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Original Research Article

# SINONASAL POLYPOSIS ASSOCIATED WITH FUNGAL INFECTION IN A TERTIARY CARE CENTRE

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## Abstract

**Background:** Sinonasal polyposis is often a consequence of chronic rhinosinusitis caused by allergic or nonallergic chronic inflammation. The fungal colonisation and invasion of the nasal cavity causes a hypersensitivity reaction and an imbalance of local immunity, leading to more eosinophilic inflammatory response and polyp formation. For a better understanding of this disease and its effective treatment, it is important to have knowledge of the clinical presentation and different fungal flora involved. The aim is to study the prevalence of fungal infection in patients with sinonasal polyposis and the identify the different fungal species involved. **Materials and Methods:** A cross sectional study was conducted in seventy patients with sinonasal polyposis and fungal materials from nasal cavity and sinuses, that was collected by endoscopy, were sent for fungal staining, culture and histopathological examination. **Result:** A positive fungal culture was noted in about 45.7% cases of sinonasal polyposis. The most common fungal species isolated was Aspergillus flavus. The maxillary sinus [42.8%] was the most commonly involved sinus and the least being the sphenoid sinus. Smoking and diabetes were found to be a significant determinant in the development of fungal infection in sinonasal polyposis. **Conclusion:** Fungal spores in the environment is the most common factor involved in the development of inflammatory reactions in the mucosa of the nose and paranasal sinus, causing polyp formation. Effective control of these risk factors can reduce the prevalence and recurrence of the disease.

## INTRODUCTION

Nasal polyps are benign lesions arising from mucosa of nose and paranasal sinuses, characterized by edematous hypertrophic mucosa with variable cellular infiltrate, as a consequence of chronic inflammation caused by different factors like allergic and non-allergic immunological inflammation or recurrent infections.[1] Etiology of nasal polyposis is multifactorial and most of the theories consider polyps to be the final manifestation of chronic inflammation. Therefore, conditions that lead to chronic inflammation in the nasal cavity can lead to nasal polyposis. According to results, mechanism of sinonasal polyp formation could be due to local antifungal immune reactivity in nose, local imbalance of immunity in the nasal mucosa and hypersensitivity to fungus.[2]

In the general population the overall prevalence rate of nasal polyposis ranges from 0.3%-4.2%.3 It is more common in adults than in children below 10 years of age. An association between the sinonasal polyposis and fungal organisms has been established for many years. This connection was recognized for the first time in 1981 by Millar et al. who noted a similarity between the sinus contents removed from five patients with chronic sinusitis and the typical pathologic resemblance to allergic bronchopulmonary aspergillosis.[3] Human exposure to fungi is inevitable owing to its ubiquitous nature. Elaborate culture techniques have enabled us to detect the presence of fungus in the nose and paranasal sinuses, where it may be routinely deposited during normal respiration. Superficial and saprophytic fungi which cause imbalance in local immunity of nasal mucosa are more important than the invasive fungi. Hypersensitivity to fungal organisms is said to be one of the mechanisms underlying the development of nasal polyposis.[4] Fungal colonization and invasion in nasal polyposis

should be taken into consideration for suitable treatment in addition to the routine management. Chronic Rhinosinusitis with Sinonasal polyposis belongs to the Diffuse eosinophilic CRS group.[5] Recent evidence suggests that IL-17 regulates atopic inflammation by attracting eosinophils and causing subsequent tissue reactions. Aspergillus, Penicillium, Cladosporium, and Alternaria are the most common fungi isolated from patients with CRS.[6] Immune suppression, such as that caused by diabetes, chemotherapy, or corticosteroids, creates a condition in which fungi are able to invade host tissues through normal mucosal barriers.[7]

Thus, for a better understanding of the disease, and for the selection of an effective treatment it is important to have knowledge of the prevalence of the disease, the type of fungal flora involved, varied clinical presentation and appropriate diagnostic tests. It is also important to know its classification based on immune relation between the fungus and the host as well as the level of mucosal invasion. Probably etiopathogenesis of sinonasal polyposis may not be homogenous as many coexisting mechanisms influence the formation of polyp. So, the present study is to find out the prevalence of fungal infection in patients with Sinonasal polyposis and different fungal species involved in paranasal sinuses and nasal cavity.

## MATERIALS AND METHODS

A Cross sectional study was conducted on 70 patients in the Department of ENT at Government Medical College, Kozhikode from March 2021 to July 2022. After obtaining institutional ethical committee approval, the patients who attended the ENT OPD, with a clinical diagnosis of sinonasal polyposis, between the age group of 15 to 65 years were selected for the study. Diagnostic Nasal Endoscopy was done for all patients to identify the nature of the sinonasal polyposis and the presence of pus or fungal material in the middle meatus or nasal cavities. A non-contrast CT scan of paranasal sinuses was done to assess the extent of polyposis and to study the detailed anatomy of paranasal sinuses.

All patients having persistent symptoms after medical management was taken up for Functional endoscopic sinus surgery (FESS) under general anesthesia. A polypectomy, uncinectomy, maxillary antrostomy, ethmoidectomy, frontal sinusotomy and sphenoidotomy was done, depending upon the involvement of the respective sinuses. The surgical specimens, including nasal polyp, pus, caseous debris, fungal ball or fungal elements, were sent for histopathological evaluation. These specimens were fixed separately in buffered formalin. Five-micron thick sections were cut from paraffin blocks and stained with H&E, Periodic acid Schiff and Gomori methenamine silver stains. Specimens for microbiological evaluation were transported without delay in sterile normal saline to the mycology laboratory. These specimens were homogenized in 2 ml sterile normal saline by an aseptic technique and centrifuged at 2000rpm for 10 minutes. Direct 10% KOH mount preparation was made of the specimen and examined. The pellet of tissue was cultured in multiple tubes of Sabouraud's dextrose agar (SDA) with antibiotics and incubated both at 250 and 370 C in a humid atmosphere. The culture was examined daily and continued for four weeks. A growth on such culture is further identified by a lactophenol cotton blue (LCB) mount. Slide cultures were done from fungal isolates to examine the fungal growth in its original form without disturbing the arrangement of the spores for the identification of fungi.

Patients were asked to return to our OPD after one week, three weeks, and three months. Antibiotics and antihistamines were given to the patient during the first week, and saline nasal douching would begin at the end of the first week. Steroid nasal sprays were also given to prevent the recurrence in selected cases, especially for negative culture cases. Patients during the follow-up visits were assessed for improvement in symptoms or any recurrence of the disease.

## RESULTS

The study group constituted 47.1% males and 52.9% females, with a slight female preponderance. The maximum age in the study population was 64yrs, and the lowest was 18yrs. The most common symptoms were nasal obstruction and nasal discharge. Less common symptoms included headache, hyposmia or anosmia, watering from eyes and facial pain. Diabetes mellitus was seen among 59.5% of the female population and 36.4 % of the male population. Hypertension was equally seen among males and females, while bronchial asthma was more common in females.

Anterior rhinoscopy findings revealed bilateral sinonasal polyps in 64.2%, unilateral polyps in 24.2% and no polyp were detected in 11.4% of the population. Both bilateral and unilateral polyps were more common among males, while18.90 % of females had no polyp on anterior rhinoscopy examination. Diagnostic nasal endoscopy of the study group showed multiple bilateral nasal polyps in 84.3% cases and unilateral polyp in 15.7 % cases.

In CT scan of the nose and paranasal sinuses, opacification of the bilateral maxillary sinus was seen in 69% of males and 78.3% of females, while left maxillary sinus alone was involved in 12.10% males and 16.20 % females. Bilateral ethmoid sinuses were involved in 73% of the total cases. Frontal sinus involvement was noted in 54.2% of the total study population, while the sphenoid sinus showed the least opacification (26%). A FESS showed the maxillary sinus to be the most common sinus involved, in 100% of the males and 94.6% of the female population. Sphenoid sinus was the least commonly involved sinus.


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KOH fungal staining was positive in 15.20% of male patients and 45.9 % of female patients, while the fungal culture was positive in 33.30% males and 56.8% females. The fungal organism identified were mainly Aspergillus, Candida, Cladophialophora, Penicillium, Fonsecaea and Mucor genus. Specimen obtained from FESS samples were subjected to fungal culture in Sabouraud's medium and fungal organisms were isolated in 32 patients. Aspergillus species was the predominant organism isolated, which accounted to 32.9% and among them, Aspergillus flavus (27.1%) was the most common. Aspergillus was the most common fungal species grown from the maxillary sinus, which accounts 24.3% of all the fungal species. Aspegillus flavus was even the most common fungal species isolated from the ethmoid sinus (30%), frontal sinus (12.9%) and sphenoid sinus (5.7%). Other organisms identified were Aspergillus niger, Aspergillus terreus, Fonsecaea pedrosoi, Penicillium and Mucor.

The association of various risk factors for fungal growth were included in the study. It was found that smoking had a statistically significant relationship with sinonasal polyposis associated fungal infection. [p value = 0.009]. However, there was no statistically significant relationship between other variables and fungal infection associated with sinonasal polyposis.

## DISCUSSION

Multiple factors contribute to the aetiopathogenesis of sinonasal polyposis and several hypotheses have been proposed to explain its pathogenesis. One of the most accepted etiology is chronic inflammation. Consequently, any condition that can provoke an inflammatory response would result in polyp formation. The ethmoidal air cell system is the most frequent site of an inflammatory response, and polyps typically develop at this location. Nasal polyps are regarded as the culmination of chronic inflammation. As a subtype of CRS, allergic fungal rhinosinusitis is strongly associated with nasal polyps. Fungi are present in the mucus of CRS patients, and these fungi induce the production of cytokines, resulting in a more eosinophilic inflammation in CRS patients than in normal individuals. Fungi can also induce eosinophilic airway inflammation symptoms even without an IgE mediated systemic reaction. This histological picture is caused by the inhalation of fungal spores in the environment and their subsequent entry into the mucosa of the nose and paranasal sinuses. Some claim that they cause chronic irritation of the osteomeatal complex, which leads to mucosal edema and ostia obstruction. With bacterial overgrowth and the release of inflammatory mediators, mucociliary clearance is eventually diminished. Inhaled fungal spores would stimulate eosinophils, which in turn assemble around and attack the fungal elements, resulting in the release of toxic mediators and a secondary inflammatory response. It is hypothesized that the role of fungi in causing an imbalance in the local immunity of nasal mucosa is more significant than that of invasive forms. Hypersensitivity to fungal organisms is one of the primary causes of nasal polyp formation. If not adequately treated, polyps can be devastating, causing bone erosion, orbital involvement, and even intracranial extension.

Seventy patients with Sinonasal polyposis were included in the present study.

The minimum age of patients included in the study was 18 years and the maximum age was 64 years; 29 (41.4%) patients were between 41 and 50 years of age. In a study conducted by Sajjad et al., the most prevalent age group was between 31 to 40 years.[8] In a separate study by Taimoor Latif et al., the predominant age range was between 31 and 40 years, with a mean age of 31yrs.[9] Among the presenting symptoms, nasal obstruction was present in nearly all patients, while facial pain was experienced by approximately 15.2% of males and 10.2% of females. Additionally, patients frequently complained of rhinorrhoea and postnasal drip. Anosmia or hyposmia accompanied by a change in taste were also found.

Diabetes mellitus was present in 36.4% of males and 59.5% of females, and was found to be more common in people diagnosed with sinonasal polyps associated with fungal infection. However, it was not possible to establish a statistically significant relationship between them. In a study on the effect of diabetes mellitus on CRS by Zi Zhang et al, it was found that there was increased development of sinonasal polyps among diabetic patients, and it also showed diabetes could lead to fungal infection of the paranasal sinuses.[10] In a study conducted by O.Satyanarayana, P. Krishna Dora and K.R.L.Surya Kirani on fungal isolates in nasal polyposis, prevalence was found to be around 60%.[11] In our study, 22.7% of smokers developed a fungal infection associated with sinonasal polyps, which was comparable to the findings of Ahmari et al. where 23% of smokers had sinonasal polyposis associated with fungal infection.[12] It was also found that smoking had a statistically significant correlation of fungal infection associated with sinonasal polyposis [p value =0.0009].

In our study, 15.7% of participants had unilateral polyps, while 84.3% had bilateral sinonasal polyps. Of these polyps, 97.14% were found in the maxillary sinus, followed by ethmoid sinus (88.57%), while only 22.9% were found in the sphenoid sinus. This result was similar to the study conducted by Cheng Zhong et al. in 107 patients, which showed maximum distribution in the maxillary and ethmoid sinuses.[10] Our study had a positive fungal culture in 32 patients (45.70%), with Aspergillus flavus being the most frequently identified organism in 19 (27.1%) patients. In their study, Atif et al. found 226 (69.75%) individuals with micropathologically and histopathologically confirmed underlying fungus.[13] In another study of the fungal isolates from nasal polyps in chronic rhinosinusitis patients, at a tertiary care centre in north India by Jain et al., KOH and/or


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culture were positive for fungal hyphae or yeast in 93% of patients (150/161).[6] In a study of 60 people, T. Santhi et al. found fungal elements in 35 patients among which Aspergillus fumigatus was the most common organism, found in 28 people.[14] In the study conducted by Raziuddin Ahmed et al., 17 of the 26 patients tested positive for fungal elements, with Aspergillus flavus being the most prevalent species.[15] Satyanarayana et al. found 30 positive cases in their study population of 50, among which 13 had Aspergillus flavus isolated.[11]. Even in our study, Aspergillus species were found in most patients.

In our study, direct microscopy following KOH staining was positive in 22 patients, or 31.4% of the total study population. These patients were also culture positive for fungi. Ten patients whose cultures were positive were negative upon direct microscopic examination. It was also seen that the fungus grown from 23 patients did not show up in histopathological staining. Fungal growth was found in 28 of the 59 patients with bilateral polyps, while only 3 of the 11 patients with unilateral polyps had fungal organisms.

Our study revealed that the majority of cultured fungal species were found in the maxillary and ethmoid sinuses. These include Aspergillus spp., Candida spp., Cladophialophora spp., Penicillium spp., Fonsecaea spp., and Mucor spp. The maxillary sinus was the most common site for the nasal polyposis associated with a fungal infection in 30[42.8%] patients, and it was comparable to the study on 160 patients treated with endoscopic surgery by Piere et al., which also showed maximal fungal distribution in the maxillary sinus.[16] In comparison to the findings of other studies, Aspergillus flavus, Aspergillus fumigatus, Mucor spp. and Candida albicans were identified as the causal fungi in the study on chronic fungal maxillary sinusitis by Vijay et al,[17] In 77.8% of their cases, Aspergillus species were the most common species isolated, whereas in the study by Rupa et al., it accounted for 95.8% of the fungal isolates.[18]

## CONCLUSION

The aetiology of sinonasal polyposis was found to be multifactorial. However, fungal spores in the environment can be considered the most common factor involved in the development of inflammatory reactions in the mucosa of the nose and paranasal sinus, causing polyp formation. A positive fungal culture in sinonasal polyposis was 45.7% among the study population and most common fungal species isolated was Aspergillus flavus. The maxillary sinus [42.8%] was the most commonly involved sinus in fungal infection and the least being the sphenoid sinus.

The distribution of fungal species in various paranasal sinuses depends on the anatomical accessibility and physiological characteristics of each sinus in terms of mucociliary clearance and drainage pathways. Various risk factors have paved the way for the development of fungal infection, in which diabetes and smoking were found to be a significant determinant in the development of fungal infection in sinonasal polyposis. Effective control of these risk factors can reduce the prevalence and recurrence of the disease.

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