

# Mucormycosis During the Waves of Covid 19 Pandemic; A Cross Sectional Study at Bahawal Victoria Teaching Hospital

Mucormycosis  
During the  
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Covid 19

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## ABSTRACT

**Objective:** To observe the frequency, clinical presentation and outcome in the patients of mucormycosis during the waves of COVID 19 pandemic.

**Study Design:** Descriptive cross sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Otorhinolaryngology, Bahawal Victoria Teaching Hospital, Bahawalpur, from November, 2020 to March, 2022.

**Materials and Methods:** Total 38 diabetic patients with Rhinocerebral mucormycosis which were confirmed through endoscopic, radiological and also histopathological findings. All the patients once diagnosed and included in the study were started with intravenous Amphotericin B after dose adjustment according to the body weight and baseline renal profile. Intravenous antifungal treatment was continued for every patient for the period of 6 to 8 weeks. Clinical outcome in terms of improvement/deterioration in symptoms and signs and mortality were recorded. SPSS version 21 was used for data analysis.

**Results:** The mean age was  $51.5 \pm 10.55$  years. Majority 27 patients were males (71.05%) and 11 were females (28.95%). Out of 38 patients only 16 patients were having the previous history of Covid 19 infection. 31 were having orbital involvement and 6 were having intracranial involvement. 18 patients were histopathologically confirmed as of mucormycosis. 26 patients were recovered after treatment, 10 patients could not survive and expired while 2 patients were lost against medical advice.

**Conclusion:** Patients with diabetes mellitus along with Covid 19 infection are more predisposed to have invasive fungal infection like Mucormycosis. Aggressive intravenous anti-fungal therapy and debridement can reduce patient's mortality.

**Key Words:** Amphotericin B, COVID-19, Mucormycosis, Complications, Frequency.

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## INTRODUCTION

Mucormycosis is a fatal life threatening angioinvasive fungal infection usually seen in immunocompromised host and its upsurge has been found in the different parts of the world during current COVID-19 pandemic. The causative fungus is commonly found in the environment growing over moist surfaces and decaying matter.

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The mucormycosis has been mistakenly termed as Black Fungus which is actually from a different group of fungi. There are various clinical sub types of mucormycosis but Rhino-Orbito-Cerebral Mucormycosis (ROCM) is the commonest and most lethal type and carries high mortality because of treatment delay in spite of its early diagnosis. Risk factors include immunocompromised state, uncontrolled diabetes mellitus mainly with diabetic ketoacidosis (DK), use of glucocorticoids, AIDS, burns and trauma, malignancies and stem cell transplantation.<sup>1</sup>

In the patients of uncontrolled diabetes mellitus with COVID-19 infection having dysfunctional immune system, the use of steroids may be responsible of emerging fungal infections.<sup>2</sup> The patients with advance stage of disease who require ICU admission are more at risk to develop fungal infections.<sup>3</sup> Mucormycosis has been associated in one study with underlying diabetes mellitus in 54-76 % of cases while in 8-22 % of mucormycosis patients there was associated diabetic ketoacidosis.<sup>4</sup> It has been observed that in post treated COVID-19 patients with previously having diabetes

mellitus who were given aggressive doses of corticosteroids, the things became worse in developing mucormycosis later on.<sup>5</sup>

In the literature review, the commonest form of this invasive fungal disease was found to be rhino-Orbito-cerebral mucormycosis and the commonest pathogens isolated were Rhizopus and mucorales.<sup>6,7</sup> In the management of mucormycosis the prompt and urgent steps are required so the usual modalities are surgical debridement and intravenous administration of Amphotericin B.<sup>8,9</sup> The outcome and prognosis of mucormycosis even before the COVID-19 waves were poor and late presentation and delay in the treatment carried high mortality which was primarily associated with invasive character of this disease.<sup>10</sup>

The rationale of our study is to find out the risk factors, reasons of upsurge, clinical magnitude, complications encountered and outcome after treatment given in the patients of mucormycosis arrived in our settings during COVID-19 pandemic. This study is also unique in a sense that such number of cases having this clinical disease are not reported very frequently especially in our part of province in the literature.

## MATERIALS AND METHODS

It was descriptive cross sectional frequency based study on the cases of mucormycosis during COVID-19 waves. The duration of study was from November, 2020 to March, 2022. The study was approved from Hospital Ethical Review Committee (ERC 1284/DME/QAMC). Informed written consent was taken from the study subjects. Non probable consecutive sampling technique was used. Patients with strong clinical, radiological and endoscopic suspicion of Rhinocerebral Mucormycosis were included in the study. All ages and both gender were included. All those patients who were not clinically and radiologically relevant and those with later on confirmed histopathological diagnosis of allergic fungal, noninvasive fungal rhinosinusitis and fungal granulomas were excluded from the study. Demographic detail, clinical symptoms and signs, radiological (CT/MRI) and nasal endoscopic findings, complications of disease, treatment modalities used and outcome were recorded.

All diagnosed patients of Rhinocerebral Mucormycosis were started with intravenous Amphotericin B after dose adjustment according to the body weight and baseline renal profile. Intravenous antifungal treatment was continued for every patient for the period of 6 to 8 weeks. Clinical outcome in terms of improvement/deterioration in symptoms and signs and mortality were recorded. SPSS version 21 was used for data analysis.

## RESULTS

The mean age was 51.5±10.55 years. Majority 27 patients were males (71.05%). Out of 38 patients 12

patients belonged to upper socioeconomic class (31.5%), 22 belonged to middle (57.8%) and 4 patients were from poor socioeconomic class (10.5%). Only 03 patients were previously having chronic kidney disease (CKD) (7.8%) and 16 patients were having the previous history of COVID-19 infection (42.1%) (Figure 1). Five (31.2%) out of 16 post COVID-19 patients gave the history of oxygen inhalation therapy during COVID-19 treatment. During clinical evaluation all 38 patients (100%) were having the involvement of nose and paranasal sinuses. Of 38 patients, Majority 23 (60.5%) patients were developed palatal fistula. 31 patients had orbital involvement (81.6%) and out of these 31 patients 06 patients got ptosis (19.3%), 06 were having impaired vision (19.3%) and 19 developed total loss of vision (61.2%) of the eye involved. 06 patients showed intracranial involvement (15.8%) (Table 1). Histopathology of the specimen during debridement was sent for every patient and 18 patients out of 38 were proven for mucormycosis on biopsy (47.3%). Systemic antifungal therapy and endoscopic surgical debridement were done for every patient in addition to the management of underlying co morbid disease like diabetes mellitus and chronic kidney disease (CKD).

Out of these total 38 patients 23 patients had to undergo partial medial maxillectomy (60.5%) while 15 (39.4%) got palatal resection of the involved side as well. Out of those 19 patients with total loss of vision, 05 patients had to undergo orbital exenteration of side involved (26.3%). In the outcome, 26 patients recovered with the treatment and discharged from the hospital (68.4%) while 10 (26.3%) patients could not survive and expired during the hospital stay. 02 patients were lost against medical advice (LAMA). (Table. 1). In the follow up 02 patients showed mild disease recurrence (5.3%) which was managed with endoscopic debridement under local anesthesia and oral antifungal medicines.

**Table No. 1: Demographic, outcome and patients having regional involvement with Mucormycosis (n=38)**

Variable	Frequency	%	Mean±S.D
Age (years)			51.5±10.55
<b>Gender:</b>			
Male	27	71.05	
Female	11	28.95	
<b>Involved regions:</b>			
Nose & PNS	38	100.0	
Palatal Fistula	23	60.5	
Intracranial	06	15.8	
Orbital	31	81.6	
<b>Outcome:</b>			
Recovered	26	68.4	
Expired	10	26.3	
LAMA*	02	05.3	

\*Lost against medical advice.

## DISCUSSION

Multiple factors are involved in the upsurge of the cases of mucormycosis during the pandemic of COVID-19. Preexisting diabetes mellitus remained uncontrolled among the patients of COVID-19 in the hospitals due to massive patient overload. In addition excessive steroid therapy beyond the recommended dosage to save the life might be one of the contributing factors.<sup>1,4,11</sup> As the fungal spores and other microbial are present in the environment of humans normally but these seldom cause any problem due to strong and healthy immune system of the body but as the immune system is compromised due to conditions like uncontrolled diabetes mellitus and COVID-19 infection these spores start damaging by entering through the air passages<sup>12</sup>. Two recent studies have documented the abnormal and damaged innate immunity in the patients of COVID-19 infection.<sup>13,14</sup> Hence when the fungal spores enter the body through human air passages, the dysfunctional macrophages remain unable to combat these spores which eventually transform into filamentous hyphae in mucormycosis with the common species of mucor and rhizopus group.<sup>15,16</sup> As uncontrolled diabetes mellitus plays an important risk factor in the current spurt of mucormycosis, studies have shown the endothelial damage during the autopsies of such patients due to hyperglycemia and this abnormality was widely noticed in the patients who died of COVID-19 in comparison with those having other viral infections like H1N1 influenza.<sup>17</sup> So the contribution of these three risk factors ; uncontrolled diabetes mellitus, use of steroid therapy and COVID-19 infection in the up rise of mucormycosis has been found and documented by Moorthy and colleagues in their recent study.<sup>18</sup> In our frequency based descriptive study all the patients with this invasive fungal infection were diabetic and all post COVID-19 patients had used corticosteroid therapy during the infection phase. In a study by Hartnett and colleagues it has been considered that contaminated and unsterile medical devices and supplies to the patients might be responsible for the spread of infected fungal spores to cause mucormycosis.<sup>19</sup> Searching for the source of fungus in rhinocerebral mucormycosis, Gupta has mentioned the need to find out the ICU devices like catheters, masks, humidifiers, oxygen piping and ventilators for fungal contamination.<sup>1</sup> As we have seen that 31.2 % of our study patients received oxygen inhalation therapy during their COVID-19 treatment. Early and prompt antifungal therapy with intravenous Amphotericin B and surgical debridement / resection are the established treatment modalities so far and have been used in many different studies.<sup>5,6,7,8,20</sup>

We used MRI with gadolinium contrast as an imaging tool for initial radiological diagnosis as well as for post treatment evidence of recovery as it has been documented helpful in extra sinus involvement of the

disease.<sup>21</sup> In an extensive review, Jaffar and his colleagues evaluated 14 case reports of rhinocerebral mucormycosis from different parts of the world and the cumulative findings show that the mean age of the patients were 45.7 years and 69% were males. Diabetes was present in 85.7 % of patients and steroid use was seen in 57.1% cases. Histopathological identification of the organism was present in 71.4% cases. In the review of these 14 case reports, 05(35.7%) patients had total loss of vision, 04 (28.5%) were having intracranial extension, 05(35.7%) patients had their paranasal sinuses involved, palatal rent was seen in 02(14.2%) patients and ptosis was present in 04(28.5%) patients. Out of 14 patients 13(92.8%) were given intravenous Amphotericin B and underwent surgical debridement. 07(50%) patients were recovered and 07(50%) were expired.<sup>22</sup> Pakdel et al in a descriptive cross sectional multi centric study on the patients of rhinocerebral mucormycosis with COVID-19 have found 9 out of 15 (60%) patients as male and mean age was 52 years. In our study the mean age was 51 years and 71% were male patients. Furthermore the risk factor of diabetes mellitus was common too. 33 % of patients got only antifungal treatment whereas 40 % patients received combined medical and surgical treatment with survival rate of 53%.<sup>23</sup> Our study showed survival rate of 68 % with combined medical and surgical treatment for all patients. Likewise Sen et al in their retrospective case series found all 100% male patients with median age 61.4 years having uncontrolled diabetes mellitus as risk factor with none of all could be correlated with histopathological identification. Disturbed vision, ptosis and ultimate visual loss were the clinical features. With combined antifungal and surgical treatment 83 % survival rate was observed.<sup>6</sup> Sharma and colleagues in their prospective case series also described similar pattern of age and gender distribution with identical risk factor and the predominant clinical spread of the disease was seen intraorbital (43.47%). All patients survived with combined medical and surgical treatment.<sup>20</sup> Moorthy et al in retrospective multi centric case series described male predominance with 55.5 years as median age with similar risk factor and involvement of rhino-orbito-palatal regions. All patients got Amphotericin B while 07 out of 16 (43.75%) underwent surgical debridement and 11 (68.7%) patients survived.<sup>18</sup> In our part of the world male predominance in mucormycosis can be due to more exposure of the outside environment as the responsibility of earning and outside work lies mainly upon male population. Between the ages of 40 to 60 years, the exposure of outer world is maximum and health issues like diabetes are also commoner in this age group. These factors may explain the contamination and catching of microorganisms like fungi and viruses in immunocompromised state. Despite the traditional aggressive treatment including intravenous antifungal

therapy and surgical debridement, the survival rate is not promising although better survival rates were observed in three case series when surgical debridement was used along with antifungal therapy.<sup>6,20,24</sup> We have found survival rate of 68.4 % in this study with combined treatment modality.

**Recommendation:** Authors recommend larger multi centric retrospective studies across the country to see the variation in the risk factors, age and gender distribution, clinical spectrum with complications and treatment modalities used among the patients of mucormycosis arrived in Covid-19 pandemic.

## CONCLUSION

Invasive fungal infections like mucormycosis can be more frequent and lethal in the presence of COVID-19 infection. Uncontrolled diabetes mellitus, immunocompromised status and corticosteroid therapy can collectively enhance the disease occurrence and mortality. Early diagnosis and aggressive antifungal treatment with endoscopic surgical debridement can improve outcome. At the same time risk factor identification with eradication can equally reduce the burden of problem.

### Author's Contribution:

Concept & Design of Study:	Muhammad Asim Shafique
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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