INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH
ISSN: 2395-6429, Impact Factor: 4.656
Available Online at www.journalcmpr.com
Volume 7; Issue 06(A); June 2021; Page No.5839-5842
DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20211026

Research Article

AN OBSERVATIONAL CLINICAL STUDY TO EVALUATE THE IMPACT OF COVID-19 AND CO-MORBIDITIES ON PATIENTS OF MUCORMYCOSIS IN CIMS HOSPITAL, BILASPUR, CHHATTISGARH

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ARTICLE INFO

Article History:
Received 06th March, 2021
Received in revised form 14th April, 2021
Accepted 23rd May, 2021
Published online 28th June, 2021

Key words:
Mucormycosis, Covid-19, Pandemic, Co morbidity, Black Fungus.

ABSTRACT

Background: Mucormycosis is an angio-invasive fungal infection due to fungi of the order Mucorales causes infection in humans only when the immunity is critically low, this is known to occur in patients with uncontrolled diabetes, post transplant and cancer. This fungus is normally present in environment. Diabetes mellitus (DM) is an independent risk factor for both severe COVID-19 and mucormycosis. The first case in Bilaspur was reported on 19th May 2021 during the peak of second wave of covid-19 in Bilaspur division. **Objective:** To evaluate the impact of covid-19 and co-morbidities on patients of mucormycosis in CIMS hospital, Bilaspur, Chhattisgarh. **Method**: This prospective observational clinical study is conducted in CIMS hospital Bilaspur, Chhattisgarh. The clinical data from mucormycosis (Black Fungus) ward during the covid-19 pandemic is collected, analyzed and studied. **Result**: The total IPD registered in CIMS hospital, mucormycosis ward is 36 till 15 June 2021. 10 out of 36 patients belonged to 18-45 years age group and 72.22% in >45 year age group. 63.88% patients were male whereas female patients were 13. 25 out of 36(65.44%) patients of lower socioeconomic status were registered in IPD, on the other hand 19.44% patients were of middle class economy status and only 11.11% were of upper class SES. 16 out of 36 patients were admitted with the chief complains of swelling over face out of these 27.77% patients had swelling over right side of face and rest were having that on left. Swelling over face was accompanied by dull pain which was seen in 21 patients. Swollen and black discoloration of eyes was observed in 11 patients out of that 8 were having diminished vision as well. 80.55% of admitted patients were having co-morbidities. 77.77% had Diabetes Mellitus type 2, 33.33% patients were chronic hypertensive, chronic kidney disease was found in 7 patients, 2 patients were having cardiac related problems and 3 were found to have hypothyroidism. 28 out of 36(77.77%) patients of mucormycosis had the history of covid-19 positivity and rest 22.22% patients did not have the covid-19 positive history. **Conclusion**: Majority of patients admitted in mucormycosis ward were old aged low SES male having multiple co-morbid conditions and with positive history of covid-19 infection. Painful swelling over face and eyes were seen predominately in most of the patients. Presence of Diabetes mellitus (DM) increased the risk of contracting mucormycosis and DM is associated with an increased severity of COVID-19 infection.

INTRODUCTION

COVID-19 is the disease caused by a new corona virus called SARS-CoV-2.WHO first learned of this new virus on 31 December 2019, following a report of a cluster of cases of 'viral pneumonia' in Wuhan, People's Republic of China.[1][2] The most common symptoms of COVID-19 are fever, dry cough, fatigue other symptoms that are less common and may affect some patients include loss of taste or smell, nasal congestion, sore throat, headache, muscle or joint pain, different types of skin rash, nausea or vomiting, diarrhoea, chills or dizziness.[3][4] As of now more than 170 million cases have been confirmed, with more than 3.51 million confirmed deaths attributed to COVID-19, making it one of the deadliest pandemics in history.[5] The first case of mucormycosis in Bilaspur was reported on 19th May 2021 during the peak of second wave of covid-19 in Bilaspur division. Both *Aspergillosis* and *Candida* have been reported

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as the main fungal pathogens for co-infection in people with COVID-19. [6] Recently, several cases of mucormycosis in people with COVID-19 have been increasingly reported world-wide, in particular from India. The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia), steroid-induced hyperglycemia, acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background co-morbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators. Mucormycosis is an angioinvasive disease caused by mold fungi of the genus *Rhizopus*, *Mucor*, *Rhizomucor, Cunninghamella* and *Absidia* of Order- Mucorales, Class- Zygomycetes.[7] The *Rhizopus Oryzae* is most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbital-cerebral (ROCM) form mode of contamination occurs through the inhalation of fungal spores.[8]

Objective: To evaluate the impact of covid-19 and co-morbidities on patients of mucormycosis in CIMS hospital, Bilaspur, Chhattisgarh.

MATERIAL AND METHOD

Method: This prospective observational clinical study is conducted in CIMS hospital Bilaspur, Chhattisgarh. The clinical data from mucormycosis (Black Fungus) ward during the covid-19 pandemic is collected, analyzed and studied.

Major Variables

1. Age
2. Gender
3. Socioeconomic status
4. Clinical Presentation
5. Co-morbidities
6. Association of Covid-19 with mucormycosis

RESULTS

This prospective observational clinical study involved IPD data of 36 mucormycosis patients who were admitted and treated in Black Fungus ward from 19th May 2021 to till the date. This study is conducted in CIMS hospital, Bilaspur Chhattisgarh. The results are as follows:

Age

10 out of 36 patients (27.77%) belonged to 18-45 year age group and 72.22% in >45 year age group there, were no patients below 18 yrs. This data shows that middle aged and old patients were predominantly affected by Black Fungus than young patients.

Table 1 Age wise distribution of patients

Age Range(yr)	< 18	18-45	> 45
N = 30	0	10(27.77%)	26(72.22%)

Gender

23 out of 36 (63.88%) patients were male whereas female patients were 13(36.11%); no patients of transgender community were reported. This data revealed that the mucormycosis affected the male patients predominantly than female during covid-19 pandemic.

Table 2 Gender wise Distribution of patients

Gender	Male	Female	Transgender
N = 30	23(63.88%)	13(36.11%)	0

Socio-economic status

25 out of 36(69.44%) patients of lower socioeconomic status were registered in IPD, on the other hand 19.44% patients were of middle class SES and only 11.11% were of upper class SES. This data clearly stated that the patients of lower socioeconomic strata were affected more by mucormycosis than other SES group.

Table 3 Socio-economic status wise distribution of patients

SES	Lower Class	Middle Class	Upper Class	Total
Percentage	25(69.44%)	7(19.44%)	4(11.11%)	36

Clinical Presentation wise distribution of patients

16 out of 36 patients were admitted with the chief complains of swelling over face out of these 27.77% patients had swelling over right side of face and rest were having that on left. Swelling over face was accompanied by dull pain which was seen in 21 patients. Swollen and black discoloration of eyes was observed in 11 patients out of that 8 were having diminished vision as well; toothache was complained by 6 patients.

Table 4 Clinical presentation wise distribution of patients

C/F	Swelling Face N =16	Pain over Face N = 21	Swelling over eye N=11	DOV N= 8	Toothache N = 6	Others N = 10
Right	10(27.77%)	17(47.22%)	7(19.44%)	5(13.88%)	4(11.11%)	-
Left	6(16.66%)	6(16.66%)	4(11.11%)	3(8.33%)	2(5.55%)	-

Co-morbidities wise distribution of patients

80.55% of admitted patients were having co-morbidities. 77.77% had Diabetes Mellitus type 2, 12 out of 36(33.33%) patients were chronic hypertensive, chronic kidney disease was found in 7 patients, 2 patients were having cardiac related problems and 3 were found to have hypothyroidism. This data clearly indicates that the immunity was compromised in presence of co-morbid conditions in most of the patients, making them relatively easy target for mucormycosis.

Table 5 Co morbidity wise distribution of patients

Comorbidity	DM Type 2	Hypertension	Chronic Kidney Disease	Cardiac Disorder	Thyroid Disorder	NIL
N =36	28(77.77%)	12(33.33%)	7(19.44%)	2(5.55%)	3(8.33%)	7(19.44%)

Association of Covid-19 with mucormycosis patients

28 out of 36(77.77%) patients of mucormycosis had the history of covid-19 positivity and its management consequently; only 22.22% patients did not have the covid-19 positive history. This data clearly states that mucormycosis was predominant in those patients who had the positive history of covid-19 infection.

Table 5 Association of Covid-19 with mucormycosis patients

Association with Covid-19	Covid-19 positive	Covid-19 Negative
N = 36	28(77.77%)	8(22.22%)

DISCUSSION

Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million populations, while its prevalence is nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of year 2019–2020. [9] India is already having second largest population with diabetes mellitus (DM) and was the diabetes capital of the world, until recently. [10] DM has been the most common risk factor linked with mucormycosis in India, although haematological malignancies and organ transplant takes the lead in Europe and the USA.[11] Nevertheless, DM remains the leading risk factor associated with mucormycosis globally, with an overall mortality of 46%. While long term use of corticosteroids has often been associated with several opportunistic fungal infection including aspergillosis and mucormycosis, even a short course of corticosteroids has recently been reported to link with mucormycosis especially in people with DM. A cumulative prednisone dose of greater than 600 mg or a total methyl prednisone dose of 2–7 g given during the month before, predisposes immunocompromised people to mucormycosis. [12] Surprisingly, 46% of the patients had received corticosteroids within the month before the diagnosis of mucormycosis in the European Confederation of Medical Mycology study. [13] These findings need a relook in the context of COVID-19 pandemic where corticosteroids are often being used. There has been a steep rise in case reports/series of mucormycosis in people with COVID-19 especially in India. This prompted us to conduct a study of mucormycosis in people with COVID-19, to know its association in relation to co-morbidities. Mucormycosis can involve nose, sinuses, orbit, central nervous system (CNS), lung (pulmonary), gastrointestinal tract (GIT), skin, jaw bones, joints, heart, kidney, and mediastinum (invasive type), but ROCM is the commonest variety seen in clinical practice world-wide. [14] It should be noted that term ROCM refers to the entire spectrum ranging from limited sino-nasal disease (sino-nasal tissue invasion), limited rhino-orbital disease (progression to orbits) to rhino-orbital-cerebral disease (CNS involvement). [15]

A 2019 nationwide multi-center study of 388 confirmed or suspected cases of mucormycosis in India prior to COVID-19**,** *Prakash et al*. found that 18% had DKA and 57% of patients had uncontrolled DM. [16] Similarly, in a data of 465 cases of mucormycosis without COVID-19 in India, *Patel et al.* has shown that rhino-orbital presentation was the most common (67.7%), followed by pulmonary (13.3%) and cutaneous type (10.5%). The predisposing factors associated with mucormycosis in Indians include DM (73.5%), malignancy (9.0%) and organ transplantation (7.7%). [17] Presence of DM significantly increases the odds of contracting ROCM by 7.5-fold (Odds ratio 7.55, $P = 0.001$) as shown in a prospective Indian study, prior to COVID-19 pandemic. [18] Presence of DM with or without DKA increases the risk of contracting mucormycosis and DM is often associated with an increased severity of COVID-19, Uncontrolled hyperglycemia and precipitation of DKA is often observed due to corticosteroid intake. Low pH due to acidosis is a fertile media for mucor spores to germinate. Moreover, steroid use reduces the phagocytic activity of WBC (both first line and second line defence mechanism), causes impairment of broncho-alveolar macrophages migration, ingestion, and phagolysosome fusion, making a diabetic patient exceptionally vulnerable to mucormycosis. COVID-19 often causes endothelialitis, endothelial damage, thrombosis, lymphopenia, and reduction in $CD4^+$ and $CD8^+$ level and thus predisposes to secondary or opportunistic fungal infection.

CONCLUSION

Majority of patients admitted in mucormycosis ward were old aged low SES male having multiple co-morbid conditions and with positive history of covid-19 infection. Painful swelling over face and eyes were seen predominately in most of the patients. Presence of Diabetes mellitus (DM) increased the risk of contracting mucormycosis and DM is associated with an increased severity of COVID-19 infection.

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How to cite this article:

Ashutosh Kori (2021) 'An Observational Clinical Study To Evaluate The Impact of COVID-19 And Co-Morbidities on Patients of Mucormycosis In Cims Hospital, Bilaspur, Chhattisgarh', *International Journal of Current Medical and Pharmaceutical Research,* 07(06), pp 5839-5842.

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