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Original article

A PROSPECTIVE OBSERVATIONAL CASE SERIES OF OPHTHALMIC MANIFESTATIONS AND TREATMENT MODALITY OF RHINO-OCULO-CEREBRAL MUCORMYCOSIS DURING SECOND WAVE OF COVID PANDEMIC IN A TERTIARY CARE HOSPITAL.

Sujata Padhy, Suchitra Dash, Deepika Priyadarshini, Prativa Behera*

Department of Ophthalmology, MKCG Medical College and Hospital, Odisha, Berhampur, India.

Abstract

Aim:

During the second wave of the COVID-19 pandemic in India, there has been a significant increase in the prevalence of COVID-19-associated rhino-orbital-cerebral mucormycosis (ROCM). In this investigation, the primary objective was to ascertain the ocular manifestations, risk factors encompassing comorbidities, and pharmacological interventions employed in the management of COVID-19.

Methodology:

This study presents a prospective, observational case series examining patients diagnosed with COVID-19-associated rhino-orbital-cerebral mucormycosis (ROCM) who exhibited ocular manifestations. The patients included in this study were seen at the eye outpatient department, admitted to the ear, nose, and throat department, and receiving treatment for COVID-19 at a designated COVID hospital. The study was conducted for a duration of three months, from 1st May 2021 to 30th August 2021, at MKCG Medical College and Hospital in Berhampur.

Results:

The majority of cases developed ROCM symptoms between day 10 and day 15 after COVID-19 diagnosis, with 56% developing within 14 days and 44% developing beyond 14 days. Orbital involvement, with stage 3c, comprising the majority (27%) of the total. 73% received intravenous amphotericin B, 56% underwent pa: ranasal sinus (PNS) debridement/ functional endoscopic sinus surgery (FESS), 3% received both orbital exenteration and PNS/ FESS debridement, and 15% underwent orbital exenteration. Intraorbital amphotericin B injections were administered in 22% of cases. The final follow-up revealed a 14% mortality rate.

Conclusion:

Diabetes mellitus and corticosteroids are the most significant risk factors for COVID-19-associated ROCM development. COVID-19 patients must be followed even after recovery. Successful outcome requires a high index of clinical suspicion, awareness of red flag signs and symptoms, speedy diagnosis, and early treatment initiation with amphotericin B, orbital exenteration when indicated and aggressive surgical debridement of the PNS.

Recommendation:

In case of COVID-19 patients who are suffering from diabetes mellitus and are treated with corticosteroid, physicians should be vigilant and monitor patient carefully for the occurrence of rhino-orbital-cerebral mucormycosis.

Keywords: Ophthalmic Manifestations, Treatment Modality Of Rhino-Oculo-Cerebral Mucormycosis, Second Wave Of Covid Pandemic, Tertiary Care Hospital., Submitted: 2023-08-29, Accepted: 2023-09-08

1. Introduction:

Infections caused by Mucoraceae fungi are highly contagious and often fatal. The fungus species Rhizopus oryzae causes Rhinocerebral Orbital Cerebral Mucormycosis (ROCM) [1]. The rapidly spreading, aseptate filamentous fungus causes 90% of rhinocerebral cases and has a death rate above 50%. ROCM is thought to start with nasal mucosa and sinuses colonisation and move to surrounding regions including the orbit. This can cause bone erosion in the orbital apex and extraocular muscles [2, 3]. Extreme cases may involve intracranial spread. Initial clinical suspicion, computational tomography (CT) of the paranasal sinus, brain and orbit, and potassium hydroxide (KOH) mount/calcofluor white stain microbiology establish the diagnosis. The first investigation is followed by a definitive one. For intracranial spread, contrast-enhanced CT or gadolinium-enhanced MRI is the final test. Further diagnosis may be confirmed by microbiological culture or biopsy [4].

Mucormycosis, like most fungal illnesses, is spread by inhaling fungal spores. Its propensity for angiogenesis and rapid development are the main causes of its proliferation and progression. It is rare in immunocompetent people but common in diabetics and immunosuppressed people [5, 6]. Infiltration of large blood arteries causes ischemia, necrosis, and infarction of nearby tissues. A few case reports of COVID-19-associated Rash-Oral Cavity Mucosal lesions (ROCM) were published early in the pandemic.

The first case was in February 2021 in India. The second wave of the COVID-19 epidemic has caused a sharp increase in cases in India. The treatment of IV liposomal Amphotericin B empirically and surgical debridement of the nasal cavity and paranasal sinuses has become standard during the COVID-19 pandemic [7]. This treatment reduces infective tissue and improves antifungal agent penetration to improve survival after mucormycosis diagnosis. Posaconazole may be used if amphotericin B is ineffective or intolerable. Intraorbital amphotericin B injection has been tried to increase bioavailability with mixed results. Despite the abundance of treatment options, the prognosis is poor, especially in India, where COVID-19-related mortality rates range from 33.3% to 80%. This caused widespread alarm, known as the "Black Fungus epidemic" [8]. This study examined COVID-19's ocular manifestations, risk factors, comorbidities, drugs, symptoms, and management outcomes.

2. Methods:

We conducted a prospective, observational study on rhino-orbital-cerebral mucormycosis (ROCM) patients who reported with ocular symptoms in the ophthalmology outpatient department. These patients were admitted to the ear, nose, and throat department for COVID-19 therapy in a COVID hospital. COVID-19 infection was also present or past. The study was undertaken at MKCG Medical College and Hospital in Berhampur from May 1 to August 30, 2021.

The reverse transcription polymerase chain reaction (RT-PCR) test on nasopharynx or oropharynx samples, CT chest scores or rapid antigen testing in cases where a positive RT-PCR test was not found in a patient with COVID- 19 clinical symptoms. A patient with recently controlled or concurrent ROCM and COVID-19 clinical manifestations and symptoms was investigated for ROCM. If CT scans, contrast-enhanced MRI, or diagnostic nasal endoscopy supported clinical symptoms, rhinocerebral mucormycosis (ROCM) was suspected. The notion of ROCM is based on clinical, radiographic, and microbiological evidence. This comprises direct microscopy, culture, histopathology with specific stains, or molecular diagnostics to confirm bacteria. Non-mucor fungal infections and non-COVID-19-associated ROCM were excluded from the study. The recovery from COVID-19 was determined by a negative reverse transcription polymerase chain reaction (RT-PCR) test or a 14-day delay from diagnosis.

* Corresponding author.
Email address: Prativabehera9556@gmail.com (Prativa Behera)

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3. Results:

Out of 30 patients, 16.7% were females and 83.3% were males. 64% patients were between age of 40-55 years.

3.1. COVID-19-associated ROCM risk factors:

Oral, intravenous, or both systemic corticosteroids were given to 84% of individuals, while 16% did not. Corticosteroids were given intravenously to 76% of patients, with 57% receiv- ing methylprednisolone and 43% dexamethasone. The most often used corticosteroids had a median duration of six days. For a median of eight days, 68% of individuals received oral corticosteroids. The patient cohort got oral corticosteroids only in 32% of cases and intravenous in the rest. Corticosteroids are a major risk factor, increasing with COVID-19 severity.The study indicated that 83.3% of patients needed prongs or masks to get oxygen. Diabetes Mellitus (DM) was found in 88% of patients and hypertension in 75%. Additionally, 33.33% of individuals had both diabetes and hypertension.

3.2. Clinical presentation of COVID-19-associated ROCM:

3.2.1. Signs of ROCM:

Periocular/facial edoema is 37%, visual loss 25%, ptosis 10%, proptosis 19%, and nasal discharge 11%. Clinical manifestations included eschar formation or nasal ulceration, diplopia or ocular motility impairment, facial or periocular discoloration, reduced periocular sensitivity, oral or palatal ulceration or eschar formation, facial paralysis, and cognitive function changes. Visual impairment, periorbital or face edoema, drooping eyelids, and eyeball protrusion were the main symptoms.

3.2.2. Symptoms of ROCM:

25% of instances have orbital/facial edoema, whereas 35% have periocular pain. Ptosis affects 10% of patients and vision loss 20%. Nasal block affects 11% of people. The patient also had proptosis, nasal discharge, diplopia, cephalalgia, orbital and facial erythema, odontalgia, dental mobility, epistaxis, and facial asymmetry.

3.3. COVID-19-associated ROCM diagnosis:

Diagnostic nasal endoscopy was performedin 68% patients. A complete nasal swab and specimens were taken during sinus debridement. Microbiological evidence was acquired using direct microscopy with calcofluor white and KOH staining. CT and MRI scans were done.

3.4. Management:

The preferred medicinal care was amphotericin B treatment in 61% of patients. Additionally, 20% of patients had primary FESS/PNS debridement. Patients received intravenous amphotericin B for an average of 10 days in 45%. Amphotericin B and posaconazole were prescribed to 25% of study subjects (Table 2). Orbital exenteration was performed in 3% of cases and intraorbital amphotericin B injection in 10%.

3.5. Outcome Of Management:

The majority of patients recovered. A 20% death rate was recorded among DCH patients. Orbital exenteration was performed in 3% of instances and intraorbital amphotericin B injection in 10% (Table 3). Approximately 70% of cases preserve the eye.

4. Discussion:

The elderly had the highest incidence. Due to viral immunosuppression and therapeutic corticosteroids, COVID-19 creates a hypoxic environment with increased ferritin, leukocyte phagocytic activity and glucose. Unsanitary behaviours, prolonged hospitalisation with the risk of hospital-acquired infections, immunosuppressive agents like tocilizumab, and concurrent medical conditions are other risk factors for COVID-19-associated secondary fungal infections in critically ill patients. MRI is best for detecting tissue necrosis and bone erosions. A potassium hydroxide

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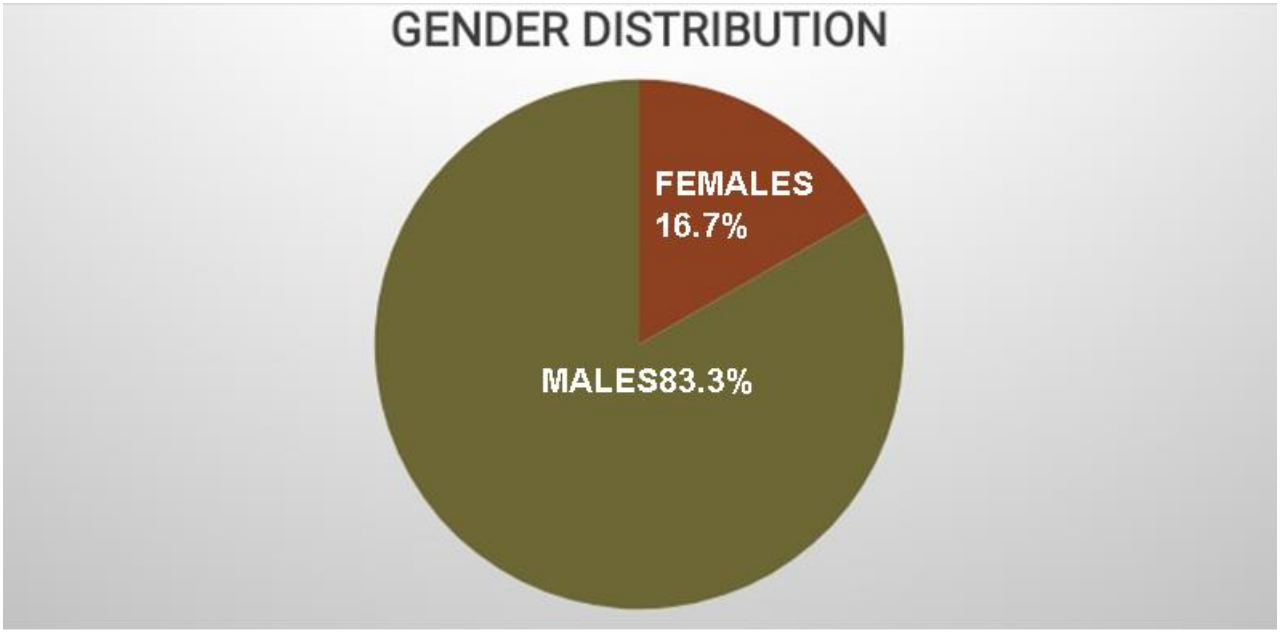

Figure 1: **Gender Distribution**

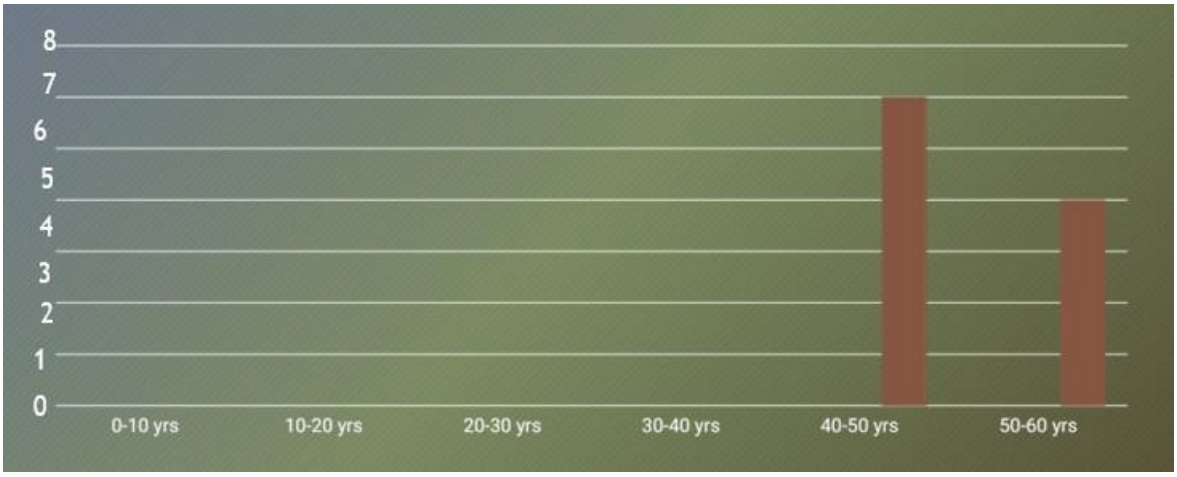

Figure 2: **: Age Distribution**

Table 1: **Risk Factors of ROCM**

Features	Number of patients	Percentage
Corticosteroids	12	100
Oxygen masks	10	83.3
Hypertension	09	75
Diabetes	08	58.35
Both diabetes and hypertension	03	33.3

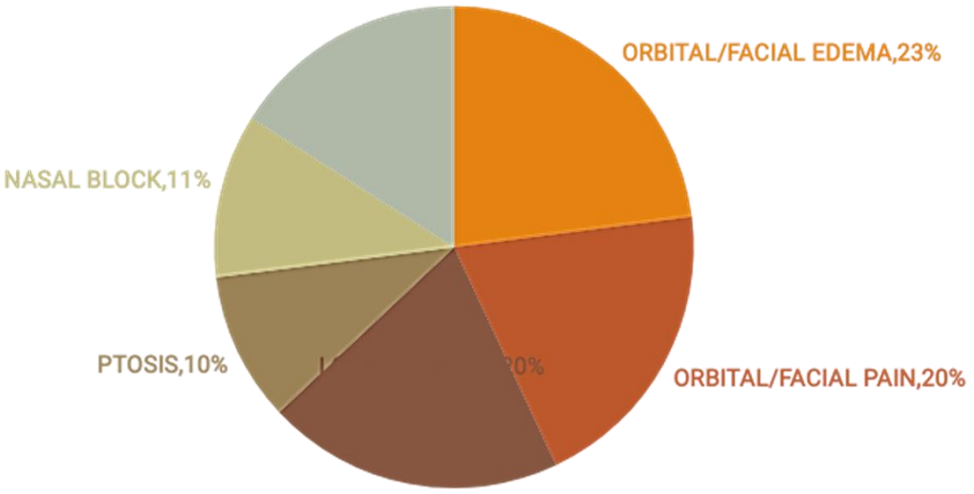

Figure 3: Signs of ROCM

Figure 4: **Loss of vision, redness, chemosis, Restriction of extraocular muscle movement, PL negative, Pupil mid-dilated & not reacting to light (RE)**

Table 2: **Management**

Treatment	Frequency
IV Amphotericin-B	4
IV Amphotericin-B + Posaconazole	3
Oral Posaconazole	3
Retrobulbar Amphotericin-B Injection	1
Exenteration	1

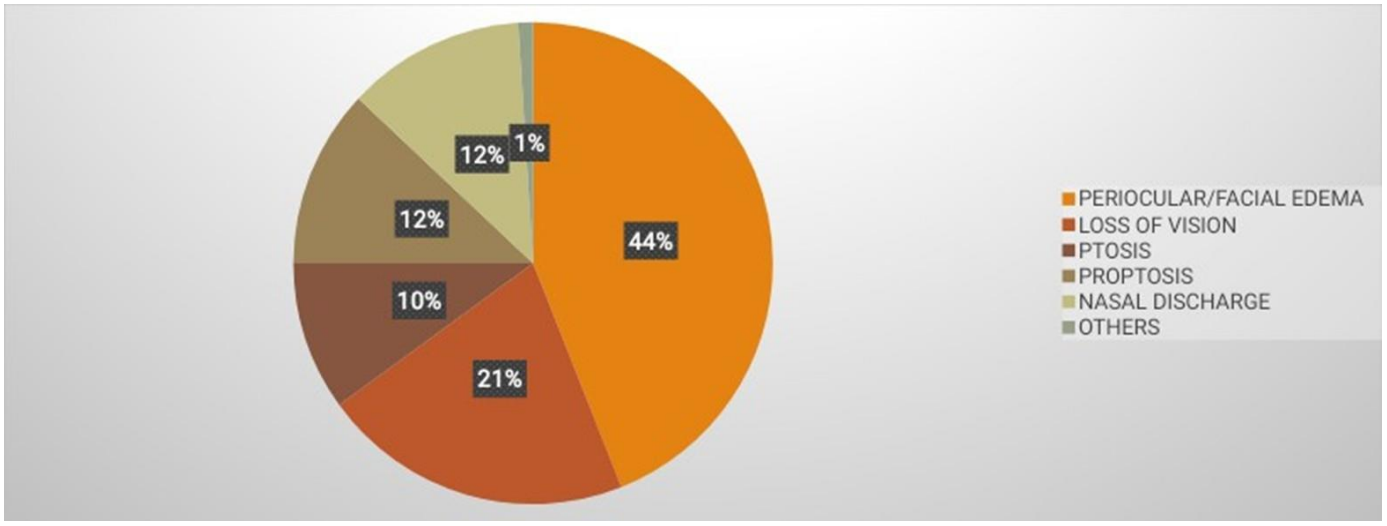

Figure 5: **Symptoms of ROCM**

Figure 6: **Sudden onset complete loss of vision, redness, Restriction of extra-ocular muscle movement, PL negative, Pupil mid-dilated & not reacting to light (both eyes) with Ptosis of 3mm (LE)**

Table 3: **Outcomes**

Features	Frequency
Orbital Exenteration	1
Eye Salvage	6
Death	5

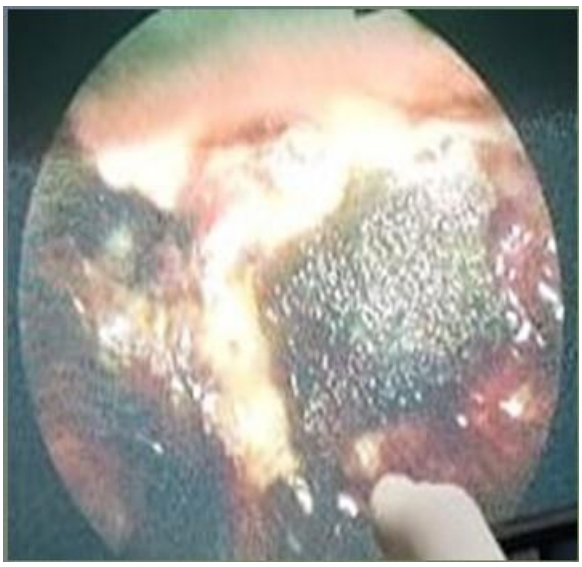

Figure 7: **Nasal endoscopy picture showing nasal mucosal involvement**

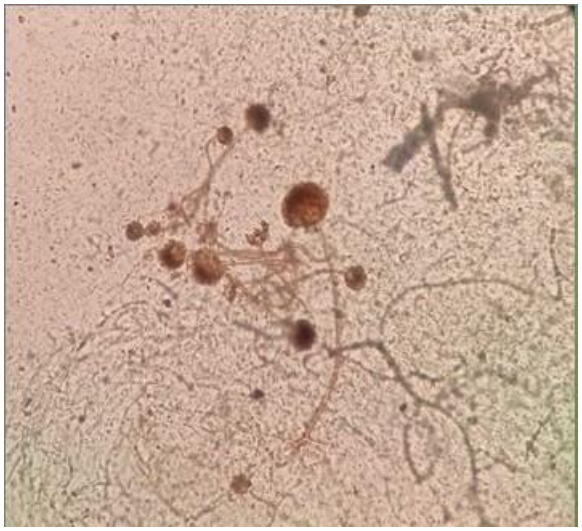

Figure 8: **KOH Mount showing broad aseptate obtuse angle branching hyphae (Ribbon-like appearance)**

(KOH) mount, diagnostic nasal endoscopy, and nasal cavity samples can quickly diagnose mucormycosis [9, 10]. Rhino-Oculo-Cerebral Mucormycosis is managed by controlling glycemic variables and other risk factors. This involves administering adequate antifungal drugs and performing optimal surgical debridement to treat the afflicted area.

5. Conclusion:

Invasive rhino-orbital-cerebral mucormycosis is life-threatening and requires a multidisciplinary approach. Ophthalmoplegia, proptosis, and reduced visual acuity were our main clinical findings. In a considerable number of cases, timely surgical surgery and systemic antifungal drugs can preserve visual acuity. In COVID-19-related mucormycosis, timely detection, careful glycemic management, rapid systemic antifungal treatment, and sinus debridement surgery save lives.

6. Limitation:

This case series considers a small size of patients as COVID-19 is a pandemic that has affected the people all around the world a more inclusive study

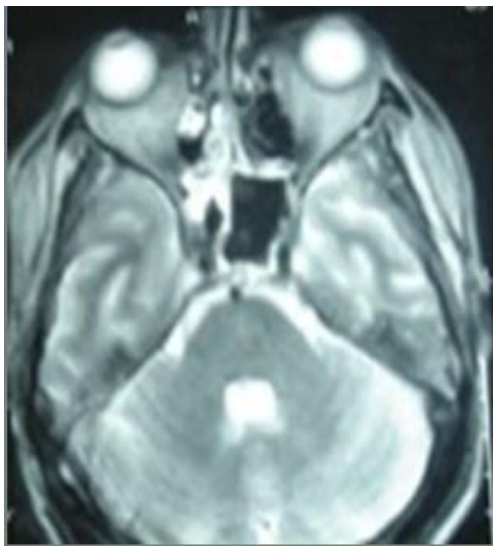

Figure 9: **Axial MRI of the orbit, paranasal sinuses, and brain showing involvement of medial orbit and abnormal fat intensity along with involvement of ethmoid sinus (LE)**

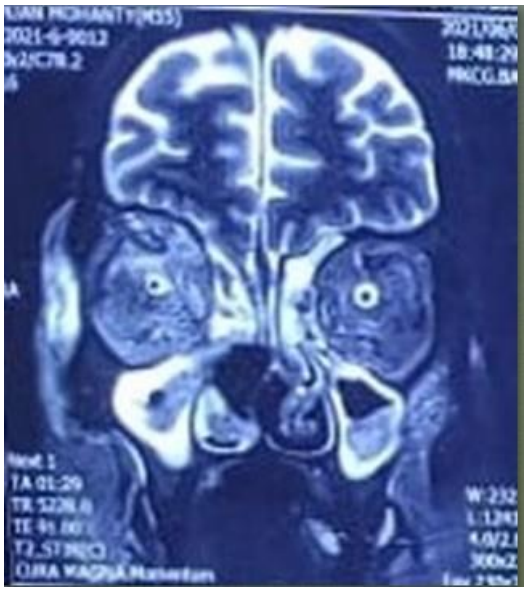

Figure 10: **Coronal MRI of the orbit and paranasal sinuses showing polypoidal mucosal thickening in maxillary sinus, ethmoid sinus and nasal cavity (RE)**

is required belonging to different ethnicity and race.

7. Recommendation:

In case of COVID-19 patients who are suffering from diabetes mellitus and are treated with corticosteroid, physicians should be vigilant and monitor patient carefully for the occurrence of rhino-orbital-cerebral mucormycosis.

8. List of abbreviation:

ROCM- rhino-orbital-cerebral mucormycosis

FESS- Functional Endoscopic Sinus Surgery

CT- Computational Tomography

RTPCR- Reverse Transcription Polymerase Chain Reaction

DM- Diabetes Mellitus

9. Acknowledgement:

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10. Conflict of interest:

None

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Author biography

Sujata Padhy Assistant Professor, Department of Ophthalmology, MKCG Medical College and Hospital, Berhampur, Odisha, India

Suchitra Dash Professor, Department of Ophthalmology, MKCG Medical College and Hospital, Berhampur, Odisha, India

Deepika Priyadarshini Senior Resident, Department of Ophthalmology, MKCG Medical College and Hospital, Berhampur, Odisha, India

Prativa Behera Junior Resident, Department of Ophthalmology, MKCG Medical College and Hospital, Berhampur, Odisha, India