

## Clinical Profile of Mucormycosis Patients Admitted in a Tertiary Care Center - A Prospective Observational Study

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### ABSTRACT

**Background :** Mucormycosis is an infection caused by a group of filamentous moulds within the order Mucorales<sup>1</sup>. India witnessed a surge of mucormycosis patients especially after the second wave of COVID 19 infection (April - June 2021). Our hospital, a tertiary care hospital in Central India also witnessed a surge in mucormycosis cases during the past three month period- April - June 2021. Therefore, present study was carried out in patients admitted to our hospital.

**Methods :** In this study a total of 83 patients of suspected mucormycosis patients were enrolled. All relevant data was recorded over a period of 2 months and analyzed.

**Results :** Amongst the 83 patients evaluated, 65% were from Nagpur district. The mean age of patients was  $52 \pm 11.39$  years with male preponderance (1.5:1). Facial pain (75.9%), headache (69.88%), nasal congestion (33.73%) were the predominant presenting symptoms. Diabetes mellitus was seen in 81.92% patients and past history of COVID 19 was seen in 86.74% patients. Steroids were used in 68.67% patients and 55.44% patients required O2 supplementation during the COVID 19 infection. All patients were treated with Injectable Amphoterecin B and endoscopic debridement was done in all patients.

**Conclusion :** Mucormycosis has emerged as a leading cause of infection in post covid patients in Indian Subcontinent and it presents with myriad of symptoms. Early diagnosis, urgent systemic antifungal therapy and sinus debridement surgery are of extreme importance for successful eradication of infection and patient survival.

### Introduction :

Mucormycosis is an acute, fulminant, often fatal fungal infection caused by fungi of the family Mucoraceae<sup>2</sup>. These fungi cause infection primarily in patients with diabetes, defects in phagocytic function (e.g., neutropenia or glucocorticoid treatment) and/or elevated levels of free iron, which supports fungal growth in serum and tissues. Devastating rhino-orbital-cerebral and pulmonary infections are the most common syndromes caused by these fungi. Mucorales have unique capability of angio-invasion causing vasculitis and thrombosis of vessels, resulting in large areas of infarction and necrosis<sup>3,4,5</sup>. Infections may result from ingestion of contaminated food, inhalation of spores into the nares or lungs, or inoculation into disrupted skin or wounds. In healthy individuals, cilia transport these

spores to the pharynx and they are cleared through the gastrointestinal tract. In susceptible individuals, infection usually begins in the nasal turbinates or the alveoli. It proliferates and spreads to the paranasal sinuses (sino-nasal mucormycosis) and then to the orbit by direct extension or through hematogenous route (sino-orbital mucormycosis). It can also spread to the brain (sino-orbitalcerebral mucormycosis) which is the commonest manifestation of mucormycosis<sup>6,7,8,9</sup>.

### Material and Methods :

After approval from the Institutional Ethical Committee of the Government Medical College and Hospital, Nagpur, prospective data of patients admitted from 1st April 2021 to 1st June 2021 of confirmed (CT/MRI/KOH mounts) mucormycosis cases were analyzed. All demographic data, detailed history, organ involvement, any comorbid illnesses were recorded. Area of residence, detailed clinical examination was done. Patients of suspected mucormycosis were subjected to investigations including complete blood count, HbA1C, CT PNS, KOH mount and nasal endoscopy. Biochemical investigations including renal function and liver

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function tests were done and recorded. All the patients received treatment, surgical treatment was endoscopic debridement or maxillectomy as per decision of ENT / OMFS surgeons. Medical treatment in form of Injection Amphoterecin and / or Tablet Posaconazole with proper standard care and anti-diabetic medications were given to all patients. Amphotericin B was given as ampotericin deoxycholate or liposomal or lipid complex as per availability in the hospital. Sample size - 83 was calculated (as per formula) and statistical analysis was done.

**Table 1 : Clinical Profile, Co-morbidities & Past History in Study Subjects**

		No. of Patients (%)
Age	< 30	1 (1.20%)
	30-39	11 (13.25%)
	40-49	20 (24.10%)
	50-59	30 (36.14%)
	> 60	21 (25.30%)
Gender	Male	50 (60.24%)
	Female	33 (39.76%)
Symptoms	Facial Pain	63 (75.90%)
	Headache	58 (69.88%)
	Nasal Congestion	28 (33.73%)
	Swelling	25 (30.12%)
Signs	Swelling of Eye	67 (80.72%)
	Discharge	34 (40.96%)
	Ptosis	28 (33.73%)
	Cranial Nerve Palsy	8 (9.64%)
Involvement	Sinusitis	83 (100%)
	Orbit	33 (39.76%)
	CNS	17 (24.29%)
Comorbid Conditions	Diabetes	68 (81.92%)
	Hypertension	31 (37.35%)
	CVE	9 (10.84%)
	IHD	6 (7.23%)
Past History of Covid	Yes	72 (86.74%)
	No	11 (13.25%)
Hypoxia	Yes	46 (55.44%)
	No	37 (44.57%)
Steroid Use	Yes	57 (68.67%)
	No	26 (31.33%)

**Table 2 : Duration between COVID 19 (Date of Swab Positivity) and Onset of Symptoms of Mucormycosis**

	Duration (Days)	Number of patients (%) n=72
INTERVAL BETWEEN	10-20	37 (51.02%)
COVID AND	21-30	32 (44.9%)
SYMPTOMS	31-40	3 (4.08%)

**Table 3 : Patients Hospitalized for Covid vs Home Based Treatment (n=72)**

TREATMENT	Number of patients (%)
Indoor	54 (72%)
Home based	18 (28%)

**Table 4 : Biochemical Profile of the Study Subjects**

	MEAN	STANDARD DEVIATION
Fasting Blood Sugar	169.15	72.29
Post Prandial Blood Sugar	254.25	100.81
Random Blood Sugar	198.26	85.42
HBA1c	9.47	2.40
Hemoglobin	10.8	1.9
Total WBC Count	9426	3998
Total Platelet Count	2,59,000	1,21,379
Blood Urea	29.95	19.98
Serum Creatinine	1	0.5
Serum Na	136	6.3
Serum K	3.8	0.77

#### Observation and Results :

During the period of April to June 2021, data of 83 patients was recorded for evaluation. The mean age of patients was  $52 \pm 11.39$  years with male preponderance (1.5:1). Majority of patients were from Nagpur district (65%), followed by Bhandara (8.4%), Amravati (6%), Chandrapur (4.8%), Gondia (3.6%) and Akola (3.1%). 72 patients had a past positive history of COVID-19 Infection and of these 18 were isolated and treated at home.

Majority of patients had Diabetes (80.7%) and Hypertension (37.35%). Clinical profile of

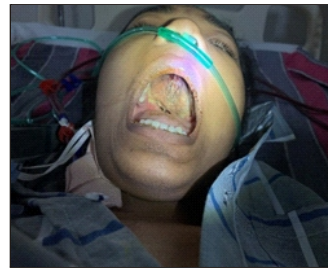
mucormycosis patients are depicted in **Table 1**. 86.74% patients had past history of covid 19, 72% patients had received indoor treatment for COVID-19.

The most common clinical presentation was facial pain (75.9%) followed by headache (69.88%), nasal congestion (33.7) and swelling of face (25%). The duration between covid 19 infection and mucormycosis symptom onset was ranging from 10 days to 36 days with a mean of 20.93 days. Laboratory parameters showed a mean random blood sugar of  $198.26 + 85.42$ , whereas the mean HbA1c was  $9.47 + 2.40$ . 31.53% of the patients had anemia ( $<10\text{g/dl}$ ), mean leucocyte count  $9426 + 3998 / \text{cmm}$ , with 2.44% patients counts less than  $4000 / \text{cmm}$  and 30.12% patients had counts more than  $11,000 / \text{cmm}$ . Platelet count was less than 1 lakh in 6.02% patients. Deranged renal parameters were seen in 15.66% patients. In our study 27.7% patients showed fungal hyphae on KOH mount.

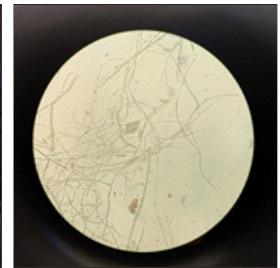
All the patients had sinus involvement in the form of sinusitis, with maximum patients having more than 3 sinus involvement, maxillary sinus being the commonest to be involved followed by ethmoidal sinus. Orbital involvement was seen in 39.76% and Cerebral involvement was seen in 24.29% of the cases. All the patients were treated with Injectable Amphotericin B and 16.8% of patients received Tab Posaconazole. All patients underwent Functional Endoscopic Sinus Surgery (FESS) under general anaesthesia and endoscopic debridement was done and wherever needed maxillectomy and orbital decompression were done as per the involvement.



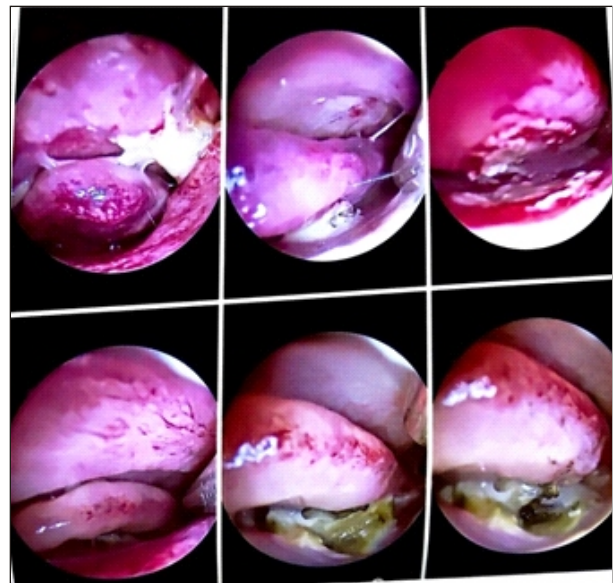
**Figure 1 : left sided orbital involvement**



**Figure 2 : showing palatal erosion**



**Figure 4 : microscopy picture showing filamentous fungi**



**Figure 3 : endoscopy images showing black crusts in middle meatus**



**Figure 5 : CT scan showing maxillary sinus involvement**

**Discussion :**

Mucormycosis is considered as an emergency, owing to the rapidly aggressive and invasive nature of the fungus<sup>10</sup>. Mucormycosis was first reported as a

cause of human disease in 1885<sup>11</sup>. During the last two decades there has been a dramatic increase in the occurrence of invasive fungal infections largely as a result of increase in the size of population at risk. It is usually an acute necrotizing fungal infection with a fulminant course due to angio-invasion. Various risk factors are associated with the development of mucormycosis. Uncontrolled diabetes is considered the key factor for predisposition to mucormycetes infection. In our study the mean age was found out to be 52 yrs. with male preponderance. In a study conducted by *Roden et al.* of 929 patients, disease was more common in males as compared to females. However no particular reason for above fact could be determined. The most common symptom was facial pain (75.9%) followed by headache (69.88%).

Rhino-cerebral mucormycosis is the commonest clinical presentation in most of the published series<sup>12,13,14</sup>. In our study, cerebral involvement was seen only in 24% patients. The infection begins with inhalation of the spores into the oral and nasal cavity. In persons with an intact immune system, infection rarely develops because the fungal spores are phagocytized by macrophages. However, in individuals with uncontrolled diabetes mellitus and in immunocompromised patients with severe neutropenia, infection develops as their immune system is weak<sup>15</sup>. From here infection spreads to the paranasal sinuses and to orbit via ethmoid and maxillary sinuses or through nasolacrimal duct resulting in orbital cellulitis<sup>16</sup>. The infection may extend posteriorly to the orbital apex, leading to orbital apex syndrome. The fungus may gain access to the cavernous sinus and to the brain parenchyma through cribriform plate, orbital apex or orbital vessels.

The study done by *Chakrabarti et al.* reported that 50% cases had uncontrolled diabetes mellitus and the association was significant<sup>12</sup>. In our study 81.92% patients had diabetes mellitus. In a study done by *Rajiv Soman et al.* COVID 19 was the risk factor in only 32.6% patients, amongst whom 78.7% received glucocorticoid treatment for COVID 19 management<sup>17</sup>. Inappropriate glucocorticoid use was independently associated with mucormycosis.

In our study 86.74% patients had previous history of COVID 19 infection; while 68.67% patients were treated with glucocorticoids with maximum number of patients receiving steroids for 6-10 days (50.90%).

Laboratory parameters showed a mean random blood sugar of 198.26 + 85.42, whereas the mean HbA1c was 9.47 + 2.40. 31.53% of the patients had Anemia (<10g/dl), mean leucocyte count of 9426 + 3998 / cmm, with 2.44% patients counts less than 4000/cmm and 30.12% patients had counts more than 11,000/cmm. Platelet count was less than 1 lakh in 6.02% patients. Deranged renal parameters were seen in 15.66% patients.

Diagnosis of invasive rhino orbital mucormycosis is made by typical clinical presentation and by detection of broad aseptate hyphae with right-angled branching in KOH mount which is pathognomonic of mucormycosis<sup>18</sup>. KOH mount can be used for quick diagnosis. In our study 27.7% patients showed fungal hyphae in KOH mount. Alternate techniques for tissue diagnosis include immunohistochemistry, polymerase chain reaction (PCR) for fungal DNA and in situ hybridization.

CT scan and MRI provides evidence for mucosal thickening, opacification of sinuses, orbital and intracranial involvement<sup>19</sup>. In our study maxillary sinus involvement was most common followed by ethmoidal. In a study by *Abdollahi et al.* maxillary sinuses were the most frequently involved sinuses (66.7%) followed by the ethmoid<sup>20</sup>.

Early diagnosis, prompt initiation of systemic antifungal therapy, control of underlying systemic condition and aggressive radical debridement of sinuses is the key in improving outcomes. Amphotericin B is the first-line drug for mucormycosis. It should be initiated as soon as the diagnosis is suspected. It is given in a dose of 1.01.5 mg/kg/day in dextrose 5% solution intravenously. The liposomal amphotericin B is more effective and less toxic facilitating prolonged administration without side effects. Due to financial constraints, our patients received the conventional form of amphotericin B. All our patients received Injection Amphoterecin B as medical management and

16.87% patients were given Tablet Posaconazole additionally. Inj. Amphotericin B was given as amphotericin deoxycholate or liposomal or lipid complex as per availability in the hospital. Endoscopic debridement or maxillectomy was done as per decision of ENT/OMFS surgeons.

### Conclusion :

Mucormycosis has emerged as a leading infection in post covid patients in Indian Subcontinent and it presents with myriad of symptoms. In our study most common risk factor associated with development of mucormycosis was past history of COVID-19, Diabetes and Steroid use. Early diagnosis, urgent systemic antifungal therapy and sinus debridement surgery are of extreme importance for successful eradication of infection and patient survival. Post COVID patients as well as doctors need to be aware of this devastating and life threatening disease. COVID patients should be advised to watch for any symptoms suggestive of mucormycosis and if so immediately seek medical advice. People need to be educated regarding stringent control of blood sugars, hand and ambient hygiene, avoid contact with dirty surfaces and wearing mask to avoid breathing mucor spores. Physicians need to be aware of judicious use of steroids and other immunosuppressants while treating COVID 19 patients.

### Limitations :

This was a prospective observational study regarding risk factors and clinical features of mucormycosis patients on admission, clinical outcome and follow up of patients was not taken into consideration.

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