Brief report

Prevalence and antibiotic susceptibility pattern of quinolones and cephalosporins resistant uropathogenic *Escherichia coli* in the north Iran

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Abstract

Escherichia coli is a Gram-negative bacillus of the *Enterobacterales* order that is considered an opportunistic pathogen. One of the places they can enter is the urinary tract, which is called the Uropathogenic *E. coli* (UPEC) strains and the infections that result from it are called urinary tract infection (UTI). The aims of this study was to obtain new information about the antibiotic susceptibility pattern of quinolones and cephalosporins resistant *E. coli*. In this retrospective cross-sectional study, all cases of urinary tract infections caused by *E. coli* isolates referred to Razi Hospital in Rasht, the North of Iran over a period of three years were evaluated. Antimicrobial susceptibility patterns were evaluated using disk diffusion method. The total number of E. coli bacteria isolated from urine samples of patients with UTIs from 2016 to 2018 was 1224 cases. Totally, 382 out of 612 tested *E. coli* isolates were ciprofloxacin resistant (62.4%). While, 251 out of 446 tested *E. coli* isolates were cephalosporins (56.3%). Among the tested isolated, 206 cases were resistant to both antibiotics (cephalosporin and ciprofloxacin), of which 71 (34.5%) were recovered from male and 135 (65.5%) from female samples. The highest antibiotic susceptibility to *E. coli* was related to amikacin (74.8%) and followed by nitrofurantoin (67.5%). The results showed an alarming rate of cephalosporin and ciprofloxacin resistance among *E. coli* causing UTI in our region. These findings suggest optimizing local stewardship programs and infection control policy.

Keywords: *Escherichia coli*, Urinary tract infection, Quinolone, Cephalosporin, Antibiotic resistance

1. Introduction

Currently, one of the most important problems of public health in the world are nosocomial infections. Nosocomial infections are caused by organisms that are resistant to or eventually become resistant to antibiotics [1, 2]. Nosocomial infections generally refer to infections that occur 48 to 72 hours after admission, or three days after discharge, or 30 days after surgery

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[3]. The World Health Organization (WHO) has conducted an epidemiological study of nosocomial infections in 14 countries and reported an overall prevalence of 8.7%. According to this report, the prevalence of nosocomial infections in Iran is 4.5%, and the most common infections are related to urinary tract, and respiratory tract infections [4].

Nosocomial infections increase the use of antibiotics and thus increase the resistance of bacteria to several drugs [5]. *Escherichia coli* is the most common of the nosocomial infections. Urinary tract infections (UTIs) is one of the most common bacterial infections in humans. Although several different microorganisms, such as fungi, viruses, and bacteria, cause UTIs, but the uropathogenic *E. coli* (UPEC) strains are responsible for 80% of these infections. They may be symptomatic or asymptomatic and in most cases will not cause death [6-8].

Antibiotic treatment is the most common way to treat infectious diseases, but overuse over the years can cause organisms to become resistant to any known antibiotic. Antibiotic resistance is one of the health problems and its increase in developing countries such as Iran is worrying [9, 10]. Beta-lactams are the most widely used antibiotics in the treatment of bacterial infections. The widespread use of these antibiotics in pathogenic bacteria leads to the production and dynamic and continuous mutation of beta-lactamases in these bacteria, which increases their range of activity against antibiotics [11]. Due to the effect of UPEC strain on a wide range of populations, it can be considered as a major target for antimicrobial therapy. Quinolones and fluoroquinolones are first-line antibiotics in the treatment of UTIs, however, treatment of infections became more complicated with the advent of quinolones resistant strains [12, 13]. Due to the importance of evidence based therapy, the present study aimed to evaluate prevalence and antibiotic susceptibility pattern of quinolones and cephalosporins resistant *E. coli* in the North of Iran.

2. Materials and Methods
2.1 Study area and subjects
This is a retrospective cross-sectional study of all cases of UTIs caused by *E. coli* isolates that were admitted to Razi Hospital in Rasht between 2016 and 2018. Razi hospital is one of the largest hospital in Guilan province, the North of Iran consists of 281 approved hospital beds and 240 active beds. In this study, the sampling method was census and from the results of the hospital archives, information about age and sex was extracted from the patients' admissions in the hospital. The results of inpatients who had a positive culture of *E. coli* isolated from urine samples were studied. Patients with incomplete file information (information about the main variables) and samples with patients with mixed culture report (simultaneous growth of two or more bacteria) and culture results of urine samples containing Gram-positive bacteria were excluded from the study.

2.2 Antibiotic susceptibility testing
Antimicrobial susceptibility patterns were evaluated using disk diffusion method based on CLSI guidelines [14]. The results of antibiogram tests, which include antibiotics of the quinolones (nalidixic acid and ciprofloxacin) and cephalosporins of the 1st to 4th generation, were extracted and the frequency of *E. coli* isolates resistant to this family was determined. The results of antibiotic susceptibility pattern of isolates causing UTIs to routine antibiotics used in the region were extracted from laboratory results and reported.

2.3 Statistical analysis
The collected and recorded results were analyzed by SPSS software version 22 (IBM Corp., USA). The results are presented as descriptive statistics in terms of relative frequency. Values were expressed as the mean ± standard deviation (continuous variables) or percentages of the group (categorical variables).

3. Results
The total number of *E. coli* isolated from urine samples of patients with UTIs from 2016 to 2018 were 1224 cases. The mean age of patients was 46 years and the age range of patients ranged from 16 to 97 years. Totally, 382 out of 612 tested *E. coli* isolates were ciprofloxacin resistant (62.4%). While, 251 out of 446 tested *E. coli* isolates were cephalosporins (56.3%). Among the tested isolated, 206 cases were resistant to both antibiotics (cephalosporin and ciprofloxacin), of which 71 (34.5%) were recovered from male and 135 (65.5%) from female samples.

The antibiotic susceptibility pattern of *E. coli* isolates resistant to cephalosporin and ciprofloxacin were listed in Table 1.

Table 1. Antibiotic resistance pattern

Type of antibiotic	Resistance	Susceptibility
Amikacin	25.2 %	74.8 %
Gentamicin	83 %	17 %
Imipenem	85.9 %	14.1 %
Nitrofurantoin	32.5 %	67.5 %

The highest antibiotic susceptibility to *E. coli* was related to the antibiotic amikacin (74.8%). The highest antibiotic susceptibility to *E. coli* was related to amikacin (74.8%) and followed by nitrofurantoin (67.5%).

4. Discussion

The wide spread of antibiotic-resistant bacterial species is one of the most serious challenges for physicians and health centers, which will lead to high costs in this regard. Research shows that the prevalence of antibiotic resistant *E. coli* is increasing in Iran; however, the patterns are varied geographically [15].

In the present study, the rate of cephalosporin resistance in UTIs caused by *E. coli* was 56.3%. Similar resistance rates are reported in some Iranian studies which does not recommend the use of cephalosporins and penicillins in the treatment of UTIs caused by *E. coli* without the laboratory report [16, 17]. In accordance to our findings, there are several reports that indicate to a high prevalence of fluoroquinolones resistant *E. coli* in Iran. Studies in the United States show that *E. coli* antibiotic resistance increased from 3 percent to 17.1 percent between 2002 and 2010 [18]. But the global data suggest that the rate of fluoroquinolones resistance is on the rise, due to multifactorial causes including the antibiotic over abuse, and emergence of multidrug-resistant clone [19-21].

Due to the retrospective nature of this study, the main limitations of the present study are the existence of a defect in the records and the lack of some clinical. Also, due to the limited study area, the results can not be generalized to the whole region and thus require more extensive studies to determine the overall status of medical and educational centers in the future.

The results of recent study determined a regional pattern of *E. coli* antibiotic resistance that causes UTIs. The results showed an alarming rate of cephalosporin and ciprofloxacin resistance among *E. coli* causing UTI in our region. These studies could lead to improved infection control programs in regional health centers as well as optimization of laboratory reports to help treat patients. Prevention of resistant isolates requires targeted optimization of treatment protocols based on laboratory results or the pattern of antibiotic resistance in the area. Due to changes in the susceptibility pattern of *E. coli*, as well as the time and place of increasing the rate of antibiotic resistance of this bacterium, continuous antibiogram tests are recommended. Also, designing prospective studies to investigate the effect of targeted use of antibiotics based on laboratory results in the process of reporting multidrug-resistant isolates can be helpful.

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