

INCIDENCE OF ALLERGIC FUNGAL SINUSITIS AMONG PATIENTS WITH CHRONIC RHINOSINUSITIS

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ABSTRACT

BACKGROUND

This study aims to evaluate the incidence of allergic fungal sinusitis among patients with chronic rhinosinusitis. Chronic rhinosinusitis (CRS) is a widely prevalent condition globally as well as in India. Fungal rhinosinusitis is classified into two subgroups: three invasive forms (acute necrotizing, chronic invasive, granulomatous invasive), and two noninvasive forms (fungal ball and allergic fungal).

MATERIALS AND METHODS

Patients attending the Department of ENT at Adesh institute of medical science & research, Bathinda (Punjab) between Jan 2016 and Dec 2016 one year duration 82 cases were included in this retrospective analysis with features suggestive of chronic rhinosinusitis. Based on clinical, endoscopic and radiological parameters, 82 cases were diagnosed to have rhinosinusitis. In these cases, postoperatively after HPE examination, 16 cases were confirmed to have mycotic infection.

RESULTS

Out of 16 cases, In Allergic fungal rhino sinusitis (AFRS), *Aspergillus flavus* (*A. flavus*) was the most common fungus isolated ten cases (71.42%). In fungal ball, *A. flavus* was isolated in two cases (14.25%) and *Aspergillus niger* (*A. niger*) was isolated in two cases (14.25%). In invasive fungal rhinosinusitis (IFRS) mucormycosis was isolated in two cases (12.5%).

CONCLUSION

The incidence of AFRS is about 12.2% of chronic rhinosinusitis. The commonest age group is second & third decade.

KEYWORDS

Allergic Fungal Rhino Sinusitis, *Aspergillus Flavus*, *Aspergillus Niger*, Invasive Fungal Rhinosinusitis, Chronic Rhinosinusitis.

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BACKGROUND

Chronic rhinosinusitis (CRS) is a widely prevalent condition globally as well as in India. Fungal rhinosinusitis is classified into two subgroups: three invasive forms (acute necrotizing, chronic invasive, granulomatous invasive), and two noninvasive forms (fungal ball and allergic fungal).¹ The typical symptoms of CRS involve nasal obstruction, posterior nasal drip, a reduction/loss of the ability to smell, facial pressure and/or pain, and nasal polyposis. Allergic fungal rhinosinusitis (AFRS) is a noninvasive form that can be distinguished clinically and histopathologically. It may represent an allergic hypersensitivity response to extramucosal fungi within the sinus cavity. Affected patients

are usually young, immunocompetent, atopic and initially present with nasal polyps.² Early diagnosis and accurate classification of fungal rhinosinusitis which depends on demonstration of fungus may help in deciding the treatment protocol and preventing multiple surgical procedures, and may lead to effective treatment. Despite advances in medical and surgical treatment, it remains a major health burden and in many cases it is extremely challenging to treat. Hence, this study was undertaken to determine the incidence of fungal agents involved in AFRS and to correlate it with the various clinical presentations. AFRS constitute a major spectrum of non-invasive fungal form causing chronic rhinosinusitis. The incidence of AFRS is estimated at 5 to 10% of all chronic rhinosinusitis (CRS) who undergo sinus surgery.^{3,4} In India, the incidence was 83.9% in patients with nasal polyps (NP).⁵

MATERIALS AND METHODS

Patients attending the Department of ENT and Head and Neck Surgery at Adesh institute of medical science & research, Bathinda (Punjab) between Jan 2016 and Dec 2016 one year duration 82 cases were included in this retrospective analysis with features suggestive of chronic

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rhinosinusitis. Based on clinical, endoscopic and radiological parameters, 82 cases were diagnosed to have rhinosinusitis. In these cases, postoperatively after HPE examination, 16 cases were confirmed to have mycotic infection.

The diagnosis of fungal infection was based on-

- Detailed history and clinical assessment was taken from each patient of feature of CRS.
- Blood investigation like AEC (Absolute eosinophil count) & Serum IgE level.
- Plain X-ray nose and paranasal sinuses (water's view),
- Diagnostic nasal endoscopy.
- CT scan nose and paranasal sinuses (Axial and coronal view).
- Microscopic examination of material like sinus mucosa and nasal polyp in wet mount KOH preparation,
- Histopathological examination of post-operative biopsy material.
- Fungal culture in Sabouraud's dextrose agar.

Information regarding age, gender, associated co-morbid diseases, clinical presentation and immune status of the patient were retrieved from records. Samples collected were allergic mucin, mucopurulent exudate at sinus cavity, nasal exudate and tissue specimens collected by endoscopic sinus surgery. A portion of surgically excised specimens was received in sterile normal saline from mycology laboratory and another part of the specimens was received in 10% formalin in the histopathology laboratory. Details about sample collection, processing and final microbiological and histopathological report were obtained from archived documents. The tissue specimens received at mycology laboratory were minced. Direct 10% KOH mount examination was performed for all these tissue specimens. Histopathological examination of the specimens was done by haematoxylin and eosin and periodic acid-Schiff stain.

Irrespective of direct KOH positivity, the specimens were subjected to fungal culture.

OBSERVATION AND RESULTS

A Retrospective study of 82 cases were diagnosed of chronic rhino sinusitis based on clinical, endoscopic and radiological Parameters. All these patients had undergone FESS. All the specimens were submitted for histopathologic examination for fungal stains and fungal culture. Of these, 16 cases were confirmed to be fungal aetiology. The patients evaluations and observations were as follows:

1. Sex- Out of 82 cases diagnosed to have CRS, 51 patients were male and 32 were female patients. The sex ratio being 1.59.
2. Age- Age varied from 17–67 years. The majority of patients belonged to the age group of second & third decade.
3. Clinical assessment- In our study 28 patients presented with feature of chronic rhinosinusitis like nasal obstruction, posterior nasal drip, reduction/loss of the ability to smell, facial pressure and/or pain & headache, 52 patients presented with polyp (Bilateral–34, Right–6,

Left–12), two were poorly controlled diabetic with black crust and necrotic change in nasal cavity.

4. Venous blood sample was taken to evaluate the absolute eosinophilic count and serum total IgE levels of the cases. Eosinophilic count higher than 500 cells per mL was considered as serum eosinophilia while IgE levels were considered raised when the counts were >100U/mL.
5. Endoscopic findings—Pre-op diagnostic nasal endoscopy was done, Finding like bilateral multiple ethmoidal polyps 34 patients, unilateral polyp in 18 cases, purulent nasal discharge in the middle meatus in 12 patients, trace of allergic mucin/fungal debris in 5 patients and dried black crusts in two cases. The remaining patients had osteomeatal complex obstruction due to deviated nasal septum, concho bullosa, etc.
6. Radiological findings— All cases underwent computed tomography scans. Most of the cases had involvement of maxillary & ethmoidal sinuses followed by frontal & sphenoidal sinuses with radiological finding like, heterogenous opacities ,mucosal thickening & heterogenous opacity with bone erosion homogenous opacities. Heterogenous opacities were seen in a majority of cases.

Bilateral-heterogenous opacities were seen in (54.25%) 45 cases, mucosal thickening was seen in (30.48%) 25 cases, heterogenous opacity with bone erosion (9.75%) 8 cases and homogenous opacities were seen in (4.87%) 4 cases.

Histopathological examination—Histopathological examination of the polyps and polypoidal mucosa was done in all 82 patients. HPE of the biopsy material with special (Lactophenol cotton blue) stain was positive for pathogenic fungi in 16 patients. Of these, culture was positive in all 16 patients (14 noninvasive & 2 invasive fungus).

Out of 16 cases, In AFRS, *Aspergillus flavus* (*A. flavus*) was the most common fungus isolated (ten cases). In fungal ball, *A. flavus* was isolated in two cases (14.25%) and *Aspergillus niger* (*A. niger*) was isolated in two cases (14.25%). In invasive fungal rhinosinusitis (IFRS) mucormycosis was isolated in two cases.

Total Patients (16)	
Invasive (2) 12.5%	Non-Invasive (14) 87.5%
IFRS (2) AFRS (10) 71.42%	Fungal ball (4) 28.5%.

Treatment—All the cases had undergone FESS. All patients (except invasive fungus) were given itraconazole 300 mg OD for 3 days then 100 mg BD for three month with systemic & localised nasal steroid given. Mucormycosis patients were treated with systemic amphotericin–B.

DISCUSSION

Rhinosinusitis is defined as the inflammation of nasal and paranasal sinus mucosa, and it is a common disorder affecting approximately 20% of the population at some point

in their lives.⁶ The prevalence is even greater in tropical countries like India. CRS is characterised by sinonasal mucosal inflammation with a history of atleast 12 weeks of persistent symptoms and signs despite maximal medical therapy.⁷ AFRS is a non-invasive fungal process representing an allergic/ hypersensitivity response to the presence of extramucosal fungi with in sinus cavity. Patients with sinus fungal ball often clinically present as unilateral nasal

obstruction, nasal polyp and discharge and is caused by the overgrowth of fungus in the nose and paranasal sinuses without an eosinophilic inflammatory reaction.⁹ AFRS patients are frequently atopic individuals clinically presenting as pansinusitis and nasal polyposis.¹⁰ which is due to the allergic response to the fungus colonizing the mucin in their sinonasal cavities.¹¹

Bent and Kuhn’s.⁸ Criteria for the Diagnosis of AFRS

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

Kupferberg et al¹² refined the endoscopic follow up into a staging system, which allows closer control of the mucosal response to medical management (i.e.) oral steroids.

Stage Endoscopic finding.

- 0 No mucosal oedema or allergic mucin
- 1 Mucosal oedema with or without allergic mucin
- 2 Polypoidal oedema with or without allergic mucin
- 3 Sinus polyps with fungal debris or allergic mucin.

Diagnostic Criteria for AFRS (2004)

Symptoms Requires ≥one of the following-

- Anterior and/or posterior nasal drainage
- Nasal obstruction
- Decreased sense of smell
- Facial pain-pressure-fullness.

Objective findings Requires all of the following-

- Presence of allergic mucin (fungal hyphae with degranulating eosinophils histopathology)
- Evidence of fungal-specific IgE
- No histologic evidence of invasive fungal disease.

Radiologic findings Highly recommended-

- Sinus CT demonstrating
- Bone erosion
- Sinus expansion
- Extension of disease into adjacent anatomic areas.

Other Diagnostic Measures

- Possible, but not required:
- Fungal culture
- Total serum IgE
- Imaging by more than one technique.

According to Karthikeyan.¹³ the majority of patients belonged to the age group of third decade. In our study the usual presentation the age group of second & third decade.

According to Bakhshae M & Collins MM.^{3,4} the incidence of AFRS is estimated at 5 to 10% of all chronic rhinosinusitis

(CRS) who undergo sinus surgery as compared to 12.2% in our study.

According to Ferguson.¹⁴ who stated that total IgE in patients with AFS is frequently elevated with a mean of 668 IU/mL. with the normal being less than 125 IU/mL. Our study revealed that the total IgE was significantly higher in patients with AFRS than those with chronic rhinosinusitis.

According to Kaur et al⁹ Bilateral-heterogenous opacities were seen in 60% of cases with a statistically significant association. Mucosal thickening was seen in 22.85% of cases. Pressure effects like bone erosion (31.42% of cases) and intracranial or intraorbital extensions (20% of cases) were also seen. Homogenous opacities on unilateral side and calcification were seen in one case each. our study revealed bilateral-heterogenous opacities were seen in (54.25%) 45 cases, mucosal thickening was seen in (30.48%) 25 cases, heterogenous opacity with bone erosion (9.75%) 8 cases and homogenous opacities were seen in (4.87%)4 cases. Various studies have reported AFRS as the most common form of fungal rhinosinusitis and it is more commonly seen in tropical climates such as that seen in India.^{15,16} In a seven-year study, 63% had AFRS among 211 patients, with 24% and 10% presenting with acute and chronic invasive sinusitis respectively.¹⁷ In this study, 71.42% of fungal rhinosinusitis patients presented as AFRS, and 28.5% of patients presented as sinus fungal ball; 12.5% of CRS were categorized as IFRS. In many studies in India, *A. flavus* was the most common isolate in AFRS cases.^{15,18,19} A study by Saravanan et al,²⁰ in Chandigarh, reported that, among the 32 patients in the AFRS group, the most common culture isolate was *A. flavus* (81%), followed by *A. fumigatus* (9%), with *Bipolaris* spp. being isolated in only 2cases (6%). our study revealed out of 16 cases, In AFRS, *Aspergillus flavus* (*A. flavus*) was the most common fungus isolated (ten cases). In fungal ball, *A. flavus* was isolated in two cases and *Aspergillus niger* (*A. niger*) was isolated in two case. Two cases of invasive fungal rhinosinusitis (IFRS) were diagnosed as mucormycosis. Patients with sinus fungal ball often clinically present as unilateral nasal obstruction, nasal polyp and discharge and is caused by the overgrowth of fungus in

the nose and paranasal sinuses without an eosinophilic inflammatory reaction.¹¹ Demonstration of fungal hyphae with characteristic cellular response or fungal culture positivity in properly collected sinus content in an otherwise characteristic patient is an important diagnostic criterion in these conditions.¹⁰ Various authors propose fungal rhinosinusitis to be a continuous spectrum of disease starting from the non-invasive to the acute invasive varieties with considerable overlap and transition from one form to another in the same patient.¹⁵ Therefore, continuous surveillance of prevalent sinonasal fungal infection and periodical monitoring of changing disease pattern of FRS patients are essential. A multi-disciplinary approach involving surgery and medical department with appropriate anti-fungals and immunotherapy is more successful in treating these patients.²¹ It was realised that prompt clinical suspicion in patients of chronic sinusitis with suspicious signs and symptoms along with timely sampling of the adequate patient specimens and the optimal and timely processing of samples by microscopy and culture and histopathological examination will go a long way for early diagnosis and management of these patients.

CONCLUSION

The incidence of ARFS is about 12.2% of chronic rhinosinusitis. The commonest age group is second & third decade. Clinical suspicion of AFRS should be made in those patients presenting with increase AEC & Serum IgE level. Diagnostic nasal endoscopy, radiological investigation, and histopathological examination of all sinus specimens have made the diagnosis much more easier. Endoscopic sinus surgery followed by antifungal therapy with systemic & localised nasal steroid plays a major role in the treatment of ARFS.

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