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Mini Review

Post-COVID Mucormycosis: An Emerging Threat in Developing Countries - A Prospective Review

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Abstract

COVID-19, with its rapidly mutating strains, poses a significant global health challenge. Recent reports of a surge in mucormycosis cases among COVID-19 patients highlight the urgent need for understanding and addressing this critical complication. This review explores the factors contributing to mucormycosis development in COVID-19 patients and outlines strategies for prevention and management. Several factors, including high glucose levels (diabetes, onset, steroid-induced hyperglycemia), low oxygen levels, elevated iron levels (especially ferritin), metabolic acidosis, and diabetic ketoacidosis, can facilitate the germination of mucor spores. COVID-19 patients with underlying conditions such as diabetes, cancer, or organ transplants are particularly susceptible to mucormycosis due to their immunocompromised state. The growth of the mucor pathogen requires free iron, which is elevated in conditions like diabetic ketoacidosis. This elevated iron level promotes the formation of Cot-H, a crucial component of fungal growth, leading to mucormycosis. Additionally, comorbidities and corticosteroids can suppress the immune system, hindering the body's ability to fight off infections like mucormycosis. Therefore, it is imperative to avoid the indiscriminate use of corticosteroids. Strict control of acute hyperglycemia and comprehensive monitoring of diabetic and immunocompromised COVID-19 patients are essential preventive measures. By addressing these factors, healthcare providers can mitigate the risk of mucormycosis in COVID-19 patients and improve overall outcomes.

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INTRODUCTION

The term "corona" is derived from the Greek word for "crown," aptly describing the appearance of the virus under a microscope: a spherical particle adorned with a crown-like structure of protein spikes, known as peplomers[1]. These peplomers enable the virus to attach to and infect host cells. Throughout history, humanity has faced numerous pandemics, including the Bubonic Plague (1665), the Spanish Flu (1918-1919), the Asian Flu (1957), the Hong Kong Flu (1968), the Swine Flu (2009), and, more recently, the COVID-19 pandemic, declared by the WHO on February 11, 2020[2]. The novel coronavirus responsible for COVID-19 was first identified in Wuhan, Hubei Province, China, in late 2019[3].

Mucormycosis, a rare but potentially fatal fungal infection, was first described by Paltauf in 1885 as phycomycosis[4] and later as mucormycosis by Baker in 1957[5]. This opportunistic infection is caused by a group of fungi, primarily from the order Mucorales, commonly found in the environment, including soil, decaying organic matter, and even the human microbiome[6]. In recent years, there has been a surge in mucormycosis cases, particularly among individuals recovering from COVID-19[7,8]. This mini review aims to explore the factors contributing to the increased incidence of mucormycosis in COVID-19 patients and to discuss preventive measures to mitigate this risk.

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PREVALENCE OF COVID-19

The COVID-19 pandemic has led to a global health crisis, with millions of deaths reported to the WHO[9]. However, the actual number of deaths may be significantly higher, particularly in countries like India, where the pandemic has been exacerbated by the emergence of mucormycosis. While the global prevalence of mucormycosis is relatively low, India has experienced a dramatic surge in cases, with a prevalence rate 80 times higher than developed countries[10,11].

Diabetes mellitus is the most common risk factor for mucormycosis in India, whereas cancer and organ transplantation are leading risk factors in Europe and the United States[12]. However, diabetes remains a significant risk factor globally, contributing to a high mortality rate of 46%[13]. Several factors, including high glucose levels, low oxygen levels, high iron levels, metabolic acidosis, and immunosuppression due to steroid use or underlying conditions like cancer or HIV/AIDS, can predispose individuals to mucormycosis[14]. The most common site of infection is the rhino-maxillary region, particularly in immunocompromised individuals with diabetes or those receiving steroid therapy[15].

MUCORMYCOSIS CASES OF COVID-19 PATIENTS

Recent studies have highlighted a concerning association between COVID-19 infection, uncontrolled diabetes mellitus, and subsequent mucormycosis. For instance, a case report involving a 60-year-old diabetic patient who tested positive for COVID-19 and received treatment with methylprednisolone, oseltamivir, and meropenem eventually developed mucormycosis, as confirmed by nasal biopsy. Similarly, a larger study involving 18 patients with poorly controlled diabetes and a history of steroid use found that 17 (94%) were diagnosed with mucormycosis[16-18]. These findings underscore the importance of vigilant monitoring for mucormycosis in high-risk individuals, particularly those with diabetes and COVID-19 (**Table I**).

Several case reports and studies have highlighted the association between COVID-19 infection and mucormycosis. For instance, a 40-year-old woman and a 54-year-old man with severe COVID-19 infection and corticosteroid treatment developed mucormycosis, confirmed by nasal endoscopy and radiological findings[19]. Similarly, a study involving 25 patients with invasive mucormycosis revealed that 11 of them had concurrent COVID-19 infection, suggesting a potential link between the two diseases, particularly in immunocompromised individuals[20]. A middle-aged diabetic woman with COVID-19 and facial pain, ptosis, and fever was diagnosed with mucormycosis through sinus endoscopy and histopathological examination[21]. A comprehensive review of 101 reported cases of mucormycosis in COVID-19 patients identified diabetes and corticosteroid use as significant risk factors[14].

Table I. Mucormycosis Cases of COVID-19 Patients.

No.	Description	Diabetes	Use of Corticosteroids	COVID-19 Positive	Mucormycosis	Treatment for Mucormycosis	References
1	60-year-old patient	Yes	Yes	Yes	Yes	Amphotericin B	16
2	Study of 18 COVID-19 positive patients	Yes	Yes	Yes	17/18 patients	-	18
3	40-year-old female and 54-year-old male patients	No	Yes	Yes	Yes	Amphotericin B	19
4	Study of 25 patients	No	Yes	11/25 patients	All 25 patients	-	20
5	Middle-aged woman	Yes	Yes	Yes	Yes	Amphotericin B	21
6	Study of 101 patients with COVID-19 and mucormycosis	80/101 patients	77/101 patients	Yes	Yes	Amphotericin B	14
7	3 patients (2 male, 1 female)	Yes	No	No	Yes	Surgery	22
8	Study of 2 male patients aged 60 and 67 years	Yes	No	No	Yes	Amphotericin B	23

CURRENT SITUATION OF MUCORMYCOSIS AND COVID-19

The rapid and ongoing spread of COVID-19, coupled with its high mutation rate, has presented a significant global health challenge. The virus's ability to evolve quickly has hindered efforts to control its transmission and develop effective countermeasures. The SARS-CoV-2 virus has undergone various mutations, leading to the emergence of several variants of concern. Notably, the B.1.617.1 (kappa) and B.1.617.2 (delta) variants were first identified in India[24]. Other significant variants include B.1.1.7 (alpha) from the UK, B.1.35.1 (beta) from Africa, P.1 (gamma) from Brazil, B.1.427/B.1.429 (epsilon) from the USA, P2 (zeta) from Brazil, and B.1.525 (eta) from multiple countries[25]. Given the rapid emergence of COVID-19, the development of a specific drug within a short timeframe has proven challenging. As such, non-pharmaceutical interventions like lockdowns and vaccination have been the primary strategies for preventing the spread of the virus and mitigating its impact. While vaccines cannot directly eliminate the virus, they effectively stimulate the immune system to generate a robust response, providing protection against infection and severe disease[26].

Several vaccines, including BNT162b2/Comirnaty Tozinameran (Pfizer), AZD1222 (AstraZeneca), Covishield (Serum Institute of India), Ad26.Cov2.5 (Janssen), mRNA-1273 (Moderna), SARS-CoV-2 (Vero cell) (Sinopharm/BIBP), and Sputnik V (Gamaleya National Centre), have received regulatory approval, while numerous others are under review or in clinical trials[27]. While vaccination remains a primary strategy to combat COVID-19, antibody-based therapies have emerged as a promising complementary approach. Monoclonal antibodies targeting the SARS-CoV-2 spike protein can neutralize the virus and prevent infection. However, the emergence of viral variants with mutations in the spike protein can reduce the effectiveness of these therapies. To address this challenge, researchers are exploring the development of antibody cocktails that target multiple epitopes on the viral surface, thereby reducing the likelihood of viral escape. This strategy has shown promise in preclinical and clinical studies and is now gaining increasing attention from scientists and clinicians[28,29].

The global health crisis caused by COVID-19 has been further exacerbated by the emergence of secondary infections, such as mucormycosis[30]. In countries like India, a significant number of COVID-19 patients have experienced severe complications due to mucormycosis[6]. This opportunistic fungal infection primarily affects individuals with underlying health conditions, including diabetes, metabolic acidosis, and diabetic ketoacidosis. Patients with elevated blood glucose levels, low oxygen saturation, and high iron levels are particularly susceptible to mucormycosis[31,32].

Iron is an essential element for both mammalian cells and pathogens[33]. In the mammalian host, iron is tightly bound to carrier proteins such as transferrin, ferritin, and lactoferrin to prevent its toxic effects. However, pathogens, including fungi, require free iron for their growth and proliferation. Diabetic ketoacidosis (DKA) can disrupt iron homeostasis by lowering the iron-binding capacity of carrier proteins, leading to increased levels of free iron in the serum. This elevated free iron concentration can provide a favorable environment for fungal growth and infection[34-36].

A compromised immune system, often resulting from long-term steroid use, cancer, organ transplantation, or other underlying health conditions, can increase susceptibility to mucormycosis[37]. While the precise pathophysiology of mucormycosis remains unclear, a proposed mechanism linking COVID-19 to mucormycosis is illustrated in **Figure 1**. The overwhelming demand for oxygen during the COVID-19 pandemic, particularly in India, led to a shortage of medical-grade oxygen cylinders. Consequently, hospitals were forced to use industrial-grade cylinders, which may have been inadequately cleaned and sterilized. This potential contamination with fungal spores could have contributed to the increased incidence of mucormycosis among COVID-19 patients[38].

While the definitive treatment for this condition remains unclear, current literature suggests that amphotericin B and surgical intervention may be potential therapeutic options[39-41]. Additionally, certain homeopathic remedies, such as arsenic album, marksol, gelsenium, nux vomica, sulphur, tuberculinum, and pulsatilla, have been reported to offer potential therapeutic benefits[42,43]. However, further rigorous scientific studies are needed to validate the efficacy and safety of these treatments.

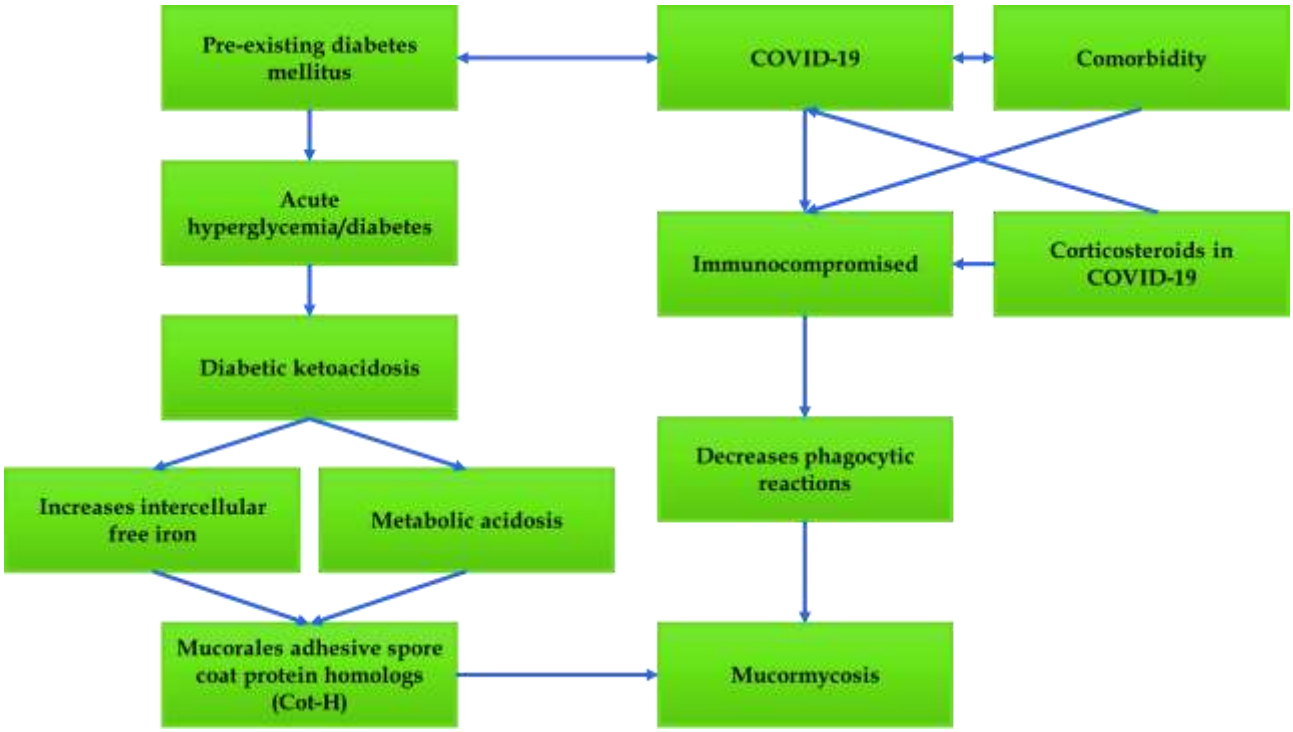

Figure 1. Pathogenesis of mucormycosis in COVID-19 patients.

CONCLUSION

the global COVID-19 pandemic has underscored the importance of comprehensive infection control measures and timely treatment of opportunistic infections like mucormycosis. To mitigate the risk of mucormycosis, it is crucial to minimize the use of corticosteroids, especially in immunocompromised individuals, and to strictly control blood glucose levels in diabetic patients. Early diagnosis and prompt initiation of appropriate antifungal therapy, such as liposomal amphotericin B, posaconazole, or isavuconazole, are essential for improving patient outcomes. Additionally, surgical intervention may be necessary to debride necrotic tissue. Ongoing research is needed to develop novel antifungal agents with improved efficacy and safety profiles, as well as to explore preventive strategies to reduce the incidence of mucormycosis in high-risk populations.

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DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this study.

REFERENCES

1. Chorba T. The Concept of the Crown and Its Potential Role in the Downfall of Coronavirus. Emerg Infect Dis. 2020;26(9):2302-5. DOI: 10.3201/eid2609.AC2609; PMCID: PMC7454052

2. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic.Acta Biomed. 2020;91(1):157-60. DOI: 10.23750/abm.v91i1.9397; PMCID: PMC7569573; PMID: 32191675

3. Chakraborty D, Yolmo NL. Fright of Covid-19 and its Future: A Review. J Palliat Care Med. 2020;10(4):1000369. DOI: 10.4172/2165-7386.1000369

4. Paltauf A. Mycosis mucorina. Archiv F Pathol Anat. 1885;102:543-64. DOI: 10.1007/BF01932420

5. Baker RD. Mucormycosis-a new disease? J Am Med Assoc. 1957; 163(10):805-8. DOI: 10.1001/jama.1957.02970450007003; PMID: 13405736

6. Mahalaxmi I, Jayaramayya K, Venkatesan D, Subramaniam MD, Renu K, Vijayakumar P, et al. Mucormycosis: An opportunistic pathogen during COVID-19. Environ Res. 2021;201:111643. DOI: 10.1016/j.envres.2021.111643; PMCID: PMC8258024; PMID: 34237335

7. Singh R, Mittal G, kakati B, Koul N. An Observational Study of Fungal Infections in COVID-19: Highlighting the Role of Mucormycosis in Tertiary Healthcare Settings. Cureus. 2024;16(3):e57295. DOI: 10.7759/cureus.57295; PMCID: PMC11059081; PMID: 38690487

8. Chillana S, Chilana KAM. COVID-19 and Mucormycosis: A Black Fungus Disaster? Indian J Dermatol. 2022;67(5):535-8. DOI: 10.4103/ijd.ijd_17_22; PMCID: PMC9971779; PMID: 36865825

9. Pollard CA, Morran MP, Nestor-Kalinoski AL. The COVID-19 pandemic has led to a global health crisis, with millions of deaths reported to the WHO. Physiol Genomics. 2020;52(11):549-57. DOI: 10.1152/physiolgenomics.00089.2020; PMCID: PMC7686876; PMID: 32991251

10. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: An Update. J Fungi. 2020;6(4):265. DOI: 10.3390/jof6040265; PMCID: PMC7711598; PMID: 33147877

11. Chander J, Kaur M, Singla N, Punia RPS, Singhal SK, Attri AK, et al. Mucormycosis: Battle with the Deadly Enemy over a Five-Year Period in India. J Fungi. 2018;4(2):46. DOI: 10.3390/jof4020046; PMCID: PMC6023269; PMID: 29642408

12. Prakash H, Chakrabarti A. Global Epidemiology of Mucormycosis. J Fungi. 2019;5(1):26. DOI: 10.3390/jof5010026; PMCID: PMC6462913; PMID: 30901907

13. Jeong W, Keighley C, Wolfe R, Lee WL, Slavin MA, Kongn DCM, et al. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. Clin Microbiol Infect. 2019;25(1):26–34. DOI: 10.1016/j.cmi.2018.07.011; PMID: 30036666

14. Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr. 2021;15(4):102146. DOI: 10.1016/j.dsx.2021.05.019; PMCID: PMC8137376; PMID: 34192610

15. Faria L, Mahin T, Qader MA, Ahmed M, Anwar MA. A Case of Post-COVID-19 Rhino-Cerebral Mucormycosis in an Immunocompromised Patient. Cureus. 2023;15(7):e42652. DOI: 10.7759/cureus.42652; PMCID: PMC10461695; PMID: 37644947

16. Mehta S, Pandey A. Rhino-Orbital Mucormycosis Associated With COVID-19. Cureus 2020;12(9):e10726. DOI: 10.7759/cureus.10726; PMCID: PMC7599039; PMID: 33145132

17. Bayram N, Ozsaygılı C, Sav H, Tekin Y, Gundogan M, Pangal E, et al., Susceptibility of severe COVID-19 patients to rhino-orbital mucormycosis fungal infection in different clinical manifestations. Jpn J Ophthalmol. 2021;65(4):515-25. DOI: 10.1007/s10384-021-00845-5; PMCID: PMC8165350; PMID: 34057620

18. Moorthy A, Gaikwad R, Krishna S, Hegde R, Tripathi KK, Kale PG, et al. SARS-CoV-2, Uncontrolled Diabetes and Corticosteroids—An Unholy Trinity in Invasive Fungal Infections of the Maxillofacial Region? A Retrospective, Multi-centric Analysis. J Maxillofac Oral Surg. 2021;20(3):418-25. DOI: 10.1007/s12663-021-01532-1; PMCID: PMC7936599; PMID: 33716414

19. Veisi A, Bagheri A, Eshaghi M, Rikhtehgar MH, Kanavi MR, Farjad R. Rhino-orbital mucormycosis during steroid therapy in COVID-19 patients: A case report. Eur J Ophthalmol. 2022;32(4):NP11-6. DOI: 10.1177/11206721211009450; PMCID: PMC9294610; PMID: 33843287

20. Satish D, Joy D, Ross A, Balasubramanya. Mucormycosis coinfection associated with global COVID-19: acase series from India. Int J Otorhinolaryngol Head Neck Surg. 2021;7(5):815-20. DOI: 10.18203/issn.2454-5929.ijohns20211574

21. Revannavar SM, Supriya PS, Samaga L, Vineeth VK. COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world? BMJ Case Rep. 2021;14(4):e241663. DOI: https://doi.org/10.1136/bcr-2021-241663; PMCID: PMC8088249; PMID: 33906877

22. Hassan FA, Aljahli M, Molani F, Almomen A. Rhino-orbito-cerebral mucormycosis in patients with uncontrolled diabetes: A case series. Int J Surg Case Rep. 2020;73:324–7. DOI: 10.1016/j.ijscr.2020.07.011; PMCID: PMC7393455; PMID: 32738774

23. Pandilwar PK, Khan K, Shah K, Sanap M, Unnikrishnan KSA, Nerurkar S. Mucormycosis: A rare entity with rising clinical presentation inimmunocompromised hosts. Int J Surg Case Rep. 2020;77:57–61. DOI: 10.1016/j.ijscr.2020.10.075; PMCID: PMC7644794; PMID: 33152595

24. El-Shabasy RM, Nayel MA, Taher MM, Abdelmonem R, Shoueir KR, Kenawy ER. Three waves changes, new variant strains, and vaccination effect against COVID-19 pandemic. Int J Biol Macromol. 2022;204:161-8. DOI: 10.1016/j.ijbiomac.2022.01.118; PMCID: PMC8782737; PMID: 35074332

25. Thakur V, Bhola S, Thakur P, Patel SKS, Kulshrestha S, Ratho RK, et al. Waves and variants of SARS-CoV-2: understanding the causes and effect of the COVID-19 catastrophe. Infection. 2022;50(2):309-25. DOI: 10.1007/s15010-021-01734-2; PMCID: PMC8675301; PMID: 34914036

26. Moore S, Hill EM, Tildesley MJ, Dyson L, Keeling MJ. Vaccination and non-pharmaceutical interventions for COVID-19: a mathematical modelling study. Lancet Infect Dis. 2021;21(6):793-802. DOI: 10.1016/s1473-3099(21)00143-2; PMCID: PMC7972312; PMID: 33743847

27. Islam MA. A review of SARS-CoV-2 variants and vaccines: Viral properties, mutations, vaccine efficacy, and safety. Infect Med. 2023;2(4):247-61. DOI: 10.1016/j.imj.2023.08.005; PMCID: PMC10774670; PMID: 38205179

28. Weinreich DM, Sivapalasingam S, Norton T, Ali S, Gao H, Bhore R, et al. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. N Engl J Med. 2021;384(3):238-51. DOI: 10.1056/NEJMoa2035002; PMCID: PMC7781102; PMID: 33332778

29. Baum A, Fulton BO, Wloga E, Copin R, Pascal KE, Russo V, et al. Antibody cocktail to SARS-CoV-2 spike protein prevents rapid mutational escape seen with individual antibodies. Science 2020;369(6506):1014–8. DOI: 10.1126/science.abd0831; PMCID: PMC7299283; PMID: 32540904

30. Hoenigl M, Seidel D, Carvalho A, Rudramurthy SM, Arastehfar A, Gangneuz JP, et al. The emergence of COVID-19 associated mucormycosis: a review of cases from 18 countries. Lancet Microbe. 2022;3(7):e543-52. DOI: 10.1016/s2666-5247(21)00237-8; PMCID: PMC8789240; PMID: 35098179

31. Sharma A, Goel A. Mucormycosis: risk factors, diagnosis, treatments, and challenges during COVID-19 pandemic. Folia Microbiol. 2022;67(3):363-87. DOI: 10.1007/s12223-021-00934-5; PMCID: PMC8881997; PMID: 35220559

32. Parfrey NA. Improved diagnosis and prognosis of mucormycosis. A clinicopathologic study of 33 cases. Medicine. 1986;65(2):113-23. DOI: 10.1097/00005792-198603000-00004; PMID: 3951358

33. Howard DH. Iron gathering by zoopathogenic fungi. FEMS Immunol Med Microbiol. 2004;40(2):95-100. DOI: 10.1016/S0928-8244(03)00301-8; PMID: 15040387

34. Howard DH. Acquisition, transport, and storage of iron by pathogenic fungi. Clin Microbiol Rev 1999;12(3):394–404. DOI: 10.1128/cmr.12.3.394; PMCID: PMC100245; PMID: 10398672

35. Gebremariam T, Lin L, Liu M, Kontoyiannis DP, French S, Edwards Jr JE, et al., Bicarbonate correction of ketoacidosis alters host-pathogen interactions and alleviates mucormycosis. J Clin Invest. 2016;126(6):2280-94. DOI: 10.1172/jci82744; PMCID: PMC4887168; PMID: 27159390

36. Ibrahim AS, Spellberg B, Walsh TJ, Kontoyiannis DP. Pathogenesis of Mucormycosis. Clin Infect Dis. 2012;54(Suppl 1):S16–22. DOI: 10.1093/cid/cir865; PMCID: PMC3286196; PMID: 22247441

37. Hassan MIA, Voigt K. Pathogenicity patterns of mucormycosis: epidemiology, interaction with immune cells and virulence factors. Med Mycol. 2019;57(Suppl 2):S245–56. DOI: 10.1093/mmy/myz011; PMCID: PMC6394756; PMID: 30816980

38. Mirza M, Verma M, Sahoo SS, Roy S, Kakkar R, Singh DK. India's Multi-Sectoral Response to Oxygen Surge Demand during COVID-19 Pandemic: A Scoping Review. Indian J Community Med. 2023;48(1):31-40. DOI: 10.4103/ijcm.ijcm_665_22; PMCID: PMC10112770; PMID: 37082381

39. Alshahawey MG, El-Housseiny GS, Elsayed NS, Alshahrani MY, Wakeel LM, Aboshanab KM. New insights on mucormycosis and its association with the COVID-19 pandemic. Future Sci OA. 2021;8(2):FSO772. DOI: 10.2144/fsoa-2021-0122; PMCID: PMC8686842; PMID: 35059222

40. Spellberg B, Walsh TJ, Kontoyiannis DP, Edwards Jr J, Ibrahim AS. Recent advances in the management of mucormycosis: from bench to bedside. Clin Infect Dis. 2009;48(12):1743-51. DOI: 10.1086/599105; PMCID: PMC2809216; PMID: 19435437

41. Smith C, Lee SC. Current treatments against mucormycosis and future directions. PLoS Pathog. 2022;18(10):e1010858. DOI: 10.1371/journal.ppat.1010858; PMCID: PMC9560507; PMID: 36227854

42. Dwivedi AK. Black Fungus/Mucormycosis and Homeopathic Treatment. Int J Sci Res. 2021:10(8):71-2. DOI: 10.36106/ijsr

43. Wolthers MS, Schmidt G, Gjørup CA, Helweg-Larsen J, Rubek N, Jensen LT. Surgical management of rhinocerebral mucormycosis: A case series. JPRAS Open. 2021;30:33-7. DOI: 10.1016/j.jpra.2021.04.013; PMCID: PMC8358096; PMID: 34401438