

## Fungal Infections of Paranasal Sinuses: Sequelae to 2020 Pandemic

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### Abstract

**Background:** In recent decades, the prevalence of fungal sinus infection has increased. It's plausible that this is related to increased awareness, antibiotic usage, and the use of immunosuppressive drugs. Furthermore, much has been written on the involvement of fungus as a causative organism.

**Objectives:** To identify fungal pathogens and correlate laboratory findings with clinical findings.

**Materials and Methods:** Patients with AIFR following recent COVID-19 infection were included. After performing potassium hydroxide (KOH) wet mounts, post-operative material was collected and cultured on two tubes of Sabouraud dextrose agar (SDA) and stored at 25°C and 37°C for isolation and identification.

**Results:** Out of 329 diabetic individuals with AIFS following COVID-19 infection, 51% exhibited mucopurulent discharge and 75.6% had unilateral involvement. Only 57.4% of KOH mount samples were positive for fungal components, however 76.3% of SDA samples exhibited positive growth, with 62% Mucorales, 8% Aspergillus, and 6% Candida species.

**Conclusion:** Mucor mycosis can develop in COVID-19 patients, particularly those with diabetes, a high and imprudent use of corticosteroids, and invasive ventilation. KOH test resulted in a preliminary diagnosis, whereas Culture remains the gold standard for identification.

**Keywords:** Invasive fungal sinusitis, Mucor mycosis, COVID-19, Diabetes mellitus

### Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) induced coronavirus illness (COVID-19) was originally detected in Wuhan, China. Until now, there has been no full research on COVID-19 sequelae.<sup>1</sup> The COVID-19 pandemic has been associated with otorhinolaryngological symptoms such as anosmia in the early stages to late-stage mucor mycosis presenting as invasive fungal sinusitis.<sup>2</sup> The hyphal invasion and symptoms take around 4 weeks to appear and be detected. Invasive fungal diseases are infections that can be fatal in immunocompromised persons.<sup>3</sup> They are also

known as Mucor mycosis infection, is caused due to decreased CD4+ and CD8+ lymphocytes associated with uncontrolled diabetes, immunosuppression, acquired immunodeficiency syndrome (AIDS), and underlying malignancies. Patients in critical care for influenza and respiratory virus infections, particularly Covid-pneumonia, have been shown to have a higher risk of acquiring invasive pulmonary fungal infections, most likely due to their reduced immunological competence.<sup>4</sup>

In recent decades, the prevalence of fungal sinus infection has increased. This might be related to antibiotic and immunosuppressant drug abuse.

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Furthermore, the involvement of fungus as a causative organism in chronic rhinosinusitis is well established.<sup>5</sup>

In moderate to severe cases with decompensated pulmonary functions and the use of immunosuppressive medicine for management increase disease severity. Without early identification and treatment, the condition may progress rapidly, with reported fatality rates of 50 to 80 % due to intra-orbital and cerebral complications.<sup>6</sup> Despite prompt treatment, mortality rates were steadily rising due to the disease's rapid progression.

## Materials and Methods

**Study Design:** Prospective Cross sectional study

**Study Setting:** Government ENT Hospital, Koti, Hyderabad

**Study Duration:** November 2021 to March 2022

**Sample size:** 329 patients

Three-month research was undertaken on 329 individuals who had clinical signs of fungal infections after recovering from COVID 19 infection.

### Inclusion Criteria

1. Patients with fungal sinusitis who have been admitted to the hospital for treatment.
2. Diabetes mellitus patients
3. Patients with suspected fungal sinusitis.

### Exclusion Criteria

1. Vaccinated against Covid-19.
2. Patients who have had no present or previous Covid-19 infection.
3. Patients who are not diabetic.
4. Patients unwilling to provide consent.

A comprehensive history was gathered from individuals who had a clinical suspicion of paranasal sinus fungal infection. Material was collected in sterile normal saline and sterile screw-capped and leak-proof universal containers after surgery (small or large surgical intervention). All samples were first inspected microscopically using potassium hydroxide (KOH) wet mounts, then cultured on two tubes of Sabouraud dextrose agar (SDA) and maintained at temperatures of 25°C and 37°C, respectively. The culture slants were incubated for 48 hours and then monitored for growth every day for up to 5

days. If colony growth happened within 5 days, the morphology of the colony was observed. For morphological identification, the fungal growth was stained with Lactophenol cotton blue (LCB). Safety precautions were used throughout the collecting and processing of materials. Gloves, N95, surgical mask, plastic apron, and PPE Kit were provided to operating employees. Before and after the procedure, the work station was thoroughly disinfected with glutaraldehyde.

**Statistical Analysis:** The SPSS 22 software was used for statistical analysis. The outcomes was presented in the form of means and percentages.

## Observation and Results

**Table 1: Distribution based on Gender and Side of involvement**

Gender	Frequency	Percentage
Male	260	79%
Female	69	21%
<b>Side of involvement</b>		
Unilateral	251	76%
Bilateral	78	24%
<b>Clinical features</b>		
Mucopurulent discharge	168	51%
Nasal Obstruction	106	32%
Facial puffiness	70	21%
Headache	65	20%
Facial pain	52	16%
Polypoid disease	46	14%
Postnasal discharge	33	10%

329 diabetic individuals with COVID-19 infection presented with AIFS (acute invasive fungal rhinosinusitis) – all of them had had COVID-19 infection therapy during the previous 10 days. Males predominated in the presenting pattern, with a mean age of 49 years.

A total of 53.1% (175) of 329 diabetic individuals with acute invasive fungal sinusitis got steroids, whereas 46.8% (154) did not. In our study, we observed that 38% (125) of individuals who got steroids required oxygen assistance, whereas 15%

(50) did not. The use of a ventilator was required by 3% of those on steroids (ten). Patients who did not get steroids were administered oxygen assistance in 30.3 % (100), 16.4 % (54) did not require oxygen, and 0.6 % (2) were intubated. Mucopurulent discharge with black particles (51 %), nasal obstruction (32 %), facial puffiness (21 %), headache (20 %), facial discomfort (16 %), polypoid illness (14 %), and post nasal discharge (10 %) were the most prevalent symptoms. Black staining and eschar development had occurred in 44% of the people. 75.6 % had unilateral involvement, whereas 24% had bilateral involvement.

Orbital complications occurred in 23 patients (7%), the symptoms being, swelling of eye (3.34%), watering from eye (1.8%), ptosis (0.9%), pain in involved eye (0.9%), orbital exenterating in 2 patients (0.6%) and blurring of vision in 1 patient. Palatal complication observed in 8 patients (2.4%), the symptoms such as tooth ache (1.2%), swelling on hard palate (0.6%) and erosion of hard palate (0.3%).

**Table 2: Percentage of samples identified in 10% KOH mount and fungal culture**

Samples identified with method	Positive	Negative
10% KOH	57.40%	42.50%
Fungal Culture	76.20%	23.70%

In 10% KOH, 57.40% of the samples were positive and with fungal culture 76.20% were positive.

**Table 3: Findings on KOH mount examination**

KOH mount findings	Frequency	Percentage
Ribbon Shaped hyphae; broad, aseptate and hyaline	89	47.00%
Septate hyphae with branching at acute angle	13	7.00%
Budding yeast cells	7	4.00%
No fungal elements	80	42.50%

In 189 samples (57.4%) of which 47% showed ribbon shaped hyaline, broad aseptate and hyaline; 7% septate hyphae with branching at acute angles; 4% showed budding yeast cells.

10% KOH mount examination was negative for fungal elements in 140 (42.5%) samples of patients

**Table 4: culture and morphological identification by LPCB**

Culture and morphological identification by LPCB	Number of samples (n=251)	Percentage
Mucorales	156	62%
Aspergillus Sp	20	8%
Candida Sp	16	6%
No growth	59	24%

Out of 329 samples, 251 (76.3%) showed fungal growth on SDA with LPCB showing 62% Mucorales, 8% Aspergillus species, 6% Candida species.

**Table 5: Distribution based on various methods used**

Methods	Number of samples	Percentage
Both KOH and culture positive	140	42.5 %
KOH positive and culture negative	49	14.9%
KOH negative and culture positive	111	33.7%
Both KOH and culture negative	29	8.8%

In 78 (23.7%) there was no fungal growth on SDA. In this study, both KOH and Culture were positive in 140 patients (42.5%) while KOH negative and culture positive in 111 (33.7%), KOH positive and Culture negative in 49 (14.9%) and both were negative in 29 (8.8%).

## Discussion

Covid-19 infection, which is caused by the new SARS-CoV-2, has been associated with broad array of symptoms, ranging from moderate cough to life-threatening pneumonia.<sup>6</sup> As we understand more about this novel disease, a plethora of symptoms and complications have been documented, and new ones are emerging and being reported almost every day.<sup>7</sup> Mucor mycosis is a fungus infection of the Mucorales family that affects diabetics with impaired immune systems. The most prevalent symptom is rhino orbital infection, which is a rare ailment.<sup>8</sup> In 2019, few cases of Mucor mycosis were reported.<sup>9</sup> The significant increase in Mucor mycosis cases during COVID-19's

second wave implies a strong correlation between COVID-19 and Mucor mycosis.<sup>10</sup>

Patients who require critical care due to Covid-19 pneumonia have risk factors and underlying conditions that make them susceptible to invasive fungal infections. A prominent predisposing condition for acute invasive fungal rhinosinusitis is uncontrolled diabetes mellitus, particularly diabetic ketoacidosis.

Song et al. studied the correlation between Covid-19 and invasive fungal sinusitis, reporting that a high number of individuals who have been exposed to Covid-19 or have recovered from it are at an elevated risk of acquiring invasive fungal infections.<sup>11</sup>

Uncontrolled diabetes and abuse of steroids are two of the most common causes of disease aggravation, and both must be addressed. If infected, seek surgical intervention and intravenous antifungal therapy as soon as possible, as post-coronavirus fungal infection can have a favorable prognosis and a less fulminant disease course.

## Conclusion

Mucor mycosis can arise in COVID-19 patients, particularly those with diabetes, an increased and imprudent use of corticosteroids, and invasive ventilation. Mucor mycosis should be suspected in diabetic patients who have had COVID. KOH-examination resulted in a preliminary diagnosis and helped define surgical margins for an invasive fungal infection. During the pandemic, early identification of fungal etiological agents using culture and LPCB benefited in prompt Mucor mycosis treatment.

**Ethical Clearance:** Ethical Clearance was obtained from the institutional ethics committee prior to the commencement of the study.

**Conflict of Interest:** Nil

**Source of Funding:** Self

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