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Original Research Article

A clinicopathological study of fungal diseases in patients with chronic rhinosinusitis and sinonasal polyposis

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ABSTRACT

Introduction: Chronic Rhinosinusitis (CRS) is a ubiquitous medical condition that has both individual and financial impacts, severely affecting the quality of life. A fungus instigated CRS is fungal rhinosinusitis (FRS) is becoming increasingly incident in recent years. However, the lack of knowledge in the etiology, pathogenesis, and natural history of the FRS complicates the disease management plan.
Aim: To study the prevalence of Fungal Diseases in all cases of Sinonasal polyposis and chronic rhinosinusitis admitted for Functional Endoscopic Sinus Surgery
Materials and Methods: This research focuses on the clinical, microbiological, and radiological analysis of FRS patients for two years. Age, gender, and occupational categorization of FRS patients were done and assessed the risk factors were based on sinus involvements based on radiology and systemic diseases.
Results: The incidence of FRS in 156 patients was higher in males within the age group of 30-40 (28%) and lower economic groups (38%). Symptoms like nasal obstruction (85%) and headache (56%) were predominantly observed. The involvement of multiple sinuses was confirmed through radiology studies. Microbiological tests revealed fungi in 18 samples (11.5%) through direct culture results and potassium hydroxide mount culture study. While Aspergillus genus pre-dominated etiological identification, A. flavus was more common in occurrence (65%), owing to the environment and living conditions that favor the exposure of spores. A recurrence study post-study period came up negative.
Conclusion: A detailed pathophysiological analysis could improve the understanding of the disease prognosis that could avoid developing complications and indiscreet administration of antibiotics, thereby improving the quality of life.

1. Introduction

Rhinosinusitis (RS) is a substantial health problem that appears to emulate the cumulative frequency of allergic rhinitis, thereby imposing a huge financial affliction on society. RS is a broad term that encompasses manifold diseases like ARS (acute RS), CRSwNP (CRS with nasal polyps), besides CRSsNP (CRS without nasal polyps).[1] Chronic RS (CRS) has been found to affect almost 15% of the overall population. CRS is a disease with varied ailments with a characteristic sinonasal mucosa inflammation. However, the pathogenesis of this inflammatory disease is greatly influenced by various genetic and environmental parameters.[2] CRS delineates physical suffering and thereby laying the physiological aspects of life at stake.

CRS instigated by fungi is fungal rhinosinusitis (FRS) is a type of CRS in which patients develop an allergic response to the fungus colonizing the sino-nasal cavities and

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thereby producing mucin.[3] FRS is an exclusive pathologic entity, distinctive by the occurrence of a thick, eosinophilic allergic fungal mucin that involves multiple sinuses, usually bilateral; however, the encompassing of unilateral sinuses are also less common.[4] Among the various fungal pathogens such as Cryptococcus neoformans, Candida sp., Sporothrix schenckii and Alternaria sp, Aspergillus sp and Mucorale fungi are the most pathogenic.[5] Also, demographic sub-type variations along with location-specific species have been reported worldwide. Common etiological FRS agents in India belong to Aspergillus sp, with a relatively higher incidence in the northern regions.[6]

FRS can be acute or chronic, broadly categorized as non-invasive or invasive based on fungal invasion into the tissue. Fungal sinusitis is seen in immunocompetent patients, although FRS is recurrently diagnosed in diabetic or immunocompromised patients. Although non-invasive FRS is required for both surgical and medical intermediation, invasive FRS can affect substantial morbidity besides mortality. FRS encompasses a wide spectrum of immune and pathological responses, including invasive, chronic, granulomatous, and allergic disease.[5] The fungus initiates hypersensitivity type I IgE reaction in patients allergic to fungus. The manifestations of the disease are predominantly driven by the eosinophilic host response to fungi within the sinuses.[7] A cumulative prevalence rate of invasive FRS is upsurging, resulting in higher degree indisposition and mortality, especially in immunocompromised state.[8] However, a clear consensus on terminology, pathogenesis, and optimal management of FRS is still lacking. Henceforth a proper diagnosis of the etiological agent is vital for controlling the prognosis of FRS for the mediation of fungal infection through targeted antifungal therapy. Hence this study was to look into the prevalence of fungal diseases in all instances with sinonasal polyposis and chronic rhino-sinusitis that were hospitalised for functional endoscopic sinus surgery.

2. Aim

To study the prevalence of Fungal Diseases in all cases of Sinonasal polyposis and chronic rhino-sinusitis admitted for Functional Endoscopic Sinus Surgery

3. Materials and Methods

This prospective observational study was done in the department of E.N.T & Head and Neck Surgery at Tirunelveli Medical College Hospital. Following approval from the Institutional scientific and ethics committee, 156 sinus secretions and polyps from patients of all age groups and of either sex who presented with radiologically proven sinusitis (CT scan) with symptoms > 12 weeks duration and undergoing functional endoscopic sinus surgery for 2 years from November 2017 to June 2019 was included in the study. Patients were interviewed by structured questionnaire after obtaining informed consent. All the patients were also clinically assessed after a detailed history, and satisfying the below-mentioned categories were included.

3.1. Inclusion criteria

All cases of CRS who underwent functional endoscopic sinus surgery in age groups and both male & female

3.2. Exclusion criteria

Patients who were on a topical or systemic steroid for the past 1 month before the study period. All cases with the characteristic appearance of fungi in DNE and during surgery. Cases with clinically appearing Malignant Nasal mass and Rhinosporidiosis

Samples of nasal sinus tissue, sinus secretions and allergic mucin from patients undergoing FESS were subjected to mycological culture. The specimen was collected in sterile saline operatively and taken to the microbiology lab as early as possible and was processed on the same day. The sample was subjected to direct microscopy with 10% potassium hydroxide (KOH) and culture.

The material was teased and placed on a clean glass slide, and a drop of 10% KOH was added. A coverslip was placed and the preparation left at room temperature for tissue digestion and then examined by microscopy for the presence of fungal hyphal elements was noticed.

The specimen was inoculated in duplicate on Sabouraud's dextrose agar with Gentamicin and Chloramphenicol. The inoculated media was incubated both at 25°C and 37°C. It was observed daily for one week and then twice weekly for three more weeks. Once fungal growth occurred, it was identified by observing its macroscopic and microscopic morphology. The microscopic morphology was studied by Lactophenol Cotton Blue (LPCB) mount. Slide culture was done when the morphology was unclear and species identification was impossible in the LPCB mount.

4. Results

Patients confirmed with CRS comprised 55% male and 45% female out of 156 samples belonging to the age category between 11 to 70. The highest percentage of infection was recorded among the age group 31 to 40 irrespective of gender, with a higher incidence in males. CRS prevalence among the age group 21-30 was also high (24%), followed by 41-50 (16%). An occupation-wise distribution study revealed the higher incidence of CRS in coolie workers (38%) followed by the housewife category (34%), a very less margin. Higher numbers of farmers were also identified with CRS.Table 1

Table 1: Distribution of patient characteristics

Patient Characteristics		Frequency	Percentage
Age group	0-10	0	0
	11-20	23	15
	21-30	38	24
	31-40	43	28
	41-50	25	16
	51-60	14	9
	61-70	13	8
	71-80	0	0
Gender	Male	86	55
	Female	70	45
Occupation	Coolie	59	38
	Housewife	54	34
	Farmers	12	8
	Others	31	20

The symptomology of CRS included detecting the presence of headache, nasal discharge and obstruction, sneezing, cough, hyposmia, and any signs in the eye. Among the observed patients, nasal obstruction was recorded in higher rates (85%) followed by headache (56%) and nasal discharge (24%). Sneezing, cough and hyposmia were recorded at relatively lower rates in 32, 30, and 23 patients, respectively. Sign of infection in the eye was observed only in one patient.Table 2

Only 19% of CRS patients were identified with systemic disease that was dominated by diabetes mellitus (10%), followed by hypertension (6%), and 3% of patients were diagnosed with both diabetes and hypertension (HT).

Table 2: Distribution of symptoms and systemic diseases

Patient characteristics		Frequency	Percentage
Symptoms	Headache	88	56.4%
	Nasal Discharge	37	23.7%
	Nasal Obstruction	132	84.6%
	Sneezing	32	20.5%
	Cough	23	14.7%
	Hyposmia	30	19.2%
	Eye Symptoms	1	0.6%
Systemic disease	Diabetes Mellitus	15	9.6%
	Hypertension(HT)	9	5.8%
	Both Diabetes & HT	4	2.6%
	Neither Diabetes or HT	128	82.1%

The DNS study in CT revealed a predominant orientation to the left (22%) and lesser to the right (17%). 96 patients displayed no DNS (Graph 6b). Among the polyps observed in DNS, the bilateral polyp was found to have a major occurrence (23%), and only 21% of the bilateral polyp was observed. 58% of CRS patients displayed no polyp.

Regarding the involvement of sinuses in CRS, 69% of observed patients displayed pansinusitis. Other sinuses such as unilateral maxillary & ethmoid sinus (15%), unilateral Maxillary Sinus (15%), bilateral maxillary & ethmoid sinus (13%), bilateral maxillary sinuses (8%), bilateral ethmoid sinus (2%), and unilateral (1%), as well as bilateral (1%) ethmoid sinus, were observed.Table 3

Table 3: Distribution of polyp

		Frequency	Percentage
Polyp in CT	Unilateral Polyp	19	12
	Bilateral Polyps	34	22
	Without polyp	103	66
Deviation in CT	DNS to right	26	17
	DNS To left	34	22
	Total patients without DNS	96	62
Polyp in DNE	Unilateral	33	21
	Bilateral	36	23
	No polyp	87	58
Sinus involvement in CT	Bilateral maxillary sinuses	13	8
	Unilateral Maxillary Sinus	24	15
	Bilateral maxillary & ethmoid sinus	20	13
	Unilateral maxillary & ethmoid sinus	24	15
	unilateral sphenoid sinus	1	1
	Bilateral sphenoid sinus	0	0
	Isolated frontal sinus	0	0
	Bilateral ethmoid sinus	3	2
	Unilateral ethmoid sinus	2	1
	Pansinusitis	69	44

Culture results confirmed fungal presence in 11.5% of tested samples, and the remaining 88.5% came out negative for the presence of fungi. Fungal positivity was found in 20 patients by direct microscopic examination (KOH mount), displaying 18 culture-positive and 2 culture-negative cases. Similarly, 136 culture-negative cases were found through KOH mount negative test. A total of 18 culture-positive and 38 culture-negative results were obtained. Fungal identification test revealed the isolates as

Aspergillus flavus (65%) and A. fumigatus (25%). A Mucor fungus was observed in samples of 2 patients. There were no recurrences recorded in a follow-up study.

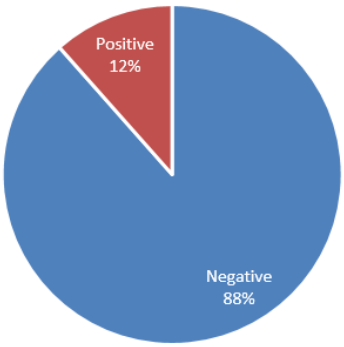

Figure 1: Fungal culture

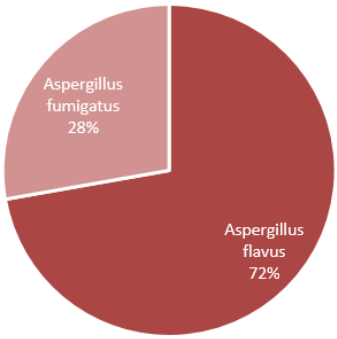

Figure 2: Distribution of fungal isolates

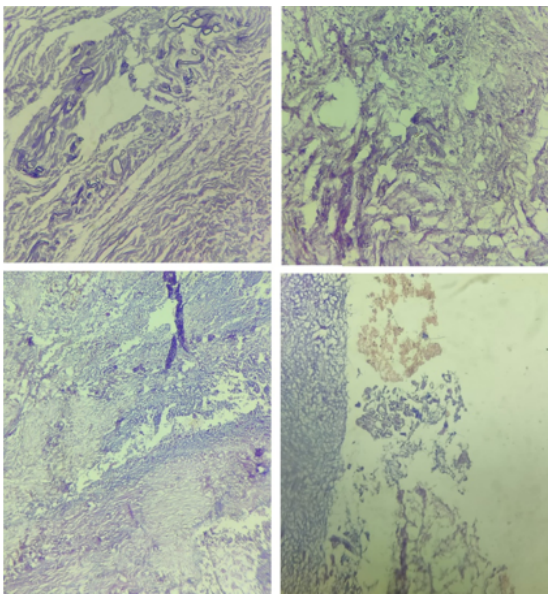

Figure 3: Mucor broad non septate hyphae

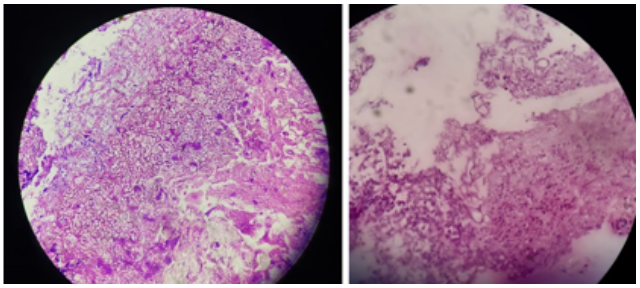

Figure 4: Aspergillus thin septate hyphae with acute angle branching

5. Discussion

Fungal rhinosinusitis is an extensive cluster of conditions instigated by fungal contagions of the paranasal sinuses. Though known for decades, the disease is gaining importance due to the increase in the incidence globally.[9] Due to the heterogeneity of the etiological components coupled with demographical influences and lacunae in the knowledge of the prognosis of the disease, management of FRS is becoming a difficult process. With the potential of FRS infection to cause a decline in the quality of life of infected patients and an upsurge in the frequency of the disease in South India, the current investigation was carried out to shed light on the prevalence, etiology, and progress of FRS in all cases of sinonasal polyposis and chronic rhino-sinusitis admitted for functional Endoscopic Sinus Surgery The study is based on clinical, microbiological, and radiological observations of FRS patients over a period of 2 years. Additionally, the analysis was also focused on associating FRS with the environmental and the presence or absence of systemic diseases among the patients.

The study encompassed patients belonging to the inclusion/exclusion category. Among 156 samples analyzed, male: female ratio of FRS occurrence was 1.3:1, who belonged to the age group of 11 to 70, with males predominantly infected. The average year of the FRS patients was 34.5, delineating the middle-aged group as more susceptible. In a similar study conducted by Das et al. in patients with a mean average age of 31 years, male patients were predominantly affected with a male:female of 1.8:1.[10] Higher incidence rates were targeted at people belonging to the third decade (28%) that were also found in the reports of Kaur et al.[11] Predominant incidence in FRS in people belonging to the lower socio-economic group, coolie was recorded. This might be due to the increased susceptibility of their exposure to fungal spores.

The symptomology was dominated by the observation of nasal obstruction trailed by headache then nasal discharge. In the symptomology study done by Ravindra et al. in FRS patients, nasal discharge was observed in higher numbers.[12] However, in another similar study carried out by Shivani et al., nasal obstruction was the most commonly occurring

symptom.[13] Risk factors associated with the disease could be attributed to diabetes mellitus followed by hypertension. Relating FRS to the immunological status of patients, many associations of fungal infections in patients with systemic diseases such as diabetes mellitus and hypertension are reported in various case studies.[14]

Radiology reports of FRS patients indicated the involvement of multiple sinuses. The common risk factor of FRS patients was designated to be the non-polyp condition compared with a polyp, which was dominated by bilateral polyps as well as the absence of DNS. Common involvement of bilateral sinuses indicates the risk factor as allergy instigated by the patient's exposure to fungal spores. Other risk factors included FRS patients without a DNS. In a study conducted by Shivani et al. nasal polyps and DNS were the major risk factors associated with FRS.[13]

Both culture and KOH mount studies revealed the presence of fungi in only 18 samples. Lower probabilities of appearance of fungi in direct culture as well as KOH mount were reported by Kaur et al. Culture studies revealed the presence of Aspergillus sp in a leading manner.[11] Among them, A. flavus was found in higher rates over A. fumigatus. A likely dominance of A. flavus in FRS patients was reported by various researchers.[9,15,16] Similar cultural characters were also reported in a clinicopathological and microbiological study of FRS conducted by Ravindra et al.[12] This could be related to the predominant presence of A. flavus spores in tropical soils and other environmental factors.[17] A fungal recurrence study after two years revealed the absence of fungal growth. Despite possessing a long historical prevalence, FRS is currently emerging as a severe disease. This study could be used to understand further the etymology and advancements of the disease that could be implemented to devise an efficient management plan.

6. Conclusion

The retrospective study involving FRS patients in the hospital proves that FRS is emerging as a common disease. With over 30% of CR patients diagnosed with FRS and increasing, the better understanding of the proper etiology and diagnosis of FRS, perilous complications, and indiscreet usage of antibiotics could be perverted for better management of FRS.

7. Conflicts of Interests

No conflicts of interests were disclosed.

8. Source of Funding

None.

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