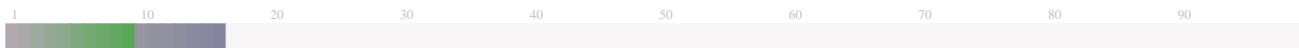


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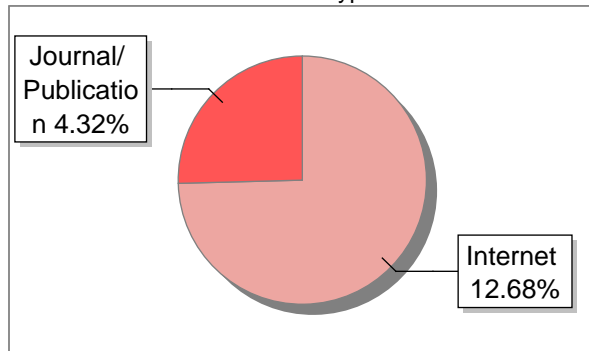
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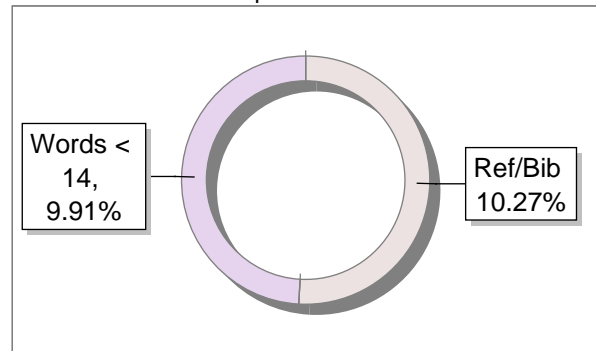
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The sensitivity pattern of ciprofloxacin and amoxicillin in chronic suppurative otitis media



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ABSTRACT

Introduction: In both poor and developed countries, chronic suppurative otitis media affects 1-46 percent of the population. The incidence of chronic suppurative otitis media is much higher in Indonesia due to various of factors, including poor sanitation, low socio-economic and nutritional status, and high population density. To reduce the occurrence of chronic suppurative otitis media, an adequate treatment is required.

Purpose: the study was to identify the bacteria that cause chronic suppurative otitis media and ciprofloxacin and amoxicillin antibiotic sensitivity pattern in Asri Medical Centre and PKU Muhammadiyah Gamping hospital, Yogyakarta.

Patients and methods: This is a prospective descriptive study with 27 patients with chronic suppurative otitis media whom met the inclusion criteria. Bacteria were isolated from ear secretions and cultured on TSA and McConkey agar medium. The antibiotics ciprofloxacin and amoxicillin were tested for susceptibility, and Gram staining, catalase test, and biochemical test were used to identify bacteria.

Results: 63 bacteria were isolated from 27 chronic suppurative otitis media patients, among of them positive gram bacteria (52%) and negative-gram bacteria (48%). The sensitivity of positive-gram bacteria and negative-gram bacteria causing chronic suppurative otitis media to ciprofloxacin was 84% and 79%, respectively. The resistance of positive-gram bacteria and negative-gram bacteria to amoxicillin by 100%.

Conclusion: *Staphylococcus* sp and *Pseudomonas aeruginosa* were the most caused chronic suppurative otitis media at the Asri Medical Centre and PKU Muhammadiyah Gamping hospital in Yogyakarta. The antibiotic ciprofloxacin is the most effective treatment for bacteria that cause chronic suppurative otitis media.

Keywords: *Staphylococcus* sp, *Pseudomonas aeruginosa*, sensitivity, resistance.

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INTRODUCTION

Chronic suppurative otitis media is a chronic inflammation of the middle ear mastoid cavity, characterized by perforation of the tympanic membrane and persistent discharge from the ear.¹ Chronic suppurative otitis media accounts for more than 50% of cases of mild to moderate conductive hearing loss. currently. Hearing loss in children affects language development, cognitive function, psychosocial, and education.^{2,3} The other complications of chronic suppurative otitis media can cause fatal intracranial infections and acute mastoiditis, especially in developing countries.² Developing countries have a higher incidence, especially in areas with low sanitation, low socio-economic conditions, poor nutrition, and high population density, and there is still a misconception that people have about this disease so that

they do not get treatment completely.^{4,5} In Otitis media Chronic suppurative bacteria reach the middle ear via the eustachian tube from the nasopharynx or the external ear canal through an intact tympanic membrane. The most common causes of aerobic microorganisms for chronic suppurative otitis media are *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus* sp., *Klebsiella* sp, *Escherichia coli*, and *Haemophilus influenza*. 50% of chronic suppurative otitis media cases are thought to be caused by Aspergillus and Candida fungi, especially in populations where the living environment is humid and hot so that the fungus develops optimally.⁶ The effective management of chronic suppurative otitis media disease is highly dependent on the level of knowledge about the causative pathogenic bacteria and the pattern of bacterial sensitivity to antibiotics. According to Ogah and Ogah,

the predominant bacteria that cause and pattern of sensitivity to antibiotics change from time to time.⁷ Therefore, it is necessary to periodically update the pattern of bacteria that cause chronic suppurative otitis media and their sensitivity so that treatment for this disease is more appropriate. The research on bacterial resistance isolated from the secretions of patients with chronic suppurative otitis media has not been widely carried out. The purpose of this study was to determine the pattern of susceptibility of bacteria that cause chronic suppurative otitis media to ciprofloxacin and amoxicillin antibiotics.

MATERIAL AND METHODS

Study Design

The research method is a prospective descriptive study with cross sectional design. The study population was all patients with chronic suppurative otitis

media treated at the Ear, nose and throat Polyclinic of Asri Medical Center hospital Yogyakarta and PKU Muhammadiyah Gamping Yogyakarta hospital. The research sample was the secretions of patients with chronic suppurative otitis media. The number of samples was 27 samples of secretions taken aseptically by the swab method.

Respondents

Respondents were 27 patients with suspected chronic suppurative otitis media who were treated at the Ear, nose and throat (ENT) Poly Asri Medical Center and PKU Muhammadiyah Gamping hospital Yogyakarta, in January-June 2022. The inclusion criteria in this study were the first time patient came for an examination and treatment at the ENT Polyclinic and were diagnosed with chronic suppurative otitis media. Exclusion criteria were patients with chronic suppurative otitis media who had used antibiotics. Research variables: types of aerobic bacteria that cause chronic suppurative otitis media, the pattern of sensitivity of bacteria that cause chronic suppurative otitis media to the antibiotics ciprofloxacin and amoxicillin.

Samples were taken by rubbing a stick in the ear canal. Then the secretions were put into Stuart's transport medium and immediately taken to the Microbiology laboratory for culture on blood agar and Mac Conkey media. Bacteria that grow are then identified by means of microscopic and macroscopic examination.

Bacterial culture isolates chronic suppurative otitis media secretions

The secretions from the Stuart transport media tube were taken with a sterilized ose, then planted on blood agar media by streaking to obtain separate colonies. Then incubated at 37°C for 24 hours. Bacterial colonies that have grown are then identified by the type of bacteria. The identification process includes Gram staining, catalase test, and biochemical test. Single colonies of bacteria were cultured with Nutrient Agar media for further sensitivity testing. Bacterial susceptibility testing was carried out according to disc diffusion and interpretation of the results referring to CLSI (Clinical and Laboratory Standards Institute). After being incubated

overnight, the next day the diameter of the inhibition zone was measured.⁸

Data analysis

The results of the sensitivity test bacteria to antibiotics obtained include in the three criteria: 1) sensitive (the possibility of the antibiotic being tested can inhibit pathogenic bacteria, so that it can be used as a guide for selecting the right antibiotic for treatment), 2) intermediate (the possibility of the antibiotic being tested is effective at higher doses, or more frequently, or only effective at certain specific sites in the body where the antibiotic can penetrate to provide adequate concentrations), and 3) resistant (antibiotics are not effective at inhibiting bacterial growth, may not be the right choice for treatment). From the data obtained, a comparison of the sensitivity test results with the total isolates was made multiplied by one hundred percent.

RESULTS

The results of the descriptive analysis of patient characteristics showed that the majority of patients examined for chronic suppurative otitis media (CSOM) secrets at the Asri Medical Centre hospital and PKU Muhammadiyah Gamping hospital in Yogyakarta were male by 48%, while the female sex was only 52%. Patients aged less than 40 years by 48%. The chronic suppurative otitis media attacks more

people with productive age / less than 40 years. The gender of CSOM sufferers between men and women is almost the same (Table 1).

The results of bacterial isolation from chronic suppurative otitis media secret specimens at the Clinical Microbiology Laboratory, Faculty of Medicine, UMY for the period January-June 2022, showed that there were 63 isolates consisting of two groups of bacteria, namely positive-gram and negative-gram bacteria. The positive-gram bacteria that can be isolated are *Staphylococcus* sp and other species, while the negative-gram bacteria that can be isolated include: *Pseudomonas aeruginosa* and other species. The results of the isolation of bacteria from chronic suppurative otitis media secret specimens were mostly shown by *Staphylococcus* (29%) followed by *Pseudomonas aeruginosa* (25%) (Table 2).

Table 3 shows the results of the examination of the sensitivity of positive-gram and negative-gram bacteria isolates from chronic suppurative otitis media secretions to the antibiotics ciprofloxacin and amoxicillin. The positive-gram bacteria that were still sensitive to ciprofloxacin and amoxicillin were 84% and 0%, respectively. The negative-gram bacteria that were still sensitive to the antibiotics ciprofloxacin and amoxicillin were 79% and 0%, respectively. The

Table 1. Distribution of examination of chronic suppurative otitis media patient secrets by age and gender at the Asri Medical Centre and PKU Muhammadiyah Gamping hospital in Yogyakarta for the period January-June 2022.

Parameter	Patient	Frequency (N=27)	Percentage (%)
Age (year)	< 40	13	48
	40-60	10	37
	>60	4	15
Gender:	Man	13	48
	Woman	14	52

Table 2. Patterns of pathogenic bacteria isolated from chronic suppurative otitis media secret specimens at the Asri Medical Centre and PKU Muhammadiyah Gamping hospital in Yogyakarta for the period January-June 2022.

Bacteria Group	Types of bacteria	Freequency	Percentage (%)
Positive-gram	<i>Staphylococcus</i> sp	18	29
	Other Species	15	24
Negative-gram	<i>Pseudomonas aeruginosa</i>	16	25
	Other Species	14	22
Amount		63	100

Table 3. The sensitivity pattern of bacteria isolated from chronic suppurative otitis media secretions to the antibiotics ciprofloxacin and amoxicillin at the Asri Medical Centre and PKU Muhammadiyah Gamping hospital in Yogyakarta.

Types of bacteria	Types of Antibiotics	Sensitivity		
		Sensitive (%)	Intermediate (%)	resistant (%)
Positive-gram	Ciprofloxacin	84	8	8
	Amoxicillin	0	0	100
Negative-gram	Ciprofloxacin	79	0	21
	Amoxicillin	0	0	100

majority of all bacterial isolates from chronic suppurative otitis media secretions were resistant to the antibiotic amoxicillin (100%). This research showed that the bacteria that cause chronic suppurative otitis media are resistant to the amoxicillin and are still sensitive to ciprofloxacin.

DISCUSSION

This study proves that *Staphylococcus* sp and *Pseudomonas aeruginosa* are the main bacteria causing chronic suppurative otitis media (CSOM) at the Asri Medical Center hospital and PKU Muhammadiyah Gamping hospital in Yogyakarta. The results of this study show the same as research in other places. *Staphylococcus* and *Pseudomonas aeruginosa* are the main bacteria causing CSOM in Bhawalpur⁹, Rawalpindi¹⁰, India¹¹, Khulna¹², Banjarmasin¹³, Medan^{14,15}, West Nusa Tenggara¹⁶, Manado¹⁷, and Padang.¹⁸ In Manado, the most common bacteria causing CSOM are *Staphylococcus* and *Streptococcus*.¹⁹

The majority of the bacteria that cause CSOM are still sensitive to the antibiotic ciprofloxacin and are already resistant to the antibiotic amoxicillin. This study is almost the same as that of Rumimpunu et al., that positive-gram bacteria that cause CSOM in Manado are still sensitive to ciprofloxacin and resistant to amoxicillin.¹⁷ Bacteria that cause CSOM are still sensitive to ciprofloxacin in Bhawalpur⁹, Rawalpindi¹⁰, India¹¹, Banjarmasin¹³, and Padang.¹⁶ Meanwhile, *Pseudomonas aeruginosa* which causes CSOM in Khulna is already resistant to ciprofloxacin.¹² Resistance of CSOM bacteria to amoxicillin was also found in Padang.¹⁸

The typical antibiotics of the quinolone group are recommended because they are

more effective than the aminoglycoside group and do not have ototoxic side effects. As for systemic antibiotics, amoxicillin/clavulanate is recommended as the first choice and quinolones as the second drug of choice in CSOM patients.²⁰ Antibiotic substances inhibit bacteria through 5 mechanisms, namely: inhibiting cell walls, depolarizing cell membranes, inhibiting protein synthesis, inhibiting nucleic acid synthesis and inhibits bacterial metabolic pathways.²¹ Ciprofloxacin is a fluoroquinolone class antibiotic. Ciprofloxacin is effective against Gram negative and Gram positive bacteria by inhibiting the replication process of deoxyribonucleic acid. The active compound ciprofloxacin binds to the DNA gyrase enzyme, resulting in double cracking of the bacterial chromosome.²²

Amoxicillin is a broad-spectrum-lactam antibiotic.²³ Amoxicillin is widely available in health centers and hospitals and is the most widely used for treatment.²⁴ Amoxicillin's mechanism of action is to inhibit the action of penicillin binding proteins so that peptidoglycan cross-links in the final stages of cell wall synthesis are not formed.²⁵ Amoxicillin regulates transpeptidase enzymes that play a role in the formation of cross-links between peptidoglycans in the formation of cell walls so that bacterial cells die due to lysis.²³

The majority of bacteria that cause CSOM are resistant to amoxicillin. The process of resistance to amoxicillin occurs because bacteria produce a β -lactamase enzyme that inactivates the β -lactam ring on the penicillin molecule.²⁶ *Staphylococcus aureus* resistance to amoxicillin occurs due to a decrease in the affinity of amoxicillin on the penicillin binding protein.²⁷ The majority of antibiotic resistance occurs

due to mutations in genes that carry the traits. Resistance genes are obtained from plasmids.²⁸ Resistance factors can be transferred from chromosomes to plasmids. The transferable plasmids are factor R plasmids or infectious plasmids. Bacteria that are resistant to many antibiotics are caused by plasmids that experience multiple resistance.²⁵ The low-dose antibiotic concentrations can increase the development of antibiotic resistance by triggering genetic changes.²⁹ Mutations occur randomly, spontaneously and are independent of the presence of antimicrobials. The mutation process known as single-step mutation causes the emergence of high levels of resistance in a short and fast period of time.²⁸ The efflux pumps show an important role in antibiotic resistance. This mechanism leads to restriction of accumulation of toxic components in cells. The efflux pumps can be drug-specific, usually expressed on chromosomes. If the pump is overproduced it will provide cross-resistance that affects several drug classes. The efflux pump on fluoroquinolones mediated by the plasmid QepA significantly increases resistance to ciprofloxacin.³⁰ The use of the wrong antibiotic will increase bacterial resistance.^{31,32} An administration of antibiotics to livestock also contributes to the increase of resistant bacteria. The nature of bacterial resistance in livestock can be transmitted to humans through consumption of these animals.^{33,34} The increase in bacterial resistance to antibiotics will limit the selection of drugs for patients and increase morbidity and mortality due to untreatable infectious diseases. The limitation of this study is that the bacteria causing CSOM were not identified at the species level. Bacteria that are already resistant to amoxicillin are not tested for beta-lactamase enzymes.

CONCLUSION

Staphylococcus sp and *Pseudomonas aeruginosa* were bacteria caused chronic suppurative otitis media at the Asri Medical Center hospital and PKU Muhammadiyah Gamping hospital in Yogyakarta. The bacteria that cause chronic suppurative otitis media are still sensitive to ciprofloxacin and are already resistant to amoxicillin. Periodic antibiotic

sensitivity testing is important to get an effective drug for chronic suppurative otitis media therapy.

FUNDING

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DISCLOSURE

There is no conflict of interest for this study.

ETHICAL CONSIDERATION

This research was approved by the Health Research Ethics Committee of the Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta. Letter of exemption Ref. No. 049/EC.KEPK FKIK UMY/VI/2021.

AUTHOR CONTRIBUTION

All authors contributed to this study's conception and design (Lilis Suryani, Asti Widuri, Muhammad Kurniawan, Bombong Nurpagino), data analysis and interpretation (Lilis Suryani, Asti Widuri), article drafting, critical revision of the article, final approval of the article, and data collection (Lilis Suryani, Asti Widuri, Muhammad Kurniawan, Bombong Nurpagino).

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