# Antimicrobial resistance in uropathogenic *Escherichia coli* strains isolated from Beasat hospital in sanandaj, Iran


## ABSTRACT

**Background and Objectives**: Urinary tract infection (UTI) is one of the most frequent infectious diseases which is caused by Gram-negative bacteria especially *Escherichia coli*. Multiple resistances to antimicrobial agents are increasing quickly in *E. coli* isolates and may complicate therapeutic strategies for UTI. The aim of this study was to determine the antibiotic resistance patterns and the multidrug-resistance (MDR) phenotypes in uropathogenic *E. coli* (UPEC).

**Materials and Methods**: A total of 153 UPEC isolates were collected from both hospitalized patients (95isolates) and outpatients (58 isolates) between March and October 2018. In order to determine the MDR among UPEC isolates, we have tested 15 antimicrobial agents on Muller Hinton agar by the disk diffusion method.

**Results**: The percentage of MDR isolates (resistant to at least three drug classes such as fluoroquinolones, penicillins, and cephalosporins) was 55.5% in the hospitalized patients and the outpatients. Antibiotic resistance to ampicillin, ceftazidime, nalidixic acid, and trimethoprim/sulfamethoxazole was higher than 60%. Meropenem, Imipenem, and norfloxacin, indicated markedly greater activity (93.3%, 80 % and 85.6%, respectively) than other antimicrobial agents.

**Conclusions**: Urinary tract infection due to MDR *E. coli* may be difficult to treat empirically due to high resistance to commonly used antibiotics, so, empirical antibiotic treatment should be reviewed periodically at local studies.



*Keywords: Antimicrobial resistance, Escherichia coli, multidrug resistance, urinary tract infections*


## 1. INTRODUCTION

Urinary tract infections (UTIs), are the most common infections and are mainly caused by Gram-negative bacteria especially uropathogenic *Escherichia coli*.

*E. coli* are a variety of bacteria with diverse species that naturally found in the intestinal tract of all humans and many other animal species. A number of *E. coli* are a cause of enteric/diarrheal disease, and another subset causes extra-intestinal disease, including urinary tract infection (UTI) [1]. *E. coli* accounts for as many as 90% of all UTIs seen among ambulatory populations [2].

A UTI is defined as a significant number of pathogenic microorganisms in the urinary system. If there are symptoms such as frequent urination, painful or blood in the urine, only 100 uropathogenic bacteria per ml of urine may be significant [3]. According to studies, urinary tract infections (UTIs), including cystitis (when infection is limited to the bladder) and pyelonephritis (when the kidney is infected), are one of the most common infections in

humans. Urinary tract infections often occur in patients with normal and functional urinary tracts [4]. The severity of the infection varies depending on the virulence of infecting bacteria and host susceptibility [5].UPEC isolates which have virulence factors such as Fimbria or Pilli adhesions stimulate colonization of the bacteria and urinary tract infection; that mediate attachment to uroepithelial cells and initiate infections [6].Clinical experiences have shown high levels of antibiotic resistance among the uropathogens. Overuse of antibiotics is the most important factor in increasing multidrug resistance (MDR) in UPEC isolates [7]. Antibiotic resistance is a serious problem in public health caused by UPEC and leading to increased mortality and morbidity. Due to the risk of kidney damage and complications, early diagnosis and treatment of the disease are important [8].UTI cause several complex symptoms, physicians begin empirical antibiotic treatment before getting the culture results because urine culture and susceptibility agent results take about 4 days to be prepared [9]. According to reports, the prevalence of MDR *E. coli* causing UTIs in the USA, Japan, China, India, Brazil, Saudi Arabia, and Nepal, is increasing [ 10,11]. Therefore the current study was proposed to determine the frequency of MDR *E. coli* among UTI isolates from a university medical center Besat Hospital, Sanandaj, Iran.

## 2. MATERIAL AND METHODS

### 2.1 Bacterial Isolates

In this study, a total 153 strains of bacteria causing UTIs collected from urine specimens in hospitalized patients or referred (outpatients) to University of Beast hospital during March to October 2018, in Sanandaj, Iran. Urine was collected by clean-catch midstream method and samples transported to the laboratory within one hour of collection. Diagnosis of *E. coli* isolates has been done according to standard microbiological methods [12]. The samples were cultured on MacConkey agar, Eosin-methylene blue agar and blood agar (Himedia Company). The plates were incubated at 35°C for 24 h. Bacteriological and biochemical tests were performed for confirmation of *E. coli* strains which included Gram-stain, oxidase, catalase, indole production, citrate utilization, methyl red-Voges Proskauer, lysine iron agar, triple sugar iron agar utilization, and urea test[10]. The positive control was tested by *E. coli* ATCC25922.

### 2.2 Antibiotic Susceptibility Test

Antibacterial susceptibility testing was performed using the Kirby–Bauer disk diffusion method on Muller Hinton agar medium. Isolates were declared as sensitive or resistant on the basis of the zone of inhibition according to the Clinical and Laboratory Standards Institute guidelines (CLSI) [13]. The antibiotic disks used in this study were ciprofloxacin (CIP) (5 µg), cefixime (CFM) (30 µg), norfloxacin (NOR)(10 µg),), nalidixic acid (NAL) (30 µg), gentamicin (GEN) (10 µg), amikacin(AMK) (30 µg), ampicillin (AMP) (10 µg), (30 µg), nitrofurantoin (NIT) (300 µg), trimethoprim/sulfamethoxazole (SXT) (1.75/23.75 µg), meropenem (10 µg), Imipenem (IPM)(10 µg), cefepime (CPM) (30 µg), ceftazidime (CAZ) (30 µg),cefotaxime (CTX) (30 µg) and Cefuroxime (CFX) (30 µg). *E. coli* ATCC25922 was used as a positive control strain. Then the data analyzed by Whonet 5.6 (WHO, Geneva, Switzerland) Software. According to the results if on isolate was resistant to at least three of the antimicrobial classes, such as fluoroquinolones, aminoglycosides, cephalosporins, or carbapenems is considered as MDR isolate.

## 3. RESULTS

A total of 153 *E. coli* strains isolated from urine specimens with a count of more than $10^5$ CFU/mL. The frequency of *E. coli* isolation was higher in females (79%) than males (21%). The age of patients ranged between 1 and 80 years. The number of *E. coli* strains were recovered from hospitalized patients and outpatients was 95(62%) and 58 (38%), respectively. Antibiotic resistance to AMP, NAL, CAZ, and SXT was higher than 60%. The rates of resistance to AMP, SXT, CAZ, NAL, and CTX in hospitalized patients were higher than outpatients. The highest antibacterial agent's susceptibility has shown in meropenem, imipenem, and norfloxacin. (Figure1). Of the 153 isolates, 85 (55.5%) isolates were multidrug-resistant.

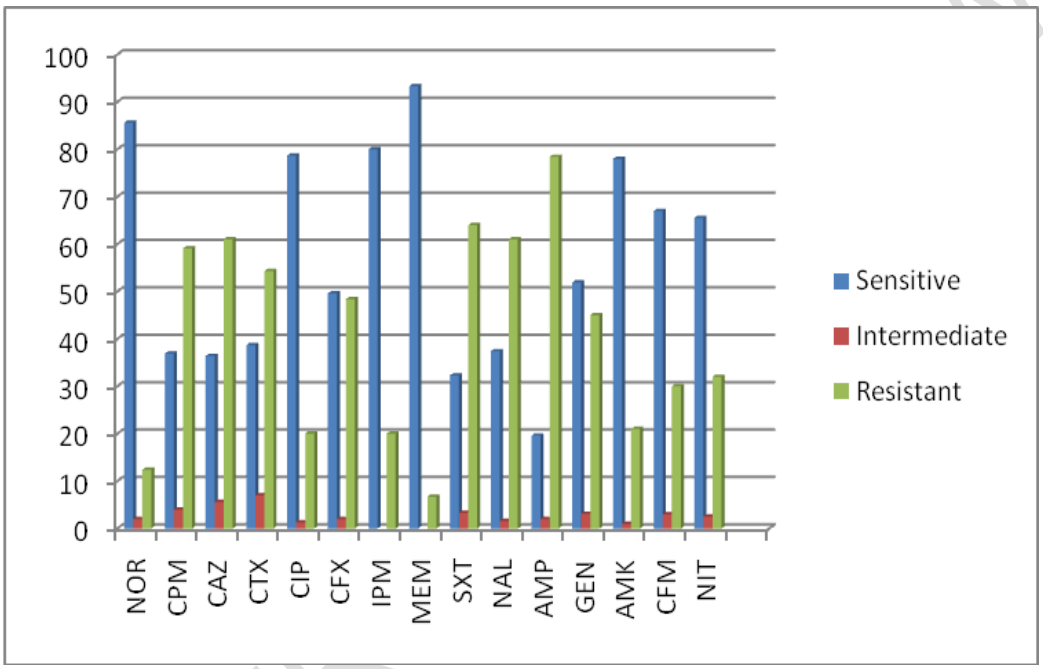


**Fig. 1. Percentages of antibiotic resistance in Escherichia coli isolated from urine samples**

## 4. DISCUSSION

UTIs are serious health affecting problems worldwide. The bacteria associated with UTI were predominantly *E. coli*. UTIs caused by uropathogenic *E.coli* are

among the most important infectious diseases leading to renal failure [14].

The results our study showed UTI in female (79%) was higher than male (21%) which is similar to the finding of Shah et al [15]. Antibacterial agents are the most important products in twentieth-century used to inhibit or kill the growth of microorganisms. Antibiotic resistance in *E. coli* isolated from UTIs is increasing and it is a major public health problem. So it is very important to determine the antibiotic resistance patterns in *E. coli* isolates for accurate and proper prescriptions.

In the current study most of *E.coli* isolates were resistant to ampicillin which indicating a cautious use of this antibiotic for the treatment of UTI, The resistance of *E. coli* to penicillins group of antibiotics have been increased in different parts of the world, but there are only a few reports which indicate 100% resistance to penicillins [16]. Resistance to other antibacterial agents such as ceftazidime (61%), cefepime (59.1%), cefotaxime (54.3%), and cefuroxime (48.4%), was also very high which according to previous studies (17]. In the present study, the resistance of *E. coli* against meropenem (6.7%) and imipenem (20%) was lower than previous studies [18, 19]. Our results have shown that the meropenem and imipenem remain as effective antibacterial agents against *E.coli*.

The significant high resistance to SXT (64%) was found in the present study while many guidelines recommend this drug for UTIs [20]. In the present study, variable resistance patterns were found for the aminoglycosides antibiotic. *E.coli* was highly resistant to gentamicin (45%) while a low level of resistance was for amikacin (21%). Quinolones, especially ciprofloxacin have been used for *E. coli* infections in recent past years. In the present study however *E. coli* was resistant to ciprofloxacin (20%), which is not similar to the previous reports [21]. Other fluoroquinolones such as norfloxacin (12.4% resistance) were found efficient for the *E. coli*. Studies from other parts of the world also show that quinolones are still active against UTI infections [21].

Multiple drug resistance (MDR) in UPEC was also determined in this study. MDR is described as resistant to at least one member from three different antibiotic classes being used for the treatment of *E. coli*. Based on the results of the current study, there is a high resistance rate to the commonly used antibiotics in the *E. coli* isolates. We found of the 153 isolates, 85 (55.5%) isolates to be resistant to three or more antibiotics. The rates of antibiotic resistance in our study were different from some studies. In a study by Tabasi et al. from Iran [22] found 79% of all *E.coli* isolates were multidrug resistant. In another study in Mexico by Ramírez Castillo etal, multidrug-resistant strain prevalence of *E.Coli* was 63.3 %[ 23].

Some behavioral factors and socioeconomic, such as misuse and use of irregular antimicrobial agents and easy access to antibiotics without a prescription can help to antibiotic resistance by hospital physicians or unskilled practitioners.

In this study, a high percentage of isolates showed an MDR phenotype. These warning resistances to the commonly used antibiotics can affect the therapeutic strategies. The successful empirical initial treatment is based on susceptibility and resistance patterns obtaining from local data. Since these susceptibility patterns are constantly changing and may vary in different geographical regions and institutions, regular monitoring of antimicrobial agents resistance seems necessary to formulate standard treatment guidelines for empirical therapy.

## 5. CONCLUSION

In our study, there is a significant antimicrobial resistance to *E.coli* isolates in UTI from community and hospital in Sanandaj, Iran. Thus, Continuous monitoring for antimicrobial resistance of UPEC in order to prevent treatment failure and to improve strategies for reducing antibiotic-resistant microorganisms and to ensure the best treatment to UTI patients is necessary.

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