

A Clinical Study of Prevalence of Fungal Sinusitis in Cases of Chronic Rhinosinusitis

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Abstract:

Background: Chronic sinusitis is a prevalent condition globally, and a notable portion of cases is linked to fungal origins, countering the prevailing notion that fungal sinusitis is uncommon. This is particularly true in countries like India, characterized by warm and humid climates in various regions and a steadily increasing prevalence of diabetes mellitus, creating an ideal environment for fungal growth. The primary objective of this study is to determine the occurrence and clinical characteristics of fungal rhinosinusitis in individuals with chronic rhinosinusitis.

Methods: All enrolled patients were introduced to the study's protocol. A comprehensive history was gathered, and thorough clinical examinations, including a detailed Ear, Nose, and Throat examination, were conducted. A total of 25 patients exhibiting clinical indications of Chronic Rhinosinusitis with suspected Fungal Rhinosinusitis underwent a meticulous history-taking and clinical examination. The investigative procedures were Complete hematogram, Blood Sugar level, Serum Electrolytes, Serum Proteins, Blood Grouping, etc. HIV/HBsAg tests were performed to assess the general condition of the patients. Relevant X-rays of the nose and paranasal sinuses were taken. Patients provisionally diagnosed with fungal Rhinosinusitis underwent CT scans of the nose and paranasal sinuses.

Results: The most common type of fungal rhinosinusitis accounted for 12 of 25 cases. The causative organism was the *Aspergillus* species. It is characterized by an allergic reaction to fungi. The second most common type of fungal rhinosinusitis accounted for nine of the 25 cases. It is characterized by the formation of a fungal mass in the sinus cavity. The table shows that fungal rhinosinusitis is most common in adults, with the average age of all patients being 43.4 years. The most common type of fungal rhinosinusitis is AFRRS followed by fungal balls. AIFRRS, CIFRRS, and CGFRS are rare fungal rhinosinusitis types.

Conclusion: Fungal ball, primarily caused by *Aspergillus* species, frequently involved the maxillary sinuses and affected both sexes equally. Allergic fungal rhinosinusitis was more common in males and consistently presented with nasal polyps and allergic mucin. Invasive forms of fungal rhinosinusitis were less common, with acute presentations being more frequent. Acute invasive fungal rhinosinusitis was predominantly caused by *Rhizopus* and exhibited a wide range of manifestations, with a higher incidence among elderly and immunocompromised individuals.

Keywords: Fungal Rhinosinusitis, Clinical Signs, Etiologic Agents, Invasive, Non-invasive, Predisposing Factors.

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Introduction

Sinusitis refers to the inflammation of the mucosa lining the paranasal sinuses. It is categorized into acute and chronic based on the duration of symptoms, where acute lasts less than 12 weeks, and chronic persists for over 12 weeks. [1] Chronic rhinosinusitis is a significant global health concern. Fungal infections are a common occurrence in

chronic rhinosinusitis, affecting both immunocompetent and immunocompromised individuals. Although significant research on fungal sinusitis has been conducted in Europe and the Americas, there is a notable lack of data from the Indian subcontinent. [2, 3] Non-invasive fungal rhinosinusitis encompasses saprophytic fungal

infection, fungal ball, and allergic fungal rhinosinusitis. Saprophytic fungal infection is characterized by visible fungal colonization of mucosal crusts observed in the nasal passages and paranasal sinuses during nasoendoscopy. [4] Patients with this condition are typically asymptomatic or may experience a foul-smelling odor. Fungal ball, more prevalent in immunocompetent middle-aged females, often manifests in individuals with a history of prior dental procedures. It involves the dense accumulation of extra-mucosal fungal hyphae, typically within a single sinus, most commonly the maxillary sinus. [5] Allergic fungal rhinosinusitis is a result of the presence of extra-mucosal fungal hyphae in the sinuses and was initially identified as an upper airway manifestation of allergic bronchopulmonary aspergillosis (ABPA) during the 1970s. [4] Numerous case series have indicated that fungi such as *Bipolaris*, *Curvularia*, and *Alternaria* are more common culprits than the previously presumed pathogen, *Aspergillus*. [6] The typical allergic fungal rhinosinusitis (AFRS) patient is a young, immunocompetent adult, typically between the ages of 21 and 33, with a higher male-to-female ratio. In 1994, Bent and Kuhn outlined diagnostic criteria for AFRS based on 15 consecutive AFRS patients, including 5 major and 6 minor criteria. [4, 7] All major criteria must be present to define AFRS, with the minor criteria serving as supporting features. The frequently implicated fungi in this condition are *Aspergillus* species and Mucorales (including *Rhizopus*, *Rhizomucor*, and *Mucor*). [8] Commonly reported symptoms encompass fever, cough, nasal mucosa crusting, epistaxis, and headaches. In some cases, persistent fever unresponsive to broad-spectrum antibiotics for 48 hours may be the initial presenting symptom. The disease typically remains localized within the sinuses, often presenting with intra-orbital or intracranial extension. Granulomatous fungal rhinosinusitis (FRS) persists for over 12 weeks, demonstrating a gradual onset, and is primarily caused by *Aspergillus flavus*, with a higher incidence in countries like India, Pakistan, and Sudan. Manifestations may include proptosis with an enlarging mass in the cheek, non-caseating granulomas with Langerhans-type vasculitis, and sparse hyphae. [9] Chronic FRS involves a slow, destructive process lasting more than 12 weeks, with *Aspergillus fumigatus* being the most common fungal species. [10] The ethmoid and sphenoid sinuses are predominantly affected, and clinical features resemble those of granulomatous FRS. Considering the rising prevalence of immunocompromised patients globally, fungal sinusitis should be considered as a differential diagnosis, particularly in cases of chronic sinusitis. This consideration is vital, especially when patients exhibit persistent and intractable symptoms despite

receiving appropriate treatment for bacterial sinusitis, allergic rhinitis, asthma, nasal polyposis, and related conditions. [11] This study was conducted particularly due to the warm and moist environment prevalent in various Indian regions and the rising incidence of diabetes mellitus, providing an ideal growth environment for fungal organisms.

Material and Methods

This prospective study was done in the Department of ENT, Rajiv Gandhi Institute of Medical Sciences (RIMS), Adilabad. Institutional Ethical approval was obtained from the institutional Ethical committee. Written consent was obtained from all the participants of the study after explaining the nature of the study in the vernacular language. Those willing to participate in the study voluntarily were included.

Inclusion Criteria

1. All cases with Rhinosinusitis with proptosis, headache, and epistaxis.
2. Aged 18 and above
3. Males and Females
4. Cases of chronic Rhinosinusitis
5. Cases of Nasal polyps and discharge.

Exclusion Criteria

1. Patients with proven bacterial sinusitis.
2. Patients with associated neoplastic lesions were excluded
3. Medically & surgically unfit patients.
4. Not willing to study.
5. Bleeding diathesis.

All enrolled patients were introduced to the study's protocol. A comprehensive history was gathered, and thorough clinical examinations, including a detailed Ear, Nose, and Throat examination, were conducted. A total of 25 patients exhibiting clinical indications of Chronic Rhinosinusitis with suspected Fungal Rhinosinusitis underwent a meticulous history-taking and clinical examination.

The following investigative procedures were systematically carried out: Complete hematogram, Blood Sugar level, Serum Electrolytes, Serum Proteins, Blood Grouping, etc. HIV/HBsAg tests were performed to assess the general condition of the patients. Relevant X-rays of the nose and paranasal sinuses were taken. Patients provisionally diagnosed with fungal Rhinosinusitis underwent CT scans of the nose and paranasal sinuses. A thorough history was obtained concerning nasal blockage, facial pain, nasal discharge, headaches, hyposmia, and fever of unknown origin after 48 hours of appropriate broad-spectrum antibiotics. Anterior and posterior rhinoscopy examinations were conducted to identify any anatomical variations predisposing to fungal infections of the

nose and paranasal sinus and to assess any pathological lesions in the nose. X-ray PNS (Water's view) and additional views, if necessary, were obtained. A comprehensive rigid endoscopic nasal examination was performed under local anesthesia. CT PNS axial and coronal cuts of 2mm slice were ordered for patients displaying evidence of pathology. A complete examination of the Head and Neck region was carried out for all selected patients, in addition to the endoscopic examination of the nose. The mental status of patients was evaluated, providing an initial assessment of CNS function. Examination of all cranial nerves, focusing on facial sensation, ocular movements, afferent pupillary reflex, and visual acuity, was conducted in cases suspected of Invasive Fungal Rhinosinusitis. The eyes were examined for conjunctival irritation or tearing. Examination of the oral cavity and oropharynx was performed to observe any palatal defects or postnasal discharge. Underlying causes of immunodeficiency were investigated, including total serum IgE level and total eosinophil count. Intraoperative microscopic evaluation of mucin along with fungal culture was conducted for suspected Allergic Fungal Rhinosinusitis (AFRS) cases, involving biopsied specimens placed in three sterile bottles: Bottle A (Specimen with Normal saline), Bottle B (Specimen with Normal saline), and Bottle C (Specimen with diluted Formalin solution). Bottles A and B were sent to the Microbiological lab within an hour of the procedure. The preferred technique in mycology and bacteriology laboratories was the KOH-Calcofluor white method, utilizing KOH to dissolve human material and calcofluor white for fluorescence microscopic examination. Bottle C was utilized for histopathological examination of the specimen under low and high-power magnification with a light microscope. The technique was based on the

concept that fungi colonize mucus, necessitating a simple non-invasive procedure to obtain as much mucus as possible for examination. Two puffs of phenylephrine (1%) were sprayed into each nostril to induce vasoconstriction. After 2 minutes, each nostril was flushed with 20ml of sterile saline, and the return was collected in a sterile pan. The collected fluid was centrifuged and sent to the mycology laboratory.

Statistical analysis: All the available data was uploaded to an MS Excel spreadsheet and analyzed by SPSS version 21 in Windows format. The continuous variables were represented by mean, standard deviations, and percentages, and categorical variables were represented by p values.

Results

Table 1 shows the distribution of cases of Fungal Sinusitis in cases of Chronic Rhinosinusitis this study shows the age and sex distribution of 25 cases of fungal sinusitis in patients with chronic rhinosinusitis. The most common age group for fungal sinusitis was 41-50 years old, accounting for 48% of cases. The least common age group was 18-20 years old, accounting for 4% of cases. There was a slight male predominance, with 17 male patients (68%) and 8 female patients (32%). The findings of this study are consistent with previous studies, which have shown that fungal sinusitis is most common in adults aged 40-50 years old and that there is a slight male predominance.

The high prevalence of fungal sinusitis in this age group may be due to several factors, including:

- Increased exposure to airborne fungi
- Decreased immune function
- Underlying medical conditions, such as diabetes or Asthma
- Prior use of antibiotics

Table 1: Distribution of cases of Fungal Sinusitis in this study

Age group	Male	Female	Total (%)
18 – 20	1	0	1(4%)
21 – 30	2	0	2(8%)
31 – 40	4	3	7(28%)
41 – 50	8	4	12(48%)
51 – 60	2	1	3(12%)
Total	17	8	25(100%)

Table 2: Distribution of symptoms reported in cases of Fungal Sinusitis in cases of Chronic Rhinosinusitis in this study shows the frequency and percentage of symptoms reported by 25 patients with fungal sinusitis in cases of chronic rhinosinusitis. The most common symptoms were nasal discharge (92%) and nasal obstruction (84%). Other common symptoms included headache (52%), facial swelling/pain (64%), and hyposmia/anosmia (56%). Ocular symptoms and mass in the nasal cavity were

less common, occurring in 4% and 8% of patients, respectively. The findings of this study are consistent with previous studies, which have shown that the most common symptoms of fungal sinusitis are nasal discharge, nasal obstruction, headache, and facial swelling/pain. Ocular symptoms, such as periorbital edema and proptosis, are less common but can be serious if not treated promptly. A mass in the nasal cavity is a rare but possible manifesta-

tion of fungal sinusitis. Other symptoms, such as cough, fever, and fatigue, may also be present.

Table 2: Distribution of symptoms reported in cases of Fungal Sinusitis in this study.

Symptoms	Frequency	Percentage
Headache	13	52
Ocular symptoms	2	4
Facial swelling/pain	16	64
Hyposmia/Anosmia	14	56
Mass in the nasal cavity	2	8
Nasal Discharge	23	92
Nasal Obstruction	21	84

In the present study, the Anterior Rhinoscopic examination of the nose revealed specific findings among the patients (Figure 1). Nasal polyps were observed in 24% of patients. Fungal debris was evident in 16% of patients. Only 2 patients displayed Facial Dymkorphism, characterized by a widening of the nasal bridge. Only 2 patients presented with ocular manifestations, including

Proptosis, periorbital swelling, excessive tearing, and vision loss. Eschars were identified in 2 patients. Two patients showed ocular symptoms such as ophthalmoplegia, proptosis, and vision loss. Only 1 patient displayed an oral sign, presenting with a fistula in the hard palate and blackish discoloration of the oral mucosa.

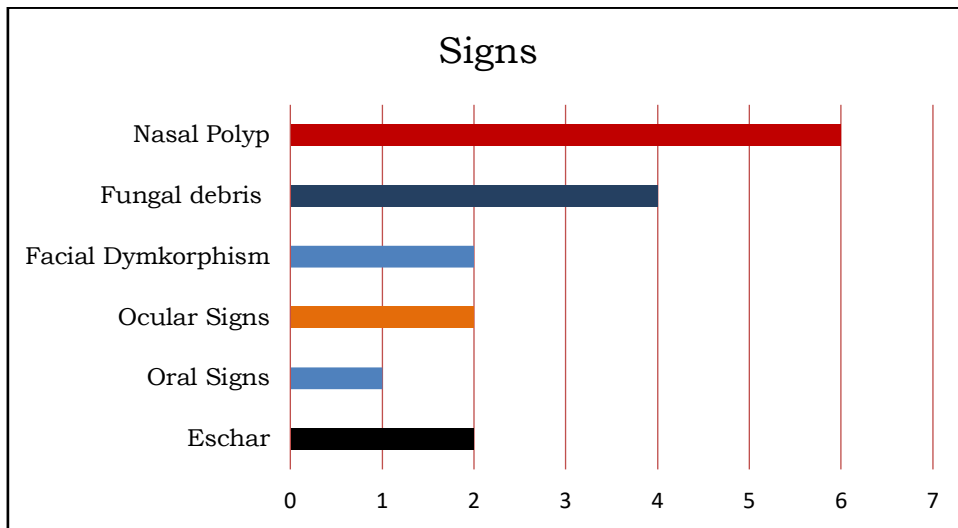


Figure 1: Distribution of signs reported in cases of Fungal Sinusitis in cases of Chronic Rhinosinusitis in this study

Among the 25 patients examined, 15 were found to be Immunocompetent, 6 exhibited an Immunologically Hyper-competent status, and 4 were identified as Immunocompromised. Notably, all cases of immunocompromised status in this study were attributed to Diabetes Mellitus (100% prevalence). In the present study, several predisposing factors for fungal sinusitis were identified, including history of chronic sinusitis in 3 cases. prior history of endodontic treatment in 1 case. Immunocompromised conditions in 4 cases. None of the patients had a history of prolonged use of steroids or antibiotics.

Table 3 shows the categorization of fungal rhinosinusitis among the 25 cases in this study. Allergic

fungal rhinosinusitis (AFRS): The most common type of fungal rhinosinusitis accounted for 12 of 25 cases. The causative organism was the Aspergillus species. It is characterized by an allergic reaction to fungi. The second most common type of fungal rhinosinusitis accounted for nine of the 25 cases. It is characterized by the formation of a fungal mass in the sinus cavity. The table shows that fungal rhinosinusitis is most common in adults, with the average age of all patients being 43.4 years. The most common type of fungal rhinosinusitis is AFRS followed by fungal balls. AIFRS, CIFRS, and CGFRS are rare fungal rhinosinusitis types.

Table 3: Categorization of fungal rhinosinusitis in 25 cases of the study

Diagnosis	Frequency	Mean age in years	Culture +ve Cases
Fungal ball	9	39.5	Aspergillus
Allergic Fungal Rhino sinusitis (AFRS)	12	38.4	Aspergillus
Acute Invasive Fungal Rhino sinusitis (AIFRS)	4	52.33	Rhizopus
Chronic Invasive Fungal Rhino sinusitis (CIFRS)	0	-	-
Chronic Granulomatous Fungal Rhinosinusitis (CGFRS)	0	-	-

In the cases of Allergic Fungal Rhinosinusitis, histopathological examination of allergic mucin stained with Hematoxylin and Eosin revealed the presence of eosinophils, Charcot-Leyden crystals, and fungal hyphae in six patients. In the present study, when examining the coronal sections of the paranasal sinuses (PNS) in the nine Fungal Ball cases, the following findings were observed: complete or subtotal opacification of the maxillary sinus was observed in five cases. Opacification of the sphenoid sinus was noted in one case. Additionally, one patient displayed opacification in both the maxillary and ethmoid sinuses, whereas another patient showed opacification in the maxillary, ethmoid, and sphenoid sinuses. Distinctive CT findings in cases of Allergic Fungal Rhinosinusitis include central areas of hyper-attenuation within the affected sinus cavity.

Discussion

In our hospital, which often receives referrals for the surgical management of chronic sinusitis, a prospective study was conducted on 25 patients with Fungal Rhinosinusitis. Our observations revealed that the majority of these patients were in the category of Non-Invasive Fungal Sinusitis. Within this category, the most common subtypes were Allergic Fungal Rhinosinusitis (48%) and Fungal Ball (36%). Conversely, the Invasive form of Fungal Sinusitis was less prevalent, accounting for only 16% of cases. It's worth noting that nearly all cases in this category were categorized as Acute Invasive Fungal Rhino Sinusitis, as instances of Chronic Invasive Fungal Rhinosinusitis and Chronic Granulomatous Invasive Fungal Rhinosinusitis were not observed (both at 0%). KT. Montone et al. [12] study found out of 400 cases with Fungal Rhinosinusitis (FRS) 87.25% were classified as non-invasive, with 45% being Allergic Fungal Rhinosinusitis (AFRS), 40% Fungal Ball (FB), and 2% representing a combination of AFRS and FB. The remaining 12.5% were invasive, with 11% being Acute Invasive Fungal Rhinosinusitis (AIFRS), 1.2% being Chronic Invasive Fungal Rhinosinusitis (CIFRS), and 0.5% categorized as Chronic Granulomatous Fungal Rhinosinusitis (CGFRS). There was one exceptional case (0.25%) involving a combined Fungal Ball and CGFRS. The most commonly isolated fungi in AFS were

Aspergillus species and dematiaceous species, while Aspergillus species predominated in cases of FB and AIFRS.

The average age in the retrospective series conducted by Ferreiro et al. [13] and colleagues was 65 years, with patients ranging from 28 to 86 years of age. deShazo [14] also reported a similar age range of 20 to 80 years in their studies. Notably, no cases involving pediatric patients were reported in these studies, aligning with the findings of the current study. [11, 12] In the current study, the incidence of fungal ball cases was within the age range of 25 to 55 years. Interestingly, elderly individuals (those over 60 years of age) were not observed in the current study, potentially due to the average age of the Indian population (63 years) and the relatively small sample size. In the present study, the maximum number of cases was between 41 – 50 years and the mean age of the cohort was 43.4 years. B. Naghibzadeh et al. [15] reported a mean age of 31.62 ± 12.56 years in their study 3, while Kasapoglu et al. [16] reported a median age of 26 patients as 43 years, with a range between 9 and 74 years. In the present study, the highest incidence of the disease was found in the fifth decade, accounting for 33.4% of cases. Combining the fourth, fifth, and sixth decades, we observed that these age groups constituted nearly 80% of the cases. The youngest patient in our study was 16 years old, and the oldest was 65 years old, resulting in a mean age of 43.81 years. The studies mentioned above consistently show a significant predominance of females. In the current study, the male-to-female ratio was approximately 2:1, which corroborates the previously observed trend. The male predominance of fungal sinusitis may be due to the fact that men are more likely to have certain occupations or hobbies that put them at increased risk of exposure to fungi, such as construction or farming.

In this study there were 16% of cases with diabetes mellitus could have caused immunosuppression which predisposes to fungal infections. Fabiana C.P. et al. [17] further concluded that clinical outcomes were linked to underlying medical conditions. Patients with aplastic anemia and diabetes mellitus were found to have a poorer prognosis, whereas individuals with hematological

diseases fell into an intermediate prognosis category. On the other hand, patients with AIDS/HIV or renal insufficiency exhibited a more favorable prognosis. Diagnosing fungal rhinosinusitis can often be delayed because the clinical features of non-invasive forms of the disease resemble those of chronic bacterial rhinosinusitis. In our study, more than 80% of the patients presented with nasal obstruction, nasal discharge, and headaches as their primary complaints. Similarly, Ragini et al. [18] also reported that most of their patients presented with nasal obstruction on the corresponding side, often accompanied by headaches and nasal discharge. Fungal rhinosinusitis can be a challenging diagnosis, often eluding definitive identification even with advanced radiological techniques. In this study, CT scans were able to conclusively diagnose fungal rhinosinusitis in all cases however only 50% of cases showed characteristic findings in CT scans. In the remaining cases, CT scans exhibited nonspecific signs of sinus and nasal mucosal inflammation, lacking the distinctive features that suggest fungal rhinosinusitis. Groppo ER et al. [19] found that magnetic resonance imaging (MRI) demonstrated a higher sensitivity (85%) than CT for diagnosing fungal rhinosinusitis. In particular, MRI was most sensitive in detecting extra sinus invasion, with a sensitivity rate of 100%. Both MRI and CT had comparable specificities, with per sinus invasion being the most specific parameter (83% for MRI and 81% for CT). The evaluation of nasal debris obtained during diagnostic nasal endoscopy or surgery confirmed the presence of fungal elements in the cases. Most histopathological examinations revealed septate fungal hyphae, typically indicative of *Aspergillus*, which is the most common environmental fungus in this region. Daniel L. et al. [20] found fungal elements in all 54 unselected chronic rhinosinusitis (CRS) cases using silver stains. This method shows promise in enhancing the diagnostic accuracy when assessing allergic mucin for the presence of fungi. However, it may prove to be highly sensitive in differentiating fungal rhinosinusitis from other cases of CRS. Given the significance of early diagnosis in the successful management of fungal rhinosinusitis, a combined approach using radiological and histopathological methods is recommended. This strategy helps avoid both false negatives and false positives in diagnosis, as the treatment of fungal rhinosinusitis has substantial implications for the patient in terms of treatment duration, side effects, and costs.

Conclusion

In conclusion, this prospective study of 25 patients with fungal rhinosinusitis revealed that non-invasive forms, particularly fungal ball and allergic fungal rhinosinusitis, were more prevalent in the

study region. Fungal balls, primarily caused by *Aspergillus* species, frequently involved the maxillary sinuses and affected both sexes equally. Allergic fungal rhinosinusitis was more common in males and consistently presented with nasal polyps and allergic mucin. Invasive forms of fungal rhinosinusitis were less common, with acute presentations being more frequent. Acute invasive fungal rhinosinusitis was predominantly caused by *Rhizopus* and exhibited a wide range of manifestations, with a higher incidence among elderly and immunocompromised individuals. Chronic invasive fungal rhinosinusitis was either absent or extremely rare in this study.

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