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Research Paper

Airway management, procedural data, and in-hospital mortality records of patients undergoing surgery for mucormycosis associated with coronavirus disease (COVID-19)



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ABSTRACT

Purpose: Although unexpected airway difficulties are reported in patients with mucormycosis, the literature on airway management in patients with mucormycosis associated with Coronavirus disease is sparse. *Methods:* In this retrospective case record review of 57 patients who underwent surgery for mucormycosis associated with coronavirus disease, we aimed to evaluate the demographics, airway management, procedural data, and in-hospital mortality records.

Results: Forty-one (71.9%) patients had a diagnosis of sino-nasal mucormycosis, fourteen (24.6%) patients had a diagnosis of rhino-orbital mucormycosis, and 2 (3.5%) patients had a diagnosis of palatal mucormycosis. A total of 44 (77.2%) patients had co-morbidities. The most common co-morbidities were diabetes mellitus in 42 (73.6%) patients, followed by hypertension in 21 (36.8%) patients, and acute kidney injury in 14 (28.1%) patients. We used the intubation difficulty scale score to assess intubating conditions. Intubation was easy to slightly difficult in 53 (92.9%) patients. In our study, mortality occurred in 7 (12.3%) patients. The median (range) mortality time was 60 (27–74) days. The median (range) time to hospital discharge was 53.5 (10 –85) days. The median [interquartile range] age of discharged versus expired patients was 47.5 [41,57.5] versus 64 [47,70] years (P = 0.04), and median (interquartile range) D-dimer levels in discharged versus expired patients was 364 [213, 638] versus 2448 [408,3301] ng/mL (P = 0.03).

Conclusion: In patients undergoing surgery for mucormycosis associated with the coronavirus disease, airway management was easy to slightly difficult in most patients. Perioperative complications can be minimized by taking timely and precautionary measures.

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Introduction

Mucormycosis is an acute-onset, aggressive, and rapidly progressive angioinvasive infection caused by saprophytic fungi of the order Mucorales. The most common underlying risk factor associated with mucormycosis is uncontrolled diabetes mellitus. Hematopoietic stem cell and solid organ transplants, corticosteroid therapy, neutropenia, or drug-induced immunosuppression are other identifiable risk factors [1,2].

There was a sudden increase in cases of mucormycosis in the second wave of Coronavirus disease (COVID-19) in India [3,4]. The

* Corresponding author. E-mail address: sushmabhatnagar1@gmail.com (S. Bhatnagar). management plan of these cases included surgical debridement, systemic antifungal therapy, sugar control, and management of systemic adverse effects related to the antifungal therapy [5]. Diabetes mellitus has been recognized as the most common coexisting concomitant disease. Attention must be given to control blood glucose [6]. In addition, airway management in these patients may be difficult due to the aggressive nature of the disease. The oropharyngeal region may be involved by fungi and edema in the supraglottic region may cause difficult endotracheal intubation and difficult ventilation [7–9]. These patients are receiving injections of amphotericin B which may have significant adverse effects such as nephrotoxicity, hypokalemia, hypomagnesemia, fever, tremor, dyspnea, and hypotension [10]. Apart from this, COVID-19 itself has harmful effects on various organs of the body. Many of these patients require surgical debridement of

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the involved tissues and anesthesiologists are involved in the multidisciplinary perioperative management of mucormycosis associated with COVID-19 [9].

The mortality rate for mucormycosis associated with COVID-19 is less known, but a study on 929 patients with mucormycosis found a mortality rate of 54%. This includes mucormycosis infections such as sinus, pulmonary, cutaneous, cerebral, gastrointestinal, generalized disseminated, kidney, and others [11]. In sinus infections, there is a risk of involvement of vital structures such as the brain and eye, so surgical debridement should be planned on an urgent basis as a delay can worsen the prognosis. There may be less time to optimize patient comorbidities, making perioperative management challenging. Since all patients in our study are positive for COVID-19, problems caused by wearing personal protective equipment, limited staffing, and supplies are additional difficulties in managing these patients [12].

Although unexpected airway difficulties are reported in patients with mucormycosis, the literature on airway assessment and management in patients with mucormycosis associated with COVID-19 is sparse. In this study, we aimed to evaluate demographics, airway assessment and management, procedural data, and in-hospital mortality records in patients undergoing surgery for mucormycosis associated with COVID-19.

Methods

Study design

A retrospective review of the medical records of patients who underwent surgery for mucormycosis associated with COVID-19 at the National Cancer Institute (Jhajjar) between 6 May 2021 and 15 June 2021 was performed [13].

Study setting and population

The study included 57 COVID-19 positive patients who underwent surgery for mucormycosis under general anesthesia. The study was approved by the Institute Ethics Committee (IEC-450/ 02.07.2021) of the All India Institute of Medical Sciences, New Delhi.

Study objectives

The primary objective was to describe airway assessment and management and the secondary objective of the study was to describe demographics, procedural data, and in-hospital mortality records.

Study protocol

Preoperative data included demographic characteristics, disease type, patient comorbidities, smoking and alcohol status, laboratory investigations, vital parameters, and airway assessment. The airway was assessed under the following headings: mouth opening, presence of loose teeth, dentures or bucktooth, whether the patient was edentulous, Mallampatti scoring, neck movements, thyromental distance, presence of short neck, presence of receding chin, and postsurgical changes [14,15]. All the surgeries were performed under general anesthesia. All anesthesiologists involved in the procedure had at least 3 years of clinical experience. As a protocol and according to recommendations, if mouth opening was adequate, we used a conventional C-MAC video laryngoscope for endotracheal intubation [9,16,17]. We calculated the Intubation difficulty score (IDS) to assess intubating conditions [18–20]. This includes the following parameters: number of intubation attempts, number of operators, number of alternative techniques, Cormack-Lehane grade, whether lifting pressure is necessary, whether or not laryngeal pressure is applied, and vocal cord mobility. IDS value = 0 represents easy intubation, a score

of >0 and <5 represents slightly difficult intubation, and a score \geq 5 represents moderate to major difficult intubation. The time required for intubation and the percentage of glottic opening (POGO) were also noted [21]. Data related to the procedure were also recorded in terms of nasogastric tube insertion, invasive monitoring, central venous catheter insertion, blood loss, urine output, etc.

The duration of anesthesia was defined as the time between induction of anesthesia and transfer of the patient to the post-anesthesia care unit (PACU) or ICU. Patients who required postoperative mechanical ventilation or who had undergone extensive surgery were transferred directly from the operation theater to the ICU. Patient data regarding length of hospital stay and mortality were obtained from hospital records. Duration of hospital stay was defined as the number of days between the date of hospitalization to the date of discharge/death. If the patient's condition was clinically stable and they completed the course of liposomal amphotericin B, we discharged them on posaconazole tablets, and asked them to follow-up after 3 months at our main hospital i.e., All India Institute of Medical Sciences, New Delhi.

Statistical analysis

The study design was descriptive in nature and followed a retrospective record review design, therefore a priori calculation of sample size wasn't performed. Instead we included the records of all patients (n = 57) who were admitted to our center and underwent surgery for mucormycosis related to COVID-19. The study period corresponds to the peak phase of 2nd wave of COVID-19 pandemic in the country with high mucormycosis admissions, so a non probabilistic, convenience sample selection of the patient records was performed. Data related to the variables selected in the study were extracted from the records and entered into MS Excel software version 16.0 (Microsoft Inc.) for summative analysis. Data were summarized using the median with the interquartile range [25th, 75th] or median (range) for continuous variables and numbers and proportions (%) for categorical variables. Statistical review of the data was performed using IBM SPSS version 24 (SPSS Inc., Chicago IL, USA). A P-value of less than 0.05 was considered statistically significant.

Results

The demographic and clinical characteristics of the patients are presented in Table 1. The 57 patients consisted mostly of men 35 (61.4%) with a median age of 49 (26,78) years. The median body weight and height were 64 (46,82) kg and 1.67 (1.45,1.81) meters. Most patients had American Society of Anesthesiologists (ASA) scores II (40.4%) and III (40.4%) [22]. Forty-one (71.9%) patients had sinonasal mucormycosis, fourteen (24.6%) had rhino-orbital mucormycosis (out of which 2 patients had a cerebral extension), and 2 patients (3.5%) was diagnosed with palatal mucormycosis. The diagnosis of mucormycosis in our study was based on clinical suspicion, potassium hydroxide (KOH) stain examination, culture, and histopathology. Total 44 (77.2%) patients had co-morbidities. The most common co-morbidity was Diabetes Mellitus 42 (73.6%), followed by hypertension 21 (36.8%) and Acute kidney injury 14 (28.1%). A total of 22 (52.4%) out of 42 diabetic patients were recently diagnosed with diabetes mellitus at presentation.

The severity of COVID-19 in patients was defined as per the guidelines of the All India Institute of Medical Sciences, the Indian Council of Medical Research, and Ministry of Health and Family Welfare [23]. The severity of COVID-19 disease, the treatment history of COVID-19 before the detection of mucormycosis, and days without oxygen therapy before surgery are mentioned in Table 1. All the patients on oxygen therapy were weaned off from it before their surgery.

Airway assessment and management, and procedural data parameters are presented in Table 2. In all 57 patients, mask ventilation was

Table 1

Demographic and clinical characteristics of included cases in the study.

Variables	Frequency (%)/ Median [IQR]
1 Age (Years)	49 [41 5 59 5]
2. Weight (Kilograms)	64 [58.70]
3. Height (meters)	1.67 [1.58,1.71]
4. Sex:	
Male	35 (61.4)
Female	22 (38.6)
5. Diagnosis:	
Sino-nasal	41 (71.9)
Rhino-orbital	14 (24.6)
Palatal	2 (3.5)
6. Symptoms	42 (75 4)
Facial Palli Hoodosho	43 (75.4)
Swelling on face	28 (40 1)
Diminished vision	10(175)
Ptosis	6 (10.5)
Deviation of angle of mouth	4(7.1)
Nasal discharge	12 (21.1)
Tooth pain	26 (45.6)
Eye pain	18 (31.6)
Eye swelling	17 (29.8)
7. Onset of Symptoms of mucormycosis (Days)	6 [5,8]
8. Days from COVID-19 infection to detection of	10 [7,17]
mucormycosis	
9. Treatment history of COVID-19 in patients at	
presentation No troatment	6 (10 5%)
No fiedifient	0(10.3%) 17(20.8%)
Antiallergics Antitussives Bronchodilators)	17 (25.6%)
Supportive treatment + intravenous/oral	20 (35.1%)
steroids	20 (00110)
Oxygen therapy + Supportive	14 (24.6%)
treatment + intravenous/oral	
steroids + Anticoagulants	
10. Severity defined as per AIIMS, ICMR &	
MOHFW COVID-19 severity protocol) \rightarrow	
Mild	41 (71.9%)
Moderate	14 (24.6%)
Severe	2 (3.5%)
I I. FUNGUS ISOlated	
Asentate Hyphae	45 (78 9)
- Septate + Aseptate Hypahe	3 (5 3)
- Negative	9(15.8)
Culture	- ()
- Rhizopus Species	31 (54.3)
-Mucor Species	2 (3.5)
- Rhizopus Species + Fusarium Species	1 (1.8)
 Mucor Species+Aspergillus Species 	1 (1.8)
- Lichtheimia Species	1 (1.8)
- Negative	21 (36.8)
Histopathology	40 (20.4)
- Mucormycosis Mucormycosis Condidicaia	40(70.1)
- Mucormycosis+Candidasis	2 (3.5)
- Mucorniycosis+Asperginosis	2 (5.2) 2 (5.2)
- Reports Inconclusive/Not available	9(158)
12. Days off oxygen before surgery (14 patients)	7 [4.3.17.8]
13. Days from detection of mucormyscosis to	14 [12.20]
surgery (days)	
14. Duration of Pharmacological treatment before	7 [5,8]
surgery (days)	
15. Clinical Outcome	
Discharged	50 (87.7)
Expired	7 (12.3)
16. ASA Grade	11 (10 2)
1	11(19.3)
2	23 (40.4) 22 (40.4)
17 Comorbidity	23 (40.4)
Diabetes	42 (73.7)
Hypertension	21 (36.8)
Acute Kidney Injury	14 (28.1)
Chronic Kidney Disease	2 (3.8)
-	

Variables	Frequency (%)/ Median [IQR]
Hypothyroidism	2 (3.8)
Coronary artery disease	2 (3.8)
Asthma	1 (1.8)
18. Pre-operative HbA1C values (%)	9.1[6.1,10.9]
19. Smoking Status*	10 (17.5)
20. Alcohol intake Status*	10(17.5)
21. Pre-operative Pulse Rate (per minute)	89 [79.5,100.5]
22. Pre-operative Systolic Blood Pressure	125 [117.5,136.5]
23. Pre-operative Diastolic Blood Pressure	75 [66.5,84.5]
24. Pre-operative Respiratory rate (breaths per	22 [20,24]
minute)	

*Items are mutually non-exclusive.

without difficulty. Fifty-six (98.3%) patients underwent oral endotracheal intubation using a conventional C-MAC laryngoscope. One patient which had rhino orbital mucomycosis has restricted mouth opening (<1 finger), for which we performed nasotracheal intubation using a fiberoptic bronchoscope. The first pass intubation success rate was 92.9%. We calculated the Intubation difficulty score to assess intubating conditions and we found a score of 0 (Easy) in 11 patients, a score of >0 to <5 (slightly difficulty) in 42 patients, and a score ≥ 5

Table 2
Airway Assessment and management with Procedural Data.

Variable	Frequency (%)
1. Mouth opening	
>3 Fingers	49 (85.9)
2.5–3 Fingers	3 (5.3)
2–2.5 Fingers	4(7.0)
<1 Fingers	1(1.8)
2. Loose tooth	5 (8.8)
3. Artificial tooth	3 (5.3)
4. Edentulous	2 (3.5)
5. Buck tooth	2 (3.5)
6. Mallampatti Score	
1	3 (5.3)
2	44 (77.2)
3	8 (14.0)
4	2 (3.5)
7. Neck Movements	56 (98.2)
8. TMD (adequate)	46 (80.7)
9. Short neck	7 (12.3)
10. Receding chin	2 (3.5)
11. Post-surgical changes	0(0)
12. No. of attempts	
1	53 (92.9)
2	4(7.0)
13. No. of operators	
1	56 (98.2)
2	1 (1.8)
14. Cormack Lehane grade	
1	24 (42.9)
2	28 (50.0)
3	4(7.0)
15. Lifting force required	
Normal	24 (42.9)
Increased	32 (57.1)
16. Vocal cord mobility	
Abduction	57 (100)
17. External laryngeal maneuver	21 (36.8)
18. Esophageal intubation	0(0)
19. Intubation Stylet used	2 (3.6)
20. Intubation difficulty score ($n = 56$)	
0	11 (19.6)
1	13 (23.2)
2	17 (30.4)
3	11 (19.6)
4	1(1.8)
5	3 (5.4)
21. Extubated	41 (71.9)
22. Shifted to ICU (Intubated)	16(28.1)

(continued)

Table 3

Pre-operative Investigations of patients.

Variable	Median [IQR]
1. Pre-Op Blood sugar (mg/dL)	146 [122.5,171]
2. D-dimer (ng/mL)	407 [227,657.75]
3. Fibrinogen (mg/dL)	484 [415.75,556]
4. Prothrombin Time (sec)	11.8 [10.97,12.97]
5. INR	1 [0.93,1.14]
6. Hemoglobin (g/dL)	11.35 [10.32,12.7]
7. WBC Count ($/\mu$ L)	8.84 [7,11.94]
8. Platelet Count ($/\mu$ L)	235.5 [181.25,303.75]
9. Neutrophils (%)	77.3 [69.5,85.05]
10. Ferritin (ng/mL)	862.85 [495.62,1381.57]
11. Lactate dehydrogenase (units/L)	295 [225,349]
12. C-reactive protein (mg/L)	11.22 [5.02,14.99]
13. Procalcitonin (ng/mL)	0.09 [0.04,1.17]
14. Interleukin-6 (pg/mL)	17.5 [8.7,43]
15. Total Bilirubin(mg/dL)	0.43 [0.3,0.58]
16. Direct Bilirubin(mg/dL)	0.18 [0.1,0.26]
17. Alanine aminotransferase (U/L)	29 [17,45]
18. Aspartate Aminotransferase (U/L)	24 [20.5,35]
19. Total Protein(g/dL)	5.9 [5.31,6.4]
20. Albumin (g/dL)	3.2 [2.8,3.6]
21. Albumin/Globulin Ratio	1.27 [1.07,1.43]
22. Alkaline Phosphatase (IU/L)	98 [87,138.5]
23. Urea (mg/dL)	34.2 [21.2,48.15]
24. Creatinine (mg/dL)	0.87 [0.69,1.7]
25. Calcium (mg/dL)	8.11 [7.87,8.64]
26. Sodium (mmol/L)	136 [134,139]
27. Potassium (mmol/L)	4 [3.55,4.7]
28. Uric Acid (mg/dL)	4.3 [3.3,5.1]

(moderate to major difficulty) in 3 patients (all 3 patients had sino nasal mucormycosis).

The median percentage of glottic opening (POGO) score was 80 (20,100)% and the time required for intubation was 15 (10,180) seconds. All patients received crystalloids while 2 patients additionally received blood transfusions. For long-term pharmacoloigical management with liposomal amphotericin B, we performed peripherally inserted central catheterization in 47 (82.5%) patients and internal jugular vein cannulation in 7 (12.3%) patients. In 3 patients, internal jugular venous cannulation was performed before their surgery in the ward, because they had difficult peripheral intravenous access. Nasogastric tube insertion was performed in 19 (33.3%) and Foley catheterization was performed in 19 (33.3%) patients. The median blood loss was 150 (50,500) ml and urine output was 250 (200,300) ml. Preoperative investigations are listed in Table 3. The median duration of anesthesia was 150 (90,270) min. Forty-one (71.9%) patients were extubated after surgery in the operation theater. Sixteen (28.1%) patients were transferred to the intensive care unit for postoperative elective mechanical ventilation. The reason for postoperative elective mechanical ventilation was extensive surgery in 14 patients and inadequate reversal from anesthesia in 2 patients. Eight out of 16 patients were extubated on postoperative day 0, 6 patients on postoperative day 1, and 2 patients on day 2. After extubation, a high flow nasal cannula (HFNC) is required in one patient for 10 days. The patient was later weaned from it.

In our study, mortality occurred in 7 (12.3%) patients during the hospital stay. The median mortality time was 60 (range, 27–74) days. The median (range) mortality time was 60 (27–74) days. The median (range) time to hospital discharge was 53.5 (10–85) days. Five (12.2%) of 41 patients with sinonasal mucormycosis and 2 (14.3%) of 14 patients with rhino orbital mucormycosis (cerebral extension in 1 patient) expired. None of the patients with palatal mucormycosis expired. Of the 7 patients who died, five were those who had extensive surgery, their condition later worsened, and two other patients also worsened during their stay in the hospital. Their condition was not responding to even high dose of antifungal therapy. Due to worsening illness and subsequent hypoxia, they were mechanically ventilated, and later died during their hospital stay.

The causes of death were identified as suspected pulmonary embolism with septic shock in 1 patient, cardiogenic shock in 1 patient, septic shock in 2 patients, septic shock with severe acute respiratory distress syndrome (ARDS) in 1 patient, middle cerebral artery infarction with septic shock and severe ARDS in 1 patient, and septic shock with acute kidney injury in 1 patient. According to the initial severity of COVID-19, 4 patients with mild disease, 2 patients with moderate disease, and 1 patient with severe disease died during their hospital stay. The median (range) time to hospital discharge was 53.5 (10–85) days. We did a comparative analysis between discharged patients and expired patients. The median [interquartile range] age of discharged versus expired patients was 47.5 [41,57.5] versus 64 [47,70] years (P = 0.04), and median (interquartile range) p-dimer levels in discharged versus expired patients was 364 [213, 638] versus 2448 [408,3301] ng/mL (P = 0.03).

Discussion

Surgical debridement of mucormycosis is an invasive procedure and airway management of patients can be challenging. Involvement of the oropharyngeal region by fungus and supraglottic edema can lead to difficulties with mask ventilation and endotracheal intubation [8]. In one study, 3 patients had fungal debris in the oropharyngeal region, and in one of these patients, due to supraglottic edema, a video laryngoscope was used for endotracheal intubation [24]. In our study, mask ventilation was not difficult in any of our patients. First pass intubation success was 92.9%. Two attempts were made in 4 (7.0%) patients. Two patients required an intubation stylet for their endotracheal intubation and two patients had difficulty guiding the endotracheal tube through the glottis on the first attempt but the second attempt was successful. In one patient, restricted mouth opening was present, therefore, fiberoptic bronchoscope-guided intubation was performed. Rest all patients are intubated by C-MAC video laryngoscope as per departmental COVID-19 protocol. We did not find any fungal debris in the oropharyngeal region and supraglottic edema in any of our patients. The intubation difficulty score was calculated with the help of the intubation difficulty scale. Eleven patients had no intubation difficulty, 42 patients had slight intubation difficulty (score 1-4), 3 patients had moderate to major intubation difficulty (score ≥ 5).

We had a dedicated COVID-19 operation theater with all the healthcare staff wearing level 3 personal protective equipment [25]. We checked all equipment and drugs for anticipated or unanticipated difficult airway management. We had masks of different sizes, stylets, bougies, laryngeal mask airways of different sizes, video laryngo-scope (C-MAC) blades of different sizes, fiberoptic bronchoscope, 2 working suction apparatus, and an emergency tracheostomy trolley for management of the unexpected difficult airway.

COVID-19 is a major contributor to morbidity and mortality due to dyspnea, poor functional status, chest pain or tightness, hypercoagulability, endocrine abnormalities especially impaired glycemic control, etc. This, in addition to mucormycosis, makes the prognosis worse in these patients [26]. In our study 42 (73.7%) patients had a history of diabetes which was managed by administration of insulin perioperatively. Central venous catheters may be required peri-operatively for blood or blood product transfusions, for fluid replacement, inotropic or vasopressor support, and long-term infusion of amphotericin B [27]. We used Groshong® PICC catheter (4 and 5 Fr) in 47 patients and internal jugular venous cannulation in 7 patients. The use of systemic amphotericin B in the management of mucormycosis associated with COVID-19 has its distinct toxicities, the most important being nephrotoxicity. There are other side effects of amphotericin B such as hypokalaemia, hypomagnesemia, fever, dyspnea, shivering, and hypotension [28]. In our study, 14 patients had preoperative amphotericin B-induced nephrotoxicity.

The primary objective of surgical management is to debride all necrotic tissues. Our patients received both antifungal treatment and surgical treatment. The overall mortality rate of mucormycosis reported in a study of 929 patients was 54%, with disseminated, gastrointestinal, pulmonary, rhinocerebral, and renal infections having the highest mortality rates. Mortality rates in sino-nasal and rhinocerebral mucormycosis have been reported to be 16 and 62 percent, respectively [11]. The mortality rate of mucormycosis associated with COVID-19 is still unknown. In our study, mortality occurred in 7 (12.3%) of 57 patients during their hospital stay. Five (12.2%) of 41 patients with sinonasal mucormycosis (cerebral extension in 1 patient) expired.

Elevated D-dimer levels has been associated with increased risk of severe disease and mortality in COVID-19 patients. [29] Some previous studies found increased levels of D-dimer values in patients with COVID-19 associated mucormycosis [30,31]. In our study, we also found increased levels of pre-operative D-dimer levels in our patients and that patients who died had statistically increased D-dimer levels compared with discharged patients. Increased age is also considered a risk factor for mortality associated with COVID-19 associated mucormycosis [32]. We also found a statistically increased mortality in older patients.

We focused on airway difficulties related to mucormycosis related to COVID-19 in addition to procedural data and in-hospital mortality records. This is prime strength of our study as the literature on airway difficulty in patients with mucormycosis is sparse. Secondarily, there are only a fraction of studies showing records of mortality in patients with mucormycosis associated with COVID-19. Our article adds to existing literature related to this topic which can be instrumental in developing clincal guidelines and further study protocols.

Our study has some limitations. First, the study had a retrospective nature from a single center and was based on analysis of anesthesia and hospital records that may be subject to selection bias. Second, we used the video laryngoscope as a first-line tool for endotracheal intubation in accordance with the COVID-19 recommendations. Difficulties may be greater if a direct laryngoscope has been used as an tool for endotracheal intubation. Third, in our study we did not reported long-term follow-up of the discharged patients. At long-term follow-up, the mortality rate can be high. Fourth, the number of expired patients was comparatively small (7 patients) for statistical comparison with those who were discharged (50 patients).

Conclusion

In patients undergoing surgery for mucormycosis associated with the coronavirus disease, airway management was easy to slightly difficult in most patients. Perioperative complications related to airways, the effect of COVID-19 and diabetes mellitus, systemic effects of amphotericin B can be reduced by taking timely and precautionary measures.

Author's contributions

- Prashant Sirohiya was involved in the conceptualization of the study, study design, patient care, data collection, statistical analysis, and in writing the first draft of the manuscript and agrees to be the guarantor of the manuscript taking responsibility for the integrity of the work as a whole, from inception to published article
- Saurabh Vig and Jitendra Meena were involved in the conceptualization of the study, study design, patient care, data collection, statistical analysis, and critique of the manuscript
- Tanmay Mathur, Gitartha Goswami, and Raghav Gupta were involved in the conceptualization of the study, study design, patient care, and in writing the first draft of the manuscript

- Smriti Panda, Abhilash Konkimalla, and Dheeraj Kondamudi was involved in the conceptualization of the study, study design, patient care, and in the critique of the manuscript
- Nishkarsh Gupta, Brajesh Kumar Ratre, Ram Singh, Balbir Kumar, Anuja Pandit, were involved in study design, patient care, and in the critique of the manuscript
- Kapil Sikka and Alok Thakar were involved in the conceptualization of the study and final critique and review of the manuscript
- Sushma Bhatnagar was involved in the conceptualization of the study, convening of the working group, study design, patient care, in final critique and review of the manuscript and agrees to be the guarantor of the manuscript taking responsibility for the integrity of the work as a whole, from inception to published article

Declaration of Competing Interest

The authors have no conflict of interest.

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References

- Patel A, Kaur H, Xess I, Michael JS, Savio J, Rudramurthy S, et al. A multicentre observational study on the epidemiology, risk factors, management and outcomes of mucormycosis in India. Clin Microbiol Infect 2020;26:944. e9-944.e15. doi: 10.1016/j.cmi.2019.11.021.
- [2] Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. J Fungi 2019;5:26. doi: 10.3390/jof5010026.
- 3] Black fungus: india reports nearly 9,000 cases of rare infection. BBC News 2021.
- [4] Elavarasi A, Sagiraju HKR, Garg RK, Ratre B, Sirohiya P, Gupta N, et al. Clinical features, demography, and predictors of outcomes of SARS-CoV-2 infection at a tertiary care hospital in India: a cohort study. Lung India Off Organ Indian Chest Soc 2022;39:16–26. doi: 10.4103/lungindia.lungindia_493_21.
- [5] Malhotra HS, Gupta P, Mehrotra D, Dandu H, Kohli N, Verma V, et al. COVID-19 associated mucormycosis: staging and management recommendations (Report of a multi-disciplinary expert committee). J Oral Biol Craniofacial Res 2021;11:569– 80. doi: 10.1016/j.jobcr.2021.08.001.
- [6] Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: an update. J Fungi 2020;6:265. doi: 10.3390/jof6040265.
- [7] Anesthetic management of rhinoorbitocerebral mucormycosis; Focus on challenges PubMed n.d. https://pubmed.ncbi.nlm.nih.gov/31399350/(accessed July 21, 2021).
- [8] Eckmann DM, Seligman I, Cote CJ, Hussong JW. Mucormycosis supraglottitis on induction of anesthesia in an immunocompromised host. Anesth Analg 1998;86:729–30. doi: 10.1097/0000539-199804000-00010.

- [9] Malhotra N, Bajwa SS, Joshi M, Mehdiratta L, Kurdi M. Second wave of COVID-19 pandemic and the surge of mucormycosis: lessons learnt and future preparedness: indian society of anaesthesiologists (ISA National) advisory and position statement. Indian J Anaesth 2021;65:427. doi: 10.4103/ija.ija_520_21.
- [10] Laniado-Laborín R, MN Cabrales-Vargas. Amphotericin B: side effects and toxicity. Rev Iberoam Micol 2009;26:223-7. doi: 10.1016/j.riam.2009.06.003.
- [11] Mucormycosis Statistics | Mucormycosis | Fungal Diseases | CDC 2020. https://www.
- cdc.gov/fungal/diseases/mucormycosis/statistics.html (accessed July 21, 2021). [12] Fan J, Jiang Y, Hu K, Chen X, Xu Q, Qi Y, et al. Barriers to using personal protective equipment by healthcare staff during the COVID-19 outbreak in China. Medicine (Baltimore) 2020;99:e23310. doi: 10.1097/MD.00000000023310.
- [13] Elavarasi A, Sagiraju HKR, Garg RK, Ratre B, Sirohiya P, Gupta N, et al. Clinical features, demography and predictors of outcomes of SARS-CoV-2 infection in a tertiary care hospital in India-A cohort study. Infectious Diseases (except HIV/AIDS) 2021. doi: 10.1101/2021.08.10.21261855
- [14] El-Ganzouri AR, McCarthy RJ, Tuman KJ, Tanck EN, Ivankovich AD. Preoperative airway assessment: predictive value of a multivariate risk index. Anesth Analg 1996;82:1197-204.
- [15] Mi Mouri, Krishnan S, Maani CV. Airway assessment. StatPearls, Treasure Island FL): StatPearls Publishing; 2021.
- De Jong A, Pardo E, Rolle A, Bodin-Lario S, Pouzeratte Y, Jaber S. Airway manage-[16] ment for COVID-19: a move towards universal videolaryngoscope? Lancet Respir Med 2020;8:555. doi: 10.1016/S2213-2600(20)30221-6.
- [17] Cook TM, El-Boghdadly K, McGuire B, McNarry AF, Patel A, Higgs A. Consensus guidelines for managing the airway in patients with COVID-19: guidelines from the difficult airway society, the association of anaesthetists the intensive care society, the faculty of intensive care medicine and the royal college of anaesthetists. Anaesthesia 2020;75:785-99. doi: 10.1111/anae.15054.
- Adnet F, Borron SW, Racine SX, Clemessy J-L, Fournier J-L, Plaisance P, et al. The Intubation Difficulty Scale (IDS). Anesthesiology 1997;87:1290-7. doi: 10.1097/ 00000542-199712000-00005.
- [19] Angadi SP, Frerk C. Videolaryngoscopy and Cormack and Lehane grading. Anaesthesia 2011;66:628-9. doi: 10.1111/j.1365-2044.2011.06777.x.
- [20] Seo S-H, Lee J-G, Yu S-B, Kim D-S, Ryu S-J, Kim K-H. Predictors of difficult intubation defined by the intubation difficulty scale (IDS): predictive value of 7 airway assessment factors. Korean J Anesthesiol 2012;63:491-7. doi: 10.4097/kjae.2012. 63.6.491

- [21] O'Loughlin EJ, Swann AD, English JD, Ramadas R. Accuracy, intra- and inter-rater reliability of three scoring systems for the glottic view at videolaryngoscopy. Anaesthesia 2017;72:835-9. doi: 10.1111/anae.13837.
- [22] Doyle DJ, Goyal A, Bansal P, Garmon EH. American society of anesthesiologists classification StatPearls Treasure Island (FL): StatPearls Publishing: 2021
- [23] CLINICAL GUIDANCE FOR MANAGEMENT OF ADULT COVID-19 PATIENTS | AIIMS Covid Information Portal n.d. https://covid.aiims.edu/clinical-guidance-for-management-of-adult-covid-19-patients/(accessed August 26, 2021).
- Karaaslan E. Anesthetic management of rhinoorbitocerebral mucormycosis; Focus [24] on challenges. J Mycol Medicale 2019;29:219-22. doi: 10.1016/j.mycmed.2019. 07 001
- [25] 2019-02-11-aide-memoire-for-levels-of-personal-protective-equipment-ppefor-healthcare-workers-for-patient-care. 2022 pdf n.d.
- [26] Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. Cureus 2022;12:e10726. n.d. doi: 10.7759/cureus.10726.
- [27] Scoppettuolo G, Biasucci DG, Pittiruti M. Vascular access in COVID-19 patients: smart decisions for maximal safety. J Vasc Access 2020;21:408-10. doi: 10.1177 129729820923935
- [28] Kulkarni P.K., Reddy N.B., Shrinivas B., Takkalki V.V. Anesthetic considerations in the management of mucormycosis 2015. https://doi.org/10.4103/2230-8598.165986.
- Shah S, Shah K, Patel SB, Patel FS, Osman M, Velagapudi P, et al. Elevated D-dimer [29] levels are associated with increased risk of mortality in coronavirus disease 2019: a systematic review and meta-analysis. Cardiol Rev 2020;28:295-302. doi: 10.1097/CRD.000000000000330.
- [30] Dravid A, Kashiva R, Khan Z, Bande B, Memon D, Kodre A, et al. Epidemiology, clinical presentation and management of COVID-19 associated mucormycosis: a single centre experience from Pune, Western India. Mycoses 2022;65:526-40. doi: 10.1111/myc.13435
- [31] Goddanti N, Reddy YM, Kumar MK, Rajesh M, Reddy LS. Role of COVID 19 inflammatory markers in rhino-orbito-cerebral mucormycosis: a case study in predisposed patients at a designated nodal centre. Indian J Otolaryngol Head Neck Surg Off Publ Assoc Otolaryngol India 2021:1–7. doi: 10.1007/s12070-021-02970-6.
- [32] Patel A, Agarwal R, Rudramurthy SM, Shevkani M, Xess I, Sharma R, et al. Multicenter epidemiologic study of coronavirus disease-associated mucormycosis, India. Emerging Infect Dis J - CDC 2021;Volume 27(Number 9) n.d. doi: 10.3201/ eid2709.210934