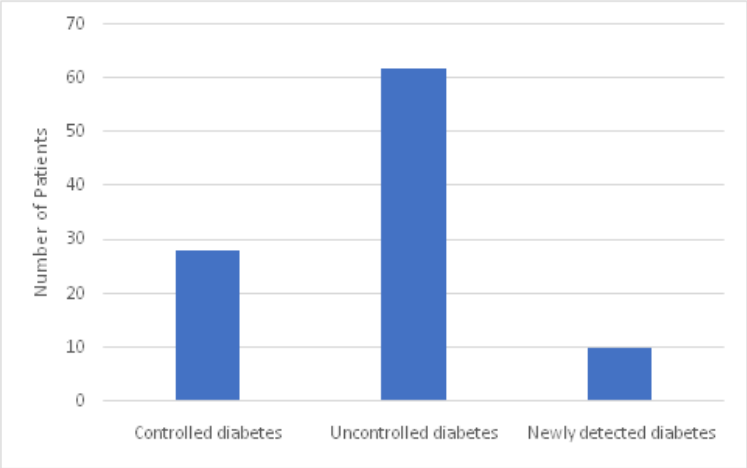

Figure 2: Glycaemic Status of Study Participants

Results

A total of 100 study participants were included in the analysis. As shown in Table 1, the majority of participants belonged to the 41–60 years age group (46%), followed by those aged >60 years (32%) and 18–40 years (22%). Males constituted a higher proportion of the study population (68%) compared to females (32%). Regarding glycaemic status (Table 2), most patients had uncontrolled diabetes (62%), while 28% had controlled diabetes and 10% were newly detected cases.

The association between glycaemic control and development of mucormycosis is presented in Table 3. Mucormycosis was significantly more common among patients with uncontrolled diabetes, with 90.3% affected, compared to 42.9% in the controlled diabetes group and 80.0% among newly detected diabetics. This association was found to be statistically highly significant ($p < 0.001$), indicating poor glycaemic control as a major risk factor for mucormycosis.

Steroid use also showed a significant association with mucormycosis (Table 4). Among patients who received steroids, 85.3% developed mucormycosis, whereas only 56.3% of those who did not receive steroids were affected. This difference was statistically significant ($p = 0.002$), suggesting steroid therapy as an important contributing factor.

Comparison of mean glycaemic parameters between patients with and without mucormycosis (Table 5) revealed significantly higher values in affected patients. The mean fasting blood sugar (198 ± 42 mg/dL vs. 136 ± 28 mg/dL), postprandial blood sugar (276 ± 56 mg/dL vs. 182 ± 34 mg/dL), and HbA1c levels ($9.1 \pm 1.4\%$ vs. $6.8 \pm 0.9\%$) were all significantly elevated in the mucormycosis group compared to those without mucormycosis ($p < 0.001$ for all parameters). These findings further emphasize the strong relationship between poor glycaemic control and the development of mucormycosis.

Discussion

The present study highlights the critical role of glycaemic control and steroid use in the development of mucormycosis, reinforcing observations reported during recent surges of this opportunistic fungal infection, particularly in diabetic patients. In our cohort of 100 participants, a predominance of middle-aged and elderly individuals was observed, with the majority belonging to the 41–60 years age group. This age distribution aligns with previous studies, which have reported higher susceptibility to mucormycosis in older individuals due to age-related immune dysregulation and a higher prevalence of comorbidities such as diabetes mellitus [11,12]. The male predominance seen in our study is also consistent with existing literature and may be attributed to higher exposure to risk factors, delayed health-seeking behavior, and a greater burden of uncontrolled diabetes among males [13].

A key finding of this study is the strong association between poor glycaemic control and mucormycosis. Patients with uncontrolled diabetes showed a significantly higher prevalence of mucormycosis (90.3%) compared to those with controlled diabetes. Hyperglycaemia creates a favorable environment for fungal proliferation by impairing neutrophil chemotaxis, phagocytosis, and intracellular killing [14]. Additionally, diabetic ketoacidosis and elevated free iron levels enhance the growth of Mucorales species, further increasing susceptibility [15]. The high proportion of mucormycosis among newly detected diabetics in our study underscores the possibility that undiagnosed or recently diagnosed diabetes may already be associated with prolonged periods of poor glycaemic control.

Steroid use emerged as another significant risk factor in the present study, with 85.3% of steroid-treated patients developing mucormycosis.

Corticosteroids are known to induce hyperglycaemia and suppress cell-mediated immunity, thereby increasing vulnerability to opportunistic infections [16]. During recent outbreaks, irrational or prolonged steroid use, often in the absence of strict glycaemic monitoring, has been strongly implicated in the rising incidence of mucormycosis [17]. Our findings support the need for judicious steroid prescription, particularly in diabetic patients, with close monitoring of blood glucose levels.

The analysis of glycaemic parameters further strengthens the association between poor metabolic control and mucormycosis. Significantly higher mean fasting blood sugar, postprandial blood sugar, and HbA1c levels were observed in patients with mucormycosis compared to those without. HbA1c, which reflects long-term glycaemic control, was markedly elevated in affected patients, indicating chronic hyperglycaemia rather than transient glucose fluctuations [18]. This suggests that sustained poor glycaemic control may be more detrimental than short-term hyperglycaemia in predisposing patients to invasive fungal infections.

Our results are comparable with several Indian and international studies that have identified uncontrolled diabetes as the most common underlying risk factor for mucormycosis, often in combination with steroid therapy [19,20]. The clinical implications of these findings are substantial, emphasizing the importance of early detection and strict control of diabetes, rational use of steroids, and regular monitoring of glycaemic parameters in high-risk patients. Preventive strategies focusing on metabolic optimization could play a pivotal role in reducing morbidity and mortality associated with mucormycosis. Despite its strengths, the study has certain limitations. Being a single-center study with a relatively small sample size, the findings may not be generalizable to all populations. Additionally, other potential confounding factors such as duration of diabetes, presence of ketoacidosis, and concomitant immunosuppressive conditions were not analyzed in detail. Future multicentric studies with larger cohorts are warranted to further elucidate the complex interplay of metabolic and therapeutic factors in the pathogenesis of mucormycosis. In conclusion, the present study demonstrates a strong and statistically significant association between poor glycaemic control, steroid use, and the development of mucormycosis. These findings reinforce the need for stringent diabetes management and cautious steroid use to mitigate the risk of this life-threatening infection.

Conclusion

The study highlights a strong association between poor glycaemic control, steroid use, and the development of mucormycosis, with middle-aged and elderly males being the most affected. Uncontrolled diabetes was identified as the primary risk factor, with significantly higher rates of mucormycosis compared to controlled or newly diagnosed diabetics, emphasizing the role of chronic hyperglycaemia in disease pathogenesis. Elevated fasting and postprandial blood sugar levels, along with higher HbA1c, indicate that sustained poor metabolic control, rather than transient hyperglycaemia, increases susceptibility to invasive fungal infections, making HbA1c a valuable risk indicator. The study also underscores the impact of steroid therapy in exacerbating hyperglycaemia and impairing immune defenses, reinforcing the need for cautious use. Overall, early diabetes diagnosis, stringent glycaemic monitoring, optimal metabolic control, and judicious steroid use are critical strategies to prevent mucormycosis and improve outcomes in high-risk populations.

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