

**Original research article****Imaging for COVID-19 infection and unfolding of mucormycosis-unravelling the connection****<sup>1</sup>Dr. Akash Aradhya S, <sup>2</sup>Dr. Ashwini P**<sup>1</sup>Assistant Professor, Department of ENT, BMCH, Chitradurga, Karnataka, India<sup>2</sup>Assistant Professor, Department of Dermatology, BMCH, Chitradurga, Karnataka, India**Corresponding Author:**

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**Abstract**

As the SARS-CoV virus impairs cell-mediated immunity by decreasing the CD4+ and CD8+ cell counts, an increased susceptibility to fungal infections is noted in these patients. In view of high risk of development of complications and higher mortality rates, it is imperative to supplement clinical diagnosis with investigative modalities. Patients diagnosed with mucormycosis based on clinical and radiological findings, at Basaveshvara Medical College Hospital Chitradurga were the study subjects. A total of 99 patients (86.08%) required hospitalization and mean length of hospital stay was 10.3 days. A total of 31 patients (26.9%) required ICU stay with mean duration of ICU care being 7.5 days. The Mean CT severity score was 12.2. A total of 115 patients (100%) were administered systemic corticosteroids. 67.8% (n=78) of cases received supplemental oxygen therapy and 11.3% (n=13) of patients required invasive ventilation. Around 71.3% (n=82) of the patients had prior history of diabetes mellitus as compared to 13.9% (n=16) of cases who were newly diagnosed cases of diabetes. Rhino-orbital mucormycosis was the most common manifestation observed. Mortality was noted in 21.7% (n=25) of the patients while 2.6% (n=3) patients were lost to follow up.

**Keywords:** COVID-19 infection, mucormycosis, corticosteroids**Introduction**

Mucormycosis is a fulminant fungal infection caused by the fungi belonging to the order Mucorales of the class Zygomycetes. It is an aggressive opportunistic infection occurring in the immunocompromised patients suffering from diabetes mellitus, AIDS, post chemo/radiotherapy or post-transplant patients etc. This ubiquitous pathogen found naturally in the environment, the body surface, and orifices produces spores that enter the host via inhalational route. On inoculation of the nose, paranasal sinuses and the nasopharynx, gradual spread to the orbit, intracranial cavity, oral cavity etc. can occur in patients with decreased cellular and humoral defenses. Common manifestations of mucormycosis include rhino-orbital, sino-nasal, rhino-orbital-cerebral (ROCM) and rhino-cerebral, with pulmonary, cutaneous and gastrointestinal forms being rarer. In subsequent stages of the disease, the vascular lamina gets invaded and aggravation of inflammation with subsequent infarction and necrosis of affected tissues occurs. Hence, early diagnosis and timely aggressive treatment remains the key to tackle this deadly disease. There has been a resurgence of cases of sino-nasal and other manifestations of mucormycosis during the current COVID-19 pandemic <sup>[1, 5]</sup>.

As the SARS-CoV virus impairs cell-mediated immunity by decreasing the CD4+ and CD8+ cell counts, an increased susceptibility to fungal infections is noted in these patients. In view of high risk of development of complications and higher mortality rates, it is imperative to supplement clinical diagnosis with investigative modalities <sup>[6]</sup>.

In the presence of clinical suspicion of COVID-19 infection, WHO advocates the usage of chest imaging as part of diagnostic workup of COVID-19 disease whenever there is delay in availability of RT-PCR or CBNAAT test results, lack of facilities for RT-PCR testing or initial negative RT-PCR test in symptomatic patients <sup>[4]</sup>. A reporting scheme developed by the Dutch Radiological Society called COVID-19 Reporting and Data System (CO-RADS), has categories 1 to 5, designed to report the severity of pulmonary involvement in the plain chest computed tomography scans of COVID-19 patients. It is also a useful tool in predicting COVID-19 infection in patients with moderate to severe symptoms. CORADS is a structured and fast reporting system which reduces ambiguity in the communication with referring physicians <sup>[2]</sup>. Early COVID-19 infection has certain typical imaging manifestations such as patchy, rounded, segmental or sub-segmental ground-glass opacities with or without consolidation. Yang *et al.* conducted a study at Chongqing Three Gorges Central Hospital, Chongqing, China, in 2020 and devised a semi-quantitative method for assessing severity of COVID-19 infection in the initial chest CT images. A CT-Severity Score (CT-SS) score less than 19.5 helped rule

out severe disease with a high negative predictive value of 96.3%. Thus, CT-SS can be used to hasten triage of patients in need of hospital admission [3].

**Methodology**

**Source of data:** Patients diagnosed with mucormycosis based on clinical and radiological findings, at Basaveshvara Medical College Hospital Chitradurga.

**Study setting:** Basaveshvara Medical College and Hospital, Chitradurga.

**Study design:** Ambispective observational cohort study.

**Study period:** May 14, 2021-November 30, 2022.

**Study area:** BMCH, Chitradurga.

**Sample size:** 43.

**Inclusion criteria**

Patients diagnosed with mucormycosis during the study period, based on clinical and radiological findings.

All patients with past history of or ongoing COVID-19 infection.

Both immunocompromised and immunocompetent patients with mucormycosis will be included.

**Exclusion criteria**

Patients not diagnosed with COVID-19 infection either through RTPCR or HRCT thorax.

**Results**

**Table 1:** Baseline characteristics of Mucor mycosis and its association with CTSS

Parameters		CTSS			Chi-square value	p-value
		<8	8 to 14	15 to 25		
Age	20-40 years	7 (35%)	0	6 (27.3%)	1.832	0.947
	40-60 years	11 (55%)	1 (100%)	13 (59.1%)		
	>60 years	2 (10%)	0	3 (13.6%)		
Gender	Male	16 (80%)	1 (100%)	19 (86.4%)	0.911	0.741
	Female	4 (20%)	0	3 (13.6%)		
Co-morbidities	Nil	13 (65%)	0	8 (36.4%)	4.269	0.093
	Diabetes Mellitus	10 (50%)	1 (100%)	18 (81.8%)	5.15	0.064
	DM and Hypertension	4 (20%)	1 (100%)	5 (22.7%)	2.865	0.349
	AIDS	1 (100%)	0	0	3.1	0.48

**Table 2:** COVID-19 parameters and its association with CTSS

Parameters		CTSS			Chi-square value	p-value
		<8	8 to 14	15 to 25		
Oxygen requirement	Mechanical ventilation	0	0	11 (50%)	40.543	<0.001
	BIPAP	1 (5%)	0	7 (31.8%)		
	NRBM	3 (15%)	0	3 (13.6%)		
	Simple mask	11 (55%)	0	0		
	Nasal prongs	1 (5%)	1 (100%)	1 (4.5%)		
	Home O <sub>2</sub> delivery	4 (20%)	0	0		
Steroid Usage	Nil	12 (60%)	0	9 (40.9%)	16.742	<0.001
	< 5days	7 (35%)	1 (100%)	1 (4.5%)		
	> 5days	1 (5%)	0	12 (54.5%)		

**Table 3:** Mucormycosis parameters and its association with CTSS

Parameters		CTSS			Chi-square value	p-value
		<8	8 to 14	15 to 25		
Clinical presentation	Sinonasal	18 (90%)	0	11(50%)	27.96	<0.001
	Rhino-orbital	1 (5%)	0	0		
	Rhino-cerebral	0	1 (100%)	1 (4.5%)		
	Rhino-orbitocerebral	0	0	9 (40.9%)		
	Mandibular	1 (5%)	0	0		
	Pulmonary	0	0	1 (4.5%)		
Surgical Intervention	Debridement	1 (5%)	0	0	24.007	<0.001
	Sinonasal debridement	19 (95%)	1 (100%)	8 (36.4%)		
	SND with Orbital exenteration	0	0	2 (9.1%)		
	SND with Craniotomy and evacuation	0	0	7 (31.8%)		
	Not operated	0	0	5 (22.7%)		
ICU stay	Nil	19 (95%)	0	7 (31.8%)	23.76	<0.001

	Intubated	1 (5%)	0	13 (59.1%)		
	Not-intubated	0	1 (100%)	2 (9.1%)		
Outcomes	Recovery	19 (95%)	0	7 (31.8%)	22.104	<0.001
	Recovery with ICU stay	1 (5%)	1 (100%)	6 (27.3%)		
	Death	0	0	9 (40.9%)		

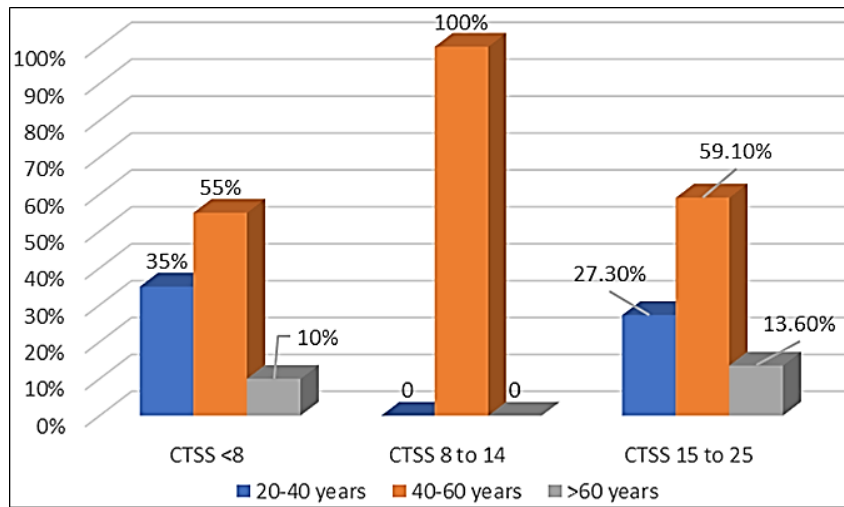


Fig 1: Age distribution of mucormycosis according to CTSS

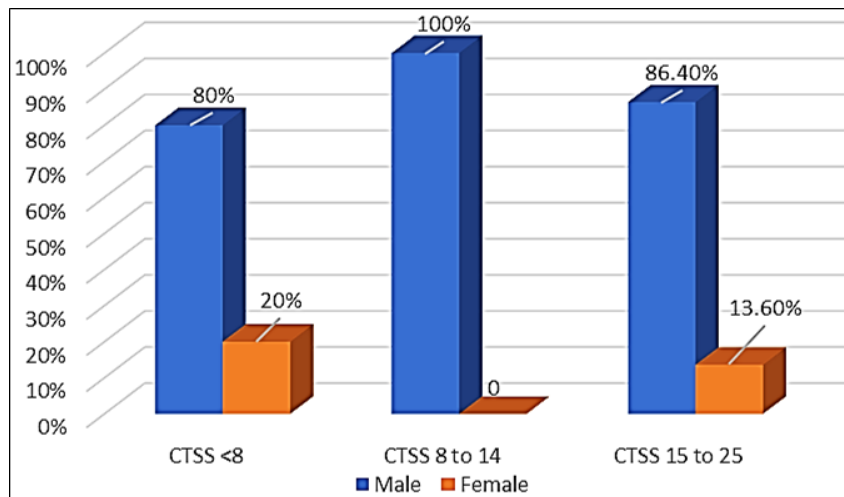


Fig 2: Gender distribution of mucormycosis according to CTSS

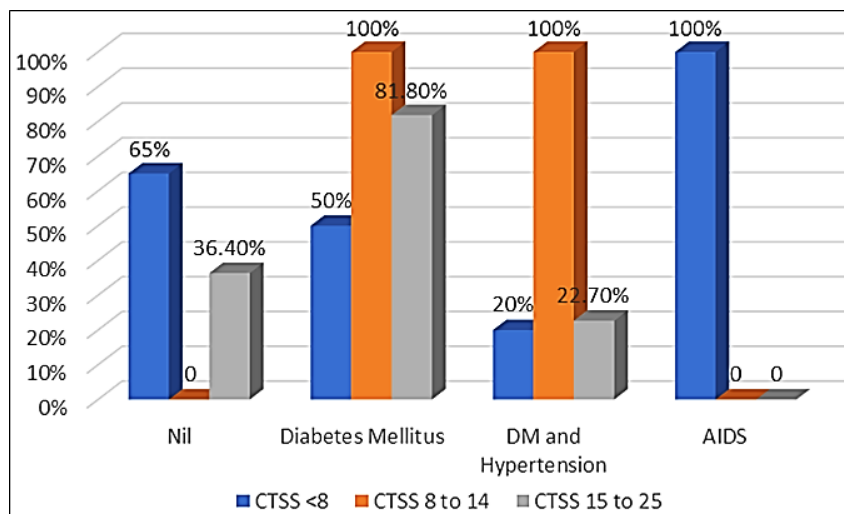


Fig 3: Comorbidities of mucormycosis according to CTSS

**Discussion**

Mucormycosis is a fungal infection caused by fungi belonging to Mucorales. It is highly aggressive with a tendency for contiguous spread. The organisms commonly implicated include *Mucor*, *Rhizopus*,

*Rhizomucor*, *Abidia* and *Apophysomyces*. These fungi usually exist as a commensal in the nasal mucosa. Fungal spores enter the host via inhalation and subsequently enter the paranasal sinuses. Patients usually present with acute sinusitis, fever, nasal congestion, purulent nasal discharge and headache [6].

There are several factors which increase the risk of invasive fungal infections and mucormycosis in patients with COVID-19 [5]. COVID-19 pneumonia predisposes patients to secondary infections that contribute significantly to morbidity and mortality. Though secondary fungal infections are less common than the bacterial infections, these are usually more invasive with worse outcomes. COVID-19 causing mucormycosis in the backdrop of unchecked hyperglycemia and steroid usage has been reported extensively.

A majority of the reported mucormycosis cases before and during the COVID-19 epidemic were from India.

There was also a significant association between CT severity scoring of COVID-19 pneumonia and mortality due to mucormycosis.

This is because patients with more severe pneumonia tend to receive higher doses of corticosteroids as well require supplemental oxygen and invasive ventilation, all of which are risk factors for mucormycosis [5].

A descriptive multisite study conducted by Gupta *et al.* included 115 patients with COVID- associated mucormycosis.

The mean age of patients was 54.2 years with majority of patients being males.

(n=81, 70.4%) as compared to females (n = 34, 29.6%).

A total of 99 patients (86.08%) required hospitalization and mean length of hospital stay was 10.3 days.

A total of 31 patients (26.9%) required ICU stay with mean duration of ICU care being 7.5 days. The Mean CT severity score was 12.2. A total of 115 patients (100%) were administered systemic corticosteroids. 67.8% (n=78) of cases received supplemental oxygen therapy and 11.3% (n=13) of patients required invasive ventilation.

Around 71.3% (n=82) of the patients had prior history of diabetes mellitus as compared to 13.9% (n=16) of cases who were newly diagnosed cases of diabetes.

Rhino-orbital mucormycosis was the most common manifestation observed.

Mortality was noted in 21.7% (n=25) of the patients while 2.6% (n=3) patients were lost to follow up.

Only the CT scan-based score for severity of pulmonary involvement was found to be associated with mortality, as per the logistic regression analysis (OR 0.82, 95% CI 0.68e1.0, P value 0.0464) [5].

A descriptive, multicentre, observational study on CT thorax severity score was carried out by Selarka *et al.* Majority of patients, that is 91.5% cases (n=43) had moderate-to-severe COVID-19 pneumonia with CT score of 8 or more. Mechanical ventilation was needed in 42.6% (n=20) of the cases (n = 20) as compared to need for supplemental oxygen therapy, which was necessary in 80.9% patients (n=38). All patients received systemic corticosteroids as part of their treatment. With 61.7% cases (n=29) receiving intravenous and 95.7% cases (n=45) receiving oral corticosteroids. A total of 45 patients (95.7%) had evidence of pan-sinusitis.

Extension of the infection beyond the paranasal sinuses was around 78.7% (n= 37) of cases, had evidence of infection spreading beyond the paranasal sinus and the mosr frequently encountered finding was orbital invasion (n=19, 40.4%). A total of 9 patients (19.1%) developed of the central nervous system complications.

About 23.4% of the patients (n=11) died and 90.9% (n=10) of these patients had uncontrolled diabetes mellitus. A total of 9 out of 11 cases (81.8%) required invasive mechanical ventilation and 4 out of 11 patients (36.4%) developed central nervous system complications. All the patients (n=11, 100%) who succumbed to the disease had evidence of moderate-to-severe COVID-19 pneumonia (100%) [6].

A study conducted by Saeed *et al.* in Abu Dhabi showed significant correlation ( $p<0.05$ ) between CT severity score and the male gender, raised inflammatory markers, maximum O2 requirement, length of hospital stay (LOS), need for intubation and clinical outcome. Oxygen requirements increase with the increasing CT severity. Death rate was significantly increased among patients with severe CT findings, as per their study [4].

CO-RADS, for COVID-19 Reporting and Data System, is a systematic assessment scheme for CT thorax in patients suspected of COVID-19, representing the level of suspicion for pulmonary involvement.

It offers a standardized assessment protocol with simplified reporting system. A five-point scale of suspicion for lung involvement of COVID-19 on chest CT is used. The scale ranges from 1 (very low suspicion for pulmonary involvement) to 5 (very high suspicion).

CO-RADS 0 implies that none of the five categories can be assigned in view of incomplete or of insufficient quality of scans, caused due to artifacts as a result of coughing or breathing.

CO-RADS 1 signifies a very low level of suspicion for pulmonary involvement by COVID-19 wherein, we find normal CT or CT findings of non-infectious etiology.

CO-RADS 3 denotes equivocal findings for pulmonary involvement of COVID-19 based on CT features, which suggests that these findings may also be found in other infectious or non-infectious etiologies.

Perihilar ground-glass, homogenous extensive ground glass opacities with or without sparing of some

pulmonary lobules are some of the findings.

CO-RADS 4 implies a high level of suspicion for pulmonary involvement by COVID-19 based on CT findings that are characteristic of COVID-19 but displaying some overlap with other pneumonias. CT findings are similar to CO-RADS 5 with the exception that the lesions are not present in contact with the visceral pleura or are present strictly unilaterally, are in a peribronchovascular area, or are coexisting with other diffuse pre-existing pulmonary abnormalities.

CO-RADS 5 signifies a very high level of suspicion for pulmonary involvement by COVID-19 based on typical CT findings such as ground-glass opacities, with or without consolidations, located close to visceral pleural surfaces, and presence of bilateral lesions <sup>[2]</sup>.

Specialists treating severely ill patients with COVID-19 and concomitant uncontrolled diabetes should have a high index of suspicion of mucormycosis, especially in the setting of corticosteroids usage during the course of disease. Hence, care must be taken to use corticosteroids only in severe COVID-19 pneumonia.

Goal must be to achieve glycaemic control and timely commencement of antifungal therapy together with surgical debridement to improve chances of survival of the patients with mucormycosis <sup>[6]</sup>.

Hence, we propose the prompt and timely usage of CT scan thorax as an investigative modality in clinical suspicion of moderate to severe COVID-19 disease, so as to initiate timely therapy.

## Conclusion

Prompt control of COVID-19 disease along with treatment of other concomitant immunosuppressive diseases, will help curb development of mucormycosis in these patients. The CT-severity score can be used as a tool to predict development of mucormycosis in this vulnerable population.

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