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Bacterial patterns and antibiotics sensitivity in culture tests of diabetic foot ulcer

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ABSTRACT

Background: Diabetic foot ulcers are one of the complications of DM which can cause a decrease in productivity in patients. Diabetic ulcers make it easier for bacteria to grow and infect the body. Some pathogenic bacteria that are often found are Staphylococcus aureus, *And Coli, Pseudomonas aeruginosa, Klebsiella pneumonia,* and Proteus is wonderful. Antibiotics play an important role in the management of diabetic ulcers infected with bacteria, where the most sensitive antibiotics are Amikacin, Erythromycin, Meropenem, Ciprofloxacin, and Ampicillin. Therefore, this study aims to determine the bacterial patterns and bacterial sensitivity to antibiotics in diabetic ulcer patients in the surgical inpatient room of RSUDZA Banda Aceh.
Method: This research is descriptive observational with a retrospective approach using medical record data from diabetic ulcer patients from August 2021 – August 2022. Sample collection was carried out randomly. *non-probability sampling* namely with total sampling. Data will be analyzed using univariate analysis
Results: There were 60 samples of diabetic ulcer sufferers who underwent pus culture examination and antibiotic sensitivity testing in this study. Based on gender, men are the most likely to suffer from dibasic ulcers, namely 41 samples. The average age of diabetic ulcer sufferers was above 65 years in 19 samples. From the pus culture examination, it was found that the 4 most commonly found bacteria were: *Staphylococcus aureus* (13), *E. Coli* (13), *Klebsiella pneumonia* (10), and *Pseudomonas aeruginosa* (8). Based on the antibiotic sensitivity pattern, Meropenem has the strongest sensitivity to bacterial pneumonia and *E. coli*. Meanwhile, Levofloxacin has the strongest sensitivity to bacteria Staphylococcus aureus and *Pseudomonas aeruginosa.*
Conclusion: It can be concluded that the cause of most diabetic ulcer infections are Staphylococcus aureus and E. Coli, while the antibiotics of choice are Meropenem and Levofloxacin because they have the highest sensitivity.

Keywords: *antibiotics, bacterial, diabetic foot ulcer*.
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INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disease with hyperglycemia characteristics that occur due to abnormalities in insulin secretion and insulin work which includes decreased insulin secretion, decreased glucose use by body cells, and increased glucose production into the blood caused by environmental and hereditary factors.[1] Diabetes mellitus is referred to as *the great imitator* Because it causes various acute and chronic complications.[2] DM complications are the 3rd highest cause of death in Indonesia. One of the most watched complications of DM is diabetic ulcers. Diabetic ulcers lead to a decrease in productivity in patients with diabetes mellitus.[3]

Diabetic ulcers are caused by hyperglycemia in patients with diabetes mellitus which then causes blood vessel abnormalities and neuropathy. Neuropathy disorders cause changes in the skin and muscles which then cause changes in the distribution of the soles of the feet, especially on the plantar surface of the foot, namely in areas that get high pressure, such as areas that line the metatarsal caput and other areas that line bone deformities and further facilitate the occurrence of diabetic ulcers.[4]

The risk of ulcer events in people with DM is 29 times greater. The entry of bacteria into the beginning of ulcers and high glucose levels in people with diabetes mellitus can be a good place for bacterial development.[3] In general, aerobic and anaerobic bacteria are very easy to multiply in diabetic ulcer infections. The most commonly found pathogenic bacteria are *Staphylococcus aureus, Streptococcus pyogenes, Staphylococcus epidermidis, E. coli, Pseudomonas aeruginoa, Klebsiella pneumonia, Acinetobacter spp., Proteus spp., dan Enterococcus* are some of the anaerobic bacteria that commonly cause tissue damage and lead to tissue necrosis, gangrene and ischemia of tissues.[5,6] Research conducted by Ni Luh Ayu in 2018 reported that from 60 samples of diabetic foot ulcer patients, the percentage of bacteria was obtained *Escherichia coli* (33,3%), *Pseudomonas aeruginosa* (21,7%), *Klebsiella pneumonia* (10%), *Proteus mirabilis* (10%), *Morganella morganii* (6,6%), *Proteus vulgaris* (3,3%), *Pseudomonas lutea* (3,3%), *Burkholderia cepacia* (1,7%), *Enterobacter aerogenes* (1,7%), *Providencia Stuartii* (1,7%), *Serratia marcescens* (1.7%) and *Sphingomon paucimobilis* (1,7%).[7]

Bacterial infections in diabetic ulcers can slow healing and the risk of

amputation becomes greater. One of the factors causing the high incidence of amputation in diabetic foot ulcer patients is errors in the use of antibiotics. The drugs most often used in bacterial infections are antibiotics. The use of appropriate antibiotics will greatly help patients in the healing process both in terms of cost and healing time.[8] Inaccuracy in using and choosing antibiotics will result in difficulty healing ulcers.[2]

In one study, it was found that the most sensitive antibiotics in diabetic ulcer bacteria were Amikacin (88.8%), Imipenem (87%), Meropenem (84.6%), Erythromycin (75%) and Cefoperazone/ Sulbactam (68.9%). Meanwhile, the most resistant antibiotics in diabetic ulcers are Ciprofloxacin (100%), Cotrimoxazole (100%), Ampicillin (97%), Ceftriaxone (89%), Cefotaxim (88%) and Levofloxacin (84%).[6] The selection of antibiotics in diabetic ulcer infections should be based on the results of bacterial culture in the patient which is then tested for bacterial sensitivity to antibiotics. Data obtained from the results of bacterial culture and bacterial sensitivity tests to antibiotics can be used as a basis for empirical therapy. This is because the pattern of bacteria and antibiotic sensitivity in each region and hospital is different.[3]

Based on the above background, researchers are interested in determining bacterial patterns and bacterial sensitivity to antibiotics in diabetic ulcer patients in the surgical inpatient room of RSUDZA Banda Aceh.

METHODS

The type and design of this study is a descriptive cross-sectional with a retrospective approach to secondary data where researchers only describe the characteristics of bacterial patterns and sensitivity to antibiotics in pus culture tests of diabetic foot ulcer patients in the surgical inpatient room of RSUDZA Banda Aceh. A sample is a part of a population that is selected in such a way that it is considered to be representative of its population. The samples in this study were taken using the total sampling method. The samples in this study were all medical records of diabetic foot ulcer patients in the surgical inpatient room of RSUDZA Banda Aceh from August 2021 to August 2022. Sensitivity test evaluation is carried out by assessing the sensitivity of an antibiotic that is still good for inhibiting microbes. Sacriter-sensitive is said to be sensitive to an antibiotic if the diameter of the inhibitory zone exceeds the upper limit of the antibiotic's breakpoints. Bacterial intermediates are said to be intermediate to an antibiotic if the diameter of the inhibitory zone is within the range of the antibiotic's breakpoints. Bacterial resistance occurs if resistant to an antibiotic if the diameter of the inhibitory zone is less than the lower limit of the antibiotic's breakpoints. Data analysis of this study used univariate analysis. Each variable is grouped into its category and presented in the form of a frequency distribution table.

RESULTS

This research has been carried out from November 1 – January 1, 2023, at RSUD dr. Zainoel Abidin. After data collection in the form of pus culture examination results on diabetic foot ulcer patients at RSUD dr. Zainoel Abidin in August 2021 – August 2022, a total of 60 samples were obtained that had met the inclusion and exclusion criteria. The distribution of characteristics of diabetic foot ulcer patients at RSUD dr. Zainoel Abidin by sex can be seen in Table 1.

Patient characteristics by age

The distribution of characteristics of diabetic foot ulcer patients at RSUD dr. Zainoel Abidin by age can be seen in Table 2.

Based on Table 2 below, it was found that 60 samples showed the most patients in the elderly age range (>65 years) with a total of 19 samples (31.7%), followed by the late elderly age (56-65 years) as many as 16 samples (31.5%). These results follow research conducted by Fitria, et al (2017) that diabetic ulcer patients were found most in the age range of late elderly and elderly with a total of 34 samples (59.7%).[4] Another study conducted by Gaol (2018) stated that at Dr. M. Jamil Padang Hospital, it was found that the highest incidence of

Table 1. Patient Characteristics by Sex

Gender	Sum	%
Man	41	68,3
Woman	19	31,7
Total	**60**	**100**

Table 2. Patient Characteristics by Age

Age	Sum	%
Late Adult (36-45 years old)	12	20,0
Early Elderly (46-55 years)	13	21,6
Late Elderly (56-65 years old)	16	26,7
Geriatric (>65 years old)	19	31,7
Total	**60**	**100**

Table 3. Bacterial Patterns in Diabetic Foot Ulcer Patients

Bacteria	Frequency (n)	%
Klebsiella pneumonia	10	16,7
Proteus mirabilis	4	6,7
Escherichia coli	13	21,6
Pseudomonas aeruginosa	8	13,3
Enterococcus facials	5	8,3
Enterobacter cloaceae	1	1,7
Staphylococcus sp	1	1,7
Staphylococcus epidermidis	1	1,7
Staphylococcus pseudintermedius	1	1,7
Staphylococcus aureus	13	21,6
Staphylococcus haemolyticus	3	5,0
Total	**60**	**100**

diabetic ulcers occurred in the age range of >50 years, which was 108 patients (73%).[5]

The elderly was one of the risk factors for the development of neuropathy complications in diabetics, these neuropathy can lead to ulceration of the feet. Neuropathy, vascular damage, and infection are three problems that can cause the development of the disease into diabetic ulcers.[9] Diabetic ulcers often occur at the age of >50 years due to decreased physiological body functions such as decreased secretion or insulin resistance, so the ability of body functions to control high blood glucose is less than optimal. Uncontrolled blood sugar levels will lead to long-term chronic complications, both macrovascular and microvascular, one of which is diabetic ulcers.[3]

Bacterial Pattern of Diabetic Foot Ulcer Patients

The distribution of bacterial patterns in diabetic foot ulcer patients at RSUD dr. Zainoel Abidin can be seen in Table 3.

Antibiotic Sensitivity Patterns

The distribution of antibiotic sensitivity patterns to bacteria was carried out by pus culture examination in diabetic foot ulcer patients at RSUD Dr. Zainoel Abidin can be seen in Table 4.

Table 4 shows that bacteria *Klebsiella pneumonia* has the highest sensitivity to the antibiotics Doripenem and Meropenem 100%. As well as bacteria *Escherichia coli* has the highest sensitivity to Doripenem, Meropenem, Amikacin, and Gentamicin at 100%.

DISCUSSION

Based on Table 1 above, it was found that from 60 samples there were more male patients with 41 patients (68.3%) than men with 19 patients (31.7%). The results are as reported by Gaol (2018), that patients with male sex (54%) are found to suffer more diabetic ulcers than women (46%). This is associated with men having more diabetic ulcer risk factors where smoking is one of the risk factors.[5] Smoking can affect the incidence of diabetic ulcers because nicotine contained in cigarettes causes endothelial damage and attachment as well as platelet aggregation which causes lipoprotein lipase thereby slowing blood fats and facilitating atherosclerosis. Atherosclerosis results in insufficiency vascular so that blood flow to the dorsalis pedis, popliteal, and tibial arteries will also decrease which can cause macroangiopathy and tissue hypoxia so that it can become a diabetic ulcer. This is different from the research conducted by Sari, et al (2018) at RSP Dr. M. Jamil Padang reported that there were more female patients than male patients with 17 female patients (60.72%) and 11 male patients (39.28%).[2] The same study conducted by Farida (2018) also reported that diabetic ulcer patients were more in women, namely 39 people (71%) while male patients amounted to 16 people (29%).[9]

Women who have entered menopause will decrease estrogen production, causing a decrease in blood vessel elasticity which will subsequently lead to atherosclerosis and hypertension. Atherosclerosis will result in obstructed blood flow, besides that high blood pressure will damage blood vessels and cause lesions in the endothelium which will then cause macroangiopathy and tissue hypoxia which will form diabetic foot ulcers.[3]

In postmenopausal women, the presence of metabolic disorders, obesity, and steroid hormone disorders increases the incidence of metabolic syndrome, type 2 diabetes mellitus, cardiovascular diseases, and malignancy. The sooner a woman goes through menopause, the more at risk of type 2 diabetes mellitus.[3,4] The most patients in the elderly age range (>65 years) with a total of 19 samples (31.7%), followed by the late elderly age (56-65 years) with as many as 16 samples (31.5%). These results follow

Table 4. Patterns of Antibiotic Sensitivity to Bacteria in Diabetic Foot Ulcer Patients

Bacteria	Antibiotic Sensitivity Pattern (%)										
	DOX	LVX	GEN	AMC	AMX	AMP	CTX	CRO	CASE	DOP	MEP
Klebsiella pneumonia (10)	10	20	30	30	0	0	20	20	30	100	100
Proteus mirabilis (4)	0	50	50	50	0	0	50	50	100	-	100
Eschericia coli (13)	15,0	77,0	100	100	0	0	15	15	30	100	100
Pseudomonas aeruginosa (8)	-	100	100	87,5	-	-	0	-	87,5	25	75
Enterococcus facials (5)	-	40	-	100	100	100	-	-	-	-	-
Enterobacter cloaceae (1)	1	0	0	0	0	0	100	100	100	100	100
Staphylococcus sp (1)	100	100	-	0	-	0	100	100	-	-	-
Staphylococcus epidermidis (1)	-	100	0	0	0	-	0	0	-	0	0
Staphylococcus pseudintermedius (1)	-	0	0	-	-	-	-	-	-	1	1
Staphylococcus aureus (13)	92	100	77	38	0	-	38	38	23	23	38
Staphylococcus haemolyticus (3)	100	100	-	0	0	-	0	0	0	0	0

N.B: DOX=Doxycycline, LVX=Levofloxacin, GEN=Gentamicin, AMC=Amikacin, AMX=Amoxicillin, AMP=Ampicillin, CTX=Cefotaxime, CRO=Ceftriaxone, CAZ=Ceftazidine, DOP=Doripenem, MEP=Meropenem, 0= Resistance, -- = Not Tested.

research conducted by Fitria, et al (2017) that diabetic ulcer patients were found most in the age range of late elderly and elderly with a total of 34 samples (59.7%).[4] Another study conducted by Gaol (2018) stated that at Dr. M. Jamil Padang Hospital, it was found that the highest incidence of diabetic ulcers occurred in the age range of >50 years, which was 108 patients (73%).[5]

The elderly was one of the risk factors for the development of neuropathy complications in diabetics, these neuropathy can lead to ulceration of the feet. Neuropathy, vascular damage, and infection are three problems that can cause the development of the disease into diabetic ulcers.[9] Diabetic ulcers often occur at the age of >50 years due to decreased physiological body functions such as decreased secretion or insulin resistance, so the ability of body functions to control high blood glucose is less than optimal. Uncontrolled blood sugar levels will lead to long-term chronic complications, both macrovascular and microvascular, one of which is diabetic ulcers.[3]

Based on Table 3, results were obtained from 60 samples, showing that the most bacteria found were *Escherichia coli* with 13 samples (21.6%) and Staphylococcus aureus with 13 samples (21.6%). The second most common bacteria found was *Klebsiella pneumonia* with 10 samples (16.7%). The third most common bacterium was *Pseudomonas aeruginosa* with 8 samples (13.3%). This is in line with research conducted by Utami (2018) at the Laur Force Hospital, Dr. Ramelan Surabaya also reported that bacterial isolates in patients with the most diabetic ulcers are bacteria *Escherichia coli* as many as 20 samples (33.3%), *Pseudomonas aeruginosa* A total of 13 samples (21,7%) and *Proteus mirabilis* A total of 6 isolates (10,0%).[7]

A study conducted by Akbar, et al (2014) in Makassar reported that the most common bacteria found in diabetic ulcer patients were gram-negative (73.52%), namely *Klebsiella pneumoniae*.[3] Research by Bulolo (2018) at Adam Malik Hospital Medan found that the most bacteria found in pus culture are *Klebsiella pneumoniae* A total of 11 samples (33,3%) and *Eschericia coli* A total of 8 samples (24.2%).[6]

Research conducted by Agistia, et al (2017) reported the most gram-negative bacteria found in patients' pus cultures were *Staphylococcus aureus*.[10] *Staphylococcus aureus* that enters the tissues releases a great many toxins that kill the cells, as a result of which inflammation proceeds much faster than multiplication and spread *Staphylococcus* itself, the study also showed bacteria *Klebsiella pneumonia* It is the second most common bacteria found in diabetic foot ulcer patients.[10] This research is also in line with a study conducted by Cahyopoetro, et al (2015) which reported that the most gram-positive bacteria found in diabetic ulcer patients are *Staphylococcus aureus* (13,%).[11]

According to a study conducted by Farida (2016) diabetic ulcer patients often found leukocytosis which is one of the signs of the severity of diabetic ulcers at a severe level. In severe infections, the etiology is generally caused by polymicrobials, especially Gram-negative rod bacteria as infection-concomitant bacteria.[12]

The results of this study are in line with research conducted by Hamid, et al (2020) in Sudan reporting that *Klebsiella sp* has a high sensitivity to antibiotics and Meropenem by 65%.[13] The results of this study are following research conducted by Utami (2018) in Surakarta obtained results that the level of sensitivity of Meropenem to bacteria *Escherichia coli* still high at 90%, and in bacteria *Klebsiella pneumonia* obtained results that are very sensitive to Meropenem and Amikacin antibiotics by 100%.[7] Research conducted by Razak (2012) reports that *Klebsiella sp* sensitivity to antibiotics Meropenem.[5]

The results of this study also showed bacteria *Staphylococcus aureus* have a high level of sensitivity to antibiotics Levofloxacin by 100% and Doxycycline by 87%. In bacteria, *Pseudomonas aeruginosa* showed a high level of sensitivity to the antibiotics Levofloxacin and Gentamicin at 100%, while Amikacin and Ceftazidine at 87.5%.

This is following research conducted by Elvira (2020), showing that bacteria *Staphylococcus aureus* has a high sensitivity to the antibiotic Levofloxacin by 83%.[14] Akbar's research (2014), showed that Amikacin and Meropenem antibiotics have the highest level of sensitivity of 100% to bacteria *Pseudomonas aeruginosa*.[15] Meropenem is a carbapenem class antibiotic that has a broad spectrum and is more active against Gram-negative aerobic bacteria. Meropenem can inhibit bacteria by preventing bacterial cell wall transpeptidase reactions so that it can inhibit and prevent the formation of bacterial cell walls.[13]

Sugiyono's research (2019), shows that the definitive pattern of antibiotic use given to diabetic ulcer patients is single and combination antibiotic therapy. Where the single antibiotic therapy that is widely used is ceftriaxon, metronidazole, and meropenem, while the combination of 2 antibiotics that are widely used are ceftriaxon + metronidazole and ceftazidim + meropenem.[16] Ceftriaxone, ceftazidim, and meropenem are broad-spectrum antibiotics that are the antibiotics of choice in the treatment of diabetic ulcers. Ceftriaxone and ceftazidim are used as antibiotics that control infection with Gram-negative bacteria including Pseudomonas and have low efficacy against Gram-positive bacteria. Meropenem is a carbapenem class antibiotic that has a broad spectrum against most Gram-negative and positive bacteria.[16]

CONCLUSION

The number of diabetic ulcer patients in this study was 60 patients, where more patients were male with 41 patients (68.3%). The age range of diabetic ulcer patients is the most elderly (>65 years) with 19 patients (31.7%). The bacteria that cause diabetic ulcers based on the results of the most patient pus cultures were obtained, namely *Escherichia coli* and *Staphylococcus aureus bacteria* as many as 13 samples (21.6%). The results of this study showed that most bacteria have a high level of sensitivity to the antibiotics Meropenem, and Levofloxacin.

The selection of the right antibiotic for the management of diabetic foot ulcer patients is carried out based on the results of bacterial culture and antibiotic sensitivity tests. If it cannot be done culture examination. The results of this study can be used as a reference in the selection of appropriate antibiotics in patients with diabetic foot ulcers to prevent the occurrence of antibiotic resistance. Health

workers such as doctors and nurses can provide education and supervision of antibiotic use as a preventive effort to prevent antibiotic resistance control.

DISCLOSURE

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Conflict of Interest

No conflict of interest.

Author Contributor

TRF and LM are involved in conceiving, designing, and supervising the manuscript. TRF and LM conduct the study. All authors prepare the manuscript and agree for this final version of the manuscript to be submitted to this journal.

Ethical Statement

This study has received ethical clearance from local authorities.

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