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RESEARCH ARTICLE

OCULAR MUCORMYCOSIS MAY NEED A MULTI-PRONGED APPROACH ON A WAR PATH - AN OBSERVATIONAL STUDY

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Abstract

Mucor mycosis is a rare, fatal fungal infection caused by the species Rhizopus of family Mucoraceae. It has been on rise since the advent of COVID-19 pandemic due to a plethora of reasons. Ours is an observational study of ten cases of Rhino-orbito-cerebral form of mucor mycosis (ROCM) with an intention to spread awareness regarding the significant implications of ROCM. Early diagnosis and prompt treatment is the need of the hour with a multi-pronged approach with an ultimate goal of salvaging the lives. Always, clinicians should have a high suspicion of involvement of the central nervous system especially in cases with orbital involvement.

Introduction:-

Mucor mycosis is a fatal fungal infection caused by the Mucoralesfungi. Its was a rare entity in the pre-covid era with aworldwide prevalence of0.005–1.7 per million population but now has become an epidemic causing an alarming spikein India.[1,2]Mucorinfection is usually noticed in patients with uncontrolled diabetics, chronic renal failure, patients on immune-suppression. COVID-19 infection provided acongenial environment for Mucorales growth secondary to immune-suppression, hyperglycemia, hypoxia, acidic medium, high ferritin levels, neutropenia.[3]Orbital involvement is critical indicator of an impending life-threatening cerebral involvement.[4] Hence, all cases with orbital involvement need special care.

Materialsandmethods:-

After taking the approval from the institutional ethic committee, we started this observational study comprising ten patients admitted to our hospital during the period June 2021 to November 2021. The patients presented either during covid-19 infection or after getting cured, with conjunctival congestion, chemosis, peri-orbital or facial pain and swelling, restriction of eye movements, eye discharge, ptosis and diminished vision. [Figures 1,2] Informed consent was taken from all the patients. The patients were thoroughly investigated to rule out non-Mucor orbital cellulitis. Imaging studies like contrast enhanced CT and MRI scans of orbit and brain were done and microscopy was done from the swabs collected from eye discharge or during diagnostic nasal endoscopy. [Figure 2(b)]

All the patients were examined under slit-lamp bio-microscopy for anterior segment evaluation. Fundus examination was done using slit lamp and 78-D lens. A multi-disciplinary approach was followed by involving ENT surgeons, neurosurgeons, dermatologists and general physicians as per the requirement and their findings are noted.

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Progression of the disease, treatment protocols and patient response to treatment were closely followed. The chosen treatment modes were pharmacotherapy – intravenous or transcutaneous retrobulbar Amphotericin-B, intravenous or oral posaconazole, surgical – functional endoscopic sinus surgery (FESS), exenteration surgery or abscess drainage. More than one of these treatments were chosen on a patient specific basis based on the site, extent of infection and the clinical severity of the disease. [Figure 3]

Results:-

A total of ten patients were included as the part of the study. The mean age of presentation with the symptoms of ROCMwas 51 years. Three of them were females and seven were males.[Figure4]The age distribution across the study group was depicted in Table -1. There were two patients with age less than 40y, three between ages 41-50y, two between 51-60y and three in above 60yr age group.

The risk factors associated with the patients affected by ROCM included diabetes (80%), hypertension (40%), steroid usage (80%) and oxygen supplementation during covid-19 infection (60%), diabetic ketoacidosis (DKA) and chronic kidney disease (CKD) each in 20% of the study group. [Figure 5] Among the clinical signs observed, the most common is total ophthalmoplegia (70%) followed by ptosis and proptosis with lid edema (60% each), defective vision without perception of light (40%), cherry red spots on fundus (30%), endophthalmitis (20%) and the least common is melted cornea in 10% of the study group. [Figure 6]

All the patients studied were affected by ROCM after 10 days of diagnosis of covid-19 infection. Half of them (five patients) were affected between 10-20 days, four patients between 20-30 days and one patient was affected after 1 month from covid-19 infection. [Table 2]

All of the patients underwent FESS on either side at least once during the entire clinical course. One of them needed twice. Six of the ten patients studied needed the exenteration surgery as a life saving treatment modality in spite of initial anti-fungal pharmacotherapy. One patient had a recurrence in the contralateral eye after exenteration. Two patients recovered after transcutaneous retrobulbar injections (TRAMB). Two patients had temporal lobe abscess, one male and one female. One of them recovered with abscess drainage and exenteration and the other passed away despite drainage of the abscess. [Table 3]

Discussion:-

The consequences COVID-19 pandemichad a life changing impact on the community at large. Several problems arose either owing to lack of previous evidence on the protocols to tackle the novel health related complications or to lack of experience of managing certain situations that resultedfrom the health crisis. The clinicians faced an uphill task of creating awareness among the people against misconceptions spread across various platforms regarding the treatment protocols of COVID-19 infection. One such consequence is the secondary infection like Mucor mycosis, which was otherwise rare opportunistic infection in the immune-compromised. It is a lethal angio-invasive fungal infection with involvement of nose, nasal sinuses, orbit and brain in two-thirds of those affected.[5,6] The viral infection, immunosuppressive medications and the co-morbidities like diabetes, hypertension, renal disease etc acted in tandem to create a brooding ground for the fungal infections – candidiasis, aspergillosis and mucor mycosis. Lack of awareness of the fungal infections in the people often caused delayed presentation to the health care centers and dire consequences.

COVID-19 associated ROCM is multifactorial. Pre-existing comorbidities, viral infection associated changes in internal milieu and immunosuppression secondary to steroid usage are all the culprits along with the tropical climate of India.[7,8] Males have higher risk of infection due to greater outdoor exposure. Even in our study, the males are more in number than females (7:3). The mean duration of ROCM after COVID-19 diagnosis in our patients was almost 2 weeks. This is in agreement with the literatureavailable. The most common associated risk factors in our study were diabetes and corticosteroid use during COVID-19 infection (80%) followed by oxygen supplementation during their treatment which could be the possible nosocomial source of spreading the fungal spores. Endogenous infection could be the source in those patients who didn't have these common associated risk factors nor admitted in hospital ruling out the possible nosocomial spread.[9]

Clinical suspicion of ROCM based on certain presenting complaints like restriction of eye movements, orbital/facial pain, periocular/facial edema, ptosis, nasal discharge, loss of vision etc especially after recovery from COVID-19

infection helps in early diagnosis and prompt treatment to save the lives of the individuals. CNS involvement was reported to be seen in 37% of the cases of COVID-19 associated ROCM.[9] Hence, there is no reason to delay further evaluation to find out the extent of the infection and initiate necessary treatment. It has to be done with a high level of suspicion and needs a multi-disciplinary approach involving ophthalmologists, ENT surgeons, neurosurgeons and general physicians. The management involves prompt initiation of anti-fungal pharmacotherapy – Amphotericin -B (the drug of choice), posaconazole; surgical debridement of PNS/ exenteration in cases of orbital involvement/ abscess drainage and cerebral decompression along with optimisation of the general condition of the patient by proper glycemic control, steroid tapering, management of hypertension, CKD and other associated co-morbidities strictly monitoring drug dosage and combinations to avoid adverse effects on the patients. In our series, all the patients received pharmacotherapy – Amphotericin B was given intravenous and/or retrobulbar and posaconazole was only given during the non-availability of the former. Salvage of vision wasn't the deciding factor of aggressiveness in surgical intervention due to high mortality rates.[3] Surgery had better outcome than medical management in ROCM without CNS involvement. However, surgery didn't have impact on the survival of the patient with CNS involvement.[9,10]Even our study infers the similar prognostic opinion on management modalities. Two patients with CNS involvement had severe disease and one of them succumbed to the infection in spite of all possible surgical interventions. This indicated the seriousness of the involvement of brain, the need for prompt diagnosis and initiating early treatment.

Conclusion:-

ROCM associated with COVID-19 infection should be dealt with on an emergency protocol owing to the lack of awareness among the public, late presentation and very high mortality associated with the fungal infection. Salvage of vision is secondary to salvage of life. A multi-disciplinary approach has to be taken up on a war path to save the life of the patient. Removing the foci of infection while optimising the general condition of the patient should be goal of management.

Figures

Figure 1: Clinical presentation of Ocular mucor mycosis with 1(a) periorbital swelling, ptosis and 1(b) restricted eye movements.

Figure 2: 2(a) Clinical presentation of Ocular mucor mycosis with eye discharge. 2(b) Microscopic photograph of the fungal hyphae isolated from the swab taken from the eye discharge.

Figure 3: Exenteration - 3(a) Intra-operative and 3(b) post-operative images of exenteration performed in a patient affected by ROCM. 3(c) Before TRAMB injection and 3(d) Recovery after TRAMB injection.

Figure 4: Sex distribution in the study – Out of ten patients, seven were males and three were females.

Figure 5: Risk factors associated with the patients affected by ROCM in the study group.

Figure 6: Clinical signs in the patients affected by ROCM in the study group.

Figure-1(a),1(b)

Figure 2(a)

Figure 2(b):-

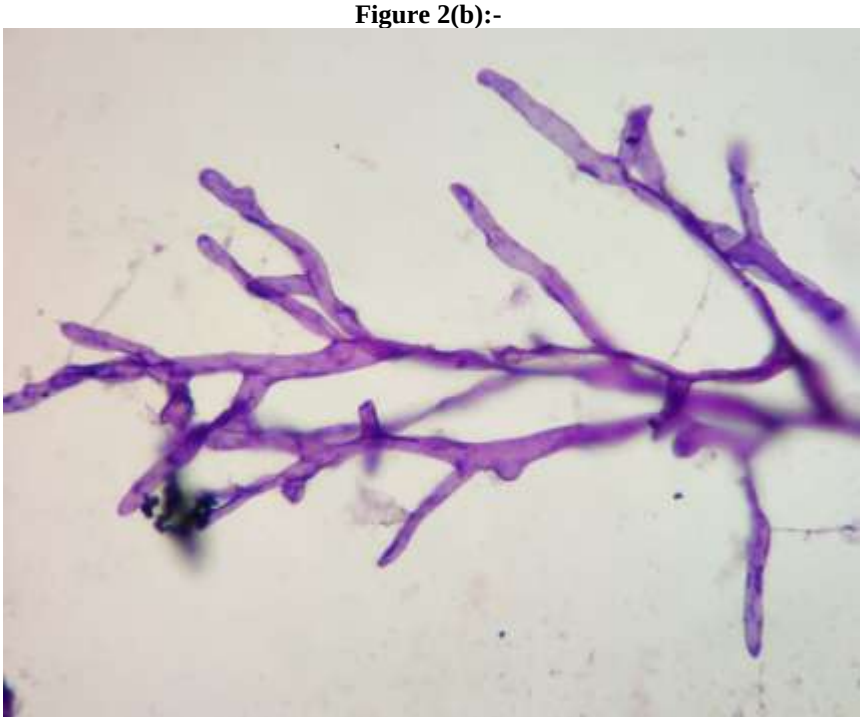


Figure 3(a), 3(b), 3(c), 3(d):-

Figure 4:-

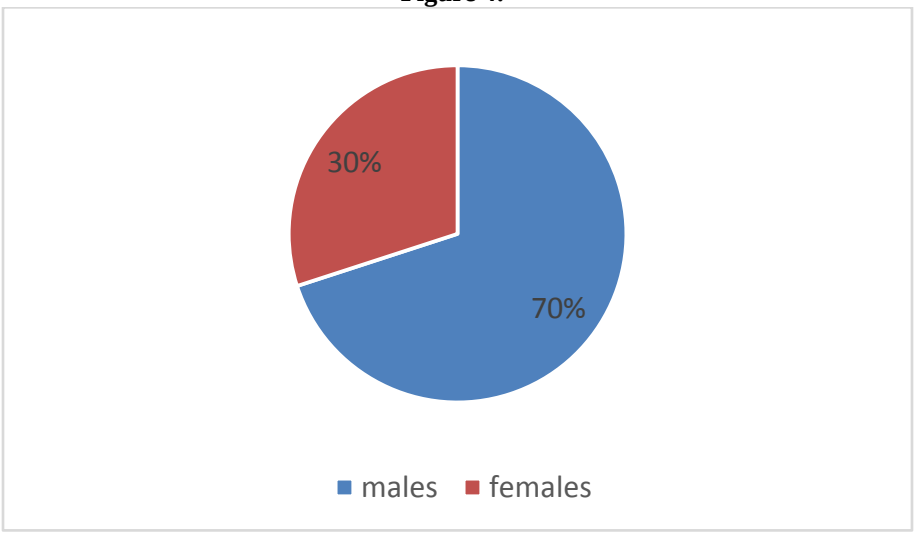


Figure 5:-

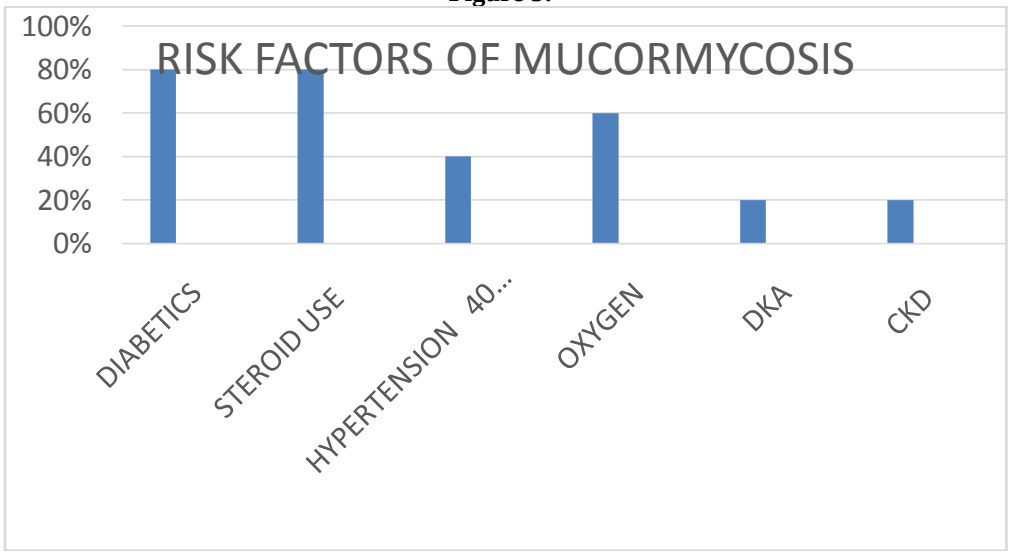
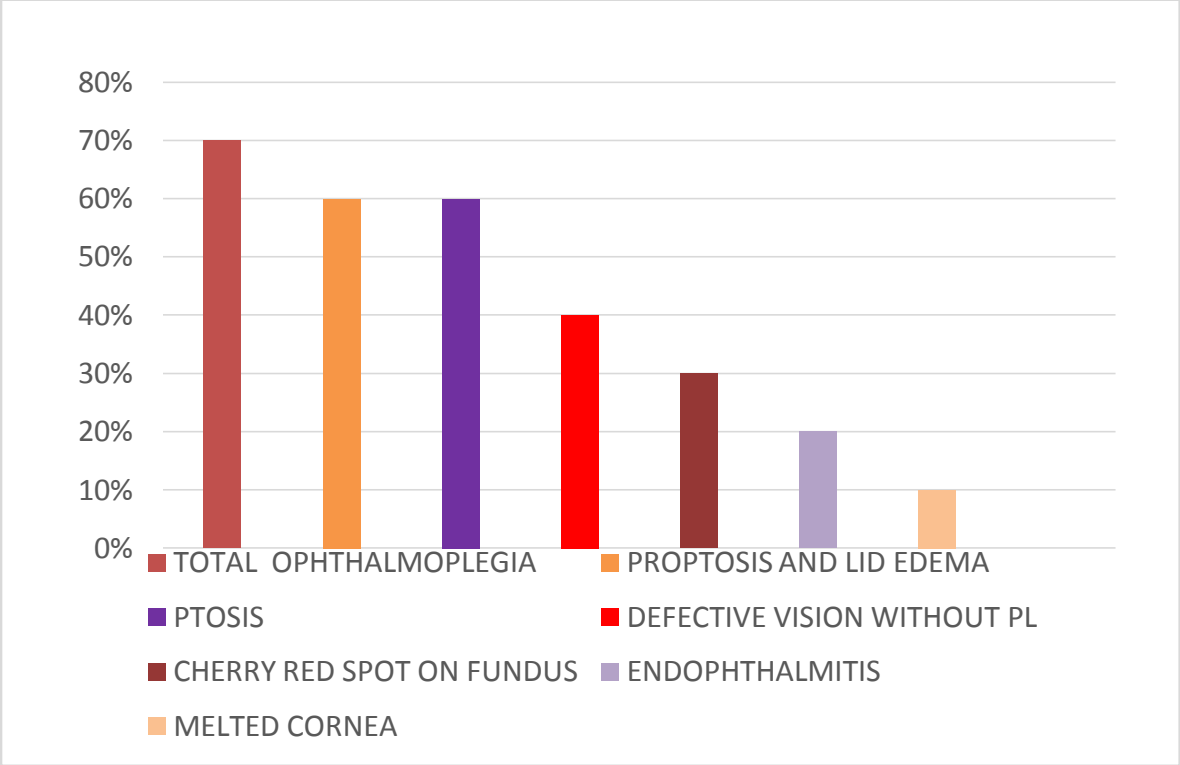


Figure 6:-



Tables

Table 1: Age distribution in the study sample.
Table 2: Duration of onset of mucor mycosis after COVID-19 infection in the study group.
Table 3: Treatment modalities and outcome in each of the ten patients included in the study.

Table-1:-

Age distribution	Frequency of cases	Percentage
<40 years	2	20%
41-50 years	3	30%
51-60 years	2	20%
>60 years	3	30%

Table-2:-

Day of mucor onset after COVID - 19	Number of people	percentage
0-10 days	0	0%
10-20 days	5	50%
20-30 days	4	40%
>30 days	1	10%

Table 3:-

Pt. no	IV AMPB	IV POS	TAB POS	FESS	TRAMB	EXENT	OTHERS	OUTCOME
1	+		+	+	+	+		Exenterated
2	+		+	TWICE	+			Improved with TRAMB
3	+		+	+		+		Exenterated.
4	+		+	+	+			Improved with TRAMB
5	+		+	+		+		Disease Recurrence
6	+		+	B/L FESS		+	Temporal abscess drainage	Exenterated
7	+		+	+		+		exenterated
8	+		+	+		+	Left temporal abscess drainage	death
9		+		+		+		Exenterated
10		+		+		+		exenterated

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