Section: Anesthesiology

Original Research Article

PERIOPERATIVE ANAESTHETIC CONSIDERATION FOR COVID ASSOCIATED MUCORMYCOSIS (CAM)- A RETROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background: Introduction: One of the dreaded complications of covid 19 infection is rhino orbital cerebral mucormycosis. Operating these patients on emergency basis is a challenge for anaesthesiologists because of various reasons like hyperglycemia, electrolyte imbalance, organ dysfunctions and difficult intubation. In addition, post covid sequalae like post covid lung fibrosis, thromboembolic complications etc. can complicate perioperative period. **Aim and objective:** To assess prevalence of difficult intubation in the patients posted for mucormycosis emergency surgery in maxillofacial surgery operation theatre. Secondary objective is to get prevalence of comorbidities in post covid status patients and perioperative complications. **Materials and Methods:** Retrospective single centre study carried out from month of April 2021 to august 2021 of patients undergoing debridement, sequestrectomies, maxillectomies under general and local anaesthesia for CAM patients. Standard surgical and anaesthesia procedures are followed along with medical management of mucormycosis and comorbidities. **Observation:** Out of total 56 patients 22 patients were operated under general anaesthesia and 18 patients operated under monitored anaesthesia care (MAC) with various local blocks. There was male preponderance and median age was 48yrs. Significant number of patients were with comorbidities like DM, HT, renal dysfunction, cardiac dysfunction etc. Diabetes mellitus was major risk factor for CAM along with steroid use. In 8 patients difficult mask ventilation and in 6 patients more than 2 attempts of intubations were needed along with use of stylate and bougie. One episode of hypoxia occurred while intubation. Restricted mouth opening, airway edema are major determinants of difficult intubation. Post operative complications like ketoacidosis, delayed awakening, stroke etc are managed aggressively. Mortality in this study was 3.57%. **Conclusion:** Covid associated mucormycosis needs multidisciplinary approach for its surgical and medical management for minimising perioperative complications and reducing mortality which is quite high worldwide.

INTRODUCTION

Covid 19 pandemic came with its enumerable complications like post covid fibrotic lung disease, restrictive lung disease, new onset diabetes mellitus, thromboembolic events like acute ischemic stroke, venous thromboembolism including peripheral veins /cerebral veins, acute coronary events, cardiomyopathies and mucormycosis. Especially after second wave these are reported globally.[1] Post covid comorbidities of multiple systems is challenging while managing these patients perioperatively. Covid associated rhino orbital cerebral mucormycosis (CAM) is one such complication which warrants multidisciplinary and emergency approach for management to minimise complications like intracerebral extension etc.

Covid associated mucormycosis have predisposing factors like presence of (I) diabetes mellitus (II) uncontrolled hyperglycemia due to corticosteroid use (III) steroid use reduces the phagocytic activity of WBC (IV) COVID-19 often causes endothelialiatis and endothelial damage predisposing to secondary or opportunistic fungal infection (V) Free available iron is an ideal resource for mucormycosis.[2,3]

The incidence rate of mucormycosis globally varies from 0.005 to 1.7 per million population whereas, in Indian population its prevalence is 0.14 per 1000, which is about 80 times higher than developed

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countries. The fatality rate of mucormycosis is 46% globally.[4,5,6] However, factors like intracranial or orbital involvement, irreversible immune suppression increases fatality to as high as 50% to 80%. Covid 19 second wave uncovered insufficient health care infrastructure not only in countries like India but globally. Scarcity of amphotericin B (AmB) is one such factor leading to extensive mucormycosis spread. In addition, there are AmB-related side effects like nephrotoxicity, hypotension, hypokalaemia, hypomagnesemia, arrhythmias and fever.

Difficulty in securing airway in mucormycosis patients have been reported in various case reports. There are only few case reports and case series from India describing the perioperative challenges faced by anesthesiologists in CAM patients.[7,8]

Aim of our study to find prevalence of difficult intubations in covid associated mucormycosis (CAM) patients undergoing various surgeries like debridement, sequestrectomies, maxillectomies, zygomatic resections in maxillofacial surgery operation theatre. Secondary objective was to assess prevalence of preoperative comorbidities for risk stratification and assess prevalence of perioperative complications like haemodynamic instability, post operative respiratory insufficiency, requirement of oxygen therapy, need of ICU etc.

MATERIAL AND METHOD

Single centre retrospective study carried out in patients undergoing combined medical and surgical treatment for covid associated rhino orbital (CAM) mucormycosis in tertiary care hospital between April 2021 to August 2021. Inclusion criteria includes patients enrolled in maxillofacial surgery department for covid associated mucormycosis for combined medical and surgical treatment in maxillofacial OT.

Diagnosis was done by clinical features, CT scan (face, paranasal sinuses, brain) and histopathology. Presenting symptoms includes history of preceding covid 19 infections with steroid use in most of the patients. There was variable time lag from weeks to months before presenting with CAM. Symptoms includes teeth mobility, blood-tinged blackish nasal discharge, intraoral abscess, facial numbness, nasal blockade, ulceration and perforation of palate, pain in facial region, peri-orbital or peri-nasal swelling, facial discoloration and induration etc. Histopathology showing fungal hyphae (broad ribbon like irregular, aseptate) with right angle branching.

Total 56 patients got operated for mucormycosis. 22 patients operated under general anaesthesia (GA), 18 patients operated under monitored anaesthesia care (MAC) and local nerve blocks. Decision to operate under local anaesthesia or general anaesthesia is taken after discussion with surgical team and considering patients cardiopulmonary status (ASA status), extent of spread of disease etc. Preoperative anaesthetic evaluation done which includes test like CBC/KFT/ ECG /echo/HBA1C/X RAY chest etc.

After 8 hrs of fasting for solids and 2 hrs of fasting for liquids, patient is taken to operation theatre after appropriate consent. Difficult intubation cart was kept ready. After attaching multipara monitor showing spo2/NIBP/ECG /etco2, supplemental oxygen is administered as most of patients had preceding covid pneumonia. So, these patients are thought to have compromised respiratory reserve. Pulmonary fibrosis, decreased FRC due to recent illness, restrictive lung disease and difficult mask ventilation /difficult intubation (due to airway edema, restricted mouth opening due to pain, nasal blockade) were anticipated. Large bore intravenous access obtained. Fluids used were RL/NS/DNS with fractionated doses of insulin as per requirement. Patients were premedicated with inj. midazolam 0.03 mg/kg, and inj. Fentanyl 2mcg/kg. Preoxygenation done with 100%oxygen. Patients were induced with inj propofol 2mg/kg in titrated doses considering reduced oral intake due to oral pathology and also suppressed adrenal gland due to chronic steroid usage. inj succinyl choline 1.5 mg /kg was used for intubation. No patient had hypotension during induction as patients were adequately co-loaded. One patient had episode of desaturation during intubation due to extensive pulmonary fibrosis. All patients were intubated orally. In one patient submental intubation was done for surgical reasons (involving zygoma). Intraoperative anaesthesia is maintained with oxygen:nitrous oxide 40:60 ratio, sevoflurane, inj vecuronium/atracurium and inj paracetamol 1gm /inj tramadol 1mg/kg for post operative pain. Patients were reversed with neostigmine, glycopylorate.

Image 1: Palatal Perforation

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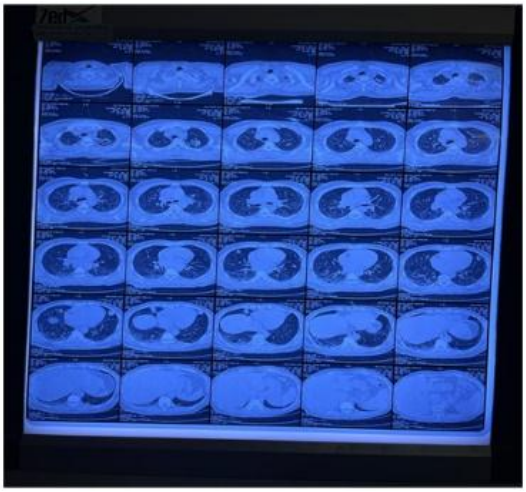

Image 2: Pulmonary fibrosis with fungal cavity

RESULTS

All the data were entered in Excel Sheet and SPSS software 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. We came across 56 patients of CAM during month of April 2021 to AUGUST 2021. 22 pts were operated in maxillofacial surgery OT under GA for open surgical approach. 18 patients were operated under monitored anaesthesia care (MAC). 15patients were operated endoscopically in ENT department. One patient was transferred to ophthalmology.

Perioperative records of 56 patients were evaluated and we observed that the median age of our patients was 48 years. Out of 56 pts 35 were male and 21 were female. The incidence of CAM and its associated surgery was more in males than females.

Out of 56 patient 22 patient had diabetes mellitus (39.28%), 7 patients were with recently diagnosed DM after covid 19 infection, 10 patients with hypertension, 2 patient had recent stroke, 12 patients had history of oxygen therapy and ICU admission during covid 19 infection, 5 patients had creatinine more than 1.5 mg/dl out of which one patient needed dialysis during covid 19 infection, one patient had acute non-alcoholic pancreatitis during covid infection. 4 patients had ischemic heart disease out of which one elderly patient had left ventricular ejection fraction less than 20 % and one patient with history of recent MI. One patient was with invasive pulmonary mucormycosis with cavitary lesions bilaterally. 4 patients with extensive pulmonary fibrosis with having baseline spo2 less than 94% and spo2 below 90% after 6-minute walk test. Out of 56 patients 53 patients had history of treatment with steroids mainly methyl prednisolone or dexamethasone making it 94% of steroid use. Mean haemoglobin was 10.5, baseline mean hba1c 10.06 in diabetics.

Mean RBS was 96mg% in non-diabetic patients.

Table 1

AGE	**Median age of 48.3 (range, 23-84) years.**	
MALE	35/56	62.5%
FEMALE	21/56	37.5%
MEAN HB	10.5	
MEAN HBA1C	10.06	
COMORBIDITIES		
DM	22/56	39%
HT	10/56	17%
ISCHEMIC HEART DISEASE	4/56	7%
RENAL IMPAIRMENT	5/56	8.9%
PULMONARY FIBROSIS	4/56	5.3%
STROKE	2/56	3.5%
INTRAPULMONARY FUNGAL CAVITARY LESION	1/56	1.7%
ACUTE PANCREATITIS	1/56	1.7%
ICU ADMISSION FOR COVID	12/56	21.4%
STEROID USE	53/56	94.6%
ASA I	15/42	35.7%
ASA II	18/42	42.8%
ASA III	6/42	14.2%
ASA IV	1/42	2.3 %

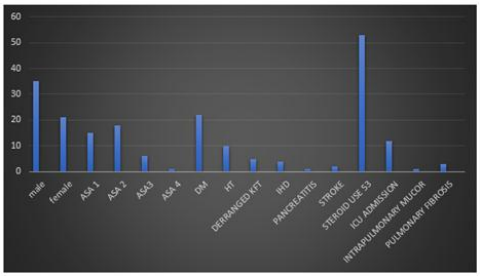

Figure 1: Pre-Operative Demographic Data

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Table 2

Criteria	MPC grading		Difficult mask ventilation	Cormac and Lehane grading		Stylate	Bougie	Peri intubation hypoxia	>2 intubation attempt
Number of patients	I	13	8	I	12	9	3	1	6
	II	7		II	7				
	III	2		III	2				
	IV	nil		IV	1				

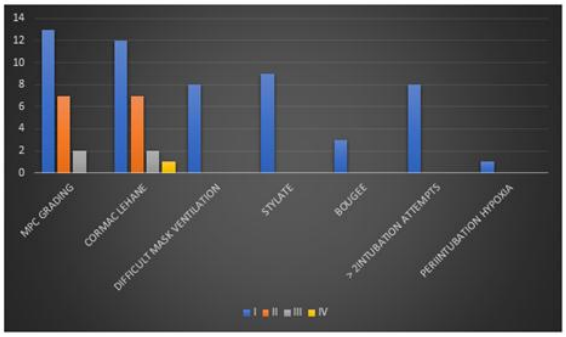

Figure 2: Difficult Intubation Data

ASA grading is shown in figure1, table 1 for 44 patients operated under GA/MAC in maxillofacial OT and airway management data is shown in table 2, figure 2 for 22 patients operated under GA. In 8 patients difficult bag mask ventilation encountered which was managed using nasopharyngeal airway and /or 2-person technique. In 6 patients more than two attempts for intubation were required. The difficulty in intubation was managed using stylet in 9 patients and bougie in 3 patients. One patient had episode of desaturation while intubation because of pulmonary fibrosis but it was quickly resolved by 100% oxygen bag mask ventilation and use of bougee in subsequent attempt. All patient were extubated in OT. Overall 9 patients (16.07%) required post-operative oxygen therapy. None patient was having any episodes of hypotension which was not corrected by intravenous fluid. Many patients were hypokalemic preoperatively due to amphotericin B infusion and insulin. Hypokalemia was corrected with both oral and intravenous potassium. One patient had multiple ventricular premature complexes and episode of ventricular bigeminy intraoperatively not compromising haemodynamic status. One patient's procedure was abandoned as he had sinus tachycardia and hypertension post induction not amenable to increase in anaesthesia depth who was operated subsequently after BP control. Postoperative period was uneventful except 2 patients who needed blood transfusion due to a anemia, one patient had developed diabetes ketoacidosis on second post op day which was managed successfully. 2 patients had delayed recovery due to underling renal derangement.

Patients operated under MAC were underwent surgery uneventful except one patient with low left ventricular ejection fraction (20%) died on 4th postoperative day because of acute stroke and aspiration pneumonia. One patient died after getting discharged of sudden cardiac event.

DISCUSSION

Mucormycosis is rapidly spreading fungal infection especially in immunocompromised individuals e.g. uncontrolled DM, haematological and other malignancies, organ transplantation, prolonged neutropenia, immunosuppressive and corticosteroid therapy, iron overload or hemochromatosis, etc. Mucormycosis can involve nose, sinuses, orbit, central nervous system, lung, gastrointestinal tract, skin, jaw bones, joints, heart, kidney, and mediastinum, but rhino orbital cerebral mucormycosis is the commonest presentation seen in clinical practice worldwide.

By July 15, 2021, India had recorded 45,374 cases of COVID-19-associated mucormycosis (CAM) and around 4300 related deaths.[9] Literature review shows that rhino-orbital cerebral mucormycosis associated with COVID-19, has a poor prognosis.[10,11] Current study shows mortality of 2/56 which is 3.57% due to aggressive surgical as well as medical management requiring multidisciplinary approach. Another study from India reported mortality of 8.9% [12]

ASA III and ASA IV pts who were high risk for general anaesthesia are operated under MAC in staged manner after discussion with surgeon.

Difficult intubation and difficult mask ventilation is reported in mucormycosis as patients have multiple mobile teeth, facial induration, restricted mouth opening, palatal perforation, significant airway edema, loss of facial tissue and bony framework especially during second debridement etc.[13,14,15] Difficult airway should be managed by prompt anticipation and preoxygenation with 100% oxygen, use of adjuncts like flex tip laryngoscope /fibreoptic bronchoscope, stylate, bougie etc. A difficult airway cart with tracheostomy back up is must.

Table 3

Perioperative complications	Number of patients
Hypotension	nil
Arrythmias	2
Post operative ICU need	3
Diabetic ketoacidosis	1
Blood transfusion	2
Delayed recovery	2
Post op oxygen therapy	9
Death	2

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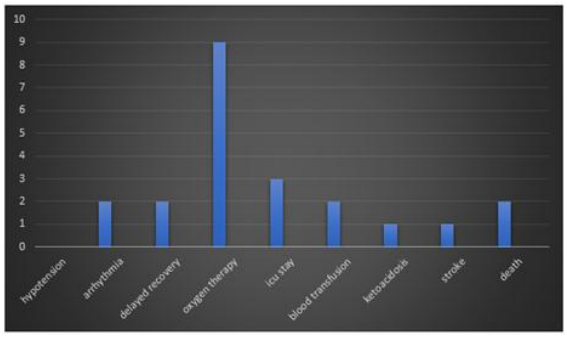

Figure 3: Post Operative Complications

Table 4

Procedures done	No. Of patient
SINUS DEBRIDEMENT AND SEQUESTRECTOMY	27
MAXILLECTOMY	12
ZYGOMATIC RESECTION	1

Optimal glycemic control should be the approach for tackling rising CAM cases.[16] In post covid patient's new onset diabetes is to be promptly detected and managed. Surgical and anaesthesia stress further aggravates hyperglycemia that can lead to ketoacidosis which further increases mortality. Amphotericin b injection is to be given in dextrose solution so additional doses of neutralising insulin are needed. Nevertheless in such patients for aggressive glucose management fractionated insulin is used along with long acting insulin. One such patient landed in ketoacidosis is managed in ICU.

Covid 19 patients can have stress-induced cardiomyopathy and also acute coronary events. We evaluated all CAM pts for any cardiovascular dysfunction by looking at NYHA SCORING, ECG, ECHO which helped for risk stratification and better planning.[17]

Post covid pneumonia patients can have pulmonary fibrosis and restrictive lung disease.[18] We recorded baseline spo2 and spo2 after 6 min walk test for all patients, so also single breath counts to assess respiratory reserve. Any abnormal recordings were further assessed by x ray chest, chest CT scan, ABG and PFT in appropriate patients for risk stratifications. 4 pts were having baseline spo2 less than 94% which was further decreases by 6 min walk test. Preop deep breathing exercise, spirometry, nebulisation, chest physiotherapy was advocated for optimisation.

Thromboembolic complications are known complications due to hyperinflammatory stage in covid 19 illness. We had one patient with acute stroke in post operative period who died on 4th post operative day. Another reason for stroke could be his low cardiac reserve that could be again sequele of covid 19 infection.

Antifungal treatment was initiated early. Liposomal or conventional Amphoteresin B with or without Posaconazole is used as per availability and baseline renal function.[19] All patients had mandatory renal function tests conducted on admission and on alternate days during hospital stay. Patients with amphotericin B-related side effects were medically managed throughout the perioperative period.

The present retrospective study highlighted the difficult airway management in CAM patients so also possible complications. These challenges can be anticipated by anesthesiologists managing mucormycosis in future.

However the limitation of this study was being a retrospective study and also we reviewed 5 months data in maxillofacial OT only which could be a limiting factor. ENT or ophthalmology OT data inclusion could have shown additional issues perioperatively.

CONCLUSION

Perioperative management of post covid mucormycosis is challenging to anaesthesiologists due to difficult intubation, organ dysfunctions etc. Multidisciplinary approach along with discussion with surgical team for type of anaesthesia /type of surgery (open or endoscopic surgical debridement) can decrease the magnitude of perioperative complications. Good post operative care will give better outcomes and reduced mortality.

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