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# Resistance Profile Antibiotics Pathogenic Bacteria from SWAB Wounds of Pontianak City Diabetes Treatment Clinic Patients

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ABSTRACT

Diabetes mellitus (DM) is a type of metabolic disorder where the sufferer has high blood sugar levels due to the body's failure to respond or produces insufficient amounts of insulin, or a metabolic disorder caused by hyperglycemia due to abnormalities in insulin secretion and insulin action or both. One of the complications of diabetes is ulcers, where a superficial infection occurs on the sufferer's skin and becomes a strategic location for bacterial growth. Most of the drugs that are widely used to inhibit or kill bacteria that cause infections in humans are antibiotics which carry the risk of drug resistance. Antibiotic resistance is a growing problem in many parts of the world. Antibiotic resistance can occur due to inappropriate or excessive use of antibiotics. This study aims to determine the susceptibility of pathogenic bacteria to several antimicrobial agents or antibiotics and to determine the percentage of antibiotic resistance in diabetes mellitus patients who experience complications, which will make it easier to choose the right antibiotic for healing. This research uses a descriptive method using samples of bacterial isolates which have been identified as 11 samples of Staphylococcus aureus bacterial isolates, 11 samples of Pseudomonas aeruginosa isolates and 39 samples of Klebsiella pneumoniae bacterial isolates. Antimicrobial susceptibility test (AST) disk diffusion method (Kirby & Bauer test) using Mueller Hinton media. With eight different types of antibiotics, this test was carried out to prove antimicrobial activity by measuring the diameter of the antimicrobial activity inhibition zone. Resistance test results were obtained in Staphylococcus aureus experiencing the highest resistance to the antibiotic Gentamycin (CN) at 63.63%, in Pseudomonas aeruginosa experiencing high resistance to the antibiotic Ampicillin (AMP) at 54.54%, and in Klebsiella pneumoniae experiencing the highest resistance. against the antibiotic Ampicillin (AMP) was 41.02%. Preventing antibiotic resistance in wound healing is very important to ensure antibiotics remain effective in treating infections. Therefore, this research was carried out in order to determine the correct type of antibiotic for healing wounds in diabetes mellitus sufferers.

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## 1. INTRODUCTION

Globally, there are 537 million adults aged 20 to 79 years suffering from diabetes and the International Diabetes Federation (IDF) estimates that the number of people with diabetes will gradually increase to 643 million in 2030 and to 784 million in 2045 [1]. Diabetes mellitus (DM) is a metabolic disorder characterized by persistent hyperglycemia. Insufficient insulin production or tissue dissatisfaction with insulin[2]. The disease manifests in two forms: primary deficiency of insulin production in type 1 diabetes (T1D) or progressive insulin resistance and decreased sensitivity to insulin secretion in type 2 diabetes (T2DM).[3].

Due to the progressive nature of diabetes, it ultimately causes complications, especially microvascular and macrovascular. These complications have major consequences for the anatomy, structure and function of cells, tissues and certain organs, as well as affecting the patient's health

status[4]. Diabetes mellitus (DM) is also a group of metabolic disorders characterized by high blood sugar levels over a long period of time. Additionally, diabetes can cause many complications such as neuropathy and serious long-term complications including cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and eye damage.[5].

Diabetes Mellitus can be triggered by environmental factors and unhealthy lifestyles such as overeating, fatty foods, lack of activity and stress. Diabetes Mellitus can also arise due to hereditary factors. Diabetes mellitus can cause various complications, including gangrene. The rate of diabetic gangrene in Indonesia is around 15%, the amputation rate is 30%, and amputation is one of the main causes of patient hospitalization. It was found that 68% of diabetic gangrene sufferers were male, and 10% of gangrene sufferers recurred. The death rate due to diabetic gangrene is 16%. Within one year after amputation, 14.3% of diabetic gangrene patients were declared dead, and the remaining 37% died within three years after surgery. [6].

Diabetic foot ulcers (DFU) are also one of the most frequent, serious, and expensive complications associated with diabetes mellitus (DM). About 19 to 34% of people with DM develop DFU during their lifetime, and about 50% of them will become infected. Diabetic foot infection (DFI) may have more severe outcomes, resulting in increased morbidity, increased costs, and reduced quality of life. If this infection reaches bone tissue, it often causes osteomyelitis, which spreads to deep tissue. This occurs in 20% and 50-60% of patients with moderate and severe infections, respectively. Several local characteristics such as the average evolution time of DFU of more than 30 days, traumatic causes, wounds extending to the bone, and others are risk factors for the development of DFU. Several studies have tried to pinpoint these risk factors such as a history of previous injuries, repeated injuries, previous amputations, peripheral arterial disease (PAD), loss of protective sensation, and the presence of kidney failure. [7].

The global epidemic of prediabetes and diabetes has led to an epidemic of complications caused by these diseases. The most common complication is neuropathy, in which loss of sensory function begins in the distal lower extremities, characterized by pain and significant morbidity. Over time, at least 50% of people with diabetes will experience diabetic neuropathy[8]. Any type of neuropathy (sensory, motor, and/or autonomic) can contribute to wound damage. For example, autonomic neuropathy decreases sweat gland activity causing dry, cracked skin, increasing the risk of itching and infection, thereby inhibiting wound healing.[9]. Diabetic ulcers are chronic clinical wounds that are difficult to heal with a prevalence of 8.1% in diabetes patients aged over 50 years. This disease is prone to infection, local circulatory disorders and nerve damage, thus significantly increasing the rate of amputation and death in patients if not immediately controlled.[10]

Infection is when microorganisms reside in tissue or body fluids and cause local or systemic symptoms. Bacteria, fungi, viruses and parasites are the four groups of infections that can occur. The form of pus is evidence of the body's reaction to infection. Pus, also called pus, is a fluid originating from an inflammatory process consisting of leukocytes (cells), tissue fluid, and cellular debris. Culture testing is necessary to determine the species of infecting bacteria because pus that persists for a long time in an infected wound indicates continued bacterial growth. Infections are often the result, not the cause, of diabetic ulcers in people with diabetes. The severity of diabetic foot infections varies, ranging from simple cellulitis to life-threatening necrotizing fasciitis. These infections can be difficult to treat and despite repeated antibiotic treatment, the prospects for clinical resolution of these infections are poor and repeated use of antibiotics risks exacerbating antibiotic resistance.[11]. Diabetic ulcer infections can also include various species of pathogenic bacteria, such as Staphylococcus aureus, Pseudomonas aeruginosa, and Klebsiella pneumoniae[12].

The emergence of antibiotic-resistant pathogenic bacteria poses a serious public health challenge worldwide. Many species of bacteria developed tolerance to antibiotics long before humans began mass producing them to prevent and treat infectious diseases[13]. The drug-resistant nature of bacteria slows down the healing process of infections, requiring new antibiotics to treat existing infections[14]. Antibiotics are drugs used to prevent and treat bacterial infections. In contrast, antibiotic resistance occurs when bacteria change as a result of antibiotic use. A situation in which bacteria evolve and stop responding to drugs, making the infection more severe, difficult to cure, and increasing the risk of disease transmission, severe illness, and death[15]. In fact, antibiotic resistance

has become a significant threat to individual health globally. Some species of pathogenic bacteria can evolve and therefore, over time, many species become resistant to antibiotics[16].

The discovery of antibiotics and their development for the treatment of infectious diseases is the greatest success story in the history of chemotherapy. However, the widespread and indiscriminate use of antibiotics in the last 70 years has led to the emergence of strains resistant to every antibiotic that has been introduced so far. The first antimicrobial agents, such as sulfonamides, developed resistance in the late 1930s. Even before penicillin was widely used in clinical practice, penicillinase was discovered in 1940 in Staphylococcus aureus and Streptococcus pneumoniae providing evidence that mechanisms of resistance to penicillin already existed in the natural environment. Similarly, after the introduction of methicillin (semi-synthetic penicillin) to treat penicillin-resistant S. aureus infections, resistance was once again observed in strains now referred to as MRSA (Methicillin-resistant Staphylococcus aureus). Antibiotic modification is a commonly used strategy to render antibiotics ineffective, especially in the case of aminoglycoside antibiotics (e.g., kanamycin, gentamicin, and streptomycin), chloramphenicol, and ÿ-lactams. A large number of aminoglycoside modifying enzymes (AME), including N-acetyl transferase (AAC), O-phosphotransferase (APH), and O-adenyl transferase (ANT) that acetylate, phosphorylate, or adenylate aminoglycoside antibiotics, respectively, are known to be present in producer bacteria. Although this enzyme was first identified in the producer species Streptomyces in the early 1970s, it performs biochemical reactions identical to those seen in antibiotic-resistant clinical strains.[17].

Antibiotic resistance is a global health problem associated with human, animal, and environmental factors. Antibiotic resistance requires a multidisciplinary, multisectoral, and coordinated approach to address health threats at the human-animal-environment interface [18]. Antibiotic resistance in bacteria has become a major concern in recent years. The threat posed by infectious bacteria and their level of resistance to antibiotics[19]. Infections caused by antibiotic-resistant microorganisms are increasingly common and increasing globally[20]. One of the pathogenic bacteria is Staphylococcus aureus (S. aureus) which is a type of bacteria that causes infections in hospitals or health facilities and can cause many diseases, such as infections of diabetic ulcers.[21]. This research aims to determine bacterial resistance to antimicrobials or antibiotics. Based on this description, researchers want to conduct research to determine and determine the pattern of antibiotic resistance in diabetes patients with complications related to diabetic ulcers at the Pontianak City Diabetes Treatment Clinic. When you know the type of bacteria and its resistance characteristics, choosing an antibiotic will be easier.

## 2. METHOD

Research methods are ways of collecting data and then processing the data so as to produce data that can solve research problems. This research method uses a descriptive method, which is a type of research method used to describe or explain conditions/phenomena or research objects without manipulating or changing the observed variables. Descriptive research methods are used to solve and answer problems that occur today. This research uses a qualitative approach which is a descriptive approach and tends to use analysis where processes and meaning are emphasized and the theoretical basis is used as a guide so that the research focus is in accordance with the facts in the field. Research using qualitative descriptive methods describes existing phenomena or realities, both natural and human engineered, where usually this research pays more attention to the quality, characteristics and relationships between activities. The research was carried out in May 2023 and carried out at the Bacteriology Laboratory, Health Analyst Campus, Pontianak Health Polytechnic.

The research population is colonies of pathogenic bacteria that have been identified and isolated from wound swabs of patients with diabetes mellitus obtained from the Pontianak City Diabetes Mellitus Treatment Clinic. First, the researchers carried out a preliminary study by looking at data from bacterial identification results obtained from diabetes mellitus patients and the samples collected were 61 isolate samples from wound swabs from patients diagnosed with diabetes mellitus at the Pontianak City Diabetes Mellitus Treatment Clinic. From the bacterial identification data, three types of pathogenic bacteria were found, namely Staphylococcus aureus with 11 isolate samples, Pseudomonas aeruginosa with 11 isolate samples, and Klebsiella pneumoniae with 39 isolate

samples. In the AST test research, eight types of antibiotics were used with different concentrations. The antibiotics used are Vancomycin (VA), Gentamycin (CN), Erythromycin (E), Chloramphenicol (C), Ciprofloxacin (Cip), Ampicillin (AMP), Amikacin (AK) antibiotics, and antibiotics. Piperacillin/ Tazobactam (TZP).

**Antibiotic Sensitivity Test**

In the research carried out, data processing was carried out by measuring the diameter of the inhibition zone of each disk and then categorizing it using the standards contained in CLSI (Clinical and Laboratory Standard Institute) in order to calculate the percentage of antibiotic resistance levels.[22]. The antimicrobial susceptibility test (AST) was carried out using the disk diffusion method. In the disc diffusion test, bacterial isolates are tested for their susceptibility to different antibiotics. A clearly visible large ring around the antibiotic disc called the zone of inhibition indicates growth inhibition by effective (susceptible) antibiotics while bacterial growth is not affected by ineffective (resistant) antibiotics. With a standard test inoculum the organism corresponds to a McFarland turbidity of 0.5 and is inoculated onto Mueller Hinton Agar media. Then a disc-shaped antibiotic with a certain concentration is attached to the agar medium. Then the disk was incubated at a temperature of 35˚C-37˚C for 16-24 hours. The inhibition zone formed is measured manually with a ruler and interpreted based on the diameter of the inhibition zone according to WHO and shows the sensitivity test standard for an antimicrobial disk using the Kirby Bauer method published by CLLSI[23][24].

**Table 1** Standard CLSI (Clinical Laboratory Standard Institute)

| Antibiotics | Medicinal Potential | Inhibition Zone Diameter (mm) | | |
|---|---|---|---|---|
| | | Resistant | Intermediate | Sensitive |
| Amikacin | 30 mcg | ≤14 | 15-16 | ≥17 |
| Ampicillin | 10 mcg | ≤11 | 12-13 | ≥14 |
| Erythromycin | 15 mcg | ≤13 | 14-17 | ≥18 |
| Gentamicin | 10 mcg | ≤12 | 13-14 | ≥15 |
| Chlorampenicol | 30 mcg | ≤12 | 13-17 | ≥18 |
| Piperacillin | 100 mcg | ≤14 | 15-17 | ≥18 |
| Ciprofloxacin | 30 mcg | ≤15 | 16-20 | ≥21 |
| Vancomycin | 30 mcg | ≤9 | 10-11 | ≥12 |

## 3. RESULTS AND DISCUSSION

Based on the results of research that has been carried out, with a sample of 61 bacterial culture isolates that have been identified from wound swabs of diabetes mellitus patients at the Diabetes Treatment Clinic in Pontianak City. An interpretation of the results of measuring the diameter of the antibiotic resistance zone against bacteria was obtained using the Kirby Bauer method of AST sensitivity testing for 8 different types of antibiotics. To see the test interpretation resultsbacterial sensitivityagainst antibiotics and the percentage of resistance levelsantibiotics, see the table below.

**Table 2.** Results of measuring the diameter of the barrier zone for antibiotics or antimicrobial substances against bacteria

| Bacteria | Amount Sample | Total Resistance to Antibiotics | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | VA | C.N | E | C | Chip | AMP | AK | TZP |
| Staphylococcus aureus | 11 | 1 | 7 | 5 | 3 | 2 | 4 | 1 | 0 |
| Pseudomonas aeruginosa | 11 | 3 | 3 | 2 | 4 | 1 | 6 | 0 | 0 |
| Klebsiella pneumoniae | 39 | 2 | 11 | 5 | 15 | 11 | 16 | 2 | 0 |

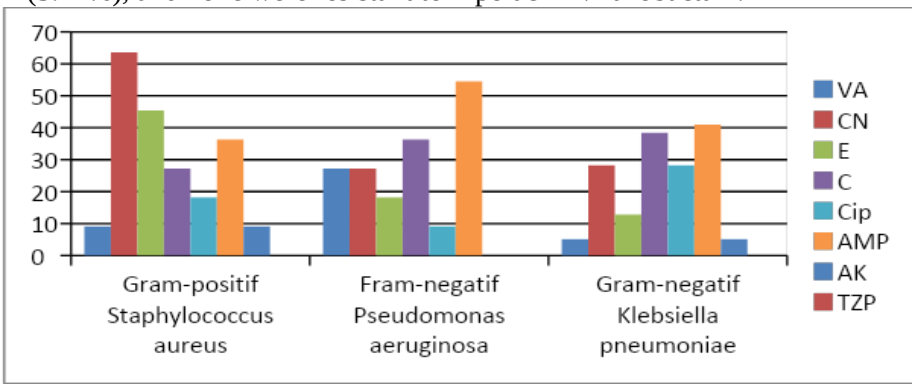
**Table 3.** Percentage Results of Resistance Levels of Antibiotics or Antimicrobial Substances Against Bacteria

| BACTERIA | NUMBER OF ISOLATE | RESISTANCE PERCENTAGE (%) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | VA | C.N | E | C | Chip | AMP | AK | TZP |
| Staphylococcus aureus | 11 | 9.09 | 63.63 | 45.45 | 27,27 | 18.18 | 36.36 | 9.09 | 0 |
| Pseudomonas aeruginosa | 11 | 27,27 | 27,27 | 18.18 | 36.36 | 9.09 | 54.54 | 0 | 0 |
| Klebsiella pneumoniae | 39 | 5.12 | 28,20 | 12.82 | 38.46 | 28,20 | 41.02 | 5.12 | 0 |

Description: Vancomyin (VA); Gentamycin (CN); Erythromycin (E); Chloramphenicol (C); Ciprofloxacin (Cip); Ampicillin (AMP); Amikacin (AK); Piperacillin/Tazobactam (TZP)

Based on the table above, describe the percentage of resistance levels for antibiotics or antimicrobial agents against bacteria. In bacteriaGram-positive Staphylococcus aureus was resistant to Gentamycin (63.63%), Erythromycin (45.45%), Ampicillin (36.36%), Chloramphenicol (27.27%), Ciprofloxacin (18.18%), Vancomycin and Amikacin (9.09%), and none were resistant to Piperacillin/Tazobactam.

Gram-negative bacteria Pseudomonas aeruginosa experienced resistance to Gentamycin (27.27%), Erythromycin (18.18%), Ampicillin (54.54%), Chloramphenicol (36.36%), Ciprofloxacin (9.09%), Vancomycin (27.27%), and none resistant to Amikacin and Piperacillin/Tazobactam. In Gram-negative bacteria Klebsiella pneumoniae, resistance to Gentamycin (28.20%), Erythromycin (12.82%), Ampicillin (41.02%), Chloramphenicol (38.46%), Ciprofloxacin (28.20%), Vancomycin and Amikacin (5.12%), and none were resistant to Piperacillin/Tazobactam.




**Graph 1.** Percentage Results of Resistance Levels of Antibiotics or Antimicrobial Substances Against Bacteria

Description: Vancomycin (VA); Gentamycin (CN); Erythromycin (E); Chloramphenicol (C); Ciprofloxacin (Cip); Ampicillin (AMP); Amikacin (AK); Piperacillin/Tazobactam (TZP);

**Discussion**

In this study, colony samples were used resulting from isolates identified as pathogenic bacteria from wound swabs of patients with diabetes mellitus obtained from the Pontianak City Diabetes Mellitus Treatment Clinic. And it has been identified, namely the bacteria Staphylococcus aureus, Pseudomonas aeruginosa, and Klebsiella pneumoniae. The resistance test research used eight different types of antibiotics. The antibiotics used are Vancomycin (VA), Gentamycin (CN), Erythromycin (E), Chloramphenicol (C), Ciprofloxacin (Cip), Ampicillin (AMP), Amikacin (AK) antibiotics, and antibiotics. Piperacillin/Tazobactam (TZP). The results of antibiotic resistance tests on Gram-positive bacteria Staphylococcus aureus were 11 samples, experiencing resistance to Gentamycin (63.63%), Erythromycin (45.45%), Ampicillin (36.36%), Chloramphenicol (27.27%), Ciprofloxacin (18.18% ), Vancomycin and Amikacin (9.09%), and none were resistant to Piperacillin/Tazobactam.

Gram-negative bacteria Pseudomonas aeruginosa experienced resistance to Gentamycin (27.27%), Erythromycin (18.18%), Ampicillin (54.54%), Chloramphenicol (36.36%), Ciprofloxacin (9.09%), Vancomycin (27.27%), and none resistant to Amikacin and Piperacillin/Tazobactam. In Gram-negative bacteria Klebsiella pneumoniae, resistance to Gentamycin (28.20%), Erythromycin (12.82%), Ampicillin (41.02%), Chloramphenicol (38.46%), Ciprofloxacin (28.20%), Vancomycin and Amikacin (5.12%), and none were resistant to Piperacillin/Tazobactam.

From the research that has been carried out, it can be seen the percentage of resistance levels of pathogenic bacteria that have been isolated from wound swabs of patients with diabetes mellitus to several antibiotics. From the results of this research, resistance can occur due to two factors, namely natural resistance and acquired resistance [25]. As a result of giving antibiotics that are not according to indications and giving the wrong dose, and long-term use of antibiotics[26].

## 4. CONCLUSION

Wounds in diabetics are often prone to infection, and various types of bacteria can infect these wounds and can become a place for bacteria to quickly multiply due to impaired blood flow and tissue damage. This can result in infections that are difficult to treat and even spread to other parts of the body. Antibiotic resistance occurs when the bacteria that cause an infection become insensitive to the antibiotics usually used to treat the infection. This research was carried out in order to find out the right type of antibiotic for healing wounds in diabetes mellitus sufferers. Based on the results of the research above, it can be concluded that the resistance pattern obtained from the resistance test was determined in that Staphylococcus aureus had a high level of resistance to the antibiotic Gentamycin (CN) of 63.63%, Pseudomonas aeruginosa had a high level of resistance to the antibiotic Ampicillin (AMP ) was 54.54%, and Klebsiella pneumonia had a high level of resistance to the antibiotic Ampicillin (AMP) with resistance of 41.02%. Preventing antibiotic resistance in wound healing is very important to ensure antibiotics remain effective in treating infections. Therefore, this research was carried out in order to determine the correct type of antibiotic for healing wounds in diabetes mellitus sufferers.

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