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A RETROSPECTIVE STUDY TO EVALUATE THE RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF MUCORMYCOSIS IN POST COVID PATIENTS - IN A TERTIARY CARE HOSPITAL

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Abstract

The primary objective of this research was to identify the risk factors present during COVID-19 infection that contributed to the development of life-threatening mucormycosis. We retrospectively investigated 40 patients diagnosed with Post COVID Mucormycosis admitted under ENT Department of Saveetha Medical College and Hospitals during May 2022 – October 2022 for whom repeat RT PCR, CT paranasal sinuses, MRI Brain with Orbit, KOH Stain, Fungal c/s, histopathology were done after admission. All Patients underwent medical and surgical management. History of COVID positive status (within the last 6 months), pre - existing comorbidity, newly diagnosed diabetes mellitus during the COVID infection, history of exposure to oxygen and steroids during the active covid infection, history of hospitalisation during the covid infection, and hyperglycaemic state during steroid therapy was recorded . COVID positive status in the past with either COVID RTPCR POSITIVE or POSITIVE CORADS scores was taken into account. The medical records of all the 40 patients were evaluated in detail for the same management. The data collected from this study showed that out of 40Mucormycosis patients, pre-existing type 2 diabetes mellitus was seen in 28(70%). 11(27.5%) had history of oxygen usage, 21(52.5%) had history of steroids intake and 12(30%) were newly diagnosed diabetes mellitus after steroid usage. Covid19 patients with exposure to oxygen and steroids with or without pre - existing diabetes mellitus were at increased risk for hyperglycaemia that in turn led to angio-invasive mucormycosis, even in previous healthy young adults. Immunocompromised patients have an inflammatory state potentiated by the activation of antiviral immunity to SARS – CoV2, which favours secondary infections. Such data is useful for highlighting the necessity of judiciously using oxygen and corticosteroids in the management of COVID-19 to prevent subsequent complications.

Keywords: Post Covid Mucormycosis, Steroids, Oxygen, İmmunocompromised State, Risk Factors.

INTRODUCTION

Mucormycosis is a fatal angio invasive infection by the fungal species of the order Mucorales, which includes the genera of ubiquitous fungi such as *Mucor* and *Rhizopus* [1]. Mucormycosis is known to be characterised by infarction and necrosis of the host tissues. It is classified based on the anatomical sites of involvement, such as rhino-cerebral, pulmonary, gastrointestinal, cutaneous, and disseminated forms. The most common form affecting people is rhino-cerebral mucormycosis, which occurs by the inhalation of spores to a host with predisposing factors within them, which includes diabetes mellitus, particularly diabetic ketoacidosis, and treatment with glucocorticoids (steroids) in the past, haematologic malignancies, haematopoetic stem-cells or solid organ transplantation, iron- overload, and malnutrition also. The diagnosis of mucormycosis solely relies upon the identification of organisms in the tissue taken by biopsy sent for histopathology with culture confirmation [1-9]. The main reason for the invasive infections in the post COVID-

19 infected patients is due to the impairment of innate defense mechanisms that are present in normal healthy individuals, like reduced ciliary clearance, and lack of lymphatic immune response against the fungal invasion during COVID-19 infection [10]. The use of corticosteroids against COVID-19 to reduce the risk of mortality, most likely is the reason that makes patients more prone to many other opportunistic infections especially mucormycosis. Mucormycosis is known to invade the arteries, and forms thrombi within the micro vessels and causes necrosis of the surrounding hard and soft tissues [11,12]. Treatment of mucormycosis usually involves a combination of surgical debridement of all the involved tissues and targeted anti-fungal therapy [12,13]. Intravenous (IV) amphotericin B (a lipid formulation) is the drug of choice for initial therapy [14,15]. Posaconazole is used as step-down therapy for patients who have responded well to amphotericin B treatment. Elimination of all the predisposing factors resulting in the infection, such as hyperglycaemia, metabolic acidosis, immunosuppressive drugs, and neutropenia, is very essential. The overall mortality of mucormycosis in India is 15-31% [16].

MATERIALS AND METHODS

A retrospective observational study was carried out at Saveetha Medical College and Hospitals, Chennai, Tamil nadu, India from May 2022– October 2022. 40 COVID Associated mucormycosis positive patients admitted in the department of Oto-rhinolaryngology were included in this study.The diagnosis of mucormycosis in all enrolled patients was confirmed by KOH mount examination or nasal or gingival biopsies, or palatal scrapings.

Study design**:** Retrospective cohort study.

Inclusion Criteria:

- History of COVID Positive status with in the last 6 months – either with a positive Covid RT PCR test or Positive CORADS score (3 – 6) on CT Thorax.
- Proven histopathology report of mucormycosis was mandatory.
- Patients Aged 18 years and above.
- Both Males and females.
- With or without pre-existing/newly diagnosed Comorbidities.
- History of hospitalisation due to COVID-19 infection.

Exclusion Criteria

- Age less than 18 years.
- No previous proven record of COVID positive status within the last 6 months.
- No history of hospitalisation for COVID 19 infection.
- Patients tested positive for aspergillosis in KOH mount.

METHODOLOGY

The diagnosis of mucormycosis was confirmed identifying broad aseptate fungal hyphae with right-angled branching either on fungal KOH or histopathological examination of nasal or gingival biopsies, or palatal scrapings.In some cases, fungal

culture and sensitivity testing on Sabouraud's dextrose agar yielded positive results for Rhizopus.

Repeat RT PCR test, Non contrast CT scan of para nasal sinuses [Fig 1,2] and MRI Brain with Orbit was done for all patients to evaluate the present COVID status and extend and severity of mucormycosis.

Fig 1: Coronal view of CT para nasal sinuses showing involvement of left maxillary sinus, nasal conchae, and ethmoidal sinus extending till frontal sinus.

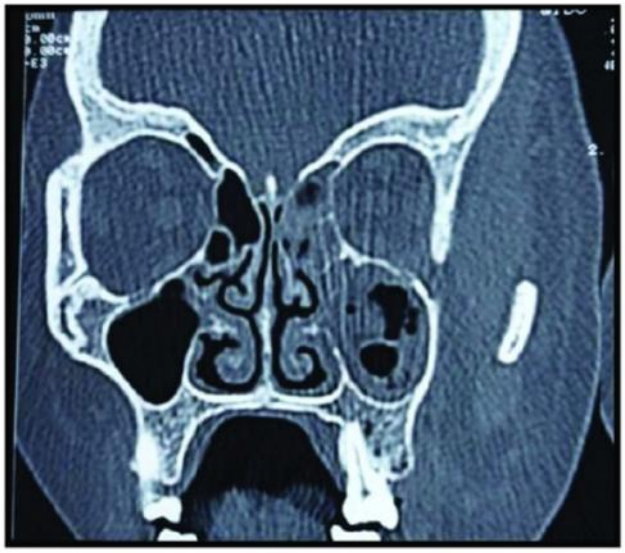
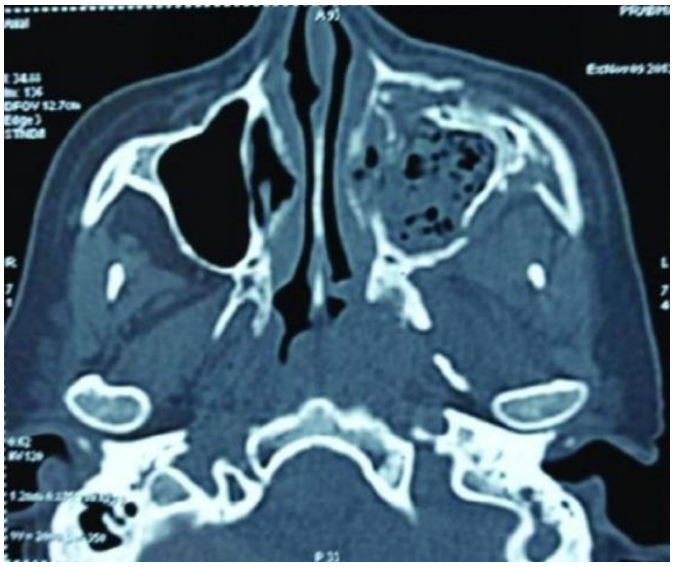


Fig 2: Axial view of CT para nasal sinuses showing erosion and destruction of posterior, medial and anterior walls of left maxillary sinus



Management began with antifungal therapy, starting with oral Posaconazole at 300 mg twice daily on the first day, followed by 300 mg once daily for two months. Intravenous Amphotericin B was administered in doses ranging from 1 to 2.5 grams per day, depending on the severity of the infection. Surgical intervention included debridement of all affected paranasal sinuses and either orbital decompression or exenteration as needed.

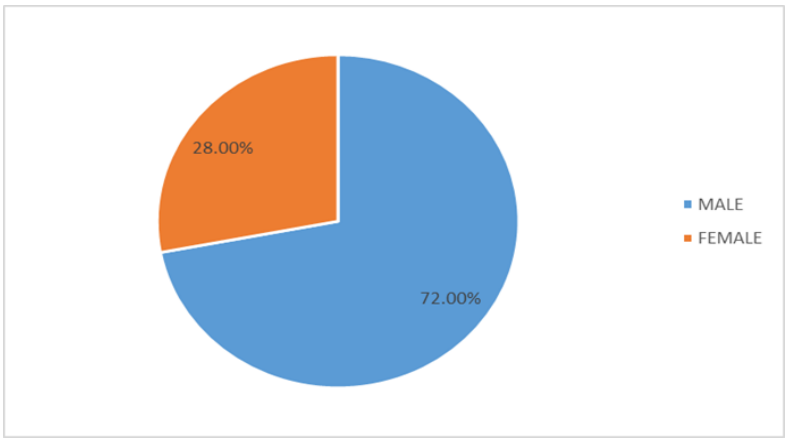
Patient's renal function and cardiac status, including ECG monitoring, were regularly assessed. Diabetic patients were managed with insulin and oral hypoglycemic agents as necessary.

Retrospectively the medical records of all these patients were evaluated in detailed for history of patients including age, gender, occupation, presenting complaints with duration, diabetic status, other comorbidities, history of covid-19 recently and associated management that was taken for the condition. Descriptive statistics were used to describe the continuous and categoral variables.

RESULTS

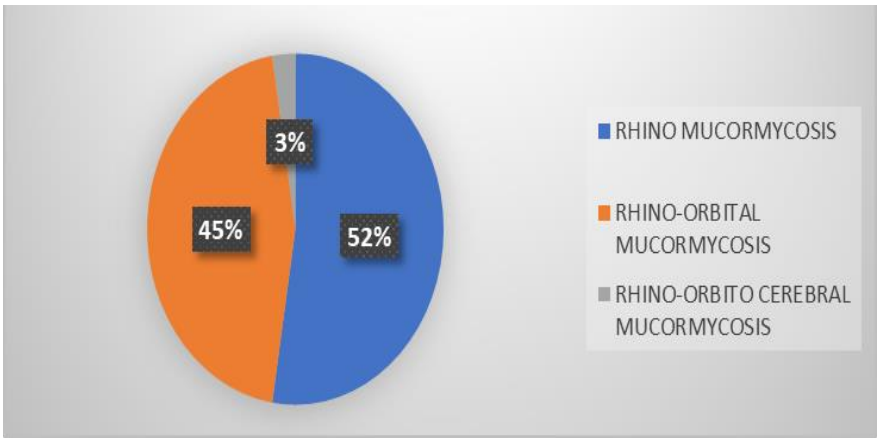
Out of 40 Mucormycosis patients 29(72.5%) were males and 11 were (27.5%) females [Fig.3].

Fig 3: Pie chart showing gender distribution of COVID associated mucormycosis



18(45%) patients had rhino-orbital mucormycosis and 1(2.5%) patient had rhino-orbito-cerebral mucormycosis and 21(52.5%) patients had only sinus involvement [Fig 4].

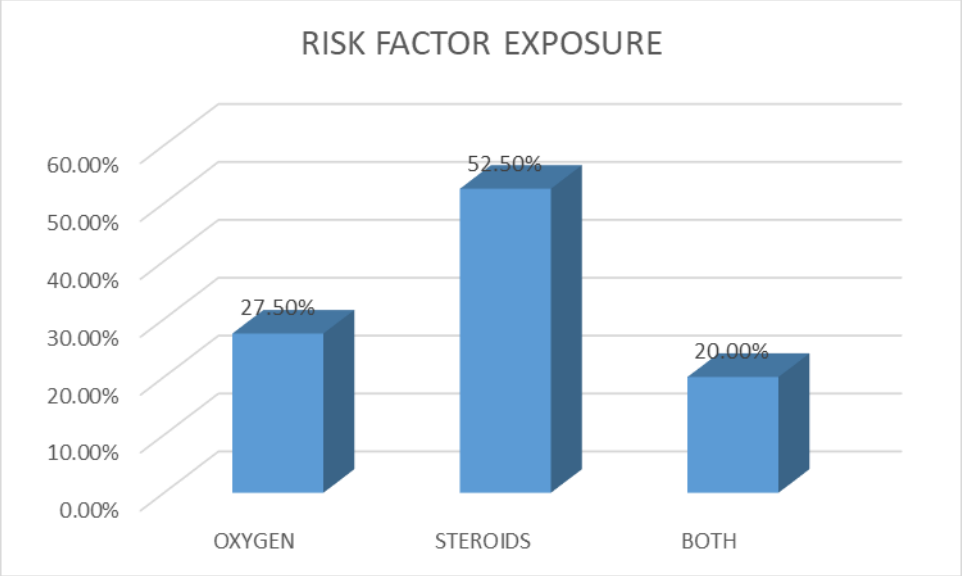
Fig 4: Pie chart showing frequency of presentation of mucormycosis



32(80%) patients had previous history of COVID positive (RT PCR) status, whereas 8(20%) patients had positive CO – RADS score in the in the last 6 months. Pre - existing type 2 diabetes mellitus was seen in 28(70%) patients.

11(27.5%) had history of oxygen usage, 21(52.5%) had history of steroids intake. 8(20%) had history of both oxygen and steroid usage [Fig 5]. 12(30%) were newly diagnosed diabetes mellitus after steroid usage during previous COVID illness.

Fig 5: Clustered column chart showing distribution of risk factors in patients with mucormycosis



DISCUSSION

Prior to the COVID-19 pandemic, mucormycosis was most commonly reported only in severely immunocompromised patients with uncontrolled diabetes [1].In few patients, it was a diabetes-defining illness. The most common clinical presentation of mucormycosis is rhino-orbital-cerebral infections. Hyperglycemia, mostly with an associated metabolic acidosis, is the most common underlying condition [1]. All cases had a history of administration of broad-spectrum antimicrobials. 11(27.5%) of the cases had a history of non-invasive oxygen supplementation. Of the patients, 70 % were previously diagnosed as diabetics and/or were treated with high-dose corticosteroids for COVID 19; both are considered risk factors for immunosuppression. Insulin was used to treat the deranged glycaemic status caused by the use of high-dose steroids. Twelve of these cases were known cases of hypertension, and four of them had obesity. All the cases had variable disease involvement in the eye, CNS, and paranasal sinuses [14,15]. Mucormycosis usually presents as acute sinusitis with or without fever, nasal congestion, purulent nasal discharge, headache, and sinus pain. All the sinuses can be involved and it spreads to contiguous structures, like the palate, orbit, and brain and usually progresses rapidly over the course of a few days. The hallmarks of spread beyond the sinuses include tissue necrosis of the palate that further results in palatal eschars, destruction of the nasal turbinates, perinasal swelling, erythema, and cyanosis of the facial skin overlying the involved sinuses and/or orbit. Signs of orbital involvement like periorbital edema, proptosis, and blindness is also seen in most of the cases. Facial numbness is not rare and results from infarction of sensory branches of the fifth cranial nerve. Spread from the sphenoid sinuses to the adjacent cavernous sinus may result in cranial nerve palsies, thrombosis of the sinus, and involvement of the carotid artery. Diagnosis is generally made by histopathological examination of the specimens obtained by endoscopic

evaluation, that is looked for broad, non-septate hyphae with right-angle branching. Further evaluation for the extent of spread of the disease is done by computed tomography (CT) or MRI.

CONCLUSION

Mucormycosis which was considered to be a very rare life threatening phenomenon, but during the second wave of the COVID-19 pandemic in India, was found to be unfortunately widespread and associated with significant morbidity and mortality. The most vital learning point is that in a patient with a recent history of COVID-19 infection, uncontrolled diabetes mellitus, and high-dose steroid supplementation are the most important risk factors that eventually results in the development of fatal mucormycosis. The most essential elements to be considered for successfully managing this fatal, life threatening infection are by controlling the predisposing factors resulting in the infection, early detection with a high suspicion in patients with contributing factors, anti-fungal drugs, and surgical debridement is essential of the involved tissues. Amphotericin-B-associated nephrotoxicity is also a severe cause of morbidity during the treatment of mucormycosis patients. Hence special care must be taken by giving adequate hydration and performing regular renal function tests. COVID-19 vaccines are also proven to provide strong protection against serious illness, hospitalization, and, hence reduces the development of mucormycosis later in life.

Statements And Declaratıons

Conflicts of interest

All authors have declared that they have no conflict of interest.

Ethical Approval

The manuscript has been read and approved by all authors, the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work.

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