



## CLINICAL PROFILE OF RHINO-OCULO-CEREBRAL MUCORMYCOSIS PATIENTS IN TERTIARY HEALTH CARE CENTRE.

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**ABSTRACT** **BACKGROUND-** The objective of this study was to determine the clinical profile and risk factors associated in the patients of mucormycosis. **METHODS** – It was a descriptive hospital-based study in conducted in tertiary health care for a period of 5 months Detailed history, clinical examination, laboratory investigations were documented and SION score was calculated for each patient **RESULTS** – The study group consisted of 70 male (59%) and 49(41%) female, with mean age being 55 years 80 (67%) patients were known case of diabetes mellitus patients. 99 (83%) patients had history of covid 19 infection, while history of steroid administration was seen in 36 (6%) patients. Most common presenting symptom was facial, nasal followed by orbital complains. It was observed that patient with history of steroid intake had higher SION score compared to those who did not and showed a positive correlation between steroid administration and SION score(1) with p value being 0.043. **CONCLUSION-** Uncontrolled diabetes and over use of steroids in COVID management are two main risk factors associated with post covid 19 mucormycosis. A strong suspicion based on clinical features helps in early diagnosis and treatment and therefore a better outcome.

**KEYWORDS :** Rhino-oculo-cerebral mucormycosis, covid 19, diabetes mellitus, steroids.

India tackled a furious 2nd covid 19 wave with only 3% of population vaccinated with predicted 3rd wave. [2] Under these circumstances, the country had also seen an increase in cases of rare but fatal disease, rhino-oculo-cerebral mucormycosis. Mucormycosis is an uncommon angio-invasive fungal infection caused by filamentous fungi belonging to the mucoraceae family. It is subdivided into Absidia, Rhizopus and rhizomucor(mucor)[3]. It typically affects immunocompromised individuals with an impaired neutrophilic response. Patients with uncontrolled diabetes, iatrogenic immunosuppression, acquired immunodeficiency syndrome and those undergone organ transplant are at higher risk [4]. Mucormycosis is characterised by the presence of hyphal invasion of sinus tissue and a time course of less than four weeks.[5] Clinically, ROCM can present with typical signs and symptoms similar to complicated sinusitis, such as nasal blockage, crusting, proptosis, facial pain and oedema, ptosis, chemosis, and even ophthalmoplegia, with headache and fever and various neurological signs and symptoms if intracranial extension is present.[2] A black necrotic eschar is often seen in the nasal cavity or over the hard palate region which is a classical sign, it occurs as it causes mycotic infiltration of blood vessels, vasculitis with thrombosis, tissue infarction, haemorrhage and acute neutrophilic infiltrate.[6]

Furthermore, as covid 19 is a life threatening, infectious disease, affected patients show an overexpression of inflammatory cytokines, and impaired cell mediated immunity with decreased cluster of differentiation of CD4 and CD8 T cell counts, indicating susceptibility to fungal co-infection. With the extensive and irrational use of steroids and other immunomodulating drugs such as remdesivir, tocilizumab as the mainstay in treatment of covid19, may have given rise to exponential rise in number of ROCM cases post covid 19 infection.

This study was undertaken with the aim to determine the patient demographics and population at risk, presenting symptoms and signs, the role of comorbidities and medications used to treat COVID-19. The information provided by such a study may help medical professionals to recognize the early clinical features of ROCM, have a high index of suspicion in the presence of typical symptoms and signs, appropriately triage patients with possible ROCM to confirm the diagnosis, establish staging, and initiate early protocol-based, multidisciplinary management.

### MATERIALS AND METHOD

A descriptive hospital-based study was conducted among the patients that were admitted in mucormycosis ward for a period of 5 months. IEC approval was obtained before conducting the study.

### INCLUSION CRITERIA

- A recovered Covid-19 suspect/confirmed case(recovered) who were put on steroids/remdesivir/tocilizumab/voriconazole/any other immunosuppressive drug/s and/or suffering from any immunosuppressive medical condition/s / diabetes/ malignancies /CKD/ liver disease/ HIV/AIDS etc.

- Patient having signs and symptoms suspicious of mucormycosis
- Positive 10% KOH mount for mucormycosis
- Positive radiological findings in CT/MRI
- Culture/HPE Positive findings on tissue biopsy

### EXCLUSION CRITERIA

- Patients admitted in mucormycosis ward who have been diagnosed with other pathology on DNE (Diagnostic Nasal Endoscopy).
- Patients admitted in mucormycosis ward whose MRI & CT suggest paranasal sinusitis but KOH negative for mucormycosis.
- Patients with active covid 19 symptoms and/or admission RTPCR report positive will not be taken into study.
- Patients who do not give consent for the study.

### PATIENT EVALUATION AND DATA COLLECTION

All patient provided informed consent before undergoing the study. All adult patients admitted in mucormycosis ward falling in inclusion Criteria will be included in study. Epidemiological data of all case like age, sex, systematic illness especially DM (Diabetes Mellitus), tobacco, smoking, organ transplant will be noted. Rapid antigen test and RTPCR sample will be taken and those who are positive (active) will be excluded from the study.

Detailed history regarding past history of covid 19, history regarding hospitalization/home isolation, O2 therapy, usage of immunosuppressant drugs like tocilizumab, steroids, remdesivir, favipiravir will be taken. History of use of other antifungals like voriconazole will be asked. In case of home isolation, history of over-the-counter use of drug will be asked.

Patients will be examined by Ophthalmologists, Otolaryngologist and Dental surgeon to diagnose mucormycosis. Examination by Physician will be done to rule out co-morbidities. Patients suspected of ROCM will be advised MRI orbit and PNS.

Blood investigations like FBS, PPBS, HbA1C, Serum ferritin, RFT, LFT, CBC will be done. Nasal endoscopy will be done for confirmation of ROCM and KOH and culture samples. Tissue biopsy will be sent for histopathological examination.

Findings will be recorded in detailed proforma and SION based scoring system was used to score based on fundus findings, radiological findings and ophthalmological findings.

### STATISTICAL ANALYSIS

Qualitative data like gender, morbidities, and outcome will be analysed as frequency and percentages. Quantitative data like age, laboratory values will be presented as mean and standard deviation with 95% confidence interval.

### RESULTS

In the current study, total 119 patients were studied who were

diagnosed as cases of mucormycosis clinically, radiologically or by histopathology reports.

The study group consisted of 70 male (59%) and 49(41%) female showing male preponderance, aged 27-95 years old with mean age being 55 years with SD of 15.5. It was observed that highest number of patients fall into the age group of 45-60 years.

**Table1 – age and gender distribution of 119 patients.**

DEMOGRAPHIC DATA			
		No	percentage
Age	25-34	4	3.36
	35-44	15	12.6
	45-54	28	23.52
	55-64	44	36.97
	65-74	25	21
	75-84	2	1.68
gender	Male	70	58.82
	Female	49	41.17

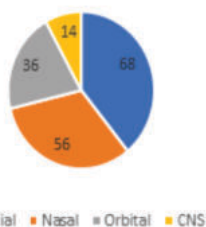
It was observed that diabetes mellitus was invariably present among the patients who presented with signs and symptoms of mucormycosis. In the present study 80 (67%) patients were known case of diabetes mellitus, out of which 52 patients had uncontrolled blood sugar levels on admission. 40 patients were hypertensive, however no significant role of hypertension has been studied in association with mucormycosis. Past history of COVID 19 infection has been a significant risk factor, which was positive in 99 patients. Irrational use of steroids as a part of treatment in Covid19 infection has been an important risk factor in causation of mucormycosis. In the present study, 36 patients had positive history of steroid administration orally or Intravenous. Total 36 (30%) patients required oxygen support, with 8 patients requiring BIPAP support and 28(23.5%) requiring nasal cannula or venturi mask.

**Table 2 – Risk factors**

RISK FACTORS(N=119)			
	Present		%
Comorbidities	DM	80	67.22
	HTN	40	33.61
	DM + HTN	38	31.93
	DM + HTN + CKD	2	1.68
Steroids		36	30.2
COVID 19		99	83.19
Oxygen requirement	Bipap	8	6.7%
	venturi mask	28	23.5%

The most common presenting sign or symptom in the study group was facial(57%) which included facial pain, swelling, numbness which is most commonly seen with sinusitis, as in mucormycosis 1st to be involved are the paranasal sinuses, followed by nasal complains(47%) like discharge, congestion, blockage followed by ophthalmic complains(30%) which was decreased vision, orbital pain, watering, chemosis or ophthalmoplegia whereas CNS complains included headache and altered consciousness which is usually seen when there is intracranial spread which was the least common presenting symptom. In the present study group, only 1 patient had oral complain of loosening of teeth.

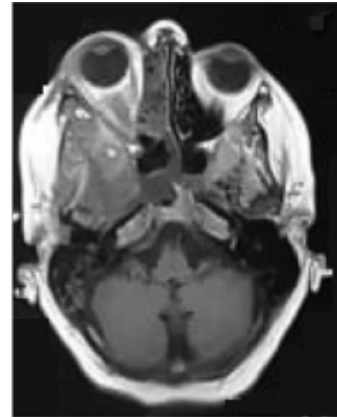
**Symptoms**



**Chart 1- Distribution of symptoms**

All the patients had neutrophilic leucocytosis in the complete blood picture with elevated ESR. The mean ESR in this study was 68. The mean HbA1c levels were 11.8. All the patients had undergone Computed Tomography and Magnetic resonance imaging, in which 14

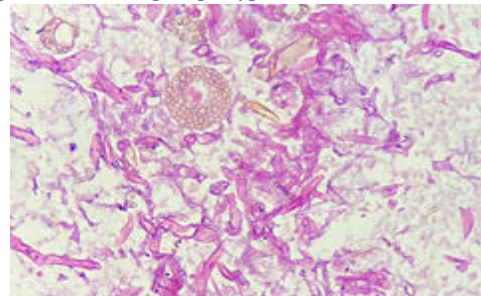
patients showed intracranial involvement which was in the form of meningeal enhancement, cavernous sinus thrombosis. 36 patients showed orbital involvement in the form of extraocular muscle involvement, intra-orbital fat involvement, orbital wall erosion, optic nerve compression. Rest 68 patients had mucosal thickening with sinus wall erosion suggesting of complicated fungal sinusitis.



**Image 1 – CT scan showing intraorbital extension**

All the patients had undergone diagnostic nasal endoscopy (DNE) and 42 patients had black eschar as a finding over hard palate or black necrotic material over nasal mucosa. All the patients who underwent DNE, samples were sent for KOH. Broad non septate hyphae resembling mucor were seen on KOH smears in 58 patients and Histopathology showed invasive mucormycosis in 42 patients, all of them showing rhizoids and collapsed columellae compatible with Rhizopus species. Mixed fungal infection was seen in 4 patients (aspergillosis and mucormycosis).

**Image 2- HPE showing fungal hyphae**



**SION SCORE<sup>11</sup>:-**

The scoring system is based on 3 main criteria, namely: (1) clinical signs and symptoms. (2) Direct and Indirect Ophthalmoscopy. (3) Imaging. The Sion Hospital Scoring System is an accurate and promising measure to solve the dilemma that is associated with orbital exenteration in rhino-oculo-cerebral mucormycosis. Based on observation, patients who had score of 23 or more were eligible candidates for orbital exenteration.

Statistical Analysis: Normality of Sion Orbital score has been checked using the Kolmogorov-smirnov test. Sion Orbital score don't follow the normality so, nonparametric Mann -whitney nonparametric test applied to know the significance of score.

Use of Steroid	N	Mean Rank of Score	MEDIAN (IQR) Score	P- value
No	83	55.92	5(5-12)	0.043
Yes	36	69.42	8(5-15.25)	
Total	119			

Patients with past history of steroid intake had higher SION score, p value of 0.043 showed significant correlation between the two.

All the patients who were clinically diagnosed as mucormycosis were treated with amphotericin b and broad-spectrum antibiotics according to standard guidelines<sup>(7)</sup>.

**DISCUSSION**

Mucormycosis is an opportunistic, fatal infection with low incidence rate of 0.005 to 1.7 per million population, which has suddenly increased with the ongoing covid 19 pandemic<sup>(8)</sup> Patients with history

of Covid 19 infection are more susceptible to mucor infection as these patients have ideal environment to help the spores germinate which are low oxygen levels, high blood sugar levels (recently diagnosed DM, steroid induced) , acidic media (metabolic acidosis , DKA), high ferritin levels and immunosuppression (SARS-CoV-2 mediated, steroid-mediated)and other comorbidities like CKD .

In the present study, the mean age was 55 years, comparable to study by Rajoor UG et al which is 50 years (9). Usually, mucormycosis has no predilection for a particular gender, in present study males were affected more than females which is similar to be found in study by Talmi et al (10).

Uncontrolled DM (67.2%) was the most common underlying risk factor found to associated with mucormycosis in the present study similar to study by Rajoor UG et al (9).

History of COVID 19 was seen in 99(83%), which makes mucormycosis a post covid sequelae which was evident in many other studies by song et al (11) and white et al (12).

Orbital and nasal findings are the most common presenting clinical features in the present study, which was also observed in study by S.K Gupta (13).

History of steroid intake was found in 36 patients (30%) in the present study, while the study by Anas M et al (14) showed that 93.3% patients and a study by John TM et al (15) had history of steroid intake who were diagnosed with mucormycosis.

In the present study, SION score[1] was calculated for each patient and it had positive correlation with steroid intake with p value being 0.043

## CONCLUSION

We are learning more about the new and long-term manifestations of the Covid-19 infection. Its association with invasive mucormycosis is dangerous and must be given serious consideration.

mUncontrolled diabetes and over-zealous use of steroids are two of the main factors aggravating the illness, and both of these must be properly checked.

- If detected, early surgical intervention and intravenous anti-fungal treatment should be sought for management, as a good prognosis and less fulminant disease course can be achieved in cases of post-coronavirus mucormycosis.

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