

## SOCIODEMOGRAPHIC AND CLINICAL PROFILE OF MUCORMYCOSIS PATIENTS ADMITTED IN TERTIARY HEALTH CARE HOSPITAL

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### Abstract

**Background:** Invasive fungal infections caused by the members of Mucorales (mucormycosis) are relatively rare but have increased in the last years. The incident rate of mucormycosis varies from 0.005 to 1.7 per million population globally whereas in India, the reported prevalence was 0.14 per 1000, approximately 80 times higher than that in developed countries, making it the country with the highest burden of mucormycosis. There lies a large lacuna in the understanding of the disease progression and the co-infection of mucormycosis with COVID-19 and the various predisposing factors. As limited data is available, the current study was undertaken to study the sociodemographic profile, clinical profile, and the outcome of mucormycosis in COVID-19 patients. To study sociodemographic profile of Mucormycosis patients admitted in tertiary health care hospital and to study Clinical profile of Mucormycosis patients admitted in tertiary health care hospital. **Materials and Methods:** Study design: Record-based cross-sectional study. Study duration: 1st May 2021 to 31st October 2021. Study population: Mucormycosis patients admitted at tertiary health care hospital. **Result:** Out of 200 patients 131(65.5%) were male and 69(34.5%) were female. Mean age group of mucormycosis subjects was  $53.98 \pm 13.39$  years. There was significant association in deaths due to mucormycosis and diabetes ( $X^2 = 5.46p = 0.01945$ ). **Conclusion:** Physicians caring for severely ill patients with COVID-19 and concomitant poorly controlled diabetes should have a high index of suspicion of mucormycosis, especially if corticosteroids are used during the course of disease.

## INTRODUCTION

Invasive fungal infections caused by the members of Mucorales (mucormycosis) are relatively rare but have increased in the last years. Mucormycosis is a fungal infection caused by the fungus Mucor of the class Phycomycetes (order Mucorales).<sup>[1]</sup> Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) has been associated with a wide range of opportunistic bacterial and fungal infections. Both Aspergillus and Candida have been reported as the main fungal pathogens for co-infection in people with COVID-19. Several cases of Mucormycosis in people with COVID-19 have been increasingly reported worldwide, especially in India.<sup>[2]</sup>

The immune dysregulation associated with COVID-19 is further aggravated by concomitant medical conditions such as diabetes mellitus, and the widespread use of immunosuppressive agents and broad-spectrum antibiotics. In addition, COVID-19 patients are more susceptible to develop secondary infections if they have decompensated pulmonary functions or require invasive mechanical ventilation. Previous reports observed that fungal infections were more likely to develop during the more advanced stages of COVID-19 infection, with substantially higher mortality among patients with a fungal co-infection.<sup>[3,4]</sup>

The incident rate of mucormycosis varies from 0.005 to 1.7 per million population globally whereas in India, the reported prevalence was 0.14 per 1000, approximately 80 times higher than that in developed countries, making it the country with the

highest burden of mucormycosis. Mucormycosis is difficult to diagnose. Despite early diagnosis and aggressive combined surgical and medical therapy, the prognosis for recovery from mucormycosis is poor.<sup>[5-8]</sup>

Rhino-orbital infection with mucorales species of fungus is a dreaded condition with higher mortality rate even with treatment. It is an opportunistic infection with invasion of the blood vessels by fungal hyphae, infarction, and necrosis of host tissue. Mucormycosis has long been known to affect immunocompromised patients particularly those with uncontrolled diabetes.<sup>[9]</sup>

There lies a large lacuna in the understanding of the disease progression and the co-infection of mucormycosis with COVID-19 and the various predisposing factors. As limited data is available, the current study was undertaken to study the Sociodemographic profile, clinical profile, and the outcome of mucormycosis in COVID-19 patients.

### Aim and Objectives

1. To study Sociodemographic profile of Mucormycosis patients admitted in tertiary health care hospital.
2. To study Clinical profile of Mucormycosis patients admitted in tertiary health care hospital.

## MATERIALS AND METHODS

We conducted a record based cross sectional study of mucormycosis patients admitted at tertiary health care hospital of Ambajogai, Beed in state of Maharashtra during the period of 1st May 2021 to 31st October 2021. 200 Case papers with complete data of mucormycosis patients were selected. Ethical clearance from institutional ethics committee was obtained. It's a record based study so data was obtained from administrative records after taking the permission from hospital administration.

Statistical Analysis: Data was analyzed using Microsoft Excel 2010, Open EPI-Info Version 3.01 updated on 2013/04/06. Categorical variables were presented as proportions (n, %) and group differences were analyzed using the chi-squared test. Vancouver system of listing and citing of reference was used.<sup>[10]</sup> The references were numbered according to their appearance in the text and listed accordingly.

## RESULTS

During the study 200 papers of mucormycosis patients were analyzed, as shown in figure 1, out of 200 patients 131(65.5%) were male and 69(34.5%) were female. majority of cases were belonging to age group ranging from 61-70 (26.5%) followed by 41-50 (25.5%) and 51-60 years (22%). Mean age

group of mucormycosis subjects was  $53.98 \pm 13.39$  years. [Table 1].

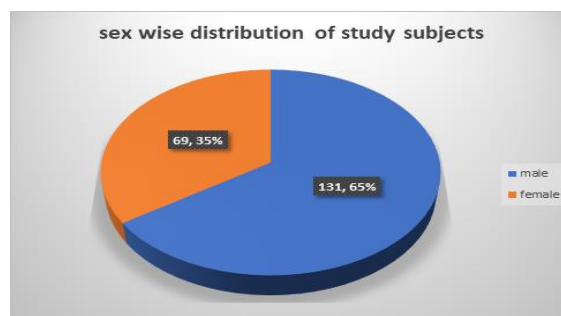


Figure 1: Sex-wise distribution of study subjects

As shown in [Table 2] significant proportion of subjects had a background history of diabetes mellitus (n =113, 56.5%), 20 (10%) were on medications for hypertension, 3 (1.5%) were having kidney disease and 2(1%) were having IHD. Out of 200 subjects 197 (98.5%) had history of covid positive test either RTPCR or Antigen test. Supplementary oxygen and steroid treatment in last 6 months was given to a in a significant proportion of subjects (n =145, 72.5%).

All patients initially presented with nasal congestion with or without discharge consistent with sinusitis. Most patients with mucormycosis experienced a non-descript localized or generalized headache (n = 160, 80%).

As shown in [Figure 2] out of 200 subjects 98 (49%) were having only sinus involvement, 3(1.50%) were having only orbital involvement, 6(3%) were having only palatal involvement, 58 (29%) having both sinus and orbit involvement, 28(14%) having sinus plus palatal involvement and 7(3.50%) were having all three sinus, orbit, palate involvement.

As shown in [Table 3] total of 35 (17.5%) patients succumbed to their disease. Sub-group analysis of these cases revealed their mean age as  $54.03 \pm 13.39$  years.

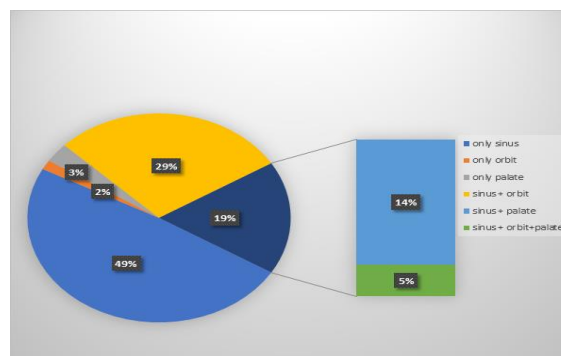


Figure 2: No. of patients according to site of involvement (%)

**Table 1: Age wise distribution of study subjects.**

Age group in years	n (%)
11-20.	2 (1%)
21-30	10(5%)
31-40	23(11.5%)
41-50	51(25.5%)
51-60	44(22%)
61-70	53(26.5%)
71-80	16(8%)
81-90	1(0.5%)
Total	200

**Table 2: Comorbidities among study subjects.**

Comorbidity	n = 200
Diabetes	113 (56.5%)
Hypertension	20 (10%)
Kidney disease	3(1.5)
IHD	2(1%)

**Table 3: Age-wise distribution of Deaths due to mucormycosis.**

Age Group Years	Male	Female	Total
31-40	2	1	3
41-50	4	4	8
51-60	4	4	8
61-70	10	3	13
71-80	3	0	3
Total	23	12	35

**Table 4: Distribution of study subjects with Co-Morbidity and Outcome**

Diabetes Mellitus	Outcome			X <sup>2</sup> - 5.46 p = 0.01945
	Death	Cured	Total	
Yes	26	87	113	
No	9	78	87	
Total	35	165	200	

Deaths among study subjects with history of diabetes were 26 (74.28%) while deaths among study subjects without diabetes were 9 (25.72%). There was significant association in deaths due to mucormycosis and diabetes ( $X^2$ - 5.46p = 0.01945).

**Table 5: Distribution of study subjects with oxygen and steroid treatment and Outcome**

Oxygen + steroid therapy	outcome			Yates corrected X <sup>2</sup> -6.517 p = 0.01069
	Death	Cured	Total	
Yes	32	113	145	
No	3	52	55	
Total	35	165	200	

Deaths among study subjects with history of oxygen and steroid treatment were 32 (91.42%) while deaths among study subjects without oxygen and steroid treatment were 3 (8.58%). There is significant association between deaths due to mucormycosis and history of oxygen and steroid treatment ( $X^2$ - 6.517p = 0.01069).

**Table 6: Distribution of study subjects according to no. of sites involved and Outcome.**

No. Of Sites Involved Among Sinus, Orbit, Palate	Outcome			X <sup>2</sup> - 6.296 p = 0.01210
	Death	Cured	Total	
Only 1 Site Involved	12	95	107	
>1 Site Involved	23	70	93	
Total	35	165	200	

Deaths among study subjects with only 1 site involvement are 12 (34.28%) while deaths among study subjects with >1 site involvement are 23(65.72%). There is significant association between mucormycosis deaths and number of sites involved among sinus, orbit, palate ( $X^2$ -6.296p = 0.01210).

## DISCUSSION

Mucormycosis is the third most common cause of invasive fungal infection after *Aspergillus* and *Candida* in humans.<sup>[11]</sup>The most common type of mucormycosis is rhino- cerebro-orbital (44%–49%), followed by cutaneous (10%–19%)pulmonary (10%– 11%), disseminated (6%– 11%) and gastrointestinal (2%– 11%).<sup>[12]</sup>

Uncontrolled diabetes is the single most common predisposing factor for mucormycosis in India, being reported in more than 50% of cases of mucormycosis.<sup>[13]</sup>

In the present study [Figure1, Table1], out of 200 patients 131(65.5%) were male and 69(34.5%) were female and mean age group of mucormycosis subjects was  $53.98 \pm 13.39$  years. Similarly Mrittika Sen et al,<sup>[9]</sup> observed that out of 2826 mucormycosis patients 71% were male and 29% were female and the mean age of mucormycosis patient was 51.98 years. Mean age of mucormycosis patients in study by Neeraj Singla et al,<sup>[14]</sup> was  $50.697 \pm 13.51$  years. Monalisa Sahu et al,<sup>[15]</sup> in their retrospective study observed that out of 217 mucormycosis patients 177(82%) were male and 109 (50%) were belonging to age group 37-54 years.

In the present study [Table2] significant proportion of subjects had diabetes mellitus as a comorbidity (n =113, 56.5%). Neeraj Singla et al found that out of 109 mucormycosis patients 86 (78.89%) were having diabetes mellitus with mean duration of 4.889 years. Mrittika Sen et al observed that out of 2826 mucormycosis patients 2194(78%) were having diabetes.

In the present study [Figure2] out of 200 subjects 98 (49%) were having only sinus involvement, 3(1.50%) were having only orbital involvement, 6(3%) were having only palatal involvement, 58 (29%) having both sinus and orbit involvement, 28(14%) having sinus plus palatal involvement and 7(3.50%) were having all three sinus, orbit, palate involvement. Monalisa Sahu et al,<sup>[15]</sup> in their retrospective study observed that out of 217 patients mucormycosis involved the nasal sinuses most commonly (n = 95, 44%) followed by rhino- orbital (ROM, n = 69, 32%), rhino-cerebral (RCM, n = 3), rhino-orbito-cerebral (ROCM, n = 15, 9%), pulmonary (n = 25, 12%), gastrointestinal (n = 6, 3%), isolated cerebral (n = 2) and disseminated mucormycosis (n = 2).

The mortality in the patients of mucormycosis depends on the stage of mucormycosis at the time of presentation, general condition of the patient, type of fungus, and the site affected. In the present study [Table3] mortality among mucormycosis patients was 17.5% similarly Monalisa Sahu et al,<sup>[15]</sup> in their retrospective study observed that total of 31 (14%) patients died due to mucormycosis during the 6 weeks follow-up. Of these, 8 (26%) had sinus involvement, 9 (29%) had ROCM, 6 (19%) had pulmonary involvement, 5 (16%) had GI involvement, 1 (3%) had cerebral, 2 (7%) had disseminated mucormycosis. on the contrary A. Patel et al,<sup>[16]</sup> observed that out of 465, 223 were survived and 242(52%) were died.

In the present study [Table4,5] it was observed that diabetes ( $X^2= 5.46p = 0.01945$ ), oxygen therapy and steroid treatment ( $X^2=6.517p = 0.01069$ ) were strongly associated with deaths due to mucormycosis. Shitij Arora et al,<sup>[16]</sup> observed that the non-survivors also had a higher median HbA1C

of 9.6 (IQR 8.3–11.8) compared to 8 (IQR 6.9–10.0) among the survivors and Among those treated with corticosteroids, the non-survivors were treated with a higher median daily dose of 53 mg prednisone equivalent compared to the survivors (median dose 50 mg prednisone equivalent, IQR 40–53.3).

## CONCLUSION

Mucormycosis can occur among COVID-19 patients, especially above 40 years with poor glycaemic control, widespread use of corticosteroids and oxygen therapy. The incidence of mucormycosis in the setting of the COVID-19 pandemic is likely to rise and result in significant morbidity and mortality. Owing to the high mortality, high index of suspicion is required to ensure timely diagnosis and appropriate treatment in high-risk populations. Physicians caring for severely ill patients with COVID-19 and concomitant poorly controlled diabetes should have a high index of suspicion of mucormycosis, especially if corticosteroids are used during the course of disease. The use of antifungal therapy together with surgical debridement may help to improve the survival of mucormycosis patients. Caution needs to be exercised with regard to the widespread usage of corticosteroids and broad-spectrum antibiotics, with an emphasis to administer corticosteroids only in severe COVID-19 pneumonia and to reduce super-infections. Mortality associated with mucormycosis in India is considerably high due to delays in seeking medical attention and diagnosing the disease, and challenges in managing the advanced stage of infection. It is necessary to conduct population-based studies in India to determine the exact prevalence of mucormycosis in diverse at-risk populations, which would help draw attention of medical authority to the early diagnosis and managing the disease.

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