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Incidence of Anaerobes in Patients with Chronic Rhinosinusitis

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Abstract: ***Background: Chronic sinusitis (CS) is an inflammatory disorder of the upper airways, which lasts longer than 12 weeks, often causing residual damage to the sinus mucosa, leading to long-term symptoms. CRS is a multifactorial morbidity, in which the complex microbiome plays a pathogenic role. The present study has been undertaken to determine the incidence of anaerobic microbes in cultures, secretions, and/or mucosal fragments acquired from CRS patients. Materials and Methods: This prospective study was conducted in the Department of ENT & Head Neck Surgery, Moti Lal Nehru, Medical College, and Swaroop Rani Nehru Hospital, Prayagraj from August 2020 to July 2021. The patients of CRS with or without polyp are willing to participate in the study and having age group between 18-45yr irrespective of gender was included in the study. Methods used for obtaining the sample were swabs obtained from middle meatus or ethmoid sinus during FESS or from osteomeatal complex secretions through endoscopy in OPD patients used for quantitative culture sensitivity and identification of organisms. Result and discussion: The mean age of patients was 26.55 ± 7.58 years. Most of the patients fall between the age of 18-24 (51.66%) years. Out of 60 cases, 33(55%) were male and 27(45%) were females. Nasal obstruction was seen in the majority 65% of patients presented with CRS followed by nasal discharge in 18.33%. As per the distribution of microorganisms, aerobes account for (55%), followed by anaerobes (40%), polymicrobial infection (1.67%), and sterile culture were isolated in 2(3.33%) samples. In the present study, we observed that Macrolides (azithromycin), Quinolones (levofloxacin), Cephalosporins (cefuroxime), Penicillin plus β-lactamase inhibitors (Amoxicillin+clavulanic acid), and Linezolid were quite efficient against the bacteria identified in our investigation. Conclusion: This study was conducted to underline the significance of the identification of specific microorganisms especially anaerobes which seem to be a major cause of chronicity and to assess their susceptibility to specific antimicrobials for targeted therapy and minimization of empirical use of antibiotics.***

Keywords: chronic sinusitis, anaerobic bacteria, prospective, microbiology, otolaryngology

1. Introduction

Chronic rhinosinusitis (CRS) is a huge disease burden worldwide, impacting at least 11% of the population1 and imposing a significant cost burden on healthcare systems, individuals, and the economy due to lost productivity at work.[1, 2]

The term rhinosinusitis refers to a group of disorders characterized by inflammation of the ciliated respiratory mucosa of the nose and paranasal sinuses, as they are contiguous with each other and it is rare for one to be affected in isolation. [3]

The rhinosinusitis task force of the American Academy of Otolaryngology-Head and neck surgery has classified rhinosinusitis based on timeframes and clinical presentation into Acute Rhinosinusitis (ARS), Recurrent Acute Rhinosinusitis (RARS), Sub Acute Rhinosinusitis (SRS), Chronic Rhinosinusitis (CRS), and Acute Exacerbation of Chronic Rhinosinusitis (AECRS) [3].

Chronic rhinosinusitis occurs when symptoms last longer than 12 weeks. These symptoms are facial pain/pressure, nasal obstruction/blockage, nasal discharge, hyposmia/ anosmia, fever, headache, halitosis, fatigue, dental pain, cough, ear pain/pressure/fullness, pus on nasal examination is some of the symptoms. These symptoms have been classified as major and minor, with major symptoms being facial pain/pressure, nasal obstruction/blockage, nasal discharge, hyposmia/anosmia, pus on nasal examination, and rest being minor symptoms. Two major or one major with two minor symptoms when present is clinically diagnostic of chronic rhinosinusitis.[3]

Rhinosinusitis is widely believed to comprise a spectrum of inflammatory and infectious diseases, simultaneously affecting the nose and paranasal sinuses.

Inflammation of the nose and paranasal sinuses can be caused by a variety of factors. A few notable causes are cystic fibrosis, anatomic abnormalities such as concha bullosa, septal spur, paradoxical turbinate, allergic or immune disorders, trauma, noxious chemicals, microorganisms, post-surgery medications, etc. [3] Pathogenic bacteria and fungi have a variety of roles, including acting as the principal initiator or perpetrator of disease in several CRS subtypes. Pathogenic organisms, on the other hand, may have no or just a minor role in other CRS symptoms, such as polypoid variations. The interpretation of microbiological data is based on the patient's overall clinical, radiographic, and pathological results. Endoscopically collected mucopurulent secretions can be cultured for precise antibiotic sensitivity testing and focused medical therapy in CRS patients with suspected infections.

According to some researchers, anaerobes eventually replace aerobic and facultative species as chronicity progresses. [4] This change could be the result of antimicrobial medications exerting selective pressure on resistant organisms, as well as the creation of conditions conducive to anaerobic growth, such as a decrease in oxygen tension and an increase in acidity within the sinus. [5] Anaerobe growth in CRS patients may arise as a result of a changing microenvironment caused by local inflammation. [5, 6, 7, 8]. The identification of anaerobes in CRS microbiological tests ranges from 0% to 88 percent. [9, 10, 11] This heterogeneity could be explained by the challenges encountered in growing its culture despite following technical methods. Prevotella species (31.1%), anaerobic Streptococci (21.9%), and Fusobacterium (15.6%) species were the most commonly isolated anaerobes. Streptococcus species, Haemophilus spp, Staph aureus, and Moraxella catarrhalis were the most common aerobes.[12,13]

The presence of resistant aerobic and anaerobic organisms can be linked to failure to respond to β-lactam antibiotics, tetracyclines, quinolones, or macrolides. Peptostreptococcus spp, Fusobacterium nucleatum, Pigmented Prevotella, and Porphyromonas spp. were such bacteria among the anaerobes. These transitional dynamics that occur in the microbiology of maxillary sinusitis are responsible for the progression of infection from acute to chronic sinusitis. [4]

Thus, identifying the microorganisms in a patient with CRS can aid in providing specific treatment and preventing the recurrence of the disease following medical or surgical intervention. Therefore, the goal of this study is to determine the incidence of anaerobic microbes in cultures, secretions, and/or mucosal fragments acquired from CRS patients.

2. Materials and Methods

This prospective study was conducted in the Department of ENT& HNS, Moti Lal Nehru, Medical College, and Swaroop Rani Nehru Hospital, Prayagraj from August 2020 to July 2021. This study was conducted after due clearance from the Institutional Ethics Committee. Patients were properly informed about the nature of the disease, its potential outcome, and the procedure to be done for obtaining the sample. Written informed consent was taken from the patients before participating in the study.

Subjects

Patients attending the ENT & HNS, Moti Lal Nehru, Medical College, and Swaroop Rani Nehru Hospital, Prayagraj were selected for the study. Patients of CRS with or without polyps are willing to participate in the study and having an age group between 18-45 years irrespective of gender were included in the study.

Methods

Patients attending the ENT Outpatient Department (OPD) were properly accessed by taking a clinical history, examined by anterior and posterior rhinoscopy, nasal endoscopy, and radiological investigations like CT scan Nose /PNS, and blood investigations like Total IgE, absolute eosinophil count, and patient were selected for our study.

Methods used for obtaining the sample were swabs obtained from Middle Meatus or Ethmoid sinus during FESS or from osteomeatal complex secretions through endoscopy in OPD patients for quantitative culture sensitivity and identification of organisms.

Swabs were taken from the middle meatus for the study of the bacteriological spectrum and were immediately transferred into transport Trypticase Soy Broth (TSB) media. Swabs were kept in the incubator for six hours and at that point, the pathogen will be in the log phase. This fluid was centrifuged in sterile tubes at a rate of 3000 rpm for 15 minutes and the supernatant was to be discarded, leaving 0.5 ml (centrifuged deposit). In the centrifuged deposit, 10 ml of sterile distilled water was added, and the mixture was shaken vigorously on Vortex for 30 sec. This mixture was then divided into 4 parts 1 ml, 3 ml, 3 ml, and 3 ml each.

1 ml is further divided for staining characteristics like Gram Stain, Z.N. stain, and Lactophenol Cotton Blue film, while 3 ml in FA bottle for isolation of Aerobes, 3 ml in FN bottle, and the remaining 3 ml in MP bottle for the isolation of anaerobes and mycobacterium respectively. These three inoculated bottles were further incubated in the Bact-Alert 3D system following standard protocols. The isolated pathogens were examined microscopically to ensure the staining and morphologic characteristics of an organism. Further identification was done at the species level by the Vitek-2 system.

Once the organisms were isolated, antibiotic sensitivity testing was carried out to discover possible antibiotics that could be provided to patients to combat that specific pathogen.

3. Result and Discussion

A total of 60 patients of Chronic Rhinosinusitis (CRS) with or without polyps aged between 18 and 45 years who were willing to undergo FESS were enrolled in this study. The mean age of patients was 26.55 ± 7.58 years. Most of the patients fall between the age of 18-24 (51.66%) years followed by 25-31 (23.33%).

In a large cross-sectional survey of 10,636 people, done by Shi et al., (2015)14 chronic rhinosinusitis was found to affect 8.0 percent of the general population and 8.2 percent of adults. However, they did not mention any specific age-related risk of chronic rhinosinusitis. Another study by Kim et al. (2018) [15] concluded that the overall prevalence of CRS was 5.88%. However, they discovered that CRS was more common at 6.55% in the elderly (≥ 65 years) age group than in the adult (19- 64 years) population which was 5.69%.

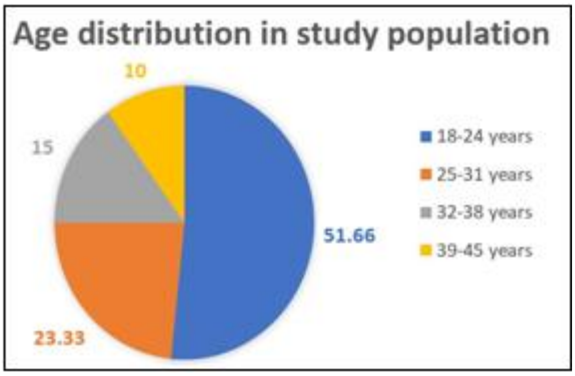


Figure 1: Distribution of study populations according to different age groups

Figure 2: Distribution of study populations according to gender

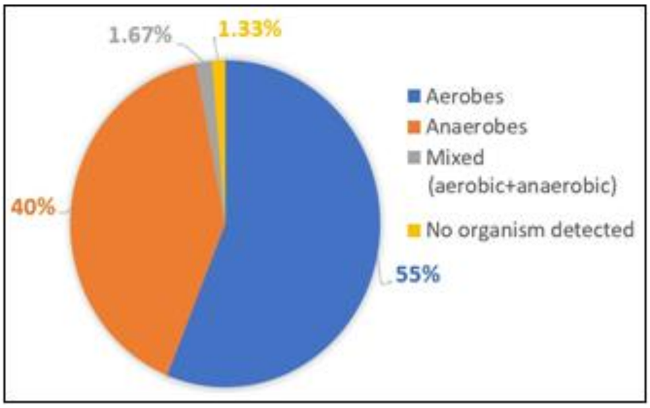
Out of 60 cases, 33 (55%) were male and 27 (45%) were females. Study shows that males (55%) were slightly higher in numbers than females (45%) in patients with chronic rhinosinusitis. Similarly, **Shi et al., in 2015** [14] in their study concluded that the prevalence of CRS was slightly higher among males (8.79%) than females (7.28%) ($p > 0.05$). Differing from our study, **Gokale et al** observed higher dominance of males (64%) than females (36%) cases. [16]

Table 1: Distribution of study populations according to Major Symptoms

Major Symptoms	n	%
Nasal obstruction	39	65.00
Nasal discharge	11	18.33
Headache	7	11.67
Facial pain	3	5.00
Total	60	100.0

Table no. 1 represents major symptoms in patients enrolled for the study. Facial pain (5%), headache (11.67%), nasal discharge (18.33%), and Nasal obstructions (65%) were some of the presenting symptoms. Among these, nasal obstruction was seen in the majority 65% of patients presented with CRS followed by nasal discharge in 18.33%. Similarly, other authors concluded a comparable presence of the symptoms.

A study by **Amodu et al.,**[17] found symptoms of nasal obstruction and nasal discharge in 100% of cases, facial pain (13.33%), and headache in 10% of patients. Another study by **Soler et al.,** [18] evaluated nasal obstruction in 95%, nasal discharge in 93%, facial pain in 92%, and headache in 83% of patients, with headache being the most commonly reported disabling condition. **Damm et al.**, [19] found nasal obstruction in 92%, postnasal drip in 87%, and headache in 64% of patients. **Kamami et al.**, [20] stated that nasal obstruction is the most frequent symptom making the patient visit an otorhinolaryngology clinic. Facial pain was seen in 13.3% of patients in a study by **Amodu et al.,** [17] although according to **West and Jones** '[21] study, only one out of every eight patients with facial pain/pressure was genuinely suffering from CRS.



As per the distribution of microorganisms, aerobes account for (55%), followed by anaerobes (40%), polymicrobial infection (1.67%), and sterile culture were isolated in 2 (3.33%) samples.

Table 2: Distribution of microorganisms according to Anaerobes, Aerobes, Mixed (aerobes + anaerobes) and no organisms detected

	Microorganisms	n=60	%
Anaerobes (n=24)	Peptococcus	21	35
	Fusobacterium	3	5
Aerobes (n=33)	Staphylococcus aureus	31	51.66
	Micrococci	2	3.33
Mixed (aerobes+anaerobes)	Peptococcus+staphaureus	1	1.67
No organism detected	Sterile culture	2	3.33

It was observed from the study that **Peptococcus** (35%) was the most common microorganism identified among anaerobes followed by **Fusobacterium** (5%). Among aerobes, **Staphylococcus aureus** (51.66%) was the most commonly isolated microorganism followed by **Micrococci** (3.33%). A single 1.67% sample revealed polymicrobial infection (**Peptococcus + Staphylococcus aureus**), and in 2 (3.33%) of the samples, no organisms were found. The microbiological profile of chronic rhinosinusitis microflora has been observed to vary significantly between investigations.

Similar to our study, **Drago et al.** (2019) [22] discovered that peptostreptococcus is the only anaerobe that can be isolated from patients with acute and chronic sinusitis. Similarly, **Vipula et al** (2018) [23] discovered Staphylococcus aureus (14.74%) to be the most dominant pathogen, as also demonstrated in our investigation. **Brook I,** in 2016 [24] revealed a wide range of potential microorganisms including Streptococcus pneumoniae, Haemophilus influenza, Moraxella catarrhalis, Streptococcus pyogenes, Staphylococcus aureus, and Anaerobic organisms (*Prevotella and Porphyromonas, Fusobacterium, and Peptostreptococcus spp*).

Antibiotic Sensitivity Test

Table no. 3 shows that ***Peptococcus*** demonstrate maximum sensitivity to Azithromycin (90.48%) followed by Levofloxacin (80.95%), Ofloxacin (76.19%), Clarithromycin (66.67%), Moxifloxacin (61.90%), Cefuroxime (57.14%), Ceftriaxone (52.38%), Clindamycin (47.62%), Ofloxacin (42.86%), Amoxycillin+ clavulanic acid (38.10%), Piperacillin+tazobactam (33.33%) & Doxycycline (19.05%).

Fusobacterium demonstrated maximum sensitivity (66.7%) to Amoxycillin+ clavulanic acid, Piperacillin+tazobactam, Cefuroxime, Linezolid, Levofloxacin, Azithromycin, and Doxycycline which was 66.67% followed by Ceftriaxone (33.33%), and was 100% resistant to Cefoparazone+ sulbactam, Ofloxacin, Moxifloxacin, Clindamycin, and Clarithromycin.

Table 3: Antibiotic Sensitivity test in microorganisms in anaerobic group

ANAEROBES (n=24)		Fusobacterium(n=3)		Peptococcus (n=21)	
		N	**%**	**N**	**%**
Amoxycillin+clavulanic acid	Sensitive	2	66.67	8	38.10
	Resistant	1	33.33	13	61.90
Piperacillin+tazobactam	Sensitive	2	66.67	7	33.33
	Resistant	1	33.33	14	66.67
Cefuroxime	Sensitive	2	66.67	12	57.14
	Resistant	1	33.33	9	42.86
Ceftriaxone	Sensitive	1	33.33	11	52.38
	Resistant	2	66.67	10	47.62
Cefoparazone+sulbactam	Sensitive	0	0.00	5	23.81
	Resistant	3	100.00	16	76.19
Ofloxacin	Sensitive	0	0.00	16	76.19
	Resistant	3	100.00	5	23.81
Linezolid	Sensitive	2	66.67	9	42.86
	Resistant	1	33.33	12	57.14
Levofloxacin	Sensitive	2	66.67	17	80.95
	Resistant	1	33.33	4	19.05
Moxifloxacin	Sensitive	0	0.00	13	61.90
	Resistant	3	100.00	8	38.10
Clindamycin	Sensitive	0	0.00	10	47.62
	Resistant	3	100.00	11	52.38
Clarithromycin	Sensitive	0	0.00	14	66.67
	Resistant	3	100.00	7	33.33
Azithromycin	Sensitive	2	66.67	19	90.48
	Resistant	1	33.33	2	9.52
Doxycycline	Sensitive	2	66.67	4	19.05
	Resistant	1	33.33	17	80.9

Table no. 4 shows that **Staphylococcus aureus** was most sensitive to Levofloxacin (67.74%) followed by Azithromycin (64.52%), Linezolid (61.29%), Piperacillin+Tazobactam (54.84), Ofloxacin (51.61), Doxycycline (51.61%), Cefuroxime (48.39%), Amoxyclav (45.16), Moxifloxacin (38.71%), Clindamycin (32.26%), Clarithromycin (32.26%), Cefoparazone + sulbactam (29.03%).

Table 4: Antibiotic sensitivity test in microorganisms in the aerobic group

AEROBES (n=34)		Micrococci (n=2)		Staphylococcus aureus (n=31)	
		N	**%**	**N**	**%**
Amoxycillin+clavulanic acid	Sensitive	2	100.0	14	45.16
	Resistant	0	0.0	17	54.84
Piperacillin+tazobactam	Sensitive	1	50.0	17	54.84
	Resistant	1	50.0	14	45.16
Cefuroxime	Sensitive	1	50.0	15	48.39
	Resistant	1	50.0	16	51.61
Ceftriaxone	Sensitive	0	0.0	13	41.94
	Resistant	2	100.0	18	58.06
Cefoparazone+sulbactam	Sensitive	0	0.0	9	29.03
	Resistant	2	100.0	22	70.97
Ofloxacin	Sensitive	2	100.0	16	51.61
	Resistant	0	0.0	15	48.39
Linezolid	Sensitive	0	0.0	19	61.29
	Resistant	2	100.0	12	38.71
Levofloxacin	Sensitive	2	100.0	21	67.74
	Resistant	0	0.0	10	32.26
Moxifloxacin	Sensitive	2	100.0	12	38.71
	Resistant	0	0.0	19	61.29
Clindamycin	Sensitive	2	100.0	10	32.26
	Resistant	0	0.0	21	67.74
Clarithromycin	Sensitive	1	50.0	10	32.26

	Resistant	1	50.0	21	67.74
Azithromycin	Sensitive	2	100.0	20	64.52
	Resistant	0	0.0	11	35.48
Doxycycline	Sensitive	0	0.0	16	51.61
	Resistant	2	100.0	15	48.39

Micrococci was most sensitive (100%) to Amoxycillin+clavulanic acid, Ofloxacin, Levofloxacin, Moxifloxacin, Clindamycin, Azithromycin, followed by 50% sensitivity to Piperacillin+tazobactam, Cefuroxime & Clarithromycin. Rest antimicrobials including Ceftriaxone, Cefoparazone+sulbactam, Linezolid, and Doxycycline show 100% resistance.

In the present study, we observed that Macrolides (azithromycin), Quinolones (levofloxacin), Cephalosporins (cefuroxime), Penicillins plus β-lactamase inhibitors (Amoxicillin+clavulanic acid), and Linezolid were quite efficient against the bacteria identified in our investigation. Similarly, Brook, I in 1984 [25] observed that clindamycin, chloramphenicol, cefoxitin, imipenem, metronidazole, and a combination of a β-lactamase inhibitor (clavulanic acid) plus penicillin (amoxicillin or ticarcillin) are highly effective antimicrobial agents against aerobic and anaerobic β-lactamase-producing microbes.

4. Conclusion

This study was conducted to underline the significance of the identification of specific microorganisms, especially anaerobes, which seem to be a major cause of chronicity and to assess their susceptibility to specific antimicrobials for targeted therapy and minimization of empirical use of antibiotics. This also helps in the reduction of economic burden to patients, better drug compliance, a significant decrease in the rate of recurrence, and improvement in quality of life.

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