

# Epidemiological and Mycological Features of MUCORMYCOSIS in Covid -19 Pandemic in a Tertiary Care Hospital

DR.K. Aarathi<sup>1\*</sup>, DR. Jagannadha Phaneendra .D.S<sup>2</sup> and DR.K. Nagamani<sup>3</sup>

<sup>1</sup>M.D. Microbiology, Assistant Professor, Department of Microbiology, Neelima institute of medical sciences, Hyderabad

<sup>2</sup>M.D. Biochemistry, Professor & HoD, Department of Biochemistry, Neelima institute of medical sciences, Hyderabad

<sup>3</sup>M.D. Microbiology, Professor & HoD, Department of Microbiology, Government Medical College, Vikarabad

**Corresponding Author:** Aarathi, M.D. Microbiology, Assistant Professor, Department of Microbiology, Neelima institute of medical sciences, Hyderabad

Received: 📅 2024 Nov 08

Accepted: 📅 2024 Nov 15

Published: 📅 2024 Nov 29

## Abstract

**Introduction:** Incidence of mucormycosis was increased during COVID pandemic. Uncontrolled DM, usage of corticosteroids is an important risk factor for ROCM.

**Aims & Objectives:** To find Clinical, Epidemiological profile of Covid associated Mucormycosis patients in a Tertiary care hospital in covid 2<sup>nd</sup> wave surge. To delineate clinical, Epidemiological profile of Covid associated mucormycosis patients. To identify Causes, Risk factors. To describe symptoms, signs & microbiological features of Covid associated Mucormycosis.

**Materials and Methods:** A patient proforma was prepared for patients admitted from May to August 2021, collected their history of Covid symptoms, treatment taken and their biopsy samples were sent to microbiology laboratory, analyzed using KOH mount and culture on SDA, DRBC agar plates and LPCB results were noted

**Results:** Out of 101 patients, 75.7% are males, 26.2% are females. 71 patients were on steroid treatment of Covid. 45 were Renovo of DM, 56 were chronic diabetic. 24 patients had visionless, 64 had periorbital edema, 56 had facial pain, 15 had loss of eye movements, 14 had hard palate necrosis, each patient having one or more signs. On KOH mount, 55 broad aseptate hyphae, 8 narrow aseptate hyphae, 3 yeasts. In 7 samples, no fungal elements were seen. 28 were KOH positive & culture negative. On Culture, Rhizopus species was isolated in 43 patients, Aspergillus species were isolated in 8, Candida was isolated 3 patients, Demeticious fungi in 1 patient & "no fungal growth" in 40 patients.

**Conclusion:** Covid -19 infection increased the risk of mucormycosis. Awareness of symptoms and signs, high clinical suspicion, prompt diagnosis, and early initiation of medical & surgical intervention are essential for successful outcome.

**keywords:** Covid-19, Mucormycosis, Rhizopus, ROCM

## 1. Introduction

Mucormycosis also called "ZYGOMYCOSIS" because these fatal diseases are caused by fungi that belongs to class "Zygomycetes" and Order "Mucorales" The organisms found from clinical specimens are mainly *Rhizopus* species (most common), & *Mucor*. Others like *Rhizomucor*, *Saksenia*, *Cunnighamella* etc., are less common [1].

*Rhizopus Oryza* is most common fungi causing 60% of cases of Mucormycosis & 90% cases of ROCM. Globally its prevalence ranges from 0.005 to 1.7 per million population, but highest (80%) 0.14/1000 population in India when compared to other developed countries. Although members of MUCORACEAE are ubiquitous in nature, they are usually

found on dead & decaying matter. Mucormycosis is caused by inhalation or exposure of fungal spores on mucosa or disrupted skin respectively. Occurrence of mucormycosis differs in developing & developed countries. In developed countries Diabetes mellitus & hematological malignancies receiving chemotherapy & allogenic stem cell transplants are the causative factors & in developing countries especially in India uncontrolled DM & trauma are the main factors [2-7].

Mucormycosis also known as "Black fungus" is actually a rare infection, surged suddenly during 2<sup>nd</sup> wave of COVID Pandemic in India. COVID -19 is a novel corona viral infection was detected firstly during December in the year 2019. Though COVID -19 is a respiratory infection, it can

be associated with fungal coinfection .During 2<sup>nd</sup> wave of COVID pandemic , increased fungal infections, mainly Rhino orbital mucormycosis(ROCM) had been documented. Hyperglycemia and ketoacidosis due to use of corticosteroids during COVID-19 infection increased mucormycosis in them as they (hyperglycemia & ketoacidosis) are supportive for fungal growth. Mucormycosis is a life-threatening condition & has high death rate of 50%. So, Early diagnosis, timely medical & surgical intervention is necessary [8-12].

In the present study, we have taken 101 samples from patients of mucormycosis (both ROCM, Pulmonary) admitted in our Hospital and taken epidemiological factors, clinical symptoms & undergone KOH, LPCB & conventional culture on Sabaraud's dextrose agar (SDA) & Dichloran Rose Bengal Agar (DRBC).

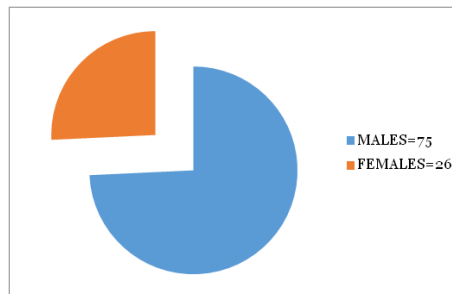
## 2. Materials and Methods:

The study was conducted in Gandhi hospital during COVID

pandemic from May 2021 to August 2021. A total no. of 101 patients were taken and analysed their history, demographic profile, clinical features, associated comorbidities and treatment were taken. The history was taken with their concern and ethical clearance was given. A structured patient proforma was prepared and their history, symptoms related to COVID, treatment received were collected. These patients were having clinical symptoms & signs of mucormycosis. The biopsy taken from orbit, nasal cartilage, sputum samples were received at microbiology laboratory & were observed by performing 10% potassium hydroxide & Lactophenol cotton blue mount. And tissue specimens were inoculated on SDA & DRBC agar plates and results were noted. Results were examined and arrayed on Microsoft Excel sheet.

## 3. Results:

Out of 101 patients, 75 are Males, 26 are Females with male preponderance. All patients are associated with COVID except 2 patients (Figure-1).



**Figure 1:** Gender Distribution of Patients Affected with Mucormycosis

Out of total, 71 patients were on treatment of steroids for COVID, & 30 patients were not. 45 patients were DENOVO diabetic whereas 56 were Chronic Diabetic (Table-1).

TYPE OF DIABETES	NO.OF PATIENTS
DE NOVO	45
CHRONIC DIABETES	56

**Table 1:** No. of Patients With De Novo & Chronic Diabetic

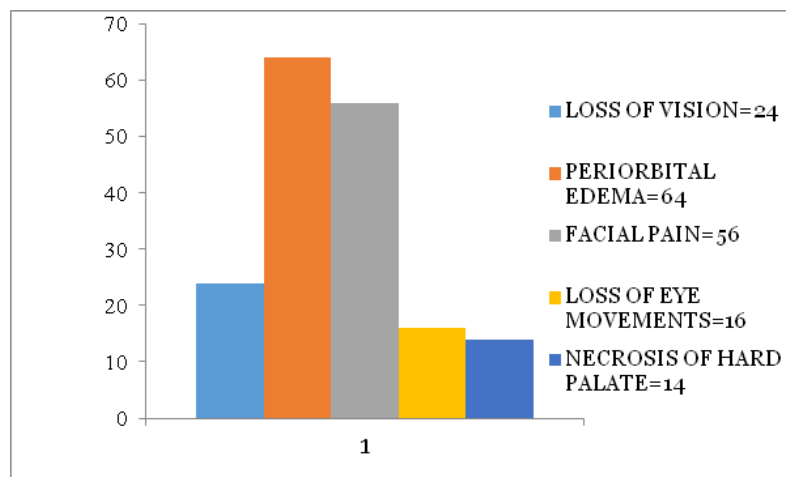
Characteristics	Characteristics	Number of patients
Age	Median age group	47.9
Gender	Male ,Female	75 (74.2%) 26(25.7%)
Duration between COVID & mucormycosis	Median days	10days
Comorbid illnesses	Diabetes mellitus,Hypertension Obesity	93(92%) 31(30.6%) 9(8.9%)
Steroid usage in recent COVID-19	Received I/V steroids , broad spectrum antibiotics	71(70.2%) 91(90%)
Symptoms of mucormycosis	Loss of vision Periorbital edema Facial pain Loss of eye movements Necrosis of hard palate	24(23.7%) 64(63%) 56(55%) 16(15.8%) 14(13.8%)
Type of diabetes	de novo DM chronic DM	45(44.5%) 56(55.4%)
Treatment taken at (for COVID-19)	Home isolated	74(73.2%)

**Table 2:** Demographic Profile, Risk Factors & Clinical Features

Sample size	Mean age	Time lag b/n Covid & rock	Risk factors	Symptoms, signs	Study
1	60 years	10 days	Chronic diabetes	Periorbital cellulitis,	Mehta <i>et. al</i> , Mumbai <sup>19</sup> (Case report)
70	44.5		DM, HTN, Prior steroid usage	Edema of eye, proptosis, ptosis	Ramaswamy <i>et al</i> <sup>18</sup>
11	46.8	2-11 days	Chronic diabetes (>7 years)	Proptosis, periorbital swelling, ophthalmoplegia, CRAO	Saroj Gupte <i>et. al</i> , Bhopal, India <sup>17</sup>
11	73+/-7 years	12.1+/-4.4 days	Chronic diabetes, i/v steroids	Proptosis, periorbital swelling, ophthalmoplegia, CRAO	Saroj Gupte <i>et. al</i> , Bhopal, India <sup>17</sup>
10	53	17	DM, HTN, CKD, CAD	Periorbital cellulitis, Endophthalmitis	Bayram <i>et al</i> , Turkey <sup>15</sup>
101	47.9	10 days	Diabetes, steroid usage	Headache, facial swelling, blurred vision	Arjun <i>et al</i> <sup>25</sup>
101	47.9	10 days	Diabetes, steroid usage	Loss of vision, periorbital edema, necrosis of hard palate	Present study

**Table 3: Mean Age, Risk Factors & Symptoms, Signs B/N Present Study and Other Previous Studies**

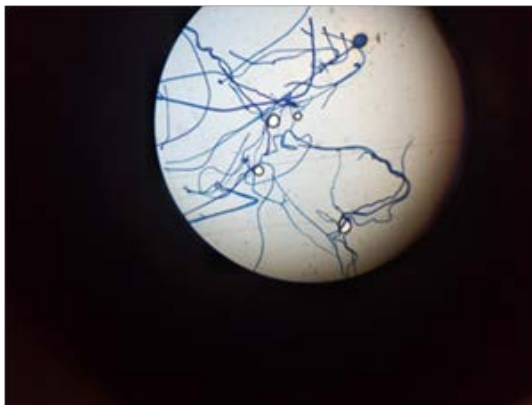
In total patients (N=101), 24 patients had loss of vision, 64 had periorbital edema, 56 had facial pain, 16 had loss of vision, 14 had necrosis of hard palate with each patient having one or more symptoms & signs. (Figure-2).

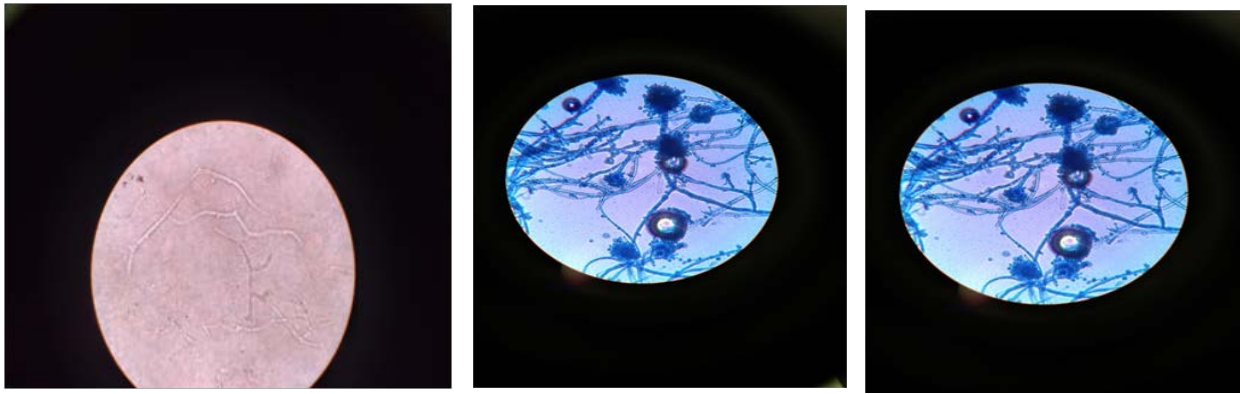


**Figure 2: Clinical Symptoms & Signs Associated with Mucormycosis Are**

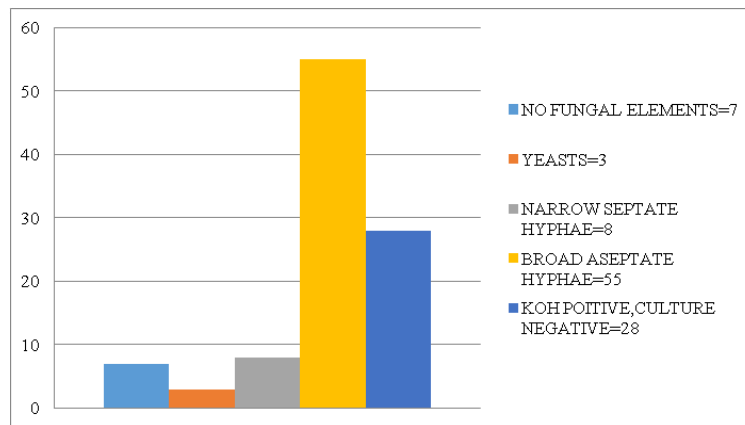
Samples were taken and KOH Mount and LPCB mount were done. On KOH mount, we got 55 broad aseptate hyphae, 8 narrow aseptate hyphae, 3 yeasts. In 7 samples, no fungal

elements were seen. 28 were KOH positive & culture negative (Figure-3,4).





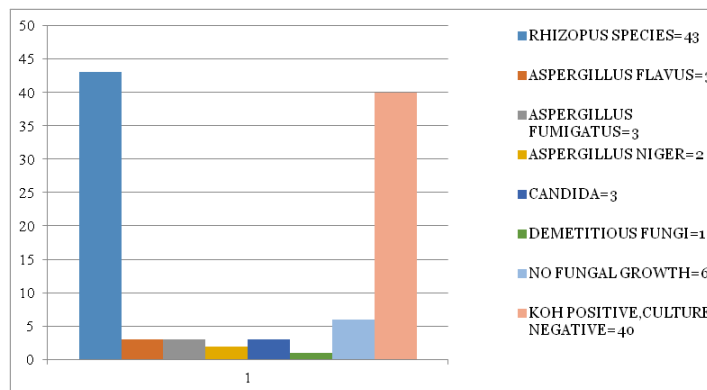
**Figure 3:** (A)Rhizopus On LPCB Mount (B)Broad Aseptate hyphae on Koh(C) Septate hyphae on Koh Mount (D) Aspergillus Fumigatus on Lactophenol Cotton Blue Mount (Aspergillus Flavus On Lactophenol Cotton blue Mount



**Figure 4:** Koh Mount Findings

All the samples were processed for culture. On culture (SDA & Draggers) we got 43 Rhizopus species, 8 Asprgillus species (3 flavus ,3 fumigatus and 2 niger) 3 were Candida, 1 was

Demetecious fungi, 40 were culture negative, 6 were KOH & culture negative (Figure-5).



**Figure 5:** conventional culture results

**4. Discussion**

Several factors are associated with mucormycosis like Diabetes Mellitus, ketoacidosis ,immunosuppressive therapy in stem cell transplantation ,hematological malignancies etc., and there is an alteration in the immune mechanisms due to decline in CD4 & CD8 cells & conversely increased IL2R,IL6,IL10 & TNF alpha leading to immunosuppression in COVID -19 patients following treatment for COVID .Other factors like free use of broad spectrum antibiotics

which affects natural microbiota of body disturbing innate immunity .Iron overload in diabetic ketoacidosis is also an important cause in diabetic patients (including de novo affected diabetes patients) as iron contributes spread of infection in the body as it is beneficial for fungal growth. In our patients ,92% had Diabetes mellitus,30.6% were hypertensive & 8.9% were Obese. Wide spread use of broad spectrum antibiotics, steroids & oxygen support may also increase the susceptibility of patients to mucormycosis[15].

In our study 90% & 70.2% of patients received broad spectrum antibiotics & steroids respectively, 54 (53%) received oxygen inhalation support as a part of COVID-19 treatment. 45 patients were attacked by diabetes after steroid treatment & 56 patients were chronic [13-15].

The fungi can also be present in the nasal mucosa of a healthy person as the spores are inhaled. So, the first affected parts are nasal cavities, causing ROCM, which is m/c type of mucormycosis. From nasal mucosa, they directly spread to turbinates, palate, orbit & brain. hyphae are vaso-invasive and fungal proliferation can cause ischaemic necrosis. And WBC have low efficacy to fight with fungal hyphae, so they proliferate easily. In a normal person, spores are usually eliminated by phagocytes unlike in immunocompromised persons where spores are transformed to hyphae. Risk factors associated with mucormycosis are chronic diabetes and corticosteroids usage respectively which correlates with many of the studies. In the present study, the mean age group is 47.9 correlating with Saroj Gupte *et al*, Bhopal whose mean age group is 46.8. The mean age group of study of Ramaswamy *et al* whose mean age group is 44.5. In our study, time lag between COVID -19 & ROCM is 10 days correlating with Mehta *et al* (10 days) and Saroj Gupte *et al* (2-11 days). Males are affected more than females correlating with Sen *et al* [13-20].

Risk factors for mucormycosis for Post covid patients are Diabetes mellitus & usage of steroids. Studies done by Ramaswamy *et al*, Bayram *et al* & Sen *et al* also stated the same. Early diagnosis, control of systemic associated factors like DM, DKA & aptly initiating systemic, retrobulbar antifungal therapy, retrobulbar injection of Amphotericin - B in patients with deep ocular infection and surgical debridement of involved maxillofacial organs like paranasal sinuses can improve patient outcome & reduce morbidity and mortality. 1ml of Retrobulbar injection of amphotericin B (1ml=3.5mg) is to be given. Liposomal amphotericin - B is the first choice (DOC) of antifungal drug to be used in mucormycosis patients. Mechanically it destroys fungal cell wall and to be prescribed in higher doses (5- 10mg/kg). Amphotericin with liposomal formulation reduces nephrotoxicity. Combination therapy is recommended as it reduces mortality. Follow up and maintenance therapy is to be given with liposomal amphotericin B for several weeks depending upon the patient response. Posaconazole is step down treatment. Along with these medical treatments surgical debridement of organs is highly recommended as blood vessels are occluded and drugs cannot reach deep into the tissues. Surgical excision is done to remove necrotic tissue till perfused tissue has appeared. This procedure is repeated until improvement comes. Orbital exenteration may be unavoidable [13-25].

## 5. Conclusion

COVID -19 infection increased the risk of Mucormycosis. Corticosteroids and Diabetes mellitus are the most important predisposing factors in the development of COVID-19-associated ROCM.

Awareness of red flag symptoms and signs, high clinical suspicion, prompt diagnosis, and early initiation of treatment with Amphotericin B, aggressive surgical debridement of the PNS, and orbital exenteration, where indicated, are essential for successful outcome.

## Conflicts of Interest:

No

## Acknowledgement:

I am thankful to my college, faculty, colleagues, and family members in helping to complete my work.

**Conflicts of Interest:** There are no conflicts of interest.

Ethical Ref. No: Ref no: IEC/GMC/2021/3/13 dated 27th July 2021).

**Presentations & Awards:** COVID WARRIOR AWARD in the year 2021

## References

- Petrikkos, G., Skiada, A., Lortholary, O., Roilides, E., Walsh, T. J., *et al.* (2012). Epidemiology and clinical manifestations of mucormycosis. *Clinical Infectious Diseases*, 54(suppl\_1), S23-S34.
- Singh, A. K., Singh, R., Joshi, S. R., Misra, A. (2021). Mucormycosis in COVID-19: a systematic review of cases reported worldwide and in India. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 15(4), 102146.
- Talmi, Y. P., Goldschmied-Reouven, A., Bakon, M., Barshack, I., Wolf, M., Horowitz, Z., *et al* (2002). Rhino-orbital and rhino-orbito-cerebral mucormycosis. *Otolaryngology—Head and Neck Surgery*, 127(1), 22-31.
- Ibrahim A, Edwards JE Jr, Filler SG, eds. Mucormycosis. Philadelphia: *Harcourt Brace*, 2004.
- Spellberg, B., Edwards Jr, J., Ibrahim, A. (2005). Novel perspectives on mucormycosis: pathophysiology, presentation, and management. *Clinical microbiology reviews*, 18(3), 556-569.
- Prabhu, R. M., Patel, R. (2004). Mucormycosis and entomophthoromycosis: a review of the clinical manifestations, diagnosis and treatment. *Clinical Microbiology and Infection*, 10, 31-47.
- Chakrabarti, A., Das, A., Mandal, J., Shivaprakash, M. R., George, V. K., *et al.* (2006). The rising trend of invasive zygomycosis in patients with uncontrolled diabetes mellitus. *Sabouraudia*, 44(4), 335-342.
- World Health Organization. Coronavirus. <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200423-sitrep-94-covid-19.pdf>. Accessed 22 May 2021.
- Mohan, B. S., Nambiar, V. (2020). COVID-19: an insight into SARS-CoV-2 pandemic originated at Wuhan City in Hubei Province of China. *J Infect Dis Epidemiol*, 6(4), 146.
- Dyer, O. (2021). Covid-19: India sees record deaths as "black fungus" spreads fear.
- AK, Gupta V. Rhino-Orbital Cerebral Mucormycosis. 2023 Apr 24. In: StatPearls [Internet]. Treasure Island (FL):

- StatPearls Publishing; 2024 Jan-. PMID: 32491361.
12. Ferguson, B. J. (2000). Mucormycosis of the nose and paranasal sinuses. *Otolaryngologic Clinics of North America*, 33(2), 349-365.
  13. Veisi, A., Bagheri, A., Eshaghi, M., Rikhtehgar, M. H., Rezaei Kanavi, M., et al. (2022). Rhino-orbital mucormycosis during steroid therapy in COVID-19 patients: A case report. *European journal of ophthalmology*, 32(4), NP11-NP16.
  14. Prakash, H., Chakrabarti, A. (2019). Global epidemiology of mucormycosis. *Journal of Fungi*, 5(1), 26.
  15. Bayram, N., Ozsaygılı, C., Sav, H., Tekin, Y., Gundogan, M., et al. (2021). Susceptibility of severe COVID-19 patients to rhino-orbital mucormycosis fungal infection in different clinical manifestations. *Japanese journal of ophthalmology*, 65(4), 515-525.
  16. Maini, A., Tomar, G., Khanna, D., Kini, Y., Mehta, H., et al. (2021). Sino-orbital mucormycosis in a COVID-19 patient: a case report. *International Journal of Surgery Case Reports*, 82, 105957.
  17. Gupta, S., Goyal, R., Kaore, N. M. (2020). Rhino-orbital-cerebral mucormycosis: battle with the deadly enemy. *Indian Journal of Otolaryngology and Head & Neck Surgery*, 72(1), 104-111.
  18. Sundaram, N., Bhende, T., Yashwant, R., Jadhav, S., Jain, A. (2021). Mucormycosis in COVID-19 patients. *Indian Journal of Ophthalmology*, 69(12), 3728-3733.
  19. Salil, M., Abha, P. (2020). Rhino-Orbital Mucormycosis Associated With COVID-19. *Cureus*, 12(9).
  20. Sen, M., Honavar, S. G., Bansal, R., Sengupta, S., Rao, R., Kim, U., et al. (2021). Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India—Collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. *Indian journal of ophthalmology*, 69(7), 1670-1692.
  21. Buil, J. B., van Zanten, A. R., Bentvelsen, R. G., Rijpstra, T. A., Goorhuis, B., et al. (2021). Case series of four secondary mucormycosis infections in COVID-19 patients, the Netherlands, December 2020 to May 2021. *Eurosurveillance*, 26(23), 2100510.
  22. Sundaram, N., Bhende, T., Yashwant, R., Jadhav, S., Jain, A. (2021). Mucormycosis in COVID-19 patients. *Indian Journal of Ophthalmology*, 69(12), 3728-3733.
  23. Kontoyiannis, D. P., Lewis, R. E. (2011). How I treat mucormycosis. *Blood, The Journal of the American Society of Hematology*, 118(5), 1216-1224.
  24. Rapidis, A. D. (2009). Orbitomaxillary mucormycosis (zygomycosis) and the surgical approach to treatment: perspectives from a maxillofacial surgeon. *Clinical Microbiology and Infection*, 15, 98-102.
  25. Arjun, R., Felix, V., Niyas, V. K. M., Kumar, M. A. S., Krishnan, R. B., et al. COVID-19-associated rhino-orbital mucormycosis: a single-centre experience of 10 cases. *QJM: An International Journal of Medicine*, 114(11), 831-834.