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FUNGAL RHINOSINUSITIS: A CLINICOPATHOLOGICAL, MICROBIOLOGICAL AND RADIOLOGICAL CORRELATION

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ABSTRACT

Background:
Fungal rhinosinusitis (FRS) ranges from non-invasive to invasive life-threatening forms. Accurate diagnosis requires integrated clinical, radiological, microbiological, and histopathological evaluation. With the rise of invasive forms in the post-COVID era, early recognition is critical for better outcomes.

Objectives:
To correlate clinical, radiological, microbiological, and histopathological findings in patients with fungal rhinosinusitis and analyze their association with risk factors.

Methods:
This observational cross-sectional study was conducted over 18 months at a tertiary care center in Mumbai and included 100 patients. Clinical evaluation, CT imaging, KOH mount, fungal cultures, and histopathology were performed. Data were analyzed using chi-square and t-tests with $p < 0.05$ considered significant.

Results:
Most patients were middle-aged (40–60 years, 46%) with equal gender distribution. Nasal obstruction (71%) and headache (54%) were the commonest symptoms. Uncontrolled diabetes (58%) and prior COVID-19 infection (29%) were the major risk factors, both strongly associated with invasive disease. The maxillary sinus was most frequently involved (80%), with bone erosion in 46%. Acute invasive fungal rhinosinusitis was the predominant subtype (57%). Mucor (44%) was the leading pathogen, followed by Aspergillus species (14%). Histopathology confirmed invasive disease in 58% of cases.

Conclusion:
FRS in the post-COVID era is characterized by a predominance of invasive forms, mainly due to Mucor, with uncontrolled diabetes and COVID-related immunological compromise as key risk factors. Maxillary sinus involvement and frequent bone erosion highlight its aggressive course. Early multidisciplinary diagnosis remains vital to improve outcomes.

Key words: *Fungal rhinosinusitis, invasive fungal sinusitis, Mucor, diabetes mellitus, COVID-19, CT scan, histopathology.*

INTRODUCTION:

Fungal rhinosinusitis (FRS) represents a complex spectrum of sinonasal disease, divided histopathologically into invasive and non-invasive types, with further subdivisions including allergic fungal rhinosinusitis (AFRS), fungal ball, saprophytic colonization, acute and chronic invasive forms, and chronic granulomatous disease.[1,2]

Its prevalence has notably risen over recent decades, likely due to heightened diagnostic awareness, advanced imaging techniques, and increasing populations with immunocompromised states.

Accurate diagnosis of FRS hinges on a multidisciplinary approach combining clinical assessment, radiological imaging, microbiological culture, and histopathological confirmation. Radiologically, noncontrast CT is the frontline imaging modality, aiding in diagnosis and differentiation of FRS subtypes, while MRI may be utilized in cases with suspected bone erosion or intracranial involvement.[3] Chronic invasive FRS often presents with features such as bone erosion and hyperattenuating soft tissue on CT scans, suggesting aggressive disease behavior.[4]

Microbiologically, the detection rates of fungal agents vary by subtype. In a recent Serbian study of 26 patients operated via endoscopic sinus surgery (ESS), fungus identification rates reached 72.2% in AFRS and 33.3% in fungal ball specimens.[5] Cladosporium spp. and dematiaceous molds were most frequently isolated, with other cases showing hyaline molds.[6]

These studies collectively underscore the importance of integrating clinical, radiological, microbiological, and histopathological findings to improve diagnosis, guide tailored treatment strategies, and enhance patient outcomes. A comprehensive correlation of these facets is especially vital given the variable presentation patterns, fungal etiologies, and disease behavior across FRS subtypes.

In this context, the current study aims to systematically correlate clinical presentation, radiological findings, microbiological profiles, and histopathological characteristics in patients with fungal rhinosinusitis, thereby reinforcing the value of a multidisciplinary diagnostic framewo

METHODOLOGY

This observational cross-sectional study was conducted over a period of 18 months at a tertiary care centre in Mumbai. The study population comprised patients presenting with features suspicious of fungal sinusitis. A total of 100 patients were included in the study using a consecutive sampling method.

Inclusion Criteria:

- All age groups
- All cases of chronic rhinosinusitis with features suspicious of fungal sinusitis (at least two among clinical, microbiological, pathological, or radiological positivity).
- All cases of nasal polyps with nasal discharge, with features suspicious of fungal sinusitis.

Exclusion Criteria:

- Clinically suspicious patients with negative microbiological and radiological findings.
- Histopathology positive patients with negative clinical, microbiological or radiological findings.

Written informed consent was obtained from all participants after explaining the study procedure in their preferred language (English/Hindi/Marathi). Detailed history, clinical assessment, and computed tomography (CT) scans of the nose and paranasal sinuses were performed for diagnosis. Specimens such as sinus mucosa and nasal polyps were collected for microscopic examination in wet potassium hydroxide (KOH) mount, mucin examination for Charcot–Leyden crystals, histopathological evaluation using special stains, and fungal culture on Sabouraud's dextrose agar.

Data were recorded using a pre-designed case record form while ensuring confidentiality. The collected data were entered into Microsoft Excel and analyzed using SPSS software. Descriptive statistics such as frequency, proportion, mean, and standard deviation were computed. Categorical variables were analyzed using the chi-square test, and continuous variables were compared using the t-test or Mann–Whitney U test as appropriate. A p-value of <0.05 was considered statistically significant. Results were presented in tables and graphs.

The study was conducted after obtaining approval from the Institutional Ethics Committee (IEC) and in compliance with ICMR ethical guidelines. All departmental permissions were secured prior to initiation. Any deviations from the planned methodology were to be reported to the IEC, and changes were implemented only after approval.

RESULTS AND OBSERVATIONS

Table 1: Age and Gender Distribution

Age in years	**Frequency**	**Percent**
< 20	4	4
20 - 40	33	33
40 - 60	46	46
> 60	17	17
Total	100	100
Gender Distribution	**Frequency**	**Percentage**

Female	51	51
Male	49	49
Total	100	100

Table No. 1 showed the age and gender distribution of the study population. The age distribution revealed that 4% of patients were below 20 years, 33% were between 20–40 years, 46% were between 40–60 years, and 17% were above 60 years. Regarding gender, 51% of the patients were female and 49% were male, indicating an almost equal distribution between both sexes.

Table 2: Clinical Symptoms

Symptoms	Frequency	Percentage
Nasal blockage	71	71
Nasal Discharge	41	41
Headache	54	54
Facial pain	34	34
Facial swelling	31	31
Periorbital edema	24	24
Blurring vision	17	17
Fever	34	34

Table No. 2 showed the distribution of clinical symptoms among the study participants. The most common presenting symptom was nasal blockage, observed in 71% of patients. Headache was reported by 54% of patients, while nasal discharge was seen in 41%. Facial pain and fever were each noted in 34% of cases, followed by facial swelling in 31%, periorbital edema in 24%, and blurring of vision in 17% of the patients.

Table 3: Risk Factors

Risk Factors			Frequency	Percentage
Uncontrolled Diabetes	Non invasive	2		

	Invasive	44	58	58
	Histopathology negative	12		
Chronic Sinusitis			16	16
COVID			29	29
Chronic Kidney disease			8	8
Dental procedures			16	16
Bronchial Asthma			14	14
Uncontrolled Diabetes with COVID history			20	20

Table No. 3 showed the distribution of risk factors among patients with fungal rhinosinusitis. Uncontrolled diabetes was the most common associated risk factor, seen in 58% of cases, out of which 44 patients had invasive fungal rhinosinusitis, 2 had non-invasive disease, and 12 were histopathology negative. A history of COVID infection was present in 29% of patients, while 20% had both uncontrolled diabetes and a history of COVID infection. Chronic sinusitis and dental procedures were reported in 16% each, bronchial asthma in 14%, and chronic kidney disease in 8% of patients.

Table 4: DNE,CT Scan and Intraoperative findings

Findings	**Frequency**	**Percentage**
Mucosal Discolouration	48	48
Nasal polyp	24	24
Septum involvement	33	33
Inferior turbinate	33	33
Middle turbinate	42	42
Palatal erosion	43	38
Allergic mucin	14	14

Bone erosion	46	46
Orbital extension	16	16
Unilateral sinus involvement	34	34
Intracranial extension	12	12
Hyperdense deposits	10	10
Paranasal Sinus Involvement	**Frequency**	**Percentage**
Maxillary sinus	80	80
Ethmoid sinus	57	57
Sphenoid sinus	45	45
Frontal sinus	37	37
Multiple sinus	68	68

Table No. 4 showed the diagnostic nasal endoscopy (DNE), CT scan, and intraoperative findings of patients with fungal rhinosinusitis. The most common finding was mucosal discolouration, observed in 48% of patients, followed by bone erosion in 46% and nasal polyp in 24%. Middle turbinate involvement was seen in 42% of cases, while septum and inferior turbinate were each involved in 33% of patients. Palatal erosion was noted in 38% of cases, allergic mucin in 14%, orbital extension in 16%, unilateral sinus involvement in 34%, intracranial extension in 12%, and hyperdense deposits in 10% of patients.

Regarding paranasal sinus involvement, the maxillary sinus was most commonly affected (80%), followed by the ethmoid sinus (57%), sphenoid sinus (45%), and frontal sinus (37%). Multiple sinus involvement was observed in 68% of the patients

Table 5: Categorization of FRS on the basis of histopathology

Disease Type	Frequency	Percent

AFRS	12	16
Fungal ball	3	4
Saprophytic	2	3
Acute invasive	43	57
Chronic invasive	12	16
Chronic granulomatous invasive	3	4
Total	75	100

Table No. 5 showed the categorization of fungal rhinosinusitis based on histopathological findings. The most common type observed was acute invasive fungal rhinosinusitis, seen in 57% of cases, followed by allergic fungal rhinosinusitis (AFRS) and chronic invasive fungal rhinosinusitis, each accounting for 16% of cases. Fungal ball and chronic granulomatous invasive fungal rhinosinusitis were noted in 4% each, while saprophytic fungal infection was identified in 3% of patients

Table 6: Culture Organism

Culture Organism				**Frequency**	**Percent**
	Mucor			44	44
	Aspergillus	A. Fumigatus	7	14	14
		A. Flavus	5		
		A.Niger	2		
	Others			4	4
	Culture negative			38	38
	Total			100	100

Table No. 6 showed the distribution of fungal organisms isolated from culture. Mucor species were the most commonly isolated organism, found in 44% of cases. Aspergillus species were identified in 14% of patients,

of which A. fumigatus was seen in 7 cases, A. flavus in 5 cases, and A. niger in 2 cases. Other fungal organisms were detected in 4% of samples. Culture was negative in 38% of patients.

Table 7: Correlation between Histopathology, KOH and Culture

		KOH positivity		Culture positivity	
		Yes	No	Yes	No
Histopathology Positive (n=75)	Invasive(n=58)	30	28	39	19
	Non Invasive(n=17)	9	8	8	9
Histopathology Negative (n=25)		9	16	15	10
Total		48	52	62	38

Table No. 7 showed the correlation between histopathological findings, KOH mount, and culture results. Among the 58 cases of invasive fungal rhinosinusitis, KOH positivity was observed in 30 cases, while 28 were KOH negative. Culture positivity was noted in 39 cases, and 19 were culture negative.

In the 17 cases of non-invasive fungal rhinosinusitis, KOH positivity was seen in 9 cases and culture positivity in 8 cases. Among the 25 histopathology-negative cases, 9 showed KOH positivity and 15 were culture positive. Overall, KOH positivity was found in 48% and culture positivity in 62% of the total cases studied.

DISCUSSION

Fungal rhinosinusitis (FRS) encompasses a broad spectrum ranging from non-invasive forms to aggressive invasive variants, with host immunity and comorbidities playing a pivotal role in disease expression. The present study evaluated 100 patients to assess their clinico-pathological, microbiological, and radiological profiles, and compared the findings with previous literature.

In our study, the majority of patients were in the 40–60 years age group (46%), followed by 20–40 years (33%), with only 4% under 20 years and 17% above 60 years. This distribution demonstrates a clear predominance among the middle-aged, similar to the findings of Swain et al.[7] who reported the highest prevalence in the 31–50 years range. Montone et al.[8] also highlighted that middle-aged populations are most frequently affected.

Gender distribution showed a nearly equal pattern with 51% females and 49% males. Hameed et al.[9] similarly found no significant gender difference, while Swain et al.[7] reported female predominance and Montone et al. noted male predominance, suggesting that gender predisposition may vary by region and population.

Clinically, nasal blockage was the most common presenting complaint (71%), followed by headache (54%), nasal discharge (41%), facial pain (34%), fever (34%), facial swelling (31%), periorbital edema (24%), and blurring of vision (17%). These findings are consistent with Ashitha et al.[10] who reported nasal obstruction and headache as predominant symptoms, and Hameed et al.[9] who also observed nasal blockage and discharge as the leading complaints.

Uncontrolled diabetes mellitus emerged as the most significant risk factor (58%), followed by COVID-19 history (29%), chronic sinusitis (16%), dental procedures (16%), and bronchial asthma (14%). The strong association between diabetes and invasive fungal disease in our study is consistent with Hameed et al.[9] who observed diabetes in more than 90% of invasive cases. Our study further highlighted that invasive histopathology was significantly more common in patients with uncontrolled diabetes. COVID-19 history was also associated with invasive disease, supporting earlier reports that linked post-COVID immunological alterations with a surge of mucormycosis cases.

Radiologically, the maxillary sinus was most commonly involved (80%), followed by ethmoid (57%), sphenoid (45%), and frontal sinuses (37%), with multiple sinus involvement in 68% of cases. Bone erosion was observed in 46%, orbital extension in 16%, and intracranial extension in 12%. Singh et al.[11] and Montone et al.[8] also reported maxillary sinus as the most frequently affected site. The presence of bone erosion and orbital/intracranial extension underlines the aggressive nature of the invasive forms.

On histopathological classification, acute invasive fungal rhinosinusitis (57%) was the most common subtype, followed by chronic invasive (16%), allergic fungal rhinosinusitis (16%), chronic granulomatous invasive form (4%), fungal ball (4%), and saprophytic colonization (3%). Montone et al.[8] and Usha Krishnan et al.[12] reported a higher prevalence of non-invasive forms, which differs from our findings. The predominance of invasive forms in the present series can be attributed to the high prevalence of uncontrolled diabetes and post-COVID status among patients.

Microbiological culture identified Mucor (44%) as the predominant pathogen, followed by Aspergillus species (14%), while 38% were culture negative. Among Aspergillus isolates, A. fumigatus was the most common, followed by A. flavus and A. niger. Ashitha et al.[10] reported Aspergillus flavus as the commonest isolate, while Singh et al.[11] and Montone et al.[8] emphasized Aspergillus as the leading agent worldwide. The predominance of Mucor in our cohort reflects the regional burden and the post-COVID epidemic surge of mucormycosis in India.

KOH positivity was observed in 48% of cases, which is lower than the higher sensitivity rates reported in other studies. Histopathology remained the most reliable diagnostic tool, with positivity in 75% of patients compared to 62% culture positivity. The combination of histopathology, culture, and KOH enhances diagnostic accuracy, as also suggested by previous studies.

Overall, this study demonstrates that invasive fungal rhinosinusitis predominates in the current scenario, with uncontrolled diabetes and post-COVID status serving as major risk factors. The predominance of Mucor as the causative organism and the high rate of aggressive radiological features, such as bone erosion and intracranial extension, highlight the changing profile of fungal rhinosinusitis in recent years compared to pre-COVID literature.

CONCLUSION

Fungal rhinosinusitis remains a clinically important entity with a wide spectrum ranging from non-invasive to aggressive invasive forms. In our study, the disease predominantly affected middle-aged individuals, with nasal obstruction and headache being the most common presenting symptoms. Uncontrolled diabetes and post-COVID status emerged as the major predisposing factors and were significantly associated with invasive fungal rhinosinusitis. Radiologically, the maxillary sinus was the most frequently involved site, with nearly half of the patients demonstrating bone erosion. Microbiologically, Mucor was the predominant pathogen in this study, while histopathology confirmed invasive disease in the majority of cases (58%).

These findings highlight the need for early diagnosis through integrated clinical, radiological, microbiological, and histopathological evaluation. Optimizing glycemic control, cautious use of steroids, and vigilant monitoring of high-risk individuals are crucial steps to reduce morbidity and mortality associated with fungal rhinosinusitis.

The findings emphasize the importance of early detection through integrated clinical, radiological, microbiological, and histopathological evaluation. Strengthening glycemic control, minimizing irrational steroid use, and close monitoring of high-risk post-COVID patients are key to reducing morbidity and mortality. The dominance of invasive forms and the predominance of Mucor reflect a changing disease landscape, warranting continued vigilance and region-specific strategies in management.

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