ORIGINAL ARTICLE

Mucormycoses in Covid-19 Patients

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ABSTRACT

Objective: The goal of the study was to report clinical characteristics, contributing variables and outcome of patients with coronavirus disease 2019 (COVID-19)-associated mucormycosis (CAM).
Study Design: Observational/descriptive study
Place and Duration: Multan Medical and Dental College and Bakhtawar Amin Medical and Dental College. Duration Jan 2021 to July 2021.
Methods: Total 90 patients of both genders had symptoms of mucormycosis during pandemic corona virus disease were presented in this study. Patients were aged between 22-80 years. Patients detailed demographics age, sex, body mass index and duration of disease were calculated after taking informed written consent. Patients were admitted in COVID-19 emergency ward and underwent for RT-PCR and MRI. Comorbidities, symptoms and cause of mucormycosis were assessed. At the end of study mortality rate, hospital stay and ICU admission were calculated. The SPSS 20.0 version was used to examine the entire set of data.
Results: Majority of the patients 65 (72.2%) were males and the rest were females 25 (27.8%). Mean age of the patients were 51.42±12.64 years with mean BMI 28.44±8.72 kg/m². 55 (61.1%) cases had COVID-19 and 35 (38.9%) were recovered from corona virus in this study. Mean duration of mucormycosis was 18.08±7.11 days. Most common symptoms of disease were eye pain/swollen of eyes, nasal stiffness, headache and blurring of vision. Rhino-orbital mucormycosis found in 63 (70%) cases. Majority of the cases were from urban areas 60 (66.7%) and 38 (42.2%) were literate. Diabetes mellitus was the most common comorbidity found in 70 (77.8%). Frequent consumption of the steroids during pandemic disease was the most common cause found in 59 (65.6%) cases. Mortality rate was 32 (35.6%) at the end of study.
Conclusion: In this study we found that the complication of COVID-19 in high-risk patients can be mucormycosis. Poor diabetes mellitus is a significant CAM predisposing factor and frequent usage of excess steroids were the most common cause. Systematic surveillance for diabetes mellitus control and to educate the doctors are indicated for early detection of CAM.
Keywords: COVID-19, Mucormycosis, Diabetes Mellitus, Steroids, Mortality

INTRODUCTION

As a result of SARS-CoV-2, the 2019 coronavirus illness (COVID-19) has been related to a variety of opportunistic bacterial and fungal infections. Both Aspergillus niger and Candida albicans have been found to be common co-infecting fungi in COVID-19 patients[2]. There have been numerous reports of mucormycosis in individuals with COVID-19 in recent years, with the majority of these cases occurring in India. In people with COVID-19, the perfect environment appears to help with germination because of the perfect combination of low oxygen (hypoxia), high glucose (diabetes, new-coming hyperglycemias, steroid-caused hyperglycemia), high iron (increased ferritin), and low phagocytic activity in a white blood cell (WBC) acid medium (metabolic acidosis, diabetic ketoacidosis, [DKA])

Paltauf[3] published the first report of phycomycosis or zygormycosis in 1885, and Baker, a US pathologist, first introduced the word Mucormycosis in 1957 to describe an aggressive illness caused by Rhizopus. When it does occur, mucormycosis, a rare but deadly infection, tends to strike those with weakened immune systems. Rhizopus, Mucor, Rhizomucor, Cunninghamella, and Mucoral, Class Zygomycetes mold fungi produce Mucormycosis, an angio-invasive disease[5]. Human mucormycosis are caused by 60 percent of Rhizopus Oryzae strains, and rhino orbital brain (ROCM) is 90 percent Rhizopus Oryzae [6].

Inhalation of fungal spores is a mechanism of contamination.

The latest 2019–2020 prediction [7, [8], [9] shows that the prevalence of mucormycosis in India is over 80 times greater (0.14 per 1000) than in industrialized nations worldwide, ranging from 0.005 to 1.7 per million people. As a result, India has the most number of people infected with mucormycosis in the world. Despite this, India has the second-highest number of people with diabetes mellitus (DM) and was once known as the "Diabetes Capital of the World"[10]. However, in Europe and the US, hematological malignancies and organ transplantation are the primary causes of mucormycosis-related death. With a death rate of 46%[11], diabetes mellitus is still the world's leading cause of mucormycosis. It is true that DM's presence was a self-sufficient risk factor a comprehensive 2018 meta-analysis of 851 cases with seldom occurring mucormycosis found that the most common isolated species was Rhizopus (48 percent) (confidence interval: 1,77–3,54; P 0,001). Aspergillosis and mucormycosis were previously linked to corticosteroids, but a recent study found that even a brief history of corticosteroids was associated with mucormycosis, particularly in diabetes mellitus (DM) patients. Immune-compromised patients are more likely to develop mucormycosis after taking more than 600 milligrams of prednisolone in a single dosage in the

preceding month[12]. Few occurrences of mucormycosis have been reported, particularly in patients with DM, following a short course of steroid treatment (5–14 days)[13]. In the European Confederation of Medical Mycology investigation, 46% of patients received corticosteroids within one month of being diagnosed with mucormycosis[14].

These findings call into question the widespread use of corticosteroids in the COVID-19 epidemic. The frequency of mucormycosis cases among COVID-19 patients has risen dramatically, particularly in India. Similarly, there are numerous documented cases from around the world. Gray literature contains a slew of anecdotal evidence, such as print and electronic media. These findings are unique and extremely important in terms of public health, especially given the high mortality rate associated with mucormycosis. Mucormycosis, particularly when present intracranially, has a 90% fatality rate [15]. The pace at which mucormycosis disseminates has also been astonishing, and even a 12-hour delay can be fatal because 50% of mucormycosis cases have historically been detected only in post-mortem autopsy series[16].

Identifying the clinical characteristics, contributing variables, and outcome of patients with coronavirus disease 2019 (COVID-19)-associated mucormycosis is the primary goal of this study (CAM).

MATERIAL AND METHODS

This observational/descriptive study was conducted at Multan Medical and Dental College and Bakhtawar Amin Medical and Dental College, during from Jan 2021 to July 2021 and comprised of 90 patients. Patients detailed demographics age, sex, body mass index and duration of disease were calculated after taking informed written consent. Patients without COVID-19 infection, brought dead and undiagnosed fungal infections, less than 22 years of age and those did not give any written consent were excluded from this study.

The patients ranged in age from 22 to 80 years. Active COVID-19 cases were defined as patients who were laboratory confirmed for SARS-CoV-2 in the emergency department (by quick antigen or nucleic acid amplification test) and were admitted to the hospital (by rapid antigen or nucleic acid amplification test). Cases of recent COVID-19 infection were classified as those who had suffered from COVID-19 during the previous three months of presentation but were now SARS-CoV-2 negative in the emergency department. According to widely accepted criteria for post-acute COVID-19 syndrome, a three-month time limit was imposed on the investigation. Patients with mucormycosis associated with COVID-19 disease (CAM) were defined as those who have MM in addition to acute or recent COVID-19 disease.

COVID-19 symptoms, CAM clinical characteristics, current COVID-19 clinical characteristics, detailed CAM comorbidities and risks factors, COVID-19 steroid use details, CAM therapy given prior to CAM symptoms, arrival vitals, ED diagnostic evaluations (radiological and microbiological), ED medicinal therapy and final surgical disposition. Details, severity and treatment of the latest COVID-19 presentation (e.g. steroid use, oxygen supplementation) have been extracted from public

documentation. At the end of study mortality rate, hospital stay and ICU admission were calculated. Categorical variables were assessed by frequencies and percentages. Mean standard deviation was used for analyzing of data. The SPSS 20.0 version was used to examine the entire set of data.

RESULTS

Majority of the patients 65 (72.2%) were males and the rest were females 25 (27.8%). Mean age of the patients were 51.42±12.64 years with mean BMI 28.44±8.72 kg/m^2. 55 (61.1%) cases had COVID-19 and 35 (38.9%) were recovered from corona virus in this study. Mean duration of mucormycosis was 18.08±7.11 days. Most common symptoms of disease were eye pain/swollen of eyes, nasal stuffiness, headache and blur vision. Majority of the cases were from urban areas 60 (66.7%) and 38 (42.2%) were literate.(table 1)

Table 1: Baseline details of enrolled cases

Variables	Frequency (n=90)	Percentage
Mean age (years)	51.42±12.64	
Mean BMI (kg/m^2)	28.44±8.72	
Gender		
Male	65	72.2
Female	35	38.9
Mean duration of mucormycosis (days)	18.08±7.11	
Symptoms		
Eye pain/swollen	25	27.8
nasal stuffiness	23	25.6
headache	22	24.4
blur vision	20	22.2
Residency		
Urban	60	66.7
Rural	30	33.3
Literacy		
Yes	38	42.2
No	52	47.8

Diabetes mellitus was the most common comorbidity found in 70 (77.8%) followed by hypertension 12 (13.3%) and coronary artery diseases in 8 (8.9%). Frequent consumption of the steroids during pandemic disease was the most common cause found in 59 (65.6%) cases. Rhino-orbital mucormycosis found in 63 (70%) cases. (table 2)

Table 2: Comorbidities and causes of disease among the patients

Variables	Frequency (90)	Percentage
Comorbidities		
Diabetes mellitus	70	77.8
hypertension	12	13.3
coronary artery diseases	8	8.9
Use of Steroids		
Yes	59	65.6
No	31	34.4
Rhino-orbital		
Yes	63	70
No	27	30

We found that 38 (42.2%) patients were recovered, 20 (22.2%) patients were admitted to ICU and mortality rate was 32 (35.6%).(table 3)

Table 3: Outcomes of disease among all cases

Variables	Frequency (90)	Percentage
Outcomes		
Recovered	38	42.2
ICU Admission	20	22.2
Mortality	32	35.6
Total	90	100

DISCUSSION

Mucormycosis is uncommon in healthy people, but it can occur in people with weakened immune systems due to a variety of diseases. Diabetes mellitus not under control, including DKA, hematological and other cancers, organ transplantation, prolonged neutropenia, immunosuppressive and corticosteroid therapy, iron overload or hemochromatosis, deferoxime and desferrioxime therapy, voriconazole prophylaxis for transplant recipients with severe burns, AIDS, intravenous drug abuser, malnutrition and open wounds are some of these examples.[17]

In this observational study total 90 patients were presented. Majority of the patients were males 65 (72.2%). Mean age of the patients were 51.42±12.64 years with mean BMI 28.44±8.72 kg/m^2. These findings were comparable to the previous researches in which most of the patients were males with ages 30-55 years.[18,19] This study demographics compared to those of Chander et al.'s[20] study of 82 MM patients, in which two-thirds were men and between the ages of 31 and 60. It's possible that oestrogen's protective impact on systemic fungal infection contributed to a lower frequency in females because of this theory. [21] 55 (61.1%) cases had COVID-19 and 35 (38.9%) were recovered from corona virus in this study. Mean duration of mucormycosis was 18.08±7.11 days. Most common symptoms of disease were eye pain/swollen of eyes, nasal stuffiness, headache and blur vision. Majority of the cases were from urban areas 60 (66.7%) and 38 (42.2%) were literate.[22,23] MUCORYCOSIS is now an Indian notifiable disease due to an increase in mucormycosis (a black fungus infection) cases during the second COVID-19 pandemic wave, as well as its link to severe sequelae and an increased fatality rate among patients who were exposed to COVID-19. The use of non-sterile medical equipment has been linked to spore contamination and a greater risk of mucormycosis infection in patients [24,25].

In current study diabetes mellitus was the most common comorbidity found in 70 (77.8%) followed by hypertension 12 (13.3%) and coronary artery diseases in 8 (8.9%). Although diabetes mellitus is prevalent, the prevalence may be higher than 50% [26-28]. There was a 2.40 odds ratio (OR) in one meta-analysis (95 percent CI 1.98–2.91) for diabetes mellitus to be related with severe illness [29], a 1.64 OR (95 percent CI 2.30–1.08) in a second meta-analysis [30], and an OR of 2.04 (95 percent CI 1.67–2.50 in a third meta-analysis).[31]Frequently consumption of the steroids during pandemic disease was the most common cause found in 59 (65.6%) cases. COVID-19 patients were given high dosage corticosteroids [32]and the use of such drugs needed to be evaluated [33].Rhino-orbital mucormycosis found in 63 (70%) cases.[34]

We found that 38 (42.2%) patients were recovered, 20 (22.2%) patients were admitted to ICU and mortality rate was 32 (35.6%).These results were comparable to the previous study.[35] There is a current need to identify potential risk factors for CAM, to recognize its various manifestations, to perform appropriate triage in the ED, and to examine vision, pupil and ocular motility as part of routine physical examination in the ED. MM has a dismal overall prognosis, although the course of treatment can make a significant difference in the final outcome. It's critical for an ER doctor to know about sending appropriate investigations, initiating systemic antifungals early, avoiding the overuse of antibiotics and systemic steroids, and supporting early multidisciplinary surgical debridement, including lateral canthotomy in the ED. A risk-based approach for patients at risk of mucormycosis must be developed in light of the ongoing COVID-19 pandemic and the growing number of SARS-CoV-2-infected critically ill patients, based on the epidemiological burden of mucormycosis, prevalence of diabetes mellitus and the severity of COVID-19 disease and the use of immune modulating agents, including the combined use of steroids and immunosuppressive agents in cancer and transplant patients.. Patients infected with SARS-CoV-2 need to be treated with a comparable technique for treating mucormycosis, which was developed for treating aspergillosis in COVID-19 [36].

Patients with COVID-19 should be monitored for glycemic levels and treated with corticosteroids judiciously. They should also take proper hygiene and sanitization steps to help restrict the spread of this fungal infection. To learn how COVID-19 causes mucormycosis infections in patients, further research is needed.

CONCLUSION

In this study we found that the complication of COVID-19 in high-risk patients can be mucormicosis. Poor diabetes mellitus is a significant CAM predisposing factor and frequently usage of excess steroids were the most common cause. Systematic surveillance for diabetic mellitus control and educated doctors are indicated on early detection of CAM.

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