Original Article

A Case-Control Study on Mucormycosis in Tertiary Care Hospital, Bhopal

Manju Toppo, Devendra Gour, Rama Singodiya Lodha, Mugdha Kamble, S. Keerthana
Department of Community Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Abstract

Background: The term mucormycosis refers to any fungal infection caused by fungi belonging to the Mucorales order. The disease often manifests in the skin and also affects the lungs and the brain. A large number of Mucormycosis cases were detected in Delhi, Maharashtra and Gujarat, and Madhya Pradesh. **Objectives:** (1) To describe the epidemiology, management, and outcome of individuals with mucormycosis. (2) To evaluate the risk factors associated with cases and control. **Methodology:** A case–control study, conducted in Hamidia Hospital, Bhopal, for 5 weeks. One hundred and sixty-eight patients diagnosed clinically with radiological or pathological findings was considered a case of Mucormycosis. Control was taken from March 2020 to May 28, 2021, the list of COVID-19-positive patients obtained from IDSP, MP. **Results:** Majority of the study participants were among the age group of 51–60 years and comprising 69.6% of males. Diabetes mellitus is the major comorbidity found in both cases (87.58%) and in controls (20.0%). **Conclusion:** There is a need to stress to control hyperglycemia, and monitor blood glucose levels after discharge following COVID-19 treatment.

Keywords: Black fungus, case–control study, COVID-19, mucor, mucormycosis

Introduction

A rare but serious fungal infection, known as mucormycosis and colloquially as "black fungus," is being detected relatively frequently among COVID-19 patients in some states of India. We share our world with fungi. They are ubiquitous in nature; current estimates put the number of fungal species to be as high as 5.1 million.[1] Common fungi that cause illness are Aspergillus species, *Candida albicans*, Cryptococcus neoformans, blastomyces dermatitis, and Rhizopus species. In developed countries, the disease remains uncommon and, at present, is mostly seen in patients with diabetes mellitus and hematological malignancies, those who are undergoing chemotherapy and those who had received stem cell transplants. In contrast, in developing countries, especially in India, Mucormycosis cases, although sporadic, occur mainly in patients with uncontrolled diabetes or trauma patients.[2]

Mucormycosis is an infectious disease caused by fungi belonging to the order Mucorales (subphylum Mucormycotina).[3] It has an angioinvasive pathology with high morbidity and mortality rates and mainly affects patients whom are weak immune systems.[4] The exact incidence of Mucormycosis in India was unknown due to the lack of population-based studies. The estimated prevalence of mucormycosis was around 70 times higher in India than globally.[5] The *Mucorales* have a unique capability of angio-invasion causing vasculitis and thrombosis of vessels, resulting in large areas of infarction and necrosis.[6] Poor drug penetration in devitalized tissue mandates the need for surgical debridement. In low- and middle-income countries, including India, Mucormycosis is associated with high mortality (45%–90%).[7]

The probable reasons include a delay in diagnosis and the high cost of managing mucormycosis. Many studies suggest that the epidemiology of mucormycosis is different in India compared with the developed world.[8]

Access this article online

Quick Response Code:

Website: www.ijcm.org.in

DOI: 10.4103/ijcm.ijcm_1320_21

Address for correspondence: Dr. Manju Toppo, H.N. 9, Crystal Ideal City, Awadhpuri, Bhopal - 462 022, Madhya Pradesh, India.
E-mail: drmtoppo@gmail.com

How to cite this article: Toppo M, Gour D, Lodha RS, Kamble M, Keerthana S. A case-control study on mucormycosis in tertiary care hospital, Bhopal. Indian J Community Med 2022;47:396-9.

Received: 23-10-21, **Revision:** 17-02-22, **Accepted:** 26-03-22, **Published:** 10-10-22

However, the existing data are from small studies, and there is a lack of data. Mucormycosis is being increasingly diagnosed in Bhopal in recent days. Herein, this study is planned to know the epidemiology, predisposing factors, microbiology, management, and outcome of patients with mucormycosis in Bhopal.

Methodology

A centre based case control study was conducted in a tertiary care hospital in Bhopal over a period of 5 weeks.

CASE-Admitted patients having symptoms and signs related to Mucormycosis and history of COVID-19 from 3rd week of May to 1st week of June 2021 in CONTROL-All COVID-19 positive patients from March 2021 to 28 May 2021 list obtained from IDSP cell MP were included.

All seriously ill patients and those who not willing to participate were excluded.

Written informed consent was taken from the admitted patients. The patients were then interviewed using a predesigned pretested pro forma. The demographic details of the patients were taken along with the history and duration and course of COVID-19 infection. A preventive practice against COVID-19 infections adopted by the patients was interviewed in detail. A detailed history on other comorbidities, past history of accidents, HIV infection, malignancy, if any, and history of burns and organ transplant/donation was also interviewed. This was followed by brief history taking of occurrence of Mucormycosis in the patients. The patients who are compatible clinically with radiological findings or pathologically confirmed was considered a case of Mucormycosis. A total of 168 cases of mucormycosis were interviewed.

The controls were selected specifically in accordance with incubation period of Mucormycosis. Controls were then matched with 1:1 ratio as per age, gender and rural and urban, and history of hospitalization. Controls were selected through random number generator online from the list of positive cases obtained from IDSP. Many of the phone numbers of controls were switched off, not responded, wrong number or refused to take part in the study; in that case the available member in that age group was contacted. Thus, 168 controls were selected randomly or through available members in that group. After identification of participants, telephonic verbal consent was obtained from the controls. Following consent, sociodemographic information was taken about the controls. A brief history of COVID-19 infection was taken regarding the onset of symptoms, date of testing, treatment taken, use and practice of wearing masks, and other comorbidities as well.

The epidemiology, risk factors, management, and outcome of COVID-19-associated Mucormycosis were also assessed and its correlation with COVID-19 infection in cases and control was evaluated. Data thus collected and were entered in Epi Info-7 and analyzed.

Institutional Ethical clearance from was obtained.

Results

A total of 168 individuals were diagnosed with Mucormycosis during the study period. In our study, the mean age ± standard deviation (years) of cases was (50.95 ± 11.79) [Table 1] and comprising 69.6% of males in both cases and 68.8% in controls. Diabetes mellitus is the major comorbidity found in both cases (87.58%) and in controls (20.0%). Para-nasal region involvement was the most common site of involvement (92.85%) [Table 2]. Our study revealed the median duration of onset of Mucormycosis symptoms from the date of diagnosis was 20 days. Radiological investigation was sought in 78.4% of the cases, followed by microscopic confirmation (i.e.,) 53.8%.

Diabetic patients were 5.1 times more risk in contracting COVID-19-associated Mucormycosis than nondiabetic patients. Similarly, patients with uncontrolled diabetes mellitus have 4.8 times more risk than controlled diabetic patients.

Table 1: Sociodemographic profile of cases and controls of mucormycosis

Variable	Case (*n*=168), *n* (%)	Control (*n*=168), *n* (%)
Age (years)		
<20	2 (1.2)	2 (1.2)
21-30	4 (2.4)	4 (2.4)
31-40	28 (16.7)	28 (16.7)
41-50	45 (26.8)	46 (27.4)
51-60	58 (34.5)	58 (34.5)
61-70	26 (15.5)	23 (13.7)
>70	5 (3.0)	7 (4.2)
Gender		
Male	117 (69.6)	100 (68.8)
Female	51 (30.4)	54 (32.1)
Area		
Urban	94 (56.0)	104 (61.9)
Rural	74 (44.1)	64 (38.1)
Occupation		
Unemployed	59 (35.1)	50 (29.8)
Government	21 (12.5)	39 (23.2)
Private	43 (25.6)	27 (16.1)
Business	24 (14.3)	9 (5.4)
Farmer	21 (12.5)	43 (25.6)
Education		
Illiterate	33 (19.6)	22 (13.1)
Primary	29 (17.3)	14 (8.3)
Secondary	37 (22.0)	31 (18.5)
Higher secondary	16 (9.5)	32 (19.0)
Graduate	40 (23.8)	43 (25.6)
Postgraduate	13 (7.7)	26 (15.5)
Comorbidities[#]		
Diabetes	127 (87.58)	29 (20.0)
Hypertension	39 (26.89)	22 (15.17)
Heart disease	6 (4.13)	4 (2.75)
Others	3 (2.06)	6 (4.13)
No comorbidity	15 (10.34)	19 (13.1)

[#]Multiple responses

Practice of steam inhalation and use of Khada is associated with occurrence of Mucormycosis odds ratio = 0.29 ($P = 0.002$) and 0.342 ($P = 0.009$), respectively [Table 3].

Patients who had undergone steroid therapy were 1.5 times at more risk than who have not taken steroids. Odds of disease in patients who had oxygen administration were 1.52 times more than who had no oxygen administration. In cases that had a history of oxygen therapy, 35.17% accounts for the medical grade.

Among the mask wearers, 47.61% had been changing their masks daily among cases as compared to 67.85% in controls. About 61.3% had undergone functional endoscopic sinus surgery and debridement, 10.1% had undergone radical resection, and 51.8% had undergone debridement and only 13.1% had been given only medical treatment. The most commonly used antifungal drugs were Liposomal Amphotericin B (88.96%), followed by Posaconazole (49.65%).

Among the 168 cases, 35.11% were recovered and discharged from the hospital and 52.38% were readmitted due to recurrences. 5.3% of patients Left against Medical Advice. About 7.1% of cases died during the course of illness.

Discussion

This study was one of its kind conducted in Bhopal, describing the epidemiology, predisposing factors, diagnosis, management practices, and outcome of mucormycosis. Several risk factors were identified associated with morbidity and mortality in mucormycosis, mainly including disseminated infection of mucormycosis, COVID-19 infection, prolonged oxygen and steroid therapy, uncontrolled diabetes mellitus. Diabetes mellitus was the predominant risk factor. Similar findings were observed in the study Chakrabarti *et al*. 2019.[9]

Mucormycosis can occur any time after COVID-19 infection, either during the hospital stay or several days to a couple of weeks after discharge (Garg *et al*. 2021).[5]

Patients who underwent combined medical and surgical management had better outcomes as surgical debridement of necrosed tissues allow better penetration of antifungals (Spellberg B *et al*. 2005).[3]

The favorable outcome in the current case was probably because of the better glycemic control in-hospital, and the timely initiation of liposomal amphotericin B. Previous studies have shown that amphotericin B is generally well-tolerated and can be safely administered.[7,10]

Conclusion

Clinicians should be vigilant for mucormycosis in the patients recovering from COVID-19 illness, especially among patients with new or previously diagnosed diabetes mellitus, steroid therapy, oxygen administration, and clinical manifestations of facial pain, orbital pain or black/blood-stained nasal discharge. Therefore, there is a need to stress to control hyperglycemia and monitor blood glucose levels after discharge following COVID-19 treatment. Similarly, steroid

Table 2: Clinical presentations of mucormycosis cases

	n (%)
Clinical presentation[#]	
Para nasal sinuses involvement	156 (92.85)
Orbital involvement	99 (58.92)
With brain involvement	51 (30.35)
Pulmonary involvement/gut involvement	3 (1.78)
Cutaneous involvement	1 (0.59)
Patients who have past history of COVID	135 (80.35)
Duration of onset of mucor symptoms from date of COVID diagnosis* (20 days)	
Onset of symptoms (>18 days)	111 (66.07)
Onset of symptoms (≤18 days)	57 (33.92)

*Median value, [#]Multiple responses

Table 3: Multivariate logistic regression of cases and controls of mucormycosis (*n*=168)

Variables	β	*P*	OR	95% CI for OR	
				Lower bound	Upper bound
Intercept	−1.198	0.007			
History of DM					
Yes	24.657	0.00*	5.10	9.6	2.7
No	0[b]				
Diabetes status					
Controlled	−21.608	0.00*	4.1	8.09	2.1
Uncontrolled	−19.137		4.8	4.88	4.88
No DM	0[b]				
History of keto-acidosis					
Yes	−1.374	0.192	0.253	0.032	1.995
No	0[b]				
Steroid therapy					
Yes	0.407	0.354	1.502	0.635	3.553
No	0[b]				
Oxygen therapy					
Yes	0.423	0.301	1.527	0.685	3.403
No	0[b]				
Zinc therapy					
Yes	−0.245	0.567	0.782	0.338	1.811
No	0[b]				
History of steam therapy					
Yes	−1.208	0.002*	0.299	0.139	0.641
No	0[b]				
History of nebulizer					
Yes	1.613	0.002*	5.018	1.769	14.233
No	0[b]				
History of Kadha					
Yes	−1.073	0.009*	0.342	0.153	0.763
No	0[b]				
History of Giloy					
Yes	0.031	0.951	1.031	0.381	2.789
No	0[b]				

0[b]: Reference category, *P<0.05 statistically significant. OR: Odd ratio, CI: Confidence interval, DM: Diabetes mellitus

usage must be limited to no more than necessary with strict blood glucose control. While administering oxygen, water for humidification must be sterile and there should be no leakage from the humidifier.

The take-home messages are opportunistic fungal infections are occurring in COVID-19 patients, awareness among health-care worker and the public is important, early diagnosis, aggressive treatment, and keeping diabetes under control are paramount for improving outcomes in an otherwise dismal disease.

Acknowledgement

We would like to extend our sincere gratitude to the Dean of Gandhi Medical College Bhopal, IDSP cell, ENT department and Pathology department for their cooperation in successfully conducting the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Blackwell M. The fungi: 1, 2, 3. 5.1 million species? Am J Bot 2011;98:426-38.
2. Chayakulkeeree M, Ghannoum M, Perfect J. Zygomycosis: The reemergingfungal infection. Eur J ClinMicrobiolInfect Dis 2006;25:215-29.
3. Spellberg B, Edwards JJr, Ibrahim A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. Clin Microbiol Rev 2005;18:556-69.
4. Bouza E, Muñoz P, Guinea J. Mucormycosis: An emerging disease? Clin Microbiol Infect 2006; 12 Supp l7:7-23.
5. Garg D, Muthu V, SehgalI S, Ramachandran R, Kaur H, Bhalla A, *et al*. Coronavirus disease (COVID-19) associated mucormycosis (CAM): Case report and systematic review of literature. Mycopathologia 2021;186:289-98.
6. Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis: Are view of the clinical manifestations, diagnosis and treatment. Clin Microbiol Infect 2004;10 Supp l1:31-47.
7. Anaissie EJ, Mattiuzzi GN, Miller CB, Noskin GA, Gurwith MJ, Mamelok RD, *et al.* Treatment of invasive fungal infections in renally impaired patients with a mphotericin Bcolloidal dispersion. Antimicrob Agents Chemother 1998;42:606-11.
8. Prakash H, Chakrabarti A. Epidemiology of Mucormycosis in India. Microorganisms. 2021;9:523. doi: 10.3390/microorganisms 9030523. PMID: 33806386; PMCID: PMC8000977.
9. Chakrabarti A, Das A, Mandal J, Shivaprakash MR, George VK, Tarai B, *et al*. The rising trend of invasive zygomycosis in patients with uncontrolled diabetes mellitus. Med Mycol 2006;44:335-42.
10. Wood JE, Mahnensmith MP, Mahnensmith RL, Perazella MA. Intradia lyticad ministration of amphotericin B: Clinical observationson efficacy and safety. Am J Med Sci 2004;327:5-8.