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EMPIRICAL ANTIBIOTIC TREATMENT OF COMPLICATED APPENDICITIS

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ABSTRACT

Background: There are many cases of complicated appendicitis, and there is a risk of life-threatening if not treated properly. The first line of treatment for complicated appendicitis is surgery and administration of appropriate empiric antibiotics. **Method**: This study employs a retrospective design with a cross-sectional approach. Sampling was conducted using consecutive sampling. The data taken comes from secondary data, namely the results of culture and sensitivity tests of complicated appendicitis cases in the microbiology department of the Haji Hospital, Surabaya, in 2021-2023. **Results**: Data collected from the microbiology section of the Haji Hospital, East Java Province, 57 cases of complicated appendicitis were obtained, which underwent aerobic culture, and the results of germ growth. Anaerobic culture examination was not conducted because the necessary facilities did not yet exist. The distribution of male patients was 64.91%, and that of female patients was 35.09%. From the culture results, 100% of the isolates were gram-negative aerobic bacteria. The examination results were based on the types of bacteria: Escherichia coli ESBL (43.86%), Escherichia coli (42.11%), and Klebsiella pneumoniae (7.02%)—as determined by the results of the antibiotic sensitivity examination. Escherichia coli ESBL is sensitive to meropenem, amikacin, and cefepime. Escherichia coli is sensitive to ceftriaxon, meropenem, amikacin, and cefepime. **Conclusion**: The dominant microbe that causes complicated appendicitis is Escherichia coli ESBL, which is resistant to ceftriaxone. The second most common bacteria is Escherichia coli, which remains sensitive to ceftriaxone. Careful consideration is needed for clinicians to determine the type of empirical antibiotic based on the patient's clinical findings.

KEYWORDS: Complicated appendicitis, Escherichia coli ESBL.

INTRODUCTION

Acute appendicitis is a typical abdominal emergency. If acute appendicitis is treated late, it is at risk of becoming complicated appendicitis. Complicated appendicitis is a perforated or gangrenous appendix found during surgery or with symptoms of peritonitis. Vermiform appendicitis or inflammation of the appendix is a medical condition commonly referred to as appendicitis. Appendicitis, often known as acute abdominal inflammation, is mainly caused by an obstruction of the appendix. The appendix's function is unclear; it is believed to play a role in the immune system in the digestive tract. An appendectomy is performed immediately to minimize the possibility of additional complications, such as peritonitis or abscess formation. Appendectomy is a surgical procedure that requires immediate action, so it has the potential to cause anxiety in patients (Soewito, 2020).

The World Health Organization (WHO) reported that in 2018, the incidence of abdominal surgery related to appendicitis was the most common. Appendectomy incidents are the most common emergency in the United States; in 2017, there were 734,138 cases of this condition; in 2018, the number increased to 739,177 cases (Fadhla et al., 2023).

According to a 2018 survey in Pujiati (2021), the prevalence of appendectomy is significant in most regions of Indonesia, affecting more than 7% of the total Indonesian population, or approximately 179,000 people. The rate of surgical intervention in Indonesia reached 12.8%, ranking it 11th among 50 existing disease patterns. Appendectomy is the most frequently performed surgical operation. According to the findings of the Household Health Survey conducted in Indonesia, acute appendicitis was identified as a causative factor of acute abdomen and was associated with various indications for emergency abdominal surgery (Mulya, 2020).

The mainstay of treatment for appendicitis is surgery and appropriate antibiotics. Proper administration of the right type and dose of antibiotics is believed to be essential in reducing more severe complications. Several studies have been conducted worldwide in an effort to review the epidemiology of bacteria and suggest empirical antibiotic options. Due to significant regional differences among studies, there is no universal consensus. At the Haji Hospital of East Java Province, patients with a diagnosis of acute appendicitis will receive ceftriaxone therapy, and if the diagnosis is complicated appendicitis, they will receive ceftriaxone and metronidazole therapy. In this study, we aim to evaluate the recommendation for empirical antibiotic administration based on the latest evidence.

METHODS

This study employs a retrospective design with a cross-sectional approach. Sampling was conducted using consecutive sampling. The study was conducted at the Haji General Hospital, Surabaya. The purpose of this study was to evaluate the recommendation for empirical antibiotic administration based on the latest evidence.

The sample in this study was patients with a diagnosis of acute appendicitis who would receive ceftriaxone therapy, and if the diagnosis was complicated appendicitis, they would receive ceftriaxone and metronidazole therapy. Research on bacterial cultures was conducted at the Clinical Microbiology Laboratory of the Haji Hospital, East Java Province. The data taken came from secondary data, namely the results of culture and sensitivity tests of complicated appendicitis cases in the microbiology department of the Haji Hospital, Surabaya in 2021-2023. General characteristic data in the assessment data collection sheet are arranged in a table, where the data is tabulated and processed statistically.

RESULT

Based on the characteristics of respondents diagnosed with appendicitis, 57 respondents experienced appendicitis, and bacterial culture will be carried out.

Table 1: Respondent Characteristics by Sex.

Sex	n	Percentage (%)
Male	37	64.91%
Female	20	35.09%
Total	57	100%

Based on table 1, it was found that the gender most often experiencing appendicitis was male, which was 37 people (6.91%). In contrast, 20 respondents were female (35.09%).

Table 2: Respondent characteristics based on the year of examination.

Examination Year	n	Percentage (%)
2021	15	26.32%
2022	24	42.11%
2023	18	31.58%
Total	57	100.00%

Based on the characteristics of the respondents, it was found that 2021 was the year with the most examinations, with 24 respondents (42.11%). Meanwhile, the year with the fewest respondents was 2021, with 15 respondents (26.32%), followed by 2023, which had 18 respondents (31.58%).

Table 3: Examination results based on microorganism type.

Gram	n	Percentage (%)
Negative	57	100.00%
Positif	0	0.00%
Total	**57**	**100.00%**

The examination results, categorized by type of microorganism, revealed that all respondents, namely 57 respondents (100%), were infected with Gram-negative bacteria.

Table 4: Examination results based on type of microorganism.

No	Organism	Gram	n	Percentage (%)
1	*Escherichia coli ESBL*	-	25	43.86%
2	*Escherichia coli*	-	24	42.11%
3	*Klebsiella pneumoniae*	-	4	7.02%
4	*Citrobacter freundii*	-	1	1.75%
5	*Klebsiella oxytoca*	-	1	1.75%
6	*Pseudomonas aeruginosa*	-	1	1.75%
7	*Salmonella Paratyphi A*	-	1	1.75%
	Total		57	100.00%

Based on the examination results, the most common type was Escherichia coli ESBL, which was identified in 25 respondents (43.86%). Escherichia coli bacteria were 24 respondents (42.11%). Klebsiella pneumonia bacteria were found in 4 respondents (7.02%), Citrobacter freundii bacteria in 1 respondent (1.75%), Klebsiella oxytoca in 1 respondent (1.75%), Pseudomonas aeruginosa in 1 respondent (1.75%), and Salmonella Paratyphi A in 1 respondent (1.75%).

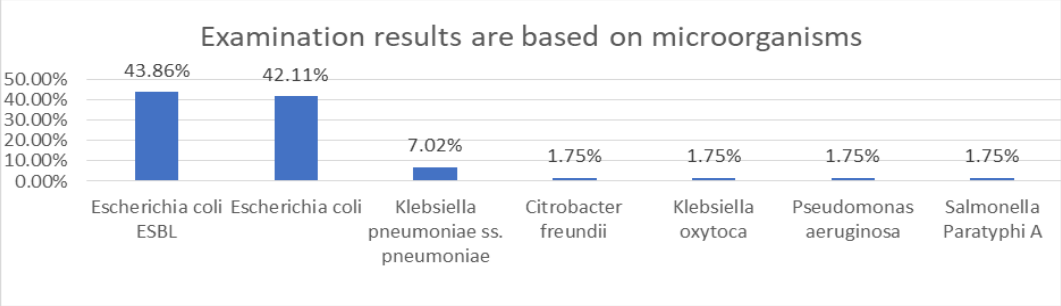

Figure 1: Types of microorganisms.

No.	Organism	AMK	AMP	ATM	CAZ	CZO	CIP	CRO	ETP	FEP	NIT	GEN	MEM	SAM	SXT	TGC	TZP
1	*Escherichia coli ESBL*	95.7	4.2	26.1	58.3	0	8.3	0	100	86.4	90	45.8	100	41.7	20	100	90.9
2	*Escherichia coli*	100	20.8	100	95.8	31.8	75	95.8	100	100	95.7	91.7	100	30.4	50	100	91.3
3	*Klebsiella pneumoniae*	100	0	100	100	0	100	100	100	100	0	100	100	100	100	100	100
4	*Citrobacter freundii*	100	0	100	100		100	100		100	100	100	100	0	0	100	100
5	*Klebsiella oxytoca*	100	0	100	100	0	100	100		100	100	100	100	100	100	100	100
6	*Pseudomonas aeruginosa*	100		0	100	0	100			100		100	100			0	100
7	*Salmonella Paratyphi A*	0	100	100	100	0		100	100	100	100	0	100	100	100	100	100

Ket : ■ < 30% : tidak direkomendasikan untuk digunakan; ■ 30-60% : dapat direkomendasikan dengan pertimbangan; ■ >60% : direkomendasikan untuk digunakan

AMK : Amikacin
ATM : Astreonam
AMP : Ampicillin
CAZ : Ceftazidime
CZO : Cefazolin
CIP : Ciprofloxacin
CRO : Ceftriaxone
ETP : Ertapenem
FEP : Cefepime
NIT : Nitrofurantoin
GEN : Gentamicin
MEM : Meropenem
SAM : Ampicillin/Sulbactam
TGC : Tigecycline
SXT : Trimethoprime / Sulfamethoxazole
TZP : Pipperacillin / Tazobactam

Figure 2: Bacterial Sensitivity Pattern in Pus/Pus Specimens.

DISCUSSION

Many cases of appendicitis come to the emergency unit, and some of them are complicated appendicitis. Complicated appendicitis is perforated or gangrenous appendicitis, even causing generalized peritonitis. The gold standard for treating appendicitis is surgery and antibiotics. At Haji Hospital Surabaya, all cases of appendicitis receive antibiotics from the emergency unit. The antibiotic of choice for acute appendicitis is ceftriaxone, and for complicated appendicitis, it is ceftriaxone and metronidazole.

In this study, the dominant germ in complicated appendicitis cases was Escherichia coli ESBL (43.87%) resistant to the cephalosporin group. ESBL or extended-spectrum beta-lactamases are enzymes produced by certain bacteria. This enzyme causes bacteria to be resistant to antibacterial drugs (antibiotics). This condition makes infections caused by ESBL-producing bacteria challenging to overcome. In this study, Escherichia coli ESBL bacteria were sensitive to the antibiotics amikacin, meropenem, and cefepime, which are included in the strict restriction antibiotic group and can be administered only upon the recommendation of the antibiotic resistance control committee.

Research in Switzerland in 95 patients presented with a complicated appendicitis, and 11 (12%) developed postoperative infectious complications. This research aims to decrease the rate of postoperative infectious complications due to amoxicillin-clavulanate-resistant E. coli in complicated appendicitis. These findings accentuate the need to implement evidence-based treatment protocols based on local microbiology profiles and resistance rates to optimise postoperative antibiotics in complicated appendicitis (Gerber, 2022). The growing prevalence of resistant strains was observed over the decade. Piperacillin/tazobactam provided the best coverage (69.8%) against resistant bacterial strains in our patients. Early escalation of antibiotics failed to reduce postoperative complications and the duration of antibiotics (Kwok, 2021).

Recent studies are discordant regarding postoperative use of piperacillin/tazobactam (PT) versus ceftriaxone/metronidazole (CM) for pediatric complicated appendicitis. Some argue that the broader spectrum PT decreases intra-abdominal abscess formation; however, antibiotic stewardship and once-a-day dosing favor CM. We aim to compare outcomes of postoperative antibiotic utilization using a large administrative database (Zeineddin et al., 2023).

Among 2805 patients diagnosed with acute appendicitis, 167 (6%) were <18 years old. The positivity rates for culture among children and adults were 33% and 18%, respectively. In total, 367 aerobes and 207 anaerobes were isolated. The predominant aerobic gram-positive coccus was viridans group streptococci (8.9%), the most common aerobic gram-negative bacillus was *Escherichia coli* (27.9%), and the most common anaerobic microorganism was *Bacteroides* spp. (27.7%). The results of antibiotic susceptibility testing of the predominant microorganisms revealed that 86.3% of gram-positive aerobes were susceptible to ampicillin, 76.3% of gram-negative aerobes were susceptible to gentamicin, and all anaerobic isolates were susceptible to metronidazole (Yu et al., 2024).

The second cause of complicated appendicitis is Escherichia coli (42.11%), which is sensitive to ceftriaxone, amikacin, meropenem, and cefepime. In this condition, clinicians need to make a wise choice of antibiotics. Initial administration in cases of complicated appendicitis is ceftriaxone and metronidazole. The clinical response after antibiotic administration is critical. If the clinical condition does not improve, coordination with the antibiotic resistance control committee is needed to administer amikacin, meropenem, or cefepime.

Complicated appendicitis involves perforation, abscess, or peritonitis, requiring both surgical intervention and effective empirical antibiotic therapy. The infection is usually polymicrobial, involving aerobic Gram-negative bacilli (e.g., Escherichia coli) and anaerobes (e.g., Bacteroides fragilis). Target pathogens: Aerobic Gram-negative rods and anaerobic bacteria are the main targets. Common regimens: Piperacillin-tazobactam monotherapy is frequently recommended due to its broad spectrum. Combination therapy includes a third-generation cephalosporin (e.g., ceftriaxone) plus metronidazole.

In patients allergic to beta-lactams, a fluoroquinolone (e.g., ciprofloxacin) plus metronidazole is an alternative. Duration of Treatment Is usually 4–7 days post-source control, as prolonged antibiotic therapy has not shown additional benefit and may increase the risk of resistance. The World Society of Emergency Surgery (WSES) 2016 guidelines recommend empirical coverage against both aerobic and anaerobic pathogens and support the use of piperacillin-tazobactam or ceftriaxone plus metronidazole as first-line therapy for complicated appendicitis (Gomes et al., 2016).

A 2017 multicenter randomized trial by Sawyer et al. demonstrated that shorter courses (4 days) of antibiotics after adequate source control are as effective as longer courses (10 days), reducing antibiotic exposure without compromising outcomes (Sawyer et al., 2017). Recent meta-analyses also support the combination of ceftriaxone and metronidazole as effective empirical therapy with low complication rates (Di Saverio et al., 2018). Culture-directed de-escalation is recommended once microbiological data are available. Avoidance of unnecessary broad-spectrum antibiotics helps reduce antimicrobial resistance.

CONCLUSION

This study found that the dominant microbe causing complicated appendicitis was Escherichia coli ESBL, which was resistant to ceftriaxone. The second most common microbe was Escherichia coli, which was still sensitive to ceftriaxone. Clinicians must consider the patient's clinical findings wisely when determining the type of empirical antibiotics.

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