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Original Research Article

Evaluation of clinicomycological profile in patients of chronic rhinosinusitis

Dimple Sahni[1], Sandeep Kaur[1], Sangeeta Aggarwal[2], Amandeep Kaur[1]*, Priya Sahni[3]

[1]Department of ENT, Government Medical College (GMC), Patiala, Punjab, India
[2]Department of ENT, Gian Sagar Medical College, Rajpura, Punjab, India
[3]Department of Social and Preventive Medicine, All India Institute of Medical Sciences (AIIMS), Bathinda, Punjab, India

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***Correspondence:**
Dr. Amandeep Kaur,
E-mail: 2k7amandeep@gmail.com

ABSTRACT

Background: Rhinosinusitis (RS) poses a major health problem, substantially affecting quality of life, productivity, and finances.
Methods: This prospective clinical study was conducted in the Department of ENT at Government Medical College, Patiala, from March 2022 to June 2024 (2 years) involving 60 patients diagnosed with Chronic Rhinosinusitis (CRS) based on the diagnostic criteria outlined in the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS-2012).
Results: The study comprised patients with a mean age of 37.42 years (±14.43) with male to female ratio of 1.22:1. Mycological evaluation showed fungal filaments on KOH mount in 35% patients and *Aspergillus flavus* being the most frequently isolated species on culture. Histopathological analysis confirmed fungal rhinosinusitis in 30% of patients, with allergic fungal rhinosinusitis being the most common finding, followed by fungal ball.
Conclusions: In our study, *Aspergillus flavus* being the most commonly isolated fungus, followed by *Aspergillus fumigatus* and Mucorales species. These findings highlight the common fungal association in CRS. Mycological identification is essential for accurate diagnosis, guiding appropriate treatment and preventing complications.

Keywords: Aspergillus, Chronic rhinosinusitis, Fungal sinusitis, Nasal polyposis

INTRODUCTION

Chronic rhinosinusitis is defined as a chronic inflammatory process of nasal mucosa and paranasal sinuses lasting more than 12 weeks, without complete resolution of symptoms.[1] It reflects a dysfunctional immune interplay between different host susceptibilities and environmental modifiers that are responsible for the chronic inflammatory response.[2]

CRS is classified into two phenotypes: CRS without nasal polyposis (CRSsNP) and CRS with nasal polyposis (CRSwNP). CRSwNP is frequently associated with asthma, aspirin-exacerbated respiratory disease (AERD), and allergic fungal rhinosinusitis (AFRS).[3]

The European position paper on Rhinosinusitis and nasal polyps (EPOS2012) outlined diagnostic criteria for CRS in adults. Diagnosis typically requires two or more of the following symptoms: nasal blockage or congestion, nasal discharge (anterior or posterior), facial pain or pressure, and a reduced or lost sense of smell, endoscopic signs like nasal polyps, mucopurulent discharge from the middle meatus, or mucosal obstruction mainly in the middle meatus. CT scan findings, such as mucosal changes in the

osteomeatal complex or sinuses, also support the diagnosis.[1]

Various conditions can predispose individuals to developing chronic sinusitis which include anatomical abnormalities such as septal deviation, concha bullosa, and uncinate process deviation, other conditions like allergic rhinitis, sensitivity to aspirin, asthma, nasal polyps, and non-allergic rhinitis. Immunological disorders like cystic fibrosis, primary ciliary dyskinesia and Kartagener syndrome. Other factors like smoking, environmental pollutants, gastroesophageal reflux disease (GERD), dental diseases, and systemic diseases such as granulomatosis with polyangiitis and sarcoidosis, further increase susceptibility to chronic sinusitis.[4]

Bacteriology includes *Staphylococcus aureus* (both methicillin susceptible and methicillin-resistant strains), coagulase-negative *Staphylococci*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, *Streptococcus intermedius*, *Pseudomonas aeruginosa*, *Nocardia species*, and anaerobic bacteria such as *Peptostreptococcus*, *Prevotella*, *Porphyromonas*, *Bacteroides*, and *Fusobacterium species*.[5,6]

Specific groups of immunocompromised patients on immunosuppressive therapies, cancer chemotherapy, intensive care treatments, conditions like Covid-19, diabetes, AIDS, hematologic disorders, organ transplantation medications increase risk of FRS.[7]

Fungal sinusitis categorized into two broad groups i.e. Invasive and non-invasive based on the presence or absence of fungus in tissue (mucosa, blood vessel or bone). Non-invasive fungal rhinosinusitis includes saprophytic fungal infection, fungal ball and allergic fungal rhinosinusitis.

The saprophytic fungal infection refers to fungal colonies within mucosal crusts in nose and paranasal sinuses with mostly asymptomatic or may have foul smelling discharge.[8] Sinus fungal ball is non-invasive accumulation of dense fungal hyphae within sinuses mainly maxillary sinus, common in middle aged females with prior history of dental procedure.[9]

Allergic Fungal Rhinosinusitis (AFRS) is prevalent with common species including *Alternaria*, *Bipolaris*, and *Curvularia*. These fungi provoke an allergic response in the sinuses, leading to the production of allergic mucin and the development of nasal polyps. AFRS primarily affects younger age groups and have male predominance.[10]

Bent and Kuhn developed the diagnostic criteria for AFRS with 5 major and 6 minor criteria.[11] Invasive fungal rhinosinusitis includes acute, granulomatous and chronic invasive fungal rhinosinusitis.

Acute fulminant invasive fungal sinusitis is most life threatening and rare form of fungal sinusitis, with duration less than 4 weeks primarily affecting severely immunocompromised patients. Aspergillus or members of the Zygomycetes class (such as Mucor and Rhizopus) are commonly responsible, with a mortality rate exceeding 50%, as this fungus rapidly invades sinus tissues, bones, extending into surrounding areas like the brain and orbit.[12] Nasal endoscopy reveals necrotic tissue, eschar formation and microscopically, fungal invasion of blood vessels can be observed, causing tissue necrosis.[13]

Chronic invasive fungal sinusitis progresses slowly and exhibits a less aggressive course. Vascular invasion is rare, and there is minimal inflammatory response with limited involvement of surrounding structures. This form effects patients with diabetes mellitus, AIDS, and those on long-term corticosteroid therapy. It primarily affects the ethmoid and sphenoid sinuses and persists for more than three months. Aspergillus fumigatus is common causative fungus.[14] Granulomatous invasive fungal sinusitis is more frequently observed in patients from Sudan, India, Pakistan, and Saudi Arabia. The disease progresses slowly, lasting over three months. It typically presents with an enlarging mass affecting the cheek, orbit, nose, and paranasal sinuses in immunocompetent individuals. Proptosis is often a prominent clinical feature.[15]

The purpose of this study was to assess the presence of fungal organisms in nasal samples, sinus secretions, and surgically removed nasal polyps and to identify the type of organisms involved in 60 patients of Chronic Rhinosinusitis at Government Medical College and Rajindra Hospital Patiala.

METHODS

This prospective clinical study was conducted from March 2022 to June 2024 (2 years) involving 60 patients diagnosed with Chronic Rhinosinusitis (CRS) based on EPOS-2012 criteria at Government Medical College, Patiala. Patients included with age ranges from 11 to 65 years, of both sexes, diagnosed cases of chronic rhinosinusitis and patients giving consent for the study. Patients with pregnancy, acute sinusitis, malignancy of nose and PNS, children below 10 years of age, treated cases of CRS, and patients not giving consent for study was excluded.

A detailed clinical history, including nasal obstruction, discharge, sneezing, headache, epistaxis, snoring, hyposmia, nasal mass, facial pain, and mouth breathing, was recorded for each patient. Blood investigations, diagnostic nasal endoscopy, X-ray (water's view) and CT of nose and PNS or MRI were done as per requirement. Microscopic examination of specimens collected as nasal swabs during nasal endoscopy, nasal crusts, allergic mucin, nasal washings and tissue excised during nasal surgery i.e. Sinus mucosa and nasal polyp subjected to wet KOH mount, mucin examination for Charcot-Ley den crystals, histopathological examination of biopsy material

with special stain and fungal culture in Sabouraud's dextrose agar. All data collected from patients' history, examinations, radiological, microbiological and histopathological investigations recorded in proforma.

Results of fungal mounts and fungal cultures were reviewed and correlated with clinical, histopathological and radiological findings to reach at final diagnosis and characterization of Fungal Rhinosinusitis. Statistical analysis of the data was performed using appropriate statistical tests.

Figure 1: Yellow brown growth of *Aspergillus flavus* on SDA media.

RESULTS

The study of 60 chronic rhinosinusitis (CRS) patients revealed that the majority were aged 26-40 years (mean 37.42±14.43), while fungal rhinosinusitis (FRS) patients ranged from 11-65 years (mean 37.33 years), with a male to female ratio of 1.22:1 (Figure 2).

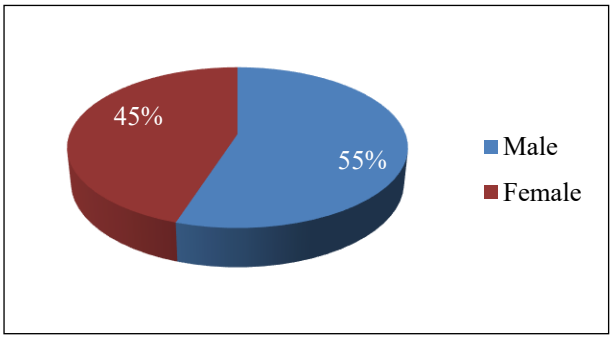

Figure 2: Distribution of patients of chronic rhinosinusitis based on gender.

The most common effected with CRS were farmer (25%), followed by student (18.33%), service class (16.67%), and housewife (15%). A significant proportion belonged to lower middle (46.67%) and lower (33.33%) socioeconomic strata, with most residing in rural areas (65%). Nasal discharge was the predominant symptom in both CRS and FRS groups, followed by nasal obstruction. In FRS group, nasal discharge was observed in 17 (89.47%) patients followed by nasal obstruction in 11 (57.89%) patients (Figure 3).

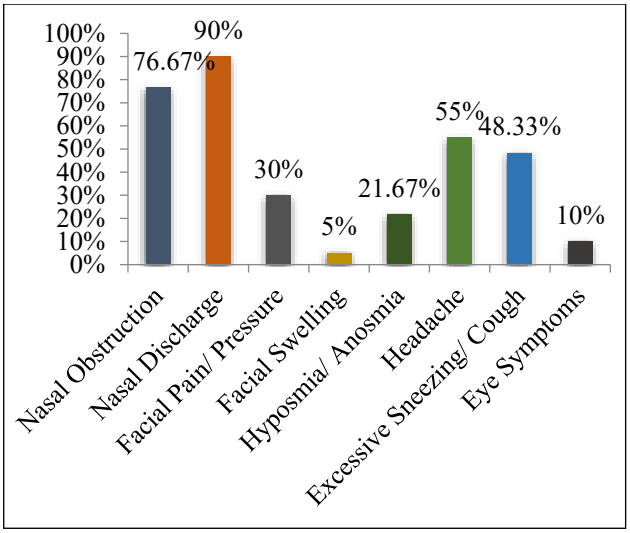

Figure 3: Distribution of patients of chronic rhinosinusitis based on symptoms.

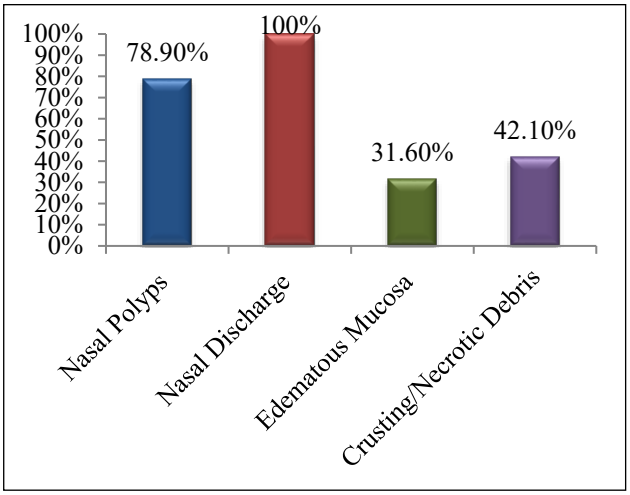

Figure 4: Endoscopic appearance in fungal rhinosinusitis patients.

Table 1: Sinus involvement on CT scan in patients of fungal rhinosinusitis.

Sinuses involvement	Fungal rhinosinusitis patients (n=19)	Percentage
Maxillary sinus	19	100
Anterior ethmoid sinuses	18	94.74
Posterior ethmoid sinuses	15	78.95
Frontal sinus	14	73.68
Sphenoid sinus	13	68.42
OMC	17	89.47
Pansinusitis	6	31.58

Diagnostic nasal endoscopy in the CRSwNP group showed nasal polyps (100%), discharge (70.37%), edematous mucosa (57.14%), and crusting (2 patients). In

the CRSsNP group, discharge (29.63%), edematous mucosa (42.86%), crusting (6 patients), and necrotic debris (4 patients) were noted. The FRS group presented with nasal polyps in 78.9% (Figure 4). The mean Lund Mackay endoscopic score was 4.43±1.04 for CRSwNP and 1.60±1.23 for CRSsNP. Mean polyp scores were slightly higher in CRS than FRS.

The maxillary sinus was most commonly involved in both CRS (nearly all patients) and FRS (100%) (Table 1).

In present study of 60 patients, KOH mounts were performed to assess for fungal elements and 21 patients (35%) tested positive for fungal elements (Table 2).

In the current study, fungal culture was tested positive in 19 out of 60 constituting 31.67% of the total patients and *Aspergillus flavus* was most common isolate (42.11%) (Figure 5).

Table 2: KOH mount.

KOH mount	Patients (60)	Percentage
Positive	21	35
Negative	39	65
Total	60	100

In the present study, *Aspergillus flavus* was the most frequently identified species, found in 8 cases (42.11%), with manifestations including 4 cases of AFRS, 3 cases of fungal ball and 1 case of granulomatous invasive fungal rhinosinusitis. *Aspergillus fumigatus* was identified in 3 cases (15.79%), with 1 case of AFRS and 2 cases of fungal ball. *Aspergillus niger* accounted for 2 cases (10.53%), involving 1 case each of AFRS and chronic invasive fungal rhinosinusitis (CIFRS). Candida was isolated in 1 case (5.26%), diagnosed as AFRS. Mucor was found in 3 cases (15.79%), as acute invasive fungal rhinosinusitis (AFRS). *Rhizopus arrhizus* and *Fusarium* each represented 1 case (5.26%) of CIFRS and chronic inflammatory polyp, respectively.

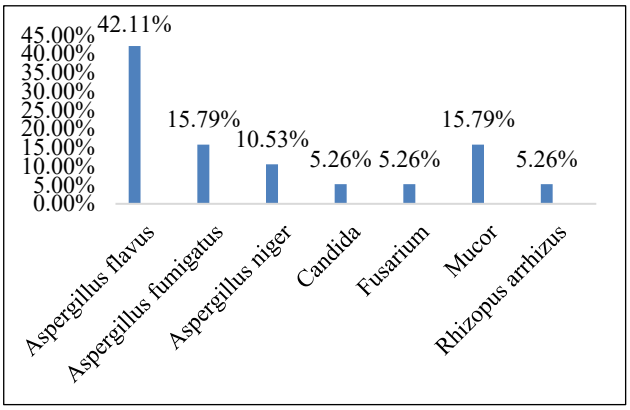

Figure 5: Fungal isolates in culture positive patients.

Table 3: Characterization of chronic rhinosinusitis patients on the basis of histopathological examination.

Histopathological findings	Chronic rhinosinusitis patients (n=37)	Percentage
AFRS	7	18.91
AIFRS	3	8.12
Antrochoanal polyp	1	2.71
Granulomatous IFRS	1	2.71
Chronic IFRS	2	5.41
Chronic inflammatory polyp	17	45.91
Fungal ball	5	13.52
Sinonasal papilloma	1	2.71
Total	37	100

Table 4: Distribution of fungal isolates among various histopathological types of fungal rhinosinusitis.

Fungal species (N=19)	AFRS	Fungal ball	AIFRS	GIFRS	CIFRS	Chronic inflammatory polyp	Total	Percentage
***Aspergillus flavus* (N=8)**	4	3	0	1	0	0	8	42.11
***Aspergillus fumigatus* (N=3)**	1	2	0	0	0	0	3	15.79
***Aspergillus niger* (N=2)**	1	0	0	0	1	0	2	10.53
***Candida* (N=1)**	1	0	0	0	0	0	1	5.26
***Mucor* (N=3)**	0	0	3	0	0	0	3	15.79
***Rhizopus arrhizus* (N=1)**	0	0	0	0	1	0	1	5.26
***Fusarium* (N=1)**	0	0	0	0	0	1	1	5.26
Total	7	5	3	1	2	1	19	100

Table 5: Sensitivity and specificity of mycological and histopathological examination for fungal rhinosinusitits.

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
KOH mount	100	95.12	90.48	100	96.67
Histopathological examination	94.74	100	100	100	98.33

DISCUSSION

Fungal rhinosinusitis (FRS) encompasses a range of disease processes characterized by diverse clinical presentations, histologic features, and biological implications. The widespread use of nasal endoscopy and CT scans, coupled with surgeons routinely submitting excised tissues for biopsy and pathologists conducting special fungal stains on suspected specimens, has led to a significant increase in positive reports of fungal infections, which is crucial for guiding targeted antifungal therapy effectively. *Aspergillus* is identified as the predominant fungal pathogen causing sinusitis. Patients with zygomycotic infections have reported the highest mortality rate of 33.3%.[16]

The present study was conducted on 60 patients of CRS in the age group of 11-65 years with mean age of patients was approximately 37.42 years with a standard deviation of ±14.43.

Among 19 patients of fungal rhinosinusitis age range was 11-65 years with mean age of 37.33 years.

In a similar study conducted by Krishnan et al age varied from 14 years to 62 years with majority of patients (37%) belonging to age group 21-40 years.[17]

In our study, there were 33(55%) males and 27(45%) females with a male to female ratio of 1.22:1 (Figure 2). Among 19 fungal rhinosinusitis patients, 10(52.63%) were males and 9 (47.37%) were females. A study done by Uzma et al also observed male predominance with 58.9% male and 41.1% female patients.[18]

In this study, predominant occupation among CRS patients was farming, 25% of cases followed by students 18.33%. In fungal rhinosinusitis 26.3% were farmers, 21.05% were housewives, 15.79% each belonged to service and unemployed group. A case series published by Milosev et al showed a higher incidence of fungal rhinosinusitis among farmers.[19] The individuals working in hot and dry climates sustain frequent mucosal injuries in their paranasal sinuses and acquire fungal agents from the fields.[20]

In the present study, 65% patients were from rural areas, whereas 35% were from urban areas. In similar study by Choudhary et al 52% of patients were from the rural area and 48% from the urban area.[21]

In our study of 60 CRS patients, the most common symptoms were nasal discharge (90%) and nasal obstruction (76.67%) (Figure 3). Among 19 fungal rhinosinusitis patients, nasal discharge was present in 89.47%, nasal obstruction in 57.89%, and headache in 52.63%. Excessive sneezing and cough, facial pain/pressure, and olfactory dysfunction were seen in 42.11%, 21.05%, and 26.32% of patients, respectively.

In the research conducted by Munjal et al nasal discharge was the predominant complaint in 37.2% cases, followed by nasal blockage in 23.6% and eye symptoms in 11.8%, mostly associated with the invasive form of the disease, results were similar to present study.[22]

In this study, 38.33% chronic rhinosinusitis patients had deviated nasal septum, 6.67% had diabetes mellitus, 16.67% had hypertension and 8.33% had bronchial asthma as predisposing factor,1.67% patients had history of previous FESS. A similar study conducted by Munjal et al, 20.9% cases had associated co-morbidities like bronchial asthma and diabetes 56.5% and 26.5% respectively.[22]

According to Lund Mackay scoring system on diagnostic nasal endoscopy nasal polyps were seen in 78.9% fungal rhinosinusitis patients, Nasal discharge in 100%, edematous mucosa in 31.57% and crusting was present in 42.11% fungal rhinosinusitis patients and 21.05% patients had necrotic debris (Figure 4). Similarly, in a study conducted by Ravindra et al the most common endoscopic finding in fungal rhinosinusitis cases was mucopurulent discharge (91%), followed by presence of polyp (83%), edematous mucosa (75%), inspissated debris (33%), and necrotic tissue (8%).[23]

In 19 fungal rhinosinusitis patients, CT scan of 3.57% patient showed homogenous opacities, 21.67% patients had heterogenous opacities, and 8.33% patients had heterogenous opacities with bone erosion. In study conducted by Kaur et al heterogeneous opacities were predominant, observed in 60% of cases with a statistically significant association.[24]

In our study in 60 CRS patients, the maxillary sinus was most commonly involved sinus in 100% patients. In fungal rhinosinusitis the maxillary sinus was involved in 100% patients, followed by anterior ethmoids in 94.74%, posterior ethmoids in 78.95%, frontal in 73.68% and sphenoid in 68.42% patients. Osteomeatal complex was blocked in 89.47% patients and Pansinusitis seen in 31.57% patients (Table 1). In a study conducted by Ravindra et al, among the 12 patients with fungal rhinosinusitis, maxillary sinus involvement was the most common (91%), followed by anterior ethmoid (9%), posterior ethmoid (9%), sphenoid (3%), and frontal sinus (2%). In 2% of cases there was involvement of all the paranasal sinuses.[23]

Out of 60 patients, 21(35%) patients showed fungal filaments on KOH mount (Table 2). On further inoculation on culture media for 4 weeks, growth was seen in 19 patients and 2 had no growth. Kaur et al conducted a study where direct microscopy showed positivity in 25 cases (71.42%), all of which exhibited septate hyphae. Additionally, culture results were positive in 32 out of 35 cases examined.[24]

In present study out of 19 culture positive patients,

Aspergillus flavus was the most common isolate detected in 8 (42.11%) patients, *Aspergillus fumigatus* in 3 (15.79%) and *Aspergillus niger* in 2 (10.53%) patients. Candidal growth was seen in 1 (5.26%) patient. Sinonasal mucormycosis was seen in 3 (15.79%) patients. *Fusarium* and *Rhizopus arrhizus* species were detected in 1 (5.26%) patient each (Figure 5). Our study aligns with findings from Prateek et al where *Aspergillus spp.* (76.19%) was the predominant isolated species among cases of fungal rhinosinusitis. Specifically, *Aspergillus flavus* (57.14%) emerged as the most frequently identified fungal isolate, followed by *Aspergillus fumigatus* (14.29%).[25]

In the present study, histopathological examination for nasal and sinus specimens was done in 37 patients. Out of 37 patients, 17 (45.91%) patients had findings suggestive of chronic inflammatory polyp, 7 (18.91%) had allergic fungal rhinosinusitis, 5 (13.52%) patients had fungal ball findings, 3 (8.12%) had histopathological findings suggestive of acute invasive fungal rhinosinusitis, 2 (5.41%) patients had chronic invasive fungal rhinosinusitis. Antrochoanal polyp and sinonasal papilloma was seen in 1 (2.71%) patient each. 1 (2.71%) patient had granulomatous invasive fungal rhinosinusitis (Table 3).

Ajay et al conducted a study where histopathological classification of fungal rhinosinusitis (FRS) included 14 patients categorized as follows: 9 (64.2%) diagnosed with Allergic Fungal Rhinosinusitis (AFRS), 1 (7.14%) with fungal ball, 2 (14.2%) with Chronic Invasive Fungal Rhinosinusitis (CIFRS), 1 (7.14%) with Granulomatous Invasive Fungal Rhinosinusitis (GIFRS), and 1 (7.14%) with Acute Fulminant Invasive Fungal Rhinosinusitis (AFIFRS).[26]

In the present study, the sensitivity and specificity for diagnosing fungal elements by KOH mount was 100% and 95.12% respectively. The PPV was 90.48% and NPV was 100% with overall accuracy of 96.67%. The sensitivity and specificity for diagnosing fungal infections by histopathological examination was 94.74% and 100% respectively. The PPV and NPV were 100% with overall accuracy of 98.33% (Table 5).

Suresh et al conducted a study in which the sensitivity of microbiology examination in diagnosing fungal rhinosinusitis was 50%, but specificity was 100%. The sensitivity and specificity of pathologic examination was 76.67% and 100%, respectively. There was a statistically significant correlation for microbiology and pathologic examination in the diagnosis of fungal rhinosinusitis.[27]

CONCLUSION

In our study, 31.67% of the 60 chronic rhinosinusitis patients were found to have fungal rhinosinusitis. *Aspergillus flavus* was the predominant fungus isolated in the cultures, followed by *Aspergillus fumigatus* and *Mucorales species*. These findings confirm that fungal association is common in patients with chronic rhinosinusitis. Mycological identification plays a crucial role in diagnosing and categorizing CRS and provides therapeutic guidance for other specialties, especially in cases of atypical presentation and infections with less common agents.

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