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# Resistance Analysis Of Several Antibiotics in Samples of Clinical Isolates With Salmonellosis

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**ABSTRACT**

Typhus is a systemic infection caused by Salmonella typhi bacteria, which is usually transmitted through contaminated food or drink, usually treated with antibiotics. Inappropriate use of antibiotics causes various problems, one of which causes resistance. This resistance problem has become a global problem, including in Indonesia where there is an increase in bacterial resistance from 2013 which is 40%, 2016 as much as 60% and in 2019 reached 60.4%, due to irrational use of antibiotics so that bacteria become resistant to drugs. This study aims to determine the description of resistance to several antibiotics in clinical isolates of patients with Salmonellosis This study is a pre-experimental study, with a cross sectional approach. The samples used were pure isolates of Salmonella typhi bacteria obtained from blood samples of Salmonellosis patients, then tested for resistance with 5 different types of antibiotics (Ciprofloxacin, Amoxicillin, Levofloxacin, Cefotaxime and Sulfamethoxazolle-trimethopim) with the disk method (Kearby Beaure). The number of experimental units is 25 units, with the number of replications is 5 replications. The results showed that the five types of antibiotics were sensitive to Salmonella typhi bacteria with the highest antibiotic sensitivity being Ciprofloxacin while the antibiotic that had the lowest sensitivity was Amoxicillin. From the results, it can be concluded that the resistance test of the five antibiotics (Ciprofloxacin, Amoxicillin, Levofloxacin, Cefotaxime and Sulfamethoxazolle-trimethopim) is sensitive.

## INTRODUCTION

Typhus is a systemic infection caused by the bacterium *Salmonella typhi*, which is usually transmitted through food or drink contaminated with the feces or urine of an infected person. Typhus is a disease characterized by prolonged fever, headache, nausea, loss of appetite and constipation or sometimes diarrhea. Symptoms are often non-specific and clinically variable, and severe cases can lead to serious complications or even death. It is mainly caused by poor sanitation and lack of clean drinking water. According to recent estimates, there are about 21 million cases and 222,000 typhus-related deaths worldwide each year. Typhus disease is usually treated with antibiotics (Sarmadi, 2021).

Some antibiotics commonly used in the treatment of typhus are ceftriaxone, chloramphenicol, ciprofloxacin, ampicillin, and cotrimoxazole (Sarmadi, 2021). Antibiotics are chemical compounds produced by microorganisms to prevent or destroy toxic microbes

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(Hardiyanti Rahma, 2020). Appropriate and rational use of antibiotics provides cost-effective effects, improves clinical efficiency, minimizes drug toxicity and minimizes the development of resistance. At the same time, inappropriate use of antibiotics causes various problems, such as incurable diseases, increasing the risk of drug side effects, and increasing treatment costs and resistance (Rahman, 2019).

This resistance problem has become a global problem, including in Indonesia. According to the Antimicrobial Resistance Control Committee, in Indonesia there was an increase in bacterial resistance from 2013 which was 40%, 2016 as much as 60% and in 2019 it reached 60.4%. According to the Indonesian Minister of Health, Endang Rahayu Sedyaningsih, 92% of Indonesian people are still not right in using antibiotics, causing resistance (Utami, 2018). The large number of inappropriate uses of antibiotics has led to the problem of antibiotic resistance (Yulia *at al,*. 2019). Resistance is the ability of bacteria to adapt or survive against antibiotics. Antibiotic resistance is a condition of microorganisms such as bacteria that become resistant to drugs (Pratomo & Dewi, 2018). Cases of antibiotic resistance in clinical isolates of *Salmonellosis* patients, such as Sulfamethoxazole resistance to *Salmonella typhi*. Frequent use of antimicrobials, irrational use of antimicrobials, excessive use of new antimicrobials and prolonged use results in resistance to these antibiotics (Rahman, 2019). This antibiotic-resistant infection can increase the risk of transmission to others. Therefore, a resistance test is carried out to determine the appropriate antibiotic administration. Resistance test is a test used to determine the resistance of bacteria to antibiotics (Sumampouw J O, 2018).

The antibiotics used in this study were Ciprofloxacin, Amoxicilin, Levofloxacin, Sulfamethoxazole-trimethopim and Cefotaxim. For positive control using Cloramphenicol. Cloramphencol is a broad-spectrum antibiotic effective against a wide variety of bacteria and anaerobes. This antibiotic has bacteriostatic and bactericidal effects at high doses. Its broad spectrum also includes the antibiotic Amoxicillin, which is used as a treatment for respiratory tract infections and typhoid fever. This antibiotic is effective against Gram-positive and Gram-negative bacteria because it can penetrate the pores of the outer phospholipid membrane (Sumampouw J O, 2018). At the same time, its broad spectrum also includes the antibiotic Levofloxacin, which is a quinolone class drug, which works by inhibiting the action of the bacterial DNA gyrase enzyme. As a result, DNA replication stops (Yuliana, 2015).

Based on the results of research conducted by (R. Sukma, C. Indriputri, 2023), that the antibiotic ciprofloxacin has a fairly high level of resistance (70%) and sensitive (30%) to *Salmonella typhi* bacteria, chloramphenicol antibiotics are (3.3%) resistant and (96.6%) sensitive to *Salmonella typhi* bacteria, as well as to amoxicillin antibiotics resistant (26.6%) and sensitive (73.3%) to Salmonella typhi bacteria. Further research conducted by (Silfia *at al* 2022) found the results of chloramfenicol antibiotics showed a strong sensitive state, while erythromycin showed resistance to *Salmonella typhi* bacteria.

Based on this background, researchers are interested in conducting research with the title "Analysis of Multiple Antibiotic Resistance in Clinical Isolate Samples of *Salmonellosis* Patients".

## MATERIALS/METHOD

This study is a *pre-experimental* study, with a *cross sectional* approach. The samples used were pure isolates of *Salmonella typhi* bacteria obtained from blood samples of *Salmonellosis* patients, then tested for resistance with 5 different types of antibiotics (Ciprofloxacin, Amoxicillin, Levofloxacin, Cefotaxime and Sulfamethoxazolle-trimethopim) with the disk method (*Kearby Beaure*). The number of experimental units is 25 units, with the number of replications is 5 replications. Data analysis was carried out *descriptively*, the potential of Ciprofloxacin, Amoxicillin, Levofloxacin, Cefotaxim and Sulfamethoxazolle-trimethopim antibiotics was known by observing the clear zone formed around the antibiotic disk by measuring the diameter of the inhibition zone. Data is presented in the form of figures and tables.

## RESULTS AND DISCUSSION

The results of the study obtained resistance test data of 5 (five) types of antibiotics (Ciprofloxacin, Amoxicillin, Levofloxacin, Cefotaxim, Sulfamethoxazolle-trimethopim) against *Salmonella typhi* bacterial strains on each antibiotic can be seen in the following table:

**Table 1.** Resistance Test Results

| No | Replication | Antibiotic (mm) | | | | | Control (+) | Control (-) |
|---|---|---|---|---|---|---|---|---|
| | | Cip | Amox | Lfx | Ctx-m | Smz-Tmp | | |
| 1 | r1 | 38 | 30 | 38 | 40 | 38 | 40 | 0 |
| 2 | r2 | 40 | 38 | 40 | 38 | 38 | | |
| 3 | r3 | 40 | 30 | 39 | 40 | 38 | | |
| 4 | r4 | 40 | 34 | 36 | 38 | 36 | | |
| 5 | r5 | 40 | 36 | 32 | 40 | 36 | | |
| Average | | 39,6 | 33,6 | 37,0 | 39,2 | 37,2 | | |
| criteria | | S | S | S | S | S | | |

Based on table 1., the inhibition zone measurement results show that Ciprofloxacin antibiotics have an inhibition zone with an average of 39,6 mm. The interpretation of the inhibition zone size for the sensitive category according to the Clinical and Laboratory Standards Institute (CLSI, 2020) is more than 31 mm. Amoxicillin antibiotic has an inhibition zone with a mean of 33,6 mm with the interpretation of the size of the inhibition zone for the sensitive category according to CLSI which is more than 18 mm. Levofloxacin antibiotic has an inhibition zone with a mean of 37,0 mm with the interpretation of the size of the inhibition zone of the sensitive category according to CLSI which is more than 21 mm. Cefotaxim antibiotic has an inhibition zone with a mean of 39,2 mm with the interpretation of the size of the inhibition zone of the sensitive category according to CLSI which is more than 26 mm. Sulfamethoxazole-trimethopim antibiotic has an inhibition zone with a mean of 37,2 mm with the interpretation of the size of the inhibition zone of the sensitive category according to CLSI which is more than 16 mm.

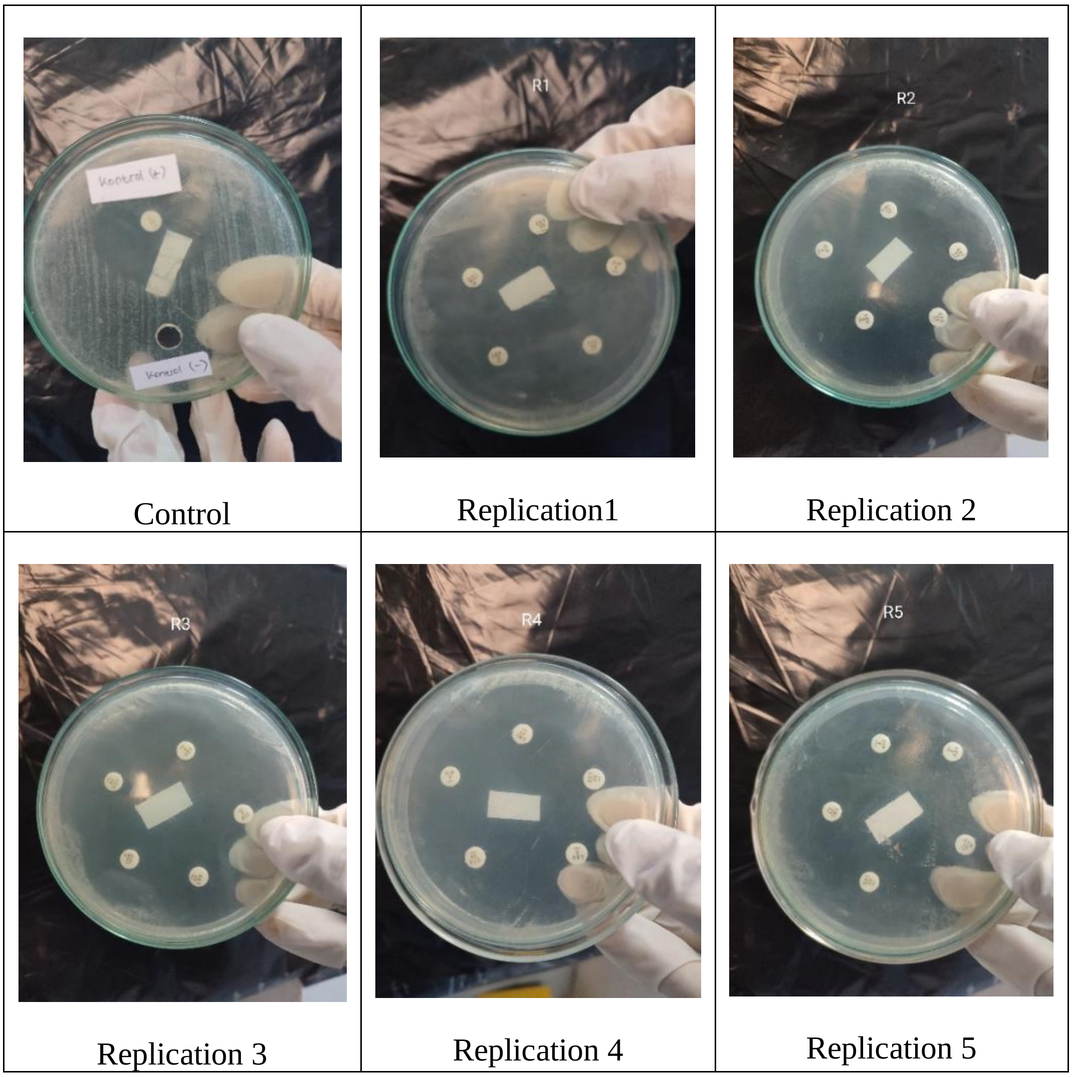


**Figure 1.** Antibiotic Resistance Test Results Against *Salmonella typhi* Bacteria

Antibiotic resistance tests carried out on isolates of *Salmonellosis* patients with 5 different antibiotics namely Ciprofloxacin, Amoxicillin, Levofloxacin, Cefotaxim, and Sulfamethoxazolle-trimethopim showed that all five types of antibiotics were sensitive to *Salmonella typhi* bacteria, with the highest antibiotic sensitivity being Ciprofloxacin and antibiotics that had the lowest sensitivity being Amoxicillin. This can be caused by the class and function of the antibiotic itself. Where Ciprofloxacin antibiotics are included in the quinolone group whose function inhibits the synthesis of microbial cell nucleic acids while Amoxicillin is included in the penicilin / β-lactam group whose function inhibits cell wall synthesis. For Levofloxacin antibiotics belong to the flouroquinolone group whose function is to inhibit DNA synthesis, Cefotaxime antibiotics belong to the cephalosporin group whose function is to inhibit microbial cell wall synthesis, Sulfamethoxazole-trimethropim antibiotics (Contrimoxazole) belong to the sulfonamide group whose function is to inhibit microbial cell metabolism and for positive control, namely Chloramphenicol antibiotics belong to the tiamfhenicol group whose function is to inhibit microbial cell protein synthesis.

The results of this study are in accordance with previous research conducted by (Budi & Sembiring, 2022) which shows Ciprofloxacin antibiotics are still sensitive to *Salmonella typhi* bacteria, while the results of this Amoxicillin antibiotic study are different from Dzullhidayat's research in 2022 which states Amoxicillin is resistant to *Salmonella typhi* bacteria. The results of the Amoxicillin antibiotic resistance test differ in each region can be caused by rationality in its use. This is Amoxicillin is a market drug that is widely known by the public for consumption and also because of its low price. The mechanism of resistance to this drug occurs due to the formation of betalactamase enzymes, the inaction of autolysin enzymes so that bacteria are tolerant to drugs (Juwita *at al*., 2012). The Levofloxacin antibiotic test is also in accordance with previous research conducted by (Yuliana, 2015) which states that Levofloxacin antibiotics are sensitive to *Salmonella typhosa* bacteria and in the Cefotaxime antibiotic test, according to (Yanto *at al*., 2021) states that Cefotaxime antibiotics are resistant to Staphylococcus auresus. The results of this Sulfamethoxazolle-trimethopim (Cotrimoxazole) antibiotic research are in accordance with the results of previous research conducted by (Juwita *at al*., 2012) which states Sulfamethoxazolle-trimethopim (Cotrimoxazole) antibiotics are still sensitive to *Salmonella typhi*.

The difference in antibiotic resistance test results with previous studies occurs because many factors influence the emergence of bacteria that are resistant to antibiotics. According to the FKUI Microbiology Textbook, there are various mechanisms that cause a bacterium to become resistant to antibiotics, namely, microorganisms produce ensymes that damage the action of drugs, changes in bacterial permeability to certain drugs, changes in certain places / loci in the cells of a group of certain microorganisms that are the target of drugs, changes in metabolic pathways that are the target of drugs, and encymatic changes occur so that although bacteria can still live well but are less sensitive to antibiotics.

From the point of view of Basic Pharmacology, resistance to an antibiotic due to lack of dosage, too short / too long administration of antibiotics, or improper methods of administering antibiotics, all cause the concentration of antibiotics to be unqualified in the patient's body (and ultimately unable to stop bacterial growth). Bacteria will try to maintain their existence by mutating. So, there are 3 factors that play a role in the occurrence of resistance, namely the microorganism itself, host factors, and drug factors (Ruslami *at al* 2017).

Bacterial resistance to antibiotics occurs due to changes in the DNA of microorganisms that undergo spontaneous mutations, so that the drug target has also changed, and due to the transfer of DNA from one microorganism to another through plasmids. Plasmids are extrachromosomal genetic elements that can replicate independently and carry genetic codes related to bacterial resistance to antibiotics (Ruslami *et al.,* 2017).

Other mechanisms are changes in gene expression, resulting in changes at the target site (such as resistance to quinolones), a decrease in drug levels in cells due to decreased drug penetration ability or an efflux system that releases drugs that have entered microorganism cells. The last mechanism is the inactivation of drugs by enzymes produced by microorganisms. Antibiotic resistance can spread from human to human (by bacteria), from bacteria to other bacteria (by plasmids), and from plasmids to other plasmids (by transposomes / pieces of DNA) (Ruslami *et al*., 2017).

According to (Juwita *at al*., 2012) bacterial resistance to antibiotics can also result from the use of antibiotics in a relatively long period of time and continuously, allowing the bacteria to memorize how the antibiotic works and can form a self-defense mechanism if later attacked by the same antibiotic. Unlike the case with the use of new antibiotics or those that are rarely used in treatment, the bacteria need a long time to create a defense mechanism against new antibiotics, so that antibiotics are still classified as sensitive. The compliance factor of the patient can also affect the occurrence of antibiotic resistance if the patient does not have compliance in taking antibiotics properly. Irrational use of antibiotics also causes increased resistance problems. Efforts to reduce the level of resistance can be done by providing education about antibiotic resistance to be used appropriately and providing an understanding of the impact of antibiotic resistance.

According to Basic Pharmacology, to prevent resistance, several things need to be remembered, namely, antibiotics should only be given when needed, according to indications, and given in appropriate doses (not excessive and not too small). The use of prophylactic antibiotics (prevention of infection with drugs) should be limited because the benefits obtained clinically must be greater than the losses so as to achieve therapeutic success, avoid side effects, and prevent resistance (Ruslami *et al*., 2017).

**NCLUSIONS**

From the results of the study of Multiple Antibiotic Resistance Analysis in Clinical Isolates of *Salmonellosis* Patients, with the *Kirby-Bauer* disc diffusion method, it can be concluded that the five antibiotics (Ciprofloxacin, Amoxicillin, Levofloxacin, Cefotaxim, and Sulfamethoxazolle-trimethopim) are Sensitive.

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