

1 **Antimicrobial resistance in uropathogenic *Escherichia coli* strains isolated from Beasat**
2 **hospital in sanandaj, west of Iran**
3

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

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

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

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

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

25 **1. INTRODUCTION**

26 Urinary tract infections (UTIs), are the most common infections and are mainly caused by Gram-
27 negative bacteria especially uropathogenic *Escherichia coli* [25].

28 *E. coli* is a kind of bacteria with diverse species that naturally found in the intestinal tract of all
29 humans and many other animal species. A number of *E. coli* are a cause of enteric/diarrheal
30 disease, and another subset causes extra-intestinal disease, including urinary tract infection (UTI)
31 [1]. *E. coli* accounts for as many as 90% of all UTIs seen among ambulatory populations [2].

32 A UTI is defined as a significant number of pathogenic microorganisms in the urinary system. If
33 there are symptoms such as frequent urination, painful or blood in the urine, only 100

34 uropathogenic bacteria per ml of urine may be significant [3]. According to studies, urinary tract
35 infections (UTIs), including cystitis (when infection is limited to the bladder) and pyelonephritis
36 (when the kidney is infected), are one of the most common infections in humans. Urinary tract
37 infections often occur in patients with normal and functional urinary tracts [4]. The severity of
38 the infection varies depending on the virulence of infecting bacteria and host susceptibility
39 [5].UPEC isolates which have virulence factors such as Fimbria or Pili adhesions stimulate
40 colonization of the bacteria and urinary tract infection; that mediate attachment to uroepithelial
41 cells and initiate infections [6]. Clinical experiences have shown high levels of antibiotic
42 resistance among the uropathogens. Overuse of antibiotics is the most important factor in
43 increasing multidrug resistance (MDR) in UPEC isolates [7]. Antibiotic resistance is a serious
44 problem in public health caused by UPEC and leading to increased morbidity and mortality. Due
45 to the risk of kidney damage and complications, early diagnosis and treatment of the disease are
46 important [8].UTI cause several complex symptoms, physicians begin empirical antibiotic
47 treatment before getting the culture results because urine culture and susceptibility agent results
48 take about 4 days to be prepared [9]. According to reports, the prevalence of MDR *E. coli*
49 causing UTIs in the USA, Japan, China, India, Brazil, Saudi Arabia, and Nepal, is increasing [
50 10,11]. Therefore the current study was proposed to determine the frequency of MDR *E. coli*
51 among UTI isolates from a university medical center Besat Hospital, in Sanandaj west of Iran.

52 2. MATERIAL AND METHODS

53 2.1. Bacterial Isolates

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

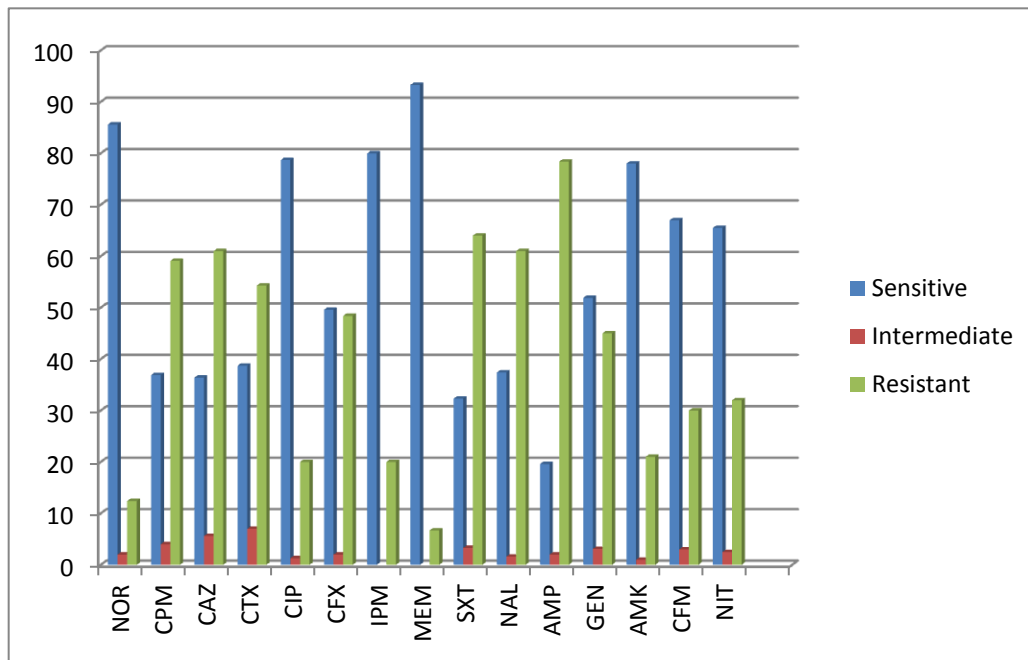
64 2.2. Antibiotic Susceptibility Test

65 Antibacterial susceptibility testing was performed using the Kirby–Bauer disk diffusion method
66 on Muller Hinton agar medium. Isolates were declared as sensitive or resistant on the basis of the
67 zone of inhibition according to the Clinical and Laboratory Standards Institute guidelines (CLSI)
68 [13]. The antibiotic disks used in this study were ciprofloxacin (CIP) (5 µg), cefixime (CFM) (30
69 µg), norfloxacin (NOR)(10 µg), nalidixic acid (NAL) (30 µg), gentamicin (GEN) (10 µg),
70 amikacin(AMK) (30 µg), ampicillin (AMP) (10 µg), nitrofurantoin (NIT) (300 µg),
71 trimethoprim/sulfamethoxazole (SXT) (1.75/23.75 µg), meropenem (MEM)(10 µg), Imipenem
72 (IPM)(10 µg), cefepime (CPM) (30 µg), ceftazidime (CAZ) (30 µg), cefotaxime (CTX) (30 µg)
73 and Cefuroxime (CFX) (30 µg). *E. coli* ATCC25922 was used as a positive control strain. Then
74 the data analyzed by Whonet 5.6 (WHO, Geneva, Switzerland) Software. According to the
75 results if on isolate was resistant to at least three of the antimicrobial classes, such as
76 fluoroquinolones, aminoglycosides, cephalosporins, or carbapenems is considered as MDR
77 isolate.

78 3. RESULTS

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

87



88

89 **Fig1.** Percentages of antibiotic resistance in *Escherichia coli* isolated from urine samples

90 **DISCUSSION**

91 UTIs are serious health affecting problems worldwide. **Urinary tract infections caused by**
 92 **uropathogenic *E. coli* are one of the most common infectious diseases that lead to renal failure**
 93 [14]. **The results of our study showed that UTI in females (79%) was higher than males (21%)**
 94 which were similar to the findings of Shah *et al* [15]. Antibacterial agents are the most important
 95 products in twentieth-century used **to kill or inhibit** the growth of microorganisms. Antibiotic
 96 resistance in *E. coli* isolated from UTIs is increasing and it is a major public health problem.
 97 Therefore, it is very important to determine the antibiotic resistance patterns in *E. coli* isolates
 98 for accurate and proper prescriptions.

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

106 19]. **The results of our study** showed that the meropenem and imipenem remain as effective
107 antibacterial agents against *E.coli*.

108 The significant high resistance to SXT (64%) was found in the present study while many
109 guidelines recommend this drug for UTIs [20]. In addition, variable resistance patterns were
110 found for the aminoglycoside antibiotics. In our study, *E.coli* was highly resistant to gentamicin
111 (45%), while a low level of resistance was observed for amikacin (21%).**In a study by Ghazvini**
112 **and *et al* (21) *E.coli* resistance to gentamicin was 36.6%, which was lower compared to our**
113 **study.**

114 Antibacterial agents including quinolones, especially ciprofloxacin have been used for *E. coli*
115 infections in recent past years. In the present study, however, *E. coli* was resistant to
116 ciprofloxacin (20%), which is not similar to the previous reports. Other fluoroquinolones such as
117 norfloxacin (12.4% resistance) were found efficient for the *E. coli*. The studies from other parts
118 of the world show that quinolones are still active against UTI infections [22].

119 Multiple drug resistance (MDR) in UPEC was also determined in this study. MDR is described
120 as resistant to at least one member from three different antibiotic classes being used for the
121 treatment of *E. coli*. Based on the results of the current study, there is a high resistance rate to the
122 commonly used antibiotics in the *E. coli* isolates. From 153 *E.coli* isolates, 85 (55.5%) isolates
123 were resistant to three or more antibiotics. The rates of antibiotic resistance in our study were
124 different from some studies.

125 **The high percentage multidrug- resistant of all *E.coli* isolates reported by Tabasi *et al* in 2015**
126 **(79%) [23] and in another study by Castillo *et al* in 2018, multidrug-resistant strains prevalence**
127 **of *E.coli* was 63.3 % [24].**

128 Some behavioral factors and socioeconomic, such as misuse and use of irregular antimicrobial
129 agents and easy access to antibiotics without a prescription can help to antibiotic resistance by
130 hospital physicians or unskilled practitioners. In this study, a high percentage of isolates showed
131 an MDR phenotype. These **alert** resistances to commonly used antibiotics can affect the
132 therapeutic strategies.

133 The **successful empirical initial treatment is based on the susceptibility and resistance patterns**
134 **acquiring from local data. Since these susceptibility patterns are constantly variable and may**

135 change in different geographical regions and institutions, regular monitoring of antimicrobial
136 agents resistance may be necessary to formulate standard treatment guidelines for empirical
137 therapy.

138 5. Conclusion

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

144 **There are no conflicts of interest**

145 This study was approved by the ethical committee of the Kurdistan University of Medical
146 Science, Kurdistan, Iran (IR.MUK.REC.1397/5033)

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