Antibiotic Sensitivity Pattern of Bacterial Isolates Among Diabetic Outpatients with Urinary Tract infection in Pontianak

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Diabetic patients are associated with a higher risk of infection. The research purposed to identify antibiotic susceptibility patterns among diabetic outpatients with urinary tract infection in Pontianak. An experimental study was performed for 13 bacterial isolates of diabetic outpatients with urinary tract infection in the Clinic of Diabetes Mellitus, Sultan Syarif Mohamad Alkadrie Hospital, Pontianak. The disc diffusion method was used to perform the susceptibility of antibiotics to the bacterial isolates. Among 13 isolates, the most common causative agent of urinary tract infection was Escherichia coli (53.85%), followed by Pseudomonas aeruginosa (30.77%), Klebsiella spp., and Enterobacter aerogenes were 7.69%. Most isolates of bacteria of the study had a high sensitivity to Cefepime (92.31%), then followed by Levofloxacin, Amikacin, and Meropenem for 84.62%. The study revealed low sensitivity of bacteria to Amoxicillin/Clavulanate, Co-Trimoxazole, Cephazoline, and Ceftriaxone (30.77%, 23.08 %, 23.08%, 23.08%, respectively). All bacterial isolates had high resistance to Ampicillin. Moreover, multidrug resistance observed among bacterial isolates.

Key words: antibiotic susceptibility, diabetes, urinary tract infections

The successful therapy for urinary tract infection depends on the identification of microbial agents and the selection of antimicrobial against them (Gutema et al. 2018). The main bacteria associated with urinary tract infection in diabetes are Escherichia coli, Enterococcus spp., Klebsiella spp., Proteus spp., Pseudomonas aeruginosa, Staphylococcus aureus, and coagulase-negative streptococcus. Other studies showed that fungi, namely, Candida spp. and Actinomyces spp., also have a role as urinary tract infection agents in diabetes mellitus (Borj et al. 2017; Gutema et al. 2018).
Antibiotic susceptibility is diverse among species and areas. Therefore, determining the sensitivity of antibiotics to bacterial isolates is essential. Furthermore, there is an increase in the antibiotic resistance prevalence due to the widespread and indiscriminate use of broad-spectrum antibiotics (Al-tulaibawi 2019). Data showed about 30% of urinary tract infection bacterial agents are resistant to ciprofloxacin and levofloxacin (Triono and Purwoko 2012; Rahman 2017). Thus, this study was performed to provide local data about the susceptibility pattern of antibiotics among diabetic outpatients with urinary tract infection in Pontianak.

MATERIALS AND METHODS

Research Design. An experimental study was conducted at the Microscopic Laboratory, Faculty of Medicine, Universitas Tanjungpura, Pontianak, during the period November 2019 to July 2020. The research procedures were approved by Ethics Committee of the Faculty of Medicine, Universitas Tanjungpura.

Bacterial Isolates. Bacterial isolates were derived from diabetic outpatients with urinary tract infection in the Clinic of Diabetes Mellitus, Sultan Syarif Mohamad Alkadrie Hospital, Pontianak. All patients were from Pontianak. Isolation of bacteria were inoculated in MacConkey Agar (Merck) and identification of bacteria by biochemistry test. All procedures were done by previous study. A total of 13 bacterial isolates were inoculated in MacConkey (Merck) agar plates using a standard inoculating loop for bacterial regrowth and incubated (Memmert) at 37 °C for 24 hours.

Antibiotic Susceptibility Test. McFarland 0.5 of bacterial suspensions were inoculated in Mueller Hinton Agar (Merck) to undergo antibiotic susceptibility testing using the disk diffusion method. Sterile cotton swab was dipped in the suspension and the excess liquid pressed. The sterile cotton swab was swab on the agar plate surface and repeated three times by rotated 60 °C of the plate. Antibiotic disks were placed on inoculated agar surface and incubated at 37 °C for 24 hours. The inhibition zone was examined according to the Clinical and Laboratory Standard Institute guidelines (Clinical and Laboratory Standards Institute 2020). Antibiotic agents that were used are Co-trimoxazole (SXT, 25 µg, Oxoid), Ciprofloxacin (CIP, 5 µg, Oxoid), Levofloxacin (LEV, 5 µg, Oxoid), Nitrofurantoin (F, 300 µg, Oxoid), Amikacin (AK, 30 µg, Oxoid), Ampicillin (AMP, 10 µg, Oxoid), Amoxicillin/Clavulanate (AMC, 30 µg, Oxoid), Cephazoline (KZ, 30 µg, Oxoid), Ceftriaxone (CRO, 30 µg, BD BBL), Cefepime (FEP, 30 µg, BD BBL), Gentamicin (GM, 10 µg, BD BBL), Meropenem (MEM, 10 µg, BD BBL), and Tobramycin (NN, 10 µg, BD BBL).

RESULTS

Generally, antibiotic susceptibility patterns for urinary bacterial isolates from diabetic patients showed high sensitivity to Cefepime (92.31%), then followed by Levofloxacin, Amikacin, and Meropenem for 84.62% each. The study revealed low sensitivity of bacteria to Amoxicillin/Clavulanate, Co-Trimoxazole, Cephazoline and Ceftriaxone (30.77%, 23.08%, 23.08%, 23.08%, respectively). All bacterial isolates had high resistance to Ampicillin. E. coli, as the main causative agent in the study, was sensitive to Amikacin and Cefepime (100%, for each). P. aeruginosa was sensitive to Levofloxacin, Amikacin, and Meropenem (100%, for each), followed by Ciprofloxacin, Cefepime, Gentamicin, and Tobramycin (75%, for each). E. pyogenes were 100% sensitive to Co-Trimoxazole, Levofloxacin, Amoxicillin/Clavulanate, and Cefepime. At the same time, Klebsiella spp. appeared sensitive to Cefepime and Meropenem (100%, for each). Detail of antibiotic sensitivity profile and inhibition zone diameter, as seen in Table 1 and Table 2, respectively.

DISCUSSION

Globally, antibiotic resistance rates are on the increase. Meanwhile, antibiotic sensitivity is a primary concern in the treatment of patients with infection. Patients with diabetes are prone to have an infection, commonly urinary tract infection because of the impaired immune response, dysfunctional bladder, and other mechanisms (Alrwithey et al. 2017). Other studies demonstrated that diabetic patients with urinary tract infections are vulnerable to have resistant pathogens as the causative agent (Nitzan et al. 2015). Our study revealed bacteria that cause urinary tract infection in patients with diabetes mellitus, namely E. coli (7/13), Klebsiella spp. (1/13), E. aerogenes (1/13), and P. aeruginosa (4/13). Several studies reported that E. coli is the most common bacteria in urinary tract infection in diabetic or non-diabetic patients (Nitzan et al. 2015; Borj et al. 2017; Gutema et al. 2018; Al-tulaibawi 2019).
Table 1 Antibiotic sensitivity profile of bacterial isolates from diabetic patients with urinary tract infection

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>*n</th>
<th>SXT</th>
<th>CIP</th>
<th>LEV</th>
<th>F</th>
<th>AK</th>
<th>AMP</th>
<th>AMC</th>
<th>FEP</th>
<th>KZ</th>
<th>CRO</th>
<th>GM</th>
<th>MEM</th>
<th>NN</th>
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</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>7</td>
<td>2 (28.57)</td>
<td>5 (71.43)</td>
<td>6 (85.71)</td>
<td>1 (14.29)</td>
<td>7 (100)</td>
<td>0 (0)</td>
<td>3 (42.86)</td>
<td>7 (100)</td>
<td>3 (42.86)</td>
<td>1 (14.29)</td>
<td>5 (71.43)</td>
<td>6 (85.71)</td>
<td>6 (85.71)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>4</td>
<td>0 (0)</td>
<td>3 (75)</td>
<td>4 (100)</td>
<td>0 (0)</td>
<td>4 (100)</td>
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<td>3 (75)</td>
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<td>2 (50)</td>
<td>3 (75)</td>
<td>4 (100)</td>
<td>3 (75)</td>
</tr>
<tr>
<td><em>Klebsiella spp.</em></td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><em>Enterobacter pyogenes</em></td>
<td>1</td>
<td>1 (100)</td>
<td>(0)</td>
<td>1 (100)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>13</td>
<td>3 (23.08)</td>
<td>8 (61.54)</td>
<td>11 (84.62)</td>
<td>1 (7.69)</td>
<td>11 (84.62)</td>
<td>0 (0)</td>
<td>4 (30.77)</td>
<td>12 (92.31)</td>
<td>3 (23.08)</td>
<td>5 (38.46)</td>
<td>8 (61.54)</td>
<td>11 (84.62)</td>
<td>9 (69.23)</td>
</tr>
</tbody>
</table>

*n*: Number of isolates

Table 2: Inhibiton zone diameter of disk diffusion among bacterial isolates from diabetic patients with urinary tract infection

<table>
<thead>
<tr>
<th>Isolate</th>
<th>SXT</th>
<th>CIP</th>
<th>LEV</th>
<th>F</th>
<th>AK</th>
<th>AMP</th>
<th>AMC</th>
<th>FEP</th>
<th>KZ</th>
<th>CRO</th>
<th>GM</th>
<th>MEM</th>
<th>NN</th>
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<tr>
<td>1</td>
<td>0</td>
<td>21.60**</td>
<td>22.52*</td>
<td>0</td>
<td>26.13*</td>
<td>7.02</td>
<td>9.33</td>
<td>28.67*</td>
<td>0</td>
<td>15.33</td>
<td>17.67*</td>
<td>25.33*</td>
<td>20.67*</td>
</tr>
<tr>
<td>2</td>
<td>23.60*</td>
<td>26.08*</td>
<td>25.60*</td>
<td>10.40</td>
<td>23.08*</td>
<td>0</td>
<td>8.18</td>
<td>30.27*</td>
<td>9.50</td>
<td>22.12**</td>
<td>11.06</td>
<td>29.53*</td>
<td>15.13*</td>
</tr>
<tr>
<td>3</td>
<td>18.82*</td>
<td>27.15*</td>
<td>27.29*</td>
<td>17.23*</td>
<td>20.02*</td>
<td>0</td>
<td>26.84*</td>
<td>33.66*</td>
<td>26.40*</td>
<td>30.60**</td>
<td>16.68*</td>
<td>30.33*</td>
<td>16.68*</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>11.28</td>
<td>16.08</td>
<td>14.66</td>
<td>28.67*</td>
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<td>0</td>
<td>25.67*</td>
<td>0</td>
<td>19.33</td>
<td>19.17*</td>
<td>19.03</td>
<td>20.41*</td>
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<td>32.18*</td>
<td>32.40*</td>
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<td>19.16*</td>
<td>0</td>
<td>11.17</td>
<td>32.00*</td>
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<td>30.33*</td>
<td>17.50*</td>
<td>29.00*</td>
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<td>0</td>
<td>24.32*</td>
<td>24.46*</td>
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<td>17.33*</td>
<td>0</td>
<td>9.16</td>
<td>13.83</td>
<td>0</td>
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<tr>
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<td>14.94</td>
<td>20.32**</td>
<td>14.73</td>
<td>10.80</td>
<td>0</td>
<td>11.56</td>
<td>30.00*</td>
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<td>34.84*</td>
<td>15.16*</td>
<td>29.50*</td>
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<tr>
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<td>27.30*</td>
<td>15.14**</td>
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<td>8.52</td>
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<td>10</td>
<td>21.02*</td>
<td>23.16</td>
<td>25.61*</td>
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<td>9.32</td>
<td>20.96*</td>
<td>30.20*</td>
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<td>16.06**</td>
<td>18.03*</td>
<td>12.51</td>
<td>27.53*</td>
<td>31.62*</td>
<td>28.52*</td>
<td>28.59**</td>
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<td>29.08*</td>
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<td>27.68*</td>
<td>26.85*</td>
<td>0</td>
<td>19.57*</td>
<td>12.06</td>
<td>26.11</td>
<td>32.80*</td>
<td>0</td>
<td>27.38*</td>
<td>16.51*</td>
<td>30.72*</td>
<td>17.38*</td>
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<tr>
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<td>16.16</td>
<td>22.34*</td>
<td>16.06**</td>
<td>19.06*</td>
<td>0</td>
<td>9.22</td>
<td>26.24*</td>
<td>9.04</td>
<td>21.62**</td>
<td>17.02*</td>
<td>28.32*</td>
<td>17.32*</td>
</tr>
</tbody>
</table>

*Sensitive, **Intermediate, Resistant
Isolate no. 1, 5, 6, 12 *P. aeruginosa*; no. 2-4, 8, 9, 11, 3 *E. coli*; no. 7 *Klebsiella*; no. 10 *E. aerogineses*
Table 1 demonstrated that all bacteria isolates are resistant to Ampicillin (100%). Ampicillin is an antibiotic effective for Gram-positive and Gram-negative microorganisms. However, some microorganisms develop resistance to Ampicillin. Studies have shown an increasing trend in ampicillin-resistance (Aamodt et al. 2015; Richey et al. 2015). Contradict to other studies, Nitrofurantoin showed the second rank of the highest antibiotic resistance (92.31%) (Gardiner et al. 2019; Zubair and Shah 2019).

Table 2 showed majority isolates have resistant to 5 antibiotics (30.76%) and 2 isolates demonstrated resistant to 9 antibiotics (15.38%). There is an increasing trend in antimicrobial resistance among uropathogenic. The primaryantibiotic resistance mechanism for Gram-negatives are the production of β-lactamases and frequently aminoglycoside modifying enzymes (Khoshnood et al. 2017; Bitsori and Galanakis 2019). Bacteria classified as Enterobacteriaceae with sensitivity test results resistance or intermediate towards third-generation cephalosporin antibiotic should be tested for the production of Extended Spectrum β-lactamases (ESBL). A previous study in Dr.Soetomo Hospital Surabaya found a more significant rate of ESBL producing E.coli compare to non-ESBL producing E. coli (Fitri et al. 2015). Pathogen that produce ESBL represent resistance to third-generation cephalosporin, monobactam, as well as to newer β-lactam antibiotics (Bitsori and Galanakis 2019). Further test is needed to reveal ESBL bacteria in this study.

Based on our study, Cefepime was reported as an antibiotic for urinary tract infection with the highest sensitivity compared to others (92.31%). Cefepime is classified as beta-lactam, fourth-generation cephalosporin antibiotic. It is used to treat uncomplicated pyelonephritis as second-line therapy and as an alternative therapy in urosepsis, renal diseases, and Extended-Spectrum Beta-Lactamases bacteria (Baldwin et al. 2008; Seputra et al. 2015; Bonkat et al. 2018; Kim et al. 2018).

E. coli isolates exhibited sensitivity towards Amikacin and Cefepime (100% for each), followed by Levofloxacin, Meropenem, and Tobramycin (85.71%, for each), Ciprofloxacin (73.41%). Less sensitivity is shown towards Amoxicillin/Clavulanate, Cephazoline (42.86%, for each), Co-Trimoxazole (28.57%), Nitrofurantoim and Ceftriaxone (14.29%, for each), whereas another study has shown the opposite result (Gutema et al. 2018; Al-tulaibawi 2019; Zubair and Shah 2019).

P. aeruginosa was shown as the highest sensitivity towards Levofloxacin, Amikacin, and Meropenem (100%, for each), Ciprofloxacin, Cefepime, Gentamycin, and Tobramycin (75%, for each) and less sensitivity for Ceftriaxone (50%). Other antibiotics do not affect P. aeruginosa. P. aeruginosa is known to have resistance towards multiple antibiotics, such as aminoglycoside, quinolones, and β-lactams through some mechanisms (Pachori et al. 2019; Pang et al. 2019). P. aeruginosa demonstrated intrinsically, acquired, and adaptive resistance(Pang et al. 2019).

Further research using a larger population or samples and different hospitals should be conducted. This study results may be used as data to improve the treatment of diabetic patients with urinary tract infections based on the pattern of antibiotic susceptibility. Antibiotic susceptibility pattern is required for the rational use of antibiotics and the prevention of resistant urinary pathogens. Furthermore, the rise of antibiotic resistance should be a significant concern for clinicians in treating diabetic patients with urinary tract infection, as demonstrated in this study.

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REFERENCES


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