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Prevalence and pattern of antibiotic resistance of gram-negative bacteria isolated from urinary tract infections in patients referring to Neka Laboratories-Iran

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ABSTRACT

Introduction: Urinary tract infection (UTI) is one of the most common bacterial infections. Increased drug resistance has identified the need to evaluate antibiotic resistance patterns to improve experimental therapy. The aim of this study was to identify bacterial agents and determine their drug resistance pattern in patients referring to the Neka diagnostic laboratories.
Methods: This descriptive cross-sectional study was conducted from December 2016 to April 2017 in patients referred to the Neka Diagnostic Laboratories. Morphological study and identification of isolated bacteria by using hot dyeing and differential biochemical tests were performed. Antibiotic resistance of bacteria was determined by Disc diffusion method in Muller Hinton Agar medium.
Result: Of the 573 patients, the most commonly isolated bacteria in the urine included 258 isolates of *Escherichia coli* (45%), 69 isolates of *Enterobacter* (12%), 18 isolates of *Klebsiella* (3.14%), and 7 *Pseudomonas* isolates (1.22%). *Escherichia coli* isolates showed the highest and lowest resistance, respectively, to Sulfamethoxazole (30.23%) and Norfloxacin (0.39%) and to the highest sensitivity to Gentamicin (56.59%).
Conclusion: The results of this study indicate an increase in the resistance of the strains of *E.coli* to the Sulfamethoxazole and Ciprofloxacin antibiotics, which may be due to the overdose of these antibiotics. The report of antibiotic susceptibility to commonly occurring organisms in this area can be considered by physicians in experimental treatments.

Introduction

Urinary tract infection is an inflammatory response of the urethra to the invasion of pathogenic microorganisms (1). This infection is of the highest importance after respiratory tract infection and is the second most common infection in children and adults and the most important infection in infants. In the world, every year, 150 million people are affected by this infection, and includes 35% of hospital infections (2-4). Urinary tract infections are one of the most common infections that occur at different ages and mis-treatment of it can lead to serious complications such as disorders of the urinary tract, hypertension, uremia and early delivery and even abortions in pregnant women. More than 50% of women get UTIs at least once in their lifetime. The severity of these infections depends on factors such as bacterial virulence. The risk factors for urinary tract infection include host characteristics, host behavior, and bacterial characteristics. Sexual activity and contraceptive methods are also important risk factors for the development of symptomatic urinary tract infection. Cell receptor characteristics, anatomy differences and host genetics are risk factors for recurrence of infection (5-6). Urinary tract infections

are caused by the presence of pathogenic microorganisms in the urethra or without signs and symptoms; In an asymptomatic infection, colonization of the bacterium is observed without any signs in the urinary tract; But in the symptomatic infection simultaneous with colonization symptoms such as: microbial invasion and inflammation in the urinary tract are observed. From the microbiological point of view, urinary tract infection occurs when pathogen microorganisms are observed and disassociated in the urine, urinary tract, bladder, kidney or prostate. According to statistics, about 2% of hospitalized patients suffer from urinary tract infections during their hospitalization, causing about 900,000 cases of hospital related urinary tract infection every year (8). Among the common bacteria in this infection are E. coli, Proteus vulgaris, Klebsiella pneumonia, Staphylococcus epidermium, Enterobacter, Citrobacter and Pseudomonas aeruginosa. Since the E. coli bacteria is the most common cause of urinary tract infections in both genders and almost all ages, the most appropriate and effective antibiotics should be selected for rapid onset of treatment (9). The basis of proper treatment for urinary tract infections is the selection of a good and inexpensive antibiotic, and the main problem in treating urinary tract infections caused by Escherichia coli is bacterial resistance to a large number of common antibiotics. On the other hand, the spread of antibiotic resistance is associated with an increase in the consumption of antibiotics. Antimicrobial resistance can vary from one region to another or from hospital to hospital, and awareness of the antibiotic resistance pattern in the final or experimental treatment of this type of infection is necessary. The emergence of resistant bacterial strains is often due to the genetic characteristics of the bacteria, increased population, travel, as well as the high consumption of antibiotics (10-11). Elderly are more prone to urinary tract infections due to decreased immune function, insufficient nutritional status, and loss of resistance to infection. In the United States, after upper respiratory tract infection, urinary tract infections are second, and many women and men suffer from it throughout life. More than eight million patients refer to doctors in the United States each year, which a significant percentage of urinary tract infections are without clinical symptoms (12-13). The aim of this study was to evaluate the prevalence of pathogenic bacteria and to determine the antibiotic resistance pattern of bacteria isolated from people with urinary tract infection in Neka medical diagnostic laboratories during 2016-2017.

Methods

This descriptive cross-sectional study lasted from December 2016 until the end of April 2017 in the Neka medical diagnostic laboratories located in Mazandaran province. For this purpose, 6767 urine samples were collected in sterile containers by Midstream method from patients referred to laboratories. A definite measure of urinary tract infection was based on positive urine culture, which was ≤105 colonies per milliliter of urine. All specimens were cultured on Indian blood agar (HI-media), Eosin methylene blue and German Macconkey (Merck) and incubated at 37 ° C for 24 hours. In order to identify the grown colonies, standard biochemical and microbiological tests were used such as gram stain, indol motility (SIM), Simmon Citrate, Methyl Red Voges Proskauer (MR-VP), Triple Sugar Iron agar (TSI), Urea consumption and Lysine decarboxylase to identify the gram-negative bacteria. The hypersensitivity test was performed according to the disc diffusion method in accordance with the principles of the International Clinical and Laboratory Standards Institute 2017. In short, in this test, after preparation of the Müller-Hinton agar medium, a microbial suspension was prepared, equivalent to half-McFarland turbidity, and cultured massively on the plate. Then the antibiotic discs of ciprofloxacin, sulfamethoxazole, nalidixic acid, norfloxacin, gentamicin, ceftriaxone, cefotaxime and imipenem provided from the Padtan Teb Co. were placed at a distance of at least 2.5 cm from each other on the medium and incubated for 24 hours at 37 C. SPSS 2016 was used to analyze the data.

Ethical considerations

Sample collection was performed with complete satisfaction of patients and in accordance with commitment no report was provided from name and characteristics of patients. Tests did not incur any costs to the patient. In this study, ethics codes of 1, 2, 17 and 20 were observed.

Results

Out of 6767 samples, 573 cases (8.5%) had positive culture, of which 489 (85.3%) were female and 84 (14.7%) were male. Three age groups were studied in this study, which included infants to age 7, 20 to 40, and 50 to 75 years old. The highest infection rates were 20 to 40 years' category. Analysis of urine specimens showed that the most common isolate was Ecoli which was isolated from 258 (45%) of the cultures and from 258 samples, 215 (83.33%) were female and 43 (16.66%) were male. Pseudomonas isolates had the lowest abundance (22.1%). The level

of resistance of pathogenic bacteria isolated from the patient's urine to different antibiotics divided by the bacterial genus has shown in Table 1. The results of the gel emission test showed that gram negative bacteria had less resistance to norfluxacin and cefotaxime. After Escherichia coli, Enterobacter (12%), Klebsiella (3/14%) and Pseudomonas (1/22%) respectively were in the following ranks. In this study, Escherichia coli was identified as the main cause of urinary tract infection and showed the highest and lowest resistance to sulfamethoxazole (30.23%) and norfluxacin (0.39%), respectively. Escherichia coli strains showed the highest sensitivity to gentamicin (56.59%), ciprofloxacin (45.35%) and ceftriaxone (34.5%) antibiotureics (Table 2).

highest urinary cultures were related to Escherichia coli and the rate of infection was significantly higher in women than in men, most likely due to the proximity of the vagina and anus in women. Similar

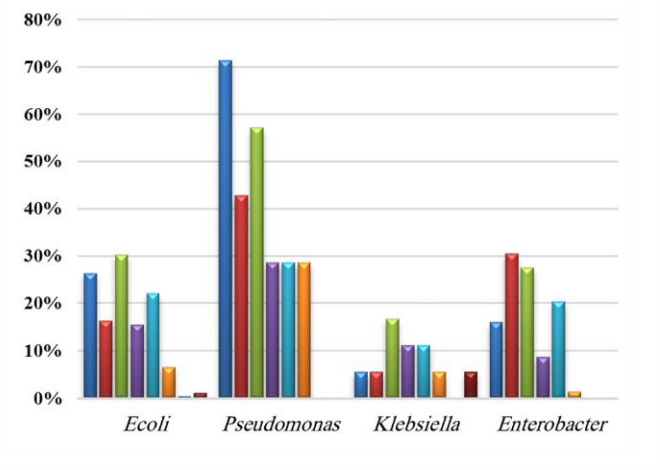

Figure 1: Frequency of resistant strains

Table 1: Frequency distribution of antibiotic resistance according to the type of isolated organism

Bacteria name	CIP	NA	SXT	GM	CRO	IPM	NOR	CTX
Ecoli	36.26%	28.16%	23.30%	50.15%	22%	59.6%	39.0%	16.1%
Pseudomonas	43.71%	86.42%	14.57%	57.28%	57.28%	57.28%	0%	0%
Klebsiella	56.5%	56.5%	67.16%	11.11%	11.11%	56.5%	0%	56.5%
Enterobacter	94.15%	43.30%	54.27%	70.8%	29.20%	45.1%	0%	0%

Table 2: Frequency distribution of antibiotic susceptibility according to the type of isolated

Bacteria name	CIP	NA	SXT	GM	CRO	IPM	NOR	CTX
Ecoli	35.45%	5.17%	33.33%	59.56%	50.34%	67.16%	81.5%	88.3%
Pseudomonas	29.14%	0 %	29.14%	57.28%	29.14%	29.14%	0%	29.14%
Klebsiella	44.44%	0%	50%	50%	78.27%	44.44%	11.11%	11.11%
Enterobacter	52.56%	23.36%	42.59%	22.65%	7.55%	25.7%	35.4%	45.1%

Discussion

Urinary tract infections are one of the most commonly hospital infections, with around 150 million people affected every year and its empirical antibiotic therapy needs to know about urinary pathogens and their antibiotic susceptibility (3). Women have a high risk of developing urinary tract infections. In this study, the as the most common cause of urinary tract infection (19-17). Diagnosis and timely treatment of urinary studies in other parts of the world have reported this bacterium tract infection is essential, especially in cases of involvement of upper parts of the urinary system, because delaying treatment causes irreversible damage to the kidney, causing side effects such as

pyelonephrosis, kidney abscess, or chronic pyelonephritis, it can also lead to chronic renal failure. Due to the lack of an accurate culture of consumption of antibiotics in our community, most of the cultures of referred patients were reported negative as a result

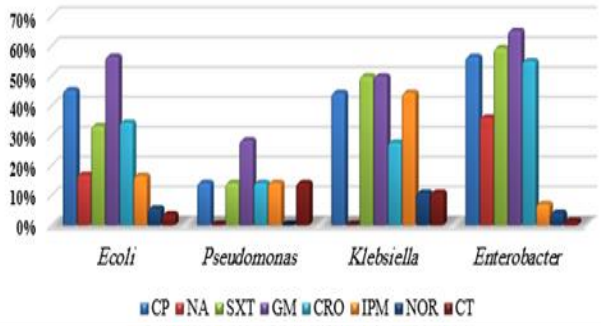

Figure 2: Frequency of susceptible strains

of previous self-therapies. In many cases, treatment is based on the most commonly used urinary tract infections and their antibiotic susceptibility. Therefore, it is necessary to draw a general pattern of antibiotic susceptibility to urinary pathogens in any country or city (21-20). Drug resistance to antibiotics in different regions of Iran and the world is different due to genetic changes in the strains, differences in antibiotic use and differences in access to antibiotics (25). The resistance of bacteria to antibiotics is inherited and acquired. In inheritance resistance, inborn and inherited traits of the cell cause inhibition of effect of antibiotic (27-26). Therefore, due to the importance of urinary tract infections, this study was conducted in Neka city. Quinolones and fluoroquinolones are a group of antibacterial synthetic drugs that are now widely used in the treatment of bacterial infections. Nalidixic acid, the first member of the quinolone group, was discovered in 1962. Placing the fluorine atom at position 6 was the first change in the base structure of quinolones, which improved their antibacterial properties and made quinolones useful drugs for the treatment of systemic urinary and respiratory infections (31 -30). In the present study, resistance to ciprofloxacin and nalidixic acid antibiotics in E. coli was 26.36% and 16.28%, respectively, and in Pseudomonas 71.9% and 42.86% respectively, which showed an increase in resistance level. Given that since the production of Nalidixic acid in 1962 as the first kinolone drug has been passed around for about six decades, and since it was used initially for the treatment of urinary tract infections, so it is expected that resistance to Nalidixic acid is higher than other quinolone antibiotics (32). In the study of Bilaway et al., The bacteria of Escherichia coli and Klebsiella showed the highest resistance to Nalidixic Acid (90%) and Ciprofloxacin (60%) (3). Also, in Rahim Abadi study, E. coli strains were resistant to Nalidixic acid (12.25%) and in Jalalpur research were resistant to Nalidixic acid and Ciprofloxacin antibiotics (30.3% and 27.8%) (4). Norfloxacin is a chemical compound of the second generation of fluoroquinolones that had 0.39% resistance to E. coli in our study, which is lower that the results of similar studies conducted by Mullah Abbaszadeh in Tabriz and Heidari Chaleshtari in Shahrekord, which showed resistance rate of 29.01% and 16.30%, respectively. In the research of Heydari Chalesteri et al., Which was conducted in 1995, the highest isolate was E. coli, with the highest resistance to ampicin, tetracycline and sulfamethoxazole, and the least resistance to gentamicin; Also, in the study of Afrug et al. In the year 2012, Escherichia coli was the most isolated organism from urine, with a prevalence of 67%, and the highest resistance to sulfamethoxazole and cefalutin (21-25); this results were consistent with our results. In the study of Taba'i et al. (2012-2014), The most abundant bacteria isolated from the urine was Staphylococcus aureus with the most resistant to sulfamethoxazole and the least resistance to ciprofloxacin (19); These results were not consistent with our study and studies by Zaidabadi Nejad et al. In the year 2014 that the most isolated bacteria was Escherichia coli (28). The cause of differences and similarities in the type and frequency of pathogen factors can be due to environmental differences and conditions in the region, including health status and education and health. In the study of Laripour et al., Infection were reported with E.coli (31.4%), Enterobacter (4.76%) and Klebsiella (2.8%); These results are consistent with our results, which are as follows: Escherichia coli (45%), Enterobacter (12%) and Klebsiella (14.3%) and it is not in consistent with study of Seraj et al. that the rate of infection was as follows: Escherichia coli (46.24%), Klebsiella (16.92%) and Enterobacter (73.7%) (5-10); The difference in the prevalence of infection with different factors can be due to differences in lifestyle, culture and the economic and social status of individuals. In this study it was identified that the E. coli isolate showed the highest resistance to sulfamethoxazole and the most susceptibility to gentamicin, which was similar to the results of Nowruzi in Jahrom, Mohammadi et al. In Ilam and Mahmoudi et al. at Hamedan (9-11-12). It was also in consistent with the study of George G. H. Zhanel and et al. in Canada and the United States (13). Several studies in different parts of the world have shown that the type of bacteria and the pattern of sensitivity and antibiotic resistance

have been constantly changing over the years. In our study, Ecoli was the most isolated isolate, that were most of the isolated bacteria from the body's mormal flora; these results were consistent with the studies of David and Gales and Ronald in 2002 (16-14). In Kulkarni et al. study, in 2017, in the northeast of Carnataka, the highest infection was with Escherichia coli, with an increase in resistance to ampicillin up to 82.53% and an increase in sensitivity to imipenem up to (96.71%) (30). In the Alcántar study in 2015, Escherichia coli showed the highest resistance to cephalosporin and showed the highest susceptibility to carbapenem and amikacin (29), which is contradicted with the data from our study. The cause of creating different resistance and sensitivity patterns can be the unnecessary use of antibiotics and, consequently, drug resistance. The results of our study indicate an increase in urinary tract infection in the age group of 20 to 40, which was consistent with the results of Borji Kermani et al. In 2013 in Kerman (24) and Barzan in 2012 in Tehran (27).

Conclusion

Due to the increasing prevalence of resistance to antibiotics, rapid and timely diagnosis of resistant strains is necessary in order to select appropriate treatment options and to prevent the increase of resistance. It is also recommended that the treatment of urinary tract infections, which is of particular importance, should be done according to the susceptibility and resistance pattern of the area in order to prevent the occurrence of a drug resistance and treatment failure that leads to the complication of the infection. In general, it is recommended that according to the pattern obtained for the treatment of Ecoli-induced urinary tract infections, in cases of severe clinical suspicion, use gentamicin for the involvement of the upper parts of the system, and in the case of mild UTIs, which are limited to the lower parts of system use relatively weak antibiotics Like cefotaxime and norfloxacin.

Ethical disclosure

Before performing the research, it was explained to the participants. An informed consent was obtained from all participants included in the study.

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Author Contributions

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interest

The authors declare that they have no conflict of interest.

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