

**Original Research Article****Mucormycosis in post-COVID patients: An Anaesthesia perspective**

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**Abstract**

COVID-19 pandemic has presented as a major health problem worldwide. There has been wide range of presentation of COVID-19 ranging from mild (flu-like symptoms) to severe life-threatening pneumonia with multi-organ involvement. Steroids have shown some ray of hope in its management. Although, systemic steroids have shown to have survival benefits but rampant use of glucocorticoids have resulted in secondary bacterial and fungal infections. Invasive fungal infections have been found in large number of COVID19 treated patients during the second wave. Mucormycosis is a life-threatening fungal infection that is commonly encountered in immunocompromised patients. Despite aggressive therapy, which includes disfiguring surgical debridement and frequently adjunctive toxic antifungal therapy, the overall mortality rate is high. We studied nearly 40 post COVID patients that were posted for mucormycosis endoscopic debridement in our hospital over a period of 2 months. We hereby present the anaesthesia challenges and mortality in these patients. Demographics, hemodynamic parameters, invasive monitoring methods, surgical procedures, hospital records, and mortality rates of these patients were studied. We concluded that an aggressive postoperative ICU care is important for recovery and for improving the survival in these patients.

**Keywords:** COVID-19, Mucormycosis, post COVID sequelae, co-morbidities.

**Introduction**

COVID-19 pandemic has presented as a major health problem worldwide. There has been a wide range of presentation of COVID-19 ranging from mild (flu-like symptoms) to severe life-threatening pneumonia with multi-organ involvement<sup>[1]</sup>. Now, since more than one year, we are still struggling with the definitive management of COVID-19. Although, systemic steroids have shown to have survival benefits but rampant use of glucocorticoids has resulted in secondary bacterial and fungal infections<sup>[2]</sup>. This increased incidence of secondary infections could be associated to pre-existing co-morbidities such as diabetes mellitus, lung diseases, malignancy and immunocompromised state. The first wave of the pandemic had less than 1% of secondary fungal infections<sup>[3]</sup>. Opportunistic bacterial infections are the most common cause of secondary infection seen in COVID-19 but recent reports showed a steep rise in systemic fungal infections, particularly invasive molds. Mucormycosis is a life-threatening fungal infection that is commonly encountered in immune-compromised patients. Despite aggressive therapy, which includes disfiguring surgical debridement and toxic antifungal therapy, the overall mortality rate is high. The major risk factors for mucormycosis include uncontrolled diabetes mellitus, ketoacidosis, other forms of metabolic acidosis, patients on corticosteroids, organ or bone marrow transplantation, neutropenia, trauma and burns, malignant hematologic disorders, and deferoxamine therapy in patients receiving hemodialysis<sup>[4-6]</sup>. Mucormycosis is an infection caused by fungi belonging to the order mucorlaes. Rhizopusoryaze is the most common organism causing 70% of all cases of mucormycosis. Overall mortality rate of mucormycosis is >50%. The post-COVID sequelae involving pulmonary, myocardial, renal dysfunction, and difficult airway secondary to mucormycosis, pose various anaesthetic challenges in these patients. We report our anaesthesia experience of 40 post COVID patients that were posted for surgical debridement of mucormycosis.

### Materials and Methods

A cross-sectional study was carried out among 40 patients of post-COVID mucormycosis that came for debridement surgery which presented to the Department of ENT in Multi-speciality Deepak Hospital, Jalna Maharashtra over a period of 2 months from 1<sup>st</sup> March 2021 to 31<sup>st</sup> May 2021. Most of the patients had unilateral facial swelling, retro-orbital pain, and headache. Crusts were taken from nasal cavity of all patients and sent for calcoflour KOH stain to rule out invasive fungal sinusitis. A contrast enhanced CT (PNS) including orbital cuts were done to look for rhino-orbital involvement. CT Brain was also done to rule out cerebral involvement. All the 40 patients were post -COVID out of which 35 were diabetic. All the patients were seen preoperatively and all baseline investigations like complete hemogram, serum electrolytes, liver function tests, kidney function test, HBA1C in diabetic patients were done. COVID19 RT-PCR, ECG, and 2D echo were done. HRCT chest and ABG was also. Written informed consent for general anaesthesia was taken from all patients. Non-invasive blood pressure, ECG, SPO2, and ETCO2 monitoring was done for all patients intra-operatively.

After preoxygenation, all patients received injection glycopyrrolate 0.004mg/kg, injection Midazolam 0.001mg /kg and injection pentazocin.0.03 mg/ kg. Patients were induced with injection propofol 2 mg/kg and injection succinylcholine 1.5mg/kg and were intubated with appropriately sized endotracheal tube. Injection vecuronium was used as long-acting muscle relaxant. Anaesthesia was maintained with O2 and air 50:50 and isoflurane in 1 MAC concentration. Mixture of Mgso4 and lidocaine 1.5mg/kg and injection dexmedetomidine was used at time of induction. Intraoperatively few patients required inj. nitroglycerine (NTG) infusion and dexmedetomidine infusion for maintenance. Injection paracetamol 1 gm iv and injection diclofenac 75mgs iv was given for analgesia. Injection tramadol 50 mg IV was used in patients with raised creatinine. Ringer lactate was used as maintenance fluid intraoperatively. Out of 40 patients, one patient had hypokalaemia which was corrected intra-operatively by giving potassium chloride infusion through central line. Intraoperative sugar monitoring was done and strict glycaemic control was maintained by using insulin infusion as per the sugar levels. All patients were given injection tranexamic acid 10 mg/kg by bolus after induction. In the end, after fulfilment of reversal criteria, all patients were given injection neostigmine 0.05mg/kg and injection glycopyrrolate 0.008mg/kg and all patients except 2 were extubated on table. Those 2 patients had respiratory acidosis and required post-operative ventilation. They were extubated the next day of surgery. There were no intraoperative complications. All patients were monitored after surgery for 24 hours in ICU.

### Statistical analysis

The data collected was entered in to Microsoft Excel and analysed. Descriptive data is presented in the form of frequency and percentage using pie chart and bar diagrams.

### Results

We studied a total of 40 patients over a period of 2 months that underwent mucormycosis debridement in tertiary hospital at Jalna.

**Table 1:** Age and gender wise distribution of mucormycosis cases

Age-wise mucormycosis cases	No.	Percentage
< 40 year	05	12%
40 to 60 year	28	70%
> 60 year	07	18%
Gender-wise mucormycosis cases		
Male	33	78%
Female	07	22%
Total	40	100%

It was seen from Table 1 that out of 40 patients, 28 patients were between 40-60 yrs of age, and 5 patients were below 40yrs and 7 patients were above 60 yrs of age. Thus, the incidence of 70% mucormycosis was found in age group of 40- 60 years in our study. We found 18% incidence in above 60 years which is quite high. Out of the 40 mucormycosis patients, 33 were male and 7 were female. There was no significant difference in the presentation of males and females with respect to gender.

**Table 2:** Incidence of diabetes & non-diabetic patients presenting with mucormycosis

Diabetes & Non-Diabetes mucormycosis Cases	No.	Percentage
Diabetes	30	75%
Non-Diabetes	10	25%
Total	40	100%

It was seen from Table 2 that out of 40 patients, 75% of patients were diabetics and remaining 25% were non diabetic. Thus, showing that the incidence of mucormycosis is higher amongst the diabetic patients.

**Table 3:** Clinical grading of Mucormycosis

Clinical presentation of mucormycosis cases	No.	Percentage
Mild	16	40%
Moderate	20	50%
Severe	04	10%
Total	40	100%

It was seen from Table 3 that out of the 40 mucormycosis patients, 50% patients presented with moderate symptoms, 40% presented with mild disease and 10% had severe involvement of mucormycosis.

**Table 4:** Site of involvement of mucormycosis

Involvement of sites mucormycosis cases	No.	Percentage
Maxillary	35	85%
Intra -Orbital	04	10%
Intra -Cranial	02	05%
Total	40	100%

It was observed from Table 4 that out of the 40 cases,85% patients had maxillary involvement where as 10% had intra-orbital and 5% had intra-cranial infection.

**Table 5:** Mechanical Ventilation post-debridement

Ventilatory support in mucormycosis cases	No.	Percentage
On table Extubation	38	95%
Post -operative Ventilatory Support	02	5%
Total	40	100%

It was seen from Table 5 that out of the 40 patients, 95% of patients got extubated on table after surgery but 5% of patients required post-operative mechanical ventilation on account of their lung involvement post-COVID.

**Table 6:** Follow-up survival rate after 2 months of mucormycosis surgery

Post-operative status mucormycosis cases	No.	Percentage
Recovered	39	97.5%
Death	01	2.5%
Total	40	100%

It was seen from Table 6 that out of 40, 97.5 % of patients recovered fully and had good survival after 2 months of follow up but one patient (2.5%) of patient expired during the course of recovery within 2 months period.

**Table 7:** Co-morbidities associated with mucormycosis patients

Co-morbid condition of mucormycosis cases	No.	Percentage
HTN with CKD with IHD	15	79%
Stroke	01	5%
Asthma	01	5%
HBsAg Positive	01	5%
Decreased LVF	01	5%
Total	19	100%

It was observed from Table 7 that out of the 40, 19 patients had co-morbidities other than diabetes. 79% patients had hypertension and 5% patients had stroke, asthma, and low ejection fraction.

**Discussion**

The entire world has been facing the COVID-19 pandemic since last one and half years and millions of patients have succumbed to the illness. The disease has presented with a prodrome of mild flu like symptoms to severe critical conditions like acute respiratory distress syndrome, stroke, pulmonary embolism and renal failure. We have been struggling over the treatment and management of COVID since its outburst. Lately, steroids have largely helped in improving the lung mechanics in COVID patients. Neither antimicrobial antibodies nor antiviral drugs proved that promising as steroids. This led to an exaggerated usage of steroids by physicians all over the world. Not only intravenous but also steroid

nebulisations had been used. We rarely reported any secondary infections after first wave but during the second wave there had been a blast of secondary fungal infections due to an excessive usage of steroids. And this was debilitating invasive mucormycosis which is the most dreaded fungus. Mucormycosis is an opportunistic fungal infection caused by zygomycetes with a mortality rate of 35-96% depending upon the site and extent of the disease<sup>[7]</sup>. It is commonly associated in diabetic patients and immunosuppressed patients. It is known to erode bone and extend to orbits, paranasal sinuses and brain it is a lethal fungal disease with the rhino-orbital-cerebral (ROC) as the most common form. Surgical debridement of the infected area improved the survival rate in these cases<sup>[8]</sup>.

COVID infection presented with dysregulated innate immune response, ciliary dysfunction, cytokine storm and microvascular coagulation which led to post-COVID sepsis and numerous complications. Anaesthesia management of such patients presented a lot of challenges in intra-operative management and also in post-operative recovery of these patients. We studied the course of 40 post-COVID mucormycotic patients to a period of 2 months postoperative. We hereby summarize the challenges faced by us. As COVID infection had mainly affected the lungs and patients developed opacities simulating acute respiratory distress syndrome, chest X-ray, arterial blood gas (ABG) and HRCT chest must be done to know the status of lung function in these patients. The patients with CTSS (COVID score on CT chest) more than 18 with severe lung involvement could require post-operative ventilatory care<sup>[9]</sup>. These are the group of patients that had poor survival. Also, the cardiac status of these patients was evaluated which included 12 lead, ECG and 2D ECHO as post COVID cardiomyopathy and myocarditis was seen in many recovered patients<sup>[10]</sup>.

COVID presented with thrombo-embolic presentations of the lungs secondary to hypercoagulability. These patients need to be investigated for coagulation parameters prior to surgery<sup>[11]</sup>. These patients are most likely to have adrenal suppression as they had received steroids for longer duration in COVID. A single shot of injection hydrocortisone should be given in order to avoid hypotension. Difficult airway cart should be kept ready and a senior anaesthesiologist should intubate these patients. Video-laryngoscopes have proved to be quite useful in intubating these patients. Use of Mc Coy blade and airway adjuncts also may be required while intubation. Ideally the use of succinylcholine should be avoided in view of critical illness myopathy which can lead to hyperkalaemia in these patients. The patients with rhino-orbital mucormycosis present with facial swelling making mask ventilation and intubation difficult.

The use of succinylcholine should be done on the basis of loss vs benefit. Isoflurane should be used as it is known to halt the growth of fungus *in vitro* studies<sup>[12]</sup>. Depending on the involvement of the disease, there could be an extensive debridement with maxillectomy, orbitectomy or evisceration. Maxillectomy surgery are of prolonged duration and are associated with post-operative facial swelling. The patients are then electively ventilated overnight and extubated on the next post-operative day. These patients are mostly diabetic so intraoperative strict glucose control should be done and insulin infusion should be started whenever required. Patients receiving antifungal drugs like injection amphotericin have found to be associated with hypokalaemia. So preoperative fresh serum electrolytes should be asked and intraoperatively also potassium should be supplemented. A central venous cannulation should be done as these patients are admitted in wards since longer duration and receiving injection amphotericin which is quite thrombophlebitic. The lungs of these patients are prone for pulmonary oedema as already they are poorly compliant due to COVID induced injury and above that these patients are receive excessive fluids along with amphotericin. Amphotericin injection leads to increase in creatinine levels. The patients with raised creatinine and severe hypokalaemia secondary to amphotericin injection can be started with oral antifungal like tablet posaconazole. The typical dose of amphotericin is 1-1.5 mg/kg/d. The total dose given over the course of therapy is usually 2.5-3 g. Amphotericin induced hypokalemia may potentiate the effect of skeletal muscle relaxants. Arrhythmia, atrial fibrillation, bradycardia, cardiac arrest, cardiomegaly, haemorrhage, postural hypotension, and vasodilatation are reported<sup>[13-15]</sup>. Mucormycosis is a very invasive fungus which also erodes bone so the debridement is associated with blood loss. Adequate blood and blood products should be reserved and transfused. As the endoscopic debridement is done along with irrigation, the estimation of actual blood loss is difficult. These patients should be observed in intensive care after surgery considering the multiple factors and comorbidities. Post-operative monitoring of serum electrolytes, glucose and their correction whenever required should be done. Hyperbaric oxygen has been found to be fungistatic and so is used as an adjunct to aggressive surgical debridement, AmB therapy, and control of any underlying predisposing conditions. It is known to help revascularization of necrotic tissue and thereby to heal viable poorly perfused acidic and hypoxic tissues<sup>[16]</sup>.

### **Conclusion**

Successful management of Mucormycosis patients is a challenging job. A co-ordinated approach of Otorhinolaryngologist, Radiologist, Anaesthesiologist and Intensivist are needed for patient management and better survival.

### **Acknowledgement**

We the authors are deeply acknowledge the help and support of Dr. Sanjay Rakh, (Director, Deepak Hospital, Jalna), Dr. Shikha Tiwari (Anesthesiologist, Madhya Pradesh) and also my beloved parents Advocate. Mr. Suresh Rao Jadhav Patil Ex. MP (Member of Parliament), and Mrs. Rama Suresh Rao Jadhav

for their constant guidance.

**Financial Support:** Nil.

**Conflict of Interest:** There are no conflicts of interest.

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