RESERACH ARTICLE

CHANGING TREND OF ANTIMICROBIAL RESISTANCE PATTERN IN ESCHERICHIA COLI CAUSING URINARY TRACT INFECTION AMONG HOSPITALIZED PATIENTS

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ABSTRACT

Urinary tract infections (UTI) are one of the commonly encountered diseases in developing countries. This study determines the antibiotic resistance patterns of E.coli from Hospitalized UTI patients. Study was carried out in one year period. Among the E.coli isolates the resistance pattern was studied using the antimicrobial susceptibility pattern and using advanced expert system of Vitek 2 compact system. The resistant profile was analysed for Beta-lactam phenotypes and Amino glycosides phenotypes. In the Beta lactam phenotypes 62% of the isolates revealed ESBL and 8% of the isolates as Carbapenamase producers. Whereas in Amino glycosides phenotypes 35% accounts for aac (3) resistance and 50% of the isolates are wild types. This study was determined to understand the epidemiological resistant patterns in the isolated strains in the hospitalized patients. Antibiotic stewardship is becoming the growing trend in the health care systems to restrict the spread of multidrug resistant strain and to avoid the empirical treatment. This specific categorised statistical analysis will enhance the adherence of antibiotic policy in adult in with typical presentation.

Key words: E.coli, UTI, resistant, Beta-lactam, Aminoglycoside.

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INTRODUCTION

Urinary tract infections (UTI) are one of the commonly encountered diseases in developing countries. UTI can be caused by Gram-Negative bacteria such as Escherichia coli, Klebsiella species, Enterobacter species, Proteus species and Gram positive bacteria like Enterococcus species and Staphylococcus saprophyticus. E.coli is the most common organism causing both community as well as hospital acquired UTI. The drug of choice for treating E.coli infections are becoming limited due to the rise in antibiotic resistance. Antibiotics are used to treat UTI. Over time, however, many bacteria have become resistant to antibiotics. Antibiotic resistance is a serious problem for individual patients and healthcare systems; in hospitals, infections caused by antibiotic-resistant bacteria are associated with higher rates of death. The main objective of the study is to provide convincing evidence and information to educate and support professionals to reduce unnecessary use and minimize the increased risk of infection with antibiotic-resistant bacteria. In this study, the objective was to analyse the antimicrobial resistance patterns of collected E.coli strains. The resistant pattern was analysed based on the phenotypic susceptibility by analysing the resistance extended by MIC values and by the automated interpretation of Advanced Expert System (AES) reported by Vitek 2 system10. AES is based upon an extensive knowledge base that comprises over 2000 phenotypes and 20,000 MIC distributions 7. A phenotype is defined as the expression of a specific mechanism of susceptibility or resistance to a given drug class within a particular species. There are number of possible phenotypes are considered under each group of antibiotics. In this study a detailed phenotype analysis was carried out for β-lactam drugs and Aminoglycoside drugs for the selected E.coli strains. This statistical data analysis was carried out to know the epidemiological resistant pattern for about a period of one year.

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MATERIALS AND METHODS

Specimen collection: A total of 7128 urine samples were received during the study period from March 2016 to February 2017. All the samples were collected in the sterile container with the instructions “Clean catch mid-stream urine”. Urine culture was done by standard loop method, a semi-quantitative method in Blood agar and Chrom UTI agar. Colonies grown 10² and above are considered as significant and taken for further follow-up. These samples were also compared with the microscopy of the specimen.

Strains: A total of 7128 urine samples were collected in a period of about one year from March 2016 to February 2017. Among that 397 isolated E.coli strains were taken for the analysis study. Their beta lactam phenotypes, aminoglycosides phenotypes were characterized by biochemical and molecular techniques.

Identification: The organism was identified preliminary by the colour morphology in HiChrom UTI agar (MP1353 from Biomerieux). The organisms isolated from urine were then identified by Vitek 2 system (GN-ID). The antibiotic susceptibility test was also carried out by Vitek 2 system (AST-N281).

Susceptibility tests: Antibiotic susceptibilities were determined according to the manufacturer’s recommendations by using the Vitek 2 instrument. The card used (AST-N281) for the test contained the following antibiotics and concentration ranges: Amikacin 2 to 64 µg/ml; Aztreonam 1 to 64 µg/ml; Cefepime 1 to 64 µg/ml; Cefoperazone/Sulbactam 8 to 64 µg/ml; Cefazidime 1 to 64 µg/ml; Ciprofloxacin 0.25 to 4 µg/ml; Colistin 0.5 to 16 µg/ml; Doripenem 0.12 to 8 µg/ml; Gentamicin 1 to 16 µg/ml; Imipenem 0.25 to 16 µg/ml; Levofloxacino 0.12 to 8 µg/ml; Meropenem 0.25 to 16 µg/ml; Minocycline 1 to 16 µg/ml; Piperacillin/Tazobactum 4/4 to 128/4 µg/ml; Ticarcillin/Clavulanic acid 8/2 to 128/2 µg/ml; Ticycycline 0.5 to 8 µg/ml; Trimethoprim/Sulfamethoxazole 20(1/19) to 320(16/304) µg/ml. Quality control was performed as per kit manufacturer’s instructions with E.coli ATCC 25922; P.aeruginosa ATCC 27853; E.coli ATCC 35218 monthly and whenever new lot received.

Data analysis: Both the identification and susceptibility was done using Vitek 2 system. The results were analysed and statistics made. The resistant phenotype identified by the AES was compared with the resistant profile of the antibiotics, and manual methods like Disc diffusion test for ESBL and Modified Hodge test for Carbapenamase producer strains.

RESULTS

Out of 7128 urine sample received, 1306 (18.32%) samples showed significant positive growth. It includes 1058 (81.01%) Gram negative bacilli, 138(10.56%) Gram positive cocci and 110 (8.42%) Yeast like cells. Among the 1058 Gram negative bacilli E.coli was identified in 674 patients with 397 IP and 277 OP isolates. The IP had 227 female and 170 male patients. The Age category include <20 = 3 patients; 20 to 40 = 41 patients; 41to60 = 105 patients and >60 = 248 patients. The resistant phenotypes was analysed for these 397 isolates.

Species: The preliminary identification of the organisms was done by the Hi Chrom/UTI agar. (Table. 1) The final identification and AST was confirmed by VITEK 2 system. The susceptibility pattern was confirmed with the MIC values of each antibiotic.

Phenotype Analysis

The performance of AES for the species is analysed to identify resistant phenotype. The AES was analysed for the Aminoglycoside phenotype and beta lactam phenotype.

Beta lactams: The beta lactams phenotypes was categorised into 12 types including wild type (Fig.1) The brief explanation and the statistical data are below (Table 2)

Aminoglycosides: According to Cathrine Barnhart et al. 2002, there are three mechanisms of amino glycoside resistance: reduced uptake or decreased cell permeability, alterations at the ribosomal binding sites, or production of amino glycoside modifying enzymes. The enzyme modification is the most common type of amino glycoside resistance which results in high level resistance. These genes are usually found on plasmids and transposes. Most enzyme-mediated resistance in gram negative bacilli is due to multiple genes. The three types of amino glycoside modifying enzymes are:

<table>
<thead>
<tr>
<th>Gram Negatives</th>
<th>Colour in HiChrom UTI Agar</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.coli</td>
<td>Pink centred cream bordered colonies flat irregular colonies</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>Green mucoid, raised, round colonies</td>
</tr>
<tr>
<td>Enterobacter/</td>
<td>Dark green flat irregular colonies</td>
</tr>
<tr>
<td>Citrobacter</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>Pale Brown dirty cream flat irregular colonies</td>
</tr>
<tr>
<td>NFGNB</td>
<td>Cream fine round colonies</td>
</tr>
<tr>
<td>Proteus</td>
<td>Cream flat flowery colonies</td>
</tr>
</tbody>
</table>

Fig. 1. Dendogram showing the beta lactam and aminoglycoside phenotypes
the wild type amino glycosides produces no enzymatic modification. Among the β-lactam phenotypes Type 6 (ESBL) was recorded as 61.46% which was much higher than any of the other phenotypes. These strains are resistant to any one of the third generation cephalosporins, Aztreonam. The beta lactam/beta lactam inhibitors are sensitive. At the same time our resistance is much lesser when compared with other Indian studies like Niranjan & Malini (2014) reported 70%; and Sharma et al. (2016) 73%. The multiple phenotypes of β-lactams were recorded in 3 different patterns.

**Penicillin’s and Cephalosporin's resistance:** The combined phenotypes are Type 1, 2, 4 and 5 which showed up to 27.70%. As described earlier and by various authors these strains extends the resistance to Penicillin, older and newer cephalosporins, aztreonams, plus inhibitor drug combinations, cephamycins, including Plasmid – mediated AmpC, hyperproducers of Chromosomal Amp C.

**High level Cephalosporins**

The combined phenotypes are Type 6 and 7 recorded in 33.75%. These strains showed high level resistance to 3rd
generation cephalosporins with increased MIC values and partially resistant to 4th generation also.

**Carbapenemase resistance**

Type 3 Carbapenamase (+ or – ESBL), Type 8 Impermeability carba (+ESBL or HL Amp C) and Type 11 n with 8.31%, 7.30% and 0.50% respectively. The high-level resistance to carbapenems by such carbapenamases is essential of three types – KPC, MBLs and Oxacillinases. Carbapenamases are beta lactamases and by tradition the nomenclature of the beta lactamases is based on their substrates, biochemical properties, location of their discovery, location of the gene on the chromosome, strains of bacteria, patients providing the sample or even after the investigator who describe them (Camillia, 2011). The multiple phenotypes of Amino glycosides were recorded in a pattern. Which include Type 1, 2, 3, 4 and 5 in 14.60% and Type 1, 2,3 and 4 in 22.92%. All these strains show acetylation with extension of resistance from single amino glycoside to multiple antibiotics. Many patients who get antibiotics for UTIs actually have asymptomatic bacteraemia and not infections. Interventions for UTIs focus on avoiding unnecessary urine cultures and treatment of patients who are asymptomatic and ensuring that patients receive appropriate therapy based on local susceptibilities and for the recommended duration. These recommendations are possible only if the supportive professionals are educated with the categorised resistant patterns. These should be updated periodically. Reporting the resistant pattern with AES will help the clinician to understand resistant pattern with probable mutation of the genes. But in the present study the phenotypes are not confirmed with the molecular analysis, it only shows the exact data analysis with the help of susceptibility pattern. The description of the phenotype was analysed with the previous research studies and articles. However the AES was very useful for the identification of the phenotypes of gram negative isolates. The multiple phenotype resistance in E.coli strains could be due to the high prevalence of resistant strains in the community. But the percentage of resistant is less due to the strict infection control practices and adherence to standard precautions.

**REFERENCES**


