

Predictors of Mortality in operated cases of Covid associated Mucormycosis.

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Abstract

Background :

Covid associated Rhino orbital cerebral Mucormycosis is comonly seen in second wave of covidin patients with uncotrolled diabetes, or imunicompromised patients. It can be treated successfully with systemic amphotericin B and surgical debridement of necrotic tissues ,Systemic amphotericin B has a lots of side effects like fever, shivering, hypotension, hypoxia, arrhythmia and mainly nephrotoxicity. There is need for early diagnosis and surgical debridement of necrotic tissues while keeping in mind the toxic effects of systemic amphotericin B and its interaction with anaesthetic agents.

Postoperative ICU is important due to comorbidities and fungal infection with high mortality.

Aims:

Aim & objectives of our study were to access predictors of mortality in operated cases of Covid associated Mucormycosis patients

Method:

we have collected detail records clinical,pathological data , preoperative Anaesthesia status, Anaesthesia techniques ,postoperative ventilatory support,ICU stay, morbidity & mortality,of operative patients of Mucormycosis in LG hospital, AMCMET college Ahmedabad **Results:**Female Gender, presence of Uncontrolled Diabetes Mellitus, Hypertension ,Hypothyroid comorbidites,Use of steroids, perioperative Vasopressor requirements, postoperative ventilatory support , decrease PaO₂,Raised DDimer,ferittin, creatinine (Acute Kidney injury)were common predictors of mortality in Covid associated Rhino orbital cerebral Mucormycosis.

Conclusion: Uncontrolled Diabetes,use of steroids,acute kidney injury, perioperative Vasopressor requirements postoperative ventilatory support,decrease PaO₂ inspite of ventilatory assistance,raised DDimer and ferittin were strong predictors of mortality in Decedents group of study population.

Keywords: Anesthetic management; Biomarkers, ICU stay,Morbidity & Mortality in Covid mucormycosis, Rhino-orbito-cerebral(ROC) mucormycosis.

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I. Introduction

Mucormycosis is a fulminant, opportunistic fungal infection most commonly seen in diabetics and immunocompromised individuals. It is a highly lethal, locally invasive with propensity to involve multiple organs. The six accepted clinical types of mucormycosis are: Rhinocerebral, gastrointestinal, pulmonary and disseminated, burn wound, central nervous system, endocarditis, and vascular mucormycosis.

Mortality is high, death can occur within several hours to few days in spite of appropriate treatment being administered. Successful management of mucormycosis largely depends on early diagnosis, a reversal of underlying predisposing factors, prompt, and broad surgical debridement of infected tissue and rapid administration of systemic antifungal therapy. There are no established regimes for the primary treatment of mucormycosis

.Amphotrecin B used has adverse effects, likeHypokalemia, hypomagnesemia, fever, chills, dyspnea, and hypotension , Allergic reactions, seizures, anemia, and thrombocytopenia can occur.. Renal function is impaired in >80% of treated patients, and a permanent decrease in the glomerular filtration rate is likely, with 15% of patients requiring hemodialysis. Studies indicate that the anesthetic management

of patients with acute tubular necrosis leading to the development of acute renal failure is of particular concern for anesthesia providers.[3]

Anesthesia management must pay particular attention for the maintenance of an adequate mean arterial pressure and cardiac output while concomitantly avoiding further renal insults. Our patient had hypotension intraoperatively with arrhythmias that responded to treatment with lidocaine infusion. A heightened awareness for renal, electrolyte, coagulopathic, hemodynamic, and respiratory aberrancies is warranted for anesthesia providers when treating patients receiving AmB therapy.[3]

Amphotericin B acts by binding to the sterol component, ergosterol, of the cell membrane of susceptible fungi forming transmembrane channels leading to alterations in cell permeability through which monovalent ions (Na⁺, K⁺, H⁺, and Cl⁻) leak out of the cell resulting in cell death. It can also bind to the cholesterol component of the mammalian cell leading to cytotoxicity. Concurrent use of corticosteroids, ACTH and digitalis glycosides may potentiate hypokalemia, which could predispose the patient to cardiac dysfunction and digitalis toxicity. If used concomitantly, serum electrolytes and cardiac function should be closely monitored.

II. Material And Methods

In this Retrospective observational study, we have collected data of operated case of Covid associated Rhino orbital cerebral Mucormycosis (ROCM) at our tertiary care hospital. Clinical, pathological biomarkers, preoperative data was recorded in spread sheet, All patients anaesthetised with standard Anaesthesia protocol. Intraoperative or postoperative vasopressor requirements, time to extubation, postoperative ventilatory support, haemodynamic parameters, in hospital mortality also noted

Statistical analysis

Results were documented on MS Excel spreadsheet and analysis done with SpSS software IBM Armonk NY 2021. Numerical variables analysed by unpaired t test, Categorical data was analysed by chi-Square test/ Fischer exact tests.

P>0.05 is non significant (NS), P<0.05 is significant (S), P<0.001 is Highly significant (HS)

III. Results:

Table 1 patient characteristics

Parameters	Group D (Decedent) (n=13)	Group S (Survival) (n=54)	P value
Age(yrs)	59.6+/-12.9	57.14+/-14.52	>0.05
Gender(M:F)	3:10	32:22	
Hypertension /Hypothyroid	7/4(53.8/30.76)%	1/0(7.69%)	<0.001(HS)
Diabetes Mellitus	13(100%)	16(29.56%)	<0.001(HS)
Post Covid day detection of mucor	18.3+/-5	20.7+/-7.2	>0.05
HRCT score	14.3+/-6.09	13.8+/-5.9	>0.05
Revised surgery done	2(15.36%)	11(20.3%)	
Steroids given	13(100%)	49(90.7%)	<0.05(S)
Preoperative Oxygen status (RA/VM/NRBM/BiPAP)	5/2/2/4	46/0/0/8	
Perioperative Vasopressor requirements	6(46.15%)	2(3.7%)	<0.05(S)
Postoperative ventilatory support required	6(46.15%)	10(18.5%)	<0.05(S)

*RA- Room Air, VM-VentiMask, NRBM- Nonbreathing mask, BiPAP- Bilevel positive Airway Pressure

Regarding patient characteristics in Decedents females are more than male, patients have comorbidities like Hypertension 53.8%, Hypothyroid 30.76% in Decedents, whereas uncontrolled Diabetes Mellitus was in all 100% Decedents, Survivors group had Diabetes in 90% of patients but was having controlled. (HbA1c<7). In both groups preoperative Oxygen status doesn't have statistical significant parameter. In all Decedents steroids Immunomodulators were given. Perioperative vasopressor requirements & postoperative ventilatory support required statistical high in Decedents group.

Table 2 clinicopathological parameters

Parameters	Group D	Group S	P value
PH	7.44+/-0.04	7.42+/-0.08	>0.05
Po2(mm of Hg)	103.39+/-30.2	203.93+/-38.3	<0.001(HS)
Pco2(mm of Hg)	30.6+/-5.31	31.6+/-6.56	>0.05
So2	96.7+/-3.21	96.9+/-3.6	>0.05
Hco3	22.4+/-3.3	22.1+/-3.6	>0.05

Urea (mg/dl)	45+/-24.4	38.8+/-26.9	>0.05
Creatinine	1.46+/-0.8	1.18+/-0.55	<0.05(S)
LDH(unit/l)	299+/-245	268+/-247	>0.05
D Dimer(ng/ml)	1024+/-964	731+593	<0.05(S)
Ferritin(ng/ml)	1652.8+/-617	1223+/-909	<0.001(HS)
HbA1c(%)	7.8+/-2.1	6.0+/- 1.2	<0.05(S)
Acetone(Yes/No/trace)	2/8/1	5/46/3	<0.05(S)
Na/K/Cl(mean)	136/3.59/105	138/3.74/102	>0.05
CRP(mg/l)	60+/-12	55+/-17	>0.05

Regarding biomarkers,,Creatinine, HBA1C, DDimer, Ferritin, acetone raised statistical significant(S) in Decedents(p<.05), whereas PaO2 decrease highly significant in Decedents (p<0.001)

IV. Discussion

Early diagnosis, intravenous Amphotericin B, surgical debridement along with treating underlying disease leads to better prognosis in systemic mucormycosis, however attending anesthesiologists should have knowledge of intravenous AmB induced renal and C.V.S. changes and its interactions. The prevalence of mucormycosis seems to be increasing among COVID-19 patients which may be associated with increased use of steroids, the possible immunocompromised state imposed by SARS-CoV-2, or co-existing conditions such as diabetes mellitus.

The mortality of CAM is remarkably high and apart from preventive practices and rational use of immunomodulators, a high index of suspicion with early diagnosis would be key to survival.

Chakrabarti A, Das A .etal(4) had suggested that in uncontrolled Diabetes patients fungal infections are common.

JHU etal (5) narrated that COVID-19-associated mucormycosis (COVID–Mucor), manifesting as rhino-orbito-cerebral mucormycosis (ROCM), which has worsened the morbidity among vulnerable populations .SARS-CoV-2 infection , High blood sugar, corticosteroids, and iron overload all lead to phagocyte dysfunction, likely the more immediate cause of mucormycosis.

Lammaert et al.,(7) 2012 conclude that Mean serum ferritin levels, a marker of immune dysregulation and an integral part of iron metabolism, were markedly elevated among cases. In addition to hyperglycaemia and steroid use, SARS-CoV-2 infection with possible alterations in iron metabolism may have predisposed to mucormycosis .

Montefusco ,Ben Nasr M et al.,(8) 2021 showed that Hyperglycaemia lasting up to 3 months associated with COVID-19 has been reported. An aberrant cytokine milieu and insulin resistance, rather than beta cell infection, seem to be the reasons Steroid use also induces hyperglycaemia, and steroid use was significantly associated with mucormycosis (OR 28.4; P = 0.001). Despite extensive use in rheumatological diseases, the incidence of mucormycosis remains low, suggesting that steroid use in conjunction with other factors has driven the COVID–Mucor epidemic in India.**Patel et al., Agarwal R,2021(10)** in their study,The vast majority of patients, 97%, had underlying diabetes mellitus, a rate higher than that found in a multicentre COVID–Mucor study from India performed during the first wave of the COVID-19 pandemic, in which two-thirds of patients had this disease .

Staplin N, Brightling C, etal (11) have suggested use of steroids in form of Dexamethasone for

Symeonidis AS. (12) have also discuss the role of iron and iron chelators in zygomycosis.

Giovanni Pontia, (13)&Henry BM, (14)have narrated biomarkers raised in Covid mortality patients were CRP, DDimer, Ferritin.

Shah Sonal,Kapdi Manisha etal(15)have recently analyse Predictors of Mortality between Young and Elder Covid-19 Patients Admitted in Covid-19 Designated Tertiary Care Hospital& concluded that DDimer, Ferritin raise are common biomarkers raised in aged Decedents whereas in young Decedents LDH was raised more along with DDimer & Ferritin. Offcourse in their study Diabetes ,Hypertension & Hypothyroid were common comorbidites in all Decedents.

Finally, the recent surge in COVID-19 cases was associated with an unprecedented shortage of oxygen availability in India, resulting in the use of industrial-grade oxygen in some parts of the country. Although exposure to impure oxygen was thought to be a possible risk factor, only a fraction of patients in this study required oxygen or ventilatory support, suggesting that it was unlikely a significant factor.

To summarise Female Gender, presence of Uncontrolled Diabetes Mellitus, Hypertension ,Hypothyroid comorbidites,Use of steroids, perioperative Vasopressor requirements, postoperative ventilatory support , decrease PaO2,Raised DDimer,ferittin, creatinine (Acute Kidney injury)were common predictors of mortality in Covid associated Rhino orbital cerebral Mucormycosis.

V. Conclusion

In nutshell, Use of steroids, high blood sugar levels, raised Ferritin, and Creatinine, (acute kidney injury) were strong predictors of mortality in Covid associated Rhino orbital cerebral Mucormycosis. Strongest predictor was decrease PaO₂ in spite of ventilatory assistance in each deceased patient in their clinicopathological scenario.

Future Recommendations

Restricting use of steroids, immune modulators to patients with severe COVID-19 requiring oxygen therapy, and screening for and optimally controlling hyperglycaemia can prevent COVID–Mucor in a large majority.

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