CHRONIC RHINOSINUSITIS WITH OR WITHOUT NASAL POLYPOSIS - DO FUNGI HAVE ANY ROLE?

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ABSTRACT

Introduction: It is well known that fungi can play a major role in the aetiopathogenesis of chronic rhinosinusitis (CRS) with or without nasal polyposis (NP).

Objectives of the Study: Our study was aimed at looking for the presence of fungal organisms in CRS and to identify the fungal species.We also compared the efficacy of nasal wash specimen as compared to mucosa from ethmoidal sinus for detecting fungi in the nose

Materials and Methods: The study design was cross sectional. A total of 94 patients of CRS with or without nasal polyposis comprised the study group. Fungal culture of nasal washings, and fungal culture and histopathology of the ethmoid mucosa specimen were carried out.

Results: Nasal washspecimens of 21 patients (22%) were positive for fungus and the most common organism isolated was Aspergillus species. Specimen culture was positive in 21 cases (22%),the most common organism was again Aspergillusspecies. The histopathology was positive for fungus in 6 cases (6%) most common isolate being Mucorales. Out of 38 cases of nasal polyps, 22 patients were positive for fungal elements; it was significant by spearman's rho coefficient p value 0.007.

Conclusion: Each form of fungal rhinosinusitis has a characteristic presentation and clinical course, with the immune status of the host playing a critical role. Accurate diagnosis and targeted treatment strategies are essential to achieve optimal outcome.

Key words: Rhinosinusitis, Nasal polyps, Fungi, Nasal lavage, Histopathology, Culture

INTRODUCTION

Chronic rhinosinusitis (CRS)is associated with chronic inflammation of the mucosa of the nasal cavity and paranasal sinuses, with a duration of more than 12 weeks.[1]The disease is characterized by nasal discharge or obstruction, facial pain, hyposmia and with endoscopic features such as polyps, purulent discharge and mucosal oedema.[2]This disease has both personal and economic impact causing significant patient morbidity leading to poor quality of life and decreased overall productivity. The association of fungi in rhinosinusitis has been increasing over the past three decades.[1]Overall prevalence rates of fungal rhinosinusitis is 35.06% and among the patients with chronic rhinosinusitis, the prevalence is 30%.[3]Several factors have been implicated in the development of CRS. Osteum blockage by oedema, thick mucus, improper mucociliary function and mucous recirculation are some of the mechanisms that can lead to the chronicity, while anatomical abnormalities may not be really significant as believed earlier.[4]

Nasal polyposis (NP) is a chronic inflammatory disease of the mucous membrane of the nose and paranasal sinuses wherein pale, pulpy, pear shaped, painless gelatinous masses of inflamed mucosa prolapse into the nose [2]The incidence of NP is between 1% and 4% of the population.[5] The main cause of polyposis formation is not exactly understood, and the relationship between NP and chronic sinusitis is much debated.NP is considered as part of the spectrum of CRS.NP is also considered as a multifactorial disease withseveral different aetiological factors, Viral, bacterial and fungal infectionsalong with genetic factorshave been

suggested as causes of inflammation in NP.Chronic inflammation leading to reactive hyperplasia of themucous membrane results in polyp formation. [6]The presence of fungus in the noseand sinuses may be benign, or it may cause a spectrumof fungal diseases which can range from noninvasive toinvasive and fulminant. The invasive disease is differentiatedinto acute invasive, chronic invasive and granulomatoustypes. The non-invasive disease can be localised colonisation, fungal ball and eosinophil related rhinosinusitis includingAFRS.[7]Fungal isolation rates have been found to vary from 0% to 100% depending on the different techniques used for specimen collection and detection methods.[4]Ponikau et al have reported the presence of fungus in more than 90% among the controls using his novel technique of collecting the nasal washings for fungal culture.[8]

The purpose of our study was to determine the presence of fungal elements in the nasal washings and specimen of nasal polyps, the types of organisms and their role in nasal polyposis and CRS. We also compared the efficacy of nasal wash specimen with mucosa from ethmoidal sinus for the detection of fungi in the nose.

MATERIALS AND METHODS

Source of data

This study was undertaken at a tertiary care teaching hospital over a period of 18 months. This was a cross sectional study with consecutive sampling technique and included all those patients coming to ENT OPD diagnosed to have chronic rhinosinusitis as per the diagnostic criteria by European Position Paper on Rhinosinusitis and nasal polyposis. A total of 94 patients were studied during this period.Ethical clearance was obtained from the institutional ethics committee. Informed consent was obtained from all the participants.

Method of collection of data

Patients who presented with headache ofmore than 12 weeks duration were evaluated. A detailed history about nasal symptoms includingnasal obstruction,nasal discharge, sneezing,

headache, epistaxis, snoring, hyposmia or anosmia, mass protruding from nostrils, facial pain andmouth breathing were taken.

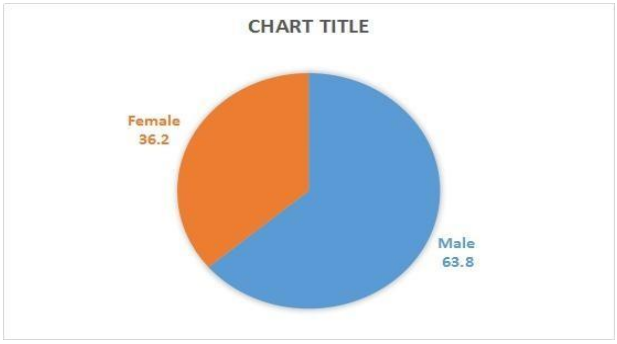
ENT examination includednasal endoscopy, otoendoscopy and throat and neck examination. A total of 94 patients satisfying the criteria and who were willing for further evaluation were subjected to collection and culture techniques of nasal lavage.From the same patients,tissue was taken from the ethmoidal mucosa during surgery and sent for histopathology.

Nasal lavage specimens were collected using the method described by Ponikau[8] in 1999. This method allows the collection of good quantity of mucus and gives a better yield of fungus in the culture medium. Two puffs of 0.1% xylometazoline/oxymetazoline nasal spray were sprayed into each nostril to produce vasoconstriction. The patient was asked to inspire deeply and after 2 min, each nostril was flushed with 20 ml of sterile saline using a sterile curved blunt needle. Patient exhales forcefully through the nose during the flushing. The return was collected in a sterile pan, put in a sterile centrifuge 50 ml tube and sent to the microbiology laboratory. This was processed and inoculated into the Sabouraud dextrose agar media with and without chloramphenicol and cycloheximide.The dish was incubated at 25°C and 37°C, as dimorphic fungi appear as mould at room temperature and as yeast at body temperature. The plates were examined at 3 days interval for a period of 30 days for fungal growth.

Endoscopic sinus surgery was tailored according to the need of the patient. Tissues were taken from the ethmoidal mucosa during the procedure.One sample was sent for histopathology as per the routine practice.The other part of the specimen was placed in a sterile container with normal saline, and sent to the microbiology department for the fungal culture of specimen. Culture of the specimen was done as described earlier.

RESULTS

Study sample included 60 males (63.8%) & 34 females (36.2%).(Figure 1) The mean age was 36.21 with standard deviation of 15.2.(Figure 2) Of the 94 patients studied majority were housewives (25-26.6%) followed by (23-24.5%)students.Most patients presented with nasal obstruction (78-82.2%) followed by facial pain (42-44.7%). (Table 1)On anterior rhinoscopy, polyps were present in 20(21.2%) cases.(Table 2)



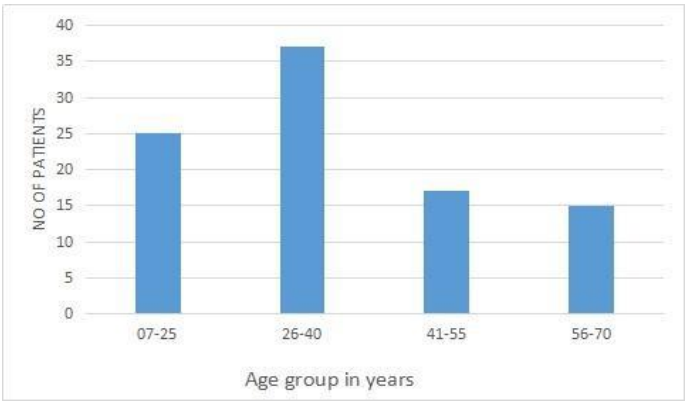


Figure 1: Sex distribution

Figure 2: Age distribution

Symptoms	**No: of patients**	**Percentage**
Facial pain/pressure	42	44.7
Nasal obstruction	78	82.8
Nasal discharge	37	39.36
Post nasal discharge	24	25.5
Hyposmia/Anosmia	18	19.14
Sneezing	32	34.04

Table1: Distribution of the symptoms presented

Findings	No: of patients	Percentage
Septal deviation	74	78.7
Inferior turbinate hypertrophy	30	32
Nasal discharge	28	30
Polyps	20	21.2
Paranasal sinus tenderness	48	51

Table 2: Clinical Examination Findings

Fungal elements in the nasal wash:

Out of 94 patients studied, 21 (22%) patients were positive for fungal elements in nasal wash.Out of these 21 patients, 8(8.5) were positive for Aspergillus fumigatus, another 8(8.5%) were positive for Aspergillus flavus, 4(4.3%) were positive for candida species and 1(1.1%) patient was positive for Rhizopus. (Figure 3)

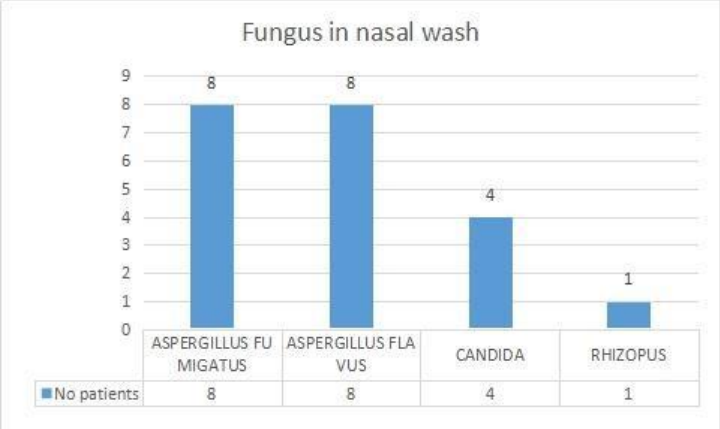


Figure 3: Different types of fungus detected in nasal wash

Fungal elements in nasal mucosa:

Out of 94 patients studied, 21 (22%) patients were positive for fungal elements in nasal Mucosa. Out of these 21 patients, 8(8.5) were positive for Aspergillus fumigatus, 7(7.4%) were positive for Aspergillus flavus, 3(3.2%) were positive for Rhizopus species, 2(2.1%) patients were positive for Fusarium and 1(1.1) patient was positive for Trichomonas species. (Figure 4)

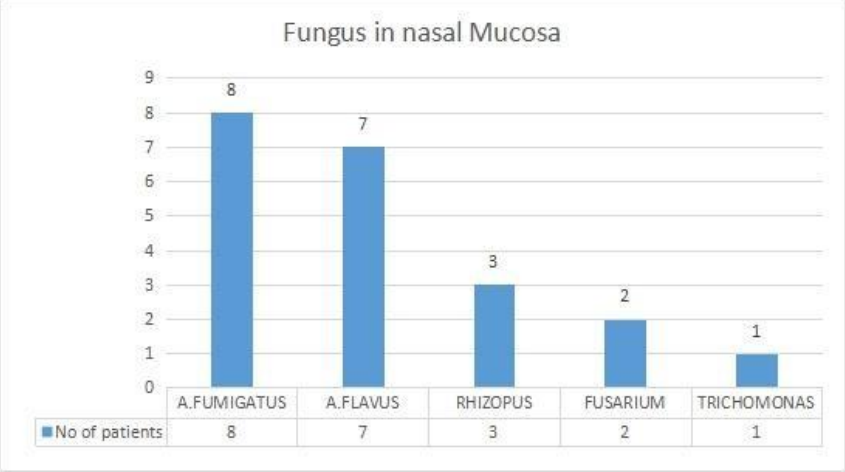


Figure 4: Different types of fungus detected in nasal mucosa

Fungus in nasal mucosa histopathology:

Out of 94 patients studied 6(6%) were positive for fungal elements and rest did not show any positive results in HPE.Out of the 6 positive cases in HPE, 5(5%) were positive for mucorales and 1(1.1%) was positive for aspergillus.

Out of 94 patients studied, 38(40%) patients were found to have nasal polyposis intraoperatively; among this group 26(27.66%) were males and 12(12.77%) were females.

The Sensitivity and specificity of various tests in detecting fungus is shown in the table 3

Test	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Nasal Wash culture	51.3	98.2	95.2	74.8

Nasal Mucosa culture	53.8	100	100	75.3
Histopathology	15.9	100	100	62.5
Nasal Wash + Nasal Mucosa	94.9	98.2	97.4	96.4
Nasal Wash +Histopathology	64.1	98.2	96.2	79.3
Nasal Mucosa + Histopathology	56.4	100	100	76.6

Table 3: Detection of fungal elements by different tests

PPV - POSITIVE PREDICTIVE VALUE NPV -NEGATIVE PREDICTIVE VALUE

DISCUSSION

Chronic rhinosinusitis is said to affect 15% of the adult population.Several factors have been implicated in the development of CRS. Blockage of the sinus openings by oedema, inflammatory mucous and dampened mucociliary function of sinonasal cavity and mucous re circulation can facilitate progress of the disease from acute to chronic. [9]Nasal polyposis has a prevalence rate of 1-4% in the general population. Histologically polyps are associated withdiffuse infiltration with inflammatory cells like eosinophils or neutrophils.[10]

Fungal rhinosinusitis can range from simple benign fungal localization to extremely complicated and aggressive invasive variant of acute fungal rhinosinusitis. The severely impaired mucociliary transport system in patients with CRS causes the stagnation of the fungal spores. The chances of detecting the spores are higher in these patients because of longer stay of inhaled spores in the airway.Clinical examination is inconclusive in most of the cases of fungal sinusitis and diagnosis is basedon high index of clinical suspicion and confirmed by microbiologicaland histopathological examination. [3]

Chronic rhinosinusitis can affect any age group. Our study had a population ranging from 7-70 years with a mean age of 36.21 years with standard deviation of 15.255. This represents

the economically productive age group of the community and reflects the probability of occupational exposure to fungus. Considering the occupations of the patients, 28(30%) people were labourers, 25(27%) were housewives and 23(24.4%) were students, rest were shop keepers, teachers and drivers. This study had 21(22%) patients positive for fungus in the nasal wash samples. The organism commonly found was aspergillus species, aspergillus fumigatus in 8 (8.5%) patients, aspergillus flavus in 8(8.5%) patients, candida in 4 (4.3%) patients and rhizopus species in 1 (1.1%) patient. Similar Study conducted by Goh et al [11] showed culture positivity of 16.7%, but most common organism in that study was rhizopusspecies.

In nasal wash culture, most common organism was aspergillus which correlates with most of the studies done till date in Indian scenario.The studies that supported the growth of aspergillus were studies conducted by Lakshmanan et al [12]in Tamil Nadu, Challa et al[13]in Hyderabad, Deshmukh et al. [14] in Maharashtra and Garg et al[15]in Delhi.Most of the international studies also revealed that aspergillus species as the most common organism.

Nasal mucosal culture

Present study showed that 21 (22%) patients were positive for fungal elements inthe nasalmucosa. Out of these, 8(8.5) were positive for Aspergillus fumigatus, 7(7.4%) were positive for Aspergillus flavus, 3(3.2%) were positive for Rhizopus species, 2(2.1%) patients were positive for Fusarium and 1(1.1%) patient was positive for Trichomonas species. These results correlated with the study of SunilGarg et al[15]which showed 48 patients(26%) positive for nasal mucosal culture and most common organism was aspergillus species. Another study by RaginiTilak et al, on 47 patients showed 10(21.2%) cases positive for fungal culture and most common organism were aspergillus species. [16]

These reportsshowing aspergillus as most common organism were in contrary to the reports from few centers in North America which have shown a high incidence of dematiaceous fungi as in the study done by SC manning et al 1991[17] and Bartynski et al[18]

Histopathology

Out of 94 patients studied, 6(6%) were positive for fungal elements and rest did not show any positive results in histopathology (HPE). Out of the 6 positive cases in HPE, 5(5%) were positive for Mucormycosis and 1(1.1%) was positive for aspergillosis. Dichotomous branching hyphae (n=5) and broad branched aseptate hyphae (n=1) were seen in tissue sections. This study correlates with a study conducted by P Kordbacheh et al[19]who reported that out of 100 patientsincluded in the study, 6 patients showed positive histopathological evidence.Other study with similar results was reported by SariAslani and B. Khademiet al. [20] who found fungal elements in 9(4.2%) patients in histopathological examination. Another study bySanthiet al [2]reported 19 cases (31.7%) positive for fungus in histopathology. Other studies by Marfani, Siddique et al [5], Goh et al[11] also showed a high histopathological evidence for fungi.

Nasal polyposis in histopathology and fungal elements

Out of 94 patients studied 38(40%) patients were positive for nasal polyposis,among this group 26(27.66%)were males and 12(12.77%) were females. A total of 39(41.89%) patients showed fungal elements by any of these three methods such as nasal wash culture, nasal mucosa culture and HPE. Out of 38 cases of nasal polyps 22(58%) patients were positive for fungal elements, it was significant by spearman‘s rho coefficient p value 0.007. These results correlated with a study by Bassiouny[21] where 60 out of 100 patients were positive for fungi and Hajiioannou J.et al[22] with 62.6% fungal growth in nasal polyposis patients.

CONCLUSION

Our findings confirm that the fungal association is frequent in patients with chronic rhinosinusitis. Aspergillus was the most frequently isolated fungus. The mere presence of fungal organisms in association with CRS is insufficient to implicate them as the causative agents in CRS. There is still a poor understanding regarding whether fungi are present as pathogens or simply as a part of the normal flora. Microscopy, histopathology and PCR assay may be considered more significant than culture alone as fungal spores are present everywhere in the environment.Accurate diagnosis provides better management of the patientpreventing the occurrence of dangerous complications and avoidinginjudicious use of antibiotics. At the same time, antifungal agents also need to be used judiciously as the debridement is more important than medications.

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