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Fungi in association with chronic bacterial rhinosinusitis; relationship with a synergistic effect: a prospective study

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ABSTRACT

Background: The role of fungi as an etiological factor in the causation of chronic rhinosinusitis remains uncertain. The interaction of fungi with bacteria can result formation of mixed biofilm which provide symbiotic relationship along with resistance from antimicrobials with an increased severity of symptoms.
Methods: The cases of chronic rhinosinusitis were diagnosed and the grading of the symptom severity was done by visual analog scale in which symptoms of nasal blockage, rhinorrhea or post nasal drip, facial pain/headache, loss of smell, sleep disturbance/fatigue were taken into consideration and each of the symptoms was graded from 1 to 10.
Results: A strong association was detected between bacteria and fungi as 37 out of 40 (92.5%) amongst cases and 31 out of 40 (77.5%) amongst controls showed growth of both the organisms. Cases who were detected of having Fungi with Bacteria were having an average score of 8.364 and cases with bacteria alone were having an average score of 6.36. taking into consideration the individual symptom score and analyzing the data, the comparison between cases having both bacteria and fungi and cases with bacteria alone was found to be statistically significant with a p one-tail= 0.010221 and p two-tail= 0.020442.
Conclusions: In chronic rhinosinusitis there is a higher incidence of poly microbial infection, and bacteria along with fungi co-exist with a synergistic effect leading to a higher morbidity.

Keywords: Sinusitis, Fungi, Bacteria, Biofilms, Symbiosis

INTRODUCTION

Fungi have long been considered a causative agent of disease in immunocompromised individuals but the scenario is fast changing and with the advancement in imaging technology, the detection of fungal pathology in the sinuses can be readily detected without any signs and symptoms. There are also reports of invasive form of fungal infection in immunocompetent individuals.[1-3]

The role of fungi as an etiological factor in the causation of chronic rhinosinusitis remains uncertain and the presence of fungi, along with eosinophilic mucin, in patients with chronic rhinosinusitis led to the fungal hypothesis of chronic rhinosinusitis which proposed that an inflammatory response to airborne fungus *Alternaria* is the underlying cause of both chronic rhinosinusitis without nasal polyps and chronic rhinosinusitis with nasal polyps, which is a form of a single disease entity varying only in severity.[4-8]

Supporting evidence is also gathered from the fact that fungi likely play a role in allergic fungal rhinosinusitis, which is a subtype of Chronic Rhinosinusitis referred to as a type 1 hypersensitivity response to fungi and eosinophilic mucin.[9-12]

Secondly, fungi exhibit intrinsic protease activity which in combination with the upregulation of protease-activated receptors in the epithelial cells of nose in patients of chronic rhinosinusitis, provide a potential pathogenic mechanism for the exacerbation of the primary inflammatory processes seen.[13-15]

There are evidence that the cell walls of fungi contain the polysaccharide polymer chitin, which has been proposed to initiate eosinophilic responses in some mouse and human studies.[16,17]

The fungal infection has been broadly divided into two categories namely non-invasive and invasive which are further subdivided. The invasive diseases include 1) acute invasive (fulminant), 2) granulomatous invasive, and 3) chronic invasive. The noninvasive diseases include 1) saprophytic fungal infestation, 2) fungal ball, and 3) fungus related eosinophilic fungal rhinosinusitis.

The interaction of fungi with bacteria can result in a mere physical association which can be planktonic, or with formation of mixed biofilm and interhyphal colonization. Association can also lead to molecular communication leading to antibiosis, signaling with chemotaxis, can bring about physiochemical changes, protein secretion, metabolite exchange, metabolite conversion, adhesion and genetic exchange. It has been seen that physical association along with molecular communication leads to alteration in either of the partners leading to altered community structure which result in altered development and altered morphology of the organisms, niche construction brings about environmental changes which facilitates the reproduction of the organism, movement and transport leads to enhanced growth of either organism, gene acquisition leads to increased survival and vitality under adverse condition, providing nutrition to each other and also increase in pathogenicity with a symbiotic relationship.[18]

Taking into consideration these interactions between fungi and bacteria a prospective case control study was taken into consideration.

METHODS

The study was conducted in the Department of E.N.T of M. M. Institute of Medical sciences and Research, Ambala, from March 2016 to September 2016, after formal ethical approval from the Institutional Ethical Committee. The cases of chronic rhinosinusitis were diagnosed on the criteria laid down by the European position paper on rhinosinusitis and nasal polyps 2012. A detailed history and examination of the patient was done and the symptom score was calculated on the initial visit of the patient using the visual analog scale in which symptoms of nasal blockage, rhinorrhoea post nasal drip, facial pain/ headache, loss of smell, sleep disturbance/ fatigue were taken into consideration and each of the symptom was graded from 1–10 according to the increasing severity (Table 1). The results obtained were analyzed with SPSS version 21 using Chi Square test.

Table 1: Visual analogue scale for nasal symptom severity score.

Symptoms	Score										
Nasal blockage	0	1	2	3	4	5	6	7	8	9	10
Rhinorrhoea/post nasal drip	0	1	2	3	4	5	6	7	8	9	10
Facial pain/ headache	0	1	2	3	4	5	6	7	8	9	10
Loss of smell	0	1	2	3	4	5	6	7	8	9	10
Sleep disturbance/fatigue	0	1	2	3	4	5	6	7	8	9	10

Procedure

Under all aseptic precautions nasal swabs were taken from the secretions present in the middle meatus under endoscopic guidance and were sent for culture and sensitivity. The nasal swab was then subjected to inoculation on appropriate bacteriological (Blood agar, MacConkey's Agar and Lowenstein Jensen Medium) and fungal culture media (KOH Mount and Sabouraud Dextrose Agar) for the identification of the organisms. The controls were considered from the subjects who were not suffering from any nasal condition.

Inclusion criteria

Patients attending the outpatient department of E.N.T with signs and symptoms as per the European position paper on rhinosinusitis and nasal polyps 2012.

Exclusion criteria

Pregnant females, children below age of 2 years and immunocompromised individuals were excluded from this study.

RESULTS

According to the data collected following results were obtained. The data was subjected to statistical analysis using SPSS version 21.

Association between bacteria and fungi

There was a strong association detected between both the organisms as 37 out of 40 (92.5%) amongst cases and 31 out of 40 (77.5%) amongst controls showed growth of Bacteria as well as Fungi on culture (Figure 1).

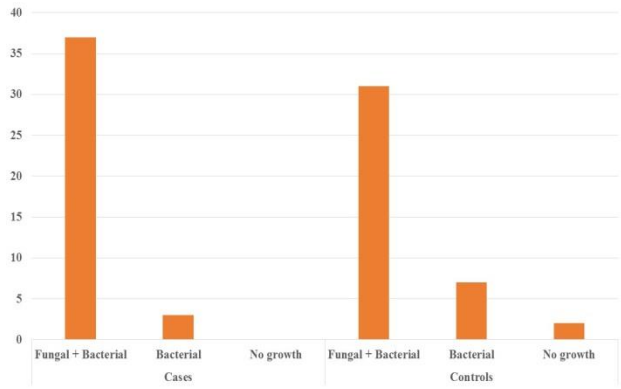

Figure 1: Growth of various organisms in cases and controls.

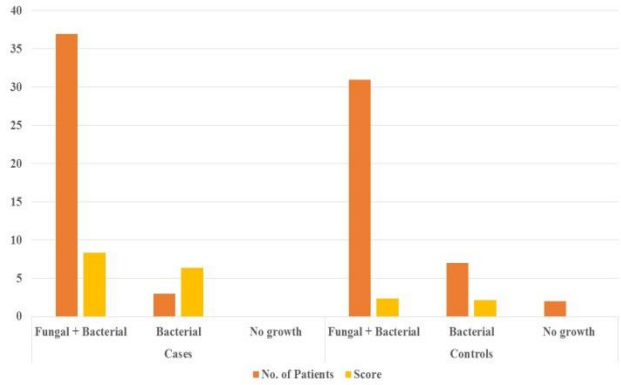

Figure 2: Association with nasal symptom severity score.

VAS score: the score obtained on visual analog scale showed remarkable differences between the cases and controls. Amongst the cases who were detected of having fungi with bacteria were having an average score of 8.364 and cases with bacteria alone were having an average score of 6.36. The VAS score amongst controls was 2.32 and 2.15 respectively (Figure 2).

Table 2: Mean individual nasal symptom severity score.

Symptoms	Cases	
	Fungal+ Bacterial	Bacterial
Nasal blockage	8.72	6.23
Rhinorrhoea/post nasal drip	7.32	7.12
Facial pain/ headache	8.52	7.15
Loss of smell	8.13	5.13
Sleep disturbance/fatigue	9.13	6.17

Individual symptom score: the various symptoms that were considered in the for the formulation of VAS score were nasal blockage, rhinorrhoea/post nasal drip, facial pain/headache, loss of smell, sleep disturbance/fatigue and the individual symptom score that were obtained are depicted in Table 2.

On analyzing the above data, the comparison was found to be statistically significant with a p one-tail= 0.010221 and p two-tail= 0.020442.

DISCUSSION

Rhinosinusitis is a common disease entity that affects approximately 20% of the population, controversies surround the role of fungi in rhinosinusitis and they accounts for >90% of all cases of rhinosinusitis, taking into consideration the classification the most commonly accepted system classifies fungal rhinosinusitis (FRS) into invasive and noninvasive diseases based on histopathological evidence of tissue invasion by fungi. The invasive diseases include 1) acute invasive (fulminant), 2) granulomatous invasive, and 3) chronic invasive. The noninvasive diseases include 1) saprophytic fungal infestation, 2) fungal ball, and 3) fungus related eosinophilic.[19] Research studies have revealed that fungi and bacteria form physical and metabolic reliant groups that have properties distinct from those of their single components.[20] The most significant relation between the two is in the formation of mixed biofilms containing both fungi (filamentous or non-filamentous) and bacteria. It has been confirmed by studies that bacterial-fungal biofilms can exist as diverse complexes of the two, or fungi may provide biotic support for the establishment of a bacterial biofilm.[21] It is also seen that Microorganisms in biofilms show enhanced resistance to antibiotic therapies; as is seen in the presence of *C. albicans* which significantly enhance Staphylococcus aureus biofilm formation and its resistance to vancomycin in serum.[22,23]

In our study there were 97.5% of the cases in which there was detection of fungi along with bacteria compared to 77.5% in controls suggesting that there is proliferation of both bacteria and fungi during the disease. Furthermore the average VAS score was 8.364 amongst individuals in which both bacteria and fungi co-existed compared to 6.36 in individuals with bacterial infestation only.

Taking into consideration the individual symptom score it was seen that the symptom scores were higher amongst cases in which there was co-existence of bacteria along with fungi. The symptoms of nasal obstruction, rhinorrhea/ postnasal drip and facial pain are related to the inflammatory process at the level of mucosa of the nose and the results suggest that there is an increase in the inflammatory process in individuals with the affection of Bacteria along with fungi compared to infection with bacteria alone. The symptom of loss of smell can be directly related to the nasal obstruction and also to the formation of mixed biofilm over the mucosal surface as the relationship between Bacteria and fungi have a higher propensity to form biofilms.

CONCLUSION

Through this study we would like to conclude that in cases of chronic rhinosinusitis there is a higher incidence

of poly microbial infection, and bacteria along with fungi co-exist with a synergistic effect leading to a higher morbidity as evaluated by the symptom score amongst cases.

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