e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(2); 199-206

Original Research Article

Anaesthetic Consideration in Mucormycosis Patients Posted for Rhino-Orbital-Dental Surgeries

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Received: 08-12-2025 / Revised: 05-01-2026 / Accepted: 07-02-2026
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Conflict of interest: Nil

Abstract:

Background: Multiple considerations exist for the anesthesiologists in covid-19 recovered patients with added problems arising due to rhino-orbital-cerebral mucormycosis and adverse effects of antifungal drugs. Overall morbidity and mortality are more in such patients. Managing such patients posted for surgical debridement presents a unique challenge to the anesthesiologist.

Methods: A retrospective analysis of 118 patients operated for surgical debridement and histopathology confirmed mucormycosis cases were analysed from the medical record. A review of preoperative clinical and laboratory data, intraoperative anaesthesia details and postoperative outcome was done.

Results: 118 confirmed mucormycosis patients were analysed. 98 patients tested covid positive, out of which 73 were hospitalized**.** 101 patients presented with diabetes mellitus. 53 patients were operated after 8 weeks of corona virus infection. 41 patients had increased creatinine levels. 7 patients presented with difficult intubation. Intraoperatively anesthesia concerns were tachycardia, hypertension, tachycardia combined with hypotension, arrythmias, hyperglycemia, raised end tidal carbon dioxide concentration (ETCO2), increased peak airway pressure and oozing in various patients. All patients were extubated. Postoperatively, 15 patients required oxygen, 92 were discharged and death resulted in 9 patients.

Conclusion: Knowledge of disease, preoperative optimization and proper preparation of patients and postoperative icu care is must for successful management of mucormycosis patients undergoing surgical debridement.

Keywords: Mucormycosis; general anesthesia; perioperative period; perioperative care; coronavirus infection; diabetes mellitus.

DOI: 10.25258/ijcpr.18.2.33

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Introduction

The introduction of covid-19 cases in December 2019 with upsurge of new and new cases surprised many clinicians worldwide. There were dynamic changes in its treatment with a step towards better management to complete cure, which somehow resulted in rapid increase in mucormycosis cases globally.

Due to presence of comorbid conditions like diabetes mellitus and lung pathologies in covid-19 patients, bacterial and fungal coinfections may coexist [1]. Rhino-orbital-cerebral mucormycosis is a rare and serious infection [1]. Many precipitating factors may be responsible for development of mucormycosis but diabetes, especially uncontrolled diabetes and concurrent high dose of steroid treatment is the main culprit as mentioned in many reviews of literature. Systemic corticosteroid can reduce the mortality in most severe courses of disease but together with immunosuppression and other clinical factors, predispose to secondary fungal disease [2]. So, the main stay of treatment lies in early diagnosis, reversal of patient's underlying predisposing factors, intravenous antifungal drugs and endoscopic surgical debridement of necrotic tissue [1]. However, it is challenging to diagnose mucormycosis as many of the clinical and radiological features of pulmonary and disseminated mucormycosis are nonspecific and overlap with covid-19 features, and also definitive diagnosis is based on histopathological examinations of biopsy specimens from the involved area [1,2]. Surgical debridement of necrotic tissue in mucormycosis patients is often indicated in presence of comorbidities and multiple organ failure [3]. Patients who were already immunocompromised

with superadded Covid19 have shown increased cases of mucormycosis [4].

In patients of mucormycosis posted for surgery, airway management is very much important, since the fungal debris in the oropharyngeal region and supraglottic edema may lead to difficult ventilation, endotracheal intubation as well as difficult nasal intubation [3]. Mucormycosis may affect any organ system and may be accompanied by hemodynamic instability. Hence, anaesthetic management may be complicated by multisystemic involvement, residual pulmonary dysfunction, immunocompromised status, adrenal suppression, difficult airway and adverse effects of antifungal drugs. Therefore, proper preoperative assessment and preoperative optimization should be done whenever possible [5,6]. Airway evaluation is more important as the greatest anesthetic challenge occurs when patients presented with airway compromise for surgical debridement [7]. Many a times these patients have higher chances of cerebral extension if surgery is delayed, so, emergency debridement is necessary [6].

Hence, this study was planned to highlight the various issues faced by the anesthesiologists in the perioperative period and to develop definite protocol for management of mucormycosis and related disease and to deliver safe and quality anesthesia services in this population. It will also help in planning of infrastructure, manpower, prepare the anesthesiologist for new emerging airborne diseases and to reframe the anesthetic approach.

Material and Methods

After approval from local institutional ethical committee and clinical trial registry, all patients who have been suspected as mucormycosis and operated for rhino-orbital-dental surgeries from May 2021-July 2021 in Government Medical College, Surat hospital were selected for this retrospective study. This study is prospectively registered with Local institutional ethical committee (GMCS/STU/ETHICS/Approval/25564/21, dated 2-11-2021) and Clinical trial registry of India (CTRI/2021/12/038566 dated: 10/12/2021). All the details of the mucormycosis patients confirmed by histopathology report were only included in this study.

Medical case record with incomplete data, cases lost to follow up or cases operated in another hospital and admitted in this hospital for medical management were excluded from the study. Also, histopathology report other than mucormycosis, like aspergillosis or other pathogens were also excluded. Details of the patients were collected from the medical records which included- age, sex, American society of physical status and duration of surgery and anaesthesia. Any details of covid illness like history of hospitalization or home isolation, history of oxygen therapy or mechanical ventilation, history of treatment with steroids or low molecular weight of heparin was noted. Information regarding patient's comorbid condition like diabetes mellitus, hypertension, pulmonary tuberculosis etc. and patient taking any medications for medical illness was noted. Details of patient's physical examination and all laboratory data or radiological data was collected from the preanesthetic record sheet. Intraoperative details about anaesthesia like-induction agent, muscle relaxants, maintenance agents and reversal agent used was collected from the noseworthy card. Also, any mention about intraoperative adverse event like bradycardia/tachycardia, hypotension/hypertension, arrythmias and medications administered for the same from anesthesia record sheet was noted. At the end of surgery, recovery of patient (extubated/oxygen therapy/noninvasive or invasive ventilation) was noted. And final outcome of patient whether discharged or death of the patient in ward or icu was noted.

Statistical Analysis

All the patients operated in the month of May 2021-July 2021 were taken as sample size by purposive sampling technique retrospectively from medical case records. The data collected was entered into Microsoft excel sheet and analysed.

Descriptive data is presented in form of frequency and percentage. Age, duration of surgery is presented as mean and standard deviation (SD).

Sample size: Target sample size was around 150 before starting of this study. But, only 118 patients were analysed, as shown in figure 1.

Result

Demographic profile of patients shown in table 1. The mean age in our study was 51.42 ± 11.24 years with minimum age 24 years and maximum age 87 years. Out of 101 diabetic patients, 27(27%) were recently diagnosed, 61(60%) suffered from chronic diabetes mellitus and status of 13(13%) was unknown. We retrieved this information solely from the case paper. therefore, we could not provide precise comments on complications related to diabetes, but based on this data, we only comment that mucormycosis was more common in diabetic patients. Rest of the population presented with other comorbid condition in lesser proportion, as detailed in table 1.

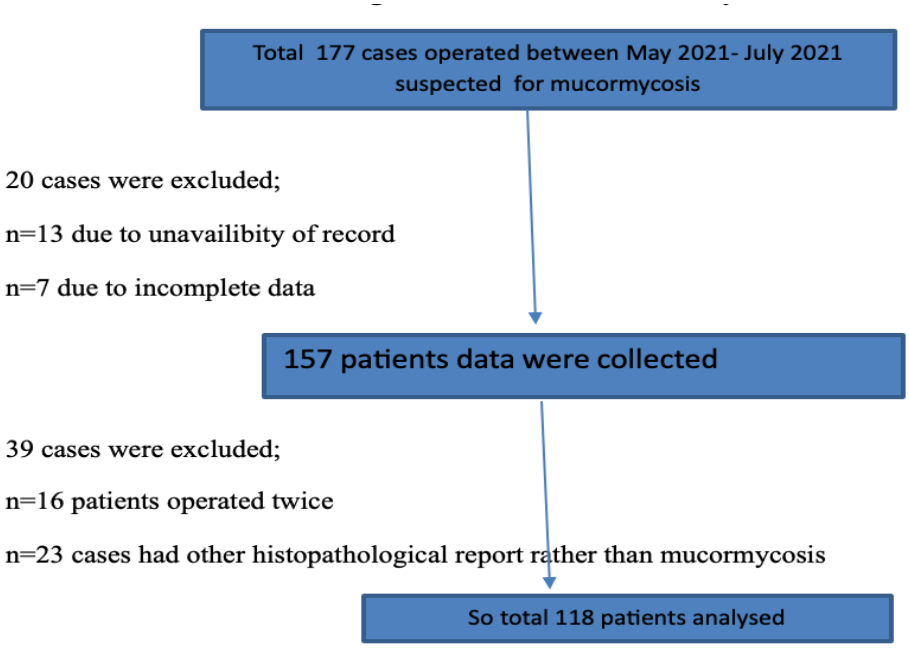

Figure 1: flow chart of the stud

Table 1: Patient's Characteristics

Variable	No of patient (frequency)
Mean Age [in year]	51.42 ± 11.24
Male/ Female	80(68%)/ 38(32%)
ASA III/IV/V with ventilatory support	57(48%)/58(49%)/3(3%)
Covid positive: negative	98 (83%): 20 (17%)
Covid positive, Hospitalization: home isolation	73(74%): 25(26%)
Out of 98 covid positive patients, Oxygen therapy/ O2+ steroid/ Only Observation	31(42%)/ 29(39%)/ 14(19%)
Predisposing factors	
Diabetes Mellitus	101(85%)
Hypertension	45(37.19%)
Diabetes Mellitus + Hypertension	40(33.05%)
Ischemic heart disease	9(7.44%)
Hypothyroidism	3(2.48%)
Asthma	2(1.65%)
Pulmonary tuberculosis	2(1.65%)
Acute kidney injury	2(1.65%)
Chronic kidney disease	1(0.82%)
Epilepsy	1(0.82%)
Cirrhosis	1(0.82%)
Duration of surgery (min)	202.33 ± 11.10
Mouth opening: ≥3 Finger breath, <3Finger breath	85(72%), 33(28%)
Mallampatti grade II: III: IV	71(60%): 15(13%): 32(27%)

Table 2: Types of surgical procedure (n=118)

Surgical procedure	Number of patients (%)
Functional endoscopic sinus surgery	94(80%)
Endoscopic sinus surgery + dental surgery	14(12%)
Endoscopic sinus surgery+ orbital exenteration	7(6%)
Orbital exenteration	3(2%)

Data are shown as n (%). Type of surgical procedure depends on area of involvement in form of nasal, sinuses, dental and orbital area.

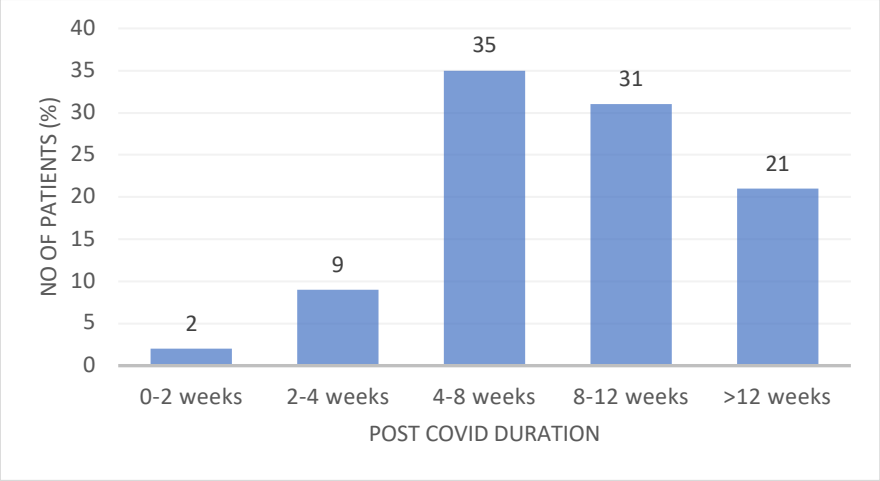

Figure 2: Timing of surgery after COVID infection [n =98]

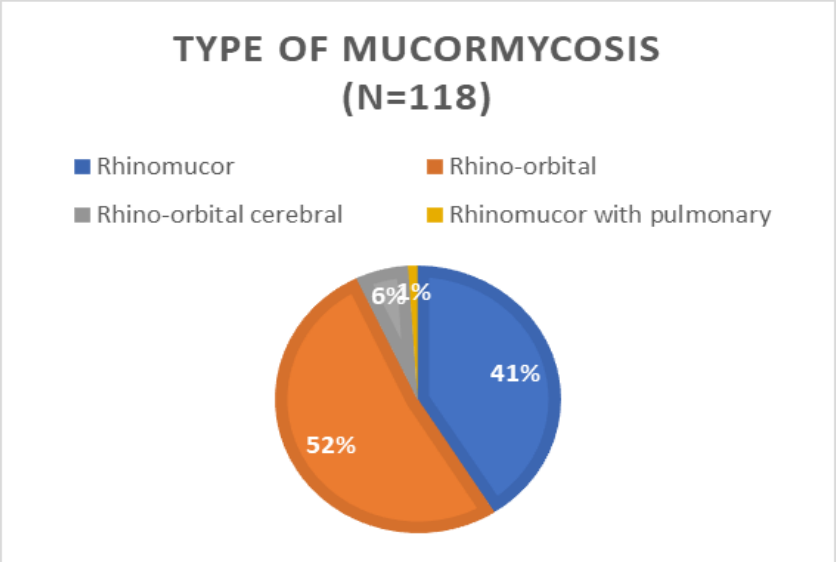

Figure 3: Type of mucormycosis(n=118).

As shown in table 3, electrolytes abnormalities were there even after correction.

Table 3: Preoperative laboratory investigations (n=118)

Preoperative Investigations	No of patients (%)
Hemoglobin- ≤8: 8-11:>11 (gm/dl)	71(60%): 3(3%): 44(37%)
Total Count- normal: leukopenia: leukocytosis	98(83%): 1(1%): 19(16%)
Platelet Count- normal: decreased: increased	95(81%): 13(11%): 10(8%)
Serum sodium (Na^+)- <135: 135-145: >145 (mmol/L)	69(58%): 48(41%): 1(1%)
Serum potassium (K^+)- <3.5: 3.5-5.5: >5.5 (mmol/L)	80(68%): 35(30%): 3(2%)
Serum creatinine: ≤1.2: >1.2 (mg/dl)	77(65%): 41(35%)

Preoperatively, mean heart rate (93.28±4.69 min), mean systolic blood pressure (126.15±19.33 mmHg), mean diastolic blood pressure (80.31±9.46 mmHg) and mean respiratory rate (18±30 min) were within normal range. Out of 118 patients 4(3.38%) patients in this study had insignificant ventricular premature beats preoperatively and were taken for operation after consultation with the cardiologist. Majority of patients (90%) 106 patients out of 180 were having oxygen saturation more than 94%. 10% (12) patients had less than 94% oxygen saturation.

Anesthetic management: Premedicant drugs used were intravenous (IV) tramadol in 49(42%), IV fentanyl in 56(47%), IV Dexmetomidine in 11(9%) and IV paracetamol in 2(2%) patients. Propofol 107(91%) was the most commonly used IV induction agent followed by sodium thiopentone in 3(2%) and etomidate in 8(7%) patients. Injection vecuronium was used as muscle relaxant in 85(72%) patients and injection atracurium in 33(28%) patients with dose titration using peripheral nerve monitoring. Intraoperatively, patients were maintained on either sevoflurane or desflurane

inhalational agent. Intraoperative crystalloid requirement was 2000ml (1000-5000ml), with colloid transfusion required in 7 (5%) patients and blood transfusion required only in 9 (7%) patients. Average urine output was 300 ml (100-1500ml).

Table 4 shows 6% patients were expected to have difficult intubation but were successfully intubated with specialized laryngoscope blades and bougie in first attempt only. Hyperglycemia managed with insulin infusion and blood sugar monitoring at regular intervals. All the patients were ventilated with low tidal volume 6-8ml/kg, high respiratory rate 18-22 breaths/min and inspiratory and expiratory ration (I:E ratio) of 1:2, volume control ventilation. Out of 118 patients, 7% patients had raised peak airway pressure and 2% patients had raised ETCO2 values, which required change in I:E ratio, respiratory rate and pressure control ventilation. 4% patients had intraoperatively excessive surgical oozing and they were managed with injection tranexamic bolus followed by infusion.

Table 4: Intraoperative anaesthesia concerns

Concerns	Number of patients (%)
Difficult Intubation	**7(6%)**
McCoy blade	3
McCoy blade with bougie	2
Macintosh blade with bougie	2
Hemodynamic parameters	
Tachycardia	28(19%)
Tachycardia+ Hypotension	8(6%)
Hypertension	6(5%)
Arrythmias	5(4%)
Hyperglycemia	14(11%)
Raised Peak and plateau pressure	7(6%)
Raised End tidal carbon monoxide	2(2%)
Oozing	5(4%)

Data are shown as n (%). Difficult intubation represents use of airway gadgets during expected difficult intubation.

All of the patients were extubated immediately after surgery with varying liters of oxygen administered via simple face mask or nasal prongs or non-invasive oxygen support in (n=15)13% of patients. Out of these 15 patients, only one patient required BIPAP support.

Out of 118 patients, 78%(n=92) patients were discharged after average 22.52± 11.10 days of ward admission. 9% (n=11) patients expired after average postoperative 16.18± 7.2 days. 9%(n=11) patients had taken discharged against medical advice. 1% (n=1) patient was transferred to another health facilities. 1% (n=1) patient was absconded.

Discussion

Mucormycosis is a devastating disease which has affected globally and majority of cases were reported from India [2]. The majority of cases in our study were males with mean age 51.42 ± 11.24 years which correlates with lancet article [2]. The majority of our patients were covid positive and most of them were hospitalized, so per guidelines, maximum number of patients received steroids. In our study, among 98 patients who tested positive for covid19, 29(39%) received steroid treatment (Table I). Many patients were not aware of steroid intake during their covid illness. So, we could not get exact data of steroid treatment in our patients.

It has been observed that covid-19 virus affects multiple organs, primarily pulmonary and cardiac systems and they may present with varying degree of illness and presentation, hence, recovery from covid-19 infection is complicated by several sequelae [8]. So, all the survivors must undergo proper evaluation before posted for elective surgery. Due to limitations of pulmonary function test and baseline 2D echo cardiography, all patients were evaluated clinically. Though anesthesiologist team were lucky to have preoperative cardiologist opinion in one patient with arrythmias.

Multiple risk factors along with the use of immunosuppressant predisposes patient to mucormycosis. Diabetes mellitus as a predisposing or confounding factor was the commonest comorbidity observed in many studies [1-6,9,10]. Similarly, in our study diabetes mellitus was found to be the most common comorbidity followed by hypertension as shown in Table 1.

The use of systemic amphotericin B in treatment of mucormycosis leads to nephrotoxicity, electrolyte imbalance, fever, shivering, dyspnea and hypotension [3]. To avoid side effects of amphotericin B, dose adjustment was done in some and liposomal amphotericin B was used in some patients. In our study, 41% patients had

hyponatremia and 30% patients had hypokalemia despite of correction on the day of surgery. Due to hospital burden and overload of patients, serum magnesium level was not available in all patients.

Computed tomography (CT) scan and magnetic resonance imaging (MRI) imaging are useful to assess sinus, brain, eye involvement, bony erosions and diagnosing soft tissue and vascular involvement. The staging is based on anatomical progression of mucormycosis [11]. Almost 41% patients were diagnosed with rhinomucor and 52% patient had rhino-orbital extension. Almost 6% patients presented with cerebral extension and 1% with pulmonary involvement. 80% patients were posted for nasal sinus debridement in our institute. Wajekar A et al [8] reported about ideal timing of surgery after covid-19 diagnosis to be more than 7 weeks. 54% patients in our study were posted after 8 weeks of covid diagnosis. Both these results are in favor of good postoperative outcome.

Many patients recovered from covid-19 may experience post-traumatic stress disorder related to prolonged hospitalization and various medical procedures [12] and any patient posted for surgery having variable level of anxiety so these might be the reason, all patients in this study were premedicated.

Patients with mucormycosis, particularly those with rhino orbital cerebral mucormycosis, may experience difficult mask ventilation and endotracheal intubation as a result of epiglottitis and supraglottic edema [3]. Nilesh Solanki et al [1] reported difficult mask ventilation in 73.68% patients and difficult intubation in 75.43% patients. Similarly, in our study, 28% patients had inadequate mouth opening and 40% patients had mallampatti grade III and IV patients, however, mask ventilation was possible in all patients and in some patients was aided with oral airway device. Difficult intubation was suspected in 6% patients and as most of the patients posted for FESS surgery, oral intubation was required. However, all patients were successfully intubated with the timely use of airway equipment and keeping in mind difficult airway algorithm. So, to deal with unanticipated airway related problems all airway equipment were kept ready and trained anesthesiologists trained in fiberoptic intubation and tracheostomy should be available.

Previous studies reported 11.5% thrombosis rate in hospitalized, non-critically ill patients and 29.4% thrombosis rate for icu patients, which may cause difficult intravenous access [12]. In our study, we did not encounter difficult IV access. However, we suggest insertion of Central venous line to guide fluid status intraoperatively and post operatively. Invasive arterial monitoring can help by beat-to-beat hemodynamic monitoring and further arterial blood gas analysis to guide post operative ventilatory requirement.

Propofol was the most common induction used as preoperative vitals were within normal range in most patients and maybe due to clear-headed recovery. Vecuronium or Atracurium was used as muscle relaxant in this study.

There is little or no documentation of ideal volatile anaesthetic agents, though many have reported antibacterial and antifungal in in-vitro studies. Nilesh Solanki et al [1] used sevoflurane/ desflurane as maintenance agent in their study. Karaaslan used desflurane in their study [3]. Barodka et al [13] reported that isoflurane inhibited the growth of Albicans. In all our cases, sevoflurane/ desflurane was used. The advantage of using sevoflurane/desflurane is its cardiovascular stability, almost nil metabolism and rapid recovery.

Intraoperatively, tachycardia and only hypertension were present in 19% and 5% patients respectively, which were managed with dexmedetomidine loading followed by infusion. Dexmedetomidine selective alpha2 agonist and recently has gained wide acceptance due to its hemodynamic stability. Prolong and excessive use of steroid may cause adrenal suppression; this might be the reason of intraoperative hypotension noted in 6% of patients or it may be due to adverse effect of amphotericin B. patients with hypotension were treated with crystalloids or colloids. In our patients none of the patients were required vasopressor support. Blood loss above maximum allowable blood loss was replaced with intra-operative blood transfusion in 9 patients.

Arrythmias in form of transient ventricular premature beats was present in 5(4%) cases, however patients remained hemodynamically stable with no other untoward consequences and were treated with injection xylocard. Increased blood sugar was present in 12% of cases and in them insulin infusion was started. For management of mucormycosis, control of blood sugar should be done.

All patients were intubated in this study. Patients with mucormycosis are likely to have residual pulmonary dysfunction (specifically in patients with postcovid mucormycosis or due to pulmonary involvement of mucormycosis) and prone for post operative pulmonary dysfunction. 7% patients had raised peak airway pressure from the beginning of surgery and in them pressure control ventilation was used to avoid further increase in airway pressure. Lung protective ventilatory strategies should be employed to prevent further lung damage. Extubation in such type of patients with expected pulmonary complication should be carried out where high level of post operative intensive care unit is

available. In our study, after administration of reversal agents, all patients were extubated at the end of surgery after adequate muscle power and tone and spontaneous respiration.

The lancet article in 2022, reported that mortality in patients with rhino-orbital cerebral disease with confirmed central nervous system (CNS) involvement was higher than in those without signs of progression to the CNS and surgery did not significantly affect survival [2]. Solanki et al [1] reported 26.31% mortality in their study. In contrast, 6% patients had cerebral involvement and mortality rate was 9% in our study.

Our strength of the study was, triage of mucormycosis patients to dedicated wards was done and top priority to surgical debridement was carried out in our institute. Almost 54% patients were operated after 8 weeks of covid diagnosis, availability of various airway gadgets to manage difficult airway, and anesthetic outcome of most of the patients were good.

Our study was limited in several ways. First, the study was single centered. Secondly, though the sample size was sufficient, some cases had to be excluded due to unavailability of complete data and follow up of other cases was not possible due to discharge against medical advice or transferred to other health care facility. clinical markers, radiological parameters and pulmonary function tests which may have important impact on anaesthesia management and patient outcome were not available in all patients. Thirdly, this study was retrospective and based on analysis of anesthesia and hospital records only. Another limitation of our study was non-availability of inflammatory markers and high-resolution computed tomography scan of chest in many cases, which could highlight many other issues.

Conclusion

Dedicated team involving all the specialties with focused approach towards timely diagnosis, proper evaluation, optimization of patient, proper planning of anaesthesia, vigilant intraoperative monitoring and high level postoperative intensive care managing rhino-orbito-cerebral mucormycosis undergoing surgical debridement is possible. Diabetes mellitus seems to have direct relationship with mucormycosis, so screening and awareness of general population should be carried out more aggressively.

Acknowledgment: We are grateful to our colleagues, ENT department, Dental department, ophthalmology department and resident doctors as a part of Anesthesia team.

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