ORIGINAL ARTICLE

Bacteriological study of antibiotic sensitivity test in chronic rhinosinusitis before and during COVID-19

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ABSTRACT

Introduction: Chronic rhinosinusitis (CRS) is an inflammation of the nasal mucosa and paranasal sinuses for more than 3 months that affects 5 to 12% of the quality of life. Antibiotics are the first line of management for CRS. Increased antibiotic resistance causes ineffective treatment of CRS. This study aims to determine the bacterial pattern that causes CRS before and during the COVID-19 pandemic. Culture sensitivity tests in rhinosinusitis patients were conducted to see changes in the bacterial resistance patterns to antibiotics before and during the COVID-19 pandemic and to determine the appropriate use of antibiotics and prevent an increase in antibiotic resistance in the ENT-HNS outward department of RSUP Dr. M. Djamil Padang.

Materials and Methods: The type of research was a retrospective study with a total sample of 174 CRS patients who had undergone culture and sensitivity tests. The study population was all CRS patients who were treated at the ENT-HNS outward department at RSUP DR. M. Djamil Padang from 2016 to 2021, underwent surgery and received antibiotic treatment at secondary health services. Antibiotic sensitivity cultures are required for surgery and to determine antibiotics use after surgery. This research was conducted from February to May at the Tertiary Hospital of Dr. M. Djamil Padang. The data collection technique used a total sampling technique. The sample in this study was taken from the medical records of patients at the ENT-HNS outward department of RSUP Dr. M. Djamil Hospital, Padang.

Results: The results showed that the prevalence of CRS with polyps before COVID-19 was 63.8% of cases. After COVID-19, the prevalence of CRS with polyps was found to be 60% of cases. Before the COVID-19 pandemic, CRS was most common among those aged ≥ 41 to 50 years (27%) and the most common bacteria causing CRS with or without polyps was Staphylococcus aureus (39%; 44%). The bacteria causing CRS with or without polyps after COVID-19 were mostly Staphylococcus epidermidis (50% of cases). Before the COVID-19 pandemic, amoxicillin-clavulanic acid had a high resistance of 75 to 100%, however, after COVID-19 there was a change in antibiotic resistance patterns and an increase in ciprofloxacin resistance of 56 to 100% was obtained.

Conclusion: This change in antibiotic resistance pattern needs attention to prevent drug resistance, especially after COVID-19.

KEYWORDS:
Chronic rhinosinusitis, polyps, nonpolyps, bacterial patterns, culture, sensitivity, pandemic COVID-19

INTRODUCTION

According to the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020), rhinosinusitis is an inflammation of the nasal and paranasal sinuses characterised by two or more symptoms. One of which must be nasal obstruction or a runny nose, and other symptoms such as facial pain, olfactory disturbances, signs on endoscopic examination (nasal polyps and/or mucopurulent discharge and/or oedema of the nasal mucosa), and/or changes in computed tomography (CT) of the sinuses and/or COM that last at least 12 weeks.[1]

Chronic rhinosinusitis (CRS) is a common health problem and affects 5 to 12% of the world's population.[1] It has two phenotypes, namely chronic rhinosinusitis with polyps (CRSwNP) and without polyps (CRSsNP).[2] In Dr. Mohammad Hoesin Palembang hospital, 13.7% of cases of CRS with polyps and 61% of cases with CRS without polyps were found.[3,4]

At the University of Silesia in Katowice in Poland, the most common bacteria causing CRS with polyps were gram-negative intestinal bacilli (40.4%). Whereas in CRS without polyps, other bacteria caused *Staphylococcus epidermidis* (33.8%).[5]

Research in Medan found that the most common causes of gram-positive bacteria were *Staphylococcus aureus* (13%) and *Staphylococcus epidermidis* (4.3%), while the gram-negative bacteria that caused polyp and non-polyp chronic rhinosinusitis were *Klebsiella oxytoca* 21.7%.[6] Studies at RSUP Dr. M.Djamil, Padang, found the bacteria that caused CRS with the most polyps, namely *Staphylococcus aureus* (35%), *Staphylococcus epidermidis* (6%), *Klebsiella sp* (13%), while the bacteria that caused CRS without polyps were *Staphylococcus aureus* (22%), *Staphylococcus epidermidis* (7%) and *Klebsiella sp* (4%).[4]

Antibiotics have an important role in the treatment of CRS.[1,7] Antibiotics can be given for 7 to 10 days. The role of macrolides in the management of CRS is more related to their immunomodulatory properties than their antibacterial properties. Macrolides reduce proinflammatory cytokines, neutrophil infiltration and oxidative damage to mucosal tissues. Doxycycline is effective in CRS with nasal polyposis

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due to its ability to inhibit matrix metalloproteinase activity. However, macrolides can increase the risk of side effects on the heart. In some literature, it is suggested to pay attention to the patient's medication and cardiac risk factors before starting therapy because there will be a risk of arrhythmia and abnormalities in the cardiac muscle. The increasing use of antibiotics has led to the emergence of antimicrobial resistance (AMR) which is a major health challenge. One strategy to prevent antibiotic resistance is to optimise the use of antibiotics, paying attention to the right dose, duration and use.[8] It is estimated that by 2050, the increase in antibiotic resistance will cause the deaths of up to 10 million people and cost as much as US$100 million.[9]

At RSUP Dr. M.Djamil Padang found a pattern of resistance for bacteria that cause CRS, namely *Staphylococcus aureus* resistant to ampicillin, ciprofloxacin and ceftriaxone.[4] Diponegoro University found 20% of bacteria were resistant to tetracycline, 4.0% to trimethoprim-sulfamethoxazole, 12% to erythromycin and 3.0% to gentamicin. A total of 10 studies using culture media found a 300-fold increase in the MIC of amoxicillin (0.25 g/ml to 75 g/ml).[10]

Langford et al. reported that 14.3% of COVID-19 patients had a secondary infection and more than 70% of patients received broad-spectrum antibiotics such as fluoroquinolones and third generation cephalosporins. In influenza sufferers, there is damage to the epithelial cells by the virus resulting in mucociliary dysfunction which results in easy passage of bacteria through their cell surfaces to bind to the nasopharynx area. As a result, a bacterial infection occurs which causes continued damage and inhibits the repair and regeneration of epithelial cells.[11]

There was a change in the pattern of bacteria before and after the pandemic. Putri et al. in the 2016 to 2017 period, the most bacteria recorded in polyp and non-polyp patients was *Staphylococcus aureus*, while the research conducted in the 2018 to 2020 period recorded the most bacteria was *Staphylococcus epidermidis*. Ortega-Pena et al. found that *Staphylococcus epidermidis* plays an important role in inhibiting the development of COVID-19 because it induces the production of type I and III interferons and reduces the expression of the SARS-COV-2 receptor in nasal epithelial cells.[12]

The pattern of bacterial resistance has changed from time to time. Mahmoudi et al. showed that *Enterobacteriaceae* isolates from COVID-19 patients had the highest resistance to co-trimoxazole (74%), piperacillin (67.5%), ceftazidime (47.5%), and cefepime (42.5%). All isolates were sensitive to amikacin (100%). *S. aureus* isolates were sensitive to vancomycin (100%) and had a resistance level of more than oxacillin, erythromycin and clindamycin (90%). *P. aeruginosa* is susceptible (90%) to imipenem. In the study conducted for the 2018-2020 period, the percentage of sensitivity to gentamicin was 80% and 95%, while the resistance to the antibiotic ampicillin with a sensitivity percentage of 5%, amoxicillin clavulanate (5 to 10%).[13]

The pattern of bacterial resistance changes from time to time, so research is needed to determine the patterns of change that happened. Changes in the pattern of bacterial resistance make treatment more difficult, worsening the patient's condition and causing high costs.[14] The high incidence of CRS and antibiotic resistance that occurred mainly in the city of Padang made researchers interested in knowing the pattern of bacteria and culture sensitivity in CRS patients in RSUP Dr. M. Djamil, Padang, between 2016 to 2021 before the COVID-19 pandemic and during the COVID-19 pandemic.

MATERIALS AND METHODS

This study is a descriptive study with a retrospective method. The sample size in this study was 174 samples. The sampling technique used was the total sampling technique. The samples in this study were taken from patient medical records at the ENT-HNS outward department of RSUP Dr. M. Djamil Hospital, Padang for the period 2016 to 2021. This study compared bacterial patterns and culture sensitivity of CRS patients before and during the COVID-19 pandemic. The variables studied were nasal polyps, age, gender, bacterial patterns, and bacterial culture sensitivity. The study population was all CRS patients who sought treatment at the ENT-HNS outward department of RSUP Dr. M. Djamil Hospital, Padang from 2016 to 2021 and received antibiotic treatment in a secondary hospital. Antibiotic sensitivity tests were carried out as a condition for surgery and for the use of antibiotics after surgery. culture and antibiotic sensitivity tests were carried out at the Microbiology Laboratory of the Faculty of Medicine, Andalas University. Data analysis was performed using SPSS to determine the distribution and percentage of bacterial patterns and culture sensitivity in CRS patients.

RESULTS

Characteristics of respondents

This study was conducted on 174 chronic rhinosinusitis patients with or without polyps in RSUP Dr. M. Djamil, Padang and Microbiology Laboratory, Faculty of Medicine, Andalas University, which met the inclusion and exclusion criteria. The characteristics of the respondents were grouped by year, presence or absence of nasal polyps, age, and gender.

The pattern of bacteria causing chronic rhinosinusitis

The results of the study found patterns of bacteria that cause CRS in RSUD Dr. M. Djamil, Hospital, Padang from 2016 to 2021. There were 20 species of bacteria that cause CRS with or without polyps. In Table II bacterial patterns are grouped by year and CRS phenotype.

Table II. Bacterial patterns of CRS patients with and without polyps at RSUP Dr. M. Djamil Hospital, Padang from 2016 to 2019 before COVID-19 and from 2020 to 2021, during COVID-19

The bacteria that caused rhinosinusitis before COVID-19 were caused by Staphylococcus aureus (39%; 44%), followed by *Klebsiella sp* (21%), while after COVID-19 the most common bacteria that caused CRS were *Staphylococcus epidermidis* (50%).

Table I: Characteristics of respondents

Variable	Frequency		%	
	2016 to 2019	2020 to 2021	2016 to 2019	2020 to 2021
Pattern of polyp and non-polyp				
CRSwNP	111	18	63.8	60
CRSsNP	63	12	36.2	40
Amount	174	30	100	100
Age (Years)				
<20	8	1	4.6	3.3
21 30	22	7	12.6	23.3
31 40	36	7	20.7	23.3
41 50	47	7	27	23.3
51 60	40	1	23	3.3
>60	21	7	12.1	23.3
Amount	174	30	100	100
Gender				
Male	81	14	46.5	46.7
Female	93	16	53.5	53.3
Amount	174	30	100	100

Table II: Bacterial patterns of CRS patients with and without polyps at RSUP Dr. M. Djamil Hospital, Padang from 2016 to 2019 before COVID-19 and from 2020 to 2021, during COVID-19

No	Bacterial species	CRSwNP				CRSsNP			
		2016 to 2019	F	2020 to 2021	F	2016 to 2019	F	2020 to 2021	F
1.	*Staphylococcus aureus*	43	39%	3	17%	28	44%	1	8%
2.	*Staphylococcus epidermidis*	22	20%	9	50%	16	25%	6	50%
3.	*Klebsiella sp.*	23	21%	3	17%	5	8%	1	8%
4.	*Coagulase-Negative Staphylococcus*	8	7%	0	0%	1	2%	0	0%
5.	*Streptococcus sp.*	5	5%	1	6%	2	3%	0	0%
6.	*Acinetobacter baumanii*	2	2%	0	0%	0	0%	0	0%
7.	*Acinetobacter lwoffii*	1	1%	0	0%	0	0%	0	0%
8.	*Citrobacter koseri*	1	1%	0	0%	0	0%	0	0%
9.	*Pseudomonas aeruginosa*	3	3%	0	0%	5	8%	1	8%
10.	*Burkholderia sp.*	0	0%	0	0%	1	2%	0	0%
11.	*Proteus mirabilis*	0	0%	0	0%	0	0%	1	8%
12.	*Raoultella ornithinolytica*	0	0%	0	0%	1	2%	0	0%
13.	*Sphingomonas paucimobilis*	0	0%	0	0%	0	0%	1	8%
14.	*Staphylococcus equorum*	0	0%	0	0%	1	2%	0	0%
15.	*Staphylococcus pseudintermedius*	0	0%	0	0%	0	0%	1	8%
16.	*Staphylococcus sp.*	0	0%	0	0%	1	2%	0	0%
17.	*Pantoea sp.*	0	0%	1	6%	0	0%	0	0%
18.	*Mycobacterium lacunata*	0	0%	1	6%	0	0%	0	0%
19.	*Serratia marcescens*	0	0%	0	0%	2	3%	0	0%
20	MRSA	3	3%	0	0%	0	0%	0	0%
Amount		111		18		63		12	

Bacterial sensitivity culture

Based on Table II data, a culture test for bacterial sensitivity to antibiotics was carried out. After data analysis, a pattern of bacterial resistance to the use of antibiotics was found. The use of the antibiotics, ampicillin, gentamicin, ciprofloxacin, ceftriaxone, meropenem, and cefoperazone has high resistance to the bacteria that cause CRS.

Before COVID-19, amoxicillin had a high level of resistance, whereas after COVID-19, there was an increase in resistance to the fluroquinolone group.

DISCUSSION

Characteristics of respondents

Based on data analysis, the prevalence of CRS with polyps at RSUP Dr. M. Djamil was 63.8%, which was higher than the prevalence of CRS without polyps, 36.2%. The Department of Otolaryngology-Head and Neck Surgery, Medical University of South Carolina, University of Colorado, University of Utah, University of Virginia, Oregon Health Sciences University found that CRS incidence with polyps was 59.7% and without polyps 40.3%.[15] The Global Allergy and Asthma European Network (GALEN) found that 445 people had CRS with polyps and 237 people without polyps.[16]

Based on the analysis of the data, it was found that there is no difference in the incidence of CRS with or without polyps before and after COVID-19. There were 60% of CRS cases with polyps in 2020 until 2021. Study by Sbeih et al. found that 5.22% of COVID-19 cases were accompanied by CRS.[17] Another study by Wang et al. showed that 6.1% of COVID-19 cases were accompanied by CRS. These results are higher than studies conducted in China and Europe, with 0 to 3% of cases.[18]

Table III: Patterns of bacterial sensitivity to antibiotics in patients of CRS with and without polyps at RSUP Dr. M. Djamil Hospital, Padang from 2016 to 2019, before COVID-19, and 2020 to 2021 during COVID-19

No	CRSwNP	2016 to 2019					2020 to 2021				
		AMC f	GM f	CIP f	CRO f	MEM f	CFZ f	AMC f	GM f	CIP f	CRO f
1	*S. aureus*	89	19	54	65	22	14			33	
2	*Kleibsiella spp*	75	26	43	48	17	9	100			
3	*S. epidermidis*	88	14	33	67	20	33			56	
4	*Streptococcus sp.*	100	20							100	
No	**CRSsNP**	**f**	**f**	**f**	**f**	**f**	**f**	**f**	**f**	**f**	**f**
1	*Kleibsiella spp*	100			40			100		100	100
2	*S. epidermidis*	75	7	50	60	18	29			67	
3	*P. aeruginosa*	100		33	100				100		
4	*Proteus mirabilis*									100	100

AMC = Amoxicilin clavulanic acid, GM = Gentamicin, CIP = Ciprofloxacin, CRO = Ceftriaxonr, MEM = Meropenem

Based on age data, the prevalence of CRS from 2016 to 2019 at RSUP Dr. M. Djamil 27% of cases are under 50 years old, and 23% of cases are over 50 years old with and without polyps. In a Canadian study, cases of CRS increased with age.[19] Nasal polyps rarely occur in children unless accompanied by comorbidities such as cystic fibrosis, which is produced by the cystic fibrosis transmembrane conductance regulator (CFTR), which is closely related to CRS and allergic fungal rhinosinusitis. In children, cellularity and lymphocytic infiltration are more prominent, whereas in adults there is a stronger eosinophilic infiltration and a glandular hyperplastic process.[20] Elderly CRS patients have characteristic inflammatory signs associated with a neutrophilic proinflammatory response.[21] Patients aged 60 years and older have higher levels of IL-1b, IL-6, IL-8, and TNF-a compared to younger patients.[22]

There is no significant difference found between age and the incidence of CRS from 2020 to 2021 after the COVID-19 pandemic. Up to 23.3% of CRS cases occurred between the ages of 21 and 50. A decrease in the incidence of chronic rhinosinusitis (3.3%) was observed at the age of 51-60. Sbeih et al. and Tunjai et al. found that there was no significant age difference between COVID-19 patients with CRS and COVID-19 patients without CRS.[16,22]

In this study, it was found that CRS is more common in women. From 2016 to 2019, 53.5 cases of CRS were found in women. The same results were also obtained between 2020 to 2021, with more women than men experiencing the CRS (53.3%). Hirsch et al. found that the prevalence of CRS was higher in women (66.7%)[23], another study conducted NHIS in the United States found fewer male sufferers than male sufferers (39.7%: 60.3%).[24] Sbeih et al. also found that 52% of chronic rhinosinusitis cases occurred in women with COVID-19.[17] Women are two times more likely to experience CRS than men. The high prevalence of CRS is associated among women with a higher level of concern for women to get services. The smaller size of the sinus ostia in women makes them more susceptible to further obstruction and infection.[16,25]

Bacteria cause Chronic Rhinosinusitis

Before COVID-19, ten species of bacteria caused CRS with polyps, and after COVID-19, seven species of bacteria that caused CRS with polyps were found in RSUP Dr. M. Djamil Padang. There were differences in the distribution patterns of the bacteria that cause CRS with polyps and without polyps in 2016 to 2019 before the COVID-19 pandemic and in 2020 to 2021 during the COVID-19 pandemic. In 2016 to 2019 before COVID-19, most CRS with polyps were caused by *Staphylococcus aureus* (39%), *Klebsiella sp*. (21%), and *Staphylococcus epidermidis* (20%) whereas, CRS without polyps was caused by *Staphylococcus aureus* (44%), *Staphylococcus epidermidis* (25%) and *Klebsiella sp*. (8%). In Medan, Staphylococcus aureus was found to be the cause of CRS with the most polyps.6 In the Beijing Tongren Hospital, it was found that the most dominant cause of CRS in polyps was *coagulase-negative Staphylococcus* (24.3%), *Corynebacterium* (19.9%) and *Staphylococcus epidermidis* (19.1%). In non-polyp CRS caused by *S. Epidermidis* (21.2%), *Corynebacterium* (21.2%), *Coagulase-negative staphylococci* (18.2%) and *Staphylococcus aureus* (13.6%). In this study, the causative bacteria varied between polyps and non-polyps.[26]

In 2020 to 2021 different results were obtained, namely the most common causes of CRS with or without polyps were *Staphylococcus epidermidis* (50%; 50%), *Staphylococcus aureus* and *Klebsiella sp.* (17%; 8%). In China it was found that *S. Epidermidis* was the most common bacterium that causes, followed by *Pseudo diphtheria, Staphylococcus aureus, Haemophilus influenza* mole and *Haemella influenzaemola*.[27] In 2021, a study was carried out in Poland to isolate the cause of CRS. The data analysis found that coagulase-negative staphylococcus and *S. Epidermidis* were the most common causes.[12] Salman et al. of the 20 studies studied, found that 40% of cases of co-infection with COVID-19 were caused by *S. Aureus*. Salman et al. suggested that there were 5.62% of cases of bacterial co-infection in COVID-19 patients.[28] The cause of secondary infection is not known with certainty, another hypothesis states that immune system dysregulation and lymphopenia are the factors which influence the incidence of secondary infection in COVID-19. Khuruna et al. found that the gram-negative bacteria *A. Baumannii* was the dominant cause of secondary infection in COVID-19 (24.3%). From the results of blood isolation it was found that 6% of *Acinetobacter sp.* was resistant to carbapenems.[29]

The research is consistent with other research conducted by various countries throughout the pandemic. The high number of S. Epidermidis bacteria that cause CRS in this study is related to the COVID-19 pandemic. This is supported by research conducted in 2022 which states that S. Epidermidis is more abundant in the anterior part of the nares than in the inside.

Bacterial Sensitivity Culture

The results of bacterial antibiogram examination in polyp and non-polyp CRS patients between 2016 to 2019, before the COVID-19 pandemic, it can be concluded that most are resistant to ampicillin and amoxicillin-clavulanic acid (75 to 100%). There are differences in the pattern of antibiotic resistance before and during the COVID-19 pandemic in CRS. During the COVID-19 pandemic, antibiotic resistance was found against the flurouquinolone class, namely ciprofloxacin. This difference in the pattern of antibiotic resistance is also related to the difference in the distribution of the bacteria that cause CRS before and during the COVID-19 pandemic (56 to 100%). Aldhwihi et al. compared antibiotic resistance before and during COVID-19. Aldhwihi et al. found a bacterial resistance level for ciprofloxacin at 84.2%.[30]

In South Korea found that patients with CRS were at increased risk for COVID-19 infection. In CRS, there is immune dysfunction, such as damage to the epithelial barrier and deficiency of specific antibodies. Viral infections can also cause CRS. Lee et al. found that CRS was caused by a viral infection which was 2.9 times higher, and 21.6% of cases were caused by a *Coronavirus* infection.[31] Sbeih and Jorge found that CRS patients using intranasal corticosteroids increased the risk of COVID-19 treatment. There is a potential difference in the density of ACE2 and TMPRSS2 affecting viral shedding in CRS. The Expression of non-eosinophilic CRS, ACE2 and TMPRSS2 was found to be higher than that of eosinophilic CRS. The increase in ACE2 and TMPRSS2 increases the risk of exposure to COVID-19 because ACE2 is the main receptor in COVID-19 infection.[17]

According to WHO, the percentage of antibiotic use during the treatment of COVID-19 reaches 94 to 100%, this percentage is higher than the reported incidence of secondary infections, which is 10 to 15%. Of the 7 to 8% of cases requiring hospitalisation and 14% of ICU admissions and 72% of patients received antibiotic treatment. This has led to an increase in antibiotic resistance or AMR. The increasing use of antibiotics causes the loss of effectiveness of antibiotics such as carbapenems which are used to treat severe bacterial infections. In addition, AMR can increase the costs and impact patient or caregiver productivity due to length of hospital stay.[32]

CONCLUSION

1. There is no difference in the prevalence of chronic rhinosinusitis (CRS) with or without polyps before and during the COVID-19 pandemic in 2020 to 2021. The prevalence of CRS with polyps at RSUP Dr. M.Djamil at 63.8%, this figure is higher than the prevalence of CRS without polyps, which is 36.2%.
2. There were differences in the distribution patterns of the bacteria that cause CRS with polyps and without polyps in 2016 to 2019 before the COVID-19 pandemic and in 2020 to 2021 during the COVID-19 pandemic. In 2016 to 2019 before COVID-19, most chronic rhinosinusitis with polyps were caused by Staphylococcus aureus (39%), Klebsiella sp. (21%), and Staphylococcus epidermidis (20%). CRS without polyps was caused by Staphylococcus aureus (44%), Staphylococcus epidermidis (25%) and Klebsiella sp. (8%). In 2020 to 2021 different results were obtained, e.g., the most common causes of CRS with or without polyps were Staphylococcus epidermidis (50%;50%), Staphylococcus aureus and Klebsiella sp (17%; 8%).
3. There are differences in the pattern of antibiotic resistance before and during the COVID-19 pandemic in chronic rhinosinusitis. Before the COVID-19 pandemic were resistant to Amoxicillin-Clavulanic Acid, (75 to 100%) while during the COVID-19 pandemic there was an increase in resistance to Ciprofloxacin (56-100%).

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