Clinical Communication

The perioperative anaesthetic management and outcomes of COVID-19 associated mucormycosis patients

INTRODUCTION

During the second wave of the coronavirus disease (COVID)-19 pandemic, many of the delta variant cases were associated with rhino-orbital cerebral mucormycosis. Due to the shortage of healthcare infrastructure and unavailability of amphotericin B, mucormycosis became more fulminant, warranting emergency radical surgical debridement, orbital 'exenteration', and maxillectomies.

Post-COVID-19 systemic sequelae like residual respiratory insufficiency, adrenocortical suppression, cardiac dysfunction, and difficult airway complicated by mucormycosis, adverse effects of amphotericin B treatment, dysregulated innate immune response, microvascular coagulation can affect the general anaesthetic management and the outcomes.[1]

We conducted a study to analyse the perioperative anaesthetic management of COVID-19 associated mucormycosis (CAM) patients and to describe their pre-anesthetic evaluation and risk stratification for emergency surgical debridement.

METHODS

This retrospective study was approved by the hospital ethics committee (RMHEC/AL/06/2022). Medical records of all patients admitted with CAM at a single tertiary care centre between April 2021 and August 2021 were analysed for patient demographic data, presenting complaints, COVID-19 status, all investigation reports, vitals monitoring recorded throughout the hospital stay, the number and type of surgeries performed on each patient, duration of anaesthesia, duration of hospital stay, risk scores, post-operative sequelae, and outcomes.

Analytical Statistical Package for the Social Sciences (SPSS) for windows version 25.0 was used for data analysis. The mean ± standard deviation (SD) and range values were calculated for quantitative variables and the percentages were calculated for categorical variables.

RESULTS

Eighty-three individuals were hospitalised with COVID-19 associated mucormycosis. Out of these, records of 67 patients could be obtained. The American Society of Anesthesiologists (ASA) physical status was grade I in one patient, II in 55 patients, III in 6 patients, and IV in 5 patients, with a median age of 48.3 ± 14.1 (range, 23-84) years.

Out of six patients with ASA grade III, five had Quick Sequential Organ Failure Assessment (qSOFA) score of 1 and Quick Systemic Inflammatory Response Syndrome (qSIRS) score of 2, while one had qSOFA score of 2 and qSIRS score of 4. For five patients of ASA grade IV, the qSOFA score was >2 and qSIRS score was >4 [Figure 1].

Six (8.9%) patients had COVID-19 complications, out of whom, one patient had severe COVID-19 illness with septic shock. Another patient had bilateral cortical venous thrombosis, while one more patient was admitted with ischaemic stroke and altered sensorium. Furthermore, in one patient, acute superior cerebellar artery infarct, and in one patient post COVID-19 bilateral axonal neuropathy and upper trunk plexopathy was diagnosed. One patient with myocardial infarction was also admitted to the intensive care unit (ICU) in a gasping state and had a cardiac arrest for which cardiopulmonary resuscitation was administered, after which spontaneous circulation was restored. This patient was planned for surgical debridement but died pre-operatively.

Ten patients (14.9%) had COVID-19 associated pneumonia and required oxygen therapy at the time of admission [Figure 2]. At admission, the mean peripheral oxygen saturation (SpO_2) was 96% (66%-100%) among the patients in the study. The mean random blood

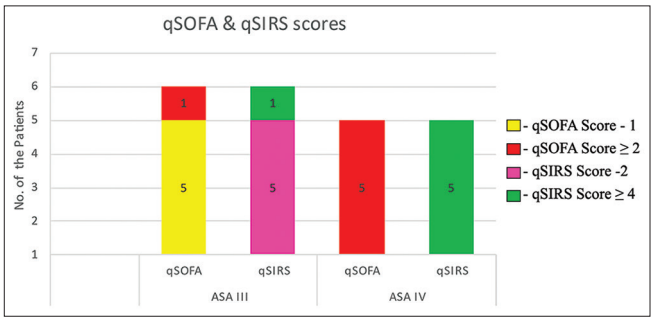

Figure 1: Pre-operative risk assessment scores. ASA - American Society of Anesthesiologists physical status. qSOFA - Quick Sequential Organ Failure Assessment score. qSIRS - Combined qSOFA and systemic inflammatory response syndrome (SIRS) score. No.-Number

glucose value of the patients was 258 ± 96.5 mg/dl and the mean glycosylated haemoglobin (HbA1c) value was 10.1 ± 1.76%.

Among 67 patients, 15 patients were newly detected with diabetes during COVID-19 illness, 41 patients were known cases of diabetes (pre-COVID-19), and 11 patients were non-diabetic. 25 patients had a history of hospitalisation with COVID-19 and had received steroids as a part of treatment, 12 patients had been home quarantined (no steroids received), and the rest of the 30 patients' files did not contain data regarding the same.

The most common clinical presentation was orbital cellulitis 37.31% (25/67), followed by facial cellulitis 31.34% (21/67), epistaxis 11.94% (8/67), headache 7.46% (5/67), and toothache 4.47% (3/67). Other symptoms included loss of vision, breathlessness, and seizures.

Sixty-five patients were operated upon. Two patients consented to non-surgical management due to advanced COVID-19 rhino-orbital cerebral mucormycosis. The computerised tomography of the paranasal sinus (CT-PNS) was done in 51 (76.11%) patients, magnetic resonance imaging (MRI) was done in 16 (23.88%) patients pre-operatively, and a repeat MRI was required in 8 (11.94%) patients post-operatively.

The most common surgery done was endoscopic sinus debridement (92.53%) [Table 1].

Thirty (44.77%) patients had high mean blood pressure >100 mmHg, 16 (23.88%) patients had a heart rate (HR) >100 beats/min, pre-operatively before induction of anaesthesia. Three patients out of sixty-five (4.61%) were shifted to the ICU for elective ventilation after surgery. The mean duration of surgery was 2.2 ± 0.8 hours (1.5-6 hours) [Table 2].

Thirty-two patients received various forms of amphotericin B, 10 patients received liposomal amphotericin B, 4 patients received lipid emulsification, and the remaining 18 received amphotericin B deoxycholate. Sixty-five (97.01%) patients received a parental/oral form of posaconazole. All patients who received amphotericin B had alternate day renal profile monitoring. Twenty-five patients received potassium correction for hypokalaemia perioperatively.

Three patients had thromboembolic events in our study, one patient had multiple cerebral infarcts, one patient developed middle cerebral artery infarct, hemiplegia, and aphasia post-operatively, and one patient was

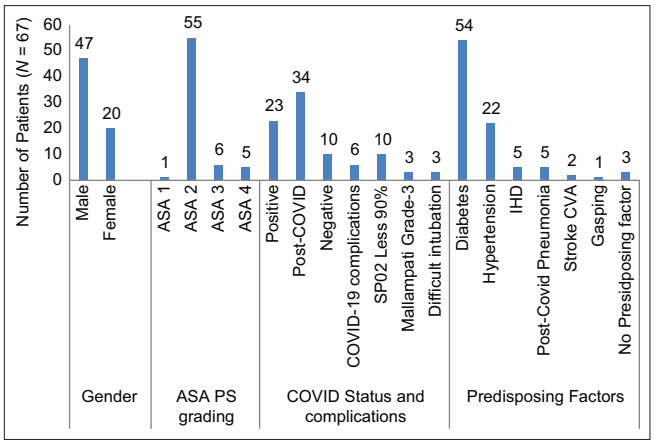

Figure 2: Pre-operative risk stratification. ASA PS - American Society of Anesthesiologists physical status, IHD - Ischaemic heart disease, CVA - Cerebral vascular accident; No. - Number; COVID-coronavirus disease

Table 1: Types of surgeries

Type of surgery	Number of subjects	Percentage
Surgery not done	2	2.9
Endoscopic sinus debridement [ESD]	62	92.5
ESD + orbital decompression	8	11.9
ESD + orbit exenteration	14	20.89
ESD + Caldwell Luc	16	23.88
ESD + partial/complete maxillectomy	8	11.9
Transfacial frontal abscess drainage	1	1.49

As many patients had repetitive surgeries, the total number of subjects was more than 67

Table 2: Post-operative outcomes

Outcomes	Results
Number of patients (percentages) shifted to ICU from OT	5 (7.69%) to ICU, 60 (92.30%) patients to ward out of 65 operated,
Number of patients (percentages) shifted to ICU from ward	3 (4.61%)
Duration of ICU stay for a total of 8 patients	8.5±4.56 (4-17 days)*
Number of patients (percentages) not extubated/extubated	3 (4.61%)/62 (95.38%)
Post-operative sequelae	Total 13, (20%), Among them Pneumonia/ ARDS/pneumothorax (6 patients), UTI/Cystitis (3 patients), MCA infarct (1 patient), Bleeding from operative site (1 patient), MRSA and Septic shock (2 patients)
Reoperated patients	15 out of 65; 23.07%
Duration of surgery	2.2±0.8 (1-6.5 hours)*
Duration of hospital stay	10.7±6.3 (1-30 days)*

ICU - Intensive care unit, ARDS - Acute respiratory distress syndrome, MCA - Middle cerebral artery, UTI - Urinary tract infection, MRSA - Methicillin-resistant Staphylococcus aureus infection, OT -Operation theatre. *Mean±standard deviation (Range)

admitted with acute cerebral infarct with a Glasgow coma scale (GCS) score of 7/15.29 patients received both injection enoxaparin 40 mg subcutaneously once daily (OD) and tablet aspirin 150 mg OD. Twenty-five patients received tablet aspirin 150 mg OD. Thirteen patients did not receive tablet aspirin.

Fifteen (23.01%) patients underwent repeat surgeries (orbital exenteration/maxillectomy) due to further spread of infection after the initial surgical debridement. Twelve (17.9%) patients had an intracranial extension. Fourteen (20.89%) patients underwent orbital exenterations. Ten patients had post-operative infections (14.9%) during their hospital stay.

With the combined treatment of emergency radical surgical resection and rapid initiation of high-dose antifungal therapy treatment, the mortality rate was reduced to 8.9% and also it decreased the duration of hospital stay. The mean duration of hospital stay was 10.7 ± 6.3 (1–30 days). The mean duration of ICU stay was 8.5+/-4.56 (4-17 days).

DISCUSSION

Literature review shows that rhino-orbital cerebral mucormycosis, mainly associated with COVID-19, has a poor prognosis.[2,3] Historically, mucormycosis is associated with high mortality rates of 25%.[3] However, our study showed a better outcome with a mortality rate of 8.9%. The post-operative outcome and improved survival rates in the mucormycosis patients in our study were influenced by aggressive pre-operative risk stratification, correction of predisposing factors, radical surgical resection, and rapid initiation of high-dose antifungal therapy.

Coronavirus has been linked to stress-induced cardiomyopathy and myocardial damage; according to conventional protocols, a comprehensive cardiac examination, including echocardiography, is recommended before surgery.[4] Post-COVID-19 individuals have been shown to have abnormal pulmonary function tests and symptoms of restrictive lung disease.[5] The risk of thromboembolic events linked with COVID-19 may impact all the systems including the central nervous system, warranting the patient's complete coagulation profile and a brain CT scan. Hence, the protocols and methods mentioned[6] needed revision and customisation as these may not always be feasible for COVID-19 positive patients and may delay the emergency surgical debridement. We hastened pre-operative optimisation and risk stratification for emergency surgeries by use of the room air saturation, arterial blood gas (ABG) analysis, previous chest radiogram or high-resolution computed tomography scans done during the patient's past COVID-19 illness, and simple bedside breath-holding tests to assess the patient's pulmonary condition. The echocardiogram was not available for emergency surgeries 24/7, so we used the 12-lead electrocardiogram, and other clinical signs like raised jugular venous pressure, and pedal oedema to stratify the cardiac condition.

qSOFA score containing alertness (GCS score <15), respiratory rate >20 breaths/min, systolic blood pressure <90 mm of Hg; and SIRS score - temperature >38.3^0 C or <36^{0}C, HR >90 beats/min, and white blood cell count >12,000 or <4,000/mm^3 were taken into consideration for pre-operative risk assessment and admission into the ICU by the attending anaesthesiologists. qSIRS (the combined qSOFA and SIRS) can improve the accuracy of the individual scores in the prediction of mortality.[7] ASA physical status grades III and IV patients with qSOFA >2, and qSIRS scores >2 with fever, and persistent hypotension in our study were pre-operatively optimised in the ICU to treat the sepsis and related multiple organ dysfunction syndrome. Arterial blood gas analysis and biochemical studies were performed at the appropriate juncture, depending upon which treatment of acidosis, electrolyte imbalances, and coagulation abnormalities was done in these patients.

Under standard anaesthetic monitoring, general anaesthesia was administered for all types of surgeries as per the post-COVID-19 mucormycosis guidelines.[8] Personal protective equipment and an intubation box were used for 23 patients within 14 days of being diagnosed as COVID-19 positive. The intubation box was devised by anaesthesiologists of our institute. Whenever intubation of a difficult airway was anticipated, C-Arm machine cover (sterile plastic cover) was used to cover the head, and neck up to the chest of the patient. Oral intubations were performed as per detailed protocols to minimise the dissemination of respiratory droplets and aerosols.[9]

Patients who achieved spontaneous ventilation (tidal volume >5 ml/kg, inspiratory pressure ≥25 cm H_2O, vital capacity >10 ml/kg) and maintained oxygen

saturation were extubated. Patients who demonstrated post-anaesthetic Aldrete recovery score <9 were shifted to the ICU with an endotracheal tube for elective post-operative ventilation.[10] They were ventilated according to the National Institutes of Health, National Heart, Lung, and Blood Institute (NIH NHLBI) therapy for acute respiratory distress syndrome (ARDS) mechanical ventilation protocol. For patients with post-COVID-19 ARDS changes, lung-protective ventilation was given with a tidal volume of 4-6 ml/kg, and P plat <35 cm H_20. Patients received ABG analysis-guided spontaneous breathing trials followed by weaning and extubation. For patients who had the partial pressure of oxygen (PaO_2), divided by the fraction of inspired oxygen (FiO_2) (P/F Ratio) <150, prone ventilation was done according to the ICU protocols.

A stress dosage of corticosteroids was given to all our patients intraoperatively, irrespective of the history of corticosteroid therapy. Blood and blood product transfusions and intraoperative inotropes were used as required depending upon the extent of surgery and pre-operative abnormalities in ASA physical status class III and IV patients to maintain intraoperative haemodynamic stability.

Perioperative hyperglycaemia management was done according to the latest updated protocols.[11] Antifungal treatment was initiated early with a high dose regimen as per the guidelines.[12] All patients had mandatory renal function tests conducted on admission and post-operatively on alternate days. Patients with amphotericin B-related side effects like nephrotoxicity, hypokalaemia, uncontrolled random blood glucose levels, and diabetic ketoacidosis were medically managed stringently throughout the perioperative period.

Patients who underwent maxillectomy and orbital exenteration were provided with prostheses and a palatal obturator. Continuous follow-up for better aesthetic, functional rehabilitation, and further psychological counselling was provided.

CONCLUSION

Superior outcomes in terms of reduced mortality in CAM patients can be achieved by aggressive pre-operative optimisation, organised anaesthetic management, and careful post-operative planning with the help of a dedicated CAM care group involving anaesthesiologists, surgeons, and intensivists. A detailed clinical examination with quick basic investigations, bedside tests, ABG analysis, and scores like qSIRS and qSOFA in those COVID-19 patients in whom conventional protocolised tests are not possible can help for emergency CAM surgeries. This can reduce the time interval between the patient's hospital admission and proceeding for surgery which can significantly improve patient recovery and survival rates. However, these results deserve validation in the context of a prospective study.

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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.

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Conflicts of interest

There are no conflicts of interest.

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