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Prevalence and Characteristics of Fungal Infections in Chronic Rhinosinusitis Patients Undergoing Endoscopic Sinus Surgery.

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ABSTRACT

Background: Chronic rhinosinusitis (CRS), a persistent inflammatory condition of the nasal passages and sinuses, is frequently associated with fungal pathogens, particularly *Aspergillus* species. Effective management necessitates thorough eradication of these pathogens and restoration of sinus function, commonly achieved through functional endoscopic sinus surgery (FESS). This prospective observational study aimed to evaluate the clinical and radiological features, determine the prevalence, and characterize the mycological profile of fungal rhinosinusitis in patients undergoing FESS.

Methods: A cohort of 50 patients undergoing treatment for CRS at Department of ENT, GIMSH, Durgapur. Nasal sinus tissues and secretions were collected intraoperatively for mycological and bacteriological analysis. Samples were processed immediately, with fungal elements identified via KOH mount and cultured on Sabouraud dextrose agar. Bacterial cultures were grown on MacConkey agar, and species identification was performed using biochemical tests.

Results: Mycological cultures revealed a 28% prevalence of fungal infection, with *Aspergillus* being the predominant species. 72% of patients had negative fungal cultures. 40 patients exhibited involvement of all sinuses, and 24 presented with nasal polyps, predominantly bilateral. 36 patients did not have diabetes or hypertension. A strong correlation was observed between KOH positivity and culture positivity (9/10), and similarly between KOH negativity and culture negativity (35/36).

Conclusions: Fungal infections represent a significant etiological factor in CRS, particularly in patients with unilateral sinus involvement. Endoscopic sinus surgery followed by appropriate antifungal therapy is crucial for effective management and improved patient outcomes.

Keywords: *Aspergillus*, Allergic fungal sinusitis, Chronic rhinosinusitis, Endoscopic sinus surgery, Fungal infection.

Introduction:

Chronic rhinosinusitis (CRS) represents a significant health burden globally, affecting a substantial portion of the population and impacting quality of life through persistent nasal congestion, facial pain, headache, and olfactory dysfunction. This inflammatory condition, characterized by inflammation of the nasal mucosa and paranasal sinuses lasting for at least 12

weeks, is a complex interplay of various factors, including anatomical variations, environmental exposures, immune dysregulation, and microbial involvement. While bacterial infections have historically been considered primary culprits, the role of fungal pathogens in CRS pathogenesis has gained increasing recognition and clinical relevance. The intricate anatomy of the paranasal sinuses, with their narrow ostia and mucosal lining, provides an ideal environment for microbial colonization and proliferation. In the context of CRS, fungal elements can contribute to the inflammatory cascade through a variety of mechanisms, including direct tissue invasion, allergic reactions, and the production of potent inflammatory mediators. The spectrum of fungal involvement in CRS ranges from simple colonization to invasive fungal rhinosinusitis (IFRS), a potentially life-threatening condition. The classification of fungal rhinosinusitis has evolved over time, reflecting a better understanding of the diverse clinical presentations and underlying pathophysiology. Allergic fungal rhinosinusitis (AFRS) is a non-invasive form characterized by the presence of eosinophilic mucus, nasal polyposis, and evidence of fungal sensitization. It is often associated with atopy and a Th2-mediated immune response. In contrast, IFRS encompasses a range of presentations, including acute invasive, chronic invasive, and granulomatous forms, typically observed in immunocompromised individuals. These forms are characterized by fungal invasion of the sinus mucosa and potentially surrounding structures, leading to significant morbidity and mortality. The etiological agents of fungal rhinosinusitis are diverse, with *Aspergillus* species being the most commonly implicated. *Aspergillus fumigatus*, *Aspergillus flavus*, and *Aspergillus terreus* are frequently isolated in both AFRS and IFRS. However, other fungal species, including *Alternaria*, *Curvularia*, and *Bipolaris*, can also contribute to the pathogenesis of CRS, particularly in specific geographic regions or patient populations. Diagnosis of fungal rhinosinusitis requires a comprehensive approach, combining clinical evaluation, radiological imaging, and mycological investigations. Computed tomography (CT) scans are essential for assessing the extent of sinus involvement, identifying anatomical variations, and detecting signs of bone erosion or intracranial extension. However, CT findings alone are often insufficient to differentiate fungal rhinosinusitis from other forms of CRS. Mycological evaluation plays a crucial role in confirming the presence and identifying the specific fungal pathogen. Direct microscopic examination of nasal secretions or sinus tissue using potassium hydroxide (KOH) preparation can provide rapid evidence of fungal elements. However, culture on Sabouraud dextrose agar (SDA) remains the gold standard for fungal identification and speciation. The management of fungal rhinosinusitis is multifaceted and depends on the specific form of the disease. Functional endoscopic sinus surgery (FESS) is a cornerstone of treatment, aiming to remove fungal debris, improve sinus drainage, and restore ventilation. In AFRS, FESS is often combined with systemic corticosteroids and topical antifungal agents to control inflammation and prevent recurrence. In IFRS, aggressive surgical debridement and systemic antifungal therapy are essential to eradicate the infection and prevent life-threatening complications. Despite advancements in diagnostic and therapeutic strategies, several challenges remain in the management of fungal rhinosinusitis. The optimal duration and route of antifungal therapy, the role of immunotherapy in AFRS, and the prevention of recurrence are areas of ongoing research. Furthermore, the increasing prevalence of antifungal resistance poses a significant threat to the effective treatment of these infections.

This study focuses on the prevalence and mycological profile of fungal infections in patients with chronic rhinosinusitis undergoing endoscopic sinus surgery. By systematically evaluating the clinical, radiological, and microbiological characteristics of these patients, we aim to provide valuable insights into the role of fungal pathogens in CRS and contribute to the development of evidence-based management strategies. This research is particularly relevant in the context of [mention your region, if applicable, e.g., the southern region of India], where

environmental factors and local microbial epidemiology may influence the prevalence and characteristics of fungal rhinosinusitis. By analyzing the data gathered, we aim to enhance our understanding of fungal infections in CRS patients and improve patient outcomes through optimized surgical and medical treatments.

Materials and Methods

Study Design and Setting:

This prospective observational study was conducted at the Department of Microbiology & ENT, GIMSH, Durgapur. A convenience sample of 50 patients undergoing functional endoscopic sinus surgery (FESS) for radiologically confirmed chronic rhinosinusitis (CRS) was included. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants. [1]

Participant Selection:

- **Inclusion Criteria:**
  - Patients of all ages and genders.
  - Radiologically confirmed sinusitis.
  - Symptoms persisting for at least 12 weeks.
  - Patients undergoing FESS.
- **Exclusion Criteria:**
  - Patients who had received topical or systemic steroids within one month prior to enrollment.

Data Collection:

Following informed consent, patients underwent a structured interview and clinical assessment. Pre-operative clinical and radiological data were recorded.

Sample Collection and Processing:

During FESS, samples of nasal sinus tissue, sinus secretions, and allergic mucin (if present) were collected under sterile conditions. Samples were immediately transported to the microbiology laboratory in sterile saline and processed on the same day.

Mycological Analysis:

1. **Potassium Hydroxide (KOH) Mount:**
   - A portion of the specimen was teased and placed on a glass slide.
   - A drop of 10% KOH was added, followed by a coverslip.
   - The preparation was allowed to digest at room temperature.
   - Microscopic examination was performed to identify fungal hyphal elements.
2. **Fungal Culture:**
   - Specimens were inoculated in duplicate onto Sabouraud dextrose agar (SDA) supplemented with gentamicin and chloramphenicol to inhibit bacterial growth.

- Inoculated media were incubated at 25°C and 37°C.
- Cultures were observed daily for one week and then twice weekly for an additional three weeks.
- Fungal growth was identified based on macroscopic and microscopic morphology.
- Lactophenol cotton blue (LPCB) staining was used to examine microscopic structures.
- Slide cultures were performed for unclear morphologies to aid in species identification.

3. **Gram staining:**
    - This procedure was used after alcohol fixation of the slides.
    - This was used to help observe any bacterial, and or fungal hyphal elements that may have been present.

Bacteriological Analysis:

1. **Bacterial Culture:**
    - Samples were inoculated onto chocolate agar, blood agar, nutrient agar, and MacConkey agar.
    - Cultures were incubated at 37°C for 18-24 hours.
    - Bacterial species identification was performed using standard biochemical tests.

Data Analysis:

Descriptive statistics were used to summarize the demographic, clinical, radiological, and microbiological findings. The correlation between KOH positivity and culture positivity was analyzed.

Results

The study population comprised 50 patients undergoing FESS for CRS. The most prevalent age group was 41-50 years (30%), followed by 21-30 years (24%) and 11-20 years (18%). Males constituted 58% of the cohort, while females represented 42%. Occupational distribution revealed equal representation of coolies and housewives (36% each), followed by other occupations (18%) and farmers (10%).

The most frequently reported symptom was nasal obstruction (86%), followed by headache (80%), allergy (70%), and sneezing (68%).

Microbiological Findings:

Fungal cultures were positive in 28% (14/50) of patients and negative in 72% (36/50) (Table 1). *Aspergillus flavus* was the most commonly isolated fungal species (8 patients), followed by *Aspergillus fumigatus* (3 patients), *Fusarium* species (2 patients), and *Rhizopus* (1 patient) (Table 2).

Clinical and Radiological Findings:

The majority of patients (36/50) did not have diabetes or hypertension. Ten patients were diagnosed with diabetes mellitus. Deviated nasal septum (DNS) was observed in 43 patients, predominantly on the left side (29 patients). All sinuses were involved in 40 patients. Nasal polyps were present in 24 patients, with bilateral polyps being more common (16 patients) than unilateral polyps (8 patients). Bilateral maxillary sinus involvement was observed in six patients, while unilateral maxillary and sphenoidal sinus involvement was observed in two patients each.

Correlation of KOH Mount and Culture Results:

Among the 14 culture-positive patients, 9 were KOH-positive, demonstrating a strong correlation between KOH and culture positivity. Among the 36 culture-negative patients, 35 were KOH-negative, indicating a strong correlation between KOH and culture negativity (Table 3).

Of the 10 KOH-positive patients, 9 (90%) were culture-positive. Of the 40 KOH-negative patients, 35 (88%) were culture-negative. The KOH mount correctly identified 64% of culture-positive patients and 97% of culture-negative patients. 90% of positive KOH results were confirmed by culture, and 88% of negative KOH results were confirmed by culture.

DISCUSSION:

This study evaluated 50 patients with chronic rhinosinusitis (CRS), revealing a broad age distribution from 11 to 80 years, with a predominance in the 40-60 year age group. The mean age of 45.5 years aligns with findings reported by Montone et al. in the USA, who also observed a similar mean age in fungal rhinosinusitis (FRS) patients. The male preponderance observed in our study (58% male, 42% female, male-to-female ratio 1.32:1) is consistent with Prateek et al.'s findings, although it contrasts with Dufour et al.'s reports of female predominance. This disparity may be attributed to increased environmental exposure to pollutants such as traffic, dust, and industrial emissions among males.

The most prevalent symptoms in our study were nasal obstruction (86%), headache (80%), nasal discharge (40%), and sneezing (68%). These findings are comparable to Shivani et al.'s observations, where nasal obstruction was the leading complaint. Our study also noted comorbidities such as nasal polyps (24 patients), deviated nasal septum (43 patients), diabetes (12 patients), and hypertension (4 patients). Shivani et al. reported nasal allergy as the most common risk factor, followed by deviated nasal septum and nasal polyps.

The significance of diabetes as a risk factor, particularly uncontrolled diabetes, was highlighted by Michael et al., who found it in 38.8% of patients with invasive fungal sinusitis. This underscores the potential for undiagnosed diabetes in our study population, a recognized issue in India. Mohapatra et al. also reported hyperglycemia in a substantial proportion of patients. The projected increase in diabetes prevalence in India, as indicated by the International Diabetes Federation, necessitates heightened vigilance for fungal rhinosinusitis in diabetic patients.

Our study revealed that CT scans of the paranasal sinuses showed multiple sinus involvement in 40 patients, consistent with Alrajhi et al.'s findings of abnormalities in all patients, with 61% showing involvement in all sinus regions.

The prevalence of fungal rhinosinusitis in our study was 28%, with fungal positivity detected in 14 patients. This aligns with findings from Klossek et al., who also reported a 30% culture positivity rate. However, our results differ from those reported by Ragini et al. (21.2% culture positive), Das et al. (61.7% culture positive), and Prateek et al. (21% culture positive). These variations may reflect differences in study populations, diagnostic methods, and geographical factors.

Aspergillus species were the predominant fungi isolated in our study (79%), with *Aspergillus flavus* being the most common. This is consistent with Saravanan et al.'s report, where *A. flavus* was the most frequently isolated species. The absence of dematiaceous fungi may reflect geographical variations in fungal distribution influenced by local climate and humidity, as noted by Michael et al.

However, several limitations should be acknowledged. The small sample size and short study duration limit the generalizability of our findings. The use of convenience sampling may introduce selection bias. The exclusion of patients on steroid therapy narrows the applicability of our results to a specific subgroup. The reliance on KOH and culture as diagnostic methods, with a 72% negative culture rate, may indicate limitations in diagnostic sensitivity. Advanced diagnostic techniques, such as PCR or sequencing, could have provided more accurate and detailed information. Furthermore, the lack of confounder adjustments in our analysis may have affected the depth and accuracy of our findings.

In conclusion, our study provides valuable insights into the prevalence and mycological profile of fungal rhinosinusitis in patients undergoing FESS. However, future studies with larger sample sizes, longer durations, and more advanced diagnostic techniques are needed to further elucidate the complex interplay of factors contributing to this condition. Additionally, investigations into the underlying immunological mechanisms and the role of environmental factors are warranted to improve our understanding and management of fungal rhinosinusitis.

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