

A Comprehensive Study of Covid Associated Mucormycosis at Our Institution

K M Elango¹, K Praveen Kumar², S Kumaresan³, T Shabarish⁴, K Jaivignesh⁴

¹Associate Professor, Department of ENT, Government Vellore Medical College, Vellore, Tamil Nadu, India, ²Assistant Professor, Department of ENT, Government Vellore Medical College, Vellore, Tamil Nadu, India, ³Professor, Department of ENT, Government Vellore Medical College, Vellore, Tamil Nadu, India, ⁴2nd Year PG Student, Department of ENT, Government Vellore Medical College, Vellore, Tamil Nadu, India

Abstract

Introduction: The incidence of opportunistic fungal infections, especially Mucormycosis, was very high during the second wave of the COVID-19 pandemic. Overall, the morbidity and mortality due to COVID-associated mucormycosis (CAM) were very high, especially in India and other high-bearing countries. Various coexisting factors had led to a high incidence of CAM.

Aim: The aim of the study is to analyze various epidemiological factors, risk factors, diagnosis, surgical management, morbidity, and mortality of CAM that occurred during the second wave of COVID-19 at our institution.

Methods of Study: All patients confirmed to have CAM by various laboratory, clinical, radiological, and histopathological methods were studied and analyzed at our institution using the data available during the study period.

Results: A total of 54 patients, who had CAM were studied. 24 patients were female, and 30 patients were male. The mean age for females was 47.83, and the mean age for males was 54.33. Diabetes and previous steroid usage were the most common risk factors associated with 16 patients had previous steroid therapy; 3 patients were HIV +ve; and the mortality rate was 5.6% among CAM patients.

Conclusion: CAM had a multifactorial etiology. Based on the site of involvement, rhinoorbital mucormycosis was the most common. Disseminated and pulmonary Mucormycosis were the least common. Most of the patients were confirmed by clinical, radiological, and histopathological methods, and most of the patients had medical treatment with injections of amphotericin or posaconazole, followed by tablets of posaconazole. Most of the patients underwent surgical debridement for clearance.

Key words: COVID-19 associated mucormycosis, COVID-19, Diabetics, Mucormycosis epidemiology mucormycosis

INTRODUCTION

For some years, fungal rhinosinusitis has become increasingly recognized, but classification and treatment are still under debate.

1. Mucormycosis is a term to describe an acute, typically opportunistic mycotic infection caused by organisms that belong to the family *Mucorales*, class *Zygomycetes* (Phycomycetes). The broad term phycomycosis is a

group of infections caused by *Rhizopus*, *Absidia*, and *Mucor*.

2. Mucormycosis belongs to the classification of acute invasive or acute fulminant Sinusitis with rapidly progressive tissue invasive and vascular invasive features, especially in immunocompromised individuals.
3. COVID-19 Pandemic produced decreased CD4 and CD8 counts and decreased granulocytic and phagocytic activities for opportunistic fungal infections like Mucormycosis, which is usually inhaled as spores from soil and produces fulminant infections.

Based on the site of involvement Mucormycosis may be: (1) Rhino mucormycosis; (2) Rhino orbital; (3) Rhino Orbito cerebral; (4) Rhino cerebral; (5) Cutaneous mucormycosis; (6) Pulmonary mucormycosis; or (7) Disseminated mucormycosis.

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Corresponding Author: Dr. K M Elango, Department of ENT, Government Vellore Medical College, Vellore, Tamil Nadu, India.

Aim of Study

The aim of the study was as follows:

1. To study the clinical and epidemiological profile of COVID-associated mucormycosis (CAM) presented to our institution during the study period
2. To study the risk factors associated with CAM during the study period
3. To study various findings (clinical, radiological, and laboratory) associated with CAM
4. To study the treatment details, morbidity, and mortality.

Study Type

This is a retrospective, observational, hospital-based study.

Study Period

June 01st, 2021–November 31st, 2021.

MATERIALS AND METHODS

Based on the data available in the institution for the period from June 01st, 2021 to November 31st, 2021, all COVID-associated mucor mycosis patients were studied with respect to age, gender, sight, etiology, and treatment-related morbidity and mortality. The following evaluation was done on patients with CAM.

1. Epidemiological patients
2. Complete case history
3. Analysis of risk factors and previous treatment history
4. Exact site and grade of disease
5. Treatment history
6. Morbidity and mortality.

Inclusion Criteria

1. All CAM patients of all ages and genders were included.
2. All CAM patients positive for COVID-19 within a 3-month period were included.
3. All CAM patients tested positive for mucormycosis by clinical, radiological, laboratory, and histopathological methods were included.
4. All CAM patients preexisting risk factors and other comorbidities were included.

Exclusion Criteria

1. Patients negative for mucormycosis were excluded
2. Patients with COVID positivity tested after 3 months were excluded
3. Patients who tested positive for other fungal infections were excluded.

Statistical Methods

The mean (SD) and percentage of frequency were used. Continuous and categorical variables were analyzed. The chi-square test was used to assess the difference between

categorical variables. $P < 0.05$ is considered as statistical significance.

RESULTS

Out of 54 patients, 24 were females and 30 were males. The mean age of presentation for males was 47.83. The mean age of presentation for females was 54.33.

Table 1: Gender Distribution of CAM

Sex	No of cases	percentage
Male	30	55.56
Female	24	44.44
Total	54	100

SEX DISTRIBUTION

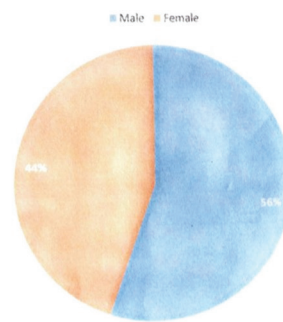
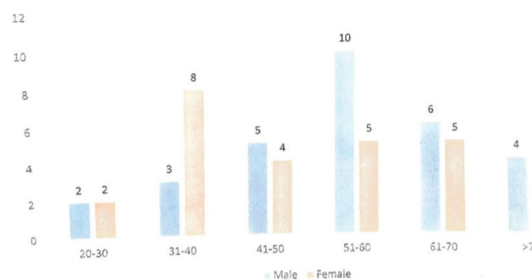


Table 2: Age wise distribution of CAM

Age in Years	Male	Female	Total
20-30	2	2	4
31-40	3	8	11
41-50	5	4	9
51-60	10	5	15
61-70	6	5	11
>70	4	0	4
Total	30	24	54

Age wise distribution of CAM



The Most Common Site of CAM

During this study, several sites of presentation occurred: rhino, rhino orbital, rhino orbital cerebral, rhino cerebral, and pulmonary mucormycosis. Cutaneous Mucormycosis, visceral of disseminated Mucormycosis. In our study, Rhino Orbital Mucormycosis was the most common.

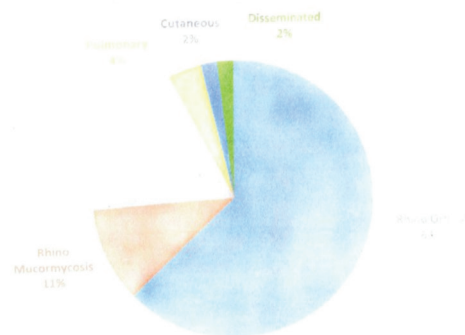
Clinical Presentation of CAM

Patients with CAM presented with various signs and symptoms; many of them had nasal congestion, rhinorrhoea, fever of varying degrees, facial and orbito-facial swelling, periorbital edema, chemosis, ophthalmoplegia, proptosis, decreasing vision to complete visual loss, erythema, cranial nerve involvement, altered consciousness, etc. The most

Table 3: Site of involvement of CAM

Site	Number	%
Rhino Orbital	34	62.96
Rhino Mucormycosis	6	11.11
Rhino Orbitocerebral	10	18.51
Pulmonary	2	3.72
Cutaneous	1	1.85
Disseminated	1	1.85

SITE OF INVOLVEMENT OF CAM



common symptoms were facial swelling, pain, and a fever of varying degrees.

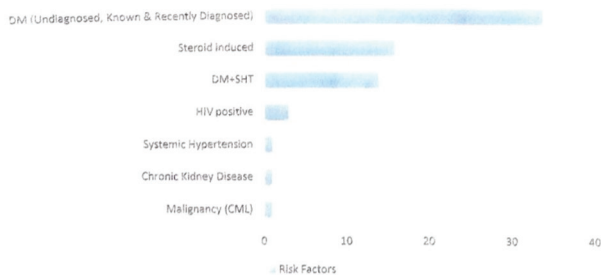
On examination, the most common finding was edematous nasal mucosa with discoloration (pale to black necrotic material). Commonly in the middle meatus and adjoining middle inferior turbinate, risk factors and etiological factors.

Most of the patients, up to 80%, had pre-existing type 2 diabetes mellitus or newly diagnosed (undiagnosed) type 2 DM. Up to 29.6% of the patients had received steroid treatment for COVID-19 previously. Up to 20% of patients had other comorbidities such as uncontrolled hypertension, HIV positivity on dialysis for renal failure, or other malignancies.

Table 4: CAM associated Risk Factors

Risk Factors	No	%
DM (Undiagnosed, Known & Recently Diagnosed)	34	62.96
Steroid induced	16	29.62
DM+SHT	14	25.92
HIV positive	3	5.56
Systemic Hypertension	1	1.85
Chronic Kidney Disease	1	1.85
Malignancy (CML)	1	1.85

CAM associated Risk Factors



Methods for Diagnosis

Various methods were followed for the identification of the case, such as clinical evaluation, radiological presentation, laboratory investigation, and histopathological diagnosis.

All patients suspected of CAM had a nasal smear for identification of mucor frozen sections and a biopsy of suspected material for histopathological and radiological evaluation.

The final diagnosis was made by examination under the microscope for fungal hyphae for mucormucosis in 100% of patients.

Treatment Done for CAM Patients

Various treatment modalities were followed in various centers. In our institution, after confirmation of CAM, the patient was treated with injection amphotericin 0.7–1 mg/kg body weight with a test dose of 1 mg in 5% dextrose on the first day of therapy.

The majority of the patients’ diagnosed positive for CAM underwent complete surgical endoscopic debridement, and five patients underwent partial maxillectomy for recurrent, residual, and extensive mucormycosis. None of the patients had orbital exenteration; one patient had a craniotomy for intracranial mucormycosis.

Table 5: Treatment Given for CAM patients

Early Endoscopic Surgical Debridement	34	62.96
Retro orbital Injection of Amphotericine	12	22.22
Surgical Debridement with partial maxillectomy	5	9.23
Craniotomy with Neurosurgical Management	2	3.70
Orbital Extraction	0	0

Treatment Given for CAM patients

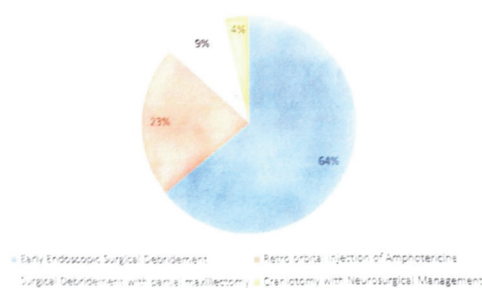
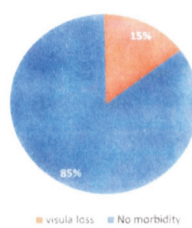


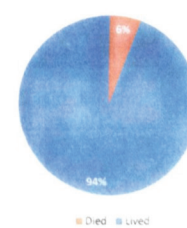
Table 6: Morbidity and Mortality of CAM

	Number	Percentage
Total number of patients who lost their visual morbidity	8	14.8%
Total number of patients who lost their lives	3	5.56%

Morbidity



Mortality



DISCUSSION

Mucormycosis fungi have Mucoïd predilection for vascular invasion of large and small arteries and veins causing thrombosis, is necrosis of tissues, or black intranasal eschar, is the pathognomonic finding in acute fulminant fungal rhinosinusitis when mucor is the predominant fungal organism.^[3] In our study, ademaïlow nasal mucosa with pale or blackish discoloration in the middle meatus and adjoining middle and inferior tubercles was the commonest finding.

Mucormycosis is acute filament fungal rhinosinusitis that occurs especially in immunocompromised status (1. AIDS, hematological disorders, type 1 diabetes, uncontrolled diabetes dh, long-standing steroids, immunosuppressive therapy, and malignancy) (2. Presumably, hyperglycemia, acidosis, and immunosuppression enhance tissue and vascular invasion and fungal growth) (3. Mucor has an active carotene reductasa system that it thorws on with increased glucose acidic pH.^[4] In our study, uncontrolled diabetes (type 2) and newly or undispensed dh with treatment of steroid for COVID-19 were also common etiological factors.

*Mucormycetes are confirmed by the presence of large, irregularly shaped, non-septal hyphae that branch at right angles of 6–50 µm in hyphae size.^[3]

In our study, we also confirmed CAN by microscopic examination and confirmed the presence of Mucor hyphae.

A commoner LT finding was Nodular Mucosal thickening of paranasal sinuses without air fluid level with spotty destruction of bony walls in our study. Another commoner finding was involvement of the orbit and cranium.

*Amphotericin-B remains the drug of choice for systemic treatment of most acute fungal rhinosinusitis.^[1,2]

In our institution, we also gave systemic amphotericin-B with careful monitoring of Renal function. For patients with altered liver and renal function, we gave systemic liposomal amphotericin at a dose of 2.5 mg/l orally and injection posaconazole for 3 weeks, followed by tablet posaconazole for 3–6 months.

Control of primary disorders is very important, even with early diagnosis. Even with early surgical debridement and

complete medical treatment, fatalities of 25–100% have been repeated. In our institution, out of 54 patients, deaths were reported, and mortality% of 5.568 patients had complete loss of vision with morbidity % of 14.8%.^[5-12]

CONCLUSION

At the end of our study, our institute was closed for a period of 6 months during the peak of COVID-associated Muconmycotis through mates was more commonly involved; uncontrolled diabetes and previous steroid treatment were the most commonly involved; unwanted diabetes and previous steroid treatment were the most common etiological and risk factors. Rhino-orbital mucormycosis was the commonest. The most common clinical findings were Nasal congestion, facial and orbital facial swelling, and pain. The most common diagnostic method was the demonstration of fungal hyphae by Microscopy, all on par with other institutions. Early diagnosis, early medical treatment, and surgical debridement were done for all patients. The morbidity rate was slightly lower in our institution when compared with other institutions. The age, gender, diagnostic criteria, clinical findings, etiological risk factors, morbidity, and mortality were well defined in the study.

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