

## Retrospective Analysis of Prevalence of Orbital Mucormycosis in Post Covid Patients in Melmaruvathur

Venkatesan C<sup>1</sup>, Santhanalakshmi R<sup>2</sup>, Divyatharini V.<sup>3</sup>

<sup>1</sup>Associate professor, Department of Ophthalmology, MAPIMS, Melmaruvathur, Tamil Nadu, India

<sup>2</sup>Professor, Department of Ophthalmology, MAPIMS, Melmaruvathur, Tamil Nadu, India

<sup>3</sup>Junior resident, Department of Ophthalmology, MAPIMS, Melmaruvathur, Tamil Nadu, India

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Corresponding author: Dr Venkatesan C.

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### Abstract

**Background:** Coronavirus 19 pandemic had a significant impact worldwide not only on health status but also on a socioeconomic level and created a major health awareness among every individual, in addition like adding fuel to the fire co infections caused by bacterial or fungal infections have worsened the situation.

**Purpose of the Study:** The main purpose of this study is to analyse retrospectively the prevalence and various patterns of presentations of mucormycosis in post covid patients.

**Methods:** In this retrospective time bound study, we have analysed the various patterns of orbital mucormycosis in patients with covid who have been taken oxygen supplementation and steroid therapy. Their immunological status is assessed by the presence of diabetic and its influence on the outcome of mucormycosis in these patients are observed by means of ocular examination, nasal swab, radiological imaging, histopathological and microbiological analysis were done in these patients for future preparedness.

**Results:** Among the 32 patients we have assessed there is a strong association between the duration of oxygen therapy and mucormycosis (p value<0.001) According to the Phi and Cramer's V Value there is 77.8 percent association between prevalence of mucormycosis among patients Oxygen Supplementation and a strong association between dosage of steroid therapy and mucormycosis (p value<0.001) in addition those with diabetes have strong association among the covid patients and severe forms of mucormycosis is seen in these patients According to the Phi and Cramer's V Value there 56.4 percent association between prevalence of mucormycosis among patients with diabetics. Intra orbital involvement is found to be 68.75 percent and intra cranial extension in 8.65 percent. Control of blood sugar in these patients has drastically improved the outcome of mucormycosis in terms of visual outcome.

**Conclusion:** Orbital mucormycosis has been like adding fuel to the fire in this covid pandemic, as ophthalmologists it is important to take necessary preventive measures regarding this sight threatening complications due to co infection. Especially diabetics when controlled properly and cautious use of steroids and oxygen supplementation in these diabetic patients will definitely improve the visual outcome in future waves.

**Keywords:** Mucormycosis, COVID, Diabetic, Oxygen supplementation, immune status, radiological changes of mucormycosis.

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## Background

Coronavirus 19 pandemic had an significant impact worldwide not only on health status but also on a socioeconomic level and created a major health awareness among every individual, in addition like adding fuel to the fire co infections caused by bacterial or fungal infections have worsened the situation[1].

The causative agent novel severe acute respiratory syndrome virus (SARS-CoV2) exhibits a wide range of disease from a mild to life threatening pneumonia and the coexisting coinfections worsens the underlying situation and impedes the prognosis of the patient, moreover the comorbidities of the patient such as diabetes mellitus and the immune status of the patient plays a key vital role in the disease progression as well as the prognosis and outcome of the patient[2].

Mucormycosis have been a newcomer to this covid situation which have been rising in alarming levels and being a deadly epidemic in this pandemic situation. Mucormycosis where there will be hyphal invasion of the paranasal sinuses causing invasive sinusitis resulting in orbital rhinocerebral mucormycosis[3,4].

Various presenting symptoms will raise the suspicion from vague signs and symptoms to facial swelling, nasal discharge, bloody discharge, proptosis etc., are presented. Since this orbital mucormycosis is a sight threatening

condition and patients immunological status, treatment regimen followed for covid management such as steroid therapy and supplemental oxygen have an influential role on the development of mucormycosis[5] we have chosen this because as ophthalmologists we can analyse the various patterns of presentation plus the factors influencing on the prevalence of mucormycosis in the covid patient retrospectively so that we can be prepared adequately for the future waves of this deadly disease, reassure the general population to avoid unduly and unnecessary fear and prevent the sight threatening condition through adequate measures and better patient care.

## Materials and Methods

A Retrospective analytical study was conducted in the post covid patients in Department of ophthalmology, Adhiparasakthi institute of medical science and research, melmaruvathur over a period of three months from May to July 2021. All patients presented with fungal sinusitis with ocular manifestations as well as invasive orbital mucormycosis at the time of covid management either on outpatient basis or departmental referral were taken into study. All the patients have undergone steroid therapy and supplemental oxygen therapy with underlying immunological status at the time of treatment were also assessed.



**Figure 1: Shows 60 year old female with sudden onset proptosis, ptosis and congestion of right eye with loss of extraocular movements**

All the patients information, comorbid status mainly diabetic control through HBA1C levels, radiological imaging of the involved sinuses plus the orbit, microbiological isolation of the fungus through swab and histopathological analysis of the biopsy done were analysed along with effectiveness of intravenous amphotericin and diabetic control over the outcome of these patients were analysed.



**Figure 2: Shows 50 year old male with headache ,swelling of eyelids ,proptosis ,nasal discharge**



**Figure 3A and 3B: Shows severe chemosis of conjunctiva with proptosis and bloody discharge from nose**

**Statistical analysis**

Analysis of Association between Prevalence of Diabetic and Occurrence of Mucormycosis. Null Hypothesis (H<sub>0</sub>): There is no Association Between Diabetic Patients and Mucormycosis.

Alternate Hypothesis (H<sub>1</sub>): There is an Association between Diabetic Patients and Mucormycosis.

**Results**

**Table 1: Cross Tabulation of Diabetic Patients and MRI Showing Orbital Involvement**

Diabetic	MRI Showing Orbital Involvement		Total
	Yes	No	
Yes	19	3	22
No	3	7	10
Total	22	10	32

Source: Computed Using Primary Data

**Table 2: Chi-Square Tests for Association between Prevalence of mucormycosis in Diabetic Patients**

Test Statistic	Value	Df	Asymptotic Significance (2-sided)
Pearson Chi-Square	10.166	1	.001**
Continuity Correction	7.712	1	.005
Likelihood Ratio	10.007	1	.002
Fisher's Exact Test			
Linear-by-Linear Association	9.848	1	.002
N of Valid Cases	32		

Note: \*\* denotes 1 % level of Significance

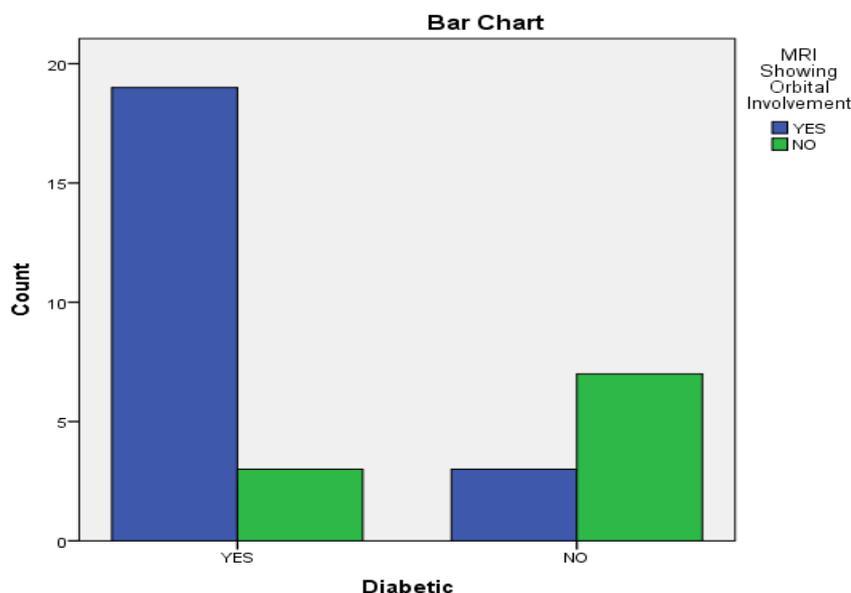
Source: Computed Using Primary Data

**Table 3: Symmetric Measures**

		Value	Approximate Significance
Nominal by Nominal	Phi	.564	.001
	Cramer's V	.564	.001
N of Valid Cases		32	

Source: Computed Using Primary Data

Based on Chi-Square value of 10.166 ( $P < 0.001$ ) the Null Hypothesis is rejected at 1% level of significance and alternate hypothesis has been accepted. According to the Phi and Cramer’s V Value their 56.4 percent association between prevalence of mucormycosis among patients with diabetics.



**Graph 1: Bar chart of Mucormycosis Prevalence of Diabetic Patients**

**Oxygen Supplementation and MRI Showing Orbital Involvement**

Null Hypothesis ( $H_0$ ): There is no Association Between Oxygen Supplementation and Prevalence of Mucormycosis.

Alternate Hypothesis ( $H_1$ ): There is an Association Between Oxygen Supplementation and Prevalence of Mucormycosis.

**Table 4: Cross tabulation of Oxygen Supplementation and MRI Showing Orbital Involvement**

Oxygen Supplementation	MRI Showing Orbital Involvement		Total
	Yes	No	
Yes	21	2	23
No	1	8	9
Total	22	10	32

Source: Computed Using Primary Data

**Table 5: Chi-Square Tests for Association between Prevalence of mucormycosis and Oxygen Supplementation**

Test Statistic	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	19.363	1	.000**
Continuity Correction	15.810	1	.000
Likelihood Ratio	19.880	1	.000
Fisher's Exact Test			
Linear-by-Linear Association	18.758	1	.000
N of Valid Cases	32		

Note: \*\* denotes 1 % level of Significance

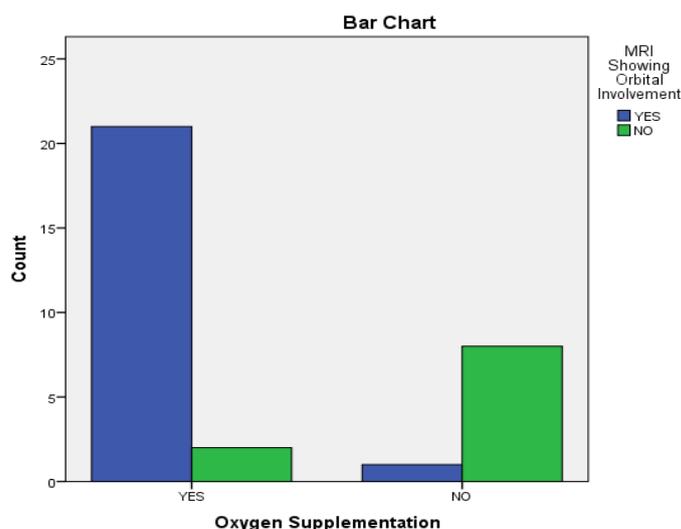
Source: Computed Using Primary Data

**Table 6: Symmetric Measures**

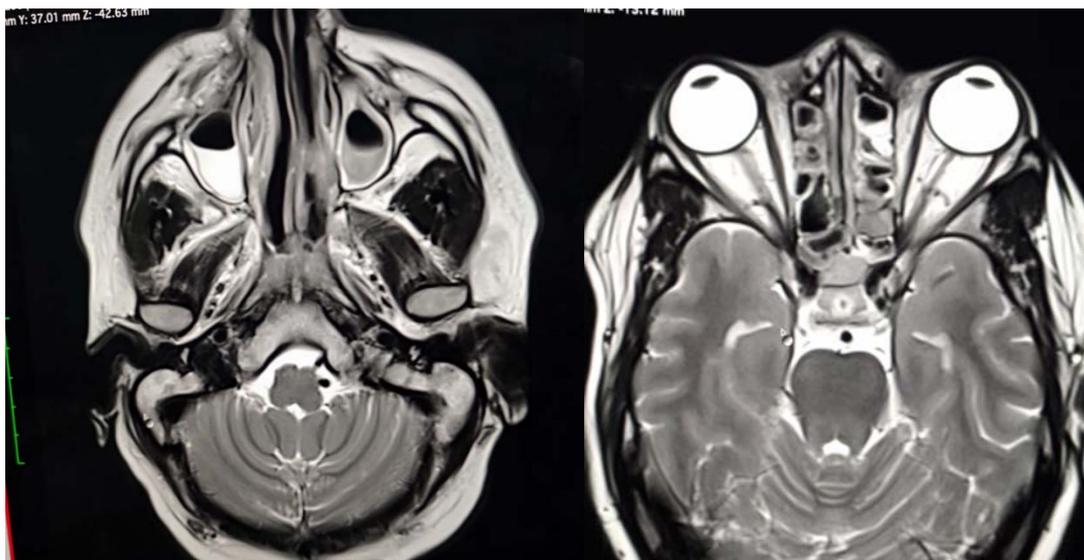
		Value	Approximate Significance
Nominal by Nominal	Phi	.778	.000
	Cramer's V	.778	.000
N of Valid Cases		32	

Source: Computed Using Primary Data

Based on Chi-Square value of 19.363 ( $P < 0.001$ ) the Null Hypothesis is rejected at 1% level of significance and alternate hypothesis has been accepted. According to the Phi and Cramer's V Value there is 77.8 percent association between prevalence of mucormycosis among patients Oxygen Supplementation.



**Graph 2: Bar chart of Prevalence of mucormycosis and Oxygen Supplementation**



**Figure 4: Shows MRI plain BRAIN of the patient note the mucosal thickening of maxillary sinuses and extra ocular muscle involvement**

A total of 32 patients presented among which 24 males and 8 females were with orbital mucormycosis and all of them have been diagnosed with coronavirus positive by RTPCR and presented with ocular symptoms of mucormycosis and sinusitis.

Out of these patients oxygen supplementation were given for all of these patients and 3 of them required intensive care management the mean duration of oxygen therapy was more than 14 days in these patients.

All of these patients were given systemic steroid therapy as a part of covid management and duration of steroid therapy was more than 10 days and as the dosage of steroid increases there is an increase in severity of the orbital mucormycosis.

Of the 32 patients, 20 of the patients have raised serum ferritin levels  $> 1000$  ng/ml and 12 of them were normal levels and all the patients were taken nasal swab and found to be positive in addition 3 of the patients biopsy was taken and sent for histopathological analysis showing evidence of invasive mucormycosis and these patients had uncontrolled diabetes Among these 22 had diabetes and 10 were non diabetic, among the 22 diabetic patients 10 were with uncontrolled

diabetes and on insulin. The diabetic patients those who were on prolonged oxygen therapy and steroid overusage with uncontrolled blood sugar has presented with more invasive and severe forms of orbital mucormycosis seen on radiological investigations for which Amphotericin B has been started and the diabetic control is achieved through insulin titrated based on their blood glucose levels.

Among the diabetic patients 12 of the patients improved symptomatically and visual outcome of orbital mucormycosis were better once the blood sugar level was strictly controlled.

### Discussion

COVID 19 pandemic have created a variety of chaos in the economy, health status and general condition of the population. In addition to this like adding fuel to the pandemic fire co infections such as rhino orbital mucormycosis has been evolved and threatening the health care officials and covid warriors in the management. A variety of clinical manifestations are presented in these patients which we see and learn day to day ranging from a simple redness of eyes, watering of eyes, nasal discharge and stuffiness to vision threatening and enucleation requiring scenarios[6].

Mucormycosis also known as phycomycosis which belongs to the family of Mucorales such as mucor, Rhizopus, abididia etc. which enter the nasal mucosa as spores through inhalation and causes fungal sinusitis but when the patients immunological status is influenced it leads to invasive sinusitis and extensive complications such as orbital extension and intracranial extension leading to morbidity and mortality[7]. It causes vascular invasion and results in thrombosis, ischemia, necrosis etc. there is a hyphal invasion of the paranasal sinuses from there it spreads to the orbit and intracranial invasion either directly or through the blood stream.

Generally, these fungal invasions are combated by our immune system especially the phagocytic leucocytes. The cell mediated immunity plays a major role in controlling the infection as soon as the fungus invades there is an active T cells proliferation and CD 4 and CD 8 cells migrate and eliminate the fungal infection. Unfortunately, the current COVID virus targets the cell mediated immunity and impairs it in a drastic manner & there is decrease in the CD ratio in these patients. The factors that influence this immune play a major role in the development of mucormycosis.

There are several forms of mucormycosis such as pulmonary mainly alveolo interstitial especially in patients who have undergone organ transplantation, gastrointestinal common among young children of premature birth and low birth weight, cutaneous after surgery or burns and finally the rhinocerebral which has been increased in the current pandemic situation and raised a lot of suspicion among ophthalmologists. The silent factor that is playing the underlying is the weakened host immune system which paves the way for the fungal invasion and in severe cases leads to disseminated forms[8]. In eye mucormycosis mainly causes a

spectrum of sympatotomy ranging from nonspecific redness of eyes, chemosis, watering of eyes, irritation discharge, limitation of extraocular movements, swelling of the eyes, proptosis, painful ophthalmoplegia associated with rhinorrhea multiple cranial neuropathies secondary to cavernous sinus involvement such as CN 3, 5, 6 and loss of vision whenever there is a focal neurological deficit indicates intracranial extension. In these patients CT revealed soft tissue thickening of the paranasal sinuses and the orbit[9].

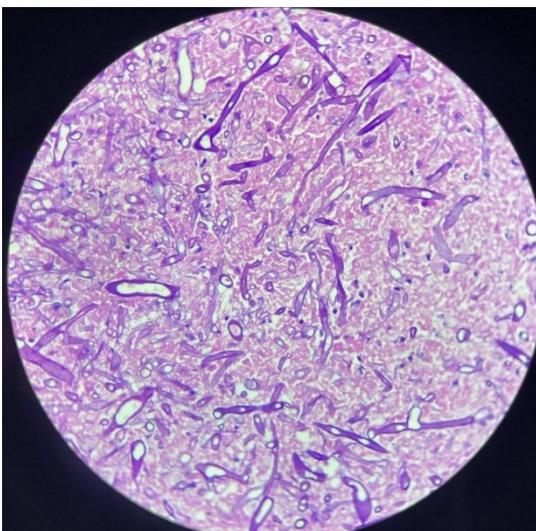
In our study the cases that have been with uncontrolled diabetes with steroid treatment for covid had developed very severe forms of mucormycosis and the prognosis have been bad, for those patients when we done a radiological imaging such as MRI T2 isointense to hypointense of tissue thickening of the paranasal sinuses earlier orbital involvement that is invasive forms has been more commonly seen. Although most of the patients showed fungal sinusitis with ethmoid being the most common sinus involved followed by maxillary and there is nonspecific thickening of the mucosa, and heterogenous post contrast enhancement has been observed. Diffusion weighed images showed increased intensity in the affected areas and restricted diffusion. Furthermore, when taken MRI brain in those patients with intracerebral extension areas of multiple infarctions, ischemia and oedema of the extraocular muscles has been noted.

We have done a nasal swab and biopsy in these patients and has sent for a KOH mount which is most commonly used for fungal isolation which showed broad aseptate hyphae with right angle branching that are ribbon like and spores. These fungal elements are more common with those with prolonged duration of oxygen supplementation in addition to immunocompromised state.

**Figure 5 A and B: Shows microbiological examination of the nasal biopsy sent for an KOH mount showed broad aseptate hyphae with right angle branching that are ribbon like and spores.**

**Figure 6: Shows the right angle branching of the fungal elements**

With histopathological examination of these specimens showed the fungal elements on eosin and hematoxylin staining showing areas of tissue necrosis, vascular invasion and neutrophilic infiltration with spores and hyphae. Periodic acid Schiff (PAS) staining was also done in these specimens showing angioinvasion[10].



**Figure 7 A and B: Shows histopathological slides of the biopsy specimen showing vascular invasion, tissue necrosis, and neutrophilic infiltration with spores and hyphae.**

In our study those patients with uncontrolled diabetes had an increased involvement of the eye and increased the morbidity, in addition the duration and dosage of steroid therapy and duration of oxygen supplementation are important influencing factors in these patients. Fatal intracranial extension is seen in those patients with uncontrolled diabetes patients, these patients were started on IV Amphotericin B were started and patient monitored and followed up periodically. Revannavar *et al* (2021) have done a case study on the orbital mucormycosis patients and have concluded that diabetic mellitus is an independent and important risk factor in the disease course and prognosis of the orbital mucormycosis patients, eventhough the orbital mucormycosis itself is debloating and sight threatening condition when its associate with diabetes especially uncontrolled diabetes such as keto acidosis the outcome of the patient is much worse and the control through medical management becomes significantly difficult. They have given radiological evidence on the presentation of mucormycosis in these diabetic patients and the effective as well as early surgical intervention benefits in these patients. In these patients when diabetes is effectively controlled the prognosis of mucormycosis was far better and judicious use of steroids and oxygen has improved the general condition of these patients

### Conclusion

Mucormycosis have been a significant threat to the current covid situation, improving one's immune status has not only improved the COVID prognosis but also the mucormycosis. Diabetics with poor glycemic control have been more vulnerable for this disease, carefull usage of steroids, oxygen supplementation, frequent changing of the oxygen masks, eye hygiene are the important precautions that we need to follow in future waves of

covid especially in these diabetes patients education and awareness regarding their blood sugar control and above measures must be followed.

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