

Challenges in Diagnosing and Treatment Plan of Mucormycosis Pre and Post Pandemic

Rishana Ashraf¹, Anitha S², Sivachandran³, Aravindhana⁴, Sathyakumar⁵,
Dr. K.T. Magesh⁶

^{1,2}BDS, SRM Kattankulathur Dental College and Hospital

^{3,4,5}MDS, SRM Kattankulathur Dental College and Hospital

⁶Professor and HOD, Department of Oral and Maxillofacial Pathology, SRM Kattankulathur Dental College and Hospital

ABSTRACT

With the current pandemic sweeping the world, science and medicine are up against enemies they have never faced before or opponents that are weaker than themselves—viruses and finally other biotic beings. Researchers are working to detect and eradicate COVID-19 variants, but opportunistic fungal infections caused by other innocuous species are rearing their ugly heads. Mucorale species cause mucormycosis, sometimes known as "Black Fungus," an aggressive opportunistic fungal illness. It spreads via blood vessels and causes necrosis, ischemia, and thrombosis. Particularly vulnerable are those who already have immunosuppressive conditions, such as diabetes mellitus, cancer, or long-term immunosuppressive pharmaceutical use. Coronavirus disease-2019 (COVID-19)-associated mucormycosis proved to be devastating because of its high death rate. Since the primary care physician is often the patient's first and often their only point of contact with a healthcare professional (especially in poor nations), they are vital to the diagnosis and treatment of this illness. To reduce mortality, early detection and diagnosis are crucial, as are preventative measures to halt the growth of the brain. A multidisciplinary approach from several professions is necessary for effective diagnosis and treatment. Surgical debridement, antifungal treatment, and excision of the affected regions are the protocols that need to be followed. Post-operative anomalies result in impairments related to phonetics, function, and appearance. Positive outcomes have been observed in congenital abnormality prosthetic rehabilitation, especially in elderly and immunocompromised individuals.

KEYWORDS: Covid19, mucormycosis, covidassociated, mucormycosis(CAM), immunocompromised, diabetes, pandemic.

INTRODUCTION

Mucormycosis is an extremely rare and severe disease that progresses over time and has a high fatality rate. Since the COVID-19 pandemic, mucormycosis has become more prevalent. Mucormycosis progression depends on early detection, prompt and effective antifungal therapy, and surgical debridement(5). The medical, surgical, imaging, and laboratory teams must work together to address mucormycosis.

The Asian region is typically home to the majority of mucorales infections; instances during the COVID-

19 pandemic were also reported in Iran, India, and other nations in the Americas and Europe. The patient experienced a slight increase in glycemic readings on occasion while receiving corticosteroid medication(1). Most research indicate that The most prevalent comorbidity in CAM is diabetes..The the pathogen's capacity and potency processes of the A coronaviral infection and the toxin mucoricin, as well as the virulence of the mucorales species, could account for the association between mucormycosis and COVID-19(3) . Cytosteroid therapy, biological therapies, CPAP, and ordysbiosis following antibiotics are iatrogenic factors associated with complementary and alternative medicine.

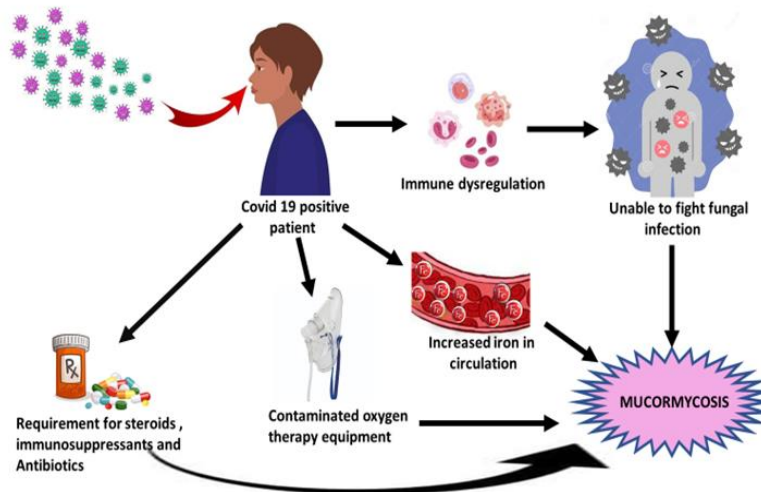
Dentists are important players in the disease mucormycosis, which mostly affects the rhinomaxillary or rhinocerebral regions, which include the palate, alveolar bone, mandibular bone, and face tissues(1). Therefore, dentists need to be aware of the symptoms of mucormycosis. The purpose of this systematic review is to identify the difficulties associated with diagnosing and treating mucormycosis both before and after COVID-19.(15)

COVID 19 HISTORY AND EVOLUTION

11th of March, 2020: The The WHO released COVID-19 to be a pandemic, and on On January 30, 2020, it was announced as a worldwide publichealth crisis. In December 2019, the illness initially surfaced in Wuhan, China, and quickly spread around the world(23). Over the course of the last ten years, a number of disease outbreaks and epidemics caused by over 20 infectious agents have surfaced globally, according to the World Health Organization (WHO). (24). One Novel infectious pathogens were responsible for a portion of these epidemics.

The frequency of mucormycosis an uncommon illness among people in general has been observed to range from 0.005 to 1.7 per million. In India, how common mucormycosis was found to be 0.14/1000 diabetic patients, which is eighty times greater than that of other countries..(24). Fortunately, we have greater tools to combat this new threat in the globe today. There's no denying that COVID-19 is a once-in-a-lifetime outbreak.(21) The world is currently experiencing unprecedented levels of global health crisis and periods of acute instability. Though the direction of this pandemic is unpredictable, undoubtedly, a new chapter in the history .

PREDISPOSING FACTORS FOR CAM



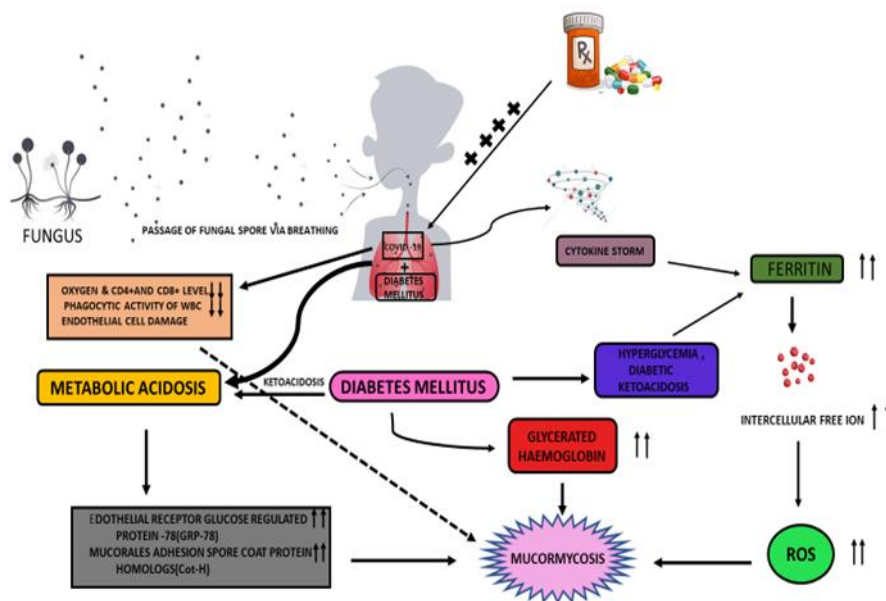
COMPLICATIONS OF COVID 19

Pulmonary

A few post-covid complications include dyspnea, fibrotic lung disease, oxygen or ventilator reliance, oxygen dependence, and abnormalities in the pulmonary function test (PFT).. Dyspnea is the pulmonary symptom most frequently reported after COVID-19(27) .

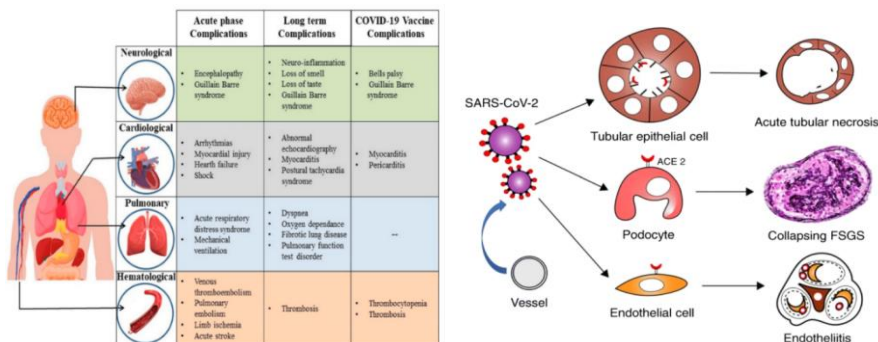
Diabetic complications

Acute diabetic decompensation, including diabetic ketoacidosis, and COVID-19 in those with type 1 and type 2 diabetes has been connected to new-onset hyperglycemia..(18) After infection, β cells that have been damaged by the virus directly or indirectly can lead to insulin secretory deficiencies and insulin resistance because of the inflammatory state(19).



Cardiovascular

Following COVID-19, cardiac issues are a common complaint after being released from the hospital..This coagulopathy has a complex etiology that includes hypoxia-induced transcription factor activation, tissue factor overexpression in response to inflammatory cytokines, and microvascular dysfunction(31)



RENAL COMPLICATIONS

Dermatological

COVID-19 cutaneous manifestation, which is followed by painful red, purple, and acral papules, urticaria, and pulovesicular rash.(34)

CASE REPORT COMPARISON BEFORE AND AFTER COVID

PRE-PANDEMIC :The precise frequency or occurrence is unknown because Limited studies are conducted on a population. and they differ in terms of snatch dates, populations, definitions,together with diagnostic techniques.,.According to a 1992–1993 study conducted in the San Francisco Bay area, there are 500 cases of mucormycosis year, or 1.7 cases per million people. Kontoyiannis et al(13). In a study published in 2016,hospitalization rates for mucormycosis was calculated to beIn the period between January 2005 and June 2014, 0.12 per 10,000 discharges. (17). Hospitalizations would rise to 0.16 per 10,000 discharges if the what mucormycosis is described was expanded to exclude the requirement for posaconazole or amphotericin B. (18).According to a based on the countrywide inhabitants survey conducted in France in 1997, there were 0.7 occurrences of mucormycosis for every million peopleSaegeman et al. found that within 2000 and 2009, there was an increase from 0.019 cases per 10,000 patient days in Belgium to 0.148 cases per 10,000 patient days.. The rate of mucormycosis incidence in India is roughly 0.14 instances per 1000 people, which is roughly eighty times more than the prevalence in wealthy nations(19). The publications mentioned above all emphasize that mucormycosis is a newly discovered illness(22).The increase in case documentation percentages by decade and culture was reported by the same authors. In the 1980s, the percentage was 50%, and in the 2000s, it was 71%(34). This may suggest that improved diagnostic techniques or greater public awareness of the illness play a role in in addition to a real rise in the frequency of cases

POST PANDEMIC : A total of 34 articles from the PubMed and Google Scholarand other databases were discovered to report the initial case (4/28). From people with confirmed (RT-PCR) diagnoses of mucormycosis, a total of 101 cases were found CIVID-19 (34). Of COVID-19 patients, India accounted for the majority of reported cases (81.2%) of mucormycosis, with 9 cases (8.9%) originating from the United States and 3 cases (3.1%) from Iran. (33). As of right now, just 19 cases (18.8%) had been reported from outside of the globe. A study conducted by Satish and colleagues, which presented 11 case-series containing mucormycosis in individuals with COVID-19 from India, was omitted from several analyses because to insufficient material regarding each patient(32). The study's combined data revealed that mucormycosis was most common in men (78.9%), as well as in those who had either recovered from COVID-19 or were actively infected (59.4%). Notwithstanding the clear overlap in the cases, was defined as individuals who were either hospitalized or released after two weeks of discovery. Three months after the diagnosis of severe COVID-19, one patient developed rhino-orbital cerebral infection, and four of the five patients with haematological malignancy developed pulmonary mucormycosis while receiving treatment for severe COVID-19 in the ICU. (28). In the patients with pulmonary, gastrointestinal, or disseminated mucormycosis .The single most significant risk element found in the majority of instances (83.3%) of mucormycosis in persons with COVID-19 was hyperglycemia at presentation (due to pre-existing DM, new-onset hyperglycemia, new-onset diabetes, or diabetic ketoacidosis [DKA]), followed by cancer (4.0%). About 15% of patients with COVID-19 and mucormycosis also had concurrent DKA, while 80% of cases had pre-existing DM. Remdesivir (20.6%) and tocilizumab (4.1%) were the most common histories of corticosteroid intake for COVID-19 therapy, accounting for 76.3% of cases(29). Nasal and sinuses were the most frequently affected organs (88.9%), then rhino-orbital (56.7%) and ROCM type (22.2%). In 30.7% of the cases, overall mortality was recorded. Mucormycosis in individuals infected with COVID-19 has been documented in 101 instances overall, of which 82 cases originated in India and 19 cases worldwide. Of those with COVID-19, those who were active (59.4%) or recovered (40.6%) were the most common gender group affected by mucormycosis (78.9%). Eighty percent of the

cases had diabetes mellitus (DM) prior to the incident, and fourteen percent also had diabetic ketoacidosis (DKA). Seventy-six.3% of cases had consumption of corticosteroids for COVID-19 therapy. Rhino-orbital was the most prevalent type of mucormycosis. (56.7%), after sinus and nose (88.9%). In 30.7% of the instances, there was a recorded death. 34% mortality is similar to that documented in the literature for patients with mucormycosis who are not COVID-19-positive. (35).

Conclusion:

The key to lowering disease-related mortality is early detection; patients with uncontrolled diabetes and Covid-19 in particular should not ignore their symptoms. The primary risk factors include the use of steroids, diabetes, the environment, overuse of antibiotics, and hypoxia. The death rate is high despite medical and surgical intervention. Improving the circumstances that lead to the formation of COVID-19-associated mucormycosis requires a comprehensive approach(35). The viruses' first and subsequent emergences, together with the hosts and vulnerability, are essential. Changing the parameters of genetic investigations to determine the host factors that make people more susceptible to a fatal disease like mucormycosis will also have a significant positive impact on public health systems in India and other countries.

REFERENCES

1. Arbune, M.; Arbune, A.-A.; Nechifor, A.; Chiscop, I.; Sapira, V. Diagnostic and Treatment Challenges of Emergent COVID-Associated-Mucormycosis: A Case Report and Review of the Literature. *Antibiotics* 2023, 12, 31. <https://doi.org/10.3390/antibiotics12010031>
2. Corresponding author at: 1351 Nile Corniche, Aghakhan, Cairo, Egypt. <https://doi.org/10.1016/j.ijscr.2021.106522>
3. Janjua, O.S.; Shaikh, M.S.; Fareed, M.A.; Qureshi, S.M.; Khan, M.I.; Hashem, D.; Zafar, M.S. Dental and Oral Manifestations of COVID-19 Related Mucormycosis Diagnoses, Management Strategies and Outcomes. *J. Fungi* 2022, 8, 44. <https://doi.org/10.3390/jof8010044>
4. <https://doi.org/10.1007/s12223-021-00934-5>
5. COVID-19 associated mucormycosis: Staging and management recommendations (Report of a multi-disciplinary expert committee) Hardeep Singh Malhotra a, Prashant Gupta b, Divya Mehrotra c, Himanshu Dandu d, Neera Kohli e, Veerendra Verma f, Apjit Kaur g, Neeraj Kumar a, Vikas Prabhu a, Manish Kumar Singh h, Riddhi Jaiswal i, Brijesh Mishra j, Bal Krishna Ojha k, Nitin Dutt Bhardwaj Virendra Atam m, Bipin Puri <https://doi.org/10.1016/j.jobcr.2021.08.001>
6. Mucormycosis in head and neck area — the emerging health problem in COVID-19 pandemic. The perspective of a dental practitioner DOI: 10.24425/fmc.2021.137228
7. Article in International Journal of Community Medicine and Public Health · April 2022 <https://www.researchgate.net/publication/360244481>.
8. Epidemiological Mucormycosis treatment and diagnosis challenges using the adaptive properties of computer vision techniques based approach: a review by Nirali & Harekrishna Kumar <https://doi.org/10.1007/s11042-022-12450-w>.
9. Mucormycosis Amid COVID-19 Crisis: Pathogenesis, Diagnosis and Novel Treatment Strategies to Combat the Spread Shreya Dogra, Akanksha Arora, Aashni Aggarwal, Gautam Passi, Akanksha Sharma, Gurpal Singh and Ravi Barnwell. | www.frontiersin.org

10. Mucormycosis infection in patients with COVID-19: A systematic review SeyedAhmad SeyedAlinaghi <https://doi.org/10.1002/hsr2.529>
11. Asmaa Abou-Bakr, Department of Oral Medicine and Periodontology, Faculty of Dentistry, The British University in Egypt, El Sherouk City, Cairo 11837, Egypt. <https://doi.org/10.1177/0022034520957289>
12. A review of COVID-19-associated mucormycosis in India <https://www.researchgate.net/publication/360244481>
13. Balkhair AA. COVID-19 Pandemic: A New Chapter in the History of Infectious Diseases. *Oman Med J.* 2020 Apr 21;35(2):e123. doi: 10.5001/omj.2020.41. PMID: 32328297; PMCID: PMC7171815.
14. Amar D Desai, Michael Lavelle, Brian C Boursiquot, Elaine Y Wan *American Journal of Physiology-Cell Physiology* 322 (1), C1-C11, 202.
15. World Health Organization. Coronavirus disease (COVID-19) pandemic. [Accessed May 21, 2020]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.
16. World Health Organization. [Accessed May 21, 2020]. Available from: [https://covid19.who.int/---WHOCoronavirusDisease\(COVID-19\)Dashboard](https://covid19.who.int/---WHOCoronavirusDisease(COVID-19)Dashboard).
17. Minami, T., Iwata, Y. & Wada, T. Renal complications in coronavirus disease 2019: a systematic review. *Inflamm Regen* 40, 31 (2020). <https://doi.org/10.1186/s41232-020-00140-9>
18. [Clinical characteristics of coronavirus disease 2019 in China](#) W Guan, Z Ni, Y Hu, W Liang, C Ou, J He, L Liu, H Shan, C Lei, [DSC Hui](#), B Du, L Li, G Zeng... *New England journal of medicine*, 2020•Mass Medical Soc
19. <https://doi.org/10.1016/j.cjco.2021.05.020>
20. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China . [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
21. <https://doi.org/10.1016/j.ijid.2020.03.017> Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis
22. Pasero D., Sanna S., Liperi C., et al. A challenging complication following SARS-CoV-2 infection: a case of pulmonary mucormycosis. *Infection.* 2020:1–6.
23. <https://pubmed.ncbi.nlm.nih.gov/35074291/>
24. <https://pubmed.ncbi.nlm.nih.gov/36805033/>
25. <https://pubmed.ncbi.nlm.nih.gov/37736777/>
26. <https://pubmed.ncbi.nlm.nih.gov/37367595/>
27. World Health Organization . 2020. Listings of who's a response to covid <https://www.who.int/news/item/29-06-2020-covidtimeline>
28. The centers for Disease Control and Prevention . 2020. Fungal diseases and covid-
29. <https://www.cdc.gov/fungal/covid-fungal.html>
30. Histopathological findings and viral tropism in UK patients with severe fatal COVID-19: a post-mortem study.
31. Aranjani JM, Manuel A, Abdul Razack HI, Mathew ST. COVID-19-associated mucormycosis: Evidence-based critical review of an emerging infection burden during the pandemic's second wave in India. *PLoS Negl Trop Dis.* 2021 Nov 18;15(11):e0009921. doi: 10.1371/journal.pntd.0009921. PMID: 34793455; PMCID: PMC8601521.
32. Balushi AA, Ajmi AA, Sinani QA, Menon V, Berieki ZA, Shezawi AA, Azri SA, Rashdi AA, Jardani AA, Baluki TA, Ghaithi SA, Reesi AA, Al-Za'abi AT, Al' Balushi MA, Maqbali TA. COVID-19-

Associated Mucormycosis: An Opportunistic Fungal Infection. A Case Series and Review. *Int J Infect Dis.* 2022 Aug;121:203-210. doi: 10.1016/j.ijid.2022.05.005. Epub 2022 May 6. PMID: 35533833; PMCID: PMC9075983.

33. Kottarathil M, Thayanidhi P, P S, Jyoti Kindo A. Rise of mucormycosis during the COVID-19 pandemic and the challenges faced. *Curr Med Mycol.* 2023 Mar;9(1):44-55. doi: 10.18502/cmm.2023.345032.1400. PMID: 37867589; PMCID: PMC10590187.
34. Al-Tawfiq JA, Alhumaid S, Alshukairi AN, Temsah MH, Barry M, Al Mutair A, Rabaan AA, Al-Omari A, Tirupathi R, AlQahtani M, AlBahrani S, Dhama K. COVID-19 and mucormycosis superinfection: the perfect storm. *Infection.* 2021 Oct;49(5):833-853. doi: 10.1007/s15010-021-01670-1. Epub 2021 Jul 24. PMID: 34302291; PMCID: PMC8302461.
35. [https://doi.org/10.1016/S2666-5247\(21\)00237-8](https://doi.org/10.1016/S2666-5247(21)00237-8)