VOL15, ISSUE 03, 2024

ISSN: 0975-3583,0976-2833

PREVALENCE AND DETERMINANTS OF PERIOPERATIVE ANAESTHESIA COMPLICATIONS IN COVID ASSOCIATED MUCORMYCOSIS (CAM) PATIENTS POSTED FOR SURGERY

Vrinda Oza¹, Vandana S. Parmar², Parthkumar D. Vadgama³, Bhavesh Kanabar⁴, Chetna Jadeja⁵ Selvendiran P.⁶, Disha Ghumaliya⁷, Magesh R.⁸, Farhan Moosani⁹

¹Assistant Professor, ²Professor and Head, ³Senior Resident Doctor, ⁵Ex-Associate Professor, Department of Anaesthesiology, P.D.U. Govt. Medical College, Hospital Chowk, Jamnagar Road, Rajkot-360001, Gujarat, India.

⁴Assistant Professor, Faculty, Department of Preventive and Social Medicine, P.D.U. Govt. Medical College, Hospital Chowk, Jamnagar Road, Rajkot-360001, Gujarat, India.

⁶Senior Resident Doctor, Department of Neuroanaesthesiology, Christian Medical College, Vellore, Tamil Nadu, India.

^{7,8,9}Junior Resident Doctor, Department of Anaesthesiology, P.D.U. Govt. Medical College, Hospital Chowk, Jamnagar Road, Rajkot-360001, Gujarat, India.

Received Date: 27/02/2024

Acceptance Date: 20/03/2024

Corresponding Author: Dr Bhavesh Kanabar, Assistant Professor, Department of Preventive and Social Medicine, P.D.U. Govt. Medical College, Hospital Chowk, Jamnagar Road, Rajkot-360001, Gujarat, India. Email: parthvadgama@gmail.com

Abstract

Background: COVID-associated mucormycosis (CAM) is an emerging complication in COVID-19 patients. These patients undergoing surgery may face high anesthesia-related risks. We aimed to determine the prevalence and risk factors for perioperative anaesthesia complications in CAM patients undergoing surgery. Objectives: This study was carried out to determine the prevalence of perioperative anaesthesia complications in CAM patients undergoing surgery and identify associated risk factors. Materials & Methods: We retrospectively analyzed 715 CAM patients who underwent surgery at a tertiary hospital in India from April 2021 to July 2021. In this study, the type of mucormycosis, comorbidities, perioperative anesthesia complications, airway management issues, and mortality were recorded and analyzed. Result: The overall anaesthesia complication rate was 51.89%. The most frequent complications were hypertension (21.53%), difficult airway (16.91%), requirement of postoperative respiratory support (13.14%), noninvasive ventilation (6.57%), reintubation (4.47%), hypotension (10.06%), and delayed recovery (9.23%). Rhinosinusitis (51.05%) and rhino-orbital mucormycosis (21.54%) predominated. Major comorbidities were diabetes (66.85%), cardiac involvement (72.73%), and chronic respiratory disease (58.74%). Increasing age, high ASA status, extensive infections, diabetes, and respiratory illness predicted complications. Mask ventilation was difficult in 17.76% and intubation in 10.91% of patients. Mortality was 5.45% within 24 hours and 12.73% by 72 hours postoperatively. Conclusion: Perioperative anesthesia complications are common in CAM surgery patients, especially those with comorbidities and extensive disease. Individualized management plans

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

are essential to optimize airway, respiratory, hemodynamic, and metabolic parameters for mitigating morbidity and mortality.

Keywords: COVID-19, mucormycosis, anesthesia, surgery, complications, perioperative care

Introduction

In the wake of the global COVID-19 pandemic, a novel and severe complication has emerged, captivating the attention of healthcare providers worldwide—COVID Associated Mucormycosis (CAM) in patients recovering from COVID-19.¹ Mucormycosis, previously called zygomycosis, is caused by fungi in the order Mucorales, which are ubiquitous in the environment.² This rare but life-threatening fungal infection, often affecting the sinuses, brain, or lungs, has presented unprecedented challenges to medical communities already grappling with the complexities of the ongoing health crisis. mucormycosis can be an aggressive, angioinvasive infection associated with high mortality, particularly in immunocompromised hosts.³ Diabetes mellitus, immunosuppression, iron overload, and trauma are established risk factors for developing mucormycosis^{4–6}. As the understanding of CAM continues to evolve, it becomes imperative to shed light on its perioperative implications, particularly in the context of anaesthetic management.

Recent case series have highlighted the growing incidence of CAM in patients recovering from severe COVID-19.^{7–9} Rhino-orbital-cerebral mucormycosis is the most common presentation of CAM, which often requires prompt surgical debridement or resection along with antifungal therapy for disease control.¹⁰ However, patients with CAM undergoing surgery may be at increased risk for perioperative morbidity and mortality given the systemic effects of severe COVID-19.

The prevalence and determinants of perioperative anaesthesia complications in CAM patients undergoing surgical interventions constitute a critical area of investigation. The interplay between the underlying mucormycosis pathology, the systemic effects of COVID-19, and the stressors imposed by surgical procedures poses a unique set of challenges for anaesthesiologists. Additionally, the antifungal therapy used to treat mucormycosis, often liposomal amphotericin B, can interact with anaesthetic medications. Amphotericin B is associated with nephrotoxicity, hypokalemia, and hypomagnesemia which can alter anesthetic management.¹¹ Little is currently known regarding the prevalence or risk factors for anesthesia-related complications in CAM patients undergoing surgery. Studies in hematopoietic stem cell transplant patients have found mucormycosis to be an independent risk factor for adverse postoperative outcomes.¹² However, COVID-19 related comorbidities may further compound surgical risk in CAM. Unraveling the intricacies of these complications is crucial not only for optimizing perioperative care but also for informing preventative strategies and enhancing patient outcomes.

This study aims to systematically explore the prevalence of anaesthesia-related complications in CAM patients undergoing surgery, identifying key determinants that may contribute to the severity and frequency of such events. By delving into the nuanced interrelationships between COVID-19, mucormycosis, and the perioperative period, this research seeks to provide actionable insights that can guide tailored anaesthetic approaches for CAM patients. Through a comprehensive analysis of patient demographics, disease characteristics, and perioperative variable this study aspires to contribute valuable knowledge to the evolving landscape of CAM management within the surgical setting.

As the medical community grapples with the multifaceted challenges posed by CAM, this investigation endeavors to enhance our understanding of the anaesthetic considerations unique to this population, ultimately fostering advancements in perioperative care for individuals afflicted by this formidable disease.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

Materials And Methodology

After getting institutional ethical committee approval (Reg. No. PDUMCR/IEC/146/2021), this cross- sectional retrospective observational study was conducted at our institute from April 2021 to July 2021 among 715 patients. Patients between age group 18-70 years of either sex with American Society of Anesthesiologists (ASA) physical status I to IV with previous history of Covid-19 (confirmed with RT-PCR) and having confirmed diagnosis of all types of mucormycosis on biopsy were from medical records available were included. Written, informed consent was taken and patients were thoroughly counselled and explained about the procedure and purpose of the study.

Pre-operative assessment and optimization was done for all patients undergoing surgery for mucormycosis. Preoperatively patients were evaluated for any major illness like diabetes mellitus (DM), hypertension (HT), obesity, ischemic heart disease (IHD), solid organ or hematological malignancy, any other immunocompromised state, chronic respiratory disease, thyroid disease etc. Patients with baseline saturation <95% were optimized by administering appropriate oxygen therapy. Preoperatively, investigations like complete blood count, random blood sugar, renal function tests, liver function tests, serum electrolytes, chest X-ray and electrocardiogram (ECG) were checked and 2D echocardiography was done when indicated. Airway was assessed by mouth opening and Mallampati grading. Altered blood sugar level and serum electrolytes were optimized according to the requirement. All the patients were kept nil per orally for at least 6 hr prior to surgery. After arrival in the operation theatre, an intravenous access with 18 G canula was secured. Airway instruments were checked and a difficult airway cart was kept ready. Multipara monitor was attached and baseline vital parameters were noted. Standard monitors i.e. NIBP, Pulse Oximeter, ECG and Capnography were used. General anaesthesia was given to all the patients with anaesthetic agents appropriate with patient's vitals and comorbidity and adequate fluid balance was maintained. Reversal and extubation as done per the protocol and transferred to ICU for further management. Continuous monitoring until 72 hr post-operatively was performed for all the patients.

All patients were administered glycopyrrolate 4 mcg/kg and ondansetron 0.1 mg/kg and additionally and fentanyl 1mcg/kg 5 minutes prior to induction. Patients were preoxygenated with 100% O₂ for 3 minutes. Induction of anaesthesia done with appropriate intravenous induction agent, 1.5mg/kg xylocaine (for attenuation of laryngoscopy response) and suxamethonium chloride 2 mg/kg according to clinical condition of the patient. Intubation done with conventional laryngoscopy or video laryngoscope (whenever difficulty in intubation anticipated). Elective oral fiberoptic intubation and tracheostomy were also considered in selected cases of anticipated difficult airway. First effective ventilation was confirmed by capnography. If required to assist the intubation, either bougie/stylet and/or the maneuvers like external laryngeal pressure were used and the number of attempts of intubation were also noted. Peri laryngeal packing was done with the sterile roller pack. Intraoperatively patients were ventilated with tidal volume to be less than 6ml/kg and plateau pressure not to exceed 30 cm of H₂O. Intraoperatively, anaesthesia was maintained with a 50:50 mixture of oxygen and air along with inhalation agent (Desflurane/Sevoflurane) and intermittent use of atracurium besylate IV. SpO₂, pulse rate, mean arterial pressure (MAP), ECG, EtCO₂, urine output were monitored throughout the procedure. Fluids and blood were replaced as per the requirement. Reversal of residual neuromuscular block was achieved using neostigmine (0.05mg/kg) and glycopyrrolate(0.08mg/kg). After oral suction and removal of oral packing, patients were extubated on establishing regular spontaneous breathing pattern, and able to open eyes to command. Patients who required ventilatory support were shifted to the intensive care unit (ICU). All the patients were transferred to Post-anesthesia Care Unit

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

(PACU) for further clinical observation. Ventilatory support was provided to the patients who couldn't be extubated. Postoperative pain relief was provided with tramadol (1mg/kg) or paracetamol (1.0 gm) intravenously, Total duration of surgery and anaesthesia was noted. Perioperative complications like airway difficulty, hemodynamic instability, desaturation (SpO₂ < 94%), altered consciousness, delayed recovery and/or respiratory distress were identified and treated accordingly. (Figure-1)

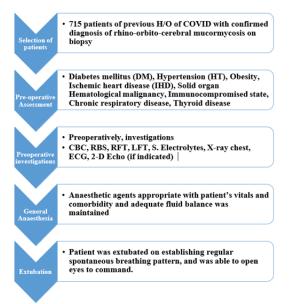


Figure 1: Study Vignette

Study instrument

It was consisting of a structured data collection tool which included following information -

- Basic details of patient i.e. age, sex
- Clinical details i.e. type of mucormycosis, types of comorbidities, peri-operative
- anaesthesia complications, details about difficult airway and mortality

Statistical Analysis

The data was compiled using Microsoft excel-2013. Quantitative data were represented as frequency and percentages.

Results

Our study found that mean duration between diagnosis of COVID-19 and diagnosis of Mucormycosis was 32 days. The age distribution among patients undergoing surgery for COVID-associated Mucormycosis (CAM) is delineated in the table. The majority of patients fall into the age groups of 41-60, constituting a substantial 62.37% of the total. This indicates that individuals in their fourth and fifth decades are prominently represented in the cohort of CAM patients requiring surgical intervention. Specifically, the 51-60 age group has the highest percentage, contributing 35.80% to the total. This suggests that individuals in their fifties are particularly affected by CAM, necessitating surgical procedures. Following closely, the 41-50 age group contributes significantly at 26.57%, emphasizing the prevalence of CAM cases in the forties and fifties. While individuals under 30 years of age account for a smaller proportion (2.80%), the 31-40 and

61-70 age groups contribute 15.10% and 15.24%, respectively. This underscores that CAM surgery is not confined to specific age brackets and affects individuals across a

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

range of ages. The elderly population, including those aged 71-80 and >80, collectively constitutes a relatively smaller percentage (4.48%) of CAM surgery cases. This distribution may reflect a trend of CAM being more prevalent in middle-aged and older individuals. [Figure 2]

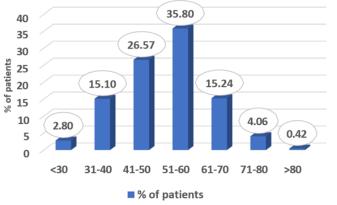


Figure 2: Age group wise distribution of patients of mucormycosis (N=715)

The gender distribution of patients undergoing surgery for COVID-associated Mucormycosis (CAM) reveals a notable predominance of male patients, constituting a substantial majority at 64.76%. This suggests a higher incidence or severity of CAM requiring surgical intervention in males compared to females. Conversely, female patients account for 35.24% of the total, indicating a comparatively lower representation in the cohort requiring surgical management for CAM. [Figure 3]

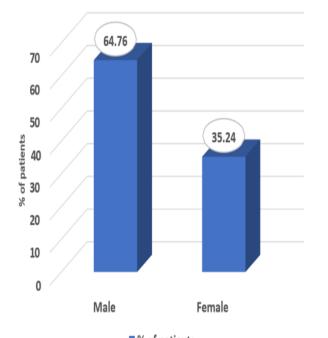


Figure 3: Gender wise distribution of patients of mucormycosis (N=715)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

The distribution of mucormycosis types among patients undergoing surgery for CAM reveals a diverse spectrum of manifestations. The predominant type is Rhinosinusitis, representing the majority at 51.05%. This suggests that a significant proportion of patients in the study experienced mucormycosis primarily affecting the nasal and sinus regions. The second most prevalent type is Rhino-Orbital Sinusitis, accounting for 21.54% of cases. This indicates an extension of mucormycosis beyond the nasal and sinus areas, involving the orbital region. The varied presentations of mucormycosis, ranging from localized (Rhinosinusitis) to more extensive (Rhino-Orbital Sinusitis), highlight the complexity and potential severity of the disease. Rhino-Orbito-Palatal Sinusitis constitutes 7.55% of cases, indicating a further extension of mucormycosis to the palatal region along with involvement in the orbital and sinus areas. Rhino-Palatal Sinusitis, representing 13.71% of cases, suggests cases where the palate is a significant site of involvement in addition to the nasal and sinus regions. This type reflects cases where the infection progresses to potentially life-threatening complications involving the brain. [Table 1]

Mucormycosis Types	No. of patients	% of patients
Rhinosinusitis	365	51.05
Rhino-Orbital Sinusitis	154	21.54
Rhino-Orbito-Palatal Sinusitis	54	7.55
Rhino-Palatal Sinusitis	98	13.71
Rhino-Orbito-Cerebral Sinusitis	44	6.15

Table 1: Types of mucormycosis among patients who have undergone surgery (N=715)

CAM patients were associated with multiple comorbidities, most common being diabetes mellitus and chronic respiratory disease. Diabetes mellitus, a well-established risk factor for mucormycosis, is highly prevalent in this cohort (66.85%), emphasizing the strong association between diabetes and the development of mucormycosis. Out of total diabetic patients, 40.27% were newly detected and 59.73% were known case of diabetes. A substantial number of patients (58.74%) had chronic respiratory diseases, highlighting the potential impact of preexisting respiratory conditions on the susceptibility to mucormycosis and perioperative morbidity and mortality. The majority of patients (72.73%) were having preoperative ECG changes, probable reasons might be the concomitant cardiac comorbidity, COVID 19 itself, hemodynamic instability and/or electrolytes imbalance. A significant proportion of patients (32.59%) were hypertensive, suggesting that vascular complications associated with hypertension might have contributed to the overall complexity of mucormycosis and perioperative anaesthesia complications. In our study, 184 (25.87%) patients had history of Amp-B consumption pre-operatively. Altered electrolyte levels are noted in a notable percentage of patients (17.20%), indicating potential disturbances in metabolic homeostasis that might have influenced the overall recovery of the patients. Obesity, though present in a relatively smaller percentage (16.64%) is still a noteworthy co-morbidity. Obesity has been associated with other comorbidities like diabetes mellitus and hypertension, altered immune responses that potentially influences the susceptibility to fungal infections, difficult airway for anaesthesia and delayed recovery from the anaesthesia. Other co-morbidities observed were Thyroid Disorder (8.25%), Cardiac Co- morbidity (7.69%), Neurological Disease (4.62%), chronic kidney disease (4.20%) This comprehensive overview of co-morbidities provides valuable insights into the reasoning behind the perioperative complications in patients undergoing surgery for CAM. [Figure 4]

ISSN: 0975-3583,0976-2833

VOL15, ISSUE 03, 2024

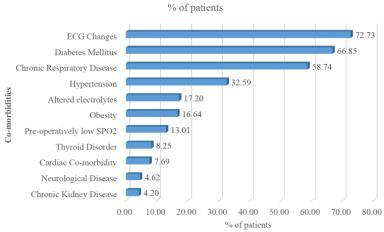


Figure 4: Type of co-morbidities among patients of mucormycosis (N=715)

Analysis of perioperative anesthesia complications shows that a significant portion of patients (21.53%) exhibited hypertension during the course of surgical procedure. Perioperative hypertension can pose challenges during anaesthesia induction and maintenance, requires careful hemodynamic management. The majority of patients (82.94%) had successful endotracheal intubation on the first attempt, indicating efficient airway management in the majority of cases. But, a considerable proportion of patients (16.91%) faced difficulties in airway management during induction of the patients. [Table 2]

Variables		No.	% of
			patients
Difficult Airway	Difficult Mask Ventilation	127	17.76
	Intubation was done in 1st attempt	593	82.94
	Intubation was done in 2nd attempt with	41	5.73
	ELP		
	Intubation required stylet/Bougie	78	10.91
Mortality	On table	0	0.00
	Within 24 Hour Post-operatively	39	5.45
	Within 72 Hour Post-operatively	64	8.95
	After 72 Hour Post-operatively	27	3.78
	On table	0	0.00

Table 2: Difficult airway	y and mortality among	patients of m	ucormycosis (I	N=715)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

Among those, 11.04% required either stylet or bougie for intubation whereas 5.87% required external laryngeal pressure (ELP) while intubation. 17.90% patients were encountered with difficult mask ventilation. Meanwhile, oral fibreoptic intubation was done in 5 patients and elective tracheostomy required in 2 patients to secure the airway before surgery. This highlights the complexity of securing the airway in patients with mucormycosis, which might have influenced by factors such as tissue inflammation or anatomical variations. A notable percentage of patients (13.14%) required non-invasive ventilatory (NIV) support in the postoperative phase. This suggests respiratory challenges persisting beyond the surgery, necessitating additional support for optimal recovery. A significant number of patients (10.06%) experienced hypotension during the peri-operative period. Managing peri-operative hemodynamics is crucial, and the occurrence of hypotension may be attributed to factors such as the use of anaesthetic agents and/or patient's underlying compromised health status. A notable percentage of patients (9.23%) encountered with delayed recovery after the surgery. This could involve various aspects, such as awakening from anaesthesia, regaining consciousness, or achieving stable physiological parameters. A subset of patients (6.57%) faced post-operative delayed recovery that necessitated ventilatory support. This indicates a more severe form of delayed recovery, possibly linked to respiratory compromise. A small but noteworthy percentage of patients (4.47%) required re- intubation during the perioperative course. Re-intubation may

be needed for reasons such as airway protection, respiratory insufficiency, or other complications. This detailed breakdown of pre-operative anaesthesia complications sheds light on the challenges associated with managing mucormycosis patients during the perioperative period. [Figure 5]

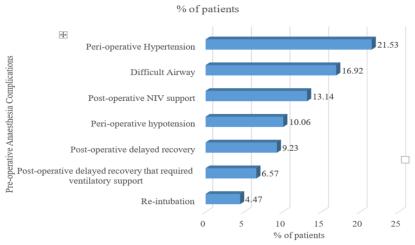


Figure 5: Perioperative Anaesthesia Complications (N=715)

No mortality occurred during the surgical procedure (on the table), indicating that immediate complications during surgery did not lead to death. A small percentage (5.45%) of patients succumbed to complications within the first 24 hours after surgery, highlighting the critical early post-operative period. A slightly higher percentage (8.95%) experienced mortality within 72 hours post-operatively, reflecting the vulnerability of these patients during the initial recovery phase. A subset of patients (3.78%) faced mortality beyond the initial 72 hours post-operatively, indicating that complications leading to death extended into the later stages of recovery. [Table 2]

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

This comprehensive assessment of difficult airway situations and mortality outcomes provides a nuanced understanding of the challenges associated with mucormycosis patients undergoing surgery. The data underscore the importance of meticulous airway management strategies and the need for vigilant post-operative monitoring to mitigate adverse outcomes.

Discussion

This retrospective observational study aimed to determine the prevalence and risk factors associated with perioperative anaesthesia complications in 715 CAM patients undergoing surgery. The most common age group affected in our study was 40-60 yr (62.37%). The gender distribution of patients undergoing surgery for COVID-associated Mucormycosis (CAM) reveals a notable predominance of male patients, constituting a substantial majority at 64.76%. Kumar *et al.* in their study also revealed similar result and demonstrated that commonly affected age group was 45-60 yr (45.5%) and 65.5% patients were males in their study.¹³

Our study found rhinosinusitis (51.05%) and rhino-orbital sinusitis (21.54%) to be the predominant manifestations of mucormycosis in surgical patients, together accounting for over 70% of cases. Desai *et al.* in their study found that most common involvement was rhino-orbito-facial followed by dental and intra cerebral mucormycosis.¹⁴ Mucormycosis is most frequently located in para nasal sinuses (39%), followed by lungs (24%), skin (19%), brain (9%), gastro-intestinal tract (7%) and other organs (6%) of cases. The spores are inhaled into the nasopharynx and tissue invasion, thrombosis and necrosis progress from the nose to the paranasal sinuses, orbit and central nervous system.⁷

The high frequency of sinus and orbital involvement likely relates to the angioinvasive growth and spread of mucormycosis from the nasal mucosa and paranasal sinuses.¹⁵ We found increasing anesthesia morbidity moving from localized rhinosinusitis to extensive rhino-orbito-cerebral infections. This aligns with pathophysiology, as greater fungal burden and tissue destruction portend worse systemic impairment.¹⁶

Moreover, orbital and intracranial complications necessitate more complex, prolonged surgeries that plausibly intensify anesthesia risks. Prospective studies are needed to confirm if mucormycosis type independently predicts perioperative outcomes when controlling for relevant factors. Understanding the distribution of mucormycosis patterns has implications for anesthesia management. Localized disease may allow more conservative, limited procedures. However, rhino-orbital-cerebral infections likely warrant extensive surgical debridement and complex reconstruction under general anesthesia.¹⁷ Anticipating extensive surgical requirements based on mucormycosis type can facilitate perioperative planning.

Our study found a high burden of comorbid illnesses among CAM patients undergoing surgery, most notably and cardiac involvement (72.73% with ECG changes), diabetes mellitus (66.85%), chronic respiratory diseases (58.74%). The heavy comorbidity load aligns with existing literature on risk factors and clinical profiles of mucormycosis patients. Diabetes, particularly with ketoacidosis, is a well-established predisposing condition for mucormycosis, presumably due to impaired immune function and microangiopathy.¹⁸ A systemic review found diabetes in up to 80% of mucormycosis cases.¹⁹

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

Similarly, chronic respiratory illness and structural lung disease are linked with mucormycosis susceptibility, plausibly due to altered mucociliary clearance and impaired macrophage function.²⁰ Pulmonary mucormycosis (PM) is known for its aggressive clinical course with a mortality rate approaching 55% with medical management alone.²¹ Hypertension and cardiac disease were also highly prevalent in our cohort. Mucormycosis is known to disseminate via invasion of vascular endothelium, potentially leading to thromboembolic phenomena.²² Endothelial dysfunction from hypertension could further propagate this angioinvasion and produce cardiac sequelae like ischemia, arrhythmias, or heart failure.²³

Our results emphasize the multi-system impact of mucormycosis and have implications for perioperative planning. Thorough preoperative optimization of diabetes, respiratory status, cardiac function, and other comorbidities is imperative. Anaesthesia management must account for complications like ischemia, fluid overload, electrolyte disturbances and drug interactions from antifungals.²⁴ Postoperatively, vigilant monitoring for cardiac, pulmonary, and metabolic derangements is essential. Future research should evaluate disease-specific protocols that balance the risks and benefits of surgery in this comorbidity-dense population. Our study found a high prevalence of anesthesia-related complications in the preoperative, intraoperative, and postoperative periods. The most frequent issues encountered were hypertension (21.53%), difficult airway (16.92%), and need for postoperative respiratory support (13.14% with NIV, 6.57% reintubation). The incidence of difficult mask ventilation and difficult intubation reported in study conducted by was kumari et al. was 7.3% and 6.4%²⁵, which is higher than that reported in the general population (5% and 5.8%, respectively)²⁶ The prevalence of difficult airway management describes potential airway challenges in mucormycosis. Both mask ventilation and endotracheal intubation can be difficult because of distorted facial anatomy, epiglottitis, and supraglottic edema.^{27,28} Moreover, most patients were diabetic in our study, in whom involvement of the atlantooccipital joint as a part of the diabetic stiff joint syndrome, makes

laryngoscopy difficult. Erden *et al.* reported a statistically significant increase in difficult laryngoscopy (18.75% vs. 2.5%) in type 2 diabetics versus non- diabetics.²⁹ In addition to anticipated difficulty, airway handling of patients with present or past COVID is strenuous due to the risk of self-infection.⁸

Hypertension was also common preoperatively, possibly due to anxiety³⁰, underlying cardiomyopathy, or undiagnosed pheochromocytoma triggered by illness.³¹ Perioperative hypotension can be multifactorial, stemming from sepsis, blood loss, decreased venous return, anaesthesia, hypovolemia, or cardiac dysfunction.³² Close hemodynamic monitoring and judicious vasopressor use is key given risks of pressure lability. Delayed emergence and recovery may relate to residual anaesthesia effects, metabolic derangements, or central nervous system impairment from severe infection.³³ Our findings reinforce the need for anticipating and mitigating potential airway, respiratory, hemodynamic, and neurologic complications throughout the perioperative course.

Future studies should investigate aesthetic techniques that optimize safety outcomes. For instance, regional anaesthesia may provide certain advantages for airway and analgesia management compared to general anaesthesia.³⁴ Additional research is critical to guide best practices for mitigating anaesthesia morbidity and mortality in this high-risk population.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

Our study found relatively low intraoperative mortality, indicating anaesthetic management was overall effective during the surgical procedure. However, nearly 1 in 10 patients died within 72 hours postoperatively, denoting the precarious recovery period in this vulnerable population. In a review conducted by Balushi *et al.*, it was reported that even with aggressive surgical debridement and systemic antifungal therapy, mortality ranged from 33.3-80% and up to 100% in disseminated disease with delayed intervention³⁵ In a systemic review and metanalysis Ostovan et al. documented that severe COVID-19 infection, history of mechanical ventilation, early CAM, comorbidities other than diabetes (malignancies, transplant, or renal failure), pulmonary and rhino- orbito-cerebral mucormycosis, and delivering only medical treatment for mucormycosis were the worst prognostic factors in CAM patients³⁶. Delayed deaths extending past 72 hours similarly highlight that complications precipitating mortality can manifest later during the postoperative course. Cerebral edema, respiratory failure from pneumonia or pulmonary embolism, uncontrolled sepsis, and metabolic disturbances are among the frequently fatal sequelae. Close postoperative monitoring, ideally in an intensive or high-dependency care setting, is imperative to promptly detect and intervene for such complications.

Future research should delineate optimal monitoring strategies, warning signs, and mitigating measures to avoid preventable adverse outcomes. Additional studies might also clarify if specific surgical techniques or approaches influence mortality risk. Our results demonstrate significant mortality concentrated in the postoperative period among CAM surgery patients. This compels healthcare systems to invest resources in enhanced postoperative care protocols and settings equipped to manage this critically ill population. Addressing the complex multisystem impacts of mucormycosis and surgery is key to improving the historically poor prognosis of this disease.

Limitations of the Study

This study provides valuable real-world data on anesthesia-related complications in CAM surgery patients but has limitations primarily related to retrospective design, single-center design limiting generalizability, and lack of controls that restrict the interpretability, possible selection bias as patients undergoing surgery could have had more severe or advanced disease versus broader CAM population. Lack of long-term follow-up data beyond the perioperative period restricts understanding of the full clinical course. We have lack of data regarding history of steroid consumption, which is an independent confounding for diabetes and development of mucormycosis.

Conclusion

This study demonstrates a substantial burden of anesthesia morbidity in CAM patients undergoing surgery The most frequent complications were hypertension, difficult airway, need for postoperative respiratory support, hypotension, and delayed recovery. Our results emphasize the importance of thorough preoperative optimization, anticipating potential airway and respiratory issues, careful hemodynamic monitoring, and planning postoperative disposition to higher-acuity settings. These measures are essential to mitigate the

high risk of anesthesia-related complications in this population. Our results provide an evidentiary basis to motivate further investigations aimed at clarifying and implementing optimal perioperative strategies for this high-risk group. Additional research should also evaluate whether specific anesthetic techniques or management protocols targeted for mucormycosis improve perioperative safety and mortality.

References

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 03, 2024

- 1. Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr. 2021;15(4):102146.
- 2. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, *et al.* Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis Off Publ Infect Dis Soc Am. 2005 Sep 1;41(5):634–53.
- 3. Skiada A, Lanternier F, Groll AH, Pagano L, Zimmerli S, Herbrecht R, *et al.* Diagnosis and treatment of mucormycosis in patients with hematological malignancies: guidelines from the 3rd European Conference on Infections in Leukemia (ECIL 3). Haematologica. 2013 Apr;98(4):492–504.
- 4. Jeong W, Keighley C, Wolfe R, Lee WL, Slavin MA, Chen SCA, *et al.* Contemporary management and clinical outcomes of mucormycosis: A systematic review and meta-analysis of case reports. Int J Antimicrob Agents. 2019 May;53(5):589–97.
- John TM, Jacob CN, Kontoyiannis DP. When Uncontrolled Diabetes Mellitus and Severe COVID-19 Converge: The Perfect Storm for Mucormycosis. J Fungi Basel Switz. 2021 Apr 15;7(4):298.
- 6. Sen M, Lahane S, Lahane TP, Parekh R, Honavar SG. Mucor in a Viral Land: A Tale of Two Pathogens. Indian J Ophthalmol. 2021 Feb;69(2):244–52.
- Sen M, Honavar SG, Bansal R, Sengupta S, Rao R, Kim U, *et al.* Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India – Collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. Indian J Ophthalmol. 2021 Jul;69(7):1670.
- 8. Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. Am J Emerg Med. 2021 Apr;42:264.e5-264.e8.
- 9. Pakdel F, Ahmadikia K, Salehi M, Tabari A, Jafari R, Mehrparvar G, *et al.* Mucormycosis in patients with COVID- 19: A cross-sectional descriptive multicentre study from Iran. Mycoses. 2021 Oct;64(10):1238–52.
- Pal R, Singh B, Bhadada SK, Banerjee M, Bhogal RS, Hage N, *et al.* COVID-19-associated mucormycosis: An updated systematic review of literature. Mycoses. 2021 Dec;64(12):1452–9.
- 11. Karimzadeh I, Heydari M, Ramzi M, Sagheb MM. Frequency and Associated Factors of Amphotericin B Nephrotoxicity in Hospitalized Patients in Hematology-Oncology Wards in the Southwest of Iran. Nephro-Urol Mon. 2016 Jul 3;8(5):e39581.
- 12. Mir SL, Ahmed S, Ghanghro L, Priya, Khatri G, Hasan MM. Mucormycosis infection in hematopoietic stem cell transplant patients: A serious threat. Ann Med Surg. 2022 Sep 9;82:104353.
- 13. Kumar A, Verma M, Hakim A, Sharma S, Meena R, Bhansali S. Epidemiology of Mucormycosis Cases During the Second Wave of COVID-19 in a Tertiary Care Institute in Western Rajasthan, India. Cureus. 14(3):e22973.
- 14. Desai D, Shah N, Cheraya N, Kalarthi B, Bavisetti S, D P, *et al.* Perioperative management of patients with post Covid rhino-orbito-cerebral mucormycosis: Prospective observational study. Indian J Clin Anaesth. 9(2):214–9.
- 15. Chikley A, Ben-Ami R, Kontoyiannis DP. Mucormycosis of the Central Nervous System. J Fungi. 2019 Jul 8;5(3):59.
- 16. Skiada A, Rigopoulos D, Larios G, Petrikkos G, Katsambas A. Global epidemiology of cutaneous zygomycosis. Clin Dermatol. 2012 Nov 1;30(6):628–32.
- 17. Ak AK, Gupta V. Rhino-Orbital Cerebral Mucormycosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Jan 24]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK557429/

- 18. Kumar RA, John NM, Ramya B, Satish HS. Management of Sinonasal Mucormycosis at a Tertiary Care Center: Our Experience. Int J Clin Rhinol. 2021 Feb 24;12(2–3):52–6.
- 19. Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr. 2021;15(4):102146.
- 20. Salazar F, Bignell E, Brown GD, Cook PC, Warris A. Pathogenesis of Respiratory Viral and Fungal Coinfections. Clin Microbiol Rev. 35(1):e00094-21.
- 21. Lee FY, Mossad SB, Adal KA. Pulmonary mucormycosis: the last 30 years. Arch Intern Med. 1999 Jun 28;159(12):1301–9.
- 22. Mahalaxmi I, Jayaramayya K, Venkatesan D, Subramaniam MD, Renu K, Vijayakumar P, *et al.* Mucormycosis: An opportunistic pathogen during COVID-19. Environ Res. 2021 Oct;201:111643.
- 23. Ambrosino P, Bachetti T, D'Anna SE, Galloway B, Bianco A, D'Agnano V, *et al.* Mechanisms and Clinical Implications of Endothelial Dysfunction in Arterial Hypertension. J Cardiovasc Dev Dis. 2022 Apr 27;9(5):136.
- 24. Sudhakaran S, Surani SR. Guidelines for Perioperative Management of the Diabetic Patient. Surg Res Pract. 2015;2015:284063.
- 25. Kumari K, Rathod D, Meshram T, Mohammed S, Raju S, Sharma A, *et al.* Perioperative anesthesia challenges and outcomes of patients with Rhino-Orbito-Cerebral Mucormycosis during the second wave of COVID-19 pandemic: An observational study. J Anaesthesiol Clin Pharmacol. 2023;39(4):615–21.
- 26. Kheterpal S, Healy D, Aziz MF, Shanks AM, Freundlich RE, Linton F, *et al.* Incidence, predictors, and outcome of difficult mask ventilation combined with difficult laryngoscopy: a report from the multicenter perioperative outcomes group. Anesthesiology. 2013 Dec;119(6):1360–9.
- 27. Karaaslan E. Anesthetic management of rhinoorbitocerebral mucormycosis; Focus on challenges. J Mycol Medicale. 2019 Sep;29(3):219–22.
- 28. Eckmann DM, Seligman I, Coté CJ, Hussong JW. Mucormycosis supraglottitis on induction of anesthesia in an immunocompromised host. Anesth Analg. 1998 Apr;86(4):729–30.
- 29. Erden V, Basaranoglu G, Delatioglu H, Hamzaoglu NS. Relationship of difficult laryngoscopy to long-term non- insulin-dependent diabetes and hand abnormality detected using the "prayer sign." Br J Anaesth. 2003 Jul;91(1):159–60.
- 30. Mulugeta H, Ayana M, Sintayehu M, Dessie G, Zewdu T. Preoperative anxiety and associated factors among adult surgical patients in Debre Markos and Felege Hiwot referral hospitals, Northwest Ethiopia. BMC Anesthesiol. 2018 Oct 30;18:155.
- 31. Howell SJ. Preoperative Hypertension. Curr Anesthesiol Rep. 2018 Mar 1;8(1):25–31.
- 32. Guarracino F, Bertini P. Perioperative hypotension: causes and remedies. J Anesth Analg Crit Care. 2022 Apr 14;2(1):17.
- 33. Cascella M, Bimonte S, Di Napoli R. Delayed Emergence from Anesthesia: What We Know and How We Act. Local Reg Anesth. 2020 Nov 5;13:195–206.
- 34. Hutton M, Brull R, Macfarlane AJR. Regional anaesthesia and outcomes. BJA Educ. 2018 Feb;18(2):52–6.
- 35. Balushi AA, Ajmi AA, Sinani QA, Menon V, Berieki ZA, Shezawi AA, *et al.* COVID-19-Associated Mucormycosis: An Opportunistic Fungal Infection. A Case Series and Review. Int J Infect Dis. 2022 Aug;121:203–10.
- 36. Ostovan VR, Tabrizi R, Bazrafshan H, Bahrami Z, Khazraei H, Khazraei S, *et al.* Mortality-Related Risk Factors for Coronavirus Disease (COVID-19)-Associated Mucormycosis: a systematic review and meta-analysis. Curr Fungal Infect Rep. 2022;16(4):143–53.