Original Research Article

The cross-sectional analytical study of COVID and post COVID mucormycosis in diabetic and non-diabetic patients and their outcomes

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ABSTRACT

Background: Mucormycosis, a rare but serious fungal infection, has shown a concerning rise in incidence among COVID and post-COVID patients, with males constituting majority of cases. This study aimed to investigate the impact of diabetes mellitus (DM) on outcomes in patients with COVID and post-COVID mucormycosis. Given the known association between DM and increased susceptibility to infections, particularly fungal ones, understanding the role of DM in exacerbating mucormycosis outcomes is crucial for clinical management.
Methods: A cross-sectional analytical study was conducted, involving a cohort of 50 patients with mucormycosis, equally divided into diabetic and non-diabetic groups. Data on morbidity, complications, hospitalization rates, and mortality were collected and compared between the two groups. Additionally, glycemic control status was assessed among diabetic patients to evaluate its impact on outcomes.
Results: Among the 50 patients analyzed, diabetic individuals displayed significantly poorer outcomes compared to their non-diabetic counterparts. This included increased morbidity, complications, hospitalization rates, and mortality. Moreover, patients with uncontrolled DM exhibited the worst outcomes, highlighting the critical importance of managing glycemic control during mucormycosis treatment.
Conclusions: The study underscores the necessity of vigilant monitoring and targeted interventions, particularly in diabetic individuals, to mitigate the adverse effects of mucormycosis in the context of COVID-19. Effective management of diabetes, especially glycemic control, is crucial for improving overall patient outcomes and reducing the burden of mucormycosis-related complications and mortality in both COVID and post-COVID scenarios. Further research is warranted to refine treatment protocols and optimize outcomes for this vulnerable population.

Keywords: COVID, Diabetes, Mucormycosis

INTRODUCTION

SARS COV2 caused a global pandemic of COVID 19 disease.[1] There were increased incidence of fungal infection during 2nd wave of covid 19 and sudden surge of angio-invasive infection of mucormycosis in COVID 19 patients.[2] Spectrum of mucormycosis ranges from rhino-orbito-cerebral/pulmonary/cutaneous/GIT and disseminated involvement of disease. The major risk factors for the disease (mucormycosis) are uncontrolled DM (m/c)/neutropenia/iron overload/corticosteroid use/ malignancy, etc.[3]

Incidence of mucormycosis and its adverse effects in COVID 19 patients with diabetes are high compared to non diabetic patients.[4] High index of suspicion, diagnostic nasal endoscopy and radio imaging helps in the diagnosis and extension of disease.[5]

This study aimed to study clinical profile, biochemical markers and imaging findings of mucormycosis in COVID and post-COVID diabetic and non diabetic patients. Also, objectives of this study were to assess risk factors, clinical profile, biochemical markers and imaging findings of mucormycosis in COVID and post COVID diabetic and non diabetic. And to compare the outcomes in diabetic (old+newly detected) and non diabetic patients of covid and post COVID associated mucormycosis.

METHODS

A cross-sectional analytical study was conducted, involving a cohort of 50 patients with mucormycosis, equally divided into diabetic and non-diabetic groups. This study was conducted in RCSM GMC and CPR Hospital Kolhapur (Tertiary care hospital) for six months from January 2022 to July 2022. The Informed verbal consent was taken from eligible patients.

Study population

Patients with active COVID and post COVID with mucormycosis with and without DM.

Procedure

A systemic search was conducted in tertiary care hospital and details of all cases that reported with mucormycosis in COVID and post COVID patients in the period of 6 months. Patients were grouped in 2 categories that is diabetics and non-diabetics based on history, BSL at presentation, HbA1C. Patients in these groups were matched for age, sex, biochemical markers, complications and mortality. comparative significant analysis in terms of p value calculated by t test and chi square test. Continuous variables were presented as mean+/- SD or median (25th and 75th percentiles) and compared using student t tests or rank tests, as appropriate. Categorical variables were described using frequencies and compared using chi-square tests.

Inclusion criteria

Patients of covid and post covid with mucormycosis. Also, those who were willing to participate in the study were included.

Exclusion criteria

Those who were not willing to participate in the study, diagnosed cases of haematological malignancies/solid organ transplant patients were excluded.

Statistical analysis

The analysis was done by IBM SPSS version 20. Chi-square test and for smaller frequencies fishers exact test

\]'/of statistical analysis is used.

RESULTS

Figure 1 shows Mucor mycosis is predominant in male patients. Table 1 shows risk factors were maximum in diabetic patients.
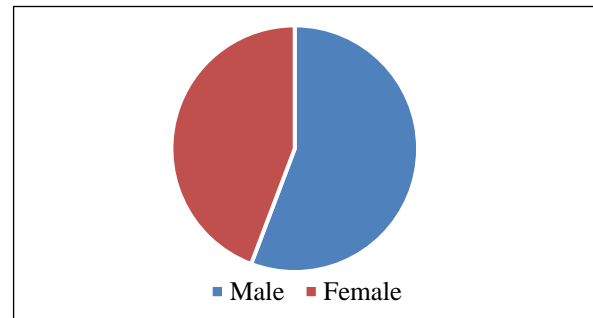

Figure 1: Sex distribution in study population.

Table 1: Risk factors among total patients of COVID associated mucormycosis in DM and non-DM.

Parameter	Diabetic (n=25)	Non-diabetic (n=25)
Hba1c level (mean)	9.67%	5.30%
Mean sugar level	243mg/dl	114mg/dl
Corticosteroids used	86%	82%

Table 2: Clinical features of presentation in mucormycosis.

Clinical feature	Percentage
Headache	82
Nasal symptoms	66
Orbital symptoms	60
CNS symptoms	8

According to table 2, most common presentation in covid was rhino-orbito Mucor mycosis and most common symptom was headache (82%).

Table 3: Vaccination status of patients in the study group.

Covid 19 vaccination	Patients
Fully vaccinated	None
Single dose of vaccine	26 patients

Table 3 shows among 50 patients that no patient was fully vaccinated and 26 patients were received single dose of covid vaccine.

Table 4 shows, biomarkers were more positive in diabetic as compared to non-diabetic patients. most common positive biomarker was serum ferritin with significant p value (0.04) followed by ESR.

Figure 2 shows that, maxillary sinus was most common site involved in mucor followed by ethmoid sinus> sphenoid sinus > frontal sinus > orbital> cerebral involvement.

Table 4: Biomarkers in patients in study population.

Biomarkers	Diabetic % (n=25)	Non diabetic % (n=25)	P value
Serum ferritin (>350ng/ml)	84 (n=21)	48 (n=12)	0.04
ESR (increased)	80 (n=20)	76 (n=19)	0.7
CRP (qualitative)	72 (n=18)	76 (n=19)	0.7
CBC n/l ratio(>3.5)	60 (n=15)	40 (n=10)	0.1
D dimer (positive)	44 (n=11)	28 (n=7)	0.2
Serum procalcitonin (>2)	24 (n=6)	8 (n=2)	0.4
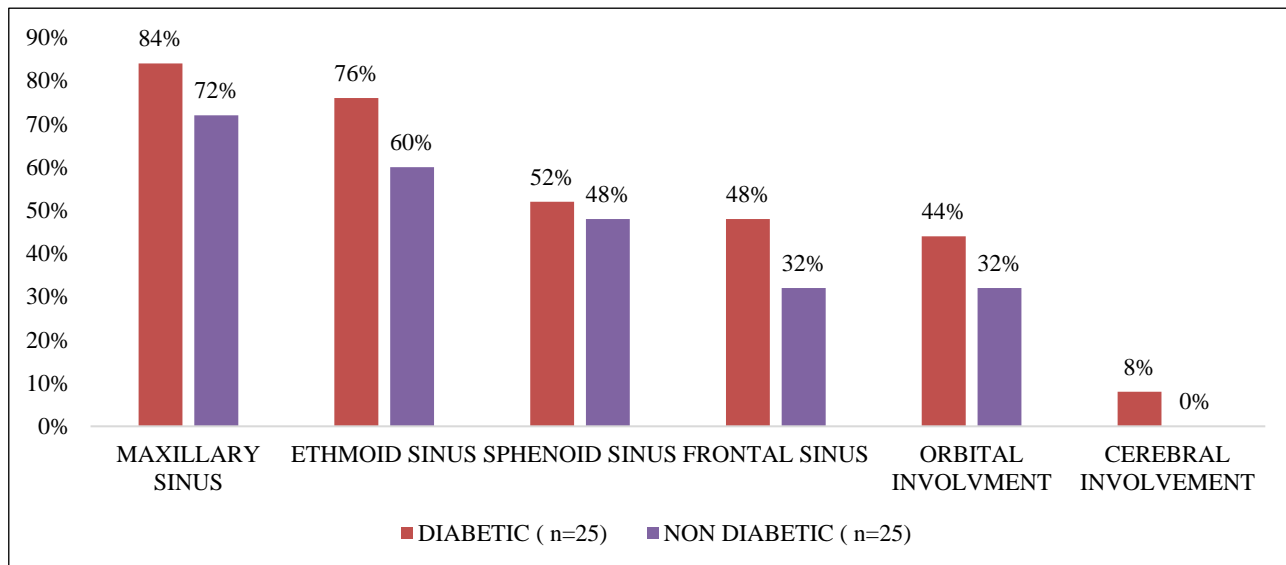
Figure 2: Extension of mucor mycosis in CT/MRI imaging in study population.

Table 5 shows that, diabetic patients had more hospital stay than non-diabetic patients.

Table 5: Hospital stay of study population.

Parameter	Diabetes	Non diabetes	P value
Mean days	30 days	21 days	0.03

Table 6 shows, thrombosis is most common complication and more commonly seen in diabetic patients.

Table 7 shows, total 5 patients died among 50 patients with mortality was more in diabetics as compared to non-diabetic.

Table 6: Comparison of complications among diabetic and non-diabetic patients.

Complications	Diabetic (n=25) (%)	Non diabetic (n=25) (%)
Thrombosis (vision loss)	10/25 (40)	7/25 (28)
Sepsis	7/25 (28)	3/25 (12)
Ophthalmoplegia	6/25 (24)	6/25 (24)
Encephalopathy	2/25 (8)	0/25 (0)

Table 7: Mortality among covid associated mucormycosis in DM and non-DM.

Mortality	Diabetics (4/25)	Non diabetics (1/25)	P value
	16%	4%	0.001

Gender Disparity: Mucormycosis predominantly affects males, constituting 56% of cases in the study population. Impact of diabetes on biomarkers: Diabetic patients exhibited significantly higher levels of serum ferritin, with 84% (n=21) having levels >350ng/ml, compared to 48% (n=12) in non-diabetic individuals (p=0.04), indicating a more pronounced inflammatory response among diabetics. Clinical presentation: Rhino-orbital mucormycosis was the most common presentation among COVID-associated mucormycosis patients, with 82% presenting with headaches. Vaccination status: None of the patients were fully vaccinated against COVID-19. Among the study population, 52% had received at least one dose of the COVID-19 vaccine. Hospital stay: Diabetic patients had a significantly longer mean hospital stay of 30 days compared to 21 days in non-diabetic patients (p=0.03), suggesting a more severe disease

course requiring prolonged medical care among diabetics. Complications: Thrombosis, particularly leading to vision loss, was the most common complication observed, with 40% of diabetic patients experiencing thrombosis compared to 28% in non-diabetic patients. Mortality: The mortality rate was significantly higher among diabetic patients, with 16% (4/25) of diabetic patients succumbing to the disease compared to 4% (1/25) among non-diabetic individuals (p=0.001). Patients with diabetes in covid and post covid mucormycosis had poor outcomes, increased morbidity, complications, hospitality and mortality as compared to non diabetic patients. Those with uncontrolled DM had poor outcome. Thus proper management of uncontrolled DM is key stone during management.

DISCUSSION

The presented cross-sectional analytical study delves into the epidemiology and clinical outcomes of mucormycosis in COVID and post-COVID patients, focusing on the influence of diabetes mellitus. The study's findings provide valuable insights into the impact of diabetic status on disease severity, treatment response, and patient outcomes.[6]

One of the notable observations of this study is the gender disparity in mucormycosis cases, with males constituting the majority of patients. This aligns with previous research indicating potential gender-specific susceptibility factors or healthcare-seeking behaviors that warrant further investigation.[7]

A pivotal aspect highlighted in the study is the significantly poorer outcomes observed in diabetic patients with COVID and post-COVID mucormycosis compared to non-diabetic individuals. These outcomes encompass increased morbidity, complications, hospitalization rates, and mortality among diabetic cohorts.[8] The study underscores the critical importance of glycemic control, as evidenced by the worse outcomes in patients with uncontrolled diabetes. Proper management of diabetes emerges as a cornerstone in mitigating the adverse effects of mucormycosis, emphasizing the need for integrated care approaches that address both fungal infection and diabetic management.[9]

The clinical presentations documented in the study, notably the prevalence of rhino-orbital-cerebral mucormycosis, align with the established spectrum of mucormycosis manifestations. Additionally, the analysis of biomarkers and imaging findings provides valuable insights into diagnostic approaches and disease extension, facilitating early detection and intervention.[10]

The findings of this study highlight the significant impact of diabetes mellitus (DM) on the clinical course and outcomes of COVID-associated mucormycosis, as evidenced by the following comparisons:

Serum ferritin levels: Diabetic patients exhibited significantly higher levels of serum ferritin compared to non-diabetic individuals, with 84% (n=21) having levels >350ng/ml, compared to 48% (n=12) in non-diabetic individuals (p=0.04).

Hospital stay: Diabetic patients had a significantly longer mean hospital stay of 30 days compared to 21 days in non-diabetic patients (p=0.03), indicating a more severe disease course requiring prolonged medical care among diabetics.

Complications: Thrombosis, particularly leading to vision loss, was more commonly observed in diabetic patients, with 40% of diabetic patients experiencing thrombosis compared to 28% in non-diabetic patients.

Mortality: The mortality rate was significantly higher among diabetic patients, with 16% (4/25) of diabetic patients succumbing to the disease compared to 4% (1/25) among non-diabetic individuals (p=0.001).

These statistical comparisons underscore the heightened vulnerability and poorer outcomes of diabetic individuals with COVID-associated mucormycosis. The elevated serum ferritin levels, prolonged hospital stays, increased incidence of complications, and higher mortality rates among diabetic patients highlight the urgent need for targeted interventions and aggressive management strategies in this population.

This is compared with a study done by Sarkar et al: In a systematic review of cases reported worldwide and in India, Sarkar and colleagues found that diabetic COVID-19 patients with mucormycosis exhibited a higher incidence of severe outcomes compared to non-diabetic counterparts.[11]

Mishra et al comparative analysis between diabetics and non-diabetics with mucormycosis in COVID-19 patients revealed that diabetic individuals had a significantly higher mortality rate and increased severity of disease manifestations compared to non-diabetic individuals.[11]

The findings of Sen et al study echoed similar trends observed in the current research, highlighting the heightened susceptibility and poorer outcomes among diabetic patients with COVID-associated mucormycosis. Key comparisons, including serum biomarker levels, hospital stay duration, incidence of complications, and mortality rates, were consistent with the results obtained in our study, further validating the observed trends.[12]

It is important to note that these observations are based on small sample size and may not be generalized to large population. The study's limitations, such as its retrospective design and relatively small sample size, warrant acknowledgment. Larger prospective studies are needed to validate the observed associations and elucidate potential causal relationships between diabetes,

COVID infection, and mucormycosis outcomes. Furthermore, while the study focused on COVID and post-COVID mucormycosis, exploring the impact of other comorbidities or treatments on disease outcomes could provide a more comprehensive understanding of the disease's pathogenesis and management.

CONCLUSION

Mucormycosis is an angioinvasive fungal infection. The disease has a recent surge in COVID 19 pandemic due to uncontrolled DM and irrational use of corticosteroids. The patients with diabetes had adverse outcome as compared to non diabetic. This study underscores the complex interplay between COVID infection, diabetes mellitus, and mucormycosis, emphasizing the need for multidisciplinary approaches to patient care. By elucidating the factors influencing disease severity and outcomes, the study contributes valuable insights that could inform clinical practice and guide future research endeavors aimed at optimizing patient management and reducing the burden of mucormycosis-associated morbidity and mortality.

ACKNOWLEDGEMENTS

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