ISSN No:2319-5886

International Journal of Medical Research and Health Sciences, 2022, 11 (7): 1-8

An Observational Study of Mucormycosis in Post-COVID-19 Patients in a Tertiary Care Hospital, Vizianagaram, Andhra Pradesh

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Received: 03-Jun-2022, Manuscript No. ijmrhs-22-65843; **Editor assigned:** 06-Jun-2022, PreQC No. ijmrhs-22-65843 (PQ); **Reviewed:** 20-Jun-2022, QC No. ijmrhs-22-65843; **Revised:** 02-Aug-2022, Manuscript No. ijmrhs-22-65843 (R); **Published:** 09-Aug-2022.

ABSTRACT

Background: *Mucormycosis is a fatal opportunistic infection caused by filamentous fungi, Mucoromycete's of the family Mucoraceae, also called as black fungus. There were mounting number of cases reported mainly during the second wave of the pandemic, even in mild and asymptomatic cases who had recovered from COVID-19 due to the immunocompromised state caused by the disease and its treatment.* ***Aim and objectives:*** *Through this study, we aim to study the clinical features and clinical outcomes of patients diagnosed and treated for Rhino-Orbito Cerebral mucormycosis.* ***Materials and methods:*** *This is a descriptive cross-sectional study conducted among 42 patients with a confirmed diagnosis of rhino-Orbito cerebral mucormycosis with post COVID-19 infections. The medical records were retrieved and the demographic findings along with clinical, histopathological and radiological data were reviewed.* ***Results:*** *The mean age of the study patients was 54.71 ± 10.11 years with majority of males (81%). Regarding the co-morbid conditions, 85.7% of the study participants had a history of diabetes mellitus and 33.3% had hypertension. 81% patients received oral/IV steroids for the management of COVID-19. Regarding the presentation of symptoms, facial complaints and nasal complaints were noted in 81% patients. Ocular complaints were present in 71.4% patients and intracranial invasion features were reported from 28.6% patients. Adequate local debridement along with FESS was done in 76.2% patients. Recurrence was seen in 42.9% patients. Regarding mortality, 19% patients died.* ***Conclusion:*** *New-onset of headache, facial/cheek swelling, black nasal discharge, periorbital swelling, visual diminution and restriction of eye movements should prompt an abrupt search for mucormycosis especially in those having history of diabetes mellitus with recent or current COVID-19 disease. Prompt diagnosis with early surgical intervention in adjunct to aggressive anti-fungal treatment could halt the spread of infection to other adjoining areas and improves the outcome.*

Keywords: Mucor mycosis, Post-COVID-19, Diabetes mellitus, Fungal infection, Vizianagaram

INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) otherwise known as the novel Coronavirus (2019-nCoV) outbreak emerged in Wuhan, Hubei province of China in December 2019 has been dwindling the world since its declaration by the World Health Organization as a pandemic on 11th March 2020 [1]. Mucormycosis, a serious angioinvasive infection caused by common filamentous fungi, that is Mucoromycete's was reported in many parts of India as a COVID-19 associated infection, where a mounting number of cases were reported mainly during the second wave of the pandemic, even in mild and asymptomatic cases who had recovered

from COVID-19. The use of steroids, which were believed as a wonder drug in the treatment of COVID-19, after the first wave is thought to play an important role in the causation of this fungal infection. High risk groups known for the occurrence of Mucormycosis are people who are immunocompromised, people with advanced age, diabetics (especially diabetic ketoacidosis), those who had a solid organ or hematopoietic stem cell transplantation, prolonged neutropenia, those on long-term use of corticosteroids, haematological malignancies (leukaemia, lymphoma and multiple myeloma) aplastic anaemia, myelodysplastic syndromes and iron overload (hemochromatosis). The risk is high in people living with HIV and in those using immunomodulating drugs and the anti-fungal medication voriconazole [2].

The disease transmission is air-borne, by inhalation of spores or by direct inoculation of the spores into disrupted skin or mucosa with the most common sites affected being sinus (39%), lungs (24%), skin (19%), brain (9%), GIT (7%), disseminated disease (6%) and other sites (6%) [3,4]. Rhino-Orbito Cerebral Mucormycosis (ROCM) is an acute, fatal opportunistic subtype with the hallmark of extensive angioinvasion with resultant vessel thrombosis and tissue necrosis invading the oral and maxillofacial areas including facial sinuses, maxilla, zygoma, orbit (Figure 1) and oral cavity [5].

Clinical presentation can be diverse. The most commonly reported signs (Figure 2) in the literature include nasal obstruction with noisy breathing, blood stained nasal discharge, headache, facial cellulitis, orbital swelling, palatal ulceration or necrosis, and black necrotic eschar in the nasal cavities [6].

Management of Rhino-Orbito cerebral mucormycosis requires surgical Sino-nasal drainage and debridement of orbital or cerebral disease, combined with a prolonged course of intravenous antifungal medication which is disfiguring and could result in adverse effects [7]. In the current study, we intend to study the clinical features and clinical outcomes of patients diagnosed and treated for Rhino-Orbito Cerebral mucormycosis in a tertiary care hospital.

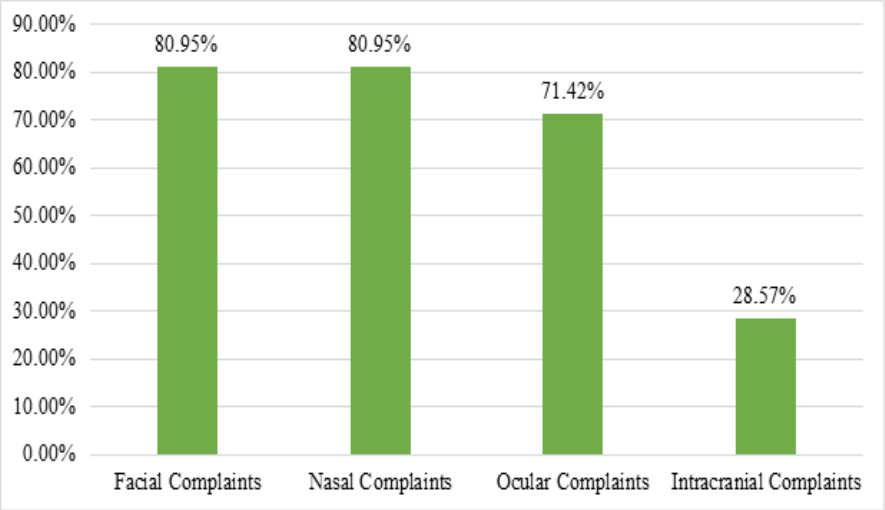

Figure 1 Presenting complaints in post COVID-19 patients with mucormycosis

Figure 2 Rt ethmoidal sinus involvements with bony destruction and non-enhancing mucosa, optic nerve involvement and tenting of eyeball

MATERIALAS AND METHODS

Study design: This is a descriptive cross-sectional study conducted among 42 patients with a confirmed diagnosis of rhino-orbit cerebral mucormycosis with post COVID-19 infection presenting to the department of Oto-rhinolaryngology and under follow up in a tertiary care hospital, Vizianagaram, Andhra Pradesh from May to September, 2021.

Data collection: The medical records were retrieved and the demographic findings along with clinical, histopathological and radiological data were reviewed. All the patients were treated very aggressively with intravenous liposomal amphotericin B and radical surgical debridement of devitalized tissue through endoscopic denker's approach was done with Functional Endoscopic Sinus Surgery (FESS) (Figure 3). After obtaining permission from the head of the department of Oto-rhinolaryngology and the Institutional Ethics Committee, Maharaja Institute of Medical Sciences, Vizianagaram, the study was commenced. Written informed consent in the local language Telugu was taken from all the participants who were included in the study for the publication of this research and accompanying images. For those who were illiterates, the consent was read out and explained to them and consent was obtained by taking their thumb impression in the presence of a witness.

Statistical analysis: Data obtained was entered in Microsoft Excel worksheet 2013 and Analysis was performed using SPSS software (Trial version 21). Descriptive statistical analysis has been carried out in the present study. Categorical variables were represented as proportions/percentages and quantitative variables were represented as mean and standard deviation.

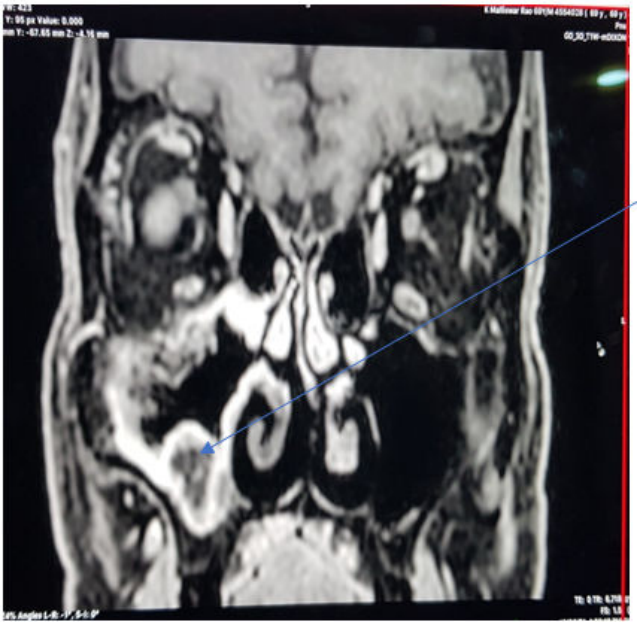

Figure 3 Rt maxillary sinus involvement with enhancing mucosa and few non enhancing areas.

RESULTS

Mucormycosis was diagnosed and treated for all the 42 patients in the tertiary care hospital. The mean age of the study patients was 54.71 ± 10.11 years ranging from 40 to 77 years, wherein majority of them are males (81%). Regarding socioeconomic status, 47.6% were above poverty line and remaining 52.4% were below poverty line. About the existing co-morbid conditions, 85.7% of the study participants had a history of Diabetes Mellitus and 33.3% had history of hypertension. Only 23.8% are vaccinated with at least one dose of COVID vaccine. The CT-severity index scores of the post COVID-19 patients were moderate in 71.4% patients and severe in 28.6% patients. Except 8 patients (19%), remaining all received oral/IV steroids for the management of COVID-19. 81% of the patients required hospital admission for COVID-19 treatment and the average duration of hospital stay was 9.05 ± 6.84 days. Among them, oxygen support was required for about 66.66% patients (Table 1).

Table 1 Results of the post COVID-19 patients with mucormycosis.

S. No	Variables	Results
1	Age (Mean ± SD)	54.71 ± 10.11 years
2	Gender	**Females:** 8 (19%)
		Male: 34 (81%)
3	Socioeconomic status	**Above Poverty line:** 20 (47.6%)
		Below Poverty line: 22 (52.4%)
4	CT Severity index	**Moderate:** 30 (71.4%)
		Severe: 12 (28.6%)
5	History of Hospitalisation for COVID-19.	**Yes**: 34 (81%)
		No: 8 (19%)
6	Period of Hospitalisation (Mean ± SD)	9.05 ± 6.84 days

7	H/O Oxygen support during hospital admission	**Required:** 28 (66.666%)
		Not required: 14 (33.333%)
8	H/O Oral/IV Steroid use during hospital admission.	**Required:** 34 (81%)
		Not required: 8 (19%)
9	Comorbid conditions	**Diabetes mellitus:** 36 (85.7%)
		Hypertension: 14 (33.3%)
10	H/O COVID-19 vaccination.	**Yes:** 10 (23.8%)
		No: 32 (76.2%)

Regarding the presentation of symptoms, facial complaints like headache, facial/cheek swelling and tingling sensation over face were noted in 81% patients. Nasal complaints like nasal block, black crusts in the nose, nasal discharge and loss of smell were present in 81% patients. Ocular complaints like orbital swelling, redness, watering from eyes and diminution of vision was found in 71.4% patients. Intracranial invasion features like Hemiparesis, altered consciousness and focal seizures were reported from 28.6% patients. All the patients had HPE and fungal smear showing broad aseptate hyphae (Figure 4) and radiological evidence of CE MRI revealing mucosal thickening of sinuses (Figure 5) and adjacent bony erosions. All the patients were treated similarly with IV amphotericin B and IV Posaconazole in addition to treatment of COVID-19 disease. Adequate local debridement of the infected and necrotic tissue by modified Denker's procedure with/without septoplasty by Functional Endoscopic Sinus Surgery (FESS) along with the medical treatment was done in 76.2% patients. Recurrence was seen in 42.9% patients. Regarding outcome, 71.4% patients got completely recovered, while 9.5% patients had serious handicap like development of oroantral fistula, septal perforation, vision loss and 19% patients died (Table 2).

Table 2 Management and outcome of the post COVID-19 patients with mucormycosis.

S. No	**Variables**	**Results**
1	Medical Management	IV Amphotericin B and IV Posaconazole: 42 (100%)
2	Surgical Management	Sino-nasal surgery (FESS, debridement): 32 (76.2%)
3	Recurrence	Yes: 18 (42.9%)
		No: 24 (57.1%)
4	Outcome	Good: 30 (71.4%)
		Poor: 4 (9.5%)

		Death: 8 (19%)

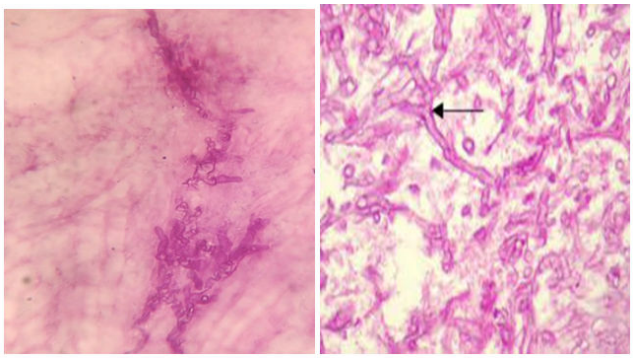

Figure 4 HPE Branched aseptate hyphae seen.

Figure 5 PRE OP–discharge seen in middle meatus.

DISCUSSION

The second wave of COVID-19 pandemic led to an alarming increase in the rate of fungal infections throughout the world. More than 20 different fungal species have been identified in hospitalized COVID-19 patients. Common agents implicated have been *Aspergillus fumigatus, Candida albicans* and Mucormycosis, of which Mucormycosis is an opportunistic fungal infection that characteristically affects immunocompromised patients, and particularly patients with uncontrolled diabetics mellitus [8]. The present study was conducted among 42 patients diagnosed and treated for mucormycosis. The mean age of the study patients was 54.71 ± 10.11 years and majority of them are males (81%). This is quite similar to the study findings of Pal R, et al. [9] and Kamath S, et al. [10]. The commonest comorbid condition observed in our study was diabetes mellitus, which was present in 85.7% of the study participants followed by hypertension in 33.3% cases. Even studies conducted by R Pal, et al. [9] and S Nagalli, et al. reported similar findings. Apart from this, even other conditions like cardiac disease, renal disease, obesity, asthma, haematological malignancies, history of transplant and immunosuppressive therapy were reported among their study participants. [9]. The CT-severity index scores of the post COVID-19 patients were moderate in 71.4% patients and severe in 28.6% patients. While Kamath S et al. reported that three out of fifteen patients of COVID-19 had severe disease with Computed Tomography Severity Scores (CTSS) more than 20/25. For the management of COVID-19, almost 80% of the patients received oral/IV steroids. Compared to this, R Pal, et al. and S Nagalli, et al. reported a little higher use of some form of steroids before the diagnosis of mucormycosis. In the current study, more than 80% of the patients required hospital admission for COVID-19 treatment and the average duration of hospital stay was 9.05 ± 6.84 days and oxygen support was required for about 66.66% patients (Figure 6).

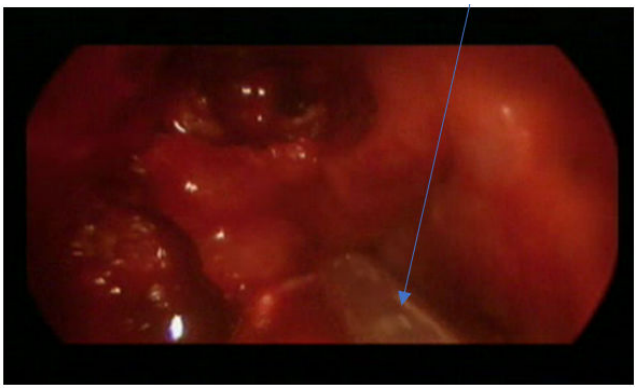

Figure 6 INTRA OP–debridement with microdebrider is seen.

Regarding the clinical characteristics, overall facial complaints like headache, facial/cheek swelling and tingling sensation over face were seen in 81% patients in the present study, while Peri-orbital/facial pain and headache were seen in 46.8% and 19.5% patients respectively in the study by S. Nagalli et al., whereas Kamath S, et al. reported it among 66.7% and 20% patients respectively. Nasal complaints like nasal block, black crusts in the nose, nasal discharge and loss of smell were present in 81% patients while unilateral nasal discharge was seen in 33.3% patients according to the study findings of Kamath S, et al. (Figure 7) [10].

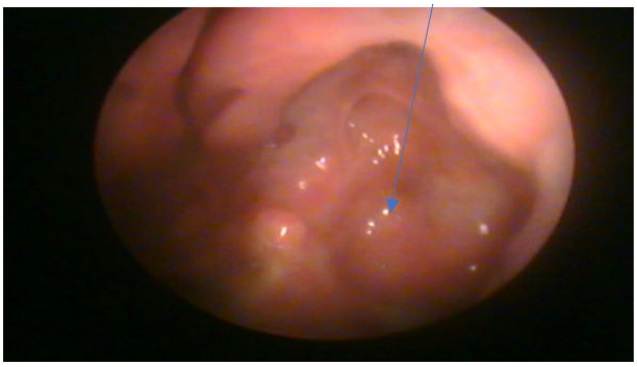

Figure 7 POST OP maxillary sinuses with healthy mucosa.

Ocular complaints like orbital swelling, redness, watering from eyes and diminution of vision was found in 71.4% patients. However, Kamath S, reported that Periorbital swelling was the most common symptom reported in 73.3% of the patients and symptoms like decreased or loss of vision, blurry or double vision were seen in 49.3% of patients according to S Nagalli, et al. Intracranial invasion features like hemiparesis, altered consciousness and focal seizures were reported from 28.6% patients while Altered sensorium is reported in 20% patients and facial deviation in 6.7% patients as per the findings of Kamath, et al. [10] apart from cranial nerves involvement (60%), with the 3rd cranial nerve being affected commonly (53.3%). All the patients were treated similarly with IV amphotericin B or IV Posaconazole in addition to treatment of COVID-19 disease similar to Kamath S, et al. However S Nagalli reported the use of Amphotericin B in 85.9% cases and Posaconazole in only 17.4% patients. Surgical treatment by local debridement of the infected and necrotic tissue along with Functional Endoscopic Sinus Surgery (FESS) was done in 76.2% patients, while it was performed only for 46.7% and 59.8% cases in the study by Kamath, et al. and S Nagalli, et al. respectively. Promisingly 90% of the cases who survived in the study by Pal R had a Sino nasal debridement in adjunct to anti-fungal treatment. Recurrence was seen in about 40% patients and overall mortality was noted in 19%. This is very less compared to the mortality rates of Pal R, et al. (34%), Kamath, et al. (40%) and S Nagalli, et al. (48.7%).

CONCLUSION

This could be due to the fact that surgical intervention was performed in adjunct to aggressive anti-fungal treatment, halting the spread of infection to other adjoining areas, particularly the brain and improving the outcome.

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