Research Article
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Antibiotic Use in Diabetes Mellitus Patients with Gangrene at Abdoel Wahab Sjahranie Samarinda Hospital

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Abstract: Gangrene is one of the complications of diabetes mellitus. Along with the rising prevalence of diabetes mellitus (DM), the prevalence of gangrene and necrosis manifestations such as ulcers and infections will ascend. The selection of appropriate antibiotics is critical in infection therapy. Inappropriate use of antibiotics will result in antibiotic resistance. Therefore, this research aims to overview demographic, clinical characteristics, antibiotic use profiles, and antibiotic-related problems for DM patients with gangrene at the Abdoel Wahab Sjahranie Samarinda Hospital. The study was retrospective research and was conducted in July-December 2021. Twenty-one patients met the inclusion criteria, and demographic data showed that most patients were men 57% (n=11), and most age was 39-59 years (57%, n=12). The longest period of suffering from gangrene was 6-10 years (14%, n=3). The most common length of hospitalization was 8-14 days, as reported by 52 percent (n=11) of patients, and the most common duration of antibiotic use was ten days, as reported by 86 percent (n=18) of patients. A single-used antibiotic was ceftriaxone (19%, n=4) patients. The most used antibiotic combination was ceftriaxone and metronidazole (81%, n=17). Fourteen patients used antibiotics appropriately in dosage, route, and frequency. Four patients were unsuitable for the benefit of antibiotics in terms of antibiotic type, and three patients were unsuitable for antibiotic use in terms of duration of administration.

Introduction

The International Diabetes Federation (IDF) estimates that at least 463 million people aged 20-79 worldwide will suffer from DM in 2019. Indonesia is ranked 7th among the ten countries with the highest number of sufferers, 10.7 million. Four provinces in Indonesia had the highest prevalence in 2013 and 2018, namely DI Yogyakarta, DKI Jakarta, North Sulawesi, and East Kalimantan (1). Diabetes mellitus is a chronic condition caused by an absolute deficiency of insulin or a relative lack of insulin due to impaired insulin secretion and work or a symptom arising from increased blood sugar levels. Various studies state that the high increase in the prevalence of DM disease impacts the occurrence of treatment patterns in DM patients (2).

Gangrene is included in microvascular complications, including sensory neuropathy, which will result in loss of pain sensations, changes in the distribution of foot pressure, and various changes in the skin and muscles that facilitate the occurrence of gangrene (3). Special treatment is needed in high DM with gangrene cases to reduce infections due to occurring wounds. One of the drug classes often used in the treatment of gangrene is antibiotics. Antibiotics are chemical substances produced by fungi and bacteria that have deadly properties or inhibit the growth of germs, while their toxicity in humans is relatively small (4). Because poly-bacterial infections are common, antibiotics used to treat gangrene must have broad-spectrum activity (5). Antibiotic combinations are also often used to synergistically treat some conditions, particularly in diabetic wounds (6). However, improper antibiotic usage might result in resistance and complicate treating infected wounds (7). Given the high prevalence of gangrene in diabetic

wounds in East Kalimantan, this study was carried out to obtain a demographic overview, clinical characteristics, antibiotic use profiles, and antibiotic-related problems for DM patients with gangrene at the Inpatient Installation of the Abdoel Wahab Sjahranie Samarinda Hospital.

Methodology

Types of research

This descriptive research design uses an observation method with a retrospective approach.

Research Population

The study population was the total number of DM patients diagnosed with gangrene hospitalised in July–December 2021 at the Abdoel Wahab Sjahranie Samarinda Hospital.

Research Sample

This study used a total sampling technique: samples from all gangrene patients who entered the hospital in a predetermined range. The number of samples obtained in July–December 2021 was 21 patients met the inclusion criteria.

Patient Sample Criteria

Patients with gangrene who received antibiotic therapy and were hospitalized with inclusion and exclusion criteria comprised the antibiotic sample used in this investigation. Inclusion criteria consisted of DM patients diagnosed with gangrene stage 0-4 (8), age >18 years, patients with complete and legible medical records, patients receiving single and combination antibiotic therapy, patients with comorbidities, and a minimal length treatment of three days. Exclusion criteria included patients with illegible or incomplete medical records, patients who underwent treatment for less than three days, and patients who died and were forced to return home.

Data Analysis Technique

Data were analyzed using Microsoft Excel (Microsoft Office 2019, Microsoft Corporation, New Mexico, America). The data copied on the collection sheet was analyzed univariately on each variable, which included patient demographic data such as age and gender presented in tabular form. Clinical data of patients related to the duration of DM, types of antibiotics, period of antibiotic use, and length of stay in the hospital were also presented. A table was created to compare the accuracy of antibiotic selection, dose, route, frequency, and duration of antibiotic administration with the literature (Use of Antibiotics Edition 1 of 2021).

Results and Discussion

The data used in this study was obtained from the medical records of DM patients with gangrene who underwent hospitalization at the Abdoel Wahab Sjahranie Samarinda Hospital from July 1 - December 31, 2021. The number of DM patients with gangrene who met the inclusion criteria of the study was 21 patients.

Patient Demographic Data

The gender and age distribution profiles of DM patients can be seen in Table 1. The gender distribution profile of DM patients with gangrene was 57% (n=12) male and 43% (n=9) female. According to the Centers for Disease Control and Prevention, males with diabetes have greater gangrene. Increased prevalence of gangrene in males is associated with decreased joint mobility and higher foot pressure (9). Research conducted by Al-Rubeaan et al. (2015) shows that the age of ≥45 will significantly increase the risk of gangrene. In that age range, there is a decrease in water content in the skin, skin elasticity, dermis-epidermal connecting integrity, and skin integrity. There is a decrease in angiogenesis and impaired physiological wound healing. Atrophy in the apocrine and sebaceous glands will cause the skin to become dry, and gangrene will occur more quickly (9).

Table 1. Patient demographic data.

Demographic Data	Amount & Percentage (n=21) patient
Gender	
Male	12 (57%)
Female	9 (43%)
Age	
18-38 years	1 (5%)
39-59 years	12 (57%)
>60 years	8 (38%)

Clinical Data of Patients

Based on the data obtained, the duration of suffering from DM, the length of hospitalization, and the duration of antibiotic use can be seen in Table 2.

Table 2. Clinical data of patients.

Clinical Data	Amount & Percentage (n=21) patient
Duration of DM	
Unrecorded DM History	16 (76%)
1-5 years	2 (10%)
6-10 years	3 (14%)
Length of Hospitalization	
3-7 days	10 (48%)
8-14 days	11 (52%)
Duration of Antibiotics Use	
<10 days	18 (86%)
>10 days	3 (14%)

The longest periods of suffering from DM were 6-10 years (14%, n = 3). This result aligns with Yelly et al.

(2018) research in IRNA internal medicine at RSUP Dr. M. Djamil Padang, where the extended duration of suffering from DM is the most cause of gangrene, usually more than five years. Long-suffering from diabetes is related to uncontrolled blood glucose levels that can cause chronic complications. Over a long enough period, it will lead to the death of tissues that will develop into gangrene (10).

In this study, the most prolonged hospitalization was 8-14 days, with 52% (n = 11) of patients. Based on research by Isna et al. (2020), the duration of treatment for DM patients with gangrene is, at most, more than eight days (7). Some patients need longer treatment due to the patient's condition has not improved, and patients get treatment again due to relapses of the disease, uncontrolled hyperglycemia, and the need for further wound care (11).

In this study, the longest use of antibiotics was ten days, with as much as 86% (n = 18) of patients. The duration of antibiotic use depends on the patient's condition. Based on the Antibiotic Use Guide Edition 1 (2021) literature, antibiotic use in DM cases with gangrene is ten days (12).

Antibiotic Use Profile

Based on the results, the type of Antibiotic given consists of single and combination antibiotics that depend on the patient's condition. The percentage of antibiotic types in DM patients with gangrene, both single and combined, can be seen in Table 3.

Table 3. Antibiotic use profile.

Antibiotic	**Amount & Percentage (n=21) patient**	**Dosage, Interval, and Route**
Monotherapy		
IV Ceftriaxone	4(19%)	1 g every 12 hours (iv)
Combination		
Ceftriaxone+Metronidazole	17 (81%)	500 mg every 8 hours (iv)

The results showed that the antibiotics given could be singular or combined. The most common type of single antibiotic used is ceftriaxone (19%, n=4). This study is in line with the research of Yelly et al. (2018), where the single use of antibiotics for DM patients with gangrene is ceftriaxone. In this study, single ceftriaxone was generally administered to patients with the general condition of the patient limp, and the wound worsened. Ceftriaxone's mechanism of action is similar to that of other antibiotics, lactams. It inhibits the synthesis of the cell wall of microorganisms by interfering with the transpeptidase reaction (13). Ceftriaxone is a broad-spectrum third-generation cephalosporin that is effective against most aerobic bacteria, both gram-positive and gram-negative. It activates against some gram-negative anaerobic bacteria commonly found in gangrene (10). Based on the recommendations of the Infectious Diseases Society of America, ceftriaxone is a drug of choice for empirical therapy in moderate to severe gangrene infections with methicillin-susceptible staphylococcus aureus (MSSA), Streptococcus spp, Enterobacteriaceae, and anaerobic bacteria (11). Single ceftriaxone is recommended for patients who show the presence of erythema, swelling, pain, and warmth around the wound without any systemic inflammatory symptoms (3).

Furthermore, antibiotics are prescribed to patients with moderate to severe infectious conditions (11). The combination of antibiotics can obtain a synergistic effect to fight microorganisms, expand the spectrum of activity, and prevent the occurrence of resistance (12). We also found the use of an antibiotic combination: ceftriaxone + metronidazole in 81% (n=17) patients. This study aligns with Liwang's (2017) study, where the most common combination used in DM patients with gangrene is metronidazole + ceftriaxone (13).

Metronidazole is vital in managing infections in diabetic gangrene because it can overcome anaerobic germs (Clostridium sp. and Bacteroides sp.), most often isolated in chronic ulcers or gangrene (14). Metronidazole is known as an antibacterial, antiprotozoal, and radiation sensitizer. Antibacterial prevents the spread of infectious agents or kills them so that they do not spread. The action mechanism is to inhibit nucleic acid synthesis by damaging DNA. As an antibacterial, metronidazole works by destroying such bacteria. Combining the two drugs is effective as empirical therapy of infection in the lower limbs because it will expand the spectrum of antibacterial activity to fight gram-positive, gram-negative, and anaerobic-aerobic bacteria.

Drug Related Problems

The data must be compared to the available literature to identify drug-related problems. Drug-related problems observed include the type of antibiotic, dosage, route, frequency, and duration of administration of antibiotics. Drug-related problems found are presented in Table 4.

Based on the findings, 17 patients and four patients have not complied with the literature regarding the types of antibiotics that must be used to treat gangrene. The four patients received ceftriaxone 2x1 g (IV), where the literature said that antibiotics must be given in combination, namely ceftriaxone 2x1 g (IV) + metronidazole 3x500 mg (IV) (9). Eighteen patients received suitable treatment. Still, three patients did

not, regarding antibiotic administration duration, even though the literature states that antibiotic treatment should last ten days. (9). The first patient used antibiotics for 12 days. The second and third patients used antibiotics for 13 days. Antibiotics were used longer since the patient required follow-up therapy to heal from gangrene infection and avoid recurrence.

The relatively high intensity of antibiotic use causes various issues and risks to public health, notably bacterial antibiotic resistance. Unnecessary or excessive use of antibiotics encourages the development of resistance and multiple resistance to certain bacteria that develop the ability to defeat antibiotics that have been designed and will spread through cross-infection. Antibiotic resistance is the ability of microbes to survive antimicrobial effects so that they are ineffective in clinical use (9).

Table 4. Drug related problems.

Drug Related Problems	Appropriate (n)	Non-Conforming (n)	(%) Appropriate	(%) Non-Conforming	Information
Types of Antibiotics	17	4	81	19	4 patients received ceftriaxone 2x1 g (iv), whereas the literature recommends combination therapy.
Dosage Antibiotics	21	0	100	-	-
Antibiotics Administration Route	21	0	100	-	-
Frequency of Antibiotics Administration	21	0	100	-	-
Duration of Antibiotics Administration	18	3	86	14	There was one patient using antibiotics for 12 days and two patients using antibiotics for 13 days

Conclusion

Demographic characteristics of DM patients with gangrene show that most gender was male, as much as 57% of patients. Most age was 39-59 years, as much as 57% of patients. The longest duration of suffering from DM was 6-10 years, as much as 14%. The length of hospitalization was at most 8-14 days for as many as 52% of patients. The longest time of antibiotic use was ten days (86%). The antibiotic used alone is ceftriaxone (19%). The antibiotic combination used was ceftriaxone + metronidazole (81%). The dose, frequency, and route of administration of ceftriaxone and metronidazole are one g every 12 hours and 500 mg every 8 hours on an IV basis, respectively. The drug-related problem in terms of antibiotic selection and duration of usage were 19% and 14%. Based on these data, it is possible to conclude that antibiotic use in the Abdoel Wahab Sjahranie Samarinda Hospital still has to be improved to handle infections in DM patients with gangrene more effectively and avoid antibiotic resistance.

Declarations

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Conflict of Interest
The authors declare no conflicting interest.

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The unpublished data is available upon request to the corresponding author.

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