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Assessing the COVID-19-associated fungal infection in Western region of India

Abstract

Objective: This study investigates the incidence and risk factors of COVID-19-associated mucormycosis (CAM) among patients in the Western region of India. Mucormycosis has emerged as a severe complication in COVID-19 patients, especially those with underlying conditions such as diabetes. The objective was to assess the prevalence, co-infections, and predisposing factors contributing to the development of mucormycosis.

Methods: A six-month case series was conducted at Metropolis Healthcare, Gujarat, involving 232 patients. Clinical samples were analyzed using fungal identification techniques, including microscopy and culture, to detect mucormycosis and associated fungal co-infections.

Results: Of the 232 cases, 56.70% were confirmed mucormycosis, while 43.29% were classified as suspected. Co-infections were identified in 14 patients with both *Aspergillus* and *Mucor* spp., while 21 had *Aspergillus* spp. alone, and 2 had *Candida* spp. The most common infection sites were the nose and sinuses (57.14%), rhino-orbital areas (22.07%), and pulmonary regions (20.77%). A significant risk factor was diabetes, present in 80% of the patients, with many undergoing steroids therapy.

Conclusion: COVID-19-associated mucormycosis presents a significant health risk, particularly in diabetic patients and those receiving steroid treatment. Early diagnosis and controlled use of steroids are crucial in mitigating the incidence of mucormycosis in COVID-19 patients. These findings underline the importance of vigilant monitoring and timely interventions.

Keywords: covid-19, mucormycosis, diabetes, corticosteroid therapy, RT-PCR

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Introduction

The Coronavirus Disease 2019 (COVID-19), a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has been associated with many secondary opportunistic bacterial and fungal conditions. Some the most frequent fungal pathogens responsible for co-infections in people with COVID-19 are Candida and Aspergillus.[1–3] There have also been reported cases of mucormycosis in COVID-19 patients globally and an increasing number seen recently, especially in India; acidic medium (metabolic acidosis; DKA), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), and Low oxygen (hypoxia). High iron levels are generally seen with very increased ferritins less phagocytic activity of WBC due to immunosuppression.[4,5]

Phycomycosis or zygomycosis was first recognized by Paltauf in 1885, and the American pathologist Baker introduced the term Mucormycosis to describe a serious Rhizopus infection. Mucormycosis is as a rare but fatal fungal infection that predominantly attacks individuals with an immunocompromised status.[6,7] Mucormycosis is an Angio invasive disease caused by the mold fungi of the Order Mucorales, Class Zygomycetes that belong to genera Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia.[8,9] Rhizopus Oryzae is the commonest type, comprising approximately 60% of human mucormycosis infections and almost highest up to 90 % cases among Rhino-orbital-cerebral (ROCM) variant. The vector of contamination is the inhalation from fungus spores.[10–12]

As per recent prophesy for the year 2019–2020, mucormycosis existed with a worldwide prevalence which ranged from around very less or negligible number of cases (1.7/million populations) to some scenarios approximately (0.14 per 1000 in India)- as brilliant opportunities whereas great threats dominated by it were noted out almost all parts of world noxious western countries.[13,14] In simple words, the highest prevalence of mucormycosis available in india. Mortality from mucormycosis is high. The fatality rate rises to 90 percent when mucormycosis extends into the brain.[15,16] Moreover, the rapid propagation of mucormycosis is a unique entity and a 12 h hesitation in diagnosis may potentially be fatal 50% of Mucorales case-patients were historically diagnosed post-mortem using autopsy series.[17,18] Here, we report a case series of 232 patients admitted as inpatients for COVID-19 infection and with mucormycosis.

Material and methods

The research was carried out over a period of 6 months on 232 patients in Metropolis Healthcare Rajkot, Gujarat, and a well-established NABL Accredited lab. Various samples (Figure 1) were collected to find out presence of fungal infection in these post covid patient with varied symptoms. This study is approved by the Ethical Committee of the Higher Research Council, which issued ethical clearance (52/1994/ACAD-1/MCA/2020/16-10-20) and administrative permis

Mucormycosis was confirmed in the patient through a positive KOH mount, and clinical symptoms strongly suggested a fungal infection. The samples were initially examined at both low and high power using a KOH mount to identify any fungal elements (Figure 2).

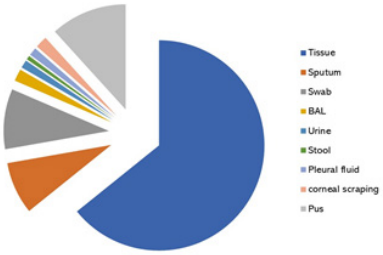

Figure 1 Various symptoms in post covid patient.

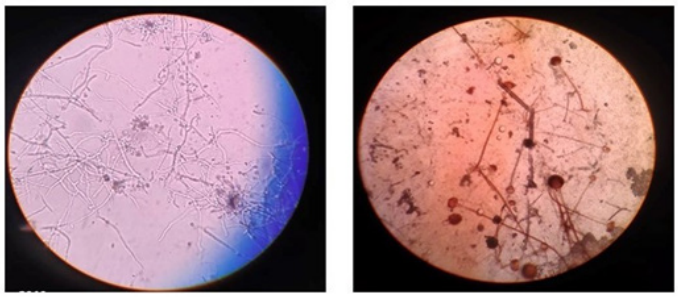

Figure 2 Direct smear with 10% potassium hydroxide.

After KOH examination the samples were steaked on Seborauds Dextrose Agar & Rose Bengal agar for fungal growth in two separate sets at 25ºC and 37ºC. The tubes were kept for at least 7 days for growth. Presence of white fluffy growth covering the whole plate or tubes were typical of Mucor spp.as they commonly known as lid lifters. The growth was confirmed with Lactophenol cotton blue stain as shown in Figure 3.

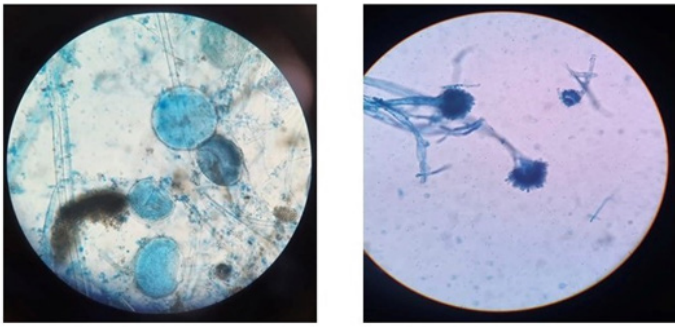

Figure 3 Hyphae with nodal rhizoids and short sporangiophores bearing round black sporangia are visible in the cultured fungi stained with lactophenol cotton blue.

Result

231 cases of mucormycosis were recorded, with 56.70% confirmed and 43.29% suspected, in individuals diagnosed with COVID-19 through RT-PCR.

Out of 131 confirmed cases of mucormycosis while 14 of them having mixed infection of Aspergillus and mucor spp. 21 were having Aspergillus spp. Infection alone while 2 of them were found to be infected with Candida spp. Nose and sinus involvement was the most frequent in mucormycosis cases (57.14%), with rhino-orbital involvement at 22.07% and pulmonary involvement at 20.77%.

Discussion

Mucormycosis is extremely rare in healthy individuals. However, the following immunocompromising diseases are its causes: poorly controlled diabetes, with or without DKA, hematological and other cancer, organ transplantation, prolonged deficit of neutrophilic granulocyte, therapy with immunosuppressive agent and corticosteroids, iron overload or hemochromatosis, deferoxamine, therapy, wounds and burns, AIDS, intravenous drug abusers, malnutrition.[17,18] Mucormycosis can affect mediastinum, kidney, heart, joints, jaw bones, skin, GIT, lungs, CNS, orbit, sinus, and nose. However, ROCM is the most common form which is observed in the worldwide clinical setup. It should be noted that the term 'rhino-orbital-cerebral disease' is considered to be a single spectrum of the disease which begins with the involvement of sino-nasal chambers and may involve limited involvement of the nose and sinuses. In addition, it may later progress to the involvement of orbits, and finally, the CNS is involved. The area of involvement varies with the underlying disease. For instance, it is mainly associated with uncontrolled diabetes and DKA and there is lung involvement in people with neutropenia, bone marrow, and organ transplant, and hematological malignancy are developing GIT infection in malnourished people.[19,20] Characterized by eosinophilic necrosis of the tissue, thrombosis, and giant cell invasion, mucormycosis is distinguished from other fungal infections through microbiological identification of hyphae, focusing on width, septation, branching angles (right or acute), and coloration.[21,22]

Published in 1950, the Smith and Krichner criteria for diagnosing mucormycosis clinically are still viewed as the gold standard and encompass the following:[23,24]

Multiple cranial nerve palsies that are unrelated to lesions that have been recorded, Ptosis of the eyelid, proptosis of the eyeball, and complete ophthalmoplegia, soft peri-orbital or peri-nasal swelling with discoloration and induration, and Blood-tinged nasal discharge and facial pain on the same side. Patel et al., found that, among the 465 non-COVID-19 mucormycosis cases examined in India, the rhino orbital type was the most prevalent at 67.7%. The pulmonary type followed with 13.3%, and the cutaneous type was the least common at 10.5%.[25,26] In Indians, the primary predisposing factors for mucormycosis are organ transplantation (7.7%), malignancy (9.0%), and diabetes (73.5%). A prospective Indian study conducted before the COVID-19 pandemic found that having diabetes increases the risk of developing ROCM by 7.5 times (Odds ratio 7.55, P = 0.001).[27,28]

According to a recent systematic review by John et al from April 9, 2021 to April 9, 2021, DM occurred in 93 percent of confirmed mucormycosis patients who had COVID-19, while 88 percent of the cases were on steroids.[29,30] This is similar to the findings of a larger case series of 231 Covid-19 associated mucormycosis patients, 80 percent of which had a known history of diabetes and more than three-quarters during their hospitalization. This data highlights what seems to be an unholy trinity of mucormycosis, diabetes, and steroid use in COVID-19.[15,31,32]

Given the high mortality associated with mucormycosis, particularly in immunocompromised individuals such as diabetic COVID-19 patients on corticosteroids, the cornerstone of management lies in early recognition, rigorous surveillance, and prompt therapeutic intervention. Integrating routine fungal screening in high-risk COVID-19 patients and maintaining a high index of suspicion, especially in the presence of suggestive symptoms (e.g., nasal discharge, facial pain, proptosis), is crucial. Additionally, the

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timely use of liposomal amphotericin B and surgical debridement, where necessary, significantly improves clinical outcomes.

Conclusion

Patients infected with COVID-19, particularly those undergoing steroid therapy with pre-existing diabetes, are highly susceptible to invasive fungal infections—predominantly mucormycosis. Therefore, meticulous clinical surveillance, early screening through rapid methods like KOH mount, and swift initiation of antifungal therapy are critical to improving survival rates. As liposomal amphotericin B remains the mainstay of treatment despite its cost and toxicity, healthcare systems must prioritize early detection strategies to minimize morbidity and avoid radical procedures like organ exenteration.

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Ethics approval and consent to participate

This study is approved by the Ethical Committee of the Higher Research Council, which issued ethical clearance (52/1994/ACAD-1/MCA/2020/16-10-20) and administrative permission.

Human and animal rights

The reported experiments on humans adhered to the ethical standards set by the institutional and national committees responsible for human experimentation, in line with the Helsinki Declaration of 1975, as revised in 2008.

AI-assisted work statement

During the preparation of this work, author(s) used the ChatGPT for language and grammar corrections. After using the tool, author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Conflicts of interest

The authors declare there is no conflict of interest.

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