

Antibiotic sensitivity pattern of bacteria from diabetic foot infections Haji Adam Malik central general hospital

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Abstract. Increasing rate of Diabetic Foot Infections (DFIs) caused by multi-drug-resistance pathogens plays a huge role in the duration of hospitalization, morbidity, and mortality of diabetic patients. The aim of the study is to assess the antibiotic sensitivity pattern of bacteria in DFIs and causative microorganisms. Using cross-sectional retrospective study, data were collected from medical records of DFIs patients previously hospitalized at Haji Adam Malik Hospital, Medan from January to July 2017. 33 patients met the criteria and got enrolled in the study. The classification of DFIs was evaluated according to Wagner's Classification. Evaluation of antibiotic sensitivity and identification of causative microorganisms were performed in standard microbiologic methods. The most common grade of DFIs was Grade-4 (48.5%), followed by Grade-3 (39.4%) and Grade-5 (9.1%). A total of 12 pathogens were identified. The most common infecting microorganism isolated on pus cultures was *Klebsiella pneumonia* (33.3%), followed by *Escherichia coli* (24.2%), *Acinetobacter baumannii* (12.1%), and *Staphylococcus aureus* (9.1%). Frequent susceptible antibiotics were Amikacin (88.8%), Imipenem (87%), Meropenem (84.6%), Erythromycin (75%), and Cefoperazone/Sulbactam (68.9%). DFIs are polymicrobial infections in this study *K. pneumonia* was the most common cause microorganism.

1. Introduction

Diabetes is one of the most major health problems that has become a big burden in any part of the world. Diabetes mellitus (DM) is a serious and complex illness that affects almost every vital organ in the body. There are approximately 415 million people worldwide suffering from diabetes. It has been estimated that this number will increase to 642 million by 2040.[1] Diabetes mellitus is the most common endocrine disorder known for its multifaceted complications, one of which is Diabetic Foot Infections (DFIs). The least expected outcome of DFIs is foot amputation. This made DFIs as a very concerning issue for diabetic patients.[2] In fact, the prevalence of foot ulcers found among diabetic patients is ranging from 4 to 10% and its lifetime incidence may be as high as 25%.[3]

Indonesia ranks seventh as the largest country for the incidence of DM after China, India, USA, Brazil, Russia, and Mexico. The 2015 estimation of DM incidence in Indonesia is about 10 million.[1] Management for DM based on the Infectious Diseases Society of America (IDSA), result in the recommended guideline in which the treatment of DFIs should be performed by a team of multidisciplinary diabetic foot care. The team should consist of an infectious disease specialist, specialist of clinical microbiology, foot surgeons, and wound-care specialists.[4]



There are several microorganisms that often cause DFIs. *Staphylococcus aureus*, *Streptococcus pyogenes*, *Staphylococcus epidermidis*, *E. coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Acinetobacter spp*, *Proteus spp* and *Enterococcus spp* are some of the most common pathogens that affect the progressivity of tissue damage.[4,5,6] The presence of obligate anaerobes in the tissue involved is associated with necrosis, gangrene, or ischemic tissue. Such condition usually occurs in severe chronic infections.[4]

The longer duration of hospitalization for diabetic patients is thought to be due to the increasing rates of DFIs. The presence of DFIs caused by the multi-drug-resistant pathogen is also contributing to the morbidity and mortality of the patients.[6] In such patients, clinicians can give empirical broad-spectrum antibiotic regimens. However, before doing so, there ought to be sensitivity tests of bacterial pathogens performed. This test would assist clinicians in choosing the appropriate antibiotic treatment regimens.[7] For acute or less severe infection, narrow-spectrum antibiotics can be administered, while the broad-spectrum antibiotics should be used in cases of chronic or severe infection.[8]

There was a limited study of the DFIs care in Indonesia.[6] This study aims to evaluate the antibiotic sensitivity pattern and to determine the causative bacteria of DFIs.

2. Methods

2.1 Design and study population

This was a retrospective cross-sectional study carried out at Haji Adam Malik Central General Hospital, Medan, Indonesia. Using consecutive sampling method, all patients who met the inclusion criteria were included in the study sample. The inclusion criteria were any patients who were hospitalized at internal medicine ward and diagnosed with DFIs in the period from January to July 2017. The exclusion criteria were all outpatients and patients with incomplete information of medical records. A total of 33 DFIs patients were enrolled, and all of them met the inclusion criteria.

2.2 Study procedures

We collected the demographic and clinical data from the patients' medical records. Demographic data collected included age, sex, length of stay in the hospital, and duration of diabetes. Laboratory parameters collected when the patients admitted to the hospital included hemoglobin, leukocytes, and HbA1c as a marker of glycemic control. Ankle-brachial index was also measured. The classification of the DFIs was evaluated according to the Wagner's Classification and distinguished over the location of infection between the left and right foot. The samples needed for isolation of bacteria and the antibiotic susceptibility test were obtained from the patients' foot ulcer, which was collected aseptically and got plated right afterward. Identification of the causative microorganisms was performed by standard microbiologic methods. Antibiotic susceptibility testing was performed using disk-diffusion method. The results were interpreted according to the guidelines of the Clinical and Laboratory Standards Institute.

2.3 Data analysis

Continuous variables were reported as mean $\pm$ SD and categorical variables as proportions. Distribution of microorganisms isolated on pus cultures, antibiotic of resistance and sensitivity were reported as frequency (percentage).

3. Results

From January to July 2017, a total of 33 DFIs patients were hospitalized and have been considered as qualified as study participants based on the inclusion criteria. We found that DFIs affected males slightly more frequent (57.5%) as compared to females (42.4%). The age range of DFIs patients was from 46 to 75 years, and the most common age group of diabetic foot patients was 54–59 years age group.

The grading of DFIs according to Meggitt–Wagner’s classification is shown in table 1. The most common cases were Grade 4 (48.5%) followed by Grade 3 (39.4%), and Grade 5 (9.1%).

Table 1. Demographic data representing sex, age, foot ulcer location, duration of diabetes, Wagner classification, laboratory and ABI (Ankle Brachial Index).

Characteristic	n =33
Sex, n (%)	
Male	19 (57.6)
Female	14 (42.4)
Mean age (years)	52.58 ± 7.75
Duration of hospitalization (%)	
< 10 days	12 (36.3)
≥ 10 days	21 (63.7)
Foot ulcer location, n (%)	
Right foot	20 (60.6)
Left foot	13 (39.4)
Mean diabetes duration (years)	6.45 ± 2.4
Wagner’s Classification, n (%)	
Grade 1	0(0%)
Grade 2	1 (3%)
Grade 3	13 (39%)
Grade 4	16(49%)
Grade 5	3 (9%)
Laboratory results	
Hb, mean ± SD (g/dl)	9.29 ± 2.27
WBC, mean ± SD (μl)	19147.76 ± 7990.98
Poor glycemic control (HbA1C ≥ 8%)	23 (69.7)
Ankle Brachial Index (ABI), mean± SD	0.86 ± 0.18

A total of 12 pathogens were identified from microorganisms isolated on pus cultures. The most common infecting microorganism isolated on pus cultures was *Klebsiella pneumonia* (33.3%), followed by *E. coli* (24.2%), *Acinetobacter baumannii* (12.1%), *Staphylococcus aureus* (9.1%). These are shown in table 2 and figure 1.

Table 2. Distribution of microorganisms isolated from pus cultures in DFIs patients.

Microorganisms	Frequency	%
<i>Klebsiella pneumoniae</i>	11	33.3
<i>E. coli</i>	8	24.2
<i>Acinetobacter baumannii</i>	4	12.1
<i>Staphylococcus aureus</i>	3	9.1
<i>Morgarella morgani</i>	1	3.0
<i>Pseudomonas aeruginosa</i>	1	3.0
<i>Erdwardsiella</i>	1	3.0
<i>Pseudomonas purida</i>	1	3.0
<i>Serratiamarcescens</i>	1	3.0
<i>Enterobacter aerogenes</i>	1	3.0
<i>Shigella sonnei</i>	1	3.0

Antibiotics showing their sensitivity most frequently were Amikacin (88.8%), Imipenem (87%), Meropenem (84.6%), Erythromycin (75%), and Cefoperazone/Sulbactam (68.9%). These are shown in table 3. Meanwhile, antibiotics showing resistance were Ciprofloxacin(100%), Cotrimoxazole (100%), Ampicillin (97%), Ceftriaxone (89%), and Cefotaxime (88%) and Levofloxacin (84%). These are shown in table 4.

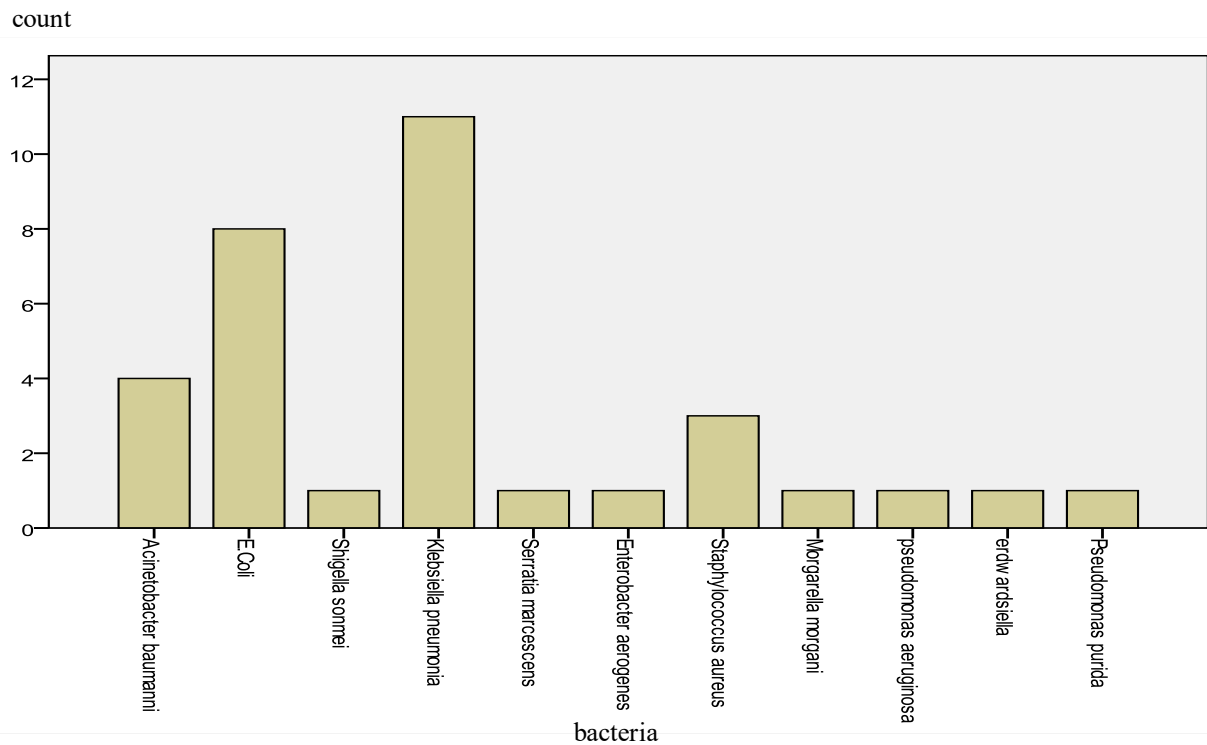


Figure 1. Graphic of microorganism.

Table 3. Antibiotic sensitivity.

Antibiotic	Frequency (n)	Sensitivity (%)
Amikacin	24	88
Imipenem	7	87
Meropenem	22	84
Erythromycin	3	75
Cefoperazone / sulbactam	20	68
Clindamycin	2	50
Vancomycin	2	50
Piperacillin-tazobactam	3	42
Gentamycin	11	34
Doxycycline	6	24

Table 4. Antibiotic resistance.

Antibiotic	Frequency (n)	Resistance (%)
Ciprofloxacin	14	100
Cotrimoxazole	9	100
Ampicillin	31	97
Ceftriaxone	24	89
Cefotaxime	23	88
Cefuroxime	6	86
Levofloxacin	21	84
Ceftazidime	25	83

4. Discussion

Diabetic foot infection is one of the complications found in diabetic patients. This is more common in the older age group compared to younger ones. In our study, we found that the group of patients most

commonly affected was those over 50 years of age. This result was similar to previous studies that showed more of the study participants acquired DFIs as a complication when they were above the age of 50.[10,11] Various studies also showed that DFIs has the longest duration of hospitalization as compared to other complications occurring in diabetic patients.[12] In this study, we found that most of DFIs patients was hospitalized for over 10 days long (63.7%). However, though, there were also some patients hospitalized for 10 days before they get discharged.

Our study found that *Klebsiella pneumonia* (33.3%) are the most common bacteria found as the etiologic agent in the DFIs, followed by *E. coli* (24.2%). The bacteria were isolated from the cultures of DFIs. In another study, it was found that the most common microorganism isolated from pus cultures was *S. aureus* (47.5%).[13,14] Another a local study conducted at Koja Regional General Hospital, Jakarta showed that *P. aeruginosa* was the most frequent bacteria isolated from DFIs.[15] Our study showed similarity with some other studies in which gram-negative microorganisms were the most common bacteria found in DFIs (*Klebsiella spp*, *P. aeruginosa spp*, and *E. coli spp*).[16] The present study confirms that multi-drug-resistant organisms (MDROs) infection are extremely common in hospitalized patients with DFIs, similar to the results of Hartmann-Heurtier et al. and Kandemir et al.[17,18] Most of the MDROs were opportunistic pathogens. A total of 51.3% of MDROs were Gram-positive bacteria, among which the top 3 were *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Enterococcus spp*. The gram-negative bacteria accounted for 48.7%, mainly including *Enterobacter spp*, *Pseudomonas aeruginosa*, and *Proteus mirabilis* bacteria.[17]

In this study, we found that the most sensitive antibiotics in treating DFIs were Amikacin (88.8%), Imipenem (87%), Meropenem (84.6%), Erythromycin (75%), and Cefoperazone/sulbactam (68.9%). Meanwhile, the most resistant antibiotics were Ciprofloxacin (100%), Cotrimoxazole (100%), Ampicillin (97%), Ceftriaxone (89%), and Cefotaxime (88%) and Levofloxacin (84%).

Diabetic foot infections are polymicrobial infections.[19] Most of the isolated bacteria showed resistance against more than one antibiotics. Therefore, we assumed that monotherapy antibiotic in treating DFIs might not be adequate. The increasing incidence of MDROs is a potential risk factor of which clinicians should be concerned in treating patients with DFIs. The local pattern of bacterial etiology and their susceptibility is also very important in choosing the correct empirical antibiotic therapy.

In terms of antibiotic therapy, there has been published guidelines about antimicrobial management for DFIs worldwide.[4,8] Generally, empirical antibiotic therapy can be administered for DFIs according to the severity of infections. For mild infections, patients could use oral antibiotics such as cephalexin, amoxicillin/clavulanate, levofloxacin or dicloxacillin, and antibiotics that cover methicillin-resistant *S. aureus* (MRSA) including clindamycin, doxycycline, and trimethoprim/sulfamethoxazole.[4,8] For moderate infections, patients can be treated initially with oral antibiotics or with parenteral antibiotics, followed by oral therapy for 1–3 weeks, whereas severe infections require hospitalization and treatment with parenteral antibiotics followed by oral therapy, for 2–4 weeks.[4]

Diabetic foot infection is one of the complications of DM that is very difficult to overcome, and therefore the management of DFIs should be performed in a multidisciplinary approach.[4,20,21] The frequency of hospitalization, previous duration of antibiotic therapy, ulcer type, ulcer size, and osteomyelitis are the independent risk factors for DFIs that need to be monitored closely in diabetic patients. The broad-spectrum antibiotics should be used parenterally in cases of chronic or severe infections.[14] In cases of mild infections, outpatients should not be treated with topical or systemic antibiotics. They should be treated with oral antibiotics for 1–2 weeks. Pharmacists also play a role in monitoring the efficacy and safety of administering antibiotics in patients.[21]

5. Conclusion

It can be concluded that DFIs are polymicrobial infections. *K pneumonia* was the most common bacteria found in DFIs. The most susceptible antibiotics were Amikacin, Imipenem, Meropenem, Erythromycin and Cefoperazone/Sulbactam.

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