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The pattern of antibiotic resistance of pathogens isolated from urine cultures of patients referred to Yazd Central Laboratory in 2012-2013

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Abstract

Introduction: Urinary tract infections (UTIs) are the second leading cause of infection in communities. Determination of antibiotic resistance in common pathogenic bacteria is important to choose an effective treatment against a particular microbe. The aim of this study was to evaluate antibiotic resistance of pathogens isolated from urine cultures of patients referred to Yazd Central Laboratory (located in Yazd, Iran). **Methods**: This was a cross-sectional study conducted on subjects who were referred to the Central Laboratory in Yazd for urine culture testing. The data was collected from all positive urine cultures. A frequency distribution table was used for descriptive statistics; Chi-square test was used to compare subgroups. Data were analyzed using Stata software version 12 (Stata Corp LP, College Station, Texas). **Results**: A total of 2014 samples of positive urine cultures were obtained during 2012-2013. Of these, 1875 (88.6%) samples were from females and 229 (11.4%) samples were from males. The prevalence of infection was most common in the age group of 50 years or older, with 594 (29.5%) cases. E. coli and Klebsiella represented 68% and 10.2% of the cases, respectively; these bacterial strains were the most prevalent in patients. The strongest antibiotic resistance in patients was towards the antibiotic ampicillin. For most of the antibiotics, the antibiotic resistance was significantly greater in males compared to females (P<0.05). **Conclusion**: Resistance to antibiotics in all investigated bacteria strains was common. For both sexes, the highest antibiotic resistance occurred in patients less than 50 years of age; the resistance was towards ampicillin. For the group over 50 years of age, the greatest antibiotic resistance was towards ceftizoxime. The subject of antibiotic resistance, therefore, should be studied in further detail since antibiotic resistance has great impact on health issues, such as UTIs.

1. Background

Urinary tract infections (UTIs) involve the presence of microbial pathogens inside the urinary tract and the resulting induction of an inflammatory response. UTIs are one of the most common infections in patients admitted in the hospital and outpatient ward [1]. Uncomplicated UTIs usually occur in patients with normal urinary system structure and function. These infections are caused by pathogens that usually are sensitive to oral antibiotic agents [2]. UTIs are the second leading cause of infection in the community. It affects 150 million people worldwide each year [3]. Evidence shows that there is a greater prevalence of UTIs in females than males. In fact, at least half of the women in the community have experienced UTIs [4].

Several studies in different societies have shown that gram-negative bacteria are the most common etiologic agent of infection. Among these bacteria, *E. coli* is responsible for more than 80% of UTIs [5]. The prevalence of UTIs in some population groups is greater than other groups, including infants, pregnant women, elderly people, patients with spinal cord injuries, people who are living with a urinary catheter (for varying lengths of time), diabetic patients, those with multiple sclerosis, and those with immunodeficiencies [6].

As a basic principle in treating UTIs, selecting an appropriate antibiotic with high efficiency and effectiveness is necessary. This is because the antibiotic resistance for pathogenic bacteria is considered to be major challenges [7]. Determination of an antibiotic resistance pattern among common pathogenic bacteria is important for designing an optimal treatment [8]. Despite the widespread ability of antibiotics, bacterial infection remains common in populations and, after respiratory tract infections, is the leading cause of infection [9].

Given the importance of the determination of antibiotic susceptibility patterns for pathogens involved in urinary system infections, this study was conducted to determine the antibiotic resistance pattern in urine samples of the patients referred to the Central Laboratory of Yazd (Yazd, Iran) from 2013-2014. Being aware of local antibiotic resistance is crucial to avoid treatment failure, and bacterial resistance, and helps in selecting an appropriate antibiotic for empiric

therapy. Findings of this study can be effective to help physicians to choose the correct treatment of antibiotics and thereby reducing medical costs.

2. Methods

This study was a cross-sectional study conducted on all subjects who were referred in the Central Laboratory of Yazd to test patient urine cultures. Data was collected for all positive urine cultures. Urine samples were collected using mid-stream method (the middle part of urine stream) in a sterile container under sterile conditions, using a calibrated loop on the agar and blood agar (using mechanical settings for culture). The samples were incubated at 37°C, then she was investigated after 24 -18 hours.

In this study, of a total 24 months, 19 months were randomly selected and all of the positive urine cultures during 19 months were studied by the census (2014 positive urine culture). Frequency distribution table was used for descriptive statistics and Chi-square test was used for compare subgroups. Data were analyzed using Stata software version 12 (Stata Corp LP, College Station, Texas). P values less than 0.05 were considered statistically significant.

3. Results

The results of the study showed that a total of 2014 samples of positive urine cultures were obtained in 2012-2013. Of the samples, 1875 (88.6%) were from females, and 229 (11.4%) were from males. The prevalence of infection was more common in patients who were over 50 years old, with 594 cases (29.5%) **Table 1**.

Table 1. Demographic distribution of participations in this study

Variable	Frequency	Percentage
Gender		
Female	1785	88.6
Male	229	11.4
Age group (year)		
<1	71	3.5
1-4	128	6.4
5-18	132	6.6
19-30	581	28.8
31-50	508	25.2
50 <	594	29.5

The frequency of *E. coli* bacteria was 1369 cases (68%), of *Klebsiella* was 205 cases (10.2%), of beta-hemolytic *Streptococci* was 170 cases (4.8%), of *Enterobacter* was 61 cases (3%), of gram-negative *Bacilli* was 46 cases (2.3%), and of non-hemolytic *Streptococci* was 42 cases (1.2%). Other bacteria cultures found in 121 cases (6%) included coagulase-negative *Staphylococci*, *Staphylococcus aureus*, *Streptococcus* group D, non-fermentative *Bacilli*, *Citrobacter*, *Proteus* and *Pseudomonas aeruginosa*, *Streptococcus* group alpha, *Staphylococcus epidermidis*, *Actinobacteria*, gram positive *Bacilli*, gram-positive cocci and pneumococci.

E.coli had the highest prevalence in males and females, with 53.3% and 69.9% of cases, respectively. In addition, for all age groups, *E. coli* had the higher frequency. After *E. coli*, *Klebsiella* was the most common bacteria type in both sexes and in all age groups **Table 2**.

Moreover, the results showed that the greatest antibiotic resistance of *Klebsiella*, *Enterobacter*, non-hemolytic *Streptococcus*, and gram-negative *Bacilli* was towards ampicillin. *E. coli* and *Streptococci* showed the greatest resistance to cotrimoxazole. The greatest sensitivity of *E. coli*, *Streptococcus*, and non-hemolytic *Streptococci* was related to nitrofurantoin. *Klebsiella* and

Table 2. Prevalence of bacteria type in investigated patients by gender and age group

Bacteria	Gender		Age Group					
	Male	Female	<1	1-4	5-18	19-30	31-50	> 50
E.coli	122(53.3)	1247(69.9)	46(64.8)	92(71.9)	95(72)	372(64)	343(67.5)	421(70.9)
Klebsiella	27(11.8)	178(10)	13(18.3)	9(7)	17(12.9)	62(10.7)	44(8.7)	60(10.1)
Beta-Hemolytic Streptococcus	14(6.1)	16(8.7)	2(2.8)	4(3.1)	6(4.5)	72(12.4)	49(9.6)	3796.2)
Enterobacter	10(4.4)	51(2.9)	0(0)	5(9.3)	2(1.5)	15(2.6)	14(2.8)	25(4.2)
Gram-Negative Bacilli	16(7)	30(1.7)	3(4.2)	7(5.5)	5(3.8)	6(1)	9(1.8)	16(2.7)
Non-Hemolytic Streptococci	6(2.6)	36(2)	1(1.4)	1(0.08)	1(0.08)	22(3.8)	8(1.6)	9(1.5)
Others	34(14.8)	87(4.8)	6(8.5)	10(7.8)	6(4.5)	32(5.5)	41(8.1)	26(4.4)

Enterobacter had the greatest sensitivity to ceftizoxime, and gram-negative *Bacilli* had the greatest sensitivity to ciprofloxacin.

In females the highest antibiotic resistance was observed in the age group of 50 years old or less; the resistance was related to ampicillin. In the group over 50 years of age, the greatest antibiotic resistance was towards ceftizoxime. The greatest sensitivity in the age group of 5 years old or less was related to ciprofloxacin. In the age group older than 30 years and between 5-18 years, the greatest sensitivity was towards nitrofurantoin. In the age group of 18-30 years old, the highest sensitivity was related to ceftizoxime. The results also showed that the greatest antibiotic resistance in the age group of 50 years or younger, for males, was related to ampicillin. In the age group over than 50 years old, for males, the greatest resistance was related to ceftizoxime **Table 3**.

Overall, our results showed that there were significant relationships between resistance to antibiotics (ceftizoxime, cephalexin, ciprofloxacin, cotrimoxasole, nitrofurantoin, norfloxacin, and nalidixic acid) to patient gender. The antibiotics resistance in males was significantly higher than in women ($P < 0.05$), but resistance to ampicillin and tetracycline were similar for both sexes ($P > 0.05$) **Table 4**.

4. Discussion

The physician's awareness regarding antibiotic resistance is crucial. Antibiotic resistance is among the major challenges in the treatment of infectious diseases. Our study showed that during 2013-2014, of the 2014 urinary tract infections diagnosed, more than 88% belonged to females. The highest prevalence of bacteria was related to *E. coli* and *Klebsiella.E. coli* was the most common bacteria in both sexes and in all age subgroups. The greatest resistance of *Klebsiella*, *Enterobacter*, non-hemolytic *Streptococcus*, and gram-negative *bacilli* was towards ampicillin. Moreover, the results showed that there was a significant relationship between patient gender and antibiotics resistance to ceftizoxime, cephalexin, ciprofloxacin, cotrimoxazole, nitrofurantoin, norfloxacin, and nalidixic acid. Consistent with our findings, Savadkouhi *et al*. [10], Vaezzade *et al*. [11] and Heidari-soureshjani et al., in their studies, showed that UTIs are more common in females [12].

Moreover, in our study herein, positive cultures were more common in the age group of 50 years old or older; this could be attributed to a weaker immune system, usually seen in this older age group. The results also showed that the highest prevalence of bacteria was related to *E. coli* in 68% and *Klebsiella* in 10.2% of the cases, respectively. Mohammadi *et al*. [13] and Abdolahi *et al*., in their studies, found that the prevalence of E.coli was greater than the other types [14]; these results are consistent with results from our study. We found that after *E. coli*, the next highest prevalence of bacteria was *Klebsiell*a. A study by Isvand et al. showed that the highest prevalence of bacteria after *E.coli* was related to *Klebsiella*, consistent with findings from our study [15].

Table 3. Antibiotic sensitivity in men and women according to age groups

Antibiotic sensitivity		Age Group <1	1-4	5-18	19-30	31-50	>50
Females	**Most Resistance**	Ampicillin (79.3)	Ampicillin (79.3)	Ampicillin (79)	Ampicillin (64.5)	Ampicillin (70.9)	Ceftizoxime (74.2)
	Most sensitivity	ciprofloxacin (96.3)	Ciprofloxacin (82.4)	Nitrofurant (89.6)	Ceftizoxi (87.8)	Nitrofurant (86.4)	Nitrofurant (85.7)
Males	**Most Resistance**	Ampicillin (90.9)	Ampicillin (90.9)	Ampicillin (83.3)	Ampicillin (70.6)	Ampicillin (74.3)	Ceftizoxime (86.6)
	Most sensitivity	Ciprofloxac (75)	Ceftizoxime (81.3)	Ciprofloxacin (100)	Ceftizoxime (75)	Ceftizoxime (62.3)	Nitrofurant (67.3)

2175
Biomed. Res. Ther. 2018, 5(5): 2271-2278

Table 4. The relationship between resistance of antibiotics and gender

Type of Antibiotic		Female	Male	Chi-Square	P-Value
Ceftizoxime	**yes**	157(75.85)	50(24.150	40.02	<0.001
	No	1379(90.60)	143(9.40)		
Cephalexin	**yes**	294(71.88)	115(28.12)	115.6	0.001
	No	1280(91.95)	112(49.34)		
Ciprofloxacin	**yes**	369(82.37)	79(17.63)	26	0.0001
	No	1175(91.16)	114(8.84)		
Cotrimoxasole	**yes**	820(87.14)	121(12.86)	4.73	0.03
	No	942(90.23)	102(9.77)		
Nitrofurantoin	**yes**	133(69.63)	58(30.37)	77.28	<0.001
	No	1642(90.77)	167(9.23)		
Ampicillin	**yes**	1246(88.31)	165(11.69)	0.66	0.41
	No	516(89.58)	60(10.42)		
Norfluxacin	**yes**	6(78.31)	18(21.69)	10.36	0.001
	No	226(91.50)	21(8.50)		
Tertacyclin	**yes**	152(87.36)	22(12.64)	1.93	0.16
	No	70(93.33)	5(6.67)		
Nalidixic Acid	**yes**	706(87.05)	105(12.95)	5.83	0.016
	No	829(90.70)	85(9.30)		

Furthermore, our research indicated that the greatest antibiotic resistance of bacteria in both sexes, and in the majority of age groups, was related to ampicillin; these findings are consistent with the findings by Madani *et al*. [16], Isvand *et al*. [15] , and Adenipekun *et al*. [17]. In our study, the lowest antibiotic resistance in males and females was related to ceftizoxime and nitrofurantoin, respectively. In a study by Glasha *et al*. in Gorgan [18] and Shekohi *et al*. [19] in Kerman, the highest sensitivity was related to nitrofurantoin; their findings were consistent with our findings. In our study, antibiotic resistance in males was significantly greater than in females ($P < 0.05$); this could be due to incorrect use and indiscriminate consumption of antibiotics in the treatment of infection in males.

5. Conclusions

Overall, our study results showed that resistance of bacteria to antibiotics was common in UTI patients. For both sexes, the highest antibiotic resistance observed in patients less than 50 years of age was related to ampicillin; the highest antibiotic resistance in patients over 50-years old was related to ceftizoxime. It is recommended that effective polices should be adopted in order to reduce the risk of resistance of bacteria against antibiotics. Prevention of spread of bacterial resistance against antibiotics warrants future quick and on-time detection of resistant strains to devise appropriate treatment strategies.

6. Open Access

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7. List of abbreviations

E.Coli: Escherichia coli **UTI**: urinary tract infection

8. Ethics approval and consent to participate

Not to be applied

9. Competing interests

The authors declare that they have no competing interests.

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Yazd University of Medical Sciences, Yazd, Iran.

11. Authors' contributions

All authors contributed to the design of the research. HP, MS, SLD and SRP collected the data. SK, ZK and SRP conducted analysis and interpretation of data. All authors drafted the first version. SRP, SK, ZK, EG and JA edited the first draft. All authors reviewed, commented and approved the final draft.

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