A Cross-Sectional Study on Mucormycosis Cases in a Tertiary Care Center of Meerut

Dear Sir,

Mucormycosis represents a group of fungal infections caused by members of the order Mucorales involving many different organs such as skin, paranasal sinuses, orbits, brain, lungs, and gastrointestinal tract. Among these, the most common site of infection is rhino cerebral, followed by cutaneous.^[1]

Following the outbreak of coronavirus disease 2019 (COVID-19), a wide spurge was seen in opportunistic bacterial and fungal infections. *Aspergillus* and Candida are the main fungal pathogens occurring as co-infection in people with COVID-19. Hence, the active case of COVID-19 or recently recovered from it contribute to the major risk factor for mucormycosis.

In India, diabetes mellitus has also been the most common risk factor linked with mucormycosis. Long-term use of corticosteroids has often been associated with several opportunistic fungal infection.

As established the unholy trinity of mucormycosis is COVID infection, diabetes, and steroids use. Risk factors for the development of mucormycosis include diabetic ketoacidosis, neutropenia, protein-calorie malnutrition, and iron overload, with or without the concomitant use of deferoxamine.^[2]

Noticing a huge rise in cases of mucormycosis in India with a high mortality rate prompted us to conduct this study with the objective to assess the association between various established risk factors of mucormycosis with the stage of disease. It was done to find out the association between various established risk factors of mucormycosis with the stage of disease.

This cross-sectional study was carried out among 83 cases of mucormycosis admitted in the ward and intensive care unit (ICU) on the day of data collection. Telephonic interview of cases was taken on predesigned pretested validated questionnaire. Informed consent was taken from each case. Interview of patients admitted in ICU was taken from their family members.

After receiving ethical approval from institutional ethic committee, the study was conducted; Data collected were entered and analyzed by Epi Info 7.2.3.1 software (Epi info 7.2.3.1, by Centre of Disease Control and Prevention, Atlanta, Georgia). Univariate analysis for association between occurrence of mucormycosis and various risk factors was assessed using Chi-square test. P < 0.05 was taken as significant.

Eighty-three mucormycosis patients including both COVID positive and COVID negative were included in the study. Out

of all the patients, 53 (63.9%) were male and 30 (36.1%) were female. Among the study participants, maximum 39.8% belong to 45–59 years of age group followed by 36.1% in 31–44 years of age group, 21.7% were in more than and equal to 60 years of age, and only 2.4% belong to 15–30 years of age group.

COVID-positive patients were 50 (60.2%), while 33 (39.8%) were RTPCR negative. In our study, out of those who were COVID positive, 24 (48.0%) were in Stage 2, while 21 (42.0%) in Stage 3 and 5 (10.0%) in stage 4, respectively. Past or present status of COVID positivity was not related to severity of disease [Table 1].

Majority patients were suffering from diabetes as 67 (80.7%) patients were diabetic in comparison to 16 (19.3%) patients who were nondiabetic. Among diabetic patients, 32 (47.8%) were in Stage 2, while 32 (47.8%) were in Stage 3 and 3 (4.4%) in Stage 4, respectively, while in nondiabetics, 10 (62.4%) were in Stage 2 and 3 (18.8%) in Stage 3 and 3 (18.8%) in Stage 4, respectively. The presence of diabetes in patient was associated with the severity of mucormycosis, and it was statistically significant [Table 1].

Among all patients, 63 (75.9%) reported zinc intake either during treatment or as preventive measure, while 20 (24.1%) did not took zinc at all. Among zinc users, 31 (49.2%) in Stage 2, while 28 (44.4%) in Stage 3 and 4 (6.4%) in stage 4, respectively. The association between zinc intake and severity at the time of presentation was found to be statistically insignificant in our study [Table 1].

Amongst all patients, 50 (60.2%) confirmed intake of steroids previously due to COVID and other medical conditions, while 33 (39.8%) denied intake of steroids. Among all those history of steroid use, 32 (64.0%) were in Stage 2, while 15 (30.0%) and 3 (6.0%) in Stage 3 and 4, respectively. Association of intake of steroids with the severity of disease was found to be statistically significant in our study [Table 1].

In COVID-positive patients, 24 (48.0%) reported oxygen use, while in 26 (52.0%), it was absent. Among 24 patients with oxygen use history, 16 (66.7%) were in Stage 2, while 6 (25.0%) in Stage 3 and 2 (8.3%) in Stage 4, respectively. Oxygen use in COVID-positive patients was found statistically insignificant with the severity of disease [Table 1].

Due to limitation in the research done under the concerned topic, we could not find any study showing relationship between severity of mucormycosis and its associated risk factors. Still, overtime several studies have been done in order to find association of various risk factors with mucormycosis.

Table 1: Association of severity of mucormycosis with various risk factors

	Staging	Stage 2, n (%)	Stage 3, n (%)	Stage 4, n (%)	Total, <i>n</i> (%)	P value
COVID status	Covid positive	24 (48.0)	21 (42.0)	5 (10.0)	50 (100.0)	Fischer exact=0.53 (Freeman-Halton extension)
	Covid negative	18 (54.5)	14 (42.4)	1 (3.1)	33 (100.0)	
Diabetes status	Present	32 (47.8)	32 (47.8)	3 (4.4)	67 (100.0)	Fischer exact=0.03 (Freeman-Halton extension)
	Absent	10 (62.4)	3 (18.8)	3 (18.8)	16 (100.0)	df=2
Zinc use	Present	31 (49.2)	28 (44.4)	4 (6.4)	63 (100.0)	χ^2 : 0.70
	Absent	11 (55.0)	7 (35.0)	2 (10.0)	20 (100.0)	df=2
						P=0.70
Steroid use	Present	32 (64.0)	15 (30.0)	3 (6.0)	50 (100.0)	Fischer exact=0.009
	Absent	10 (30.3)	20 (60.6)	3 (9.1)	33 (100.0)	df=2 (Freeman-Halton extension)
	Total	42	35	6	83	
Oxygen use	Present	16 (66.7)	6 (25.0)	2 (8.3)	24 (100.0)	Fischer exact=0.80
	Absent	18 (69.2)	7 (26.9)	1 (3.9)	26 (100.0)	df=2 (Freeman-halton extension)
	Total	34	13	03	50	

COVID: Coronavirus disease

In the present study, among the total mucormycosis patients studied, nearly 80.70% were diabetic showing diabetes to be a major risk factor associated with the disease; results were similar to the systematic review done^[3] showing diabetes mellitus to be the most commonly reported underlying condition especially in Asian countries such as India.^[3]

The results were also similar to the study by Ravani *et al.*^[4] Nearly 96.7% of the mucormycosis cases were found to be diabetic. ^[4] On assessing the COVID status of study participants, it was seen that nearly 60.2% were COVID positive and the results were almost similar to the study ^[4] where 61.2% of cases were COVID positive. Although due to limited research done under this field, a study done by Mehta and Pandey ^[5] suggests that there are specific pathophysiologic features of COVID-19 that may permit secondary fungal infections, thereby enhancing the risk of invasive fungal infections. Hence, COVID-19 can be one of the predisposing factors leading to mucormycosis.

Majority 75.9% of study participants in the present study reported intake of Zinc either as a part of their treatment or as a preventive measure. Although the association was not found to be statistically significant with the severity of the disease, but still Zinc intake could be one of the predisposing factors and more research needs to be done under it.

Nearly 60.2% of the study participants confirmed the use of steroids either as COVID treatment or as treatment for other disease and the association of the use of corticosteroids with the severity of mucormycosis was found to be statistically significant, and this finding was almost similar to the study done by Ravani *et al.* where nearly 61.2% of mucormycosis cases were on concurrent steroid use.^[4] Thereby showing that the use of corticosteroids can be one of the predisposing factors

leading to mucormycosis. Other risk factor such as oxygen use was not found to be statistically significant in the present study.

There is a high index of possibility of having mucormycosis following COVID exposure. Diabetes mellitus and irrational use of steroid are the most important risk factor showing direct association with the severity of mucormycosis. A study was done on a limited number of patients; hence, the results could not be generalized, and there is a need for more research in order to have a better perspective of the disease. Further studies are needed to evaluate steroid use in COVID-19 patients with uncontrollable diabetes mellitus.

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Conflicts of interest

There are no conflicts of interest.

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