

SPECTRUM OF COVID ASSOCIATED MUCORMYCOSIS (CAM) DURING SECOND WAVE IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Mucormycosis is not an uncommon disease in India, but there was an exponential increase in cases during the second wave of the current pandemic caused by Covid 19. **Aim:** To evaluate the spectrum of Covid Associated Mucormycosis during the second wave concerning co-morbidities and severity of disease. The study will also assess the outcome of the Management protocol during the ongoing pandemic. **Materials and Methods:** Patients presenting with clinical features of mucormycosis were included in the study. KOH staining and culture for mucorales were done in all patients; Nasal endoscopy was done whenever possible, and tissue was sent for histopathological examination. The various risk factors, complications of mucormycosis, the treatment protocol for managing mucormycosis, and treatment outcome were assessed. **Result:** Diabetes mellitus was the most important risk factor contributing to mucormycosis. Nasal endoscopy, KOH staining and Histopathological examination picked up 97% of cases of mucormycosis. Rhino orbital mucormycosis was the most typical mode of presentation (58%). **Conclusion:** Covid infection increased the risk of developing mucormycosis in Diabetic patients independent of the usage of steroids: high suspicion, Early diagnosis, Good glycaemic control, Inj. Amphotericin in adequate doses and repeated endoscopic debridement are the mainstays of treatment of CAM.

INTRODUCTION

Mucorales and Entomophthorales are two types of Zygomycetes which cause infection in humans. Mucor is seen in immunocompromised individuals, whereas entomophthorales- (basidiobolus, conidiobolus) is a chronic subcutaneous infection seen in the immunocompetent host. Mucormycosis has a plethora of presentations as Rhino Orbital, Rhino Orbito Cerebral, Cutaneous, Gastrointestinal, Pulmonary, and Renal in an immunocompromised host.^[1] Mucormycosis is not an uncommon disease in India. Still, there was an exponential increase during the second wave of the current pandemic caused by Covid 19, which was declared a notifiable disease by the GoI.^[2] Compared to global data, Mucormycosis is 70 times more prevalent in India, and the most important contributing factor to this is the already high prevalence of diabetes in the population.^[3] Unlike regular times the pandemic posed several unique problems in managing Mucormycosis. With the Medical college hospital

being converted into an exclusive Covid hospital, doctors and residents from all departments, including non-clinical specialities, were posted in Covid wards. They all had to be educated to look for clinical features of mucormycosis. The patients were then shifted to an exclusive ward for mucormycosis managed by a multidisciplinary team. Some of the patients were Oxygen-dependent which delayed the diagnosis and treatment of mucormycosis. The exponential rise in the number of cases and the rationing of essential drugs like amphotericin and Posaconazole resulted in increased disease severity, pushing the limits of the health infrastructure to the extreme.

Aim

The study aims to evaluate the spectrum of mucormycosis during the second wave of Covid concerning co-morbidities and the severity of the disease. In addition, the study will also assess the outcome of the Management protocol during the ongoing pandemic.

MATERIALS AND METHODS

The study was conducted at Government Tirunelveli medical college, Tirunelveli, during the second wave of the Covid 19 pandemic from May to July 2020. All the patients with any of the clinical features of mucormycosis were admitted. Patients were enquired regarding their previous Covid positive status and the treatment they received before admission. All patients were submitted to RTPCR for Covid at admission. Nasal endoscopy was routinely done unless the patient was very sick. KOH staining was done in all patients. Nasal / sinus mucosa was sent to histopathological examination after nasal endoscopy or surgical debridement. All patients with suspicion of Mucormycosis after endoscopy and KOH staining were started on Inj. Amphotericin as early as possible without waiting for culture or histopathology reports. A high index of suspicion was maintained in patients with orbital symptoms as rapid deterioration of visual symptoms was common. Rationing of the available resources was done, and most patients received a standard 50mg of Inj. Amphotericin daily. Patients with orbital and cerebral involvement received a higher adequate dose whenever possible. An operation theatre was exclusively allotted to the Department of ENT on all days to take care of the increasing workload. Endoscopic surgical debridement was the mainstay of treatment and was done at the earliest opportune moment. Some patients were not fit for general anaesthesia, and debridement was done under local anaesthesia. Some patients who were initially not oxygen dependent became oxygen dependent for a few days after general anaesthesia. Hence, the decision to operate under general anaesthesia had to be taken depending on the pulmonary status. Some patients were still Covid positive at the time of surgery. Regular quarantine of the workforce in rotation and the sheer magnitude of the number of cases in a short time period stretched the workforce's limits. Most of the patients were managed by Endoscopic sinus surgery and were followed up by repeated nasal endoscopy. Debridement was repeated when necessary. Some patients also needed debridement by sub-labial approach, Denker's approach, Palatal debridement, maxillectomy, Orbital exenteration etc. Patients were followed up, and the outcomes of surgery were evaluated.

RESULTS

In this study 74 patients with clinical features of mucormycosis were included. Maximum number of

patients were male 47 (63.5%) and higher of number of patients were in age group of 41 to 60 years 45 (60.8%). In this study 73 (98.6%) of patients were not vaccinated and 43 (58.1%) of patients were tested positive for covid during admission.



Figure 1: Eschar in the left nasal cavity



Figure 2: Rhino orbital mucor



Figure 3: Hard palate erosion

Table 1: Demographic details of patients (n=74)

| Patient characteristics | | Frequency | Percentage |
|-------------------------|--------|-----------|------------|
| Gender | Male | 47 | 63.5% |
| | Female | 27 | 36.5% |
| Age | <=40 | 10 | 13.5% |
| | 41-60 | 45 | 60.8% |

| | | | |
|-------------|------------------|----|-------|
| | >60 | 19 | 25.7% |
| Vaccination | One dose | 1 | 1.4% |
| | Not vaccinated | 73 | 98.6% |
| Swab test | Positive | 43 | 58.1% |
| | Negative/Unknown | 31 | 41.9% |

Most of the patients had diabetes mellitus 66 (89.2%) followed by hypertension 11 (14.9%). 27 (36.5%) of patients treated with systemic steroids before diagnosing mucormycosis. In this study 64 (86.5%) of patients had facial pain/headache, 46 (62.2%) of patients had decreased vision and 36 (48.6%) patients had nasal obstruction.

Table 2: Clinical characteristics

| | | Frequency | Percentage |
|-------------------|-------------------------------------|-----------|------------|
| Comorbidities | DM | 66 | 89.2% |
| | Hypertension | 11 | 14.9% |
| | CKD | 3 | 4.1% |
| | HIV +VE | 1 | 1.4% |
| H/o steroid usage | | 27 | 36.5% |
| Clinical features | Nasal obstruction | 36 | 48.6% |
| | Facial pain / Headache | 64 | 86.5% |
| | Decreased vision | 46 | 62.2% |
| | Ophthalmoplegia | 20 | 27.0% |
| | Palatal / Teeth involvement | 15 | 20.3% |
| | Cerebral involvement | 3 | 4.1% |
| | Blackish eschar of the skin of Face | 3 | 4.1% |
| | Dacryocystitis | 1 | 1.4% |
| | Facial palsy | 1 | 1.4% |

Table 3: Comparison of Nasal endoscopy, KOH staining & Histopathology

| Nasal endoscopy findings (n=23) | KOH Staining | HPE | Frequency | Percentage |
|--|--------------|----------|-----------|------------|
| Black crusts absent | Positive | -- | 17 | 74% |
| Black crusts absent | Negative | Positive | 4 | 17% |
| % of patients detectable if, Nasal endoscopy & KOH Staining are done | | | 67 | 91% |
| % of patients detectable if KOH Staining & HPE are done | | | 68 | 92% |
| % of patients detectable if Nasal endoscopy, KOH Staining & HPE are done | | | 72 | 97% |

In 8 patients, endoscopy was not done due to poor general condition or who expired before the procedure. KOH staining was done in all patients and yielded a high positivity rate compared to culture and histopathology. In addition, nasal endoscopy was routinely done, and Black crusts/eschar was a common finding.

Table 4: Surgical treatment – Endoscopic debridement & other

| | | No. of Repeated surgeries | No. of patients | Percentage |
|------------------------|------------------------------------|---------------------------|-----------------|------------|
| Endoscopic debridement | 4 & above | 7 | 9.5% | |
| | 3 | 14 | 18.9% | |
| | 2 | 30 | 40.5% | |
| | 1 | 19 | 25.7% | |
| Partial maxillectomy | | 8 | 10.8% | |
| Palatal debridements | | 7 | 9.5% | |
| Orbital exenteration | | 1 | 1.4% | |
| Extent of Mucormycosis | Limited to nasal cavity & PNS | 28 | 38% | |
| | Rhino orbital mucormycosis | 43 | 58% | |
| | Rhino orbito cerebral mucormycosis | 3 | 4% | |
| Outcome | Improvement in vision (n=46) | 20 | 43% | |
| | Discharged | 68 | 92% | |
| | Expired | 6 | 8% | |

DISCUSSION

The incidence of Mucormycosis, a potentially fatal disease when untreated, witnessed a substantial surge during the second wave of the ongoing Covid pandemic. The total number of patients in the current study was 74. The mean age of presentation in our study was 53 years, similar to a study by Manesh A

et al.^[4] which gives a mean age of 50.42 years. In our study, males were more affected than females in the ratio of 1.7:1, while some studies show a male predilection of 4:1.^[5] The mean presentation duration with symptoms of mucormycosis after becoming swab positive (n=43) was 20 days. Hussain S et al.⁶ cited the onset of mucor after covid as 14.59+/-6.88 days, similar to our study. Uncontrolled Diabetes mellitus was the most common co-morbidity in most patients [Table 2]. In

a study by Patel A et al.^[5] uncontrolled diabetes of 62.7% was one of the most common predisposing factors of CAM. In comparison, a study by Prakash H et al.^[7] shows 56.8% of uncontrolled diabetics. The mean Blood glucose at the time of admission was 256 mg%. The mean duration of Diabetes mellitus in patients with a history of Diabetes mellitus was 7 years. Many patients were on irregular treatment for DM. A good number of patients (17%) were recently diagnosed with DM within one month before admission⁷. In a study by Bhandari S et al.^[8] 42.1% of CAM were newly diagnosed diabetics, and steroid usage was recorded in 84.3% for a mean period of 7-14 days. However, only 36.4% of patients gave a treatment history with some form of steroids in our study. In our study, chronic kidney disease was seen in a very minimal number of patients. Facial pain and headache 86.4% were the patients' most common symptoms at admission, followed by orbital symptoms 62.1%. Patients usually presented within two weeks of symptoms' onset [Table 5]. Rhino orbital mucormycosis (ROM) is the most common type of presentation, 58% in our study, similar to a study by Patel A et al.^[5] which gives 58.2% of ROM. KOH staining was done for all patients, and nasal endoscopy was done for most patients except for very sick. The presence of blackish crusts in endoscopy was detected in 65% of patients. In the remaining 35% of patients without blackish crusts, KOH staining was positive in about 74% of patients. The absence of blackish crusts during nasal endoscopy does not rule out mucormycosis. When both endoscopy and KOH findings were taken together, the diagnostic yield was 91% of patients. This was very helpful to start treatment early without waiting for culture and histopathology reports. However, a combination of nasal endoscopy, KOH staining and histopathological examination significantly increased the yield of diagnosing mucormycosis in 97% of patients. Microscopy, either direct or histopathology, formed the cornerstone of diagnosis.^[9,10] Repeated surgical debridement was done in many patients dictated by the extent of disease and evolving complications. Most patients needed more than one surgery. Endoscopic debridement was the most commonly performed procedure, but some patients who underwent endoscopic debridement initially required palatal debridement, maxillectomy etc. Most partial maxillectomies were done using a sublabial approach, and an external incision was unnecessary. Orbital exenteration was done as a last resort in one patient, even though orbital involvement was common. Surgical debridement with Inj.amphotericin B.^[11,12] was the treatment of choice, but Raj P et al.^[11] used local nebulisation with amphotericin B as an adjunct; a Mexican epidemiology study by Leon DE et al.^[12] showed similar improvement with surgery and antifungals as combined treatment. An analysis of the extent of the disease revealed that ROM was the commonest

mode of presentation in our study. The range of ROM/ROCM in various Indian studies is 45-74%³. ROM (42%) is the most common mode of presentation, followed by ROCM (24%) in a study by Pal R et al.^[13] Further, among the 46 patients with visual symptoms, 20 patients had some visible improvement (43%). Therefore, 68 patients (92%) were discharged, and the number of deaths was 6 (8%). All the patients who were discharged were advised regular follow-up and Tab. Posaconazole.

CONCLUSION

Covid-Associated Mucormycosis (CAM) was a devastating attack on the population during the second wave of Covid. DM was the most important risk factor associated with mucormycosis. Usage of steroids for treating Covid could have aggravated the poor control of diabetes mellitus, but steroids solely may not contribute to mucormycosis. None of the patients in the study were fully vaccinated, and the role of vaccines in preventing mucormycosis needs to be analysed. High suspicion, early diagnosis, stringent glycemic control, an early advocate of Inj. Amphotericin B in adequate doses is essential to prevent a grave prognosis. Repeated endoscopic surgical debridement is still the mainstay of surgical treatment and, when done early, can prevent visual complications and help avoid mutilating surgeries later.

REFERENCES

1. Prabhu RM, Patel R. Mucormycosis and entomophthoromycosis: a review of the clinical manifestations, diagnosis and treatment. *Clinical Microbiology and Infection*. 2004; 10:31-47.
2. Rocha IC, Hasan MM, Goyal S, Patel T, et al. COVID-19 and mucormycosis syndemic: double health threat to a collapsing healthcare system in India. *Tropical Medicine & International Health*. 2021;26(9):1016-8.
3. Prakash H, Chakrabarti A. Epidemiology of mucormycosis in India. *Microorganisms*. 2021;9(3):523.
4. Manesh A, Rupali P, Sullivan MO, Mohanraj P, et al. Mucormycosis—A clinicoepidemiological review of cases over 10 years. *Mycoses*. 2019;62(4):391-8.
5. Patel A, Agarwal R, Rudramurthy SM, Shevkani M, et al. Multicenter epidemiologic study of coronavirus disease-associated mucormycosis, India. *Emerging infectious diseases*. 2021;27(9):2349.
6. Hussain S, Riad A, Singh A, Klugarová J, et al. Global Prevalence of COVID-19-Associated Mucormycosis (CAM): Living Systematic Review and Meta-Analysis. *J Fungi (Basel)*. 2021;7(11):985.
7. Prakash H, Ghosh AK, Rudramurthy SM, Singh P, et al. A prospective multicenter study on mucormycosis in India: Epidemiology, diagnosis, and treatment. *Medical mycology*. 2019;57(4):395-402.
8. Bhandari S, Bhargava S, Samdhani S, Singh SN, et al. COVID-19, Diabetes and Steroids: The Demonic Trident for Mucormycosis. *Indian J Otolaryngol Head Neck Surg*. 2021:1-4.
9. Walsh TJ, Gamaletsou MN, McGinnis MR, Hayden RT, et al. Early clinical and laboratory diagnosis of invasive pulmonary, extrapulmonary, and disseminated mucormycosis (zygomycosis). *Clinical Infectious Diseases*. 2012;54(suppl_1): S55-60.

10. Skiada A, Lass-Floerl C, Klimko N, Ibrahim A, et al. Challenges in the diagnosis and treatment of mucormycosis. *Medical mycology*. 2018;56(suppl_1): S93-101.
11. Raj P, Vella EJ, Bickerton RC. Successful treatment of rhinocerebral mucormycosis by a combination of aggressive surgical debridement and the use of systemic liposomal amphotericin B and local therapy with nebulized amphotericin—a case report. *The Journal of Laryngology & Otology*. 1998;112(4):367-70.
12. Corzo-León DE, Chora-Hernández LD, Rodríguez-Zulueta AP, et al. Diabetes mellitus as the major risk factor for mucormycosis in Mexico: Epidemiology, diagnosis, and outcomes of reported cases. *Medical mycology*. 2018;56(1):29-43.
13. Pal R, Singh B, Bhadada SK, Banerjee M, et al. COVID-19-associated mucormycosis: An updated systematic review of literature. *Mycoses*. 2021;64(12):1452-1459.