Original Article

Post-COVID-19 mucormycosis: A prospective, observational study in patients undergoing surgical treatment

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Abstract

Background and Aims: Post the second wave of COVID-19 in India, our institute became a dedicated center for managing COVID-19-associated mucormycosis (CAM), but there was a paucity of data regarding perioperative considerations in these patients. The objectives of present study was to describe the preoperative clinical profile, the perioperative complications and outcome of CAM patients undergoing urgent surgical debridement.

Material and Methods: This prospective observational study was conducted on CAM patients presenting for surgical debridement from July to September 2021. During preoperative visits, evaluation of extent of disease, any side effects of ongoing medical management and post-COVID-19 systemic sequalae were done. The details of anaesthetic management of these patients including airway management, intraoperative haemodynamic complications and need for perioperative blood transfusion were noted.

Results: One hundred twenty patients underwent surgical debridement; functional endoscopic sinus surgery (FESS) was carried out in 63% of patients, FESS with orbital exenteration in 17.5%, and maxillectomy in 12.5%. Diabetes mellitus was found in 70.8% and post-COVID new onset hyperglycemia in 29.1% of patients. Moderate-to-severe decline in post-COVID functional status (PCFS) scale was observed in 73.2% of patients, but with optimization, only 5.8% required ICU management. The concern during airway management was primarily difficulty in mask ventilation (17.5%). Intraoperatively, hemodynamic adverse events responded to conventional treatment for hypotension, judicious use of fluids and blood transfusion. Perioperatively, 10.8% of patients required blood transfusion and 4.2% of patients did not survive. Non-surviving patients were older, with a more aggressive involvement of CAM, and had comorbidities and a greater decline in functional capacity.

Conclusion: A majority of patients reported a moderate-to-severe decline in PCFS that required a preoperative multisystem optimization and a tailored anesthetic approach for a successful perioperative outcome.

Keywords: Anesthesia, COVID-19, debridement, mucormycosis, perioperative, surgical

Introduction

Concomitant with the steep surge of coronavirus disease 2019 (COVID-19) cases in May–June 2021, the second wave in India witnessed an unprecedented rise in COVID-19-associated mucormycosis (CAM) cases. More than 47,000 CAM cases were reported in three months from May to July 2021 and India accounted for over 70% of global cases.[1,2] Rhino-orbital-cerebral mucormycosis (ROCM) is caused by ubiquitous environmental molds belonging to species Mucorales. It is classically observed in patients with immunosuppressive conditions such as uncontrolled diabetes mellitus, underlying malignant diseases, neutropenia and corticosteroid therapy.[3] Several hypotheses have been proposed to explain the emergence of CAM in patients

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recovering from COVID-19. These include weakening of immunity due to viral infection, steroid treatment for mitigating cytokine storm syndrome, dysregulation of glucose homeostasis, zinc supplementation, iron overload, use of inhalational medications and industrial grade oxygen.[4] Prompt administration of antifungal medications and urgent surgical debridement is the cornerstone to reduce high mortality of patients. Previous reports have suggested that perioperatively, mucormycosis patients have increased mortality and morbidity due to coexistence of immunosuppression, sepsis, multiple organ involvement and side effects of antifungal drugs. Under anesthesia, patients may also experience difficulty in mask ventilation and endotracheal intubation as a result of edema resulting from fungal debris.[5,6]

The anesthetic management of CAM patients is challenging since patients may have multisystemic effect of SARS-CoV-2, known as post-COVID-19 sequalae. While perioperative COVID-19 infection is reported to have enhanced mortality,[7] there is paucity of evidence in literature on post-COVID sequalae having effects on perioperative management, morbidity and mortality of CAM patients who undergo urgent surgical debridement. The present study was undertaken to observe and document the preoperative clinical profile, the perioperative complications and outcome of CAM patients undergoing urgent surgical debridement.

Material and Methods

After approval from the institutional ethical committee (IEC), this prospective observational study was conducted in 120 adult patients operated from 11 July 2021 to 15 September 2021. Amid rising cases of CAM, two operation theaters at our center that had facilities for endoscopic, open or combined surgical debridement were dedicated for CAM cases.

Patients presenting for urgent surgical debridement of ROCM, who had recovered from COVID-19 infection were included in the study. Appropriate written informed consent for participation was obtained from all patients undergoing surgery during the study period.

Pre-anesthetic check-up (PAC) of all patients was conducted using institutional protocol, which, apart from the usual assessment, consisted of evaluation of extent of disease, any side effects of ongoing medical management and post-COVID-19 systemic sequalae. The details which were obtained included; the clinical course during active COVID-19 infection (duration, hospitalization, oxygen requirement, admission to intensive care unit (ICU) or high dependency unit (HDU), treatment received), any features of systemic post-COVID sequelae. The post-COVID sequelae that were assessed included persisting general well-being and constitutional symptoms, assessment of functional capacity, pulmonary abnormalities using chest X-ray and arterial blood gas analysis, and 12 lead electrocardiogram and two-dimensional echocardiograph (if deemed necessary by the attending anesthesiologist) for any cardiovascular disorder.

The patient's ability to perform activities of daily living interpreted as a functional capacity assessment was done using post-COVID-19 functional status (PCFS) scale and six-minute walk test (6MWT).[8,9] The American Thoracic Society guidelines were followed for the 6MWT.[9] Several authors have reported that 6MWT to be useful in post-COVID-19 follow-up as it correlates with severity of acute disease and functional impairment in chronic phase of COVID-19.[10]

Laboratory investigations were decided at the discretion of the attending anesthesiologist. Optimal glycemic control (blood sugar values less than 200 mg/dl), correction of amphotericin-related hypokalemia (serum potassium values more than 3.5 mmol/l), preoperative improvement of pulmonary function with nebulization, incentive spirometry and antibiotic cover (if indicated) were ensured. All patients underwent surgical procedure under general anesthesia with endotracheal intubation and controlled ventilation by a qualified anesthesiologist with more than three years of experience. Patients were premedicated with fentanyl, midazolam and glycopyrrolate. After preoxygenation for three minutes, the patients were induced with intravenous propofol or etomidate (where indicated), and after confirming mask ventilation, muscle relaxation was achieved with vecuronium or atracurium (where indicated). Para-oxygenation using nasal prongs at 15 L/min oxygen flow rate was routinely provided while intubating the trachea, as most of these patients had a pre-operative PaO_2 between 60–70 mmHg on room air. C-MAC® Video-laryngoscope (Karl Storz, Tuttlingen, Germany) was the preferred laryngoscope for laryngoscopy and intubation. Certain patients with a significantly reduced mouth opening (due to swelling, pain, deformity) were intubated by an awake fiberoptic approach.

Any adverse events relating to airway management were recorded. The following definitions were used for airway-related events:

Difficult mask ventilation: Grade 3 and/or grade 4 of Hans classification for ease of mask ventilation.[11]

Difficult laryngoscopy: Inability to view glottic inlet using standard Macintosh blade of C-MAC® video-laryngoscope.

Difficult intubation: Placement of endotracheal tube requiring more than two attempts with standard Macintosh blade or necessitating use of hyper-angulated blade of C-MAC® video-laryngoscope.

Other airway complications such as laryngospasm, significant airway obstruction requiring immediate intervention at the time of intubation/extubation were also noted.

After intubation and confirming tube placement, proper fixation of the tube was done to the left angle of the mouth (as per the surgical requirement). Oropharyngeal pack was placed with the help of laryngoscopy. Anesthesia was maintained with nitrous oxide (N_2O) and isoflurane/sevoflurane/desflurane in oxygen and patient was handed over to the surgeon. Intraoperatively, we monitored the electrocardiogram (ECG), pulse rate, non-invasive blood pressure, end-tidal carbon dioxide ($EtCO_2$), temperature and blood loss.

To decrease intraoperative blood loss, hypotensive anesthesia was provided to patients having no contraindications. Patients with coronary artery disease, uncontrolled hypertension, recent history of myocardial infarction (MI) or cerebrovascular accident (CVA), anemia, patients requiring oxygen supplementation preoperatively and the elderly were not considered for intraoperative deliberate hypotension. Intraoperative dexmedetomidine infusion or nitroglycerine infusion appropriate to the patient's hemodynamic profile were chosen for hypotensive anaesthesia. As the majority of patients belonged to the American Society of Anesthesiologists physical status III and IV (ASA PS III/IV), we used modified hypotensive anesthesia, maintaining the patient's systolic blood pressure 85–90 mmHg and a mean arterial pressure (MAP) of 60–70 mmHg in order to enhance perfusion of tissue and reduce complications related to hypotension.[12] Around 20–30 minutes after induction of anesthesia, suitability of patient to receive deliberate hypotension was decided by the attending anesthesiologist based on preoperative status and hemodynamic parameters. Invasive arterial blood pressure (IBP) monitoring was done in those receiving hypotensive anesthesia and those with significant coexisting diseases.

Occurrence of any intraoperative complication(s) was recorded by the study team. It included hemodynamic, pulmonary and renal complications, and excessive blood loss or any other surgery related complications.

The intraoperative hemodynamic complications (Hypotension, Hypertension, Bradycardia, Tachycardia, arrythmias or myocardial ischemia) and pulmonary complications such as hypoxia, bronchospasm, pulmonary embolism, pulmonary edema or any other complication(s) leading to respiratory failure were noted.

The intraoperative adverse events were graded according to Classification of Intraoperative Complications (CLASSIC) proposed by Rosenthal *et al.*[13] in which grade 1 and 2 were termed as low grade and 3 and 4 as high-grade complications.

Intraoperatively, dexamethasone was administered to patients who required multiple attempts during laryngoscopy and intubation or to patients in whom extensive surgical manipulations of the maxilla or oral cavity were observed. At the end of the surgery, after ensuring complete hemostasis, oral pack was removed, anesthetic agents discontinued, patient awakened and the trachea was extubated after giving neuromuscular reversal agents neostigmine and glycopyrrolate. Any significant events such as postoperative oxygen requirement, hemodynamic instability and ICU admission were noted. The patients were followed up during their hospital stay and occurrence of any postoperative complications and their outcome was recorded.

Statistical analysis

We used the Statistical Package for the Social Science (SPSS) version 24.0 software for the analysis. Descriptive statistics is used to describe patient demographics, type of surgery, incidence of intraoperative and postoperative complications. Categorical variables are presented in number and percentage (%) and continuous variables are presented as mean ± standard deviation (SD). *P* value of less than 0.05 is taken as significant at 95% confidence interval (CI). Logistic regression analysis was carried out to ascertain the relationship between the occurrence of intraoperative and postoperative complications and perioperative anesthesia, surgery and patient-related factors.

Results

A total of 120 patients suffering from mucormycosis underwent urgent surgical debridement under general anesthesia during the study period. The most common type of mucormycosis observed was rhino-orbital mucormycosis (65%) followed by rhino-cerebral mucormycosis (25%). The surgical procedures undertaken were functional endoscopic sinus surgery (FESS) in 63% of patents, FESS with orbital exenteration in 17.5%, FESS with palatal excision in 3.33%, and maxillectomy in 12.5%.

More than half of the patients belonged to the age group of 40–60 years (53.3%) and the majority were males (71.8%). As shown in Figure 1, 70.8% were known to have pre-existing diabetes while 29.1% were diagnosed to have new onset

hyperglycemia (post-COVID-19 patients with no prior history of diabetes having blood glucose levels of more than 200 mg/dl) following COVID-19 infection (total 99.9%). Preoperatively, 64.1% of patients with dysglycemia were on treatment with insulin injection. History of recent (within last 30 days) major adverse cardiovascular events were found in 4.1% of patients (a total of five patients; four with recent history of cerebrovascular accident and one with recent myocardial infarction). A small proportion of patients had autoimmune diseases and history of taking immunosuppressants (1.6%). During acute phase of COVID-19 infection, 57.1% of patients remained in home isolation, and 42.9% required hospitalization. Out of this, 23% required oxygen administration through low-flow oxygen delivery devices in hospital, whereas 10% of patients were hospitalized but they did not need oxygen supplementation, and ICU admission was required with respiratory support in 7.5% of patients. Around 72% took steroids during COVID illness with mean duration of treatment being 8.6 ± 6.3 days [Figure 2a and b].

The mean duration of time between COVID-19 positivity and surgical debridement for mucormycosis in the present cohort of patients was 44.8 ± 17 days. Persistence of post-COVID fatigue (subjective complaints of loss of energy or generalized sense of exhaustion or persistent tiredness despite good sleep or rest that started after the patient contracted COVID-19 infection) was reported by 64% of the study participants, and 25% of patients complained of having post-COVID breathlessness and headache. A moderate limitation of functional capacity was found in 46.6% of the patients, whereas 26.6% reported a severe limitation. The 6MWT was negative in 74.2% of patients, but it was found to be positive in 12.5% of patients and 13.3% could not perform the test. Preoperative chest X-ray abnormalities such as ground glass haze, blunting of costophrenic angles, consolidation, etc., was reported in 79% of these patients [Table 1]. However, baseline PaO_2 on arterial blood gas (ABG) analysis ranged between 60 and 70 mmHg [Table 2]. ECG abnormalities were noted in 3.3% of patients.

Table 1: Preoperative profile of patients undergoing surgical debridement

Preoperative characteristics	Percentage (%)	Number (*n*)
Post-COVID-19 symptoms		
Fatigue	64.2	77
Breathlessness	25.8	31
Headache	25.8	31
Cough	2.5	3
Others	1.7	2
Post-COVID-19 functional status (PCFS) scale		
Negligible functional limitations	2.5	
Slight functional limitations	29.1	
Moderate functional limitations	41.6	
Severe functional limitations	26.6	
Six-minute walk test		
Positive	12.5	15
Negative	74.2	89
Not able to perform	13.3	16

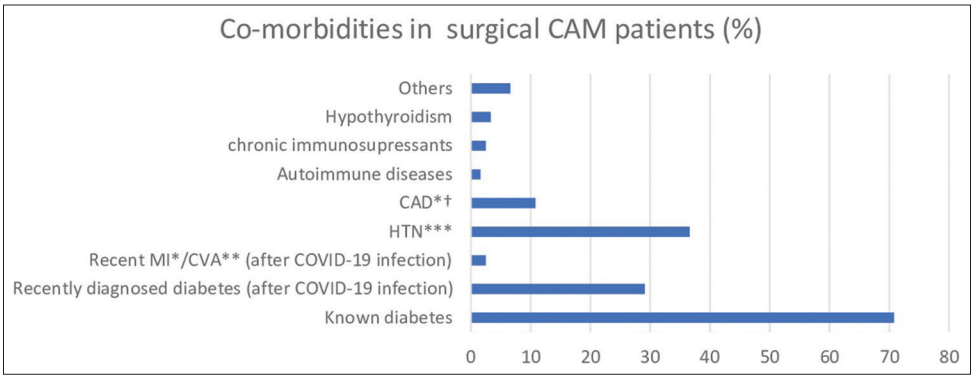

Figure 1: Comorbidities in CAM patients presenting for surgical debridement

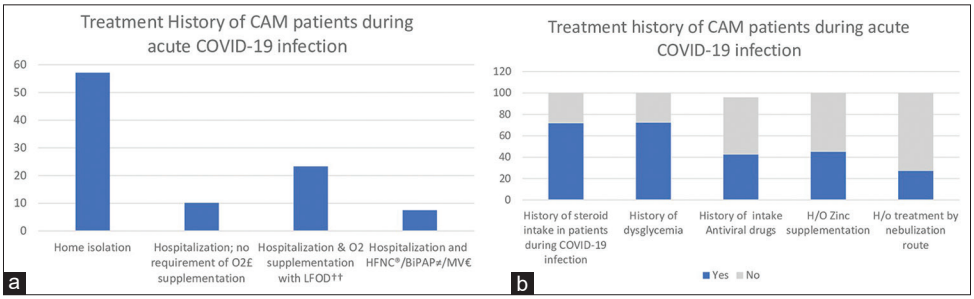

Figure 2: (a and b) Treatment history of patients during acute COVID-19 infection

During airway management, the difficulty in mask ventilation was noted in 17.5% of patients, whereas difficult intubation was observed in 5.8%. Only 2.5% of these patients needed awake fiberoptic-guided intubation. The most common intraoperative complication observed was hemodynamic instability (hypotension) in 65% of cases [Table 3]. The average blood loss intraoperatively was 404 ± 233 ml. In 12.5% of patients, intraoperative blood loss of more than 500 ml was noted and 10.8% required perioperative blood transfusion. Intraoperative deliberate hypotension was performed in 55% of patients. In 45% of patients (13 patients of CAD, 3 patients with recent MI/CVA, 25 patients aged more than 60 years and in 13 patients after blood loss more than 500 ml), it was not performed intraoperatively. Three patients sustained grade 3 intraoperative event (one patient had intraoperative massive blood loss of 2 liters, two developed laryngospasms during extubation). The mean surgical duration was 160.5 ± 67.2 minutes. Postoperative ICU admission was needed in 5.8% of these patients and respiratory failure (defined as PaO_2/FiO_2 <300 on ABG analysis) was noted in 3.3% of these patients. At the time of concluding the present study, 88.3% of the patients were discharged home while 4.2% expired, and 7.5% remained admitted in the hospital. The mean duration of hospital stay for these patients was 35 ± 12.6 days.

Table 2: Preoperative investigations of patients undergoing surgical debridement for CAM

Parameters	Mean±standard deviation
Hemoglobin (gm/dl)	10.6±1.2
TLC **(per microliter of blood)	8315±3263
Platelet count (lakhs per unit volume)	2.4±0.9
HbA1C† (%)	10.4±2.3
Blood urea (mg/dl)	26±18.3
Serum creatinine (mg/dl)	0.7±0.5
Serum sodium (mEq/l)	135.5±3.1
Serum potassium (mEq/l)	3.9±0.6
Serum magnesium (mg/dl)	1.50.3
D- dimer (ng/ml)	495±229.6
Lactate dehydrogenase (U/l)	269.7±176.5
C reactive protein (mg/l)	84.7±124.4
Serum bilirubin (mg/dl)	0.5±0.2
Aspartate aminotransferase (U/l)	22.4±56
Alanine aminotransferase (U/l)	31.8±27
Alkaline phosphatase (U/l)	78.1±93.8
Partial pressure of oxygen on ABG* on room air (mm Hg)	87±17.6

**arterial blood gas analysis, **total leucocyte count, †Glycosylated hemoglobin*

Compared to survivors, the patients who did not survive were observed to be older, with higher points on PCFS indicating they suffered from greater limitation of functional capacity. The intraoperative blood loss was found to be greater in patients who did not survive (394.8 ± 183.5 ml vs 630 ± 771.8; $P = 0.03$) and there was a significantly higher preoperative blood urea and serum creatinine levels observed in them ($P = 0.00$). Additionally, lower platelet counts, higher prothrombin time and international normalized ratio, higher D-dimer and lactate dehydrogenase (LDH) levels were observed in them [Table 4].

Discussion

The present study described the clinical characteristics of patients with CAM presenting for surgical debridement and complications arising in perioperative period in a single tertiary care health center. We found CAM to be predominantly affecting males, with more than half of the patients belonging to the age group 40–60 years. The most common comorbid condition was diabetes mellitus with 70.8% of patients having pre-existing disease while 29.1% were diagnosed to have new onset hyperglycemia following COVID-19 infection. This is in concordance with previous studies on CAM from India.[14,15]

In post-COVID-19 patients, there can be short-term and long-term deleterious multisystem sequalae leading

Table 3: Perioperative complications encountered in patients

Perioperative complications		Percentage (%) of patients	Number (*n*)
Difficult airway	Difficult mask ventilation	17.5	21
	Difficult Laryngoscopy and intubation	5.8	7
	Fiberoptic guided intubation	2.5	3
Hemodynamic instability	Required inotropes	2.5	3
	Did not require inotropes	62.5	75
Intraoperative bronchospasm		1.6	2
Blood loss more than 500 ml		12.5	15
Blood transfusion		10.8	13
Patient requiring repeat surgery		10.8	13
Postoperative ICU® admission		5.8	7
Postoperative respiratory failure		3.3	4

®Intensive care unit

Table 4: Comparison between survivors and non-surviving patients who underwent surgery

	Survivors	Non-survivors	*P*
Age (in years)	49±11.4	60±9.8	0.032
BMI*(Kg/m^2)	25.5±2.5	23.6±2.3	0.088
Time elapsed since COVID positive (in days)	44.8±17.4	44.4±12.5	0.95
Duration of onset of mucormycosis (in days)	15.1±15.9	20.6±9.1	0.44
Duration of steroid treatment during acute COVID-19 infection (in days)	8.8±6.5	8.6±4.6	0.93
Functional status	2.8±0.7	3.8±0.44	0.009
Blood loss (in ml)	394.8±183.5	630±771.8	0.03
IV® fluids given (in ml)	1715.5±357.1	1530±761.2	0.28
Duration of surgery (in minutes)	163.16±65.7	138±116.8	0.42
Days of hospitalization	35.7±12.1	24.8±8.9	0.05
Hemoglobin (gm/dl)	10.6±1.2	10.5±1.66	0.77
TLC** (per microliter)	8406.22±3308.61	8054±4417.97	0.81
Platelet count (lakh per unit volume)	2.48±0.96	1.4±0.8	0.02
HBA1C°° (%)	10.5±2.3	8.7±1.1	0.10
Blood urea (mg/dl)	24±13.8	64.2±53. 0	0.00
Creatinine (mg/dl)	0.7±0.3	2.0±1.5	0.00
Serum bilirubin (mg/dl)	0.5±0.2	0.5±0.1	0.88
Aspartate aminotransferase (units/l)	46.1±58.7	32.5±11.1	0.64
Alanine aminotransferase (units/l)	33.1±27.9	24±9.3	0.51
Alkaline phosphatase (units/l)	125.6±96.8	153±111.9	0.58
Prothrombin time (seconds)	12±1.7	13.9±3.4	0.05
INR†	1.0±0.13	1.1±0.21	0.02
Sodium (mEq/l)	135.7±3.0	133.6±1.3	0.11
Potassium (mEq/l)	4±0.6	3.6±0.5	0.19
Magnesium (mg/dl)	1.5±0.4	1.3±0.4	0.28
D-dimer (ng/ml)	485.0±218.4	785.6±362.7	0.03
Lactate dehydrogenase (U/L)	242.18±96.4	643.33±508.0	0.00
C reactive protein (mg/L)	81.9±128.3	69.6±96.6	0.89

**Body mass index, ®Intravenous fluids, ** Total leukocyte count, °°Glycosylated hemoglobin, †International normalized ratio*

to a challenging perioperative anesthetic management. The sequalae include chronic pulmonary dysfunction, myocardial involvement, musculoskeletal deconditioning and neuropsychiatric symptoms. In patients undergoing surgery amid a background of these physiological perturbances, there is probability of increased risk of adverse outcomes. It has been recommended to delay elective surgery for at least seven weeks following COVID-19 infection, as increased risk of postoperative pulmonary complications and mortality have been found in patients undergoing surgery within six weeks of COVID-19 infection. Furthermore, increased mortality was also observed in patients who were still symptomatic seven or more weeks after acquiring infection.[16]

In the present cohort, mean duration elapsed between COVID-19 infection and surgery was 44.8 ± 17 days. Moderate-to-severe reduced functional capacity was observed in 73.2% of patients. A majority of patients reporting with reduced PCFS were optimized perioperatively with multidisciplinary approach, and thereby postoperative pulmonary complications were seen in only two patients. In contrast, patients undergoing surgery during active COVID-19 infection had a much higher rate of perioperative complications despite adequate optimization.[7]

Guler *et al.*[17] found that in mild-to-moderate COVID-19 illness, overall average pulmonary function returned to normal four months after recovery, and in patients who had severe COVID illness, an impaired diffusion capacity, reduced oxygen saturation and a reduced physical performance was found beyond four months after recovery. Since our study population reported treatment within two months of their recovery period, the pulmonary function needed to be optimized preoperatively to reduce the risk of postoperative pulmonary complications. It was observed by Rinaldo *et al.*[18] that muscle deconditioning due to prolonged hospital stay, steroid intake, and direct effect of viral load on muscles led to an impaired oxygen extraction and impaired exercise response in COVID-19 survivors, which added to the respiratory morbidity in our patients.

Beyond 30 days after infection, patients with COVID-19 are at increased risk of a variety of cardiovascular (CV) diseases. At 12 months post-COVID-19 compared with contemporary

control group, for every 1000 people, there is 23.48 incidents of major adverse cardiovascular event (MACE), 19.86 incidents of dysrhythmia, 12.72 incidents of other CV disorder including 11.61 incidents of heart failure, 9.88 incidents of thromboembolic diseases, 7.28 incidents of ischemic heart disease, 5.48 incidents of cerebrovascular disorders and 1.23 incidents of inflammatory diseases of the heart.[19] It is therefore crucial to rule out the possibility of CV diseases in patients of CAM. In the present cohort, we encountered five patients with MACE: four with recent MACE and one with recent MI. As there is paucity of data for preoperative cardiac workup of post-COVID-19 patients, we limited CV workup of patients to clinical examination, 12 lead ECG and chest-X ray. Additional diagnostic workup were left at the discretion of the attending anesthesiologist.

In our study, the most common intraoperative complication observed was hemodynamic alterations in 65% of patients who required urgent intervention by the anesthesiologist. The predominant hemodynamic concerns observed were hypotension and tachycardia. Most of the patients with hypotension responded to conventional protocol of fluid bolus and titrating the dose of anesthetic agents; and only three patients required ionotropic support (2.5% of the study population). In our study, the CAM patients appeared to be sensitive to the vasodilatory effect of anesthetic agents which guided us to use them judiciously. Post-COVID-19 myocarditis occurring independent of pre-existing conditions and underlying aggressive fungal infection causing invasion of endothelial cells of blood vessels could be possible explanations for this observation.[20,21]

Patients undergoing surgical debridement of mucormycosis could develop persistent blood ooze from surgical site because of blood vessel invasion by the fungi and widespread inflammation.[22] We observed that intraoperatively, 12.5% of the patients had blood loss exceeding 500 ml, and perioperatively, 10.8% of them required transfusion. Therefore, in CAM patients with involvement of facial structures, paranasal sinus, orbits, undergoing surgical debridement, extreme caution is warranted if hypotensive anesthesia is desired by surgeons keeping the above factors in mind.

The airway management in mucormycosis patients could be problematic due to facial swelling and pain. We encountered difficult mask ventilation to be the most common airway-associated problem in these patients. The extension of infection of the oral cavity in some patients also led to tissue necrosis of palate, resulting in palatal perforation. The pain associated with maxillofacial tissue invasion by mucor also caused a reduced mouth opening in some patients. In our study, the C- MAC® video-laryngoscope (Standard Macintosh blade in most of cases) was used in majority of patients for securing the airway as it allowed careful placement of ETT (Endotracheal Tube) while visualizing its trajectory from oral cavity till glottis and reducing chances of failed intubations in these patients.

Another concern faced during the surge of mucormycosis case during second wave of COVID-19 pandemic was acute shortage of appropriate antifungal medicine, particularly the less toxic liposomal Amphotericin B. As a result, many patients at our centre received amphotericin B deoxycholate which is more nephrotoxic compared to the liposomal preparation. Patients of ROCM who do not receive any antifungal treatment have mortality rate as high as 80%, and even after treatment, there could be 40–50% mortality.[23] A recent study found a combined similar mortality rate of 45.7% at 12 weeks in both CAM and non-CAM groups. Older age, ICU admission and pulmonary or brain involvement were independently associated with a higher risk of death, whereas sequential treatment with a combination of antifungal drugs was independently linked to better survival.[14] Another study concluded that early aggressive debridement of infected tissues in mucormycosis led to improved patient outcome.[24] Our patients were all aggressively optimised and taken up early on a semi-emergency basis, we had a successful outcome in the majority of our patients.

At the end of our study, we observed that majority (88%) of our patients were discharged, 4.2% had expired whereas 7.5% were still admitted in hospital. The patients who did not survive, were older in age, had decreased functional status and a significantly greater intraoperative blood loss. Kidney function tests were deranged significantly in the patients who did not survive. Serum LDH levels, D-dimer, platelet count and prothrombin time were noted to be higher in patients who had expired. Higher D-dimer values and prothrombin time may have led to unrecognized perioperative thrombotic complications resulting in a higher mortality in this group. Fazeli *et al.*[25] observed that increased serum titers of LDH and D-dimer values might be indicative of extensive tissue involvement by invasive fungi, and coagulopathy could be related to disseminated intravascular coagulation or sepsis.

The limitations of the current study are that a limited number of patients from a single center have been included. Data from other parts of the world involving a larger number of patients are needed for supporting the results of the present study. Secondly, a majority of patients in our cohort underwent FESS which is relatively less invasive compared to other surgical procedures undertaken for debridement of mucormycosis; hence the results should be carefully extrapolated to CAM

patients undergoing surgery. Another limitation is that we used ASA-PS for risk estimation of patients undergoing urgent surgical procedure which has reduced accuracy in certain patient groups. More consistent discrimination of patient outcome is reported with risk assessment tools such as APACHE (Acute Physiology and Chronic Health Evaluation) II and ACS NSQIP (American College of Surgeons National Surgical Quality Improvement Program) universal surgical risk calculator, but they are time consuming with APACHE II used mainly in critically ill patients. Also, there is a lack of external validation for NSQIP tool which is developed based on data from American patients.[26]

As the aim of our study was to provide comprehensive perioperative patient profile and complications in CAM patients undergoing urgent surgical procedure, limited details of hemodynamic and pulmonary complications were included.

Conclusion

The surgical CAM patients constitute a group of high-risk patients having underlying comorbidities and reduced functional capacity. As early surgical debridement is vital for improving patient prognosis, anesthesiologists should be aware of anesthetic concerns in this group of patients. The preoperative assessment should be aimed to identify systemic post-COVID-19 sequalae, existing comorbidities and complications associated with mucormycosis and its treatment. Perioperative management requires a tailored anesthetic approach as these patients have multiple challenges which include difficult airway management, propensity for intraoperative hemodynamic alterations, significant blood loss and reduced pulmonary reserves. There should be judicious use of intraoperative hypotensive anesthesia. Postoperatively, these patients might need vigilant monitoring due to overall poor functional status. Their hospital stay is frequently longer than 30 days, partly due to the requirement to continue amphotericin therapy and partly owing to the increased postoperative morbidity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Ethical approval

Ethics Committee: Institutional Ethics Committee, Maulana Azad Medical College and associated Hospitals.

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Conflicts of interest

There are no conflicts of interest.

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