International Journal of Research in Medical Sciences
Taneja A et al. Int J Res Med Sci. 2023 Jul;11(7):2513-2516
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20232092

Original Research Article

Mucormycosis and COVID-19- black threat of the pandemic

Ashima Taneja[1], Baljot Singh[2]*, Sameer Kaura[4], Divjot Singh Chawla[3], Gurvansh Singh[5], Manpreet Kaur[1]

[1]Department of Obstetrics and Gynecology, [2]Department of Pulmonary Medicine, [3]Department of Microbiology Dayanand Medical College and Hospital, Ludhiana, Punjab, India
[4]Department of Oral Maxillofacial Surgery, BJS Dental College, Ludhiana, Punjab, India
[5]Intern, SGRD Medical College, Amritsar, Punjab, India

Received: 18 April 2023
Revised: 18 May 2023
Accepted: 31 May 2023

***Correspondence:**
Dr. Baljot Singh,
E-mail: baljot007@gmail.com

ABSTRACT

Background: Cases of mucormycosis in people with COVID-19 have been increasingly reported world-wide, particular from India. Globally, the prevalence varied from 0.005 to 1.7 per million population. The aim of the study was to determine the effect of mucormycosis in COVID-19 patients.
Methods: A retrospective study was conducted on 30 patients with biopsy-proven mucormycosis with RT-PCR-confirmed COVID-19 from May 21 to April 2022. Clinical and paraclinical data including demography, underlying diseases, clinical features, corticosteroid use, sites of infection, co-infections, the time between COVID-19 and mucormycosis, clinical management were recorded.
Results: Data from a total of 30 patients post covid mucormycosis was analyzed. The majority of patients were male 70%, age group 30-55 years and were immunocompromised. All of them were diabetic. 80% patients had severe COVID-19 illness. 20% had mild-moderate infection. The average interval between COVID-19 infection and mucormycosis was 15-35 days. The most common was rhinorbital cerebral infection followed by pulmonary involvement. 2 patients had cutaneous mucormycosis. Systemic antifungals were used in all the patients. 12 out of 20 patients with rhinorbital cerebral mucormycosis underwent reconstructive surgery. Debridement was done in 2 patients with mucormycosis.
Conclusions: Our study concludes that CAM (COVID-19 associated mucormycosis) is associated with high mortality and morbidity. Systemic steroids are helpful in people with severe COVID-19 infection but they can also predispose them to secondary fungal diseases. Timely diagnosis and management are challenging but can be helpful if there is an early diagnosis of infection and control of comorbid conditions.

Keywords: CAM, Mucormycosis, Rhino-orbital mucormycosis

INTRODUCTION

Many opportunistic bacterial and fungal infections are seen in patients with severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2).[1] The most common are aspergillus and candida.[1] Cases of mucormycosis in people with COVID-19 have been increasing worldwide, in particular from India. The prevalence of mucormycosis varied from 0.005 to 1.7 per million population, while its prevalence is nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of the year 2019–2020.[2-4] Government of India made mucormycosis a notifiable disease in May 2021 in several states.

Mucormycosis is an uncommon but fatal fungal infection that usually affects patients with altered immunity and is caused by mold fungi of the genus *Rhizopus* Class-

zygomycetes.[5] Mucormycosis is not a contagious disease. It affects people with diabetes especially diabetic ketoacidosis, neutropenia (a type of white blood cells), long-term systemic corticosteroid use, solid organ transplantation and iron overload. The risk is high for people living with HIV, and those using immunomodulating drugs, including the anti-fungal voriconazole in some high-risk groups.[6]

The symptoms of mucormycosis depend on where in the body the fungus is growing. The most common symptom is a sinus infection (sinusitis) which is accompanied by nasal congestion, nasal discharge, and sinus pain. Other symptoms include conjunctival injection or chemosis, loosening of teeth/discoloration of palate/gangrenous inferior turbinates, fever and headache may also occur. Worsening of respiratory symptoms, hemoptysis, chest pain, alteration of consciousness. Skin lesion that resembles blisters or ulcers are also seen. The infected area may turn black, or swelling around a wound.[7]

A case of mucormycosis was diagnosed by identification of mucorales by culture, polymerase chain reaction or histopathology, in a patient with a clinical diagnosis of invasive mucormycosis.[8] Although, diagnosis is very challenging and the following investigations are used NCCT PNS (to see bony erosion), HRCT chest (≥10 nodules, reverse halo sign, CT bronchus sign, etc.), and CT angiography, MRI brain for better delineation of CNS involvement, KOH staining and microscopy, histopathology of debrided tissue and culture, MALDI-TOF if available, presence of Ribbon like aseptate hyphae 5-15 µ that branch at right angles.[9]

Initiation of treatment timely reduces mortality. A multidisciplinary team approach is required. Treatment of mucormycosis involves the combination of surgical debridement and antifungal therapy. Treatment of choice is liposomal amphotericin B in an initial dose of 5 mg/kg body weight (10 mg/kg body weight in case of CNS involvement).[10] It has to be continued till a favorable response is achieved and the disease is stabilized which may take several weeks following which step down to oral posaconazole (300 mg delayed-release tablets twice a day for 1 day followed by 300 mg daily) or Isavuconazole (200 mg 1 tablet 3 times daily for 2 days followed by 200 mg daily) can be done. Conventional amphotericin B (deoxycholate) in the dose of 1-1.5 mg/kg may be used if the liposomal form is not available and renal functions and serum electrolytes are within normal limits.[11]

Aim of the study was to study the outcome of COVID-19 associated mucormycosis.

METHODS

A retrospective study was conducted on 30 patients came to Dayanand Medical College and hospital Ludhiana, Punjab, from May 2021 to May 2022. Total 30 patients with biopsy-proven mucormycosis and RT-PCR-confirmed COVID-19 were taken into the study. Written and informed consent was obtained from the patients. Clinical and paraclinical data including demographics, underlying diseases, clinical features, corticosteroid use, sites of infection (rhino-orbital, pulmonary, CNS), co-infections, the time between COVID-19 and mucormycosis, clinical management (systemic antifungal therapy and surgical procedures) and outcomes (overall response, survival, causes of death) were collected.

Inclusion criteria

Angio-invasive mucormycosis should be confirmed on histopathological examination using GMS, and PAS staining, confirmed case of COVID-19 by RTPCR. The interval between two infections should not be more than 3 months.

Exclusion criteria

Only rapid antigen positive cases, RT-PCR negative cases were excluded.

All the patients were subjected to CT scan orbit, PNS and lungs, and MRI to know the location and extension of mucormycosis, and appropriate treatment was given medical and surgical.

Statistical analysis was done by using chi square test. The Ethical committee of DMCH approved this study.

RESULTS

Data from a total of 30 patients post covid mucormycosis was analyzed. The Mean age of the patients was 45.17±7.697 (Table 1). The majority of patients were male (n=21) 70%. All of them were diabetic and the majority of them were immunocompromised (n=11), 30%.

Table 1: Demographic data of the patients in the study.

	N	Mean	SD
Age (years)	30	45.17	7.697
Gender	**N**	**%**	
Male	21	70	
Female	9	30	

Primary outcome

Out of 30 patients in the study, 80% (n=24) patients had severe COVID-19 illness. 20% (n=6) had the mild-moderate infection (Table 2).

The average interval between COVID-19 infection and mucormycosis was 15-35 days (Table 3).

Table 2: Primary outcome of patients with COVID-19 associated mucormycosis (n=30).

Severity of infection	No. of cases	Percentage
Mild	1	3.3
Moderate	5	16.7
Severe	24	80.0

Table 3: Time interval between COVID-19 infection and mucormycosis.

Time interval between COVID-19 infections and mucormycosis (days)	N	Mean	SD
	30	21.93	6.308

Secondary outcome

Patients with CAM had the most common rhinorbital cerebral infection 60% (n=18). Pulmonary involvement was reported in 30% (N=9) of patients. 2 patients had cutaneous mucormycosis (1 post abdominal hysterectomy wound, 1 post vaginal delivery episiotomy wound). 1 patient had disseminated mucormycosis (thyroid, tracheal and pulmonary). All of them received corticosteroids. Systemic antifungal agents amphotericin B, posaconazole, and isavuconazole were used in all the patients. 12 out of 20 patients with rhinorbital cerebral mucormycosis underwent reconstructive surgery. Surgical debridement was done in 3 patients with mucormycosis (Table 4). 83% of patients required ICU treatment. Mortality was reported in 5 out of 30 patients.

Table 4: Secondary outcome of patients with COVID-19 associated mucormycosis.

	N	Percentage
Site of infection		
Rhino-orbital	18	60.0
Pulmonary	9	30.0
Cutaneous	2	6.7
Disseminated	1	3.3
Mortality	5	16.7
ICU care	22	73.3
Surgical management	15	50.0

DISCUSSION

In this review, we describe 30 cases of COVID-19-associated mucormycosis and we observed that Mucormycosis was predominantly seen in males. (70%) In a systematic review on COVID-19 associated mucormycosis by Kumar et al, the majority were males.[1] In our study, the most common age group was of 30-55 years. which is similar to a study done by Hoenig et al.[12] Old age, men, diabetics, and smokers have a higher risk of developing mucormycosis, which is attributed to the change in their innate immunity and having more severe COVID-19 infection, using steroids concurrently.[13] The majority of them had uncontrolled diabetes and systemic corticosteroid treatment. Diabetic ketoacidosis may induce ferritin synthesis.[14] This is due to a hyperglycemia-induced inflammatory state which increases the development of COVID-19-associated mucormycosis.[15]

In our study majority of patients had severe COVID-19 infection and were associated with mucormycosis. This was similar to a study done by Jaffar et al, they reported the triad of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), corticosteroid use, and uncontrolled diabetes mellitus have been evident for the significant increase in the incidence of angioinvasive maxillofacial mucormycosis.[16] In this review, the average time interval between COVID-19 infection and mucormycosis was 15-35 days. Also, in an updated systematic review of the literature, on COVID-19-associated mucormycosis, the median time interval between COVID-19 diagnosis and the first evidence of mucormycosis infection or CAM diagnosis was 15 days.[17] Usually, the disease is seen during the COVID-19 recovery period, suggesting that multiple factors facilitate fungal colonization, but patients may overlook the symptoms as confusing with residual symptoms of COVID-19 infection and present late to the hospital.

In this study, as described above most common site reported was rhino-orbital followed by pulmonary followed 2 cases of cutaneous mucor, and one case of disseminated mucormycosis. Similar findings were seen in a study conducted by Hoenigi et al.[12] In a study conducted by Shivaraj et al, similar findings were observed.[18] The link between SARS-CoV-2 and mucormycosis is the same entry route, namely glucose-related protein 78, which is required for mucor fungi to enter nasal and paranasal sinuses. To the best of our knowledge, there is no such case reported to date. These two were the rarely reported site of cutaneous mucormycosis during the pandemic. Although a rare case also reported by Tambe et al, cutaneous mucormycosis of the axilla with severe COVID-19 pneumonia.[19] Horiguchi et al reported a fatal case report of disseminated mucormycosis to diagnose on autopsy.[20] To the best of our knowledge, our case was the rare case that survived disseminated mucormycosis after receiving combination antifungal treatment with surgical debridement. Limitation of this study was small sample size.

CONCLUSION

Our study concludes that CAM (COVID-19 associated mucormycosis) is associated with high mortality and morbidity. Systemic steroids are helpful in people with severe COVID-19 infection but they can also predispose them to secondary fungal disease. Diabetes is the most common risk factor for secondary fungal infection. Timely diagnosis and management are challenging in developing countries like India but a careful management plan can be helpful if there is an early diagnosis of

infection and control of comorbid conditions. All efforts should be done to maintain optimal glucose control and only judicious use of corticosteroids, antibiotics, and antifungals in patients with COVID-19.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee, DMCH, Ludhiana, Punjab

REFERENCES

1. 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 Clin Res Rev. 2021;15(4):102146.
2. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: an Update. J Fungi. 2020;6(4):265.
3. Chander J, Kaur M, Singla N, Punia RP, 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.
4. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. J Fungi. 2019;5:26.
5. Eucker J, Sezer O, Graf B., Possinger K. Mucormycoses. Mycoses. 2001;44(7):253-60.
6. Mucormycosis. WHO. 2018. Available from: https://www.who.int/india/home/emergencies/coronavirus-disease-(covid-19)/mucormycosis. Accessed on 22 February 2022.
7. Guideline for management of mucormycosis in COVID-19 patients background. Available from: https://dghs.gov.in/WriteReadData/News/20210517111930155598 8Mucormycosismanagementin Covid-19.pdf. Accessed on 16 April 2023.
8. Dulski TM, DeLong M, Garner K, Patil N, Cima MJ, Rothfeldt L, et al. Notes from the field: COVID-19-associated mucormycosis- Arkansas, July-September 2021. Morbid Mortal Week Rep. 2021;70(50):1750-1.
9. Jain A, Sundaram N, Bhende T, Yashwant R, Jadhav S. Mucormycosis in COVID-19 patients. Indian J Ophthalmol. 2021;69(12):3728.
10. Kumari A, Rao NP, Patnaik U, Malik V, Tevatia MS, Thakur S, et al. Management outcomes of mucormycosis in COVID-19 patients: a preliminary report from a tertiary care hospital. Med J Armed Forces India. 2021;77:S289-95.
11. 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 Japan J Ophthalmol. 2021;65:515-25.
12. Hoenigl M, Seidel D, Carvalho A, Rudramurthy SM, Arastehfar A, Gangneux JP, et al. The emergence of COVID-19 associated mucormycosis: a review of cases from 18 countries. Lancet Microbe. 2022;3(7):e543-52.
13. Farghly Youssif S, Abdelrady MM, Thabet AA, Abdelhamed MA, Gad MO, Abu-Elfatth AM, et al. COVID-19 associated mucormycosis in Assiut University Hospitals: a multidisciplinary dilemma. Scient Rep. 2022;12(1):10494.
14. John TM, Jacob CN, Kontoyiannis DP. When uncontrolled diabetes mellitus and severe COVID19-19 converge: the perfect storm for mucormycosis. J Fungi. 2021;7:298.
15. Elango D, Palanisamy P. COVID-19 associated mucormycosis: a review. J Fam Med Prim Care. 2022;11(2):418.
16. Al-Tawfiq JA, Alhumaid S, Alshukairi AN, Temsah MH, Barry M, Al Mutair A, et al. COVID-19 and mucormycosis superinfection: the perfect storm. Infection. 2021;49:833-53.
17. Pal R, Singh B, Bhadada SK, Banerjee M, Bhogal RS, Hage N, et al. COVID-19-associated mucormycosis: an updated systematic review of literature. Mycoses. 2021;64(12):1452-9.
18. Nagalli S, Kikkeri NS. Mucormycosis in COVID-19: a systematic review of literature. Infezioni in Medicina. 2021;29(4).
19. Joshi A, Tambe RR, Hinduja A, Sunil S, Varaiya A. Cutaneous mucormycosis in a patient of severe COVID-19 pneumonia: a rarer than rare case report. Indian J Crit Care Med. 2021;25(11):1318-9.
20. Horiguchi T, Tsukamoto T, Toyama Y, Sasaki T, Nakamura T, Sakurai A, et al. Fatal disseminated mucormycosis associated with COVID-19. Respirol Case Rep. 2022;10(3):e0912.

Cite this article as: Taneja A, Singh B, Kaura S, Chawla DS, Singh G, Kaur M. Mucormycosis and COVID-19- black threat of the pandemic. Int J Res Med Sci 2023;11:2513-6.