

PREVALENCE OF ALLERGIC FUNGAL SINUSITISRajlaxmi Panigrahi¹**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: Allergic fungal sinusitis (AFS) is a disease of young immune competent adults. Nasal obstruction, nasal discharge, nasal allergy and proptosis were the most common presentations. Initial diagnosis of allergic fungal sinusitis requires high index of suspicion in patients presenting with chronic rhino sinusitis, such cases should be properly evaluated. Differentiation from invasive forms of fungal sinus disease is crucial.

KEYWORDS: Sinusitis, Allergic Fungal Sinusitis, Skull base erosion, Orbital involvement, Fungal.

INTRODUCTION: Allergic fungal rhino sinusitis (AFRS) is a relatively new and incompletely understood clinical entity with characteristic clinical, radiographic, and histopathologic findings. AFRS is often misdiagnosed. Recognition and understanding of this unique disease will lead to efficient diagnosis and treatment of this curable process. Allergic fungal sinusitis (AFS) was first described in the literature in the early 1980s, when Millar et al noticed a clinical entity of sinus disease that was similar in many ways to allergic broncho pulmonary aspergillosis (ABPA).¹

AFRS is a type I hypersensitivity reaction to fungal antigens, where clinically the patients are atopic and have unilateral or bilateral nasal polyps. AFRS is a truly unique pathologic entity, defined largely by the presence of allergic fungal mucin, which is a thick, tenacious, eosinophilic secretion with characteristic histologic findings. This mucin is grossly and microscopically similar to that found in the lungs of patients with allergic bronchopulmonary aspergillosis (ABPA), and this pulmonary correlate helped guide the early understanding of the pathogenesis of AFRS.

Unique features of AFRS that can alert the clinician to a possible diagnosis include a young (mean age is 22 years), immunocompetent patient with unilateral or asymmetric involvement of the paranasal sinuses, a history of atopy, nasal casts, and polyposis, lack of significant pain and scattered mycelial filaments without tissue invasion. Nasal casts are green to black rubbery formed elements made of allergic mucin, as many as 40 % of patients with AFRS have co-existing asthma.

In 1994, Bent and Kuhn published their diagnostic criteria centered on the histologic, radiographic, and immunologic characteristics of the disease.²

Others have proposed several sets of criteria that have served to further the discussion of and investigation into this unique disease; however, the Bent and Kuhn criteria (Table 1) are largely regarded as the standard for diagnosis today. Patients must meet all the major criteria for diagnosis, while the minor criteria serve to support the diagnosis and describe individual patients but are not used to make a diagnosis.

The major criteria include a history of type I hypersensitivity by history, skin testing, or in vitro testing; nasal polyposis; characteristic computed tomography (CT) scan findings; the presence of eosinophilic mucin without invasion; and a positive fungal stain of sinus contents removed at the time of surgery. The minor criteria include a history of asthma, unilateral predominance of disease, radiographic evidence of bone erosion, fungal cultures, presence of Charcot-Leyden crystals in surgical specimens, and serum eosinophilia.

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Major	Minor
Type I hypersensitivity	Asthma
Nasal polyposis	Unilateral disease
Characteristic CT findings	Bone erosion
Eosinophilic mucin without invasion	Fungal cultures
Positive fungal stain	Charcot-Leyden crystals
	Serum eosinophilia

CT, computed tomography

BENT AND KUHN DIAGNOSTIC CRITERIA: Finally, laboratory findings are also helpful in the diagnosis of AFRS. Total immunoglobulin E (IgE) levels are generally elevated, often to more than 1,000 U/mL.

Mabry and colleagues³⁻⁵ demonstrated broad sensitivity to both fungal and nonfungal antigens, emphasizing that AFRS patients are generally atopic. Interestingly, the reactions were not fungal specific, although typically only one fungus was isolated from the culture. This finding could represent a common fungal epitope to explain the broad reactivity, or possibly—as Schubert described—the presence of a superantigen that could contribute to the nonspecific reactivity of these patients.⁶

Nasal polyps are graded on CT scan, as per the grading system of Lildholdt et al, according to a fixed anatomical landmark.

Grade	Description
1	<ul style="list-style-type: none"> • Small polyps extend just below the free edge of the middle turbinate
2	<ul style="list-style-type: none"> • Medium sized polyps reaching between the upper and lower edges of the inferior turbinate.
3	<ul style="list-style-type: none"> • Large polyps reaching below the lower edge of the inferior turbinate

According to Telmesani et al. there is a significant increase in the rate of recurrence with the increase in grade of polyps. Till date, AFRS has been a highly un-recognised clinical entity, resulting in inadequate treatment, thereby adding to physical discomfort/suffering and unnecessary economical burden to the patient.

MATERIALS AND METHOD: During a period of 1 year between July 2012 to June 13, 35 patients of nasal polyps (both recurrence and new cases) were seen in the ENT OPD, out of which 24 patients agreed to undergo investigations and treatment and gave a fully informed consent to be considered for the study.

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For the purpose of study the following details were recorded for all patients, namely, demographic data, clinical examination details, CT scan findings, serum IgE levels, intra-operative findings, histopathological findings of the operative specimen and mucin, culture. All patients were subjected to a detailed history, thorough physical and nasal examination. Medical management in the form of topical steroids, antihistamines for a period of one month were given to all cases and some patients were also given antibiotics for ten days. Those patients who failed to respond to the medical treatment were subjected to CT scans of the paranasal sinuses.

The cases with evidence of polypoidal changes/polypi and radiological typical evidence of presence of allergic fungal sinusitis with bone erosion were included in this study. A record regarding the characteristic clinical presentation, radiological extent of the disease, labs (IgE and eosinophil count) operative details including the area involved were noted as well as postoperative results (nasal symptoms, headache and visual improvement), recurrence and the treatment given was maintained. Medical specialist pre-operatively evaluated all patients for common conditions that could contraindicate the use of oral corticosteroids.

All these patients underwent surgery, which included complete removal of allergic fungal mucin from involved sinuses and creating wide access to these sinuses for ventilation and postoperative care. The surgical approach was based on the extent of the disease according to the findings of CT scan.

All the allergic mucin and polyp/sinus mucosa removed was sent for histopathological examination and KOH preparation. Pathologist was alerted for special fungal staining such as PAS (Periodic acid-Schiff) and GMS (Gomori methanamine silver stain). Postoperatively all patients received antibiotics for one week. Patients whose allergic mucin was negative for fungal hyphae on KOH preparation as well as on special staining were excluded from this study.

The follow-up period ranged 6–12 months.

RESULTS: In our study, out of the 24 cases, all 12 recurrent cases were diagnosed as AFRS, while in the fresh cases, 8 were AFRS, 3 were inflammatory polyps and one was invasive fungal sinusitis.

Prevalence rate of AFRS was 66.6% in new cases of bilateral nasal polyposis. This is higher than reported in literature. In 2006, Saravanan et al. have reported 51% prevalence of AFRS. Asthma was found to be associated with nasal polyps in 4 patients (16.67%). In most of the available literature, the rate of associated asthma in cases of AFRS ranges from 30% - 40%.

The case study had 14 male and 10 female patients and out of the whole group only 2 were diabetic.

Aspergillus flavus was the most common fungal species identified in our study. In United States, Dematiaceous fungi are the most common.

DISCUSSION: Allergic fungal sinusitis is being increasingly seen in various parts of the world with higher incidence in Southwestern states of the USA,⁷ Sudan, northern India,^{8,9} and Saudi Arabia.

The author has experienced a rising trend in Odisha which is in eastern part of India.

Nasal obstruction and discharge have been seen to be common complaints in allergic fungal sinusitis compare with invasive disease. Similarly nasal polyps on anterior rhinoscopy were predominantly present. This study describes the frequency of symptoms and techniques used for diagnosis of AFS in our patients. All patients in our series were immunocompetent and young with a

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mean age at presentation 20 years and 83% were in 2nd and 3rd decade of life, which is similar to studies reported in the common reported fungi.

This study describes the frequency of symptoms and techniques used for diagnosis of AFS in our patients. All patients in our series were immune competent and young with a mean age at presentation 20 years and 83% were in 2nd and 3rd decade of life, which is similar to studies reported in the Literature.^{9,10}

The male female ratio in our study is 1.4: 1 which is comparable to the study of Thahim et al and Richard D Desha but is contrary to the study of Scott C Manning who studied a female preponderance. Gupta et al also reported a more aggressive nature of ASF in children than in adults mandating an early diagnosis, proper management and regular follow up in children⁹ Nasal obstruction, nasal discharge, symptoms of allergic rhinitis or sinusitis and headache were the main presentation in our patients.

Patients typically complain of gradual nasal airway obstruction and production of semi-solid nasal crusts that upon inquiry match the gross description of allergic fungal mucin. The clinical features depend upon the extension of the disease, involvement of orbital or intracranial structures and presence of the concomitant bacterial rhinosinusitis. Patients with AFS are atopic, but generally their symptoms have been unresponsive to medical and surgical treatment for common allergic rhinosinusitis and chronic sinusitis.

Nasal polypi, proptosis, nasal discharge, mucin cast, Telecanthus and facial asymmetry were seen in our patients. The clinical findings in both local and international literature are more or less the same with insignificant difference in frequencies of the symptoms. Ophthalmic findings are said to occur probably due to close proximity of the orbit to paranasal sinuses and extension of the disease leads to proptosis, impaired vision and facial asymmetry. Such extrasinus extension of AFS is caused by bone resorption from pressure from the expanding allergic mucin mass and is not caused by invasion of fungi into sinus mucosa, bone or other tissue.¹¹

A higher incidence of proptosis, facial deformity, intraorbital/ intracranial extension and a higher rate of recurrence in children were reported by Gupta et al. In our study disease was bilateral in 58.3 % cases and unilateral in 41.6 % patients which is similar to the study of Bradley Marple¹² found 51% bilateral disease in 45 patients. The recurrence is more common in female and in that group of patients having bilateral disease; studies suggest as these organisms do not require light for food production, they can live in dark and damp environment. The sinuses consisting of moist, dark cavities are a natural home for fungi resulting in fungal sinusitis

Operative details showed extensive polypoid and characteristic thick peanut-buttery tan to dark-green allergic mucin in all cases, concomitant bacterial sinusitis with pus under tension in 7 cases. Similar findings are reported in world literature.^{1,2,4,9} Histopathological analysis showed fungal hyphae in all allergic mucin in our cases. We utilized various histological staining techniques to help to identify the variety of components within allergic fungal mucin. Hematoxylin and eosin (H&E) staining accentuates the mucin and cellular components of allergic fungal mucin.

Using this stain, background mucin often takes on chondroid appearance, while eosinophils and Charcot Leyden crystals are heavily stained and become easily detectable. Fungi fail to stain using this technique and therefore may be difficult to identify. The Gomori methenamine silver (GMS) stain, which turns fungi black or dark brown were used along with PAS stain.

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The use of a fungal stain complements the findings of initial H&E stain and is extremely important in the identification of fungus. No financial support was utilized so due to budget constraints, all allergic mucin were not cultured. *Aspergillus* was found in 5 specimens cultured in our study, showing prevalence of the organism in this region.^{9,13} A positive fungal culture does not confirm the diagnosis of AFS, nor does a negative culture exclude it. For example, fungi may proliferate as saprophytic growth in diseased sinuses.

Furthermore, mycology laboratories vary in capability and specimen handling significantly influences the rate of positive fungal cultures in a clinical setting. Allergic mucin remains the most reliable indicator of AFS. Because nasal polyposis and fungal disease in the sinuses are not unique to AFS, other mycotic disease in the differential diagnosis must be defined.¹⁴

The CT scan findings suggested 58.3% bilateral and 41.6% unilateral involvement of nose and paranasal sinuses and 61% double density sign. Although these findings are not specific for AFS, they remain relatively characteristic of the disease and may provide preoperative information supportive of diagnosis of AFS. Expansion, remodeling, or thinning of involved sinus walls is common in AFS and is caused by the expansile nature of the accumulating mucin and polypi. Areas of high attenuation are found within the expanded paranasal sinuses in all patients.

Other diseases can cause similar radiographic findings. Bony erosion of the sinus walls and extension into adjacent cavities have been mentioned in many reports.¹⁴⁻¹⁶ Heterogeneity in scan was initially thought to be attenuation related to hemosiderin accumulation in the mucin, but recent theories suggest accumulation of iron and manganese.¹⁸

Lab investigations showed increased level of total IgE in all our cases. Our results are matching reports of other studies. Total IgE values generally are elevated in AFS, often to more than 1,000 U/mL. Total IgE level traditionally has been used to monitor the clinical activity of allergic bronchopulmonary fungal disease. On the basis of similar IgE behavior associated with recurrence of AFS, total IgE levels have been proposed as a useful indicator of AFS clinical activity.¹⁷

Endoscopic sinus surgery included polypectomy, ethmoidectomy, maxillary antrostomy, frontal sinus trephination, and right frontal sinus exploration. The operation revealed thick, "claylike" fungal material and thick mucinous secretions throughout the sinuses. The sinus contents were removed and submitted for histologic examination.

The patient was instructed to self-administer saline irrigation with a bulb syringe and to continue taking fluticasone. A 1-month postoperative evaluation showed resolution of periocular edema with a return of facial symmetry. Postoperatively patients were discharged on 2nd postoperative day, and were followed up at 2 weeks, 1 month, 3 months, 6 months. Postoperatively, saline nasal douching for initial 2 weeks. Topical steroid spray was started at the first post-operative visit and continued for 3 months. Tablet Itraconazole was prescribed for 3 months, with a regular watch over liver function tests.

Initial diagnosis of allergic fungal sinusitis requires high index of suspicion on the part of the attending physician. Keeping in mind the results of this study and the reports of different studies showing a high prevalence of the disease, it is recommended that the diagnostic criteria for allergic fungal sinusitis should be followed strictly.

Every patient of chronic rhinosinusitis should be properly evaluated with a detailed history, thorough clinical examination, radiological investigations (CT scan), laboratory investigation (IgE level), allergic mucin along with polypoidal tissue removed from sinus should be subjected

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histopathology staining. Fungal genus or species can be accurately identified on sinus allergic mucin culture, and nasal specimen for culture should be avoided.¹⁴

Differentiation of invasive forms of fungal sinus disease is crucial, because systemic antifungal medication and extensive surgical tissue debridement are not required in allergic fungal sinusitis.

CONCLUSION: AFS is a condition having insidious features and warrants prompt attention. In the past 30years, there has been significant increase in the number of recorded fungal infections. This can be attributed to increase in public awareness, new immunosuppressive therapies and overuse of antibiotics. Allergic fungal sinusitis should be considered in all patients presenting with chronic rhinosinusitis. Differentiation from invasive forms of fungal sinus disease is crucial.

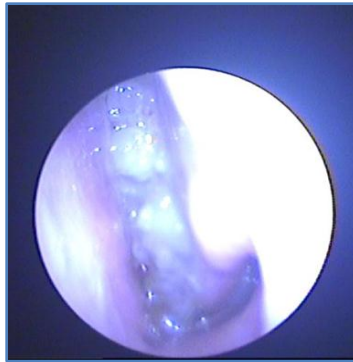


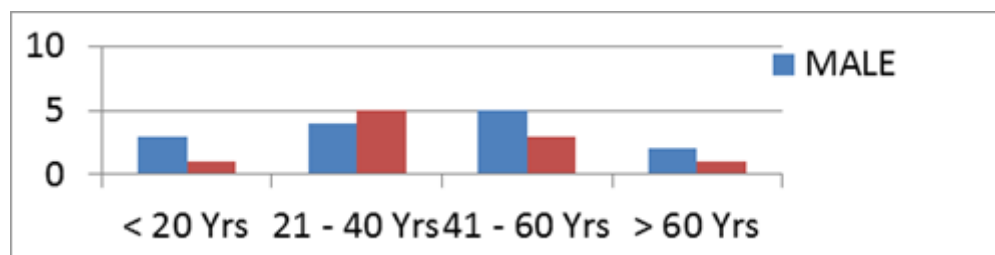
Fig-1 : Polyp with greenish allergic mucin



Fig-2 : Clay like fungal debris in Sphenoid



Fig-3 : one month post operative



The above figure depicts age group and gender distribution of the study

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CT SCAN FINDINGS	NO. OF PATIENTS	%
Bilateral Involvement of Nose and Paranasal Sinuses	14	58.3
Unilateral Involvement of Nose and Paranasal Sinuses	10	41.6
Double Density Sign	15	62.5
Orbital Involvement	5	20.8

Table 2: CT SCAN FINDINGS (pt -24)

CLINICAL FEATURES	NO. OF PATIENTS	%
Nasal Obstruction	23	95.8
Nasal Discharge	20	83.3
Post Nasal drip	18	75
History of Allergic Rhinitis	15	62.5
History of cast production	10	41.6
Loss of Smell	18	75
Headache	16	66.6
History of Asthma	4	16.6
Polyposis	24	100
Impaired Vision	5	20.8
Previous Surgeries	12	50

Table 3: CLINICAL PRESENTATION

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