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## ORIGINAL RESERCH

# Study of Mucormycosis infection and outcome at tertiary health care centre, Southern Rajasthan

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### Introduction

Mucormycosis, a serious angioinvasive infection caused by common filamentous fungi, that is, mucormycetes, constitutes the third most common invasive fungal infection following aspergillosis and candidiasis [1]. The disease can be transmitted by inhalation of spores or by direct inoculation of the spores into disrupted skin or mucosa. The etiologic agents can cause infections with high mortality in immunocompromised, mainly diabetic patients [2].

Broad aseptate hyphae (coenocytic mycelia) and zygospore production are two characteristics of mucormycetes. Several species of the order Mucorales, which are known for their propensity to disseminate, are involved in infections of the rhinocerebral, pulmonary, cutaneous, gastrointestinal, and other less common organs in immunocompetent and immunocompromised people. The hyphae invade blood vessels and cause tissue infarction and necrosis regardless of the method of infection (inhalation of airborne spores, ingestion, or direct skin inoculation). [3].

Mucor mycosis made severe chaos in India during the second wave of COVID-19 (April to July 2021) epidemic by its sudden devastating surge. Exact cause of its rise suddenly and specifically during the second wave remains debatable, it has been noted that the people who are diabetic and have recovered from COVID-19 infection are more predisposed to Mucormycosis.

Mucormycosis infection of the sinuses is a form of life-threatening invasive fungal sinusitis that typically affects immunocompromised individuals with an impaired neutrophilic response. Patients can include those with uncontrolled diabetes mellitus, acquired immunodeficiency syndrome, iatrogenic immunosuppression and haematological malignancies, and those who have undergone organ transplantation.[4]

Without early diagnosis and treatment, there may be rapid progression of the disease, with reported mortality rates from intra-orbital and intracranial complications of 50–80 per cent.[5] Even with prompt diagnosis, treatment of underlying diseases, and aggressive medical and surgical intervention, the management is often not effective, leading to an extension of the infection and ultimately death.[6]

### Aims and objectives

- To know the, risk factors, and treatment outcome of mucormycosis.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

## Materials and methods

The retrospective observational study was conducted at RNT Medical College, Udaipur, India -a tertiary care institute. It was carried out over a period of 5 months from Jan 2022 to May 2022.

All patients with invasive mucormycosis of the paranasal sinuses who presented to the ENT department, either as an out-patient or following departmental referral, and who were either coronavirus-positive or had recovered from coronavirus infection, were included in the study.

The patients' presentation details, imaging findings, co-morbidities, management details, and follow-up information were obtained, recorded and analysed. All patients were operated upon, keeping complete surgical debridement as the aim, along with intravenous amphotericin administration.

Clinico-demographic profile of the patients was examined with special reference to diabetes (new/ knowndiabetic cases and HbA1c levels) and steroid usage (type, its dosage/ quantity and its period of administration).

Information on clinical features, risk factors, laboratory and radiological findings, treatment (including medical and surgical treatment), and outcome was noted from the records. The data obtained was then analyzed using Excel and statistical software.

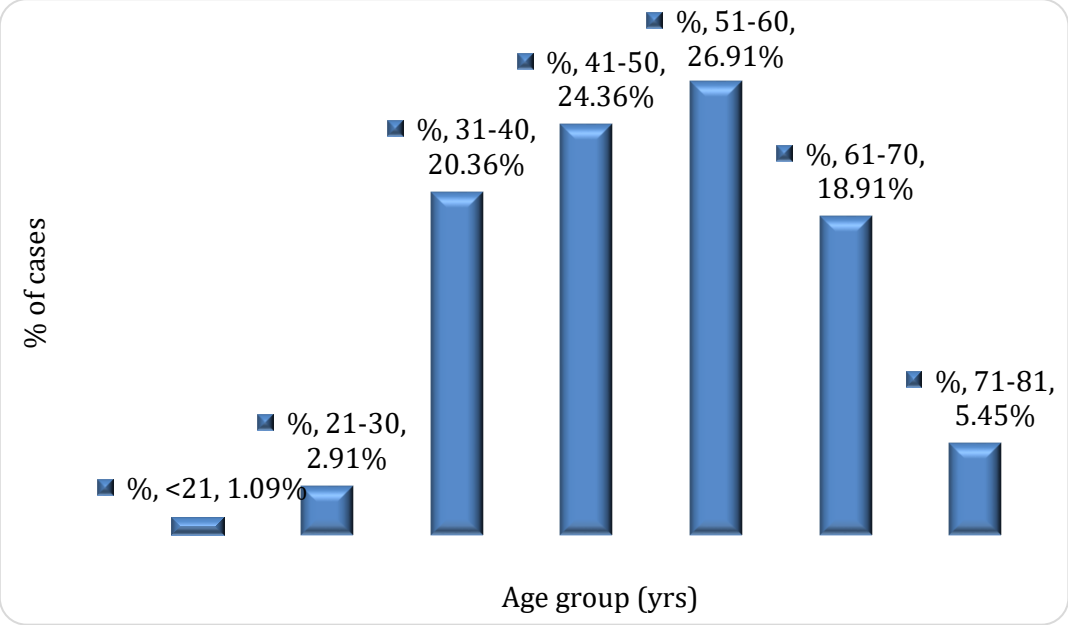
## Statistical analysis

Statistical analysis was performed using SPSS v.22. The statistically significant variables by univariate analysis ($P < 0.05$) were included in the multivariate model.

## Results

We observed 275 patients with confirmed mucormycosis evaluated between study period of 5 months from Jan 2022 to May 2022, who were given steroids and had Covid-19 infection. Out of these 275 cases, maximum 193 (70.18%) patients were in the age group of more than 40 to 70 years of age. About 20% were in the 31-40 years of age group followed by 5.45% in 71-81 years and 4% were less than 30 years of age group (Figure 1).

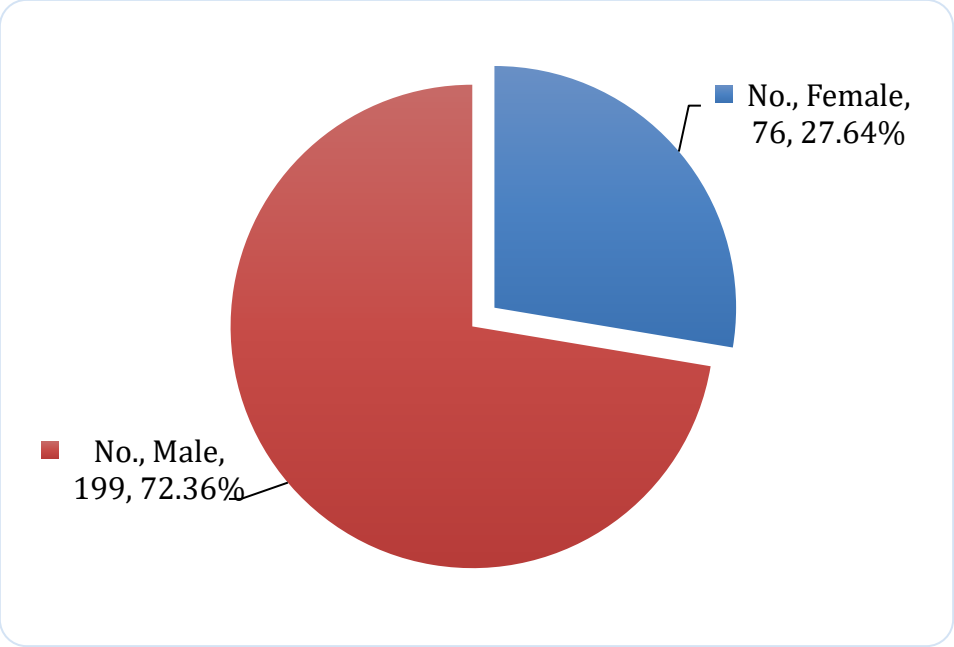
**Figure 1: Distribution of Patients According to Age Group**




72.36% of patients were male and 27.64% were females, showing male predominance. (Figure 2).

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

**Figure 2: Distribution of Patients According to Gender**




History of Covid-19 was observed in 180 (65.45%) patients as the major risk factor followed by 170 (61.81%) had diabetes, 133 (48.36%) received steroids, 85 (30.91%) received oxygen, 59 (21.45%) had immunocompetent status, 3 (1.09%) had CKD (Table 1).

**Table 1: Risk factors Associated with Mucormycosis**

| Risk factors Associated with Mucormycosis | No. | % |
|---|---|---|
| History of Covid | 180 | 65.45% |
| Diabetic | 170 | 61.81% |
| Steroids Received | 133 | 48.36% |
| Oxygen Received | 85 | 30.91% |
| Immunocompetent Status | 59 | 21.45% |
| CKD | 3 | 1.09% |
| Diabetic Ketoacidosis | 1 | 0.36% |
| Solid organ transplant | 1 | 0.36% |
| Dialysis | 1 | 0.36% |

Mean Hb1Ac levels was 9.52±1.89 gm% with 234 (85.09%) patients having ≥7.5 Hb1Ac and 41 (14.91%) had <7.5 gm% levels (Table 2).

**Table 2: Distribution according to Hb1Ac Levels**

| Hb1Ac levels | |
|---|---|
| Mean±SD | 9.52 ± 1.89 |
| <7.5 | 41 (14.91%) |
| ≥7.5 | 234 (85.09%) |

Majority of patients 228 (82.90%) were treated by Amphotericin B and Posaconazole therapy only, whereas 47 (17.10%) required surgical intervention with Amphotericin B and Posaconazole (Table 3).

**Table 3: Mode of Treatment**

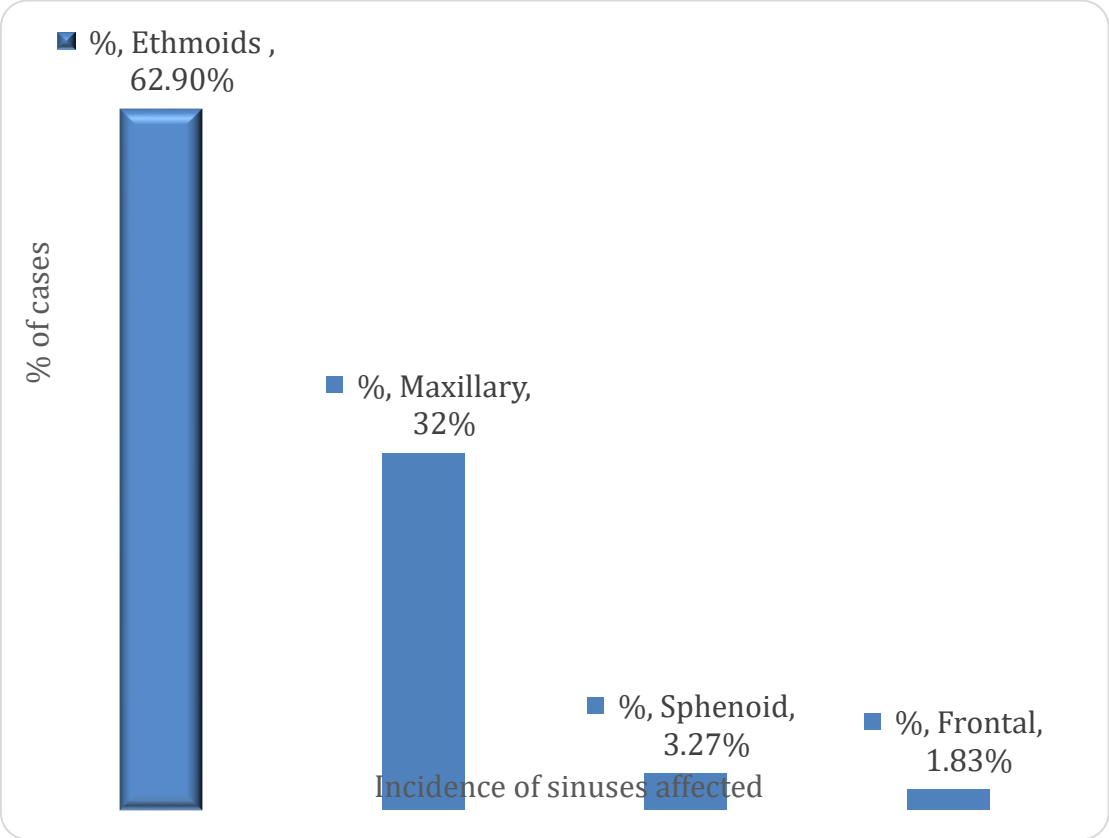
| Mode of Treatment | No. | % |
|---|---|---|
| Amphotericin B and Posaconazole therapy only | 228 | 82.90% |

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

| | | |
|---|---|---|
| Patients treated with surgery and amphotericin B and Posaconazole | 47 | 17.10% |

Ethmoids was mainly affected in 173 (62.90%) cases, followed by maxillary in 88 (32%), sphenoid in 9(3.27%) and frontal in 5 (1.83%) (Figure 3).

**Figure 3: Incidence of sinuses affected**




Out of 47 surgical procedures maxillectomy was performed in 16 cases, 2 (4.25%) patients expired, maxillectomy + alveolectomy was performed in 7 cases, 4 (8.51%) patients expired, maxillectomy + orbital exenteration was performed in 3 cases, 2 (4.25%) expired. Modified Endoscopic Denker's, FESS + Debridement and Alveolectomy + Antrostomy were performed in 15, 3 and 3 cases respectively and none expired (Table 4).

**Table 4: Type of Procedure and Outcome**

| Type of Procedure | No. (n=47) | No. of Deaths | Percentage (n=47) |
|---|---|---|---|
| Maxillectomy | 16 | 2 | 4.25% |
| Maxillectomy + Alveolectomy | 7 | 4 | 8.51% |
| Maxillectomy + Orbital Exenteration | 3 | 2 | 4.25% |
| Modified Endoscopic Denker's | 15 | 0 | 0% |
| FESS + Debridement | 3 | 0 | 0% |
| Alveolectomy + Antrostomy | 3 | 0 | 0% |

Out of total 275 patients, 222 (80.72%) were discharged alive and 53 (19.27%) expired (Table 5).

**Table 5: Outcome**

| Outcome | No. of Patients | Percentage (n=275) |
|---|---|---|

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

| | | |
|---|---|---|
| Alive | 222 | 80.72% |
| Death | 53 | 19.27% |

**Discussion**

Invasive fungal infections have dramatically increased in frequency over the past 20 years, largely as a result of an increase in the size of the population at risk. Mucormycosis is not the exception in this time of rising incidence. Acute necrotizing fungal infection with a fulminant course typically results from angioinvasion. In developing and tropical nations, an increase in the number of covid-19 incidence may be linked to an increase in the number of patients with invasive mucormycosis.

Out of 275 patients with confirmed mucormycosis, 95.63% patients were in the adult age group. Similar findings were noted in the studies of Chakrabarti et al in 2009 reported 352 (92.1%), Manesh et al in 2019 observed 177 (96.2%), Chander et al in 2018 in their study observed 78 (95.1%), Prakash et al in 2019 reported 342 (89.1%) and Patel et al in 2020 reported 438 (94.2%) in adult age group.(9,10,11,12,13)In a study conducted by Roden et alof 929 patients diagnosed with mucormycosis, the mean age was 38.8 years. (14)

72.36% of patients were male and 27.64% were females with a M:F ratio of 2.62:1. Singh et al observed similar findings with 78.9% males v/s 21.1% females in their study. More commonly observed in males. Male: female ratio in studies by Chakrabarti et al was 2.4:1, Manesh et al 2.5:1, Chander et al 2.04:1, Prakash et al 2.3:1, Patel et al 2.3:1 and by Priya et al 2.8:1.(9,10,11,12,13,15)

When Risk factors were assessed History of Covid-19 was observed in 180 (65.45%) patients as the major risk factor followed by 170 (61.81%) had diabetes, 133 (48.36%) received steroids, 85 (30.91%) received oxygen, 59 (21.45%) had immunocompetent status, 3 (1.09%) had CKD.

Ghosh AK et al reported diabetes mellitus is the most common underlying disease after history of Covid infection, followed by haematological malignancies and solid-organ transplants. (16) Diabetes mellitus was reported in 54–76% of cases. The prevalence of mucormycosis was reported at 0.16–1.72% in patients with diabetes mellitus. Prakash et al reported a higher prevalence of diabetes mellitus as a risk factor (67%) compared to Chakrabarti A et al (22%). (9,12) Similar to India, diabetes mellitus is a major risk factor in mucormycosis in Mexico (72%), Iran (75%), and the USA (52%) (17,18). Solid-organ transplantation (SOT) is a risk factor in 2.6–11% of mucormycosis cases from India (Ghosh AK), compared to 7–14% from global data (16,17,18).

Other predisposing factors associated with mucormycosis in India are chronic kidney disease (CKD), steroid therapy, pulmonary tuberculosis, and chronic obstructive pulmonary disease (COPD) [Chakrabarti A et al]. Chakrabarti A et al 2021, reported that mucormycosis patients had CKD in 9–32% of cases. Similarly, a study from Turkey reported that 18% of the patients with mucormycosis had chronic renal insufficiency (9,19). Pulmonary tuberculosis and COPD were seen in 7–46% of patients with mucormycosis(20,21,22]. Other risk factors reported in India included intravenous drug use, autoimmune disease, HIV infection, immunosuppressant drugs, malnutrition, and ICU stay.

Mean Hb1Ac levels was 9.52±1.89 gm% with 234 (85.09%) patients having ≥7.5 Hb1Ac (uncontrolled DM) and 41 (14.91%) had <7.5 gm% levels. Sharma et al reported patients with controlled diabetes mellitus9 (39.13%) and uncontrolled12 (52.17%). (7)

Majority of patients 228 (82.90%) were treated by Amphotericin B and Posaconazole therapy only, whereas 47 (17.10%) required surgical intervention with Amphotericin B and Posaconazole. Similar to ours Priya et al 2020 in their study treated mucormycosiswith amphotericin B + surgery (18.8%), surgery alone (50.0%). Patel et al 2020 reported amphotericin B + surgery (43.7%), amphotericin B + alone (61.3%), surgery alone (41.4%).

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

Prakash et al 2019 amphotericin B + surgery (32.4%), amphotericin B + alone (54.4%), surgery alone (60.9%). (12,13,15)

Bala K et al reported patient survival was significantly higher when surgery and medical treatment were combined with amphotericin B (61.5% vs. 10.3%) (P=0.04). (8) The severity of the illnesses or co-morbidities differ significantly between the surgical patients and non-surgical patients. In the current study, the group that was unable to have surgery was predominated by comorbid conditions like poor general health, hypertension, chronic renal failure, and immunosuppression. Bala et al reported that even when comparing the survival rates of liposomal and conventional amphotericin B, there is a difference (88% survival vs. 66% survival). (8)

Ethmoid sinus were mainly affected in 173 (62.90%) cases, followed by maxillary in 88 (32%), sphenoid in 9(3.27%) and frontal in 5 (1.83%). Almost similar findings were reported by Sharma et al. According to them Ethmoids 23 (100%), Maxillary 12 (52.17%), Sphenoid 5 (21.73%) and Frontal 1 (4.34%) were the commonly sinuses affected. (7)

Out of 47 surgical procedures maxillectomy was performed in 16 cases, 2 (4.25%) patients expired, maxillectomy + alveolectomy was performed in 7 cases, 4 (8.51%) patients expired, maxillectomy + orbital exenteration was performed in 3 cases, 2 (4.25%) expired. Modified Endoscopic Denker's, FESS + Debridement and Alveolectomy + Antrostomy were performed in 15, 3 and 3 cases respectively and none expired.

In present study out of total 275 patients, 222 (80.72%) were discharged alive and 53 (19.27%) expired. In the largest meta-analysis conducted by Roden et al., the overall mortality rate was observed to be 46% of the 53 patients treated in the study conducted by Chakrabarti et al. (9,14) Depending on the site of involvement, mucormycosis has a different survival rate. The higher survival rate in the Bala et al study may be attributable to the fact that the majority (92%) of the patients included for outcome analysis fell into the cutaneous or rhino-orbito-cerebral categories, which were quickly and easily diagnosed.

## Conclusion

Immunosuppressive effect of COVID-19, cannot be altered now . It is important that health care providers should be made aware about judicial use of steroid for treatment of COVID-19 and control of blood sugar levels. Uncontrolled diabetes and over-zealous use of steroids are two main factors aggravating the illness. If infected, these should be monitored daily. On diagnosis, early surgical intervention and intravenous anti-fungal treatment as per guidelines provided by local authorities should be implemented without any procrastination . Living in the era of pandemic, outlets spreading fake news , made up facts , there is a need for factual studies like ours to realign the guidelines , to make cost effective preventive strategies for further preparations of such pandemics so that egalitarian approaches that can anticipate and rapidly respond to such pandemics are developed .

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ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023


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