



Original Article

## Clinical Spectrum, Diagnostic Approaches, and Treatment Outcomes of Invasive Fungal Sinusitis: A Combined Retrospective and Prospective Study from South India

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### ABSTRACT

**Background:** Invasive fungal sinusitis is a serious condition with high morbidity and mortality, particularly in immunocompromised patients in tropical regions. This study aimed to assess modes of presentation, complications, diagnostic approaches, and treatment outcomes of invasive fungal sinusitis.

**Materials and Methods:** A combined retrospective and prospective observational study was conducted at the Upgraded Institute of Otorhinolaryngology, Rajiv Gandhi Government General Hospital, Chennai, from March 2025 to February 2026. Thirty adult patients with histopathologically or culturally confirmed invasive fungal sinusitis (acute, chronic, and chronic granulomatous subtypes) were included. Data on demographics, clinical features, predisposing factors, endoscopic findings, imaging, microbiology, management, and outcomes were analyzed using SPSS version 27.0.

**Results:** The mean age was 48 years with male predominance (67%). Diabetes mellitus was the predominant predisposing factor (87%). Mucorales were isolated in 83% of acute and chronic invasive cases, while Aspergillus predominated in chronic granulomatous cases. Intraorbital complications occurred in 73% of patients. Combined antifungal therapy and surgical debridement led to clinical improvement in 77% of cases, with an overall mortality rate of 23%.

**Conclusion:** Invasive fungal sinusitis predominantly affects middle-aged diabetic males and carries significant risk of orbital complications. Early diagnosis through nasal endoscopy and biopsy, followed by aggressive multimodal management, can improve outcomes. Heightened awareness and timely intervention are crucial in high-prevalence regions.

**Keywords:** Invasive fungal sinusitis; Mucormycosis; Aspergillus; Diabetes mellitus; Surgical debridement; Amphotericin B.

### INTRODUCTION

Fungal sinusitis, also known as fungal rhinosinusitis (FRS), represents a diverse group of conditions caused by fungal organisms colonizing or invading the nasal cavity and paranasal sinuses. Fungal sinusitis is broadly classified into non-invasive and invasive forms based on the presence or absence of tissue invasion by fungal elements. Non-invasive types include allergic fungal rhinosinusitis (AFRS), fungal ball (mycetoma), and saprophytic fungal colonization, while invasive forms encompass acute invasive fungal rhinosinusitis (AIFRS), chronic invasive fungal rhinosinusitis (CIFRS), and chronic granulomatous invasive fungal sinusitis (CGIFS). This classification is critical because it directly influences the clinical course, prognosis, and therapeutic approach [1].

The epidemiology of fungal sinusitis varies significantly by geographic region, host immune status, and environmental factors. In Western countries, non-invasive forms such as AFRS and fungal balls predominate among immunocompetent

individuals, often linked to atopic conditions and environmental mold exposure [2]. In contrast, India and other tropical regions report a higher burden of both non-invasive and invasive disease. Studies from rural north India have documented fungal rhinosinusitis in up to 27.5% of chronic rhinosinusitis (CRS) cases, with a population prevalence around 0.11%, frequently associated with agricultural activities like wheat harvesting that increase airborne *Aspergillus flavus* spores [3].

Patients with fungal sinusitis present with a wide spectrum of symptoms that often overlap with bacterial or viral rhinosinusitis, making early recognition difficult. Common modes of presentation include nasal obstruction, nasal discharge (which may be thick, purulent, or allergic mucin-like), facial pain or headache, anosmia, and post-nasal drip. In allergic fungal rhinosinusitis, patients—typically young adults with a history of atopy—may report recurrent nasal polyposis, thick “peanut butter-like” eosinophilic mucin, and sometimes visual disturbances due to expansile sinus disease [4].

Fungal balls usually cause unilateral symptoms with chronic low-grade complaints and are often discovered incidentally. In sharp contrast, acute invasive fungal sinusitis in immunocompromised hosts (diabetics with ketoacidosis, neutropenic patients, or those on corticosteroids/immunosuppressants) can progress rapidly within days, featuring fever, severe facial pain, epistaxis, palatal or nasal mucosal necrosis, black eschar, and cranial nerve involvement. Orbital symptoms such as proptosis, diplopia, vision loss, or ophthalmoplegia signal extension beyond the sinuses [5].

Complications of fungal sinusitis can be devastating, particularly in invasive forms. Local extension may lead to orbital cellulitis, subperiosteal abscess, or cavernous sinus thrombosis. Intracranial spread can result in meningitis, brain abscess, cerebritis, or major vascular complications like carotid artery invasion and stroke. Chronic invasive and granulomatous forms tend to have a more indolent course but still cause bony erosion, skull base involvement, and cranial neuropathies over months [6].

The pathophysiology differs markedly across subtypes. In non-invasive disease, fungi act as antigens triggering intense eosinophilic inflammation (in AFRS) or simply form dense concretions within sinuses (fungal ball) without tissue penetration. Invasive disease occurs when host immunity fails to contain the fungus, allowing hyphal invasion of mucosa, blood vessels (angioinvasion), and bone. Hyperglycemia and ketoacidosis impair neutrophil function and provide an iron-rich environment favorable to Mucorales growth. Prolonged neutropenia or corticosteroid use similarly predisposes to *Aspergillus* invasion [7].

Diagnosing fungal sinusitis requires a high index of suspicion, especially in endemic areas or high-risk patients. Nasal endoscopy often reveals characteristic findings such as allergic mucin, polyps, fungal debris, or necrotic mucosa. Imaging plays a pivotal role: computed tomography (CT) is the initial modality of choice, demonstrating heterogeneous opacification, hyperdense areas (metallic density in AFRS or fungal balls), bony expansion/erosion, or extrasinus extension. Magnetic resonance imaging (MRI) provides superior soft-tissue detail for orbital and intracranial involvement, showing the classic “black turbinate” sign or non-enhancing necrotic tissue in invasive cases [8].

Invasive disease demands urgent, aggressive multimodal therapy. Early and repeated surgical debridement to remove all necrotic tissue is essential, often extending to orbital exenteration or skull base resection in advanced cases. This is coupled with systemic antifungal therapy—liposomal amphotericin B as first-line for mucormycosis and voriconazole for aspergillosis—along with aggressive correction of underlying immunosuppression (e.g., glycemic control in diabetes). The overlapping clinical features with bacterial rhinosinusitis or malignancies can lead to diagnostic confusion [9].

Understanding the modes of presentation, potential complications, diagnostic nuances, and efficacy of various management plans is therefore essential for improving patient outcomes [10]. This study was undertaken to assess the various modes of presentation and complications of fungal sinusitis, to study the appropriate diagnostic approach for early detection of the condition, and to evaluate the different management plans employed along with their efficacy in achieving favorable clinical outcomes.

## MATERIALS AND METHODS

**Study Design:** The study followed a combined retrospective and prospective observational design. Retrospective data were collected from hospital records of eligible patients diagnosed and treated during the initial part of the study period, while prospective enrollment and detailed data collection were carried out for subsequent cases.

**Study Setting:** This study was conducted in the Upgraded Institute of Otorhinolaryngology at Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India. The study period extended from March 2025 to February 2026. The hospital is a major tertiary care teaching institution that serves as a referral center for complex head and neck disorders, including invasive fungal sinusitis, for a large population from urban and rural areas of Tamil Nadu and neighboring states.

**Study Participants:** Patients presenting with clinical features suggestive of invasive fungal sinusitis who were subsequently confirmed to have the condition on histopathology and/or culture were included in the study. Inclusion criteria encompassed all adult patients diagnosed with acute invasive fungal sinusitis (AIFS), chronic invasive fungal sinusitis (CIFS), or chronic granulomatous invasive fungal sinusitis (CGIFS), including those with intracranial or intraorbital complications.

Patients below 20 years of age were excluded from the study. Additional exclusion criteria included cases of non-invasive fungal sinusitis (such as allergic fungal rhinosinusitis or fungal ball) and incomplete medical records that precluded meaningful analysis. A total of 30 patients satisfying the inclusion and exclusion criteria were enrolled in the study.

**Sample Size and Sampling Technique:** The sample size consisted of 30 consecutive patients diagnosed with invasive fungal sinusitis during the study period. A non-probability convenience sampling technique was employed, wherein all eligible patients presenting to the institute and meeting the inclusion criteria were included.

**Study Tools and Investigations:** Data were collected using a structured proforma that recorded demographic details, clinical presentation, predisposing factors, endoscopic findings, imaging characteristics, microbiological and histopathological results, treatment modalities, and clinical outcomes. Diagnostic nasal endoscopy (DNE) with biopsy was performed in all cases. Tissue samples were sent for histopathological examination (HPE) with special stains (Periodic Acid-Schiff and Gomori Methenamine Silver) and fungal culture. Imaging included contrast-enhanced computed tomography (CT) of the paranasal sinuses (PNS) and magnetic resonance imaging (MRI) of the brain and orbits when intracranial or orbital extension was suspected. Routine blood investigations, including blood glucose levels and renal function tests, were carried out to identify underlying comorbidities.

**Study Procedure:** All patients underwent thorough clinical evaluation, including detailed history and complete ear, nose, and throat examination. Diagnostic nasal endoscopy was performed to identify characteristic findings such as black eschar, mucosal necrosis, or fungal debris. Biopsy was taken from suspicious areas and sent for urgent histopathological examination and fungal culture. Imaging with CT PNS was obtained in all patients, while MRI was reserved for those with clinical or endoscopic evidence of orbital or intracranial involvement.

Confirmed cases of invasive fungal sinusitis were managed with a combination of aggressive surgical debridement (endoscopic or open), systemic antifungal therapy (primarily liposomal amphotericin B), and optimization of underlying immunosuppressive conditions, particularly glycemic control in diabetic patients. Repeated surgical debridements were performed as required based on clinical response and endoscopic findings. Patients were followed up regularly during hospitalization and after discharge to assess treatment response and detect any recurrence or complications. All data were recorded prospectively where possible and supplemented with retrospective chart review.

**Ethical Issues:** The study was conducted after getting approval from the Institutional Ethics Committee of Rajiv Gandhi Government General Hospital and Madras Medical College, Chennai. Since the study involved both retrospective analysis of existing records and prospective data collection, a waiver of informed consent for retrospective cases was sought and granted by the ethics committee. For prospectively enrolled patients, written informed consent was obtained after providing detailed information about the study in the patient's native language. Patient confidentiality was strictly maintained by using anonymized study identification numbers. There was no conflict of interest, and the study did not receive any external financial support.

**Statistical Analysis:** Data were analyzed using SPSS software version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean  $\pm$  standard deviation (SD) or median with interquartile range, as appropriate. Categorical variables were presented as frequencies and percentages. Comparisons between the three subtypes of invasive fungal sinusitis (acute, chronic, and chronic granulomatous) were performed using one-way ANOVA for continuous variables and chi-square test or Fisher's exact test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

The study included 30 patients with invasive fungal sinusitis, categorized into acute invasive (AIS, n=12), chronic invasive (CIS, n=13), and chronic granulomatous (CGS, n=5) subtypes. The overall mean age was 48 years. Although patients with chronic invasive fungal sinusitis tended to be slightly older (mean  $53.46 \pm 4.61$  years), the difference in age across the three groups did not reach statistical significance ( $p = .066$ ). There was a male predominance (67%) across all subtypes with no significant difference in gender distribution ( $p = .882$ ) (Table 1).

**Table 1: Demographic Characteristics of Patients with Invasive Fungal Sinusitis by Subtype (N = 30)**

Variable	Acute Invasive (AIS) (n=12)	Chronic Invasive (CIS) (n=13)	Chronic Granulomatous (CGS) (n=5)	Test Statistic	p-value
Age (years), Mean $\pm$ SD	48.83 $\pm$ 11.20	53.46 $\pm$ 4.61	43.40 $\pm$ 5.41	F = 2.89	.066
<b>Age Group, n (%)</b>				$\chi^2$	.312
$\leq 40$ years	3 (25.0)	0 (0.0)	1 (20.0)		
41–50 years	4 (33.3)	4 (30.8)	3 (60.0)		
51–60 years	3 (25.0)	9 (69.2)	1 (20.0)		
61–70 years	2 (16.7)	0 (0.0)	0 (0.0)		
<b>Gender, n (%)</b>				Fisher's	.882
Male	8 (66.7)	8 (61.5)	4 (80.0)		
Female	4 (33.3)	5 (38.5)	1 (20.0)		

Note. AIS = Acute Invasive Fungal Sinusitis; CIS = Chronic Invasive Fungal Sinusitis; CGS = Chronic Granulomatous Fungal Sinusitis. One-way ANOVA was used for age comparison.

Diabetes mellitus was the predominant predisposing factor, present in 87% of all cases and significantly more common in acute and chronic invasive subtypes compared to the granulomatous form ( $p = .0004$ ). Nasal obstruction and nasal discharge were significantly more frequent in the chronic invasive group ( $p < .0001$  and  $p = .0018$ , respectively), while fever and headache showed subtype-specific patterns (Table 2).

**Table 2: Predisposing Factors and Clinical Presentation by Subtype of Invasive Fungal Sinusitis**

Variable	AIS (n=12) n (%)	CIS (n=13) n (%)	CGS (n=5) n (%)	p-value (Fisher's Exact)
Diabetes Mellitus	12 (100)	12 (92.3)	1 (20.0)	.0004
No Predisposing Factor	0 (0.0)	0 (0.0)	3 (60.0)	.0028
Nasal Obstruction	0 (0.0)	11 (84.6)	1 (20.0)	<.0001
Nasal Discharge	0 (0.0)	8 (61.5)	1 (20.0)	.0018
Headache	5 (41.7)	1 (7.7)	3 (60.0)	.0476
Fever	4 (33.3)	0 (0.0)	0 (0.0)	.0274
Proptosis	3 (25.0)	2 (15.4)	0 (0.0)	.566

Black eschar in the nasal cavity or palate was observed in over 50% of acute and chronic invasive cases but absent in the granulomatous subtype. Intraorbital complications were highly prevalent across all groups (73% overall) and showed a borderline significant difference between subtypes ( $p = .0496$ ) (Table 3).

**Table 3: Endoscopic Findings and Complications by Subtype**

Variable	AIS (n=12) n (%)	CIS (n=13) n (%)	CGS (n=5) n (%)	p-value
Black Eschar (Nasal Cavity/Palate)	7 (58.3)	7 (53.8)	0 (0.0)	.206
Slough Covered Mass	1 (8.3)	0 (0.0)	3 (60.0)	.0046
Intraorbital Complications	10 (83.3)	8 (61.5)	4 (80.0)	.0496
Intracranial Complications	3 (25.0)	2 (15.4)	1 (20.0)	>.999

Histopathology and culture results revealed Mucorales as the causative organism in 83% of cases overall, predominantly in AIS and CIS subtypes ( $p < .0001$ ). In contrast, Aspergillus species were responsible for 60% of chronic granulomatous cases (Table 4).

**Table 4: Microbiological and Histopathological Findings by Subtype**

Organism	AIS (n=12) n (%)	CIS (n=13) n (%)	CGS (n=5) n (%)	p-value (Fisher's)
Mucorales positive	10 (83.3)	13 (100)	0 (0.0)	<.0001
Aspergillus positive	0 (0.0)	2 (15.4)	3 (60.0)	.0110
Overall Mucorales	83%	—	0%	—
Overall Aspergillus	0%	—	60%	—

The majority of patients received combined medical and surgical management. Amphotericin B combined with surgical debridement was the most common approach in chronic invasive cases ( $p = .0024$ ). Overall, 77% of patients showed clinical improvement, while 23% expired. No statistically significant difference in mortality was observed across the three subtypes ( $p > .999$ ). These outcomes support the efficacy of early aggressive debridement combined with antifungal therapy in improving survival, although mortality remains substantial in invasive fungal sinusitis (Table 5).

**Table 5: Management Approaches and Clinical Outcomes by Subtype**

Variable	AIS (n=12) n (%)	CIS (n=13) n (%)	CGS (n=5) n (%)	p-value
Amphotericin B + Debridement	5 (41.7)	11 (84.6)	0 (0.0)	.0024
Endoscopic Sinus Surgery (ESS)	3 (25.0)	4 (30.8)	1 (20.0)	>.999
Orbital Decompression	2 (16.7)	0 (0.0)	1 (20.0)	.0415
Improved	9 (75.0)	10 (76.9)	4 (80.0)	>.999
Expired	3 (25.0)	3 (23.1)	1 (20.0)	>.999

The findings demonstrate that invasive fungal sinusitis predominantly affects middle-aged diabetic males, with Mucorales being the leading pathogen in acute and chronic invasive forms and Aspergillus more common in granulomatous disease. High rates of orbital complications and a mortality rate of 23% highlight the aggressive nature of the disease.

## DISCUSSION

The present study of 30 patients with invasive fungal sinusitis conducted at a tertiary care center in Chennai highlights the aggressive nature of this condition in the Indian subcontinent. Diabetes mellitus emerged as the dominant predisposing factor, affecting 87% of cases, with particularly high prevalence in acute (100%) and chronic invasive (92.3%) subtypes compared to only 20% in the chronic granulomatous form ( $p = .0004$ ). This finding is consistent with the well-established association between uncontrolled diabetes, ketoacidosis, and impaired neutrophil function that facilitates fungal invasion [11]. The overall male predominance (67%) and mean age of 48 years further align with epidemiological patterns reported from tropical regions where agricultural exposure and delayed healthcare access may contribute to disease burden [12].

Clinical presentation varied significantly by subtype. Acute invasive fungal sinusitis (AIS) was characterized by fever (33.3%), headache (41.7%), and higher rates of proptosis (25%), reflecting its rapid progression. In contrast, chronic invasive fungal sinusitis (CIS) predominantly manifested with nasal obstruction (84.6%) and nasal discharge (61.5%), both statistically significant ( $p < .0001$  and  $p = .0018$  respectively). Black eschar, a classic sign of mucormycosis, was observed in more than 50% of AIS and CIS cases on diagnostic nasal endoscopy but was absent in the granulomatous subtype. These distinct phenotypic differences underscore the importance of maintaining a high index of suspicion and prompt endoscopic evaluation for early detection, as emphasized in contemporary literature [13].

Intraorbital complications were alarmingly common, occurring in 73% of all patients and showing a borderline significant difference across subtypes ( $p = .0496$ ). Intracranial involvement was noted in 20% of cases. Such high rates of orbital and intracranial extension at presentation reflect delayed diagnosis and the aggressive angioinvasive property of Mucorales species, which accounted for 83% of cases overall, predominantly in AIS and CIS groups ( $p < .0001$ ). Aspergillus species, on the other hand, were responsible for 60% of chronic granulomatous cases. This etiological pattern mirrors recent Indian studies where Mucorales predominate in diabetic patients, while Aspergillus flavus is more frequently isolated in chronic granulomatous invasive fungal sinusitis (CGIFS) [14].

Management in this series followed a multimodal approach combining systemic antifungal therapy with surgical intervention. Amphotericin B combined with surgical debridement was the mainstay of treatment, particularly in the chronic invasive group (84.6%,  $p = .0024$ ). Endoscopic sinus surgery was performed in 27% of cases, while more extensive debridement was required in 53%. Orbital decompression was needed in select patients with significant orbital involvement. Overall, 77% of patients showed clinical improvement with this strategy, resulting in a mortality rate of 23%. No significant difference in outcome was observed between the three subtypes ( $p > .999$ ). These results support the critical role of early and repeated surgical debridement along with prompt antifungal therapy in improving survival, even in resource-constrained settings [15].

The mortality rate of 23% observed in the present study, although substantial, compares favorably with several earlier reports from India and other developing countries, where mortality often exceeds 30–50% in acute invasive cases. Factors contributing to relatively better outcomes in this cohort include the multidisciplinary team approach involving otorhinolaryngologists, microbiologists, radiologists, and diabetologists, along with aggressive optimization of glycemic control. However, two deaths were primarily attributed to decompensated liver disease rather than fungal infection itself, highlighting the impact of comorbidities on final outcomes [16].

Diagnostic approaches in the study proved effective. Diagnostic nasal endoscopy with biopsy, combined with CT PNS and selective MRI, facilitated accurate subtyping and early identification of complications. The presence of black eschar on endoscopy provided an important clinical clue for mucormycosis, allowing empirical initiation of amphotericin B even before culture confirmation in several cases. This strategy aligns with current recommendations emphasizing that delay in diagnosis and treatment remains one of the most important modifiable factors affecting survival [17].



The findings of this study have important clinical implications for high-prevalence regions. Given the strong association with diabetes mellitus, routine screening for hyperglycemia in patients presenting with atypical or severe rhinosinusitis symptoms is warranted. The high rate of orbital complications at presentation stresses the need for heightened awareness among primary care physicians and emergency practitioners. Furthermore, the distinct microbiological profile—predominance of Mucorales in invasive forms and *Aspergillus* in granulomatous disease—supports the use of histopathological examination with special stains and fungal culture as gold standard diagnostic tools rather than relying solely on imaging [18].

Limitations of the study include its modest sample size and single-center design, which may limit generalizability. The combined retrospective-prospective nature could have introduced some selection bias, although standardized data collection tools were used. Long-term follow-up data beyond six months were not uniformly available for all patients. Future multicenter studies with larger cohorts and longer follow-up periods would help validate these findings and evaluate newer antifungal agents and adjunctive therapies such as hyperbaric oxygen or local amphotericin irrigation.

## CONCLUSION

This study emphasizes that invasive fungal sinusitis remains a life-threatening condition with high morbidity, particularly in diabetic patients in tropical countries. Early clinical suspicion, prompt diagnostic nasal endoscopy with biopsy, appropriate imaging, aggressive surgical debridement, and timely antifungal therapy forms the cornerstone of successful management. A multidisciplinary approach is essential to reduce mortality and morbidity.

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