How to Cite:
Lavanya, S., Jeyaprakash, B., Ezhilvendhan, K., Bhava, B. S., & Rajeshkannan, R. (2022). Rhino-orbital-cerebral mucormycosis in post COVID-19 patients: A hospital based clinical study. *International Journal of Health Sciences*, *6*(S4), 11775–11782.
https://doi.org/10.53730/ijhs.v6nS4.11401

Rhino-orbital-cerebral mucormycosis in post COVID-19 patients: A hospital based clinical study

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***Abstract*---**Introduction-Mucormycosis is an angio invasive infection that occurs due to fungi Mucorales. It occurs primarily in severe immunocompromised individuals and in poorly controlled diabetes mellitus patients. Objectives-To study the clinical features and assess the severity of orbital involvement among the rhino-orbital mucormycosis patients. To study the management & outcome in post covid rhino orbital mucormycosis patients. Methods- It was a Hospital based retrospective study conducted from a period June 2021 to August 2021(3 months) in Vinayaka Mission's Kirupananda Variyar Medical College, Salem. Sample size of 50 taken from medical records section.Patient's demographic data like age, gender were noted. Data such as presenting symptoms, signs, history of presenting illness, COVID history, and associated co morbidities were noted. Findings of anterior segment evaluation (done by slit lamp biomicroscopy in ambulatory patients, torch light examination for bed ridden patients)

Manuscript submitted: 9 April 2022, Manuscript revised: 18 June 2022, Accepted for publication: 27 July 2022

were noted. SPSS (Version 22.0) was used for analysis. Results-the most common age group was 40-60 years (58%), followed by >60 years (24%), this suggest that mostly mucormycosis is more common after 40 years as per present study. most common duration was between 2-4 weeks when the symptoms of mucormycosis starts to seen from COVID seen in 58% of patients (p>0.05).sixty four percent of patients has orbital involvement in which 21(65.62%) were males and 11 (34.3%) were females and it was not significant.The most common presenting symptoms was eye pain/headache seen in 64% patients. Liposomal amphotericin B followed by oral posaconazole was given in 100% of patients along with sinus debridement also in all patients. Conclusions- Treating the immunocompromised conditions which led to the disease, systemic antifungals, and sinus debridement proved to be the main stay of treatment. Multidisciplinary timely diagnosis and prompt treatment may significantly improve the prognosis.

***Keywords*---**mucormycosis, nasal discharge, peri-orbital edema, headache, diminished vision, liposomal amphotericin B, diabetes, posaconazole.

Introduction

Rhino-orbital-cerebral mucormycosis (ROCM) is an uncommon, acute, and aggressive fungal infection occurring in several immunocompromised states including diabetes, which is the most common (60%–81%) predisposing factor.1,2 The disease originates in the nasal/sinus mucosae after inhalation of fungal spores and takes a rapidly progressive course extending to neighbouring tissues, including the orbit, and sometimes to the brain. Gregory et al in 1943 reported three cases of ROCM in patients with uncontrolled diabetes with unilateral orbital cellulitis, complete ophthalmoplegia, cerebral tissue invasion, and death.3 ROCM causes a very high residual morbidity and mortality due to the angioinvasive property of the fungus, thereby causing vascular occlusion and consequently resulting in extensive tissue necrosis.4 Impaired delivery of the antifungal drugs to the site of infection because of vascular thrombosis and limited aggressive surgery because of the complex anatomy of the rhino-orbital region cautions for early diagnosis and aggressive management in these patients. Mortality associated with invasive mucormycosis is high. Prevalence of mucormycosis is found to be high in post covid patients.5it can be categorised into rhino- orbital – cerebral, cutaneous, disseminated, gastrointestinal & pulmonary types.Mucorales- have distinct histological appearance – irregular, non-septate hyphae that branch at right angles .ROCM is the most common clinical presentation among diabetes.6 Lipid formulations of amphotericin B is the main stay treatment. This clinical study was to assess the clinical features, severity& the outcome of the disease.

Materials and Methods

It was a Hospital based retrospective study conducted from a period June 2021 to August 2021(3 months) in Vinayaka Mission's Kirupananda Variyar Medical College, Salem. Sample size of 50 taken from medical records section.
Inclusion criteria:

1. Patients who had past covid 19 infections
2. Patients diagnosed with mucormycosis by means of clinical features, nasal endoscopy, histopathological & radiological methods.
3. Patients who gave consent to the study

Exclusion criteria:

1. Patients with other ocular infections.
2. Patients who refused to give consent to the study

Methodology

Patient's demographic data like age, gender were noted. Data such as presenting symptoms, signs, history of presenting illness, COVID history, and associated co morbidities were noted. Visual acuity which was recorded at the time of presentation with Snellen's chart was noted. Findings of anterior segment evaluation (done by slit lamp biomicroscopy in ambulatory patients, torch light examination for bed ridden patients) were noted.Features of fundus examination which was done by 90D lenses in slit lamp, direct ophthalmoscope and indirect ophthalmoscopy with +20D lens, were noted. Results of imaging modalities on CT, MRI of brain, PNS & orbits were noted. Medical and surgical intervention given to the patients was recorded.Totally 50 patients fulfilling the inclusion criteria were included in the study.

Statistical Analysis

The statistical software namely statistical package for social sciences (SPSS) 22.0 was used for the analysis of the data. Categorical data represented in frequencies and proportions. Chi-square test has been used to find the significant association. $P<0.05$ is considered as statistically significant value.

Results

Table 1- Age and Gender wise distribution of study participants

AGE (in years)	NO	Percentage %
<40	9	18
40-60	29	58
>60	12	24
total	50	

As per table 1 the most common age group was 40-60 years (58%), followed by >60 years (24%), this suggest that mostly mucormycosis is more common after 40 years as per present study. Among gender distribution 62% were males and 38% were females (31 &19). Among 50 patients the most common risk factor was diabetes (70%) followed by steroids intake (64%) and Oxygen supplementation (60%).

Table 2-Day of onset of symptoms of mucormycosis from covid

DAY OF ONSET OF SYMPTOMS FROM COVID (WEEKS)	NO OF PATIENTS	%
< 2 weeks	11	22
2-4 weeks	29	58
4-6 weeks	5	10
> 6 weeks	5	10

As per table 2 days on onset of mucormycosis with symptoms are seen in which most common duration was between 2-4 weeks when the symptoms of mucormycosis starts to seen from COVID seen in 58% of patients, followed by <2 weeks (22%). And it was not significant ($p>0.05$).

Table 3- Patients with Orbital Involvement

	NO OF PATIENTS WITH ORBITAL INVOLVEMENT	%
MALE	21	65.62
FEMALE	11	34.3
TOTAL	32	64

As per table 3, sixty four percent of patients has orbital involvement in which 21(65.62%) were males and 11 (34.3%) were females and it was not significant.

Table 4- Status of Visual Acuity and Presenting Symptoms

VISUAL ACUITY	NUMBER	PERCENTAGE
NO PERCEPTION OF LIGHT	16	32%
ONLY PERCEPTION OF LIGHT	3	6
CFCF – 3 meters	5	10

CF 3 meters- 6/6	25	50

As per table 4 No Perception of light – 16, Only PL – 3, CFCF To CF at 3 mts – 6, CF 3 mts- 6/6 – 25 (32%,6%,10%,50%).This suggest that orbital involvement has significant association with visual acuity ($p<0.05$). While, the most common presenting symptoms was eye pain/headache seen in 64% patients, followed by restrictive eye movements in 60%. Nasal blockage and decreased vision seen in 44% and 42% respectively.

Table 5- Anterior Segment findings

ANTERIOR SEGMENT FINDINGS	PERCENTAGE %
Periorbital edema	64
ptosis	60
Proptosis	44
Conjunctival chemosis	28
RAPD	24
Dilated , fixed pupil	12

As per table 5 the most common anterior segment finding was periorbital oedema seen in 64% of patients, followed by ptosis (60%), proptosis (44%), chemosis (28%), RAPD (24%) and least seen was dilated/fixed pupil (12%).

Table 6- Fundus Findings

FUNDUS	NUMBER	PERCENTAGE
NORMAL	34	68
CRAO	10	20
OPTIC DISC EDEMA	2	4
OPTIC DISC PALLO& ATTENUATED BLOOD VESSELS	4	8

As per table 6 mostly the fundus findings were normal in 68% of patients but 20% patients seen CRAO and 4% showed optic disc edema.

Table 7- Management in Mucormycosis patients

MANAGEMENT	NUMBER	%
INTRAVENOUS	50	100

LIPOSOMOAL AMPHOTERICIN B FOLLOWED BY ORAL POSACONAZOLE		
SINUS DEBRIDEMENT	50	100
ORBITAL EXENTERATION	18	36
TRAMADOL INJECTION	2	4

As per table 7 liposomal amphotericin B followed by oral posaconazole was given in 100% of patients along with sinus debridement also in all patients. Orbital Exenteration was done 36% of patients and tramadol injection was given in 4 % patients.

Table 8- Outcome of Patients after Management

OUTCOME	NUMBER	%
FAVOURABLE	28	56
UNFAVOURABLE	19	38
DEATHS	3	6

As per table 8 favourable outcomes seen in 56% of patients while 38% has unfavourable outcomes. 6% had deaths.

Discussion

Mucormycosis typically originates in the nasal or oral mucosa, spreads to the paranasal sinuses, and enters the orbit via the ethmoid and maxillary sinuses or via the nasolacrimal duct.9 Intracerebral extension may occur from the orbit via orbital apex, orbital vessels, or via cribriform plate.9 Diabetes predisposes to this infection, as is seen in the majority of instances of MUCORMYCOSIS (60%–81%) in different series.1,2,5,10

Yohai et al reviewed 145 case reports of mucormycosis, 60% of them had diabetes, and analysed their ophthalmic and non-ophthalmic signs and symptoms occurring at any time during the course of disease.1 Similarly Ferry and Abedi reported 16 cases of MUCORMYCOSIS; 13 (81%) of them had diabetes.2 We have compared our observations with these two available series where the majority of the patients had diabetes.

Periorbital swelling and pain were observed in 66% and 43% of patients by us, compared with 43% and 11% respectively by Yohai et al.1 Ptosis in absence of ophthalmoplegia was reported in 3% of patients, whereas all our patients with ptosis had concomitant ophthalmoplegia. Ophthalmoplegia (89% v 67%) and proptosis (83% v 64%) were more frequently observed by us compared with

others.1 Endophthalmitis has been rarely reported (1%) with MUCORMYCOSIS but in our series two (6%) patients had it.1,6 Overall it seems that orbital manifestations were more common in our patients than reported in the literature. This could be due to delay in admission, thereby permitting spread of infection to the orbital tissue. Orbital manifestations are due to ischaemic necrosis of the intraorbital cranial nerves, orbital cellulitis, or rarely ocular invasion by mucorales.1

Computed tomography or magnetic resonance imaging is useful modalities to assess the extent of the disease. In our study paranasal sinuses were involved in all patients, with ethmoid and maxillary being the most frequent, while Ferry et al2 and Yohai et al1 reported sinuses involvement in 69% and 79% respectively. Orbital involvement observed as an orbital mass and/or thickening of the recti and optic nerve were seen in the majority (80%) of our patients.

Amphotericin B is partially effective therefore surgical debridement becomes essential.6,11Antral wash, lateral rhinotomy, pansinusectomy, orbital exenteration, and sometimes intracranial surgery are performed depending upon the extent of the disease. Extensive orbital involvement by mucorales required orbital exenteration in 11 (42%) patients and nine (82%) of them survived. This is in concurrence with other observers who feel orbital exenteration may be lifesaving in an actively inflamed orbit with a blind, immobile eye.2,3

Factors associated with poor survival in MUCORMYCOSIS include (i) delay in diagnosis and treatment, (ii) hemiparesis, (iii) bilateral sinus involvement, and (iv) facial necrosis.1 Yohai et al reported survival of 63% of patients with a lag time from seven to 12 days and 44% in those with a lag time of 13 to 30 days.1 In our analysis, 85% patients survived who had lag time from three to nine days, but only 55% survived with a lag time of 10 to 45 days. This is in agreement with observations made by others.11,12. However, our survival rate was comparable to that reported in western countries (68% v 70%–73%) in different series.1,6,10

Conclusions

Immunocompromised states like uncontrolled DM, steroid usage in covid positive patients, are major risk factors for occurrence of rhino orbital mucormycosis. CT MRI helps in early detection of extent of disease and helps in planning of management. Orbital apex & CNS involvement led to unfavorable outcome in majority of the patients. Treating the immunocompromised conditions which led to the disease, systemic antifungals, sinus debridement proved to be the main stay of treatment. Multidisciplinary timely diagnosis and prompt treatment may significantly improve the prognosis.

Source of Funding- None
Conflict of Interest- None declared

References

1. A Bhansali, S Bhadada, A Sharma, V Suresh, A Gupta, P Singh, A Chakarbarti, R J Dash. Presentation and outcome of rhino-orbital-cerebral mucormycosis in patients with diabetes. Postgrad Med J 2004;80:670674.
2. Abramson E , Wilson D, Arky RA. Rhinocerebral phycomycosis in association with diabetic ketoacidosis. Ann Intern Med 2014:1060–2.
3. Akbarov, A. N., & Xabilov, D. N. U. (2021). The condition of the oral cavity in patients who have had a viral infection COVID-19. *International Journal of Health & Medical Sciences*, *4*(4), 381-383. https://doi.org/10.21744/ijhms.v4n4.1796
4. Cohen SG, Greenberg MS. Rhinomaxillary mucormycosis in a kidney transplant patient. Oral Surg Oral Med Pathol2010;50:33–8.
5. Ferry AP, Abedi S. Diagnosis and management of rhino-orbitocerebral mucormycosis (phycomycosis): a report of 16 personally observed cases. Ophthalmology2013;90:1096–104.
6. Gregory JL, Golden A, Haymaher W. Mucormycosis of the central nervous system: a report of three cases. Bull John Hopkins Hosp2003;73:302–13.
7. Hatice Sebila Do¨kmetas¸ a,*, Ercan Canbay b , Sarper Yilmaz c , Nazif Elaldi d , Ays¸en Topalkara e , Ibrahim Oztoprak f , Esin Yildiz g. Diabetic ketoacidosis and rhino-orbital mucormycosis.Diabetes research and clinical practice 2012;32:139-142.
8. Intriago, C. Z., & Posligua, T. I. Q. (2020). Telecommunications and virtualization in times of pandemic: impact on the electrical engineering career. *International Journal of Physical Sciences and Engineering*, *4*(3), 38–44. https://doi.org/10.29332/ijpse.v4n3.630
9. Ochi JW, Harris JP, Feldman JI, et al. Rhinocerebral mucormycosis: results of aggressive surgical debridement and amphotericin B. Laryngoscope2018;98:1339–42.
10. Parfrey NA. Improved diagnosis and prognosis of mucormycosis: a clinicopathologic study of 33 cases. Medicine 2016;65:113–23.
11. Pillsbury HC, Fischer ND. Rhinocerebral mucormycosis. Arch Otolaryngol2016;103:600–4.
12. Smith JL, Stevens DA. Survival in cerebro-rhino-orbital zygomycosis and cavernous sinus thrombosis with combined therapy. *South Med J*2016;79:501–4.
13. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). The COVID-19 pandemic. *International Journal of Health Sciences*, *5*(2), vi-ix. https://doi.org/10.53730/ijhs.v5n2.2937
14. Yohai RA, Bullock JD, Aziz AA, et al. Survival factors in rhino-orbital-cerebral mucormycosis: major review. Surv Ophthalmol2014;39:3–22.
15. zafer koc, filiz koc, Deniz yerdelen, Hakan ozdogu. Rhino –Orbital –Cerebral mucormycosis With different cerebral involvements: infarcts, haemorrhage, ophthalmoplegia. Neuroscience 2007; 117:1677-1690.