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Clinico-epidemiological profile of Mucormycosis patients admitted in VIMS hospital, Ballari: Case series

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Abstract

Background: Mucormycosis is caused by the fungi belonging to the order Mucorales. Humans acquire the infection predominantly by inhalation of sporangiospores, occasionally by ingestion of contaminated food or traumatic inoculation. In the backdrop of COVID-19 expression, there has been notable increase in the incidence of invasive fungal infection (IFI), namely Mucormycosis and aspergillosis. In the present study we aim to know the Clinico-epidemiological profile of Mucormycosis patients admitted in Vijayanagar institute of medical sciences (VIMS), Ballari, Karnataka.

Methodology: A descriptive study was carried out at VIMS Hospital, Ballari, Karnataka after obtaining ethical clearance. The data was collected using structured questionnaires through interview and case records on risk factors, clinical profile and management of patients who were suspected of Mucormycosis. Frequencies and Proportion were used to describe the variables. Study period was from April 2021-June 2021.

Results: Out of 52 patients, 45(86.5%) were male and 7(13.5%) were female. Age group between 41-50 years (40.4%) were most commonly affected followed by 31-40 years (28.8%) and 50% were positive for COVID 19, 26.9% were post COVID and 23.1% were NON COVID. Twenty two patients were on steroids, 21 (95.5%) of them due to COVID 19 and 1(4.5%) due to asthma. Comorbid conditions like diabetes mellitus 38(73.1%) and hypertension 12(23.1%) were most commonly present. 12(31.6%) out of 38 patients had uncontrolled diabetes mellitus. Mucormycosis was confirmed by KOH and histopathological results and were positive in 21(43.7%) and 27(77.1%) patients respectively. Management of Mucormycosis included both medical and surgical intervention.

Conclusion: Mucormycosis is a life threatening fungal infection. The present study emphasizes the need for further understanding of the disease and to take aggressive measures for early diagnosis and management.

Keywords: Mucormycosis, Invasive fungal infection, COVID 19

Introduction

Most cases of Mucormycosis result from inhalation of fungal sporangiospores that have been released in the air or from direct inoculation

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of organisms into disrupted skin or gastrointestinal tract mucosa. Seasonal variations affect the incidence of Mucormycosis, with most infections occurring from August to November.[1]

Mucormycosis occurs in six different forms, i.e., rhino cerebral, pulmonary, cutaneous, gastrointestinal, and disseminated, and the most frequent sites of infection include pulmonary, rhino cerebral, cutaneous, and disseminated[2].

The incidence of Mucormycosis has been increasing in recent decades, mainly due to the growth of the number of severely immunocompromised patients[3]. It was thought that there might be higher chances of Mucormycosis in COVID-19 individuals who were diabetic and treated with corticosteroids. Interestingly, many COVID-19 patients who were non-diabetic and never used steroids also contracted the infection. Hence, it will be interesting to see whether COVID-19 itself possesses a risk factor by modifying the immunological markers. Prolonged hospital stay with mechanical intubation may also increase the chances of Mucormycosis. Indiscriminate and prolonged use of antibiotics may be responsible for increased susceptibility to fungal infections[4].

Early diagnosis of Mucormycosis is of utmost importance, since it may improve outcome. Studies have shown that it increases survival[5] and it may also reduce the need for or extent of surgical resection, disfigurement and suffering [6].

Both antifungal and surgical management are recognized as the backbones of the treatment; however, both pose challenging issues, such as medication toxicities and anatomic location of lesions[7].

All COVID-19 patients have to be monitored closely for sequelae of immunosuppression. The presence of risk factors adds burden in the treatment of COVID-19 patients.

In this context this study aims to know the Clinico-epidemiological profile of Mucormycosis patients admitted in VIMS hospital, Ballari.

Objective

1. To describe the clinico-epidemiological profile of Mucormycosis patients admitted at VIMS hospital, Ballari.

Materials and Methods

A prospective observational study was carried out at Vijayanagar institute of medical sciences (VIMS), Ballari, Karnataka. Ethical approval was obtained by institutional ethics committee before the start of the study.

Study participants

Individuals with features suggestive of Mucormycosis were enrolled in this study. Features suggestive of Mucormycosis are those individuals with clinically compatible disease and the demonstration of fungi in the tissue (or body fluids) either by direct microscopy (KOH), culture or molecular methods. All participants received treatment at the discretion of the treating physician. Patients admitted with suggestive features of Mucormycosis were interviewed after taking written consent in the local language (Kannada) explaining the purpose and objectives of the study.

Study tool

Pre-designed, semi-structured questionnaire was designed to gather the information like a) Basic demographic, epidemiological profile (age, sex, income, occupation, type of house etc.) b) Clinical aspects of the patients c) Predisposing factors (diabetes, corticosteroid therapy, stem cell transplantation and others) d) Comorbid conditions (Diabetes, hypertension, asthma and others) e) Investigations (Blood tests, histopathological findings, X-ray, CT and MRI scan, etc.) f) Treatment (medical, surgical) was obtained.

Study duration

3 months from April 2021-June 2021

Sample size (N) = Sample size is based on the number of patients suspected to be Mucormycosis who got admitted to VIMS Hospital, Ballari.

Inclusion Criteria

Patients presenting with features suggestive of Mucormycosis presented at the time of the study.

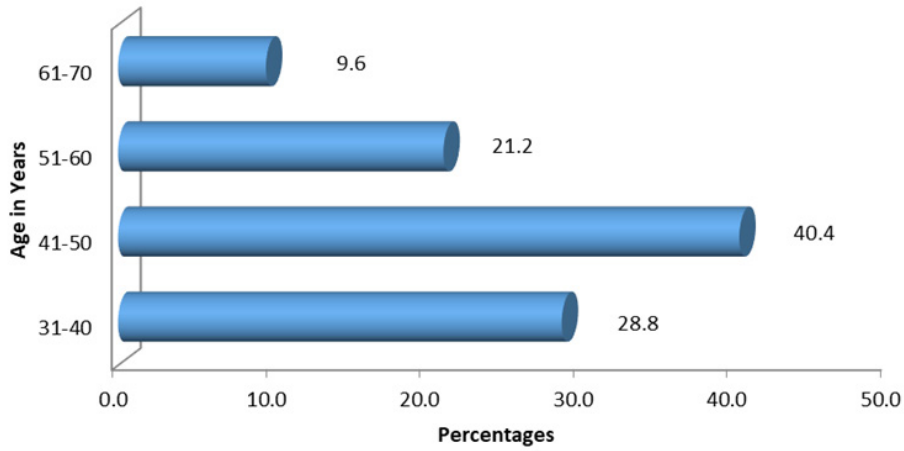
Exclusion Criteria

Severely ill patients who cannot be interviewed.

Statistical Analysis

Frequency and proportion was used for analysis.

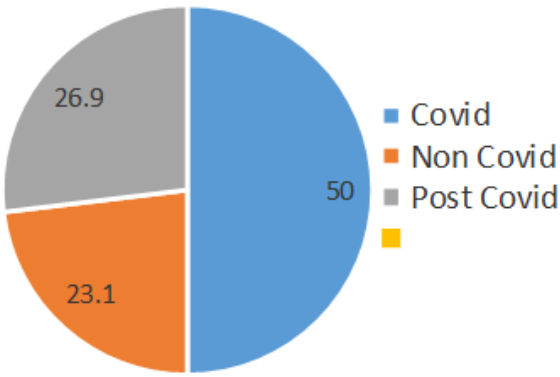
Results



Graph 1. Distribution Of Age Group

Most common age group was between 41-50 years (40.4%) followed by 31-40 years (28.8%).(GRAPH 1)

A total of 52 individuals were diagnosed with Mucormycosis during the study period, of whom 26 (50%) were positive for COVID - 19, 14 (26.9%) were postcovid and 12(23.1%) were noncovid.(GRAPH 2)



Graph 2 COVID status

Table 1. General Information (N=52)

	Frequency	Percentage
REFERRED FROM(N=5)	4	
PHC	1	80
Private hospital		20
GENDER		
Male	45	86.5
Female	7	13.5

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	Frequency	Percentage
RELIGION		
Hindu	48	92.3
Muslim	4	7.7
SOCIOECONOMIC STATUS CLASSIFICATION		
Upper	01	1.9
Upper middle	06	11.5
Middle	10	19.2
Lower middle	17	32.7
Lower	18	34.6
HISTORY OF TRAVEL (IN THE LAST TWO WEEKS)	3	5.8
OCCUPATION		
Professional	1	1.9
Skilled	9	17.3
Semiskilled	6	11.5
Unskilled	33	63.5
Unemployed	3	5.8
METHOD OF STEAM INHALATION (N=19(36.5%))		
Vaporiser	05	26.0
Utensil	14	74.0
WATER USED FOR STEAM INHALATION		
Tap water	16	84.0
Distilled water	3	16.0

The general information is summarized in Table 1.Out of 52 patients, 45(86.5%) were male and 7(13.5%) were female. 4(80%) patients were referred from PHC and 1(20%) from private hospital. Most of the patients 18(34.6%) were belonging to lower socioeconomic status followed by lower middle 17(32.7%), 33(63.5%) and 9(17.3%) were unskilled and skilled workers respectively and 48(92.3%) belonged to Hindu religion. Only 3(5.7%) of them had a history of travel in the last two weeks. Steam inhalation was used by 19(36.5%) patients, 16(84%) of them used tap water.

Table 2. Assessment Of Predisposing Factors (N=52)

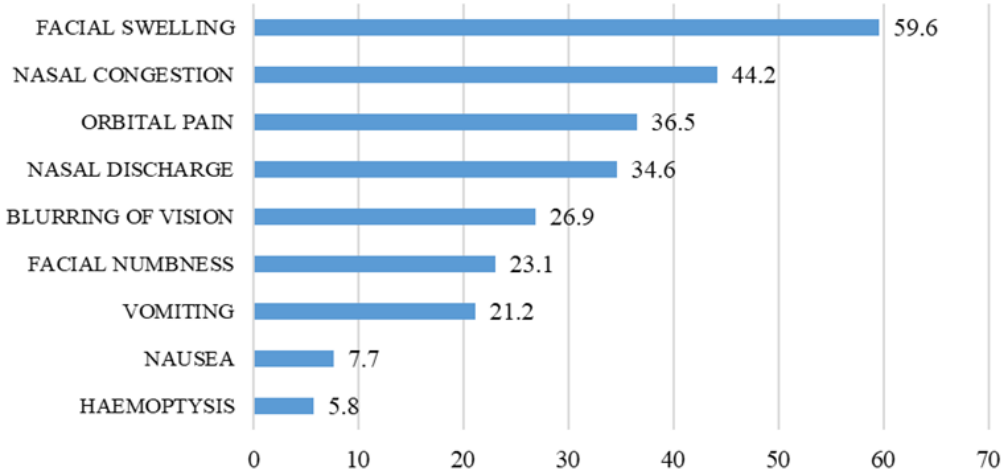
	Frequency	Percentage
Steroids intake	22	42.3
Reason		
Asthma	01	4.5
Covid-19	21	95.5
Immunomodulators intake	01	1.9
History of ICU stays (IN THE LAST MONTH)	01	1.9
Oxygen therapy(IN THE LAST MONTH)	25	48.0
History of transplant		
Stem cell	02	3.8
Voriconazole therapy(IN THE LAST MONTH)	01	1.9
Iron therapy(IN THE LAST MONTH)	07	13.5
Consumption of zinc tablets(IN THE LAST MONTH)	31	59.6
History of blood transfusion (IN THE LAST 1 MONTH)	02	3.8
Injections use IM/IV	22	42.3
On Ventilator support(IN THE LAST 1 MONTH)	03	5.7
History of intake of broad spectrum antibiotics (IN THE LAST 1 MONTH)	21	40.4

Twenty two patients were on steroids, 21 (95.5%) of them due to COVID 19 and 1(4.5%) due to asthma. Only one patient had history of Immunomodulators, ICU stay and Voriconazole therapy. Oxygen therapy and ventilator support was required in 25(48%) and 3(5.7%) patients respectively. Stem cell transplant was done in 2 (3.8%) patients. There was history of consumption of iron and zinc tablets in 7(13.5%) and 31 (59.6%) patients respectively and 2(3.8%) patients received blood transfusion in the last month. Usage of injections(IM/IV) and broad spectrum antibiotics were seen in 22(42.3%) and 21(40.4%) of the patients respectively. (TABLE 2)

Table 3. Comorbidities

Type of Comorbid condition	Frequency	Percentage
Hypertension	12	23.1
Asthma	02	3.8
Thyroid disorders	02	3.8
Cardiac disease	01	1.9
Epilepsy	01	1.9
DIABETES (N=38)		
Controlled	26	68.4
Uncontrolled	12	31.6

Comorbid conditions like diabetes mellitus 38(73.1%) and hypertension 12(23.1%) were most commonly present. 12(31.6%) out of 38 patients had uncontrolled diabetes mellitus. (TABLE 3)



Graph 3- Symptoms Pertaining To Mucormycosis

Most of the patients had presentations like facial swelling 31(59.6%) followed by nasal congestion 23 (44.2%) (GRAPH 3)

Table 4. Signs Pertaining To Mucormycosis (N=52)

Nasal Examination		
	Frequency	**Percentage**
Ulceration, necrosis and discharge	19	36.5
Nasal cavity shows a blackish discoloration of the middle turbinate	07	13.6
Nasal mucosa		
Congestion	10	19.2
Healthy	01	1.9
Sinus mucosa		
Deviated nasal septum	05	9.6
Blood clots	01	1.9
Congestion	01	1.9
Minimal crusting, b/l mucoid discharge,	01	1.9
Oedematous	01	1.9
ORAL EXAMINATION		
Sinusitis	14	26.9
Tenderness of the cheek bone	13	25.0
Black eschar on the palate	03	5.7
OCULAR EXAMINATION		
Restricted eye movement	14	26.9

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Proptosis	05	9.6
Swelling of right upper eyelid	05	9.6
Ophthalmoplegia	05	9.6
No vision PL=Negative	03	5.7
Oedema	01	1.9
Pterygium	01	1.9
Ptosis	01	1.9
FUNDUS EXAMINATION		
Cherry red spot	03	5.7
Periorbital oedema	03	5.7
Disc oedema	02	3.8

On nasal examination 19(36.5%) patients had ulceration, necrosis and discharge. 10 (19.2%) of them had nasal mucosa congestion and 5 (9.6%) of them had deviated nasal septum. On oral examination 14(26.9%) and 13(25%) of them had sinusitis and tenderness of the cheek bone respectively. 14(26.9%) had restricted eye movement on ocular examination. On fundus examination 3(5.7%) had cherry red spot and periorbital oedema.(TABLE 4)

Table 5. Investigations And Management (N=52)

	Frequency	Percentage
KOH		
Positive	21	43.7
Negative	27	56.3
BIOPSY		
Mucormycosis with ischaemic changes	3	100.0
FUNGAL CULTURE		
Positive	2	50
No fungal growth	2	50
HISTOPATHOLOGY		
Positive	27	77.1
Negative	8	22.9
CT/MRI		
Positive	26	50
Negative	2	3.8
CT Positive	7	13.5
MRI Positive	12	23.1
MRI Negative	1	1.9
MANAGEMENT OF MUCORMYCOSIS (N=52)		
Medical Management	29	55.8
Medical and Surgical Management	23	44.2

Mucormycosis was confirmed by KOH and histopathological results and were positive in 21(43.7%) and 27(77.1%) patients respectively. Biopsy and fungal culture identified etiological agent in 3

and 2 patients respectively. CT and MRI was done to assess the extent of anatomic involvement and in 26(50%) of the patients had features suggestive of Mucormycosis. Management of Mucormycosis included both medical and surgical management. 29(55.8%) of them were treated purely by medical management and 23(44.2%) of them required both medical and surgical management.(Table 5)

Discussion

Although Mucormycosis is an extremely rare in healthy individuals but several immunocompromised conditions predispose it. This includes uncontrolled DM with or without DKA, hematological and other malignancies, organ transplantation, prolonged neutropenia, immunosuppressive and corticosteroid therapy, iron overload or hemochromatosis, deferoxamine or desferrioxamine therapy, voriconazole prohylaxis for transplant recipients, severe burns, acquired immunodeficiency syndrome (AIDS), intravenous drug abusers, malnutrition and open wound following trauma[8].

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 worldwide[8]. 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) [9].

The incidence of Mucormycosis is not age or gender dependant but in the present study there is significantly higher number of males (86.5%). Teny M. John, Ceena N et al found that Thirty-four (83%) of the patients in their study were males. Out of which 71% were reported from India[10]. In a study conducted by Roden et al. of 929 patients diagnosed with Mucormycosis, the mean age was 38.8 years, and disease was more common in males (65%) as compared to females (35%). In the study conducted by Bala K, Chander J et al the mean age was 40.43 years and the most common in males (72%) as compared to females[11] (28%). In the present study 45 (86.5%) of them were male and 7(13.5%) were female.

We found 26 (50%) patients who were positive for COVID 19, 14 (26.9%) were post-covid . Song et al. studied the association between Covid-19 and invasive fungal sinusitis in April 2020, and concluded that a large number of patients affected by or recovered from Covid-19 are at increased risk of developing invasive fungal diseases[12]. Aditya Moorthy, Rohith Gaikwad,et al studied that all 18 cases in his study were positive for COVID 19[13].

Hence it becomes utmost important that clinicians pay attention to the high probability of increased incidence of fungal infections in Covid-19 affected or recovered patients, similar to the finding observed in the present study.

Data from a global fungal infection registry reports haematological malignancy (63%) to be the most important underlying condition for mucormycosis[14] .In contrast diabetes (73.07%) was the main predisposing factor in the current study. IA. Patel, H. Kaur, I. Xess, et al in a multicentre observational study on the epidemiology, risk factors, management and outcomes of Mucormycosis in India concluded that Diabetes mellitus (73.5%) was the predominant risk factor for mucormycosis[15]. In a review of 179 cases of paranasal sinus Mucormycosis, 70% of patients had diabetic ketoacidosis[16].

The situation might also be similar in other low- and middle-income countries, where diabetes is prevalent[17].

Presence of DM significantly increases the odds of contracting ROCM by 7.5-fold (Odds ratio 7.55, P ¼ 0.001) as shown in a prospective Indian study, prior to COVID-19 pandemic[11]. In a recent systematic review conducted until April 9, 2021 by John et al[18].that reported the findings of 41 confirmed mucormycosis cases in people with COVID-19, DM was reported in 93% of cases, while 88% were receiving corticosteroids.

In the present study 22 patients were on steroids, 21 (95.5%) of them due to COVID 19 and 1(4.5%) due to asthma. In a review, 62(8%) per cent of coronavirus-positive or recovered patients had secondary bacterial or fungal infections during hospital admission, with widespread use of broad-spectrum antibiotics and steroids[19].

Although according to reports published by doctors, it was remarked that patients with no history of the factors like reusing masks, not getting vaccinated; COVID-19 mutations were also infected with Mucormycosis. There were claims that one common factor involved in patients affected was "excessive steam inhalation[20]." In this study 36.5% of the patients were using steam inhalation.

The consumption of zinc tablets was found in 31(59.6%) patients. It is scientifically proven that zinc starvation inhibits microbial growth in tissues and zinc acts as key nutrition for fungal growth. In vitro study, it has been seen that zinc chelator (zinc antidote) like clioquinol or phenanthroline or other zinc chelator inhibits the growth of this fungus. It means zinc deprivation inhibit the fungal growth. Not only this, it is difficult to grow this fungus in zinc deficient tissue[21].

In the present study Mucormycosis was confirmed by KOH and histopathological results and were positive in 21(43.7%) and 27(77.1%) patients respectively. In a multicentre observational study conducted by IA. Patel, H. Kaur, I. Xess, et al confirmed Mucormycosis by direct microscopy in 406 (87.3%) participants, histopathology in 340(73.1%) participants[15].

Present study aims to understand the clinico-epidemiological profile of the patients who were suspected to be of Mucormycosis. The limitation of the study is though it is an epidemiological study the exact incidence or prevalence of Mucormycosis was difficult to assess in different risk groups. Though the predisposing factors were assessed but the strength of association could not be described as there is no control group. The study results may not be generalizable where haematological malignancy and transplantation are the dominant risk factors.

Conclusion

In conclusion, Mucormycosis is a life threatening disease and a serious problem in India with a high mortality. Present study showed that diabetes mellitus was the major predisposing factor which has to be taken into account for further understanding of the disease and to reduce the severity. Use of steam inhalation, zinc therapy and oxygen therapy were found to be predisposing factors which requires further evaluation. The breach in knowledge identified in the study need to be further addressed and there is a need of further awareness in understanding Mucormycosis so as to diagnose and provide prompt treatment.

Ethical Clearance: Ethical approval was obtained by institutional ethics committee.

Source of funding: NIL

Conflict of Interest: NO

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