



ORIGINAL RESEARCH PAPER

Medicine

RELATIONSHIP OF HYPOALBUMINEMIA WITH OUTCOME OF RHINO-ORBITO-CEREBRAL MUCORMYCOSIS (ROCM), A TERTIARY CARE CENTER BASED STUDY.

KEY WORDS: Rhino-Orbito-Cerebral Mucormycosis (ROCM), Hypoalbuminemia, Deformity, Death, Outcome.

Dr. Shyamash Mandal

Assisant Professor, Dept. Of General Medicine, BSMCH.

Dr. Souvik Das*

Post Graduate Trainee, Dept. Of General Medicine, BSMCH. *Corresponding Author

Dr. Abhisek Mallik

Senior Resident, Dept. Of General Medicine, BSMCH.

Dr. Prof. Syamal Kundu

Head of Department, Dept. Of General Medicine, BSMCH.

ABSTRACT

Mucormycosis is a serious but rare fungal infection caused by a group of molds called mucormycetes. The increasing incidence of Rhino-Orbito-Cerebral Mucormycosis (ROCM), a form of Mucormycosis in the setting of COVID-19 in India and elsewhere has become a matter of immediate concern. As far as outcome of ROCM is concerned, some patients respond only to pharmacotherapeutic agents and short surgical procedures without any deformity, whereas some patients need decapitating surgeries like Orbital exenteration and/or Maxillectomy resulting in deformity, and some patients may develop complications leading to death. Presence of hypoalbuminemia in patients with ROCM can exert poor prognosis especially where surgical organ removal is indicated. The study was a hospital based prospective cross-sectional study done on 33 ROCM patients to look for any relationship between two factors, hypoalbuminemia and outcome of ROCM. And we found out that hypoalbuminemia independently can affect the outcome of the disease.

INTRODUCTION:

Mucormycosis (previously called zygomycosis) is a serious but rare fungal infection caused by a group of molds called mucormycetes¹. These molds live throughout the environment. Mucormycosis most commonly affects the sinuses or the lungs after inhaling fungal spores from the air. It can also occur on the skin after a cut, burn, or other type of skin injury.

Mucormycosis is a potentially lethal, angioinvasive fungal infection predisposed by diabetes mellitus, corticosteroids and immunosuppressive drugs, primary or secondary immunodeficiency, hematological malignancies and hematological stem cell transplantation, solid organ malignancies and solid organ transplantation, iron overload etc². The increasing incidence of Rhino-Orbito-Cerebral Mucormycosis (ROCM) in the setting of COVID-19 in India and elsewhere has become a matter of immediate concern³⁻⁵. From the time that we first reported a series of six cases of ROCM in February 2020, there has been an exponential increase in incidence in India, in sync with the soaring second wave of COVID-19⁶. ROCM being a rapidly progressive disease, even a slight delay in the diagnosis or appropriate management can have devastating implications on patient survival⁷. However, the outcome can be optimized by early diagnosis prompted by awareness of warning signs and symptoms and high index of clinical suspicion, confirmation of diagnosis by appropriate modalities, and initiation of aggressive medical and surgical treatment by a multidisciplinary team^{7,8}.

Sayantan Banerjee, David W. Denning and Arunaloke Chakrabarti cite a study that computes India's overall mucormycosis prevalence to be 0.14 cases per 1,000 population in India⁹, or about 187,460 patients. The overall mortality in mucormycosis when well-treated ranges from 30% to 46.7%. This could translate to about 105,000 people succumbing to these infections every year in the WHO South East Asian Region (SEAR), were these numbers to be applied to the region.

ROCM can be categorized as Possible, Probable, and Proven. A patient who has symptoms and signs of ROCM in the clinical

setting of concurrent or recently (<6 weeks) treated COVID-19, diabetes mellitus, use of systemic cortico-steroids and tocilizumab, mechanical ventilation, or supplemental oxygen is considered as Possible ROCM. When the clinical symptoms and signs are supported by diagnostic nasal endoscopy findings, or contrast-enhanced MRI or CT Scan, the patient is considered as Probable ROCM. Clinico-radiological features, coupled with microbiological confirmation on direct microscopy or culture or histopathology with special stains or molecular diagnostics are essential to categorize a patient as Proven ROCM. As far as outcome of ROCM is concerned, some patients respond only to pharmacotherapeutic agents and short surgical procedures without any deformity, whereas some patients need organ removal surgeries like Orbital Exenteration and/or Maxillectomy resulting in deformities of upper jaw and hard palate, and some patients may develop complications leading to death.

Albumin has a number of important physiologic functions, which include maintaining oncotic pressure, transporting various agents (fatty acids, bile acids, cholesterol, metal ions, and drugs), scavenging free oxygen radicals, acting as an antioxidant, and exerting an antiplatelet effect. Hypoalbuminemia in adults, defined by an intravascular albumin level of <3.5 g/dl, is associated with poor postoperative outcomes in patients undergoing surgical intervention¹¹. Three theoretical constructs might explain this relationship. First, albumin might serve as a nutritional marker, such that hypoalbuminemia represents poor nutritional status in patients who go on to experience poor postoperative outcomes. Second, albumin has its own pharmacologic characteristics as an antioxidant or transporter, and therefore, the lack of albumin might result in a deficiency of those functions, resulting in poor postoperative outcomes. Or third, albumin is known to be a negative acute phase protein, and as such hypoalbuminemia might represent an increased inflammatory status of the patient, potentially leading to poor outcomes. Hence presence of hypoalbuminemia in patients with ROCM can exert poor prognosis especially where surgical debridement and organ removal is indicated.

METHODS AND MATERIALS:

- It is a prospective cross-sectional study, done in patients

admitted in ward of Department of Otorhinolaryngology, Critical Care Unit, Covid ward under Department of General Medicine, B.S.M.C.H, Bankura.

- All patients of diagnosed ROCM are included by complete enumeration method.

Inclusion Criteria:

- All the cases of ROCM diagnosed both clinically and Histopathologically, in the in-patient ward of Department of Otorhinolaryngology, Critical Care Unit, Covid ward under Department of General Medicine, B.S.M.C.H, Bankura.
- Patients who are willing to participate in the study.

Exclusion Criteria:

- Lowest serum albumin level during course of disease is >3.5.
 - Known or diagnosed cases of
 - Chronic Kidney Disease.
 - Diabetic Nephropathy.
 - Uncontrolled Hypertension.
 - Chronic Liver Disease.
 - Patients who do not want to participate in the study.
 - Patients who were referred to higher center.
- All the cases of ROCM are treated according to their situation and other associated conditions according to standard protocol.
 - All the patients are treated with 20% Human albumin according to standard protocol (Infusion 20% Human Albumin at a rate of 20 drops per minute once daily). Serum albumin value repeated every 3 days interval. Treatment continued until serum albumin reaches 3.5 gm/dl.

RESULTS AND ANALYSIS:

Table 1. Distribution of total number of ROCM patients according to outcome.

Discharged with Deformity.	Discharged without deformity.	Death.	Total.
14	13	6	33.

Total 33 patients were taken into our study, 14 (42.4%) out of them were discharged with some degree of deformity, 13 (39.4%) of them were discharged without any deformity, and 6 (18.2%) of them deceased due to course of the disease itself or associated complications (Table 1 and diagram 1).

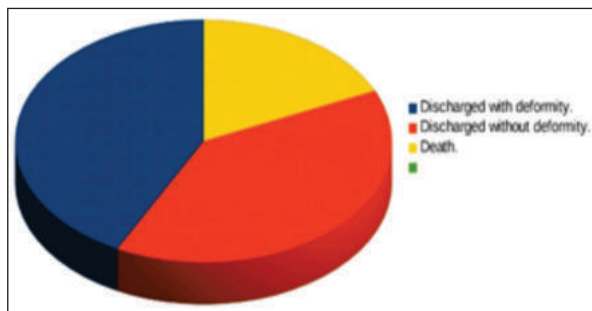


Diagram 1. Distribution of ROCM patients according to outcome.

Table 2. Relationship between hypoalbuminemia severity and ROCM outcome (P value 0.04726).

Albumin level.	Discharge with Deformity.	Discharge Without Deformity.	Expired.	Row total.
2.5-3.5 gm/dl.	8	10	1	19
<2.5 gm/dl.	6	3	5	14
Column total.	14	13	6	33

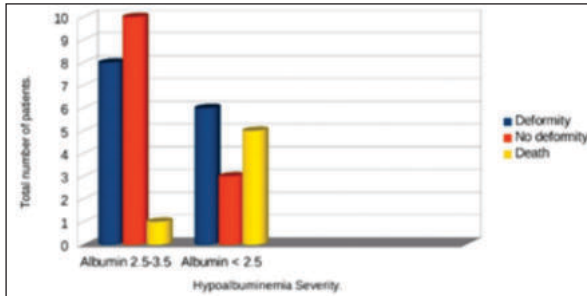


Diagram 2. Relationship between hypoalbuminemia severity and ROCM outcome.

Table 2 shows among patients with mild hypoalbuminemia, incidence of deformity is lower than that of being discharged without deformity. But in patients with severe hypoalbuminemia, deformity is more common. Among the 19 patients with mild hypoalbuminemia, 8 (42.1%) patients were discharged with deformity, 10 (52.6%) were discharged without any deformity and 1 (5.3%) died in the study period. Among the 14 patients with severe hypoalbuminemia, 6 (42.9%) were discharged with deformity, 3 (21.4%) were discharged without any deformity and case fatality rate among them was 35.7% (6). The chi-square statistic is 6.1042. The p-value is 0.04726. Hence the patient's with mild hypoalbuminemia had better surgical prognosis than patients with severe hypoalbuminemia despite of intravenous Human albumin transfusion.

CONCLUSION:

The study was a hospital based prospective cross-sectional study done on 33 ROCM patients to look for any relationship between two factors, hypoalbuminemia, a complication of the disease and outcome of ROCM. According to the data analysis, we can strongly comment that hypoalbuminemia independently can affect the outcome of the disease. And also it can be postulated that early prevention, diagnosis aggressive therapy can change the course of the disease in its process and improve the outcome.

REFERENCES:

- <https://www.cdc.gov/fungal/diseases/> postulated that early prevention, diagnosis and aggressive therapy can change the course of the disease in its process. mucormycosis/index.html.
- Ravani SA, Agrawal GA, Leuva PA, Modi PH, Amin KD. Rise of the phoenix: Mucormycosis in COVID 19 times. Indian J Ophthalmol 2021.
- Sen M, Lahane S, Lahane TP, Parekh R, Honavar SG. Mucor in a viral land: A tale of two pathogens. Indian J Ophthalmol 2021; 69:244-52.
- Sarkar S, Gokhale T, Choudhury SS, Deb AK. COVID-19 and orbital mucormycosis. Indian J Ophthalmol 2021; 69:1002-4.
- Sen M, Honavar SG, Sharma N, Sachdev MS. COVID-19 and eye: A review of ophthalmic manifestations of COVID-19. Indian J Ophthalmol 2021; 69:488-509.
- Rao R, Shetty AP, Nagesh CP. Orbital infarction syndrome secondary to rhino-orbital mucormycosis in a case of COVID-19: Clinico-radiological features. Indian J Ophthalmol 2019; 69.
- Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, et al. Global guideline for the diagnosis and management of mucormycosis: An initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. Lancet Infect Dis 2019; 19:e405-21.
- Skied A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: An update. J Fungi (Basel) 2020; 6:265.
- <https://www.thehindu.com/news/national/mucormycosis-not-uncommon-in-india-studies/article34617210.ece>
- P Aeanwit et al. The effect of serum albumin on the aggregation state and toxicity of amphotericin B. J Pharm Sci. 2000 Dec; 89(12):1589-93.
- Sunghye K, Stephen A McClave, Robert G, Keith R. Hypoalbuminemia and Clinical Outcomes: What is the Mechanism behind the Relationship? Am Surg. 2017 Nov 1; 83(11):1220-1227.