Bacterial Profile of Urinary Tract Infections and Antibiotic Resistance Pattern in a Tertiary Care Hospital

Authors:
Mangalgi Smita S, Assistant Professor,
Sanjay S Wavare, Lecturer,
Shivali Gajul, Lecturer,
Annapurna G Sajjan, Professor,
Department of Microbiology, BLDEU’s Shri B M Patil Medical College, Vijayapura, Karnataka, India.

Address for Correspondence
Mangalgi Smita S,
Department of Microbiology,
BLDEU’s Shri B M Patil Medical College,
Vijayapura – Karnataka, India.
E-mail: smitamangalgi@gmail.com.

Citation

Submitted: Oct 25, 2019; Accepted: Jan 19, 2020; Published: Feb 28, 2020

Abstract: Background: Due to emergence of multidrug resistance, empirical treatment of Urinary tract infections is becoming intricate. Aim: To know the bacteria causing UTI, their antibiogram and possibility of using fosfomycin as an empirical drug. Material and Methods: Urine sample from suspected UTI cases were cultured by standard method. Identification of bacterial isolate, antimicrobial susceptibility and ESBL production was performed by standard protocol. Results: Of the 1674 urine samples 529 samples showed significant growth of which 386 were Gram negative bacilli, 107 Gram positive cocci and 36 Candida species. Most prevalent pathogens were E. coli (47.4%) among the Gram negative group and Enterococci (13%) among the Gram positives. A good number of bacteria were susceptible to fosfomycin. Conclusions: Routine surveillance studies are needed to have knowledge about the most effective empirical treatment. Fosfomycin looms out as the drug of choice for empirical treatment of UTI in this area.

Key Words: ESBL, fosfomycin, MDR, UTI

Introduction:
Urinary tract infections (UTIs) are among the most frequent bacterial infections witnessed both in outpatients as well as in hospitalized patients leading to significant morbidity and mortality. [1] Urinary tract infection (UTI) is defined as the presence of bacteria in urine along with symptoms of infection. Uncomplicated and complicated are the two clinical categories of UTI. An uncomplicated UTI is typically seen in healthy individuals who have no structural, neurological abnormalities, are not pregnant or have not been catheterized. All other UTIs are considered complicated [2]. Common factors associated with UTI are poor hygiene, undernourishment, low socioeconomic status. [3] Though uncomplicated UTIs are mainly caused by Gram negative bacilli, occasionally may be caused by Enterococci, Staphylococcus suprophilicous. Though studies from Nigeria have reported changing patterns in prevalence of uropathogens, worldwide studies have reported E. coli to be the most frequently encountered bacteria. [4, 5] The prevalence of other bacterial species such as Klebsiella, P. mirabilis, Serratia, Enterobacter, Enterococcus, Coagulase Negative Staphylococci vary from region to region and in the same region from study to study [6-10]. Relative frequency of pathogens causing UTI is governed by various factors like age, sex, hospitalization, catheterization etc. Irrespective of the causative agent, empirical treatment has to be initiated before the culture and sensitivity results are available. Irrational use and over-the counter availability of antibiotics and poor infection prevention practices have led to the emergence of drug resistance to commonly used antibiotics. Many studies have documented the appearance of Multi Drug Resistant (MDR) variants. [11-14] An isolate with resistance to at least two antibiotics of different classes including aminoglycosides, chloramphenicol, tetracyclines and/or erythromycin is considered to be MDR. [10, 11] Currently, community-acquired UTIs due to ESBL producing Gram negative bacilli are being often reported and due to multi-drug resistance (MDR) the choice of antibacterial agent becomes limited. [15-17] Nitrofurantoin and fosfomycin have shown promising results in the treatment of UTI caused by multidrug resistant bacteria in many studies. [18-20] No reports regarding the antimicrobial resistance of uropathogenic bacteria pertaining to ESBL production and sensitivity to fosfomycin have been published from this area.

With this background, the study was undertaken with the aims to know the common bacteria accounting for UTIs and to assess the antimicrobial susceptibility pattern, production of ESBL and sensitivity to fosfomycin.

Materials and Methods
Study design: A prospective study was conducted in the department of Microbiology after obtaining the approval from the Institutional Ethical Committee and the consent from the participants. The study duration was from April 2016 to May
was used as negative control and a known in-house ESBL producer as positive control. Statistical analysis was done using InStat GraphPad software.

**Results**
During the study period 1674 urine samples from suspected cases were processed for urine culture, of which 529 (31.6%) yielded significant growth. Remaining 1145 samples showed either non-significant, mixed growth or were sterile. Among the 529 culture positive patients 343 (65.83%) were females and 178 (34.16%) were males. Mean age of patients was 52.86 ± 24.06 years (range 20 days to 90 years). About 70% of the isolates belonged to Enterobacteriaceae. *E. coli* (47.44%) was the most common isolate followed by *Klebsiella pneumoniae* (15.5%), *Citrobacter* (5.29%) and *Proteus* (1.13%). Other Gram-negative bacteria (*Pseudomonas* and *Acinetobacter*) accounted for 3.58% of the isolates. About 20.6% of the isolates were Gram-positive, major being *Enterococcus faecalis* (13.4%). *Candida* species were isolated from 6.79% of patients and more than 50% were *Candida non-albicans*. Diabetes mellitus was the major predisposing factor in the patients from whom *candida* was isolated (66.7%). There was no significant difference concerning the species according to age classes or gender. Of the 529 isolates 280 (52.93%) were multidrug resistant. Distribution of uropathogens and the frequency of MDR are given in Fig 1.

A varied level of antimicrobial resistances against commonly prescribed drugs was noted in this study (Table 1). Of the seven different antibiotics used, significantly high (P < 0.01) susceptibility was shown to fosfomycin (97.98%) followed by nitrofurantoin (72.97%) both for Gram negative and Gram positive bacteria. About 60% of Gram negative isolates were sensitive to amikacin. Most Gram negative bacteria were resistant to ampicillin (85.75%), amoxycillin (84.03%) (Table 1).

Of the 289 suspected ESBL positive isolates, 164 (56.74 %) showed positive result on confirmatory test and 125 (43.25 %) were confirmed to be ESBL negative (Table 2). Among the 164 ESBL positive bacteria majority were *E. coli* (78.04 %).
Antibiotic Resistance Pattern in a Tertiary Care Hospital

In this study UTI was more common in females than males, located in accordance with the studies by Dash et al. and Mishra et al. which signifies that these cannot be used now. [26, 35] Majority of the urinary tract isolates were found to be resistant to norfloxacin, ciprofloxacin, ceftriaxone, cefazidime, ceftaxime. These findings have great repercussion as patients in a tertiary care hospital like ours receive these drugs as an empirical or definitive treatment. Incidence of MDR uropathogens was found to be 52.93% which is in accordance with the studies by numerous other authors. [11, 16, 17, 36-38] Due to ESBL production problems in treatment of UTIs has been amplified, which also has been reported by other studies. [16, 39-46]

In the present study, of the 289 suspected ESBL producing isolates, 56.74% were confirmed to produce ESBL, which is in accordance with the studies that have reported ESBL producers in the range of 40-70%. [16, 40-44] Much less figures have been reported by some authors which does not match with the present study. [45-48] This may be because of the disparity in geographical location, study design, over the time change in the resistance pattern of the isolates. Our study reveals that most of the multi drug resistant as well as ESBL producing Gram negative isolates were sensitive to fosfomycin and nitrofurantoin. Both these drugs also showed an excellent bactericidal activity against all the Gram-positive isolates. Re-emergence of nitrofurantoin sensitivity may be correlated to its non-usage for a long period in this area. Similar findings of high susceptibility to fosfomycin and nitrofurantoin have been addressed by various authors supporting our findings. [9, 10, 35, 49-50].

Thus, fosfomycin stands out as a drug of choice in the empirical treatment of UTI caused by both Gram negative as well as Gram positive bacteria in this area.

Table 1. Antibiotic resistance pattern among uropathogens (%) | E. coli | Klebsiella | Citrobacter | Proteus | Pseudomonas | Acinetobacter | Enterococcus | S. aureus | CONS
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>98.0</td>
<td>93.9</td>
<td>89.2</td>
<td>66.6</td>
<td>100</td>
<td>66.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxiclavine</td>
<td>97.21</td>
<td>93.9</td>
<td>85.7</td>
<td>83.3</td>
<td>85.7</td>
<td>58.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>7.9</td>
<td>23.1</td>
<td>35.7</td>
<td>50</td>
<td>71.4</td>
<td>41.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>51.7</td>
<td>46.3</td>
<td>50</td>
<td>66.6</td>
<td>85.7</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>62.5</td>
<td>50</td>
<td>57.1</td>
<td>83.3</td>
<td>71.4</td>
<td>41.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperacillin</td>
<td>30.2</td>
<td>25.6</td>
<td>25</td>
<td>50</td>
<td>71.4</td>
<td>16.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Results of ESBL screening and confirmation

<table>
<thead>
<tr>
<th>Organism</th>
<th>Total isolates</th>
<th>ESBL screening test positive (%)</th>
<th>ESBL confirmatory test positive (%)</th>
<th>ESBL confirmatory test negative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.coli</td>
<td>251</td>
<td>196 (78)</td>
<td>70</td>
<td>65 (33.1)</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>82</td>
<td>67 (81.7)</td>
<td>28</td>
<td>62 (62.6)</td>
</tr>
<tr>
<td>Citrobacter</td>
<td>28</td>
<td>21 (75)</td>
<td>6</td>
<td>21.4</td>
</tr>
<tr>
<td>Proteus</td>
<td>6</td>
<td>5 (83.4)</td>
<td>2</td>
<td>33.3</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>12</td>
<td>9 (75)</td>
<td>7</td>
<td>22.2</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>12</td>
<td>9 (75)</td>
<td>7</td>
<td>22.2</td>
</tr>
</tbody>
</table>

Discussion

Urinary tract infections are the most common and serious health problem worldwide. Due to growing antimicrobial resistance management of UTI is jeopardized. Antibiotic resistance pattern of uropathogenic bacteria and frequency of MDR strains vary from region to region and in the same region from time to time. This study was aimed to know the common bacteria responsible for UTIs, to assess the antimicrobial susceptibility pattern, production of ESBL by uropathogens and likelihood of use of fosfomycin as an empirical drug.

Of 1674 urine samples collected from suspected UTI patients 529 (31.6%) yielded significant pathogens. Our findings are in accordance with the studies by Dash et al. (34.5%) from Odisha, India and Oladeinde et al from Nigeria(39.7%). [26, 27] Indian studies from Aligarh and Jaipur have reported lower culture positivity rate of 10.86% and 17.19% respectively, whereas a Mexican study has shown high culture positivity rates of 97.3%. [28-30] This wide variation in culture positivity rate might be due to the varied geographical location.

In this study UTI was more common in females than males, which agrees with most of the studies worldwide. Irrespective of geographical area E. coli and Klebsiella species remain the commonest bacteria isolated in UTI patients, which has been noted in this study as well. Other causative agents isolated in this study were Enterococcus faecalis, S. aureus, Citrobacter species etc. Similar prevalence of microorganisms has been acknowledged by many studies. [8-11]

Ampicillin and amoxicillin are often used as oral therapy for gram-negative UTIs. High in-vitro resistance noted for these drugs in this study and studies by Dash et al. and Mishra et al. signifies that these cannot be used now. [26, 35]
References:


43. Abayneh M, Tesfaw G, Abdissa A. Isolation of Extended-Spectrum ß-lactamase-(ESBL-) Producing *Escherichia coli* and *Klebsiella pneumoniae* from Patients with Community-Onset Urinary Tract Infections in Jimma University Specialized Hospital, Southwest Ethiopia. *Canadian Journal of Infectious Diseases and Medical Microbiology*. 2018; 2018.


46. Rajan S, Prabavathy J. Antibiotic Sensitivity and Phenotypic Detection Of ESBL producing E.Coli Strains Causing Urinary Tract Infection In a Community Hospital, Chennai, Tamil Nadu, India.. *Webmed Central Pharmaceutical Sciences*. 2012;3(11):WMC003840