

# Observation on Prevalence and Mechanism of Multi Drug Resistant Escherichia Coli Causing Uncomplicated Urinary Tract Infection in Female

Abha Kumari<sup>1</sup>, Santosh Kumar<sup>2</sup>, Sandeep Kumar<sup>3</sup>

## ABSTRACT

**Introduction:** In the last decade, the prevalence of drug resistance in *E. coli* has increased leading to difficulty in management. One of the most common prevalent extra-intestinal bacterial infections is the Urinary Tract Infection. The multiple drug resistant bacteria due to continued mismanaged selective pressure and been regarded as an inevitable genetic response to antimicrobial therapy. We evaluated and assessed the resistance pattern of *E. coli* causing UTI in female patients and review the literature regarding possible mechanism of MDR.

**Material and methods:** The present study included female patients between 20-50 years of age who came with suspected UTI from 2012 to 2014. The analysis was done on all *E. coli* isolates obtained from urine sample. The isolates were tested for ampicillin, cefuroxime, ceftriaxone, norfloxacin, nitrofurantoin, amoxicillin-clavulanic acid, co-trimoxazole, cefepime, ciprofloxacin, amikacin, piperacillin-tazobactam and imipenem. Streaking of the culture on the nutrient agar was done followed by assessment of the colony growth. The possible mechanism of MDR were reviewed.

**Results:** *E. coli* was the most commonly isolated micro-organism in our present study. It was isolated in 640 specimens which accounted for 55.56 percent of the total cases. *Klebsiella* species were the second most isolated species found in 162 specimens which accounted for a total of 14.05 percent of the total specimens. The next species to occur in the order of frequency of isolation was the *Pseudomonas* species which was observed in 84 of the urine specimens and accounted for 8.33 percent of the total isolates. The *Candida* species was observed in only 17 isolate specimens and accounted for 1.48 percent.

**Conclusion:** Increased occurrence of UTI due to MDR *E. coli* could either by gene transfer or by mutation or by modified Biochemical mechanism.

**Keywords:** *Escherichia coli*, Urinary tract Infection, MDR, R-plasmid.

## INTRODUCTION

One of the most common prevalent extra-intestinal bacterial infections is the Urinary Tract Infections (UTIs). It is one of the frequently met diseases affecting people from all the age groups starting from neonates and ending to geriatric age groups.<sup>1</sup> Despite of advancements and emergence of higher generations of antibiotics, these antibacterial agents have not been up to the mark in eradicating these worst diseases. One of the possible reasons responsible for this decline in therapeutic control of the disease is antibiotic resistance.<sup>2,3</sup> The multiple drug resistant bacteria due to continued mismanaged selective pressure and have credited for being responsible for genetic response to antibacterial therapy. A serious public health issue is presented by the emergence of antibiotic resistance in the management of

UTIs.<sup>4</sup> Hence; we evaluated and assessed the resistance pattern of *E. coli* causing UTI.

## MATERIAL AND METHODS

The present study was carried from 2012 to 2014. All those patients that were suffering from UTI were included for the study. Female between 20-50 years of age who came with a suspected UTI were included in the study. Urinary tract infection was clinically defined as two or more symptoms suggestive of this infection and included dysuria, frequency, urgency, pyuria and/or haematuria. Ethical committee of the institute granted the ethical permission for carrying out the present study. Also the written consent was obtained from all the patients after explaining them the research steps and procedures involved. A semi-quantitative method, mainly loop's standard method, was employed for obtaining samples from urine culture. Standard group of methods were used for the isolation and identification of micro-organisms from the urine culture.<sup>1</sup> Mueller-Hinton agar was used for doing the antibiotic sensitivity testing. Rules and guidelines of clinical and standard laboratory were used for obtaining the micro-organisms from the culture. The isolates were tested for ampicillin, cefuroxime, ceftriaxone, norfloxacin, nitrofurantoin, amoxicillin-clavulanic acid, co-trimoxazole, cefepime, ciprofloxacin, amikacin, piperacillin-tazobactam and imipenem. When antimicrobial resistance was observed against three or more antimicrobial agents, only them the isolate was categorized as MDR. Overnight incubation of the culture was done at thirty seven degree centigrade followed by streaking of the agar culture plates at oblique angles. Algorithm was used for assessment of the colonies of the micro-organisms.

## STATISTICAL ANALYSIS

SPSS software was used for the assessment of the results. Chi-square test and student t test were used for the assessment of level of significance.

## RESULTS

Figure 1 highlights the proportion of uro-pathogens among

<sup>1</sup>Assistant Professor, Department of Pharmacology, <sup>2</sup>Associate Professor, Department of Biochemistry, <sup>3</sup>Assistant Professor, Department of ENT, Rajendra Institute Of Medical Sciences, Ranchi-834009, India

**Corresponding author:** Dr. Sandeep Kumar, Assistant Professor, Department of ENT, Rajendra Institute Of Medical Sciences, Ranchi-834009, India.

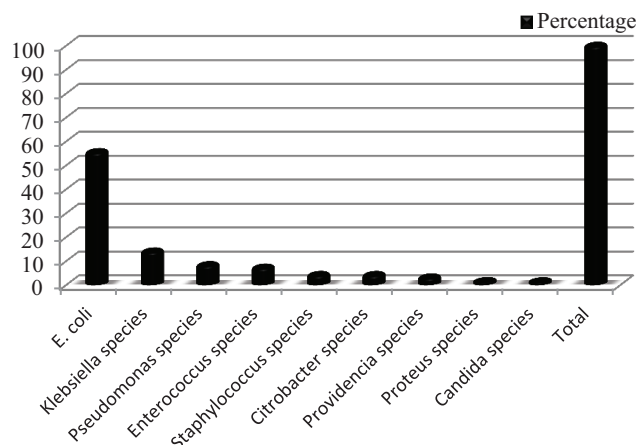
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isolates of UTI. E.Coli was the most commonly isolated micro-organism in our present study. It was isolated in 640 specimens which accounted for 55.56 percent of the total cases. Klebsiella species were the second most isolated species found in 162 specimens which accounted for a total of 14.05 percent of the total specimens. The next species to occur in the order of frequency of isolation was the Pseudomonas species which was observed in 84 of the urine specimens and accounted for 8.33 percent of the total isolates. The Candida species was observed in only 17 isolate specimens and accounted for 1.48 percent. Possible mechanism of resistance were reviewed.

**DISCUSSION**

Various gram positive species such as E.coli, Klebsiella are responsible for causing various varieties of UTIs. The commonest micro-organisms responsible for causing both communities acquired and hospital acquired UTI is E.coli.<sup>6-8</sup> Studies from various parts of India have shown occurrence of high rates of antimicrobial resistance among E coli. The cost of therapeutic approach for treating cases of UTI and difficulties encountered while making treatment planning for the cases of UTIs is increasing with time due to emergence of multi drug resistance (MDR) E.coli.<sup>9-11</sup> Hence; we evaluated the pattern of of E. coli causing UTI.

In the present study, a total of 4000 urine samples were received for culture and sensitivity during the study period. Among these, 1152 samples yielded significant bacteriuria; most of the samples showed no growth and less than 3 percent of the samples showed mixed growth. The various organisms isolated from urine culture are shown in Table 1. E. coli was the commonest accounting for more than 55 per cent of the uropathogens. The isolates were sensitive to amikacin, piperacillin-tazobactam, nitrofurantoin and imipenem; most of the E. coli isolates were multi drug resistant. Yüksel et al assessed the pattern of resistance of various urinary pathogens against the routinely used antimicrobial agents for the treatment of UTIs. They observed that the most common causative agent was Escherichia coli followed by Klebsiella pneumoniae. From the results, they concluded that nitrofurantoin could be equally useful in the treatment protocol of UTI in young adults.<sup>12</sup> Yilmaz et al evaluated and determined the pattern of antibiotic susceptibility patterns of E. coli strains isolated from adult outpatients with UTI, in Turkey. They collected data of the isolated which were collected from the patients with UTI and analyzed and assessed these isolated for the presence and frequency of occurrence of various micro-organisms. They observed that out of total 4,534 E. coli strains, antibiotic resistance rates of the isolates for female and male, respectively: Ampicillin, amoxicillin-clavulanic acid, cefuroxime, cefotaxime, piperacillin-tazobactam, amikacin, gentamicin, trimethoprim-sulfamethoxazole, and ciprofloxacin/norfloxacin. From the results, they concluded that a considerable proportion of the studied E. coli isolates were resistant to most antibiotics except amikacin.<sup>13</sup> Cullen et al analyzed the frequency, incidence and way of appearance of antimicrobial resistance occurring E.coli induced UTI and observed these findings over a period of eleven years. They observed that urinary tract infections in the urology patient population demonstrate higher antibiotic resistance rates than nosocomial or community UTIs. From the results, they concluded that



**Figure-1:** Proportion of uro-pathogens among isolates of UTI

Micro-organism	Number	Percentage
E. coli	640	55.56
Klebsiella species	162	14.05
Pseudomonas species	96	8.33
Enterococcus species	84	7.29
Staphylococcus species	49	4.25
Citrobacter species	49	4.25
Providencia species	37	3.21
Proteus species	18	1.56
Candida species	17	1.48
Total	1152	100

**Table-1:** Proportion and number of uro-pathogens among isolates of UTI

in the health care community and medical health care bases settings, the most frequent pathogen involved in affecting and causing UTI is E.coli. Over 10 years long observation period, the frequency of its incidence ranges to over than fifty percent.<sup>14</sup> Catal et al evaluated the antibiotic and antimicrobial sensitivity of the commonly affecting uropathogens. They retrospectively analyzed data from all paediatric urine samples processed at microbiology laboratory and concluded that knowledge and attitude about the local prevalence of micro-organisms might be responsible for the selection of the suitable antibiotics.<sup>15</sup> Drug resistance refers to unresponsiveness of microorganisms to an antimicrobial agent after its repeated use. Antibiotic resistance could be intrinsic or acquired. The acquired resistance develops due to widespread and irrational use of antibiotics. This type of resistance develops either by gene transfer or mutation or by modified biochemical mechanism. Much of the drug resistance encountered in clinical practice is plasmid mediated. The plasmid which carry genes resistant to antibiotics ( r-genes) are called R- plasmids. The transfer of resistant genes can occur by conjugation, Transduction, Transformation, Transposones or by Integrons. Biochemical mechanism of resistance to antibiotics are by producing an enzyme that inactivates the antibiotics, prevention of drug accumulation in the bacterium, Quorum sensing, modification/ protection of the target site and alternative pathway for metabolic requirements.<sup>16</sup>

**CONCLUSION**

The increased prevalence and frequency of occurrence of MDR strain of E. coli. This might be due to gene transfer, mutation

or by Quorum sensing. Regularly updated surveillance of local microbial prevalence and resistance pattern are needed to guide the empiric therapy of UTIs.

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