

# Fungal Rhinosinusitis: Study of Risk Factors, Outcome and Utility of Nasal Samples in Its Diagnosis

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## ABSTRACT

**Background and Aim:** Fungal rhinosinusitis (FRS) sets in following the interactivity of fungi with Sino nasal tract when the immune system is subdued. Due to the varied clinical presentation of FRS with inconclusive evidence of imaging, mycological evaluation helps to identify and speciate the fungi. Fungal rhinosinusitis can be diagnosed with biopsy tissue and/or deep nasal swabs. This study was undertaken to know risk factors, and outcomes along with the utility of nasal samples with emphasis on deep nasal swabs in diagnosing fungal rhinosinusitis.

**Materials and Methods:** A retrospective observational study was carried out on patients with suspected fungal rhinosinusitis (invasive and non-invasive). Both COVID-19-positive and -negative subjects tested by RT-PCR were included. Brief clinical history, associated comorbidities, risk factors, and outcomes were noted in these cases. Nasal swabs or tissue samples from endoscopic biopsy obtained from patients were subjected to Gram stain, KOH mount, and culture on Sabouraud dextrose agar followed by slide culture for identification.

**Results:** Of the 41 cases studied for FRS, 25 were males and 16 were females. Risk factors like post-COVID-19 infection was seen in 27 (65.8%), diabetes in 31 (75.6%), and use of steroid during COVID-19 treatment in 16 (39.02%) cases. Deep nasal swabs were received in 29 (70.7%) and tissue obtained after debridement in 12 (29.3%) cases. *Rhizopus* spp. was the most common fungi isolated followed by *Aspergillus* spp.

**Conclusion:** Both COVID and non-COVID patients were diagnosed with invasive/ non-invasive fungal rhinosinusitis from deep nasal swabs/tissue in the present study. Diabetes was an important comorbidity in non-COVID patients with FRS. Deep nasal swabs aided early diagnosis for both invasive and non-invasive FRS.

**Keywords:** COVID-19, Diagnostic Nasal Endoscopy, Deep Nasal Swabs, Fungal Rhinosinusitis, Mucormycosis

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## 1. Introduction

Fungal rhinosinusitis (FRS) is an inflammatory condition involving paranasal sinus mucosa due to fungi (1). It can be classified broadly into two categories namely non-invasive when confined to superficial epithelium and invasive when fungal hyphae develop potential for tissue/blood vessel invasion (2, 3). The non-invasive group includes saprophytic colonization, fungal balls, and allergic fungal rhinosinusitis (AFRS) whereas Invasive FRS may

be acute/chronic/granulomatous (1, 4). Predisposing risk factors for FRS include uncontrolled diabetes mellitus, immunodeficiency (neutropenia, AIDS), patients with stem cell transplant or solid organ transplant, and those who are on immunosuppressive therapy for various diseases (5, 6). *Aspergillus* species are usually responsible for non-invasive FRS cases (7). Noteworthy among the invasive ones are rhino-orbito-cerebral mucormycosis/ zygomyces (ROCM),

a life-threatening fungal infection caused by Order *Mucorales* belonging to class *Zygomycetes* followed by *Aspergillus* spp (8, 9). The most common warning signs of FRS include facial pain, nasal pain/ stuffiness, eye pain, worsening headache, nasal discharge which can be bloody, foul smelling, eyelid edema/ facial edema, eyelid/ periorbital/ facial discoloration which can be blackish or bluish, proptosis/ ptosis causing change in visual acuity, sudden loss of vision, restricted eye movement, diplopia or even fever, disorientation, seizures, or paralysis (10, 11). Clinical suspicion along with radiological, microbiological, and histopathological diagnosis prompts early treatment in patients suspected of invasive FRS specifically as it is associated with poor outcomes if surgical intervention is not done along with antifungal medication (12).

FRS, predominantly caused by fungi of the order *Mucorales* was brought to the limelight during the pandemic caused by the SARS-CoV 2 virus contributing to high morbidity and mortality not only by the virus itself but also due to associated comorbidities and steroid therapy in COVID-19 disease, resulting in further immunosuppression (2, 9, 13). There was a surge in fungal co-infections in patients with COVID-19 which was attributed to *Aspergillus* spp, *Candida* spp, *Cryptococcus* spp., and *Mucorales* (14). Around 14,872 cases of mucormycosis were reported in India by May 28, 2021 (15).

Diagnostic modalities include CT and MRI scans of paranasal sinuses (CT-PNS) along with diagnostic nasal endoscopy (DNE) for nasal biopsy (tissue)/ Swab collection (16). On clinical suspicion, the first diagnostic modality on a patient when FRS is suspected is CT-PNS followed by endoscopic evaluation of the nasal cavity and sinuses. A computed tomography (CT) scan/ Magnetic resonance imaging (MRI) helps to evaluate mucosal soft tissue edema, mucoperiosteal thickening in the sinus, bone erosions, and invasion of fungi into the orbit/brain (17). DNE helps to examine for tissue necrosis, the color of the nasal mucosa, and blackish eschar in turbinates followed by sample collection. The highest yield, along with the greatest accuracy, for presumptive diagnosis is obtained when a biopsy sample is taken from the middle turbinate (18). Deep nasal swabs can also be collected when fungal rhinosinusitis/ ROCM is suspected (19). Advantages of these deep nasal swabs include simultaneous collection during diagnostic endoscopy itself on an outpatient basis thereby avoiding patient admission which is required for nasal (biopsy) tissue collection. Microscopic evaluation including Potassium hydroxide (KOH) mount/ Gram stain and culture can also be done from these swabs, but histopathological examination is not possible as no tissue is available. Deep nasal swabs have also been

tried in many centers for sample collection in suspected FRS/ROCM due to the ease involved in the collection (20-22). A deep nasal swab is performed by inserting the swab deep into one nostril into the middle nasal meatus. The swab is collected under endoscopic guidance with gentle rotation at the middle meatus (until resistance is felt at the turbinate), as the opening of most sinuses is at semilunar hiatus which is anatomically located in the middle nasal meatus (23, 24).

There is a dearth of knowledge regarding the utility of deep nasal swabs for diagnosing suspected cases of invasive/ non-invasive fungal rhinosinusitis. Hence the present study was undertaken to analyze the usefulness of nasal samples (tissue and deep nasal swabs) for diagnosing fungal rhinosinusitis caused by fungi of order *Mucorales* or other fungal genera.

Therefore the aims of this study was 1. To know the role of nasal samples along with the utility of deep nasal swabs aiding in early diagnosis of fungi of order *Mucorales*/ other fungal genera in suspected cases of fungal rhinosinusitis along with risk factors and outcome. 2. To study the risk factors and outcome of these patients in relation to fungal isolates obtained from deep nasal swabs.

## 2. Materials and Methods

The present study was conducted at the Department of Microbiology (Mycology section) at Mamata General and Super Specialty Hospital affiliated with Mamata Medical College and Hospital, Khammam, Telangana. The study was conducted for a period of 1 year from June 2021 to June 2022 year after due to ethical committee clearance (IEC/IRB:19/22). This was a retrospective study on samples obtained from patients suspected of fungal rhinosinusitis.

### Inclusion and Exclusion Criteria for Study Participants

Deep nasal swabs or tissue received from patients suspected of fungal rhinosinusitis were included in the study. All other clinical samples like bronchoalveolar lavage, sputum, tracheal aspirates, Endotracheal secretions, and blood that were received for infections other than FRS were excluded from the study. COVID-19 infection from the patient records were cross-checked with RTPCR reports and data available from the Molecular laboratory attached to Mamata Medical College.

Clinical records of patients from Outpatient (OPD) / in-patient (IPD) departments and Intensive care unit (ICU) were noted. Patient data and relevant clinical

history were recorded. Associated comorbidities like Diabetes mellitus, COVID-19 status, use of steroids, immunosuppression, iron-chelation therapy, neutropenia, solid organ transplant, chronic kidney disease, chronic alcoholism, chronic respiratory disease, stem cell transplantation, and HIV status were noted.

#### Protocol at the Tertiary Care Center for Diagnosing FRS

Patients were suspected of fungal rhinosinusitis when one of the following symptoms and signs were present: facial pain, postnasal drip, nasal pain/stiffness, eye pain, worsening headache, nasal discharge, eyelid edema/ facial edema, eyelid/ periorbital/ facial discoloration, proptosis/ ptosis causing changes in visual acuity, sudden loss of vision, restricted eye movement. Relevant investigations like Computerised tomography (CT) scan of the paranasal sinuses (PNS) and Magnetic resonance imaging (MRI) scan were obtained. CT findings suggestive of fungal rhinosinusitis included intralesional hyperdensity or calcification within an opacified sinus/ Bone erosion or expansion/ mucosal thickening in an asymmetric fashion, and invasion of the fat surrounding the maxillary antrum for sinus involvement. MRI scan was done for invasive cases when extension into tissues/ brain/ orbit was suspected.

They were then subjected to diagnostic nasal endoscopy. Indications for collection of deep nasal swabs included inflamed/ crusted nasal mucosa, purulent discharge/ oedematous mucosa, and blackish crusts/ eschar not extending into sinuses during endoscopy itself. Tissue was collected when invasion was noted, which included blackish crusts/ eschar/ septal perforation/ mass (polyp) in the nasal cavity or paranasal sinuses after patient admission.

#### Mycological Evaluation

To confirm the clinical/ radiological findings of FRS, deep nasal swabs and tissue samples were obtained. Both the samples were then subjected to gram stain, 10% KOH mount, and culture on Sabouraud dextrose agar (SDA). Mucormycosis was identified by the presence of broad, ribbon-like aseptate/pauci-septate hyphae with right-angled branching on KOH mount/Gram stain. Non-Mucorales were identified by the presence of narrow, septate hyphae with acute angled branching. Preliminary reports of KOH mount and gram stain findings were issued and communicated to consultants telephonically. The fungus was further identified by growth on SDA slants kept at 37°C and 25°C by noting colony characteristics on the obverse and reverse for pigmentation. Slide

culture was performed for further species identification.

Thus, for this retrospective study, a diagnosed case of FRS was when clinical/ radiological and microbiological (microscopy and culture) findings were met in the case of nasal swab samples, for tissue samples, similar findings as for swabs along with histopathological evidence. The treatment and outcome of the patients were checked by medical records or by direct telephonic conversation.

Data was entered in Microsoft Excel sheet 2019. The data was transformed into IBM SPSS software version 26 and analyzed. The data were represented by means, frequency, and percentages. Fisher's exact test with continuity correction was used to analyze categorical data for smaller values. The association was considered statistically significant if the P-value was <0.05.

### 3. Results

A total of 41 cases constituted the present study. Of which 25 (60.9%) were males and 16 (39.1%) were females. The mean age of patients with suspected fungal rhinosinusitis in this study was 51.5 years. Facial pain was the most common presentation seen in 32 (78.04%) cases, followed by facial edema in 24 (58.5%) cases for both mucormycosis and other fungal infections. Headache was seen in 12 (29.2%), facial numbness in 11 (26.8%), palatal discoloration in 9 (21.9%), nasal stuffiness in 8 (19.5%), and blurring of vision in 6 cases (14.6%). Palatal discoloration (75%) and blurring of vision (62.5%) was more common in mucormycosis cases than other fungal infection cases. Risk factors like post-COVID-19 infection was seen in 27 (65.8%) cases, diabetes in 31 (75.6%), and use of steroid during COVID-19 treatment in 16 (39.02%) cases. Most patients presented with symptoms at an average of 46.9 days (range: 21-87) post steroid treatment. 34.2% of cases had no history of COVID-19 infection in the past and mucormycosis was diagnosed in 2 cases among them. Non-Mucorales infection in COVID/non-COVID cases was non-invasive. COVID-19-associated mucormycosis (CAM) could be seen in 25.9 % of patients (7/27). 2 cases had a history of chronic alcoholism, but nasal swabs yielded no fungal growth. Other risk factors like immunosuppression, iron-chelation therapy, neutropenia, solid organ transplant, chronic kidney disease, chronic respiratory disease, stem cell transplantation, and secondary immunodeficiency (HIV) were not seen in our study. Although most patients recovered (80%), outcome was poor in patients diagnosed with Mucormycosis ([Table 1](#)).

**Table 1.** Clinical profile, risk factors, and Outcome of suspected cases of Fungal rhinosinusitis

Suspected cases (n=41)	n	%	Mucormycosis-culture proven (n=8) (%)	Other fungal infections (n=8) (%)	Mixed fungal infection (n=1) (%)
Age in years (mean)	51.5		51.4	51.6	51.5
<b>Sex</b>					
Male	25	60.9	4 (50)	4 (50)	0
Female	16	39.1	4 (50)	4 (50)	1 (100)
<b>Clinical features</b>					
Facial pain	32	78.04	8 (100)	6 (75)	1 (100)
Facial oedema	24	58.5	8 (100)	6 (75)	1 (100)
Headache	12	29.2	3 (37.5)	1 (12.5)	1 (100)
Facial numbness	11	26.8	3 (37.5)	2 (25)	1 (100)
Palatal discoloration	9	21.9	6 (75)	2 (25)	1 (100)
Nasal stuffiness	8	19.5	5 (62.5)	2 (25)	1 (100)
Blurring vision	6	14.6	5 (62.5)	0	1 (100)
<b>Risk factors</b>					
Post-COVID-19 infection	27	65.8	6 (75)	4 (50)	1 (100)
COVID-19 negative	14	34.2	2 (25)	4 (50)	0
Diabetes mellitus	31	75.6	8 (100)	7 (87.5)	1 (100)
H/O Steroid use	16	39.02	6 (75)	4 (50)	1 (100)
<b>Outcome(n=40)</b>					
Recovered	32	80	1 (12.5)	8(100)	0
Expired	8	20	7(87.5)	0	1(100)

**Abbreviations:** H/O- History of.

Of the 41 patients tested, samples received were deep nasal swabs in 29(70.7%) cases and tissue obtained after debridement in 12(29.3%) cases. Overall, fungal growth was reported in 41.4% of cases (17/41) among which mucormycosis could be diagnosed in 19.5% of patients (8/41), other fungal infections in 19.5% (8/41) cases and mixed infection in 2.4% (1/41). The total fungal isolation rate for tissue was 50% (6/12) along with histopathological correlation and for deep nasal swabs, it was 48.2%

(14/29). Mucormycosis could be diagnosed from deep nasal swabs in 24.1% (7/29) cases and from tissue in 16.6% (2/12) cases. Growth was observed in 3 cases from deep nasal swabs but no fungal growth was reported due to the absence of microscopic findings, indicating false positivity of 10.3% (3/29) and none was seen with tissue. Of the total cases, 51.2% (21/41) were negative by microscopy and culture indicating false negatives by both methods (Table 2).

**Table 2.** Distribution of nasal samples showing growth of fungi of order Mucorales/other fungal genera from suspected cases of Fungal Rhinosinusitis

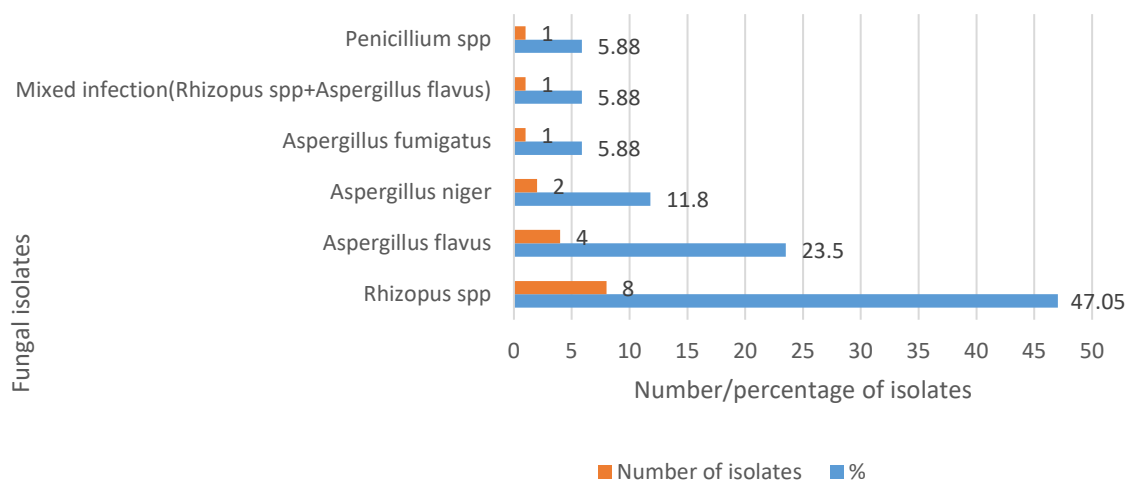
Nasal samples	N (%)	Mucormycosis	Other fungi	Mixed infection	No growth reported		
		MS+ve /C(G)	MS+ve /C(G)	MS+ve /C(G)	MS-ve	C(G)(%)	C(NG)
Deep nasal swabs	29 (70.7)	7	4	0	18	3(10.3%)	15
Tissue	12 (29.3)	1	4	1	6	0	6
<b>Total (%)</b>	<b>41 (100)</b>	<b>8 (19.5%)</b>	<b>8 (19.5%)</b>	<b>1 (2.43%)</b>	<b>24 (58.5%)</b>	<b>3(7.31%)</b>	<b>21(51.2%)</b>

**Abbreviations:** MS-Microscopy (Koh mount and/or Gram stain); MS+ve= Microscopy showed fungal elements; MS-ve= Microscopy showed no fungal elements; C(G)=Culture showed growth of fungal isolate; C(NG)= Culture showed no growth of fungal isolate

Of the total 17 fungi reported from culture, *Rhizopus* spp was isolated in 47.05% (8 cases) and one patient had isolation of *Rhizopus* spp with aspergillosis (mixed infection-5.88%). *Aspergillus flavus* was the next most

common species isolated in 23.5% (4/17) cases, *Aspergillus niger* in 2(11.8%) cases followed by *Aspergillus fumigatus* and *Penicillium* spp in 5.88% (1 case) each (Figure 1). All these 8 cases of non-

Mucorales were diagnosed as non-invasive fungal rhinosinusitis with no cerebral, orbital involvement.



**Figure 1.** Distribution of Fungal isolates grown from nasal samples (Deep nasal swab and Tissue) [n=17]

Of the total 29 deep nasal swabs received, Fisher's exact test with continuity correction showed an insignificant association of gender with the use of deep nasal swabs in isolation of Mucorales/other fungal genera ( $P=0.95$ ). An insignificant association was noted in COVID-19 patients with the use of swabs in isolation of Mucorales/other fungal genera ( $P>0.99$ ). The association was not significant either with diabetic patients /patients on steroid treatment with the use of deep nasal swabs in isolation of

Mucorales/other fungal genera with a P-value of 0.525 and  $>0.99$ , respectively. Among these 29 patients, 1 patient left against medical advice (LAMA) and thus could not be included in the outcome analysis. Of the 28 patients, outcome was significantly associated ( $P=0.041$ ) in isolation of Mucorales from deep nasal swabs, indicating more deaths were associated with patients having mucormycosis compared to other fungal infections (Table 3).

**Table 3.** Association of gender, risk factors, and outcome of patients in relation to fungal isolates obtained from Deep Nasal Swabs.

Suspected cases (n=41)	Deep nasal swabs (n=29)	n (%)	Mucormycosis (n=7)	Other fungal infections (n=4)	p-value <sup>∞</sup>
Sex	Male	20 (69.0)	4	3	0.95
	Female	9 (31.0)	3	1	
COVID status	Positive	20 (69.0)	5	3	$>0.99$
	Negative	9 (31.0)	2	1	
Steroid treatment	Present	12 (41.4)	5	3	$>0.99$
	Absent	17 (58.6)	2	1	
Diabetes mellitus	Present	18 (62)	7	3	0.525
	Absent	11 (38)	0	1	
Outcome (n=28)	Recovered	22 (75.9)	1	4	<b>0.041</b>
	Expired	6 (20.6)	6	0	

<sup>∞</sup> (Fisher's exact test with continuity correction)

#### 4. Discussion

Of the 41 cases studied, 19.5 % had culture-proven rhino-orbito-cerebral infection by *Mucorales* (ROCM) and 19.5% cases had non-invasive fungal rhinosinusitis caused by other fungal genera. Youssif *et al.* (25) reported 8.25% CAM (COVID associated mucormycosis) and Rawson *et al.* (26) found 8% of patients with secondary fungal infection with COVID-

19. Both these studies had less incidence compared to our study (19.5%). This could be due to less sample size in the present study along with the inclusion of COVID negative cases.

Male gender, old age, COVID-19, diabetes, and steroid use had a high risk of developing not only mucormycosis but also other fungal rhinosinusitis

which was seen in the present study. A study done by Aranjani JM *et al.* (9) in 2021 emphasized the significance of the above risk factors like our study. A study done by Shetty S *et al.* (27) in 2022 on invasive aspergillosis of the nose and paranasal sinuses in COVID-19 convalescents had 8 patients with associated comorbidities like diabetes and male preponderance which was similar to the present study. Facial pain (78.04%), facial edema (58.5%) followed by headache (29.2%) was the most common symptom in the present study which is similar to the study done by Abdollahi A *et al.* (28) in 2016 in the pre-COVID era. The present study contrasts a study done by Shetty S *et al.* in 2022 (27) where nasal obstruction and headache was the commonest symptom among patients with *Aspergillus* infections.

Two types of samples were received in the present study which included deep nasal swabs and biopsy-tissue. Of the total 41 samples received maximum were deep nasal swabs (70.7%) followed by tissue samples (29.3%). In a study by Ahirwar S *et al.* (20) in 2021 different samples like swabs, sputum, and BAL were received for diagnosing mucormycosis in post-COVID-19 patients in which 22.8% (8/35) were positive for fungal smear which is similar to the present study where CAM was seen in 25.9% (7/27) cases. In total, 58.5% of cases in our study were reported as having no fungal growth, this could be because non-invasive fungal rhinosinusitis tends to have low fungal growth as reported by few studies (12, 29).

*Rhizopus* spp, *Aspergillus* spp, *Rhizopus* spp with *Aspergillus* spp., and *Penicillium* spp were isolated in the present study from nasal samples (tissue & nasal swabs) received from both COVID-19 positive and COVID-19 negative patients which can be compared to study done by Nazari T *et al.* (30) in 2022 which was a systemic review of 169 patients on COVID-19 associated fungal infections (CAFI) where Mucormycosis, Aspergillosis and Fusariosis were diagnosed. As both COVID-19-positive recovered patients and COVID-19-negative patients were included in our study, we analyzed that these fungal infections in the pandemic era in COVID-19-negative cases were due to another most common risk factor like Diabetes mellitus. In a study done by Chaganti PD *et al.* (31) in 2020, *Aspergillus* spp was the most common cause of fungal rhinosinusitis in non-COVID-19 patients which was seen in the present study also. *Penicillium* spp is also one of the known causes of rhinosinusitis which was seen in our study (32).

In the present study, the utility of deep nasal swabs in isolating *Mucorales* or other fungi concerning gender, COVID-19 status, diabetes mellitus, and steroid use did not contribute to any significant finding but was significantly associated with outcome

( $P=0.041$ ). Most of the patients who were diagnosed with Mucormycosis by microscopy and culture from deep nasal swabs had bad outcomes (prognosis) compared to patients diagnosed with other fungal infections.

The tissue sample obtained for biopsy is the sample of choice for microbiological diagnosis in mucormycosis as it can be subjected to histopathological examination simultaneously to look for tissue invasion. But this requires patient admission. Although 29.3% of tissue samples were received in our study, 50% (6/12) of them showed growth of *Mucorales* or other fungi which was better compared to 37.9% (11/29) growth reported from deep nasal swabs. Deep nasal swabs although not recommended as per many literatures and guidelines are still samples of (33) choice in many institutes due to their ease of collection during DNE and adaptability involved (23, 34, 35). In a study done by Gade N *et al.* (22) in 2022, deep nasal swabs constituted 57% of samples which is less compared to the present study (70.7%).

*Mucor* /*Aspergillus* spores are present widely in the environment. They may exist in healthy individuals as commensals by inhabiting nasal mucosa/ paranasal sinuses, due to their low virulence. When such a patient's immune system is suppressed, they may germinate and spread (6). Fungal growth in culture without microscopic detection of the fungal agent usually indicates false positives as these fungi are known saprophytes (8). In addition to this, swabs collected from non-sterile sites like nasal mucosa can further accentuate diagnostic dilemmas in the absence of microscopic findings due to the non-availability of tissue for histopathology (33). In the present study, 10.3% of false positives were observed from deep nasal swabs from mycological viewpoint and retrospective analysis of cases. The false negative rate from all nasal samples was 51.2%. A study by Watkinson, J.C *et al.* (36) in 2018 showed that the sensitivity of culture in fungal ball/AFRS/Acute invasive fungal rhinosinusitis was low indicating false negatives and they concluded that if fungal cultures were negative, the presence of fungi cannot be ruled out which correlates with the present study.

For invasive FRS, a delay in commencing antifungal therapy can significantly increase the mortality of the patients. As radiological investigations may yield non-specific results, surgical intervention aids in mitigating disease burden, and improves drug bioavailability, limiting it from spreading further. It also has an important role for confirmation of diagnosis as samples can be sent for histopathological and microbiological examination intraoperatively (37). Thorough saline irrigation of sinuses with subsequent follow-up on an OPD basis was done in our study in

most cases without the need for antifungal drugs. Extensive debridement with Liposomal Amphotericin B/ Posaconazole was the drug of choice for mucormycosis and Posaconazole/ Isavuconazole/ Liposomal Amphotericin B along with surgical debridement was the drug of choice for aspergillosis when indicated at our setup (38, 39). The outcome in our patients was poor who were diagnosed with mucormycosis compared to other fungal rhinosinusitis. Management of mucormycosis is often ineffective even after early diagnosis, aggressive medical and surgical management leading to progression of infection and high fatality (6, 40).

This study analyzed nasal samples from both COVID-positive and negative patients, so all suspected cases of fungal rhinosinusitis were taken into consideration. Deep nasal swabs aided in early diagnosis due to rapid microscopy findings along with positive culture results. False positives and false negatives from deep nasal swabs could be identified from this study. As this was a retrospective study with small sample size, the utility of nasal swabs in comparison with tissue could not be done. Relation of fungal isolates with risk factors or outcomes from biopsy-tissue samples could not be attempted again due to the smaller sample size. More studies are thus needed to assess the incidence and prevalence of FRS in COVID or non-COVID patients in this pandemic era along with the utility of deep nasal swabs for diagnosing them.

## 5. Conclusion

This was one of the studies in which both COVID and non-COVID patients were included to diagnose invasive and non-invasive fungal rhinosinusitis from nasal samples. Risk factor like diabetes mellitus was a major

contributor to infections in non-COVID-19 patients. Poor outcome was significantly associated with isolation of mucormycosis obtained from deep nasal swabs. False positives and false negatives could be seen with nasal samples for FRS as the sensitivity of culture is low. In the present study, we observed that deep nasal swabs can be useful samples for expeditious diagnosis of fungal rhinosinusitis on an OPD basis during diagnostic endoscopy itself helping for better patient management.

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## Ethics Approval

The present study was conducted at the Department of Microbiology (Mycology section) at Mamata General and Super Specialty Hospital affiliated with Mamata Medical College and Hospital, Khammam, Telangana. The study was conducted for a period of 1 year from June 2021 to June 2022 year after due ethical committee clearance (IEC/IRB:19/22).

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## Conflict of Interest

The authors declared no conflict of interest.

## Reference

- Monga S, Malik JN, Sharma A, Agarwal D, Priya R, Naseeruddin K. Management of Fungal Rhinosinusitis: Experience From a Tertiary Care Centre in North India. *Cureus*. 2022;14(4):e23826. [DOI:10.7759/cureus.23826]
- Fadda GL, Succo G, Moretto P, Veltri A, Castelnuovo P, Bignami M, et al. Endoscopic Endonasal Surgery for Sinus Fungus Balls: Clinical, Radiological, Histopathological, and Microbiological Analysis of 40 Cases and Review of the Literature. *Iran J Otorhinolaryngol*. 2019; 31(102):35-44.
- Deutsch PG, Whittaker J, Prasad S. Invasive and Non-Invasive Fungal Rhinosinusitis-A Review and Update of the Evidence. *Medicina*. 2019;55(7):319. [DOI:10.3390/medicina55070319] [PMID] [PMCID]
- Chakrabarti A, Denning DW, Ferguson BJ, Ponikau J, Buzina W, Kita H, et al. Fungal rhinosinusitis A categorization and definitional schema addressing current controversies. *Laryngoscope*. 2009;119(9): 1809-18. [DOI:10.1002/lary.20520] [PMID] [PMCID]
- Palanisamy P, Elango D. COVID19 associated mucormycosis: A review. *J Family Med Prim Care*. 2022;11(2):418-23. [PMID] [PMCID] [DOI:10.4103/jfmpc.-jfmpc 1186 21]
- Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post coronavirus disease mucormycosis: a deadly addition to the pandemic spectrum. *Laryngol Otol*. 2021;135(5):442-7. [PMID] [PMCID] [DOI:10.1017-/S0022215121000992]

7. Gupta SK, Singh R, Gupta A. Incidence of Fungal Rhinosinusitis in Bihar and Its Management. *Int J Res Rev.* 2018;5(11):196-201.
8. Chakrabarti A, Das A, Mandal J, Shivaprakash MR, George VK, Tarai B, et al. The rising trend of invasive zygomycosis in patients with uncontrolled diabetes mellitus. *Med Mycol.* 2006;44(4):335-42. [DOI:10.1080/13693780500464930] [PMID]
9. Aranjani JM, Manuel A, Abdul Razack HI, Mathew ST. COVID-19-associated mucormycosis: Evidence-based critical review of an emerging infection burden during the pandemic's second wave in India. *PLOS Negl Trop Dis.* 2021;15(11):e0009921. [DOI:10.1371/journal.pntd.0009921] [PMID] [PMCID]
10. Janjua OS, Shaikh MS, Fareed MA, Qureshi SM, Khan MI, Hashem D, et al. Dental and Oral Manifestations of COVID-19 Related Mucormycosis: Diagnoses, Management Strategies and Outcomes. *J Fungus.* 2021;8(1):44. [DOI:10.3390/jof8010044] [PMID] [PMCID]
11. Ferguson BJ. Mucormycosis of the nose and paranasal sinuses. *Otolaryngol Clin North Am.* 2000;33(2):349-65. [PMID] [DOI:10.1016/S0030-6665(00)80010-9]
12. Chakrabarti A, Chatterjee SS, Das A, Panda N, Shivaprakash MR, Kaur A, et al. Invasive zygomycosis in India: experience in a tertiary care hospital. *Postgrad Med J.* 2009;85(1009):573-81. [DOI:10.1136/pgmj.2008.076463] [PMID]
13. Philip AC, Madan P, Sharma S, Das S. Utility of MGG and Papanicolaou stained smears in the detection of Mucormycosis in nasal swab/scraping/biopsy samples of COVID 19 patients. *Diagn Cytopatho.* 2022;50(3):93-8. [DOI:10.1002/dc.24924] [PMID] [PMCID]
14. Salehi M, Ahmadikia K, Badali H, Khodavaisy S. Opportunistic Fungal Infections in the Epidemic Area of COVID-19: A Clinical and Diagnostic Perspective from Iran. *Mycopathologia.* 2020; 185(4):607-11. [PMID] [PMCID] [DOI:10.1007/s11046-020-00472-7]
15. Raut A, Huy NT. Rising incidence of mucormycosis in patients with COVID-19: another challenge for India amidst the second wave? *Lancet Respir Med.* 2021;9(8):e77. [PMID] [DOI:10.1016/S2213-2600(21)00265-4]
16. Frater JL, Hall GS, Procop GW. Histologic Features of Zygomycosis: Emphasis on Perineural Invasion and Fungal Morphology. *Arch Pathol Lab Med.* 2001;125(3):375-8. [DOI:10.5858/2001-125-0375-HFOZ] [PMID]
17. Sreshta K, Dave TV, Varma DR, Nair AG, Bothra N, Naik MN, et al. Magnetic resonance imaging in rhino-orbital-cerebral mucormycosis. *Indian J Ophthalmol.* 2021;69(7):1915-27. [DOI:10.4103/ijo.IJO\_1439\_21] [PMID] [PMCID]
18. Hernández JL, Buckley CJ. Mucormycosis. [Updated 2020 Jun 26]. *Stat Pearls [Internet] Treasure Island (FL): Stat Pearls Publishing.* 2021.
19. Kewaliya R, Yadav DK, Lunia G, Jangir S. A clinicoepidemiological study of orbital mucormycosis in COVID-19 pandemic at a tertiary healthcare hospital, North-West Rajasthan, India. *Delta J Ophthalmol.* 2022;23(3):213-20. [DOI:10.4103/djo.djo\_6\_22]
20. Ahirwar SS. Emerging cases of mucormycosis in post Covid-19 disease patients. *Indian J Microbiol Res.* 2021;8(3):219-23. [DOI:10.18231/j.ijmr.2021.045]
21. Kumar DSS, Singh R. To evaluate the mucormycosis cases in post Covid-19 patients. *Eur J Mol Clin Med.* 2022;9(3):134-8.
22. Gade N, Nag S, Shete V, Mishra M. Study of Molds in Post COVID -19 Patients: An experience from Tertiary Care Centre. *J Infect Dis Microbiol.* 2022; 1(2):1-7. [DOI:10.37191/Mapsci-JIDM-1(1)-007]
23. Meher R, Wadhwa V, Kumar V, Shisha Phanbuh D, Sharma R, Singh I, et al. COVID associated mucormycosis: A preliminary study from a dedicated COVID Hospital in Delhi. *Am J Otolaryngol.* 2022;43(1):103220. [PMID] [PMCID] [DOI:10.1016/j.amjoto.2021.103220]
24. Hapugoda S, Jones J, Hacking C, et al. Hiatus semilunaris. 2022.
25. Farghly Youssif S, Abdelrady MM, Thabet AA, Abdelhamed MA, Gad MOA, Abu-Elfath AM, et al. COVID-19 associated mucormycosis in Assiut University Hospitals: a multidisciplinary dilemma. *Sci Rep.* 2022;12(1):13443-3. [PMID] [PMCID] [DOI:10.1038/s41598-022-13443-3]
26. Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis.* 2020;71(9):2459-68. [DOI:10.1093/cid/ciaa530] [PMID] [PMCID]
27. Shetty S, Shilpa C, Kavya S, Sundararaman A, Hegde K, Madhan S. Invasive Aspergillosis of Nose and Paranasal Sinus in COVID-19 Convalescents: Mold Goes Viral? *Indian J Otolaryngol Head Neck Surg.* 2022;74(Suppl 2):3239-44. [PMID] [PMCID] [DOI:10.1007/s12070-022-03073-6]



28. Abdollahi A, Shokohi T, Amirrajab N, Poormosa R, Kasiri AM, Motahari SJ, et al. Clinical features, diagnosis, and outcomes of rhino-orbito-cerebral mucormycosis- A retrospective analysis. *Curr Med Mycol.* 2016;2(4):15-23. [PMID] [PMCID] [DOI:10.18869-/acadpub.cmm.2.4.15]
29. Dufour X, Kauffmann-Lacroix C, Ferrie JC, Goujon JM, Rodier MH, Klossek JM. Paranasal sinus fungus ball: epidemiology, clinical features and diagnosis. A retrospective analysis of 173 cases from a single medical center in France, 1989-2002. *Sabouraudia.* 2006;44(1):61-7. [DOI:10.1080/13693780500235728] [PMID]
30. Nazari T, Sadeghi F, Izadi A, Sameni S, Mahmoudi S. COVID-19-associated fungal infections in Iran: A systematic review. *PLoS One.* 2022;17(7):e0271333. [DOI:10.1371/journal.pone.0271333] [PMID] [PMCID]
31. Chaganti P, Rao N, Devi K, Janani B, Vihar P, Neelima G. Study of fungal rhinosinusitis. *J NTR Univ Health Sci.* 2020(9):103-6. [DOI:10.4103/JDRNTRUHS.JDRNTRUHS\_98\_20]
32. Waghay J. Clinical study of fungal sinusitis. *Int J Otorhinolaryngol Head Neck Surg.* 2018;4(5):1307-12. [DOI:10.18203/issn.2454-5929.ijohns20183707]
33. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and Diagnosis of Mucormycosis: An Update. *J Fungus.* 2020;6(4):265. [DOI:10.3390/jof6040265] [PMID] [PMCID]
34. Farmakiotis D, Kontoyiannis DP. Mucormycoses. *Infect Dis Clin.* 2016;30(1):143-63. [DOI:10.1016/j.idc.2015.10.011] [PMID]
35. Gupta MK, Kumar N, Dhameja N, Sharma A, Tilak R. Laboratory diagnosis of mucormycosis: Present perspective. *Fam Med Prim Care Rev.* 2022; 11(5):1664-71. [PMID] [PMCID] [DOI:10.4103/-ifmpc.ifmpc\_1479\_21]
36. Watkinson JC, Clarke RW. *Scott-Brown's Otorhinolaryngology and Head and Neck Surgery. Basic Sciences, Endocrine Surgery, Rhinology.* 1. USA: CRC Press: Boca Raton, FL; 2018. [DOI:10.1201/9780203731000]
37. Sen M, Lahane S, Lahane TP, Parekh R, Honavar SG. Mucor in a Viral Land: A Tale of Two Pathogens. *Indian J Ophthalmol.* 2021;69(2):244-52. [DOI:10.4103/ijo.IJO\_3774\_20] [PMID] [PMCID]
38. Honavar SG. Code Mucor: Guidelines for the Diagnosis, Staging and Management of Rhino-Orbito-Cerebral Mucormycosis in the Setting of COVID-19. *Indian J Ophthalmol.* 2021;69(6):1361-5. [DOI:10.4103/ijo.IJO\_1165\_21] [PMID] [PMCID]
39. Baghel SS, Keshri AK, Mishra P, Marak R, Manogaran RS, Verma PK, et al. The spectrum of invasive fungal sinusitis in COVID-19 patients: experience from a tertiary care referral center in Northern India. *J Fungus.* 2022;8(3):223. [DOI:10.3390/jof8030223] [PMID] [PMCID]
40. Centers for Disease Control and Prevention. Mucormycosis statistics. 2022.