



A CASE SERIES OF MUCORMYCOSIS IN POST COVID 19 PATIENTS IN A TERTIARY CARE HOSPITAL IN TELANGANA

Dr Abdul Mujeeb*	MBBS MS ENT Assistant Professor Govt Medical College Siddipet. *Corresponding Author
Dr K Jayasree	MBBS MS General Surgery Associate Professor Govt Medical College Siddipet.
Dr V Geeta	MBBS MD Associate Professor Pathology, Government Medical College, Siddipet.
Dr K Nagaraj	MBBS MS ENT Professor Government Medical College Siddipet.
Dr Shreya	MBBS MS ENT Senior Resident Govt Medical College Siddipet.
Dr V V Shailaja	MBBS MD Microbiology Professor Govt Medical College Siddipet.

ABSTRACT **Aim:** Aim of the study is to put forth the effectiveness of surveillance by an otorhinolaryngologist in covid/post covid patients with comorbidities for early detection and containment of mucormycosis for better outcomes and to reduce the morbidity and mortality. **Materials And Methods:** The study was conducted at a tertiary care hospital/ nodal centre for covid-19 in Siddipet district of Telangana. A prospective observational study on 15 cases of post covid from the period of May - October 2021 were diagnosed with mucormycosis clinically, radiologically and with histopathological confirmation of fungus and were treated by appropriate surgical debridement followed by course of parental and oral antifungal therapy. **Results:** In our study patients with preexisting diabetes and those who were treated with parental steroids and male sex were at increased risk of mucormycosis. Surveillance played a major role in early detection of the disease limited to nose and paranasal sinuses, and prompt treatment with reduced time gap between detection and intervention was helpful in reducing the morbidity and mortality. **Conclusion:** Active surveillance and follow up of all covid patients with risk factors, irrespective of symptoms is a key to early detection of mucormycosis, which helps in identifying the disease in early stages, reduces the morbidity and mortality.

KEYWORDS : Mucormycosis, Covid-19, Diabetes, Surgical debridement, Steroids, FESS.

INTRODUCTION:

In 2019 there were reported cases of new strain of virus affecting the respiratory tract and was named novel corona virus -19. This virus soon spread throughout the world and has become pandemic. During second wave of covid-19 due to delta variant a large number of cases treated aggressively with steroids as a potential life saving drug for treating covid pneumonia, lead to neutropenia and poor control of blood sugars. In some patients who were already immunocompromised due to preexisting diabetes, use of steroids have resulted in further immunosuppression and new cases of deadly opportunistic infection by fungus called mucormycosis were reported. During covid -19 pandemic second wave, there was a sudden peak in the number of cases of rhino-orbito-cerebral mucormycosis in patients who were treated for severe covid -19 pneumonia in hospitals. This led to increase mortality and morbidity in patients such as loss of vision and facial deformities. People with preexisting medical comorbidities such as diabetes were at increased risk of developing mucormycosis. Mucormycosis is an acute and potentially fatal fungal infection caused by fungi related to the mucoraceae family.(1)These fungi are opportunist organisms and can be found in fruit, soil, feces, and may be cultured from the nasal and oral mucosa of healthy humans.(2)Mucormycosis is a rare opportunistic infection caused by fungus belonging to genus Mucorales.

These fungi usually grow in decaying vegetative matter and are ubiquitous. Rhinocerebral mucormycosis is an acute and often lethal opportunistic fungal infection typically affecting diabetic (50% of the cases) or immunocompromised patients caused by fungi of the class zygomycetes (3-5). There were reported cases of this infection in immunocompromised patients such as uncontrolled diabetes, organ transplant recipients, HIV etc. The infection has high incidence in diabetic patients due to the greater availability of glucose to the pathogen, lower response of T-cells, reduced serum inhibitory activity against the Rhizopus in lower pH, and increased expression of some host receptors that mediate the invasion of human epithelial cells through microorganism.(6)An Indian study has reported diabetes as the main risk factor in 70% of the patients.(7) Most common sites for mucormycosis are sinus (39%), lungs (24%), skin (19%), brain (9%), GIT (7%), disseminated disease (6%) and other sites (6%) (8). Clinically it may manifest with necrosis of paranasal sinuses or palate and tongue which may progress towards orbit before reaching intracranial structure (9). In our institute we have come across 15 cases of mucormycosis affecting nose and paranasal sinuses, which had properties of angioinvasion and tissue necrosis, which is rapidly fatal if

untreated. Endoscopic picture of middle turbinate necrosis is shown in figure 1.

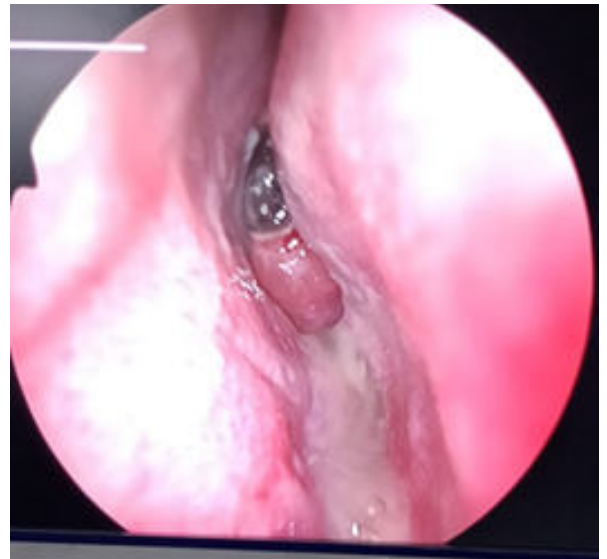


Fig 1 Endoscopic Picture Showing Blackish Discoloured Middle Turbinate.

All the cases were studied for risk factors and treated with extensive surgical debridement and Amphotericin B, and were followed up regularly.

MATERIALS AND METHODS:

Study Setting:

In our study, a total of 15 cases were part of prospective observational study, and data was collected, of which 14 patients were from our hospital, which is a tertiary care center in Siddipet district of Telangana and were diagnosed with covid 19, 1 patient was referred from outside. We have diagnosed cases based on clinical history, examination, diagnostic nasal endoscopy, CT scan, MRI of nose and paranasal sinuses, KOH mount and fungal culture findings, obtained from suspicious tissue samples intra operatively, from the period of MAY - October 2021.

Inclusion Criteria:

- 1) Adults above 18 years with clinical signs and symptoms of mucormycosis admitted in covid ward during period of May 2021- oct 2021.
- 2) Patients coming to outpatient or referred from outside with history of covid 19 with clinical signs and symptoms suspicious of mucormycosis.
- 3) Histopathological confirmed cases of mucormycosis confined to nose & paranasal sinuses in our hospital post covid 19

Exclusion Criteria:

1. Children or individual's less than 18 years
2. Non covid patients with signs and symptoms of chronic rhinosinusitis.
3. Operated cases of Fungal sinusitis with species other than mucor
4. Asymptomatic Patients with post covid coming to opd who were tested negative on KOH mount and radiological screening tests
5. Unfit cases.

All 15 cases underwent FESS with extensive endoscopic debridement of affected sinuses and the tissue samples were collected and sent for KOH mount for fungal hyphae and histopathological study. Confirmed mucormycosis cases, as shown in figure 2

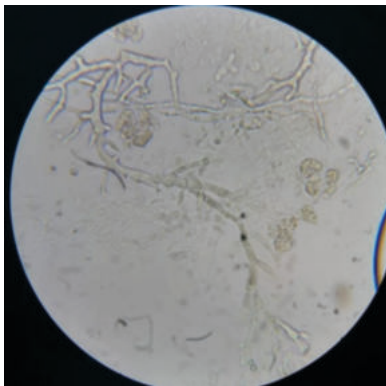


Fig 2: KOH mount showing right branching aseptate hyphae suggestive of mucor. Confirmed cases were started on liposomal Amphotericin b later shifted to oral Posoconazole therapy and followed up. All details were collected and analysed.

RESULTS:

Out of total of 15 cases 11 were male (73.3%) and 4 females (26.6%), with age between 30 and 75 years with median of 50 years. 11 out of 15 (73.3%) patients were on prolonged oxygen therapy. 8/15 patients (53.3%) were having preexisting diabetes at the time of treatment and 5/15 cases (33.3%) were hypertensive. 1 patient had completed chemotherapy for hepatocellular carcinoma. All cases were treated with steroids for covid associated disease. All cases were evaluated clinically, radiologically and were subsequently operated by FESS and extensive debridement of involved sinuses and necrotic tissue. Figure 3 shows contrast enhanced MRI scan of paranasal sinuses with areas of necrosis (non enhancing tissue) amidst areas of enhancement.

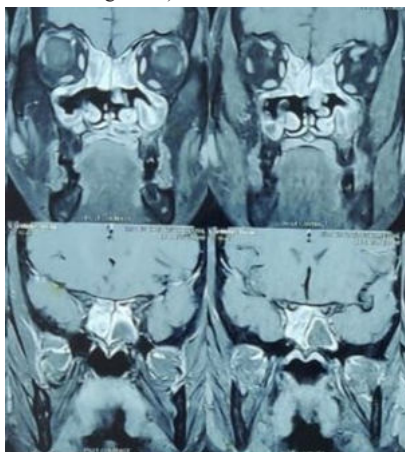


Figure 3: Showing Contrast Enhanced MRI Where Non Enhancing Areas In Nasal Cavity, Suggestive Of Devitalized Tissue

All cases were histopathologically confirmed for mucor. All cases received liposomal Amphotericin B in immediate post operative period. Liposomal amphotericin B was given in all patients in dose of 3-5 mg/kg body weight diluted in 250 ml of 5% dextrose given slowly over 4 h.(10-14).Posaconazole, a triazole that inhibits growth of the fungus, has been proposed as a promising adjunctive or alternative treatment for mucormycosis(4, 15). In subsequent follow up one patient died, which accounted for 6.6%. 1 case developed orofacial fistula, which accounted for 6.6%, which was treated with partial alveolectomy. Total of 14/15 cases, (93.3%) improved after completion of oral posaconazole therapy and were declared cured after thorough radiological and clinical evaluation, as shown in the table.

Table showing various parameters and their outcome in post covid mucormycosis.

Sr	Age	Sex	Comorbidity	Steroid	Oxygen support	Surgical debridement	Histopathological confirmation of fungal hyphae	Antifungal therapy	Outcome
1	50	male	Diabetic	yes	yes	yes	yes	yes	Cured
2	70	male	nil	yes	no	yes	yes	yes	Cured
3	50	male	Hypertension	yes	no	yes	yes	yes	Cured
4	75	male	Diabetic,hypertension, chemotherapy	yes	yes	yes	yes	yes	Cured
5	41	male	Diabetic	yes	yes	yes	yes	yes	Cured
6	70	Female	Diabetic,hypertension	yes	yes	yes	yes	yes	Death
7	52	male	nil	yes	yes	yes	yes	yes	Cured
8	50	male	nil	yes	yes	yes	yes	yes	Cured
9	52	male	Diabetic	yes	yes	yes	yes	yes	Cured
10	70	Female	Diabetic, hypertension	yes	yes	yes	yes	yes	Cured
11	50	male	Diabetic, hypertension	yes	yes	yes	yes	yes	Cured
12	57	male	nil	yes	yes	yes	yes	yes	Cured
13	41	male	nil	yes	yes	yes	yes	yes	Cured
14	70	Female	Diabetic	yes	yes	yes	yes	yes	Cured
15	45	Female	nil	yes	yes	yes	yes	Yes	Cured

DISCUSSION:

India had witnessed sudden increase in number of covid cases during second wave caused by delta strain of covid -19 virus, amidst the pandemic there were also reporting of alarming increase in number of cases of mucormycosis in patients who were hospitalised and treated for covid 19. Among those who were treated, the prevalence of mucormycosis were reported significantly higher in patients with history of preexisting comorbidities like uncontrolled diabetes, hypertension, ckd, chemotherapy. These patients must be followed up regularly and clinically evaluated for early warning signs and symptoms of mucormycosis and this plays important role in detection and early intervention there by reducing morbidity and mortality and reducing burden of disease.

India being a global hub of diabetes with second position in world with estimated 69.2 million people affected by it, diabetes is known to cause immunosuppression by reducing chemotactic and phagocytic activity of neutrophils. Impaired neutrophil and phagocyte response and increased available serum iron are the two underlying conditions in the majority of mucormycosis patients (16). Earlier studies had proven that diabetic ketoacidosis impairs chemotactic and phagocytic activity of neutrophils and increased available serum iron respectively (17). Angioinvasion by the fungi has been studied to a greater extent and is considered central to its ability to cause tissue necrosis and dissemination (16, 18). Glucocorticoids played important role in the management of covid 19 in hospitalized patients to reduce the mortality. Steroids are very well known to cause hyperglycemia and worsen diabetic control as well as immunosuppressive effect on macrophages and neutrophils accompanied by increased serum free iron levels which promotes growth of fungus like mucor species which is otherwise a rare opportunistic infection.

Mucormycosis of nose and paranasal sinuses is a rapidly fulminant infection characterized by angioinvasion and infarction and necrosis of tissue affected and rapid progression to spread to adjacent orbit and brain resulting in high mortality rate and morbidity. In our study, males(73.3%) were affected more than females (26.6%), we have patients with age as young as 30 to as old as 75 with median average age of 50 years, which is similar to the study done by balai et al(19), Gupta et al(25).Almost all cases were already admitted in covid wards and symptomatic patients with cheek pain and eye swelling were sent for screening to our department before being discharged. One patient who was treated outside for covid was referred due to presence of high risk factors i.e., diabetes and history of chemotherapy and clinically suspicious of mucor. We have found that almost 53.3% of our patients were known diabetic and 33.3% were hypertensive prior to covid19. Histopathological examination of surgical specimens can confirm the clinical diagnosis with the appearance of right-branching aseptate hyphae, which are considered typical of mucor species, along with

evidence of angioinvasion and tissue necrosis (20). Fungal cultures provide further confirmation (21). CT scans can be used to evaluate the progression of disease although correlation with the clinical findings may not always be accurate (22). All patients had a history of being treated with high doses of steroids and were performed diagnostic nasal endoscopy to look for blackish discoloration and necrosis of nasal tissue and thorough examination of oral cavity was done for palatal and dental involvement. Suspicious and symptomatic cases were further evaluated radiologically with CT scan and MRI scans to look for early signs of involvement of turbinates and sinuses. All our patients showed radiological involvement of either turbinates or sinuses in radiological screening, thoroughly worked up for surgery, blood sugars were tightly controlled and planned for extensive endoscopic debridement of involved sinuses and turbinates and necrotic and suspected tissue samples were sent for KOH mount and histopathological examination following which patients were started on iv Amphotericin B in post operative period and subsequently shifted to oral Posaconazole therapy and serial followup was done. During follow up, one patient required revision surgery for which partial alveolectomy was done and in the subsequent follow up patient improved, another patient had lost to follow up due to death, which accounted for 6.6%, which is similar to the study done by Gupta et al (23) in which the death rate was 5.7%.

In our study almost all cases were promptly referred for early screening with the disease being limited to turbinates and sinuses without involvement of eye or brain. The surgical approach should be based on the clinical state of the patient with timely interventions for appropriate debridement of infected areas (24). Spellberg et al. specify the resolution of immunosuppression, radiographical signs and clinical symptomatology as the objectives of treatment (25).

CONCLUSIONS:

Post covid mucormycosis is often a fatal condition and people with preexisting comorbidities such as diabetes are at high risk of developing it and risk is further increased by use of steroids which will worsen immunity. We recommend early screening in post covid patients with high risk factors who may or may not have symptoms, which is a very effective tool in reducing the overall morbidity and mortality. Multidisciplinary management and appropriate surgical debridement followed by antifungal therapy remains mainstay of treatment.

Acknowledgement Ethical committee: Institutional review board at Govt medical college siddipet approved the study for publication.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declarations: The authors declares that there is no conflict of interest.

REFERENCES:

- 1) T Mohindra S, Mohindra S, Gupta R, et al. Rhinocerebralmucormycosis: the disease spectrum in 27 patients. *Mycoses* 2007; 50: 290–296.
- 2) Goel S, Palaskar S, Shetty VP, et al. Rhinomaxillary mucormycosis with cerebral extension. *J Oral Maxillofac Pathol* 2009; 13(1): 14–17.
- 3) Vijayabala GS, Annigeri RG, Sudarshan R (2013) Mucormycosis in a diabetic ketoacidosis patient. *Asian Pac J Trop Biomed* 3(10):830–833
- 4) Sarrami AH, Setareh M, Izadinejad M, Afshar-Moghaddam N, Baradaran-Mahdavi MM, Meidani M (2013) Fatal disseminated mucormycosis in an immunocompetent patient: a case report and literature review. *Int J Prev Med* 4(12):1468
- 5) Herrera DA, Dublin AB, Ormsby EL, Aminpour S, Howell LP (2009) Imaging findings of rhinocerebralmucormycosis. *Skull base* 19(2):117
- 6) Mohammadi R, Meidani M, Mostafavizadeh K, Iraj B, Hamedani P, Sayedain SM, Mokhtari M (2015) Case series of rhinocerebralmucormycosis occurring in diabetic patients. *Caspian J Intern Med* 6(4):243–246.
- 7) Chakrabarti A, Das A, Mandal J, Shivaprakash MR, George VK, Tarai B, Rao P et al (2006) The rising trend of invasive zygomycosis in patients with uncontrolled diabetes mellitus. *Med Mycol* 44:335–342
- 8) Roden MM, Te Z, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL et al (2005) Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Infect Dis* 41:634–53.
- 9) Effat KG, Karam M, El-Kabani A (2005) Potts puffy tumour caused by mucormycosis. *J Laryngol Otol* 119:643–5
- 10) Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan. *China Lancet* 395(10223):497–506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
- 11) World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it 2020 [31/03/2020]. Available from: [https://www.who.int/emergencies/diseases/new-covid-19/technical-guidance/naming-the-coronavirus-disease-\(covid-2019\)-and-the-virus-that-causes-it](https://www.who.int/emergencies/diseases/new-covid-19/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it)
- 12) Ceccarelli M, Berretta M, Venanzi RE, Nunnari G, Cacopardo B (2020) Differences and similarities between severe acute respiratory syndrome (SARS)-CoronaVirus (CoV) and SARS-CoV-2. Would a rose by another name smell as sweet. *Eur Rev Med Pharmacol Sci* 24(5):2781–2783. https://doi.org/10.26355/eurrev_202003_20551
- 13) World Health Organization. Rolling updates on coronavirus disease (COVID-19) 2020 [31/03/2020]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus2019/events-as-they-happen>.
- 14) Vijayabala GS, Annigeri RG, Sudarshan R (2013) Mucormycosis in a diabetic ketoacidosis patient. *Asian Pac J Trop Biomed* 3(10):830–833
- 15) Karla S, Natally H, GuerreiroNicolau FC, de Castro I, de Giassi KS (2019) Spectrum of clinical and radiographic findings in patients with diagnosis of H1N1 and correlation with clinical severity. *BMC Infect Dis*. <https://doi.org/10.1186/s12879-019-4592-0>
- 16) Spellberg B, Edwards J, Ibrahim A (2005) Novel perspectives on mucormycosis: pathophysiology, presentation, and management. *Clin Microbiol Rev* 18(3):556–569
- 17) Kim J-G, Park HJ, Park JH, Baek J, Kim HJ, Cha I-H, Nam W (2013) Importance of immediate surgical intervention and antifungal treatment for rhinocerebralmucormycosis. *J Korean Assoc Oral Maxillofac Surg* 39:246–250.
- 18) Hosseini S, Borghei P (2005) Rhinocerebralmucormycosis: pathways of spread. *Eur Arch Otorhinolaryngol* 262:932–938
- 19) Balai E, Mummadi S, Jolly K, Darr A, Aldeerawi H (2020) Rhinocerebralmucormycosis: a Ten-Year Single Centre Case Series. *Cureus*. <https://doi.org/10.7759/cureus.11776>
- 20) 23. Lass-Flörl C (2009) Zygomycosis: conventional laboratory diagnosis. *Clin Microbiol Infect* 15(SUPPL5):60–65
- 21) Greenberg R, Scott L, Vaughn H, Ribes J (2004) Zygomycosis (mucormycosis): emerging clinical importance and new treatments. *Curr Opin Infect Dis* 17:517–525.
- 22) Talmi Y, Goldschmid-Reouven A, Bakon M, Barshack I, Wolf M, Horowitz Z, Berkowicz M, Keller N, Kronenberg J (2002) Rhino-orbital and rhino-orbitocerebralmucormycosis. *Otolaryngol Head Neck Surg* 127:22–31.
- 23) Gupta, D.P., Gupta, S., Shah, C.K. et al. Clinical Study of Surge of Mucormycosis in COVID-19 Pandemic: A Tertiary Care Center Study. *Indian J Otolaryngol Head Neck Surg* (2021). <https://doi.org/10.1007/s12070-021-02784-6>
- 24) Reed C, Bryant R, Ibrahim A, Edwards JJR, Filler S, Golderg R, Spellberg B (2008) Combination polyene-caspofungin treatment of rhino-orbital-cerebral mucormycosis. *Clin Infect Dis* 47:364–371.
- 25) Spellberg B, Walsh T, Kontoyiannis D, Edward JJR, Ibrahim A (2009) Recent advances in the management of mucormycosis: from bench to bedside. *Clin Infect Dis* 48:1743–1751