

## A HISTOPATHOLOGICAL STUDY OF RHINO-ORBITAL MUCORMYCOSIS IN CORRELATION WITH ITS RISK FACTORS AND RADIOLOGICAL FINDINGS IN COVID-19 PATIENTS

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### Abstract

**Background:** Coronavirus disease 2019 (COVID-19) first emerged in Wuhan, China in December 2019, and since then there has been a notable rise in the incidence of invasive mucormycosis. The aim of this study was to analyse our experience of the cases of invasive mucormycosis infection to draw a correlation between causative factors, histopathology and radiological findings to enable clinicians to understand an evolving disease pattern. **Materials and Methods:** The present study has been conducted on the 100 biopsy specimens of rhino orbital tissue of suspected mucormycosis cases as well as biopsy proven mucormycosis cases, received in the Department of Pathology, BRD Medical College, Gorakhpur, for histopathological examination. The study was done on RTPCR confirmed COVID-19 cases. Formalin fixed paraffin embedded histological sections were studied microscopically. All the sections were stained with H & E stains and special stain, PAS (Periodic acid Schiff). **Result:** A Total of 100 cases were included in our study. The majority of the cases 68% belonged to lower socioeconomic status. The major risk factors included corticosteroid use during COVID-19 treatment 85% cases, uncontrolled diabetes 78% cases. The most common presenting symptom was eye pain/swelling 69% cases. The most common presenting sign was visual deterioration 74% cases. The most commonly involved sinus was ethmoid 78% cases. **Conclusion:** Diabetes, COVID-19 and steroid administration- this trinity coexisted in this pandemic has self-potentiated the problem of immune dysregulation leading to fungal invasion and tissue necrosis & stage 2 and 3 radiological involvement of PNS (paranasal sinus) & orbit.

## INTRODUCTION

The health scenario of the latter part of 2019 and whole of 2020 has been dominated globally by a novel strain of severe acute respiratory syndrome coronavirus 2 (SARSCoV-2)—which, along with severe pneumonia, is also associated with strokes, venous thrombosis, renal failure, cardiomyopathy, coronary and systemic vasculitis.<sup>[1]</sup> Coronavirus disease 2019 (COVID-19) first emerged in Wuhan, China in December 2019, and since then the frequency of bacterial and fungal coinfections has been continuously rising.<sup>[2]</sup> The predominant clinical phenotype of COVID-19 manifests as an upper

respiratory infection followed by pneumonia when the virus invades the respiratory epithelium binding to angiotensin converting enzyme 2 (ACE2) receptors.<sup>[3]</sup> The more severe, second stage of this disease is caused by the systemic inflammation and coagulopathy causing direct damage to blood vessels, with hepatic, renal and cardiac injuries. The coagulopathy seen is of complement-mediated thrombotic microangiopathies.<sup>[4]</sup> It is a non-segmented negative sense RNA virus which causes profound lymphopenia. In later stages of infection, when viral replication accelerates, epithelial-endothelial barrier integrity is compromised and the inflammatory response and triggering an influx of

monocytes and neutrophils is accentuated. Collectively, endothelial barrier disruption, dysfunctional alveolar-capillary oxygen transmission and impaired oxygen diffusion capacity are characteristic features of covid-19.<sup>[5]</sup> The pathogen is ubiquitous, occurring naturally in the environment, the body surface, and orifices. The spores inoculate the paranasal sinuses and the nasopharynx with subsequent spread to the orbit and intracranial cavity in persons with decreased cellular and humoral defence.<sup>[6]</sup> Tissue necrosis, often a late sign, is a hallmark of mucormycosis, resulting from angioinvasion and vascular thrombosis Globally,<sup>[3]</sup> the prevalence of mucormycosis varied from 0.005 to 1.7 per million population, 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.<sup>[7]</sup> 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.<sup>[8]</sup> DM remains the leading risk factor associated with mucormycosis globally, with an overall mortality of 46%.<sup>[9]</sup> Besides diffuse alveolar damage with severe inflammatory exudation and coagulopathy, COVID-19 patients also have immunosuppression with a decrease in CD4 +T and CD8 +T cells.<sup>[10]</sup> High incidence of diabetes in our population and widespread use of corticosteroids as a part of treatment of covid-19 seems to be casual to this increased incidence. Covid-19 patients are prescribed with heavy doses of steroids resulting in weakened immune system and are susceptible to mucormycosis. In addition, steroids can cause blood sugar levels to spike, which is challenging for patients with uncontrolled diabetes and the acidic environment due to this condition favours the fungal (mucorales) growth.<sup>[11]</sup> Mucormycosis is difficult to diagnose which affects outcome and results in poor prognosis. Early diagnosis and treatment are essential. Delay of a week often doubles the 30day mortality from 35% to 66%. Despite early aggressive combined surgical and medical therapy, the prognosis of mucormycosis is poor.<sup>[12]</sup> Median interval of seven days from covid-19 and mucormycosis. The above finding shows the importance of this critical surveillance time for detecting mucormycosis in covid-19 patients.<sup>[13]</sup> Early diagnosis with the institution of appropriate antimicrobial therapy saves both sight and life. A definitive diagnosis of mucormycosis as the causative fungal species is achieved only after the histopathologic examination of the biopsy specimen and culture. KOH examination may be used only as a suggestive tool to identify the presence of mucormycosis.<sup>[3]</sup> Computed tomography is the first diagnostic tool used to assess the status of sinuses, although extent of extra sinus spread is best judged with MRI.<sup>[14]</sup> Given the poor prognosis of this disease and its time liability, we aim to analyse our experience of the cases of invasive fungal infection to draw the correlation between causative factors,

histopathology and radiological findings to enable clinicians to understand an evolving disease pattern.

## MATERIALS AND METHODS

The present study is prospective and retrospective observational study, has been conducted in the Department of Pathology, B.R.D. Medical College Gorakhpur, U.P. on the biopsy specimens of rhino orbital tissue of suspected mucormycosis cases as well as biopsy proven mucormycosis cases, received in the Department of Pathology send by Department of Ophthalmology and Otorhinolaryngology, Baba Raghav Das Medical College, Gorakhpur, for histopathological examination of mucormycosis cases during a period from July 2021 to June 2022. Study was done on RTPCR confirmed COVID-19 cases. Previous and present history, investigations, clinical features and history of associated risk factors were taken from all patients, case records and other information provided by COVID ward, B.R.D. Medical College Gorakhpur were evaluated thoroughly and correlation between COVID 19 riskfactors and mucormycosis were made along with its radiological and histopathological findings. In the present study a total of 100 samples of formalin fixed paraffin embedded histological sections were studied microscopically. All the sections were stained with Haematoxylin and Eosin stains and special stain, PAS (Periodic acid Schiff). Statistical analysis was done using chi square test ( $\chi^2$ ). A  $P < 0.05$  taken as statistically significant.

## RESULTS

A total of 100 cases of rhino-orbital mucormycosis associated with COVID-19 were included in our study.

**COVID-19 associated mucormycosis (CAM): Age group(N=100)**

Age of patients ranged from 21 - 68 years. Mean age of patients 51.19 years. The maximum number of cases 30% cases were in the age group of 51-60 years followed by 28% cases in age group of >60 years. Therefore, most common age group is 50-60 years.

**CAM: Gender (N=100)**

Male to Female ratio was 1.7:1, males were more commonly affected than females. This male preponderance can be associated with greater outdoor exposure and therefore, to fungal infestation. In our study, majority of the cases were male 63% cases and 37% cases were female.

**CAM: Socioeconomic status (N=100)**

Majority of the cases 68% belonged to lower socioeconomic status class followed by middle class 22% cases.

**CAM: Risk Factors (N=100)**

Uncontrolled diabetes mellitus has been identified as a predominant risk factor for COVID-19 associated rhino-orbital mucormycosis. The risk is

higher in diabetics than in general population. It is most common comorbidity associated with majority of the cases 78% including diabetic ketoacidosis in 11% cases followed by hypertension in 12% cases

and chronic kidney disease in 4% cases, ischaemic heart disease in 4% cases, malignancy in 2% cases. Comorbidities in mucormycosis cases associated with COVID-19 are shown in [Table 1].

**Table 1: Comorbidities Seen in mucormycosis cases associated with COVID-19 (N=100)**

Comorbidities	No. of cases (N)	%
Diabetes mellitus including diabetic ketoacidosis (11%)	78	78%
Hypertension	12	12%
Ischemic heart disease	4	4%
Chronic kidney disease	4	4%
Malignancy	2	2%
Total	100	100%

**CAM:** Duration of onset of covid 19 to appearance mucormycosis symptom (N=100)

Majority of cases 72% were diagnosed within one month of onset (Early onset) of covid19 infection and rest 28% were diagnosed after one month (Late onset) of COVID-19 infection.

Association of uncontrolled diabetes mellitus and COVID-19 associated rhino-orbital mucormycosis was found to be statistically significant (P<0.00001), based on Chi-square test in our study. Association of diabetes with mucorycosis in COVID-19 patients shown in.

**Table 2: Association of diabetes with mucorycosis in COVID-19 patients. (N=100)**

COVID 19 associated Mucormycosis	Diabetic	Nondiabetic	Total	$\chi^2$	P- value
Early onset (<1 month)	70	2	72	55.3687	0.00001
Late onset (>1 month)	8	20	28		

**Table 3: Grading of necrosis in COVID-19 associated mucormycosis cases**

Grades of necrosis [% of necrosis /10 low power fields]	Mucormycosis cases	%
Mild (<30%/10 lpf)	10	13.0%
Moderate(30-50%/10lpf)	39	50.6%
Severe (>50%/10 lpf)	28	36.4%
Total	77	100%

**Table 4: Distribution of mucormycosis cases associated with COVID-19 according to histopathological findings.**

Histopathological features	No. of cases	%
Necrosis	77	77%
Neutrophilic infiltration	69	69%
Angioinvasion	22	22%
Granulomatous inflammation	08	08%

**Table 5: Association of necrosis with fungal hyphae load. (N=100)**

Necrosis	Fungal load			Total	$\chi^2$	P-value
	Mild	Moderate	Severe			
Present	11	43	23	77	39.4164	<0.00001
Absent	19	3	1	23		
Total	30	46	24	100		

**Table 6: Correlation between uncontrolled diabetes and stages of mucormycosis based on radiological findings.**

Staging based on Radiological findings	Uncontrolled Diabetes			Total	$\chi^2$	P-value
	Present	Absent	Total			
Stage I (Nasal mucosa only)	4	1	5	14.4442	0.002359	
Stage II (Paranasal sinus (PNS) with nasal mucosa)	29	18	47			
Stage III (Orbit with paranasal sinus)	38	2	40			
Stage IV (CNS with orbit and PNS)	7	1	8			
Total	78	22	100			

**Table 7: Correlation of steroid use with radiological staging of mucormycosis cases associated with COVID-19.**

High dose Steroid use	Stage I	Stage II	Stage III	Stage IV	Total	$\chi^2$	P- value
	Present	4	35	39			
Absent	1	12	1	1	15		
Total	5	47	40	8	100		

**(CAM): Symptoms**

The most common presenting symptom was eye pain/swelling present in 69% cases followed by facial swelling in 68% cases, visual disturbances in 52% cases, headache in 48% cases, nasal discharge in 42% cases, fever in 34% cases, altered sensorium in 6% cases.

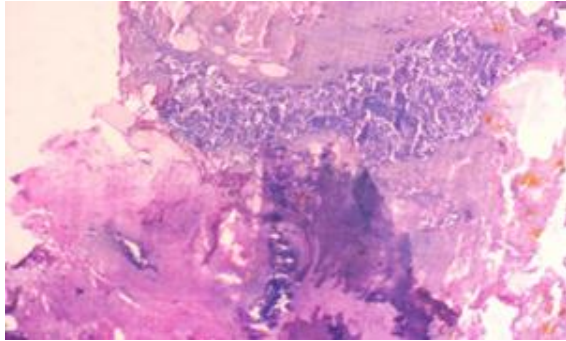
**(CAM): Signs**

The most common presenting sign was visual deterioration in 74% cases, second most common sign was facial edema in 56% cases followed by ophthalmoplegia in 44% cases, proptosis in 36% cases, keratopathy in 28% cases, nasal/palatal eschar

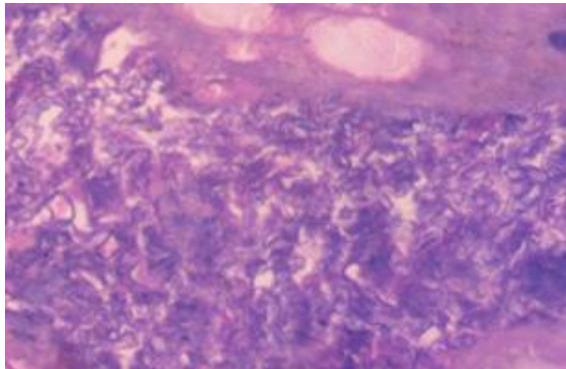
in 11% cases, periocular/ facial hypoesthesia in 5% cases, facial palsy in 3% cases.

#### **Histomorphological findings in CAM**

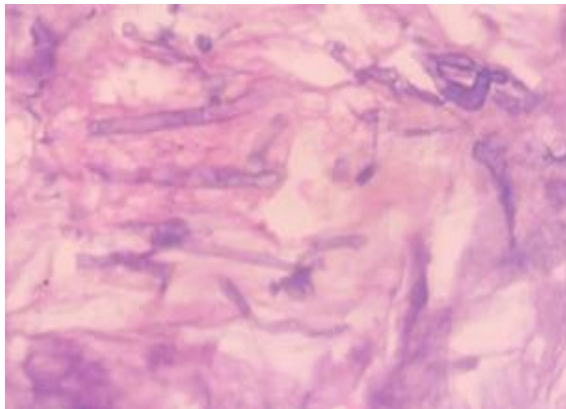
H&E stained sections showed characteristic hyphae of mucorales which were broad, ribbon like, predominantly aseptate with right angle branching. Sections were also stained with special stain, PAS for further confirmation. Pink coloured, Broad, aseptate fungal hyphae of mucor were seen.



**Figure 1: H&E staining at 10x showing mucor hyphae.**



**Figure 2: H&E staining at 40x showing broad, ribbonlike, aseptate Mucor hyphae with right angle branching.**

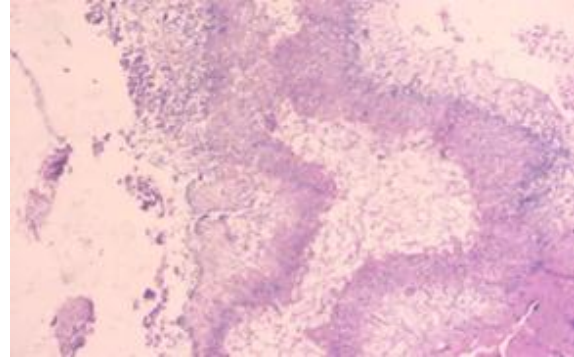


**Figure 3: H&E staining at 40x showing broad, ribbonlike, aseptate, mucor hyphae with right angle branching.**

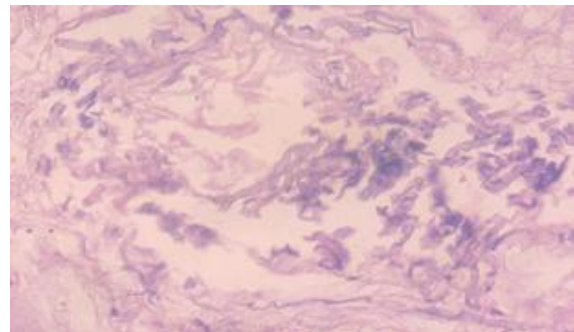
Other findings on histopathological examination were, necrosis were present in 77% cases and necrosis was graded in these cases as summarised in [Table 3].

Neutrophilic infiltration was seen in 69% cases, angioinvasion were seen in 22% cases,

granulomatous inflammation was present in 08% cases. Histological findings are shown in [Table 4].



**Figure 4: H&E staining at 10x showing angioinvasion, mucor hyphae is seen invading into the vessel.**

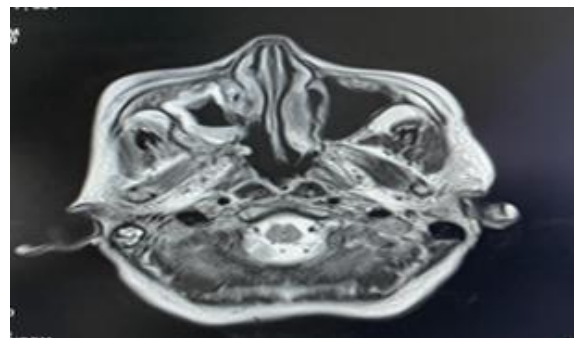


**Figure 5: P.A.S (periodic acid Schiff) staining at 40x, mucor hyphae, broad, ribbon like, aseptate hyphae with right angle branching.**

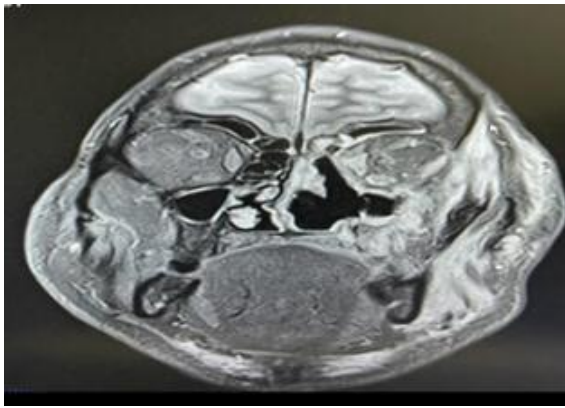
Majority of cases 46% were found to present with moderate fungal load, 30% cases showed mild fungal load while severe fungal load is seen in 24% cases. [Table 5] shows the association of necrosis with fungal hyphae load in mucormycosis cases was statistically significant based on chi-square test ( $P < 0.002359$ ). As the severity of the necrosis increases, the presence of fungal components also increases, which leads to extensive destruction of tissue.

#### **(CAM): Sinus involvement**

Radiological findings showed sinus involvement, in majority of cases most commonly involved sinus was ethmoid 78% cases followed by maxillary sinus in 74% cases followed by sphenoid in 64% cases and frontal sinus in 43% cases.



**Figure 6: T2W Axial MRI showing diffuse mucosal thickening in the right maxillary sinus along with hyperintense right pterygoid muscles suggesting edema.**

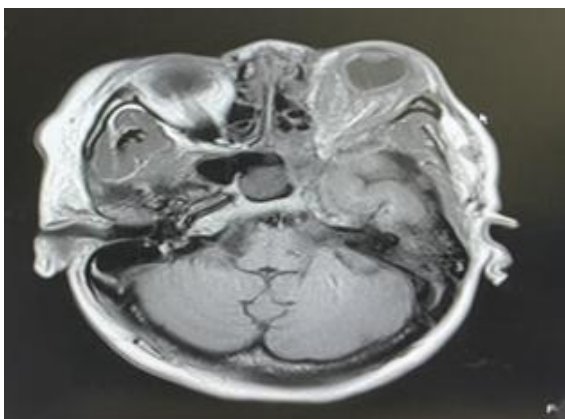


**Figure 7:** T2W coronal MRI showing mucosal thickening and enhancement in the left maxillary sinus with altered signal intensity and thickening of the perimaxillary soft tissue, infra temporal region and soft tissue of the cheek. Enlargement and heterogeneous enhancement of the left medial and inferior rectus muscle of the left orbit.

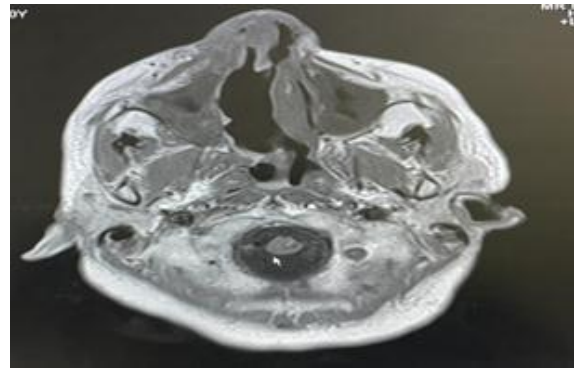
#### **CAM: Staging based on Radiological findings**

Staging of disease of COVID-19 associated mucormycosis patients based on radiological findings was done summarised in [Table 6]. Out of 100 cases, 5% cases were grouped in stage 1 they showed involvement of nasal mucosa only. 47% cases belonged to stage 2 showed involvement of paranasal sinus along with nasal mucosa. 40% cases were grouped in stage 3 showed paranasal sinus and orbital involvement. Rest 08% cases were grouped in stage 4 showed paranasal sinus, orbital and central nervous system (CNS) involvement.

Uncontrolled Diabetes which includes diabetic ketoacidosis also was statistically correlated with the radiological stages of the disease, which showed that association of uncontrolled diabetes with radiological stages of the disease was statistically significant ( $P < 0.002359$ ). Correlation based on radiological findings depicted in [Table 6]. This correlation showed that an acidotic state aids in the spread of the infection.



**Figure 8:** T1W Axial MRI showing diffuse mucosal thickening in bilateral ethmoid sinuses along with enlargement of left cavernous sinus, area of altered signal intensity in the left retroorbital fat along with soft tissue thickening in the region of orbital apex with proptosis of the left globe.



**Figure 9:** T1W Axial MRI showing diffuse mucosal thickening in bilateral maxillary sinuses along with destruction of right inferior nasal turbinate and nasal septum.

#### **CAM: History of corticosteroid use (N=100)**

History of corticosteroid use during COVID-19 treatment were present in 85% cases and 15% cases had no history of corticosteroid use.

[Table 7] shows Correlation of steroid use with radiological staging of mucormycosis cases associated with COVID-19. There was significant relationship between high dose steroid use and radiological stage of involvement of mucormycosis. The result was statistically significant in our study ( $P < 0.027636$ ), based on chi square test. Use of steroids during COVID-19 treatment exacerbate hyperglycemia and therefore, spread of infection.

## **DISCUSSION**

In present study, most patients had diabetes and history of corticosteroid therapy, with rhino-orbital mucormycosis being the most typical presentation. As the severity of the necrosis increases, the presence of fungal components also increases, which leads to extensive destruction of tissue. Therefore, early diagnosis by the study of histomorphological features of mucormycosis helps in the management.

A total of 100 cases of rhino-orbital mucormycosis associated with COVID-19 were analysed in our study.

**COVID-19 associated mucormycosis (CAM): Age group (N=100)**

Our study, showed age wise distribution of mucormycosis cases associated with COVID-19. The maximum number of cases 30% were in the age group of 51-60 years followed by 28% in age group of >60 years. This was in accordance with the study done by Gupta P Devang et al,<sup>[15]</sup> also reported that 34.3% were in the age group of >60 years, 30% in age group of 51-60 years.

**CAM: Gender (N=100)**

In our study, majority of the cases were males 67% and 37% were females. This is in accordance with the study done by Yadav H et al,<sup>[16]</sup> reported that 65.31% were males. Kumar S et al,<sup>[17]</sup> also reported similar observation that 79% were males. Chawla U

et al,<sup>[18]</sup> in their study also showed that 64.56 % were males.

#### **CAM: Socioeconomic status (N=100)**

In our study out of 100 cases ,68% cases belonged to lower socioeconomic class followed by middle class 22% and 10% were in upper class. Prakash S et al,<sup>[19]</sup> reported similar findings that 69.44% cases were belonged to lower class. Bandyopadhyay T et al,<sup>[20]</sup> also reported similar observation that 81.30% cases were belonged to lower class.

#### **CAM: Risk Factors (N=100)**

In our study, most common comorbidities/risk factors in mucormycosis associated with COVID-19 cases were diabetes mellitus in (78 %) cases, including 11% cases of diabetic ketoacidosis next commonly associated risk factor was hypertension in 12% cases. This is in accordance with the Nagalli S et al,<sup>[21]</sup> reported in their study that 77.14% of cases had diabetes mellitus, 29.5% cases had hypertension. Sahu M et al,<sup>[22]</sup> Bavishi A et al,<sup>[23]</sup> also showed the similar observations. In our study, uncontrolled diabetes and high dose steroid use was found to be predominant risk factor for mucormycosis in COVID-19 patients Yadav H et al,<sup>[16]</sup> stated in their study that, a total of 49 patients presented during the study period, with a mean age of 42.2 years. The major risk factors included uncontrolled diabetes 89.8% cases, COVID-19 positivity 51.02% cases, and concurrent steroid use 38.77% cases. The most common presenting symptom was facial pain/swelling 43.65% cases, while the most common presenting sign was deterioration in vision 75.51% cases.

#### **CAM: Duration of onset of COVID-19 to appearance mucormycosis symptom(N=100)**

In our study, majority of the cases had Duration of onset of COVID-19 to appearance of mucormycosis symptoms <1 month. Majority of mucormycosis cases, 72% were diagnosed with in one month of onset of COVID-19 infection and 28% cases were diagnosed after one month of COVID- 19 infection. Yadav H et al,<sup>[16]</sup> reported similar findings, that majority of mucormycosis cases, 72% were diagnosed with in one month of onset of COVID-19 infection.

#### **CAM: Symptoms**

In our study, the most common presenting symptom was eye pain/swelling present in 69% cases followed by facial swelling/ pain in 68% cases, visual disturbances in 52% case, headache in 48% cases, nasal discharge in 42% cases, fever in 34%, altered sensorium in 6% cases. Kamath S et al,<sup>[24]</sup> reported similar findings in their study that eye pain/swelling present in 73.3 % cases followed by facial pain/ swelling in 66.7% cases, visual disturbances in 60% cases, headache in 20% cases, nasal discharge in 33.3% cases, fever in 33.3% cases, altered sensorium in 20% cases. Nagalli S et al,<sup>[21]</sup> also reported similar findings.

#### **CAM: Signs**

In our study, the most common presenting sign was visual deterioration in 74% cases, second most

common sign was facial edema in 56% cases followed by ophthalmoplegia in 44% cases, proptosis in 36% cases, keratopathy in 28% cases, nasal/palatal eschar in 11% cases, periocular/ facial hypoesthesia in 5%, facial palsy in 3% cases. Kamath S et al,<sup>[24]</sup> reported similar findings in their study that most common presenting sign was visual deterioration in 60% cases, second most common sign was facial edema in 46.7% cases followed by proptosis in 26.75% cases, facial palsy in 6.7% cases Yadav H et al,<sup>[16]</sup> also reported similar findings.

#### **CAM: History of corticosteroid use (N=100)**

In our study, majority of cases had history of corticosteroid use during COVID-19 treatment were present in 85% cases, 15% had no history of corticosteroid use. M Anas et al,<sup>[25]</sup> reported similar findings in their study that, majority of cases 93.3% had history of corticosteroid use during COVID-19 treatment. Kumar S et al,<sup>[17]</sup> also reported in their study that, majority of cases had history of corticosteroid use during COVID 19 treatment 55%.

#### **CAM: Fungal hyphae load (N=100)**

In our study, majority of cases 46% were found to present with moderate fungal load, 30% cases showed mild fungal load while severe fungal load is seen in 24% cases. Fungal load was graded on the basis of number of microscopic fields showing fungal hyphae in 400x objective lens (High power field). It is graded as mild when hyphae were noted in <4 HPF. It is graded as moderate when hyphae were noted in 5-7 HPF and severe when fungal hyphae noted in > 8 HPF. Sree Lakshmi et al,<sup>[26]</sup> reported similar findings in their study that, majority of cases 48% cases were found to present with moderate fungal load, 27% cases showed mild fungal load while severe fungal load is seen in 25% cases. Goel A et al,<sup>[27]</sup> reported in their study that, majority of the cases, were seen with severe fungal hyphae load 63.63 % cases followed by 24.24% cases were found to present with moderate fungal load ,12.12% cases showed mild fungal load. Jain et al,<sup>[28]</sup> reported in their study that, majority of cases 68.4% were found to present with moderate fungal load, were found to present with moderate fungal load, while severe fungal load is seen in 21.0% cases, followed by 10.5% cases showed mild fungal load.

#### **Histo morphological findings in CAM**

H&E stained sections showed characteristic hyphae of mucorales which were broad, ribbon like, predominantly aseptate with right angle branching. Sections were also stained with special stain, PAS for further confirmation. Pink coloured Broad, aseptate fungal hyphae of mucor were seen. Fungal cultures were also carried out for all cases, showed growth of mucorales, produced fluffy white /grey, or brownish colonies.

#### **Other histomorphological findings.**

In our study, majority of cases, necrosis was present 77% cases followed by neutrophilic infiltration was seen 69% cases, angioinvasion was seen in 22%

cases, granulomatous inflammation were present in 08% cases. I. Sree Lakshmi et al,<sup>[26]</sup> reported similar findings in their study that, in majority of cases necrosis was present 61% cases, angioinvasion were seen in 24% cases, perineural invasion were seen in 16% cases, granulomas were present in 11% cases. This is in accordance with the study done by Goel A et al,<sup>[27]</sup>

#### **Grading of necrosis in CAM**

In our study, majority of the cases 50.6% showed moderate necrosis followed by severe necrosis in 36.4% cases followed by mild necrosis in 13% cases. Pujari D et al,<sup>[29]</sup> in their study also showed that, the cases showed mild necrosis in 53.3% followed by moderate and severe necrosis in 23.3% cases in each category. The grading was done by looking at the amount of necrosis present in 10 low power fields (lpf).

#### **CAM: Sinus involvement**

In our study, majority of the cases most commonly involved sinus was ethmoid 78% cases followed by maxillary sinus 74% cases followed by sphenoid 64% cases and frontal sinus 43% cases. Bavishi A et al,<sup>[23]</sup> also reported similar findings in their study that, in majority of cases most commonly involved sinus was ethmoid 79.2% cases followed by maxillary sinus 75% cases followed by sphenoid 66.7% cases and frontal sinus 45.8% cases. Sharma S et al,<sup>[30]</sup> reported in their study that, in majority of cases most commonly involved sinus was ethmoid 100% cases followed by maxillary sinus 52.17% cases.

#### **CAM: Staging based on Radiological findings**

Our study, showed that out of 100 cases, 5% were grouped in stage 1 they showed involvement of nasal mucosa only 47% cases belonged to stage 2 involvement of paranasal sinus along with nasal mucosa 40% cases were grouped in stage 3 paranasal sinus and orbital involvement. Rest of the cases 08% were grouped in stage 4 paranasal sinus, orbital and central nervous system (CNS) involvement. This is in accordance with the study done by Chawla U et al,<sup>[18]</sup> reported in their study that, 1.96% cases were grouped in stage 1 they showed involvement of nasal mucosa only 28.34% cases belonged to stage 2 involvement of paranasal sinus along with nasal mucosa. 56.69% cases were grouped in stage 3 paranasal sinus and orbital involvement. Rest of the cases 12.99% were grouped in stage 4 paranasal sinus, orbital and central nervous system (CNS) involvement. Yadav H et al,<sup>[16]</sup> they also reported similar observation in their study that 2.04% cases were grouped in stage 1 showed involvement of nasal mucosa only 46.94% belonged to stage 2 involvement of paranasal sinus along with nasal mucosa. 22.45% cases were grouped in stage 3 paranasal sinus and orbital involvement. Rest of the cases 28.57% were grouped in stage 4 paranasal sinus, orbital and central nervous system (CNS) involvement.

## **CONCLUSION**

Extra vigilance in immunosuppressed patients helps in reducing the morbidity and mortality due to COVID-19. A standard blanket protocol of steroid administration for COVID-19 need to be revisited and an emphasis on tight glycemic control during and after COVID-19 infection should be laid. Therefore, early diagnosis by the study of histomorphological features of mucormycosis helps in the management with suitable and aggressive antifungal medication along with surgical debridement can improve survival.

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