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FREQUENCY OF INVASIVE FUNGAL RHINOSINUSITIS AMONG COVID-19 PATIENTS OF PESHAWAR

Original Research

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ABSTRACT

Background: Acute invasive fungal rhinosinusitis (AIFR) has emerged as a severe opportunistic infection in patients with COVID-19, particularly among those with underlying immunocompromising conditions. While isolated case reports dominate existing literature, studies estimating the overall frequency of AIFR among SARS-CoV-2-infected individuals remain limited. Understanding its prevalence is essential for guiding early clinical suspicion, timely diagnosis, and effective management, especially in high-risk populations and resource-constrained healthcare settings.

Objective: To determine the frequency of acute invasive fungal rhinosinusitis in patients diagnosed with COVID-19.

Methods: This descriptive cross-sectional study was conducted at the ENT Department of Khyber Teaching Hospital, Peshawar, from 16th March 2023 to 15th September 2023. A total of 298 patients aged 10–60 years with confirmed COVID-19 via RT-PCR were enrolled using non-probability consecutive sampling. Patients with prior sinonasal surgery, facial trauma, known malignancy of the sinuses, or chronic immunosuppressive disorders unrelated to COVID-19 were excluded. Fungal sinusitis was suspected clinically and confirmed by direct microscopic examination of sinonasal tissue samples immersed in 10% potassium hydroxide (KOH). Histopathological evaluation was also performed to validate tissue invasion.

Results: The mean age of participants was 57.85 ± 7.99 years, mean BMI was 25.12 ± 1.01 kg/m², and the average duration of illness was 7.79 ± 2.65 days. Of the 298 patients, 202 (67.8%) were older than 55 years, and 152 (51.0%) were female. A BMI over 25 kg/m² was observed in 134 patients (45.0%), and 124 (41.6%) were smokers. Invasive fungal rhinosinusitis was confirmed in 65 cases, yielding a frequency of 21.8%.

Conclusion: AIFR was found in a considerable proportion of COVID-19 patients, particularly among elderly individuals and those with metabolic risk factors. Early identification is crucial to reduce morbidity and improve outcomes.

Keywords: COVID-19, Fungal Rhinosinusitis, Immunocompromised Host, Invasive Fungal Infections, KOH Microscopy, SARS-CoV-2, Sinusitis.

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Prevalence of AIFR in COVID-19 Patients

Background

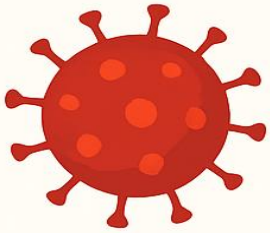
Increased risisk of acute invasive fungal rhinosinusitis (AIFR) associated with COVID-19



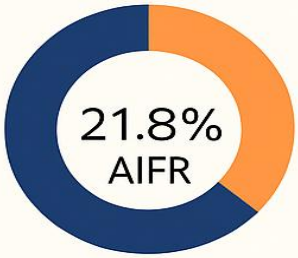
RT-PCR

KOH microscopy

Methods



SARS-CoV-2



Results

- Mean age 57.9
- 51.0% female
- Mean BMI 25,1kg/m^2

Conclusion

AIFR was found in a substantial proportion of COVI-19 patients

Conclusion

AIFR was found in a substantial proportion of COVID-19 patients

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INTRODUCTION

Coronavirus disease (COVID-19), initially referred to as the 2019 novel coronavirus (2019-nCoV), is a viral syndrome primarily targeting the respiratory tract and is responsible for a global health crisis that continues to impact healthcare systems worldwide (1–3). While the hallmark of this disease is respiratory compromise, emerging evidence has underscored its complex interplay with host immunity. COVID-19 has been linked with varying degrees of immunosuppression, primarily due to a reduction in circulating helper and cytotoxic T cells, a mechanism that compromises the body's innate and adaptive immune responses (4). Moreover, corticosteroid therapy—commonly administered to mitigate the severe inflammatory responses in COVID-19—further contributes to immunosuppression, rendering patients more susceptible to opportunistic infections. This immunocompromised state is further worsened in individuals with pre-existing conditions such as diabetes mellitus, hypertension, tuberculosis, or other chronic illnesses (5). One of the most alarming secondary complications increasingly reported in COVID-19 patients is acute invasive fungal rhinosinusitis (AIFR), a rapidly progressive and potentially fatal condition characterized by fungal invasion of the sinonasal mucosa within a period of less than four weeks (6). AIFR traditionally affects individuals with compromised immune systems, such as those with uncontrolled diabetes, malignancy, HIV/AIDS, or those undergoing immunosuppressive or chemotherapeutic treatment (6,7). The emergence of COVID-associated invasive fungal sinusitis (CAIFS) as a clinical entity has raised significant concern, particularly in regions with high COVID-19 caseloads. CAIFS poses an urgent clinical challenge, as delayed diagnosis and management can lead to devastating outcomes, including extension into orbital and intracranial compartments, resulting in neurological, vascular, or ophthalmic complications (8,9).

Several early studies began to document the incidence of fungal infections among COVID-19 patients, highlighting the need for vigilance in clinical settings. A retrospective study reported five cases of fungal infection among 99 COVID-19 patients, marking one of the earliest documented clusters of CAIFS (10). A separate investigation identified sinonasal and respiratory fungal co-infections in 5.8% of COVID-19 patients (11). Similarly, a study found that 26.3% of critically ill COVID-19 patients with moderate to severe ARDS in Germany had developed aspergillosis (12). Another study also observed that 19.4% of ICU-admitted COVID-19 patients suffered from both sinonasal and pulmonary fungal infections (13). Across multiple studies, fungal co-infections in COVID-19 patients were reported in 8% to 15% of cases, although the exact species and clinical severity varied (14-16). Despite the alarming rise in cases, most existing literature on CAIFS comprises isolated case reports or small observational series, with a notable gap in large-scale studies that quantify the incidence of AIFR in broader populations. Particularly, data from resource-constrained regions such as Khyber Pakhtunkhwa in Pakistan remain limited. Understanding the regional prevalence of AIFR in the context of COVID-19 is essential for formulating timely diagnostic protocols and therapeutic strategies. Therefore, the current study was designed to determine the frequency of acute invasive fungal rhinosinusitis among patients with active or recent COVID-19 infection in the Khyber Pakhtunkhwa region, with the aim of addressing this critical gap in local epidemiological data.

METHODS

This cross-sectional study was conducted at the Department of Ear, Nose, and Throat (ENT), Khyber Teaching Hospital, Peshawar, over a six-month period from 16th March 2023 to 15th September 2023. The study enrolled male and female patients aged 10 to 60 years with confirmed COVID-19 infection, as diagnosed by reverse transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 performed on nasal swab specimens. Patients were excluded if they had a history of facial trauma, previous sinonasal surgical interventions, known immunodeficiency states, or malignancies of the paranasal sinuses, as these factors could independently predispose them to fungal sinus infections and confound the outcomes. Acute invasive fungal rhinosinusitis (AIFR) was clinically suspected in patients presenting with symptoms of nasal congestion, post-nasal drip, and frontal headache persisting for more than four weeks. Fungal etiology was confirmed microscopically by the presence of fungal elements in specimens obtained from the paranasal sinuses, processed with 10% potassium hydroxide (KOH) and examined under light microscopy. Histopathological confirmation was also sought using tissue preserved in 85% formaldehyde. All surgical procedures, including specimen collection, were performed under sterile conditions in an operating theatre by experienced ENT consultants or specialists using standard anterior rhinoscopic techniques.

A non-probability consecutive sampling method was employed to select participants. A total sample size of 298 was calculated using the OpenEpi version 3.01 calculator, with an absolute precision of 5%, confidence level of 95%, and an expected prevalence of CAIFS at 26.3% (9). The study received ethical clearance from both the Institutional Review Board and the College of Physicians and Surgeons Pakistan (CPSP), and all patients provided written informed consent after being informed about the nature, benefits, and potential risks

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of the study. Data were collected through structured clinical questionnaires and analyzed using SPSS version 21.0. Continuous variables such as age and duration of sinonasal complaints were reported as means and standard deviations, while categorical variables, including gender, COVID-19 status, presence of fungal infection, type of fungal species, and histopathological results, were presented as frequencies and percentages. The primary outcome variable was the frequency of AIFR among COVID-19 patients. Associations between AIFR and demographic variables like age and gender were assessed using post-stratification chi-square tests. A p-value of less than 0.05 (two-tailed) was considered statistically significant.

RESULTS

The study included 298 patients with confirmed COVID-19 infection, among whom the mean age was 57.85 ± 7.99 years and the mean body mass index (BMI) was 25.12 ± 1.01 kg/m². The average duration of sinonasal symptoms was 7.79 ± 2.65 days. A majority of the participants were older than 55 years (n = 202, 67.8%), and slightly more were female (n = 152, 51.0%) compared to male participants (n = 146, 49.0%). BMI greater than 25 kg/m² was recorded in 134 patients (45.0%), while 164 patients (55.0%) had a BMI of 25 kg/m² or below. Regarding lifestyle and demographics, 124 participants (41.6%) were smokers, 169 (56.7%) were from rural areas, and 164 (55.0%) were salaried individuals. Educational background showed that 47.7% had education up to matric level, 23.8% had no formal schooling, and 28.5% had education above matric level. The prevalence of acute invasive fungal rhinosinusitis (AIFR) in this cohort was found to be 21.8% (n = 65), while 78.2% (n = 233) showed no evidence of fungal invasion. Stratification of AIFR cases by baseline characteristics revealed a statistically significant association with BMI. A higher proportion of patients with BMI ≤ 25.0 kg/m² were diagnosed with AIFR (n = 43, 26.2%) compared to those with BMI > 25.0 kg/m² (n = 22, 16.4%) with a p-value of 0.042, indicating statistical significance. No significant associations were observed between AIFR and other variables such as age group (p = 0.237), gender (p = 0.965), duration of symptoms (p = 0.514), smoking status (p = 0.090), profession (p = 0.288), or area of residence. The distribution across these categories showed variations, but none reached statistical significance. Among the 65 patients diagnosed with acute invasive fungal rhinosinusitis, fungal species identification revealed that *Mucor* was the most commonly isolated organism, found in 28 cases (43.1%), followed by *Aspergillus* in 19 patients (29.2%). *Candida* species were identified in 10 patients (15.4%), while mixed infections, predominantly involving both *Mucor* and *Aspergillus*, were present in 8 cases (12.3%). These findings highlight the predominance of mucormycosis among COVID-associated fungal sinusitis cases in the studied cohort, with implications for early empirical antifungal therapy selection. Histopathological analyses confirmed tissue invasion consistent with invasive fungal infection in all 65 cases, supporting the microbiological findings and reinforcing diagnostic accuracy.

Table 1: Descriptive statistics of study participants (n = 298)

Parameters	Mean	Std. Deviation
Age (years)	57.85	7.988
BMI (kg/m^2)	25.116	1.0110
Duration (days)	7.79	2.650

Table 2: Distribution of study participants with various parameters and invasive rhinosinusitis (n = 298)

Parameters	Subgroups	Frequency	Percent
Age (years)	55 or below	96	32.2
	More than 55	202	67.8
Gender	Male	146	49.0
	Female	152	51.0
BMI (kg/m^2)	25.0 or below	164	55.0
	More than 25.0	134	45.0
Duration (days)	7 or below	139	46.6
	more than 7	159	53.4
Profession	Salaried	164	55.0
	Business	134	45.0
Smoking	Yes	124	41.6
	No	174	58.4

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Parameters	Subgroups	Frequency	Percent
Residence	Rural	169	56.7
	Urban	129	43.3
Residence	No formal schooling	71	23.8
	Matric or below	142	47.7
	Above matric	85	28.5
Fungal Rhinosinusitis	Yes	65	21.8
	No	233	78.2

Table 3: Association of Demographic and Clinical Variables with Fungal Rhinosinusitis in COVID-19 Patients

		Fungal Rhinosinusitis		Total	P value
		Yes	No		
Age	55 or below	17	79	96	0.237
		17.7%	82.3%	100.0%	
	More than 55	48	154	202	
		23.8%	76.2%	100.0%	
Gender	Male	32	114	146	0.965
		21.9%	78.1%	100.0%	
	Female	33	119	152	
		21.7%	78.3%	100.0%	
BMI (kg/m^2)	25.0 or below	43	121	164	0.042
		26.2%	73.8%	100.0%	
	More than 25.0	22	112	134	
		16.4%	83.6%	100.0%	
Duration (days)	7 or below	28	111	139	0.514
		20.1%	79.9%	100.0%	
	More than 7	37	122	159	
		23.3%	76.7%	100.0%	
Profession	Salaried	32	132	164	0.288
		19.5%	80.5%	100.0%	
	Business	33	101	134	
		24.6%	75.4%	100.0%	
Smoking	Yes	33	91	124	0.090
		26.6%	73.4%	100.0%	
	No	32	142	174	
		18.4%	81.6%	100.0%	

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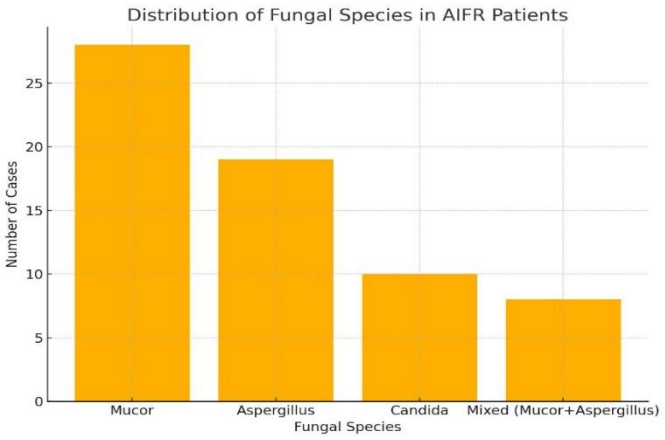


Figure 1 Distribution of Fungal Species in AIFR Patients

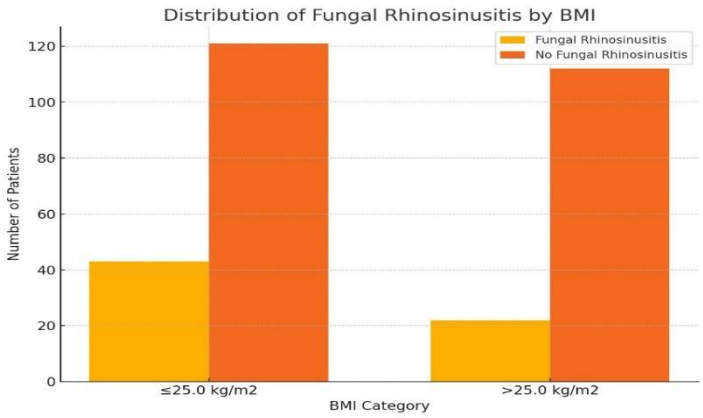


Figure 2 Distribution of Fungal Rhinosinusitis by BMI

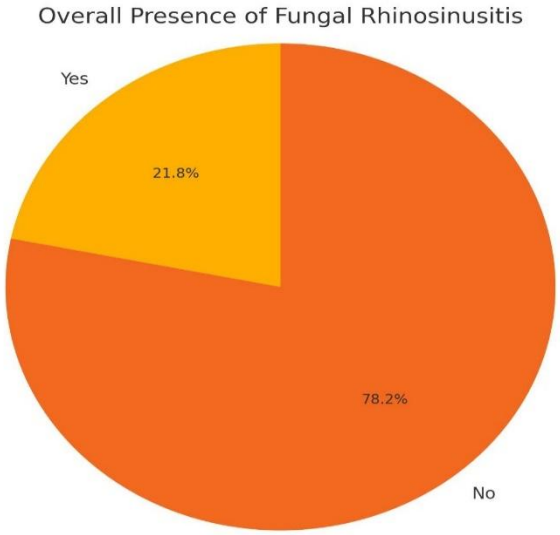


Figure 3 Overall Presence of Fungal Rhinosinusitis

DISCUSSION

The clinical presentation of COVID-19 has consistently demonstrated a broad spectrum of symptoms, ranging from asymptomatic infections to severe respiratory failure and multi-organ dysfunction. Among hospitalized individuals, common manifestations included high-grade fever, sore throat, fatigue, myalgia, dyspnea, chest tightness, and gastrointestinal disturbances, all of which reflect the virus's systemic involvement (17). Of particular interest to otolaryngologists is the early and frequent involvement of the upper respiratory tract, including chemosensory disturbances such as anosmia and ageusia. These olfactory and gustatory dysfunctions, often presenting in the absence of nasal congestion or rhinorrhea, were among the earliest reported ENT-related symptoms. Studies suggest a global prevalence of olfactory impairment as high as 47.85%, and in some cohorts, these were the only initial or isolated signs of infection, especially among younger individuals (18,19). The burden of ENT manifestations in COVID-19 patients extended beyond chemosensory complaints. Inflammatory conditions such as pharyngeal erythema, sore throat, nasal obstruction, and headaches were commonly reported, although their exact prevalence varied across different populations (20). More critically, the emergence of COVID-associated acute invasive fungal rhinosinusitis (CAIFS) has brought significant attention due to its aggressive clinical behavior and rapid progression. Mucormycosis, in particular, showed a marked increase in incidence during the pandemic, attributed to COVID-induced

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immunological alterations, widespread corticosteroid use, poorly controlled diabetes, and nosocomial exposures (21). This study also identified *Mucor* as the predominant fungal species in affected patients, followed by *Aspergillus* and *Candida*, consistent with regional patterns observed in similar post-COVID cohorts. The predominance of mucormycosis, found in over 40% of patients with AIFR in the current analysis, reinforces the need for heightened clinical vigilance, especially in patients with comorbidities and a recent history of immunosuppressive therapy.

The diagnostic complexity of CAIFS arises from its overlapping symptomatology with acute bacterial sinusitis and other less aggressive fungal infections. In clinical settings, AIFR may present as rhino-orbital, sinupalatal, or even cerebral involvement, making early and accurate identification crucial. Cases may also manifest in a localized sinonasal pattern or rapidly progress into fulminant disease with orbital or intracranial extension (22). These findings support the urgent need for tissue diagnosis and early antifungal intervention in high-risk patients. Histopathological confirmation, as implemented in this study, remains a critical gold standard for confirming invasive fungal involvement and guiding treatment. The spectrum of laryngeal involvement, including dysphonia, has also been recognized as part of COVID-19's ENT profile. Dysphonia may result from direct viral invasion of laryngeal tissues or be a consequence of mechanical trauma from prolonged intubation in critically ill patients. Reports have shown its presence in up to 26.8% of hospitalized patients, particularly those requiring intensive care or ventilatory support (23,24). Though not a focus of the present study, the laryngeal sequelae in post-COVID patients remain an important area for further exploration. This study adds value by quantifying the frequency of AIFR among a defined population in a tertiary care center and identifying demographic associations with disease occurrence. However, several limitations must be acknowledged. The non-probability consecutive sampling method introduces potential selection bias, and the exclusion of patients with pre-existing immunosuppressive conditions may have inadvertently excluded a subset at highest risk for fungal infections. Moreover, the lack of longitudinal follow-up restricts insights into treatment outcomes and long-term complications. Species-level identification, though addressed here, could be further enhanced by incorporating molecular diagnostic tools for increased precision. Nonetheless, the use of dual confirmation through KOH mount and histopathological analysis, along with structured ENT evaluation protocols, strengthens the diagnostic validity. Future studies should adopt multicenter, prospective designs and explore molecular characterization of fungal strains, risk prediction scoring models, and outcomes of antifungal therapies in COVID-associated rhinosinusitis. The findings underscore the evolving clinical landscape of post-COVID complications and emphasize the importance of integrated ENT surveillance in the comprehensive management of COVID-19 patients.

CONCLUSION

Invasive fungal rhinosinusitis has emerged as a significant complication among patients affected by COVID-19, particularly those with advanced age and underlying conditions that compromise immune function. Given that the upper respiratory tract is the primary site of SARS-CoV-2 entry, early recognition of ENT-related manifestations is essential for timely diagnosis and targeted intervention. This study highlights the importance of maintaining a high index of suspicion for fungal sinus involvement in COVID-19 patients, especially in those with known risk factors. By reinforcing the link between COVID-19 and acute invasive fungal rhinosinusitis, these findings emphasize the need for vigilant screening and prompt management strategies to reduce associated morbidity and improve patient outcomes.

AUTHOR CONTRIBUTION

Author	Contribution
Nasir Iqbal*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Israr ud din	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published

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