

## Original Research Article

# Clinicoepidemiological study of acute invasive fungal rhinosinusitis in a tertiary care centre

Rajeshree Chaurpagar, Priyanka Garud\*, Apurva Pawde, Parag Doifode,  
Bhagyashree Chiplunkar, Mohammed Badarul Muneer

Department of ENT, GMC Akola, Akola, Maharashtra, India

**Received:** 12 September 2021

**Revised:** 19 October 2021

**Accepted:** 20 October 2021

### \*Correspondence:

Dr. Priyanka Garud,

E-mail: Priyanka.garud04@yahoo.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Coronavirus disease 2019 (COVID-19) accounted for severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), which was declared a global pandemic by World health organization (WHO) in March 2020. In second wave of COVID there was notable surge in Acute invasive fungal rhinosinusitis (AIFRS). We observed that use of systemic corticosteroids in treatment of COVID 19 especially among patients with poorly controlled diabetes mellitus increased the incidence of AIFRS.

**Methods:** This is retrospective observational study carried out in a Tertiary care Hospital GMC Akola from period of February 2021 to august 2021 were patients with the suspected diagnosis of AIFRS were admitted and evaluated following a standardized protocol, including clinical examination diagnostic nasal endoscopy, radiological evaluation. Diagnosis of AIFRS was confirmed on histopathology.

**Results:** Study was conducted in GMC, Akola of 136 patients out of which 97 were males and 39 were females. In our study 78.67% patients had history of covid infection, followed by diabetes mellitus in 54.41%, history of steroid treatment found in 64.70% patients. On HPE 69.85% were positive for mucor and mixed infection (mucor and aspergillus) were found in 6.61%. Most common presenting feature was facial pain and swelling in 66.91%, palatal changes with dental pain in 45.58%, diminution of vision 17.64%, headache in 27.94% patients.

**Conclusions:** Early and prompt diagnosis in high level of clinical suspicion in suspicious patient of AIFRS is vital to improve outcomes as it is known to have high morbidity and mortality (18-80%).

**Keywords:** AIFRS, Post covid, Steroid, COVID-19

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a new disease entity caused by a novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) first documented in China in December 2019 and subsequently causing a worldwide pandemic.<sup>1</sup> In second wave of covid it was observed that there was a notable surge in Acute invasive fungal rhinosinusitis (AIFRS). Coronavirus disease (COVID-19) causes an immunosuppressed state and increases risk of secondary infections like mucormycosis.<sup>2</sup> AIFRS is a potentially fatal infection that

is remarkably found in comorbid, immunocompromised patients and considered the most aggressive subtype of fungal sinusitis with subsequent serious morbidity and mortality. AIFRS defined as presence of tissue invasion by fungal elements over an acute clinical course of less than 4 weeks. AIFRS is a time-sensitive condition that must be recognized and treated promptly to avoid life-threatening complications. Secondary infections occur mainly after severe disease and in ICU treated cases of COVID-19 comprising around 10–30% of cases. According to the Epidemiology of Mucormycosis in India reported in 2021, the estimated prevalence of

Mucormycosis was at an alarming rate of nearly 70 times higher than the global data. The incident rate of mucormycosis varies from 0.005 to 1.7 per million population.<sup>3</sup> The main objective of this study is to evaluate about the different clinical and epidemiological features of AIFRS patients in our tertiary care centre.

## METHODS

In February 2021 we observed a notable surge of AIFRS in COVID-19 patients. This retrospective observational study was done in 136 patients from February 2021 to August 2021. Patients selected in our study were diagnosed with acute invasive fungal sinusitis clinically and radiologically.

### Inclusion criteria

Subjects included in study were clinically and radiologically proven cases of AIFRS. All patients enrolled underwent detail history taking, clinical examination, nasal endoscopies and radiological evaluation.

### Exclusion criteria

Pregnant patients were excluded in our study.

This study was approved by institutional ethical committee. The statistical data was entered in MS excel 2007 and analysed using Statistical package for social sciences (SPSS) 16.0 version. In current study 78.67 % patients had history of recent covid infection with definite diagnosis of covid 19 confirmed on polymerase chain reaction. Both prompt surgical debridement with antifungal medications along with treatment of any associated comorbidity was done in all patients. Anti-fungal therapy was the prime line of management in patients proven on evaluation. Injection liposomal amphotericin B (5 mg-10/kg), depending upon the severity and extension of disease and associated comorbidity, the dosage were calculated, along with timely regular assessment of blood parameters, to rule out toxicity of drugs. Patients were discharged on Tablet Posaconazole which was continued till clinical and radiological clearance of disease. Postoperative treatment included nasal saline irrigation thrice a day for at least 3 months. In cases with bacterial coinfection, systemic antibiotic therapy was administered on the basis of nasal swab culture sensitivity. All patients were prospectively followed up through endoscopic monitoring performed within 7 days intervals and continued till 3 months after surgery.

## RESULTS

In our study of 136 patients 97 were males (66.91%) and 39 were females (28.67%). 78.67% patients were diagnosed with AIFRS in relation to COVID-19 infection. All patients were diagnosed in the recent post

COVID-19 infection period, with maximum patient 52.20% affected after 1 week of COVID infection.

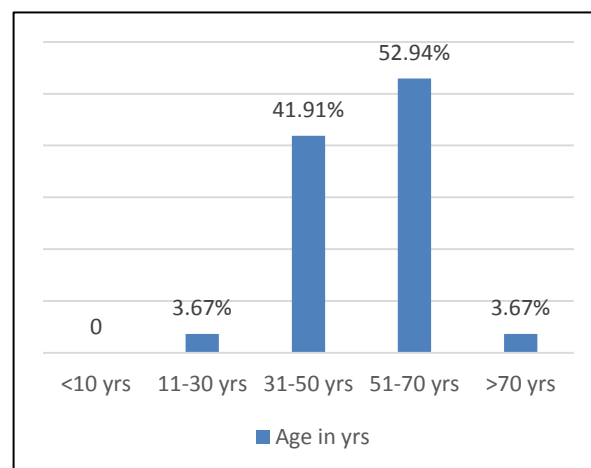


Figure 1: Age distribution of patients.

Table 1: Demographic data, associated comorbidities and histopathological evaluation.

Variable	No.	Percentage
<b>Total cases</b>	136	100
<b>Sex (male/females)</b>	97    39	71.32    28.67
<b>Comorbidities</b>		
Diabetes mellitus	74	54.41
Hypertension	25	18.38
Chronic kidney disease	14	10.29
Hypothyroid	3	2.20
Renal transplant	2	2.94
Cardiac	2	2.94
Meningioma	1	0.7

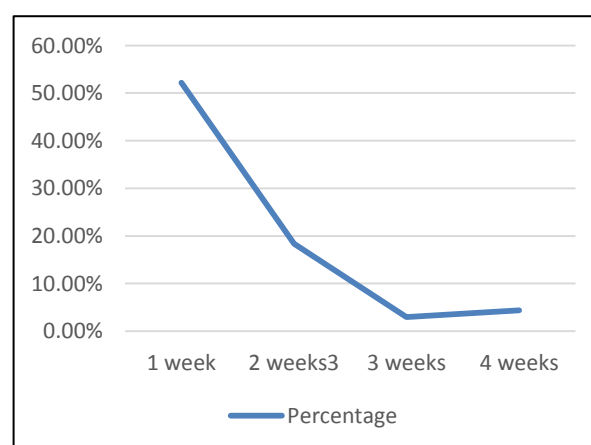


Figure 2: Interval between discharge from covid ward and onset of AIFRS symptoms.

The maximum no. of patients were in 51-70 age group i.e., 52.94%, followed by 41.91% in the age group of 31-

50 years. Demographic data associated co-morbidities is mentioned in table 1.

**Table 2: Data of clinical features, symptoms of AIFRS.**

Presenting complaints	No. of patients	Percentage
Facial Pain	91	66.91
Facial Swelling	22	16.17
Nasal obstruction/discharge	57	41.91
Palatal involvement	62	45.58
Dental pain	49	36.02
Headache	38	27.94
Diminution of vision	24	17.64
Proptosis	18	13.23
Diplopia	8	5.88
Altered sensorium	3	2.21
Change in voice	1	0.73
Giddiness	1	0.73
Skin involvement	1	0.73

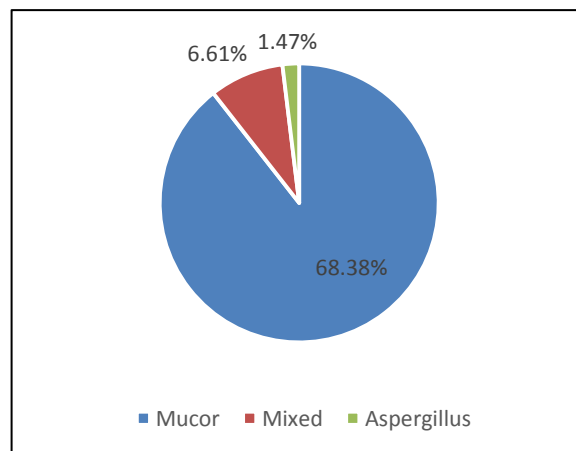


**Figure 2: MRI contrast scan showing fungal granuloma in left anteromedial temporal lobe and mucosal thickening in bilateral sphenoid sinus.**

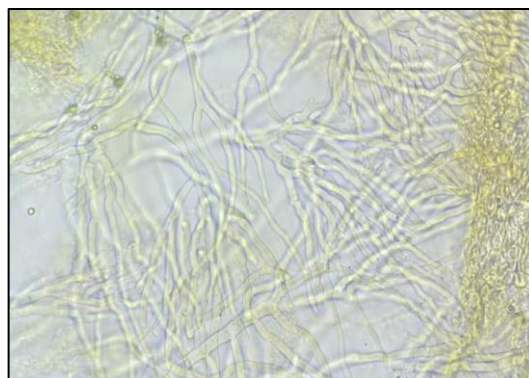
The most common associated comorbidity was diabetes mellitus seen in 74 patients, out of which 21 patients had recent onset DM caused after corticosteroid treatment given during COVID-19 treatment. Other associated comorbidities were hypertension (18.38%), chronic kidney disease (10.29%), for whom regular nephrologist consultation was taken. Four Patients of chronic renal disease were on dialysis, out of which 2 patients had history of renal transplant. In our study 21.32% patients were covid negative with no history of any COVID admission but were diagnosed to be comorbid with uncontrolled diabetes mellitus.

In current study maximum patients presented with features within 1 week (52.20%), out of which 24 patients were with active COVID infection (17.64%). In study of Selarka et al mean time elapsed from COVID-19

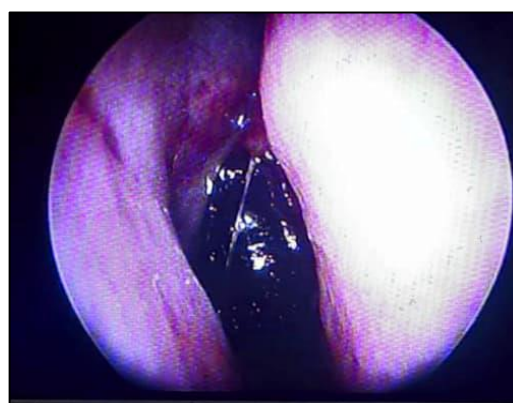
diagnosis to mucormycosis was 12.1±4.6 days, and eleven (23.4%) subjects succumbed to their disease, mostly (n=8, 72.7%) within 7 days of diagnosis.<sup>4</sup>



**Figure 3: Histopathological evaluation.**



**Figure 4: Microbiological view of Mucor showing broad aseptate hyphae.**



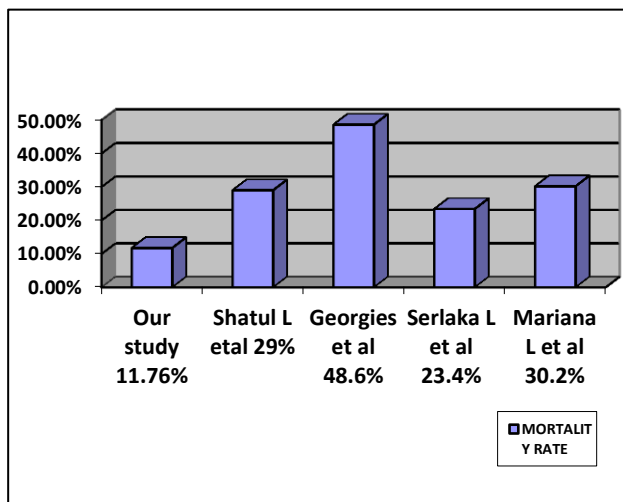
**Figure 5: Endoscopic view of mucormycosis, also known as 'Black Fungus', showing necrosed middle turbinate.**

Out of 136 patients, 107 patients (78.67%) were documented positive for covid.88 patients (64.70%) were on Steroid treatment and 9 patients in our study had received the covid vaccine out of which 4 patients had

taken one dose only. In study of Selarka et al, majority suffered from diabetes mellitus (n=36, 76.6%). Most were not COVID-19 vaccinated (n=31, 66.0%).<sup>4</sup>



**Figure 6: Clinical presentation of mucormycosis showing palatal necrosis.**



**Figure 7: Comparison of mortality rates in various studies.**

Once AIFRS is suspected, a nasal endoscopy is essential to evaluate the signs of fungal involvement. Pale mucosae, ulcers, and granulation are present in up to 75% of patients examined by endoscopy.<sup>5</sup> Endoscopic findings and MRI contrast scan showed various stages of sinonasal (100%), palatine (39.70%) orbital (35.29%), and cerebral (13.23%), involvement. MRI with gadolinium contrast is necessary in order to rule out the suspected invasion of paranasal sinus fungal ball to the surrounding structures, such as cavernous sinus, intraorbital and intracranial compartments, or remodelled bony walls.<sup>6</sup> On MRI images, fungal ball usually appears as an intrasinus mass that is iso- or hypointense on T1-w and markedly hypointense on T2-w. The lowered signal intensity on T2-w, which can extend as far as to a signal void, is caused both by high iron and manganese concentrations and the presence of calcium under the form of microcalcifications, which have all been noted as the characteristic features of AFRS.<sup>7,8</sup> The contents of

calcium and heavy metals, such as iron, zinc, and manganese, within fungal hyphae most prominently affect the appearance of FB on both CT and MRI imaging.<sup>9</sup>

In our study, maximum patients presented with complaints of facial pain (66.91%), palatal changes were seen in 45.58% patients, dental pain in 36.02%. Patients with orbital involvement had complaints of pain and sudden diminution of vision (17.64%), proptosis in 13.23% patients. Three patients presented with altered sensorium because of intracranial extension of disease, and one presented with change in voice due to laryngeal involvement. One case had necrosis of cheek area where skin involvement was seen.

Controversy remains regarding the classification of fungal rhinosinusitis, however the most accepted categorization of this entity was proposed by deShazo et al who differentiated fungal rhinosinusitis into non-invasive and invasive forms based on histopathological findings.<sup>10</sup> Histopathological evaluation of mucosal biopsies in our study confirmed that the main causative fungi were *Mucor* species in 68.38% and *Aspergillus fumigatus* in 1.47% while nine patients (6.61%) were infected with both. The remaining 32 patients (23.52%) were negative on hematoxylin and eosin staining, periodic acid Schiff, Gomori and methenamine silver staining for mucormycosis, but were strongly positive, clinically and radiologically. Histopathological evaluation of these patients who were negative for mucor showed abundant necrosis, osteomyelitis of bone and inflammation, however their tooth scrapings were positive for fungal element.

Mycological tissue culture is also helpful in evaluating AIFRS as it can determine the fungi species and direct the antifungal drug sensitivity. However, it does not show invasiveness of mucosa and, therefore, cannot establish the definitive diagnosis of AIFRS.

Moreover, it usually takes a minimum of 7-21 days to obtain the results, and a significant number of negative results is expected.<sup>11,12</sup>

In current study the commonest predilection was lateral nasal wall with maxillary involvement (82.11%) with ethmoid (78.86%) and sphenoid (61.6%) sinuses being the most commonly affected sinuses. Orbital involvement showed evidence of subperiosteal abscess in 14 patients (10.29%), extension of inflammation giving symptoms of orbital apex syndrome (21.79%). Among 18 patients with intracranial extension, 7 patients had cavernous sinus thrombosis, 3 cases had involvement of anteromedial temporal lobe, Clivus along with meckels cave was involved in 3 cases, fronto parietal lobe along with involvement of cortical and subcortical region enhancement in three patients. One patients had involvement of left cerebellar hemisphere with edema of 4th ventricle.

Injection liposomal amphotericin B was given to all patients with an induction dose ranging from 5-10 mg/kg till a cumulative dose of 2.5 gm and further till clinical and radiological clearance of disease and also according to extent of disease, along with nephrologist consultation and regular monitoring of serum creatinine and serum electrolytes. All patients were discharged on tablet Posaconazole till post op biopsy negative for fungal element. Surgical approach was purely endoscopic in 78 patients, combined endoscopic and open approaches were utilized in the remaining 58 patients. Debridement of necrotic tissues is important in AIFRS patients since the removal of devitalized tissue increases the ability of antifungal drugs to reach infected areas, reducing the fungal burden and slowing the progression of the disease. Also, this action is not only local, since it reduces the stress on the development of neutrophils, facilitating bone marrow recovery.<sup>13</sup>

Endoscopic Debridement included resection of the middle turbinate, wide middle meatal antrostomy, ethmoidectomy, sphenoidotomy, and modified denkers approach in some cases according to the involved sinuses. Orbital involvement in this case series was managed by a wide variety of surgical approaches including endoscopic evaluation of subperiosteal abscess, orbital decompression. Neurosurgery was consulted for operative intervention in the cases of intracranial extension. Palatal necrosis was managed by maxillectomy according to extension of disease and necrosis. Skin necrosis due to invasive fungal infection was managed by debridement only.

Overall survival in our study was 88.23%. Sixteen patients succumbed (11.76%), out of which 2 patients had extensive intracranial extension. Redebriement was needed in 24 patients, out of which 4 patients needed multiple debridement.

## DISCUSSION

Mucormycosis is opportunistic fungal infection characterized by infarction and necrosis of host tissues that results from invasion of the vasculature by hyphae.<sup>1</sup> Tissue necrosis, often a late sign, is a hallmark of mucormycosis, resulting from angioinvasion and vascular thrombosis. The fungi responsible for mucormycosis belong to the order Mucorales and are saprobes found in decaying matter and soil. The fungal sporangiospores enter the human body mainly by inhalation and less commonly by ingestion or direct inoculation. The large spores (example- *Rhizopusarrhizus*) commonly settle in the upper respiratory tract, while the smaller spores (for instance, *Cunninghamella*) reach the lower respiratory tract.<sup>14</sup>

The present study was carried out in department of Ear Nose Throat, Government Medical College, Akola from February 2021 to august 2021. The main purpose of this study was to evaluate the different clinical, radiological

features, and the outcome of prompt surgical intervention along with antifungal treatment. *Aspergillus* and *Mucorales* account for the majority of cases of AIFRS. COVID19 associated the onset of diabetes, and diabetic ketoacidosis (DKA) has been precipitated in newly diagnosed diabetes following COVID-19. Severe COVID-19 increases insulin resistance through enhanced secretion of stress hormones (cortisol and others) and cytokines.<sup>15</sup> The most common clinical presentation of mucormycosis is rhino-orbital-cerebral infection, believed to be secondary to inhalation of spores into the paranasal sinuses of a susceptible host.<sup>16</sup> Studies on SARS-CoV and SARS-CoV-2 have shown that both viruses belong to the same species and have similar biological and clinical characteristics.<sup>17</sup> In immunocompromised patients, these fungi can be angioinvasive, resulting in thrombosis and ischemia of the nasal mucosa.<sup>18</sup> In our study we found predominance of mucorale species in 93 patients (68.38%), and *aspergillus* was found 2 patients (1.47%), whereas mixed species was found in 9 patients (6.61%). Kasapoglu et al also reported a predominance of Mucorale involvement.<sup>19</sup> The conventional risk factors for invasive mold infections include neutropenia, hematological malignancies, solid organ transplantation, hematopoietic stem cell transplant, immunosuppressive therapies targeting T-cells (calcineurin inhibitors, tumor necrosis factor inhibitors, lymphocyte-specific monoclonal antibodies, prolonged use of corticosteroids at a dose of 0.3 mg/kg for 3 weeks in the past two months, and certain inherited immunodeficiency diseases.<sup>20</sup>

In present study most common associated comorbidity was Diabetes mellitus seen in 54.41% patients, out of which 15.44 % were recently diagnosed with diabetes mellitus after use of corticosteroid in covid infection. Diabetes mellitus was the most common underlying risk factor for Covid 19 associated mucormycosis in India than in other countries.<sup>2</sup> In other pre-COVID pandemic studies, the most common concomitant disease was also DM.<sup>21,22</sup> Diabetes mellitus is a risk factor for severe COVID-19 and is associated with increased mortality due to COVID-19.<sup>23</sup> Diabetes impairs innate immune function by impairing phagocytic function, which significantly improves following glycemic control.<sup>24,25</sup> Further, impaired dendritic cell responses delay the timely activation of adaptive immune responses.<sup>26</sup> Many fungal species, *Rhizopus*, *Mucor*, *Rhizomucor* and *Aspergillus*, were reported to cause AIFR.<sup>27</sup> Most studies reported mainly the Mucorales species.<sup>21,28</sup>

In current study, most of the patients had complaints of facial pain (66.91%), palatal changes (45.58%), nasal obstruction (41.91%), dental pain (36.02%), diminution of vision (17.64%), proptosis (13.23%), facial swelling (16.17%). Ketenci et al reported fever, facial edema, facial pain, and nasal obstruction as the most frequent symptoms.<sup>29</sup> In study of Werthman-Ehrenreich et al seventy percent of rhino-orbital-cerebral mucormycosis cases have been found to be in patients with diabetes

mellitus, most of whom had also developed ketoacidosis at the time of presentation.<sup>1</sup> Infection usually presents with acute sinusitis, fever, nasal congestion, purulent nasal discharge and headache. All the sinuses become involved, and contiguous spread to adjacent structures such as the palate, orbit, and brain results in clinical symptoms.<sup>1</sup>

Orbital compartment syndrome (OCS) results from an expansile process within the closed compartment of the orbit leading to increased orbital pressure, and potentially resulting in ischemia and vision loss.<sup>1</sup> This diagnosis should be suspected in patients presenting with acute proptosis, elevated intraocular pressure, sudden vision loss, ophthalmoplegia, fixed dilated pupil or afferent papillary defect. Causes of OCS can be retrobulbar hemorrhage (from trauma, vascular malformations, tumors), cellulitis or other infection, orbital malignancy, or previous orbital surgery.<sup>30</sup> In current study orbital involvement and intracranial extension were seen 35.29% and 13.97% patients, most of whom had uncontrolled diabetes mellitus. A multi-disciplinary approach was taken for patients with involvement of orbit and palate along with senior ophthalmologist and oro maxillofacial surgeon, and radiological. Transcutaneous retrobulbar inj Amphotericin B was given in all acute invasive fungal rhinorbital sinusitis by ophthalmologist. Improvement was seen in 30.14% cases after orbital decompression endoscopically. Orbital and intracranial extension is associated with an increased risk of death. In study of Payne et al 32.5% of patients needed at least one revision surgery.<sup>31</sup> Whereas in our current study revision debridement was needed in 17.64% cases, and multiple re-debridement were needed in 2.94%. These patients were had other associated comorbidity like uncontrolled DM, multisystem involvement.

Mortality has been reported to range from 20% to 68% in previous studies.<sup>32,33</sup> In our study mortality rate was found to be 11.76%. The fatality rate of cases reported from India (36.5%) was less than the globally reported cases (61.9%), probably due to the predominance of rhino-orbital mucormycosis.<sup>2</sup> According to The US Centre for Diseases Control and Prevention

(CDC), an overall all-cause mortality rate of 54% was reported for mucormycosis. The global mucormycosis case fatality rate is 46 percent.<sup>34</sup>

The mortality rate depends upon the underlying condition of the patient, fungus type, and affected site in the body (for example, the mortality rate reported was 46% for patients with sinus infections, 76% for pulmonary infections, and 96% for disseminated mucormycosis).<sup>35</sup>

#### **Limitations of study**

This study is limited to patients admitted in our tertiary care centre. The pathophysiology of AIFRS in non-diabetic patients, non-hospitalised covid patients with no

history of systemic corticosteroids use also remains unclear and needs further research.

#### **CONCLUSION**

Early diagnosis and treatment are essential, as a delay of even 6 days is associated with a doubling of 30 day mortality from 35% to 66%. A Histopathological study facilitates the confirmation of diagnosis, however frozen section biopsy is more desirable for early intervention and management of AIFRS. The difficulty and delay in diagnosing Mucormycosis affects the outcome of the disease and may lead to poor prognosis because of its high invasiveness and its intrinsic low susceptibility to antifungal agents. Therefore, early diagnosis and treatment are necessary. Prompt early surgical debridement with adequate dosage of liposomal Amphotericin B, facilitates early discharge and prevent fatal complications.

#### **ACKNOWLEDGEMENTS**

As it is said that, gratitude, when expressed in words, it's only half its acknowledgement. Having searched extensively through the pages of theaurus and oxford, I could not find the words to express my thanks with a great sense of gratitude to my respected teacher and guide Dr. Apurva Pawde, Professor and Head, Department of ENT; Dr Rajeshree Chaurpagar, Associate Professor, under whose guidance and supervision, I had the opportunity to carry out this work. I am also grateful to Dr Parag Doifode, Assistant Professor, Dr. Bhagyashree Chiplunkar, Assistant Professor, for their constant support and encouragement, Dr Mohammed Badaral Muneer, PG Resident for providing a helping hand which led to completion of this work. I bow in gratitude to The almighty God for inspiring me for this humble attempt to publish the article and serve the society.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

#### **REFERENCES**

1. Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. *The American journal of emergency medicine.* 2021;42:264-e5.
2. Selarka L, Sharma S, Saini D, Sharma S, Batra A, Waghmare VT, Dileep P et al. Mucormycosis and COVID- 19: An Epidemic within a Pandemic in India. *Mycoses.* 2021;40:221-4.
3. Jeong W, Keighley C, Wolfe R. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. *Clin Microbiol Infect.* 2019;25:26-34.
4. Selarka L, Sharma S, Saini D, Sharma S, Batra A, Waghmare VT, Dileep P et al. Mucormycosis and

- COVID 19,an epidemic within a pandemic in India. *Mycoses.* 2021;12(3):110-3.
5. Gillespie MB, O'Malley BW, Francis HW. An approach to fulminant invasive Fungal rhinosinusitis in the immunocompromised host. *Arch Otolaryngol Head Neck Surg.* 1998;124:520.
  6. Zinreich SJ, Kennedy DW, Malat J, Curtin HD, Epstein JI, Huff LC et al. Fungal sinusitis: diagnosis with CT and MR imaging. *Radiology.* 1988;169:439-44.
  7. Aribandi M, McCoy VA, Bazan C 3rd. Imaging features of invasive and noninvasive fungal sinusitis: a review. *Radiographics.* 2007;27:1283-96.
  8. Reddy CE, Gupta AK, Singh P. Imaging of granulomatous and chronic invasive fungal sinusitis: comparison with allergic fungal sinusitis. *Otolaryngol Head Neck Surg.* 2010;143:294-300.
  9. Nicolai P, Lombardi D, Tomenzoli D, Villaret AB, Piccioni M, Mensi M et al. Fungus ball of the paranasal sinuses: experience in 160 patients treated with endoscopic surgery. *Laryngoscope.* 2009;119:2275-79.
  10. deShazo RD, O'Brien N, Chapin K, Soto-Aguiar M, Gardner L, Swain R. A new classification and diagnostic criteria for invasive fungal sinusitis. *Arch Otolaryngol Head Neck Surg.* 1997;123:1181-8.
  11. Ghadiali MT, Deckard NA, Farooq U, Astor F, Robinson P, Casiano RR. Frozen-section biopsy analysis for acute invasive fungal rhinosinusitis. *Otolaryngol - Head Neck Surg.* 2007;136:714-9.
  12. Badiie P, Moghadami M, Rozbehani H. Comparing immunological and molecular tests with conventional methods in diagnosis of acute invasive fungal rhinosinusitis. *J Infect Dev Ctries.* 2016;10:90-5.
  13. Gillespie MB, O'Malley BW. An algorithmic approach to the diagnosis and management of invasive fungal rhinosinusitis in the immunocompromised patient. *OtolaryngolClin North Am.* 2000;33:323-33.
  14. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. *ClinMicrobiol Rev.* 2000;13(2):236-301.
  15. Affinati A, Wallia A, Gianchandani R. Severe hyperglycemia and insulin resistance in patients with SARS-Cov-2 infection: a report of two cases. *Clin Diabetes Endocrinol.* 2021;7(1):8.
  16. Cox G (2020)Mucormycosis Up To Date (8).
  17. Peeri NC, Shrestha N, Rahman MS, et al. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? *Int J Epidemiol.* 2020;49:717-26.
  18. Valera FC, do Lago T, Tamashiro E, Yassuda CC, Silveira F, Anselmo-Lima WT. Prognosis of acute invasive fungal rhinosinusitis related to underlying disease. *International Journal of Infectious Diseases.* 2011;15(12):e841-4.
  19. Kasapoglu F, Coskun H, Ozmen OA, Akalin H, Ener B. Acute invasive fungal rhinosinusitis: evaluation of 26 patients treated with endonasal or open surgical procedures. *Otolaryngol Head Neck Surg.* 2010;143:614-20.
  20. Donnelly JP, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, et al. Revision and update of the consensus definitions of invasive fungal disease from the European organization for research and treatment of cancer and the mycoses study group education and research consortium. *Clin Infect Dis.* 2020;71(6):1367-76.
  21. Bellazreg F, Hattab Z, Meksi S. Outcome of mucormycosis after treatment:report of five cases. *New Microbes New Infect.* 2015;6:49-52.
  22. Vaezi A, Moazeni M, Rahimi MT, de Hoog S, Badali H. Mucormycosis in Iran: a systematic review. *Mycoses* 2016;59:402-15.
  23. Guan W, Liang W, Zhao Y, Liang H, Chen Z, Li Y, et al. Comorbidity and its impact on 1590 patients with Covid19 in China: a nationwide analysis. *EurRespir J.* 2020;55(5):2000547.
  24. Shodja M, Knutsen R, Cao J, Oda K, Beeson L, Fraser G, et al. Effects of glycosylated hemoglobin levels on neutrophilic phagocytic functions. *Jacobs J DiabetesEndocrinol.* 2017;8(2):9-16.
  25. Lecube A, Pachon G, Petriz J, Hernandez C, Simo R. Phagocytic activity is impaired in type 2 diabetes mellitus and increases after metabolic improvement. *PLoS ONE.* 2011;6(8):E23366.
  26. Hodgson K, Morris J, Bridson T, Govan B, Rush C, Ketheesan N. Immunological mechanisms contributing to the double burden of diabetes and intracellular bacterial infections. *Immunology.* 2015;144(2):171-85.
  27. Bakhshae M, Bojdi A, Allahyari A. Acute invasive fungalrhinosinusitis: our experience with 18 cases. *Eur Arch Otorhinolaryngol.* 2016;273:4281-87.
  28. Saedi B, Sadeghi M, Seilani P. Endoscopic management of rhinocerebralmucormycosis with topical and intravenous amphotericin B *J LaryngolOtol.* 2011;125:807-10.
  29. Ketenci I, Ünlü Y, Kaya H. Rhinocerebralmucormycosis: experience in 14 patients. *J LaryngolOtol.* 2011;125:e3.
  30. Stiff H, Chung A. Orbital compartment syndrome curriculum. *Eyerounds.* 2020. Accessed on 25 July 2020.
  31. Payne SJ, Mitzner R, Kunchala S, Roland L, McGinn JD. Acute invasive fungal rhinosinusitis: a 15-year experience with 41 patients. *Otolaryngol – Head Neck Surg.* 2016;154:759-64.
  32. Parikh SL, Venkatraman G, DelGaudio JM. Invasive fungal sinusitis: a 15-year review from a single institution. *Am J Rhinol.* 2004;18:75-81.
  33. Talbot GH, Huang A, Provencher M. Invasive aspergillusrhinosinusitis in patients with acute leukemia. *Rev Infect Dis.* 1991;13:219-32.

34. Chamilos G, Lewis RE, Kontoyiannis DP. Delaying amphotericin B-based frontline therapy significantly increases mortality among patients with hematologic malignancy who have zygomycosis. *Clin Infect Dis.* 2008;47:503-9.
35. Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Foodborne, Waterborne, and Environmental Diseases (DFWED). Available at:

<https://www.cdc.gov/ncezid/dfwed/index.html>.  
Accessed on 17 May 2021.

**Cite this article as:** Chaurpagar R, Garud P, Pawde A, Doifode P, Chiplunkar B, Muneer MB. Clinicoepidemiological study of acute invasive fungal rhinosinusitis in a tertiary care centre. *Int J Otorhinolaryngol Head Neck Surg* 2021;7:1772-9.