Antibiotic Resistance Trend of Uropathogens in a Tertiary Teaching Hospital in Rasht, Iran, a Longitudinal Study

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ABSTRACT

Background: The present study was conducted to determine the most prevalent isolates in urine cultures and resistance profile of the isolated pathogens and trend of changing resistance to common antibiotics used for the treatment of urinary tract infections. Materials and methods: In this longitudinal - descriptive study, the data of 2060 positive urine cultures and the susceptibility testing results of inpatients and outpatients' urine specimens from 2007 to 2014 were studied. The susceptibility testing using Kirby-Bauer disk diffusion method according to CLSE standards was done on isolated uropathogens for t ceftriaxone, ceftazidime, gentamicin, amikacine, ciprofloxacin and cotrimoxazole, pipracillin, nitrofurantoin and imipenem. Results: The most prevalent pathogen which was isolated was E.coli, 1141 (55.4%). The resistance trend of E.coli isolates for antibiotics showed increased resistance for: ceftazidim (67% to 81%), ciprofloxacin (57%-77%), pipracillin (20%-87%): stable resistance rate for : ceftriaxone(73%-70%), cotrimoxazole (79%-74%) and decreased resistance for : nitrofurantoin (32%-8%), gentamicine (49%-37%) and amikacine (21%-13%). 50% of E.coli isolates were co-resistant to ceftriaxone and ciprofloxacine and trimetoprim-sulfamethoxazole. Conclusion: Antibiotic resistance of uropathogens for most of the important antibiotics empirically used for UTI was very high and increasing in this hospital.

Key Words: *Antibiotic resistance, urinary tract infection, E.coli, multidrug resistant*

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INTRODUCTION

Globally, it has been estimated that there are150 million urinary tract infections every year [1]. Patient morbidity, costs of treatment, rates of hospitalization, and use of broad-spectrum agents are remarkably increased by antimicrobial resistance [2]. There are a limited and predictable spectrum of organisms which lead to urinary tract infections. Considering both outpatients and inpatients, Escherichia coli has been the main urinary tract pathogen, causing 75 to 90% of the uncomplicated urinary tract infection isolates. Staphylococcus saprophyticus, Klebsiella spp., Proteus spp., Enterococcus spp., and Enterobacter spp. have been the pathogens which were less commonly isolated from outpatients [3]. Antibiotic resistance development has been a major issue for managing infections both in community and hospital settings [4]. The Infectious Diseases Society of America recommends that physicians obtain information on local resistance rates and that ongoing surveillance be carried out to check the changes in susceptibility of uropathogens [5]. The present study was conducted to determine the most prevalent isolates in urine cultures of inpatients and institutional in vitro susceptibility and resistance profile of the isolated pathogens and the trend of changing

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resistance to common antibiotics used for the treatment of urinary tract infections.

MATERIALS AND METHODS

Setting

This longitudinal - descriptive study was conducted in teaching hospitals, affiliated with Guilan University of Medical Sciences in Rasht from 2007 to 2014. For this purpose, the data of positive urine cultures and susceptibility testing results of inpatients and outpatients urine specimens from microbiology laboratory of Razi hospital (a tertiary teaching general hospital of Guilan university of medical sciences in Rasht) from 2007 to2014 was gathered. During this 7- year period, 2060 positive urine culture results were obtained.

Data Collection

Susceptibility testing using Kirby-Bauer disk diffusion method according to CLSE standards was done on isolated uropathogens for ceftriaxone, ceftazidime, gentamicin, amikacine, ciprofloxacin and cotrimoxazole on all isolates. The susceptibility testing for pipracillin, nitrofurantoin and imipenem in some periods according to the availability of disks was done.

Statistical Analysis

The obtained information was inserted into SPSS-20, and descriptive statistics (percentage, frequency) were utilized.

RESULTS

During this 7- year period (2007-2014), 2060 positive urine culture results were obtained from the hospital's microbiological laboratory. The most prevalent pathogen which was isolated was E.coli, 1141 (55.4%). 60% of specimens were obtained from women. Other pathogens in order of prevalence were: citrobacter spp (20%), enterobacter spp (9.8%), klebsiella spp (4%), enterococcus (2.8%), pseudomonas spp (2%), Staphylococcus saprophyticus (1%) (table 1).

The resistance trend of E.coli isolates for antibiotics showed the increased resistance for : ceftazidim(67% to 81%), ciprofloxacin (57%-77%), pipracillin (20%-87%); the stable resistance rate for: ceftriaxone (73%-70%), cotrimoxazole (79%-74%); and the decreased resistance for: nitrofurantoin (32%-8%), gentamicine (49%-37%) and amikacine (21%-13%)(table 2).

33% of E.coli isolates were co- resistant to ceftriaxone, ciprofloxacin and gentamicine or amikacin. 50% of E.coli isolates were co-resistant to ceftriaxone and ciprofloxacine and trimetoprim-sulfamethoxazole (MDR isolates). Citrobacter and entrobacter had very similar resistance rates: 77% and 81% for ceftriaxone, 42% and 42% for gentamicine,32% and 39% for amikacine,50% and 52% for ciprofloxacine, 84% and 85% for pipracilline ,78% and 83% for cotrimoxazole and 56% and 71% for nitrofurantoin; respectively. klebsiella.spp and pseudomonas aerogenoza showed significantly higher resistance rates than citrobacter and enterobacter (table 3).

For pseudomonas, the resistance rates for antibiotics ceftazidime and cefepime: two third generation of cephalosporine was highly active against pseudomonas aeruginosa : 90% and 86%; respectively, not shown in table 3. The resistance rates of enterococcus spp, a gram positive microorganism occasionally causing UTI also revealed very high rates: 57% for gentamicine, 67% for amikacine, 64% for ciprofloxacine. Also the resistance rates for doxycycline was (50%), for penicillin was (85%), and for ampicillin was (69%) ; the antibiotics sometimes used for infections caused by gram positive cocci, were very high (Not shown in table 3).

Table 1: microorganisms isolated from Urine cultures in Razi hospital: 2007-2014

Y	N	E.coli N (%)	Citro N (%)	Entro N (%)	Pseudo N (%)	Klebsiella N (%)	Staph sapro N (%)	Enterococus N (%)	Others N (%)
2007	183	103(56)	22(12)	29(16)	7(4)	3(1.6)	1(0.5)	5(2.7)	13(7)
2008	188	107(57)	31(17)	24(13)	6(3)	0(0)	2(1)	6(3)	12(6.3)
2009	208	110(53)	46(22)	21(10)	4(1.9)	2(0.9)	5(2.4)	5(2.4)	15(7.2)
2010	300	181(60)	65(22)	15(5)	8(3)	4(1.3)	4(1.3)	7(2.3)	16(5.3)
2011	191	114((60)	49(25)	22(19)	6(3)	3(1.6)	2(1)	5(2.6)	14(7.3)
2012	235	113(48)	63(27)	29(12)	5(2)	4(1.7)	3(1.2)	6(2.5)	12(5)
2013	330	198(60)	77(23)	30(9)	0(0)	0(0)	2(0.6)	8(2.4)	15(4.5)
2014	425	215(50)	65(15)	32(8)	11(3)	67(16)	3(0.7)	15(4)	17(4)
Total	2060	1141(55)	418(20)	202(10)	47(2.3)	83(4)	22(1)	57(2.7)	114(5.5)

Table 2: Antibiotic resistance percentage of E.coli isolated from urine cultures in Razi hospital: 2007-2014

Y	N	cefta	genta	amika	cipro	pipra	ceftria	imip	cotri	nitro
2007	103	67%	49%	21%	57%	-	73%	-	79%	32%
2008	107	66%	53%	18%	61%	-	63%	-	-	-
2009	110	70%	39%	13%	59%	-	65%	-	-	-
2010	181	78%	54%	19%	77%	-	80%	-	-	-
2011	212	57%	42%	11%	72%	20%	68%	73%	73%	12%
2012	113	82%	46%	23%	76%	50%	74%	79%	82%	15%
2013	198	81%	47%	22%	70%	39%	72%	-	66%	11%
2014	215	-	37%	13%	77%	87%	70%	-	74%	8%

Table 3: antibiotic resistance percentage of other uropathogens isolated from urine cultures in Razi Hospital: 2007-2014

pathogen	N	ceftria	genta	amika	cipro	pipra	imip	cotri	nitro
citrobacter	418	77%	42%	32%	50%	84%	-	78%	56%
entrobacter	202	81%	42%	39%	52%	85%	-	83%	71%
pseudomonas	47	-	90%	73%	100%	91%	50%	-	-
klebsiella	83	90%	75%	66%	84%	92%	-	91%	75%
enterococcus	57	-	57%	67%	64%	-	-	-	30%

DISCUSSION

In this study, the most prevalent microorganism isolated from urine cultures of patients admitted to this hospital for UTI or other diagnoses, was E.coli (mean =55% over 7-year period :range 48%-60%). As in other studies, E.coli has been consistently the most prevalent microorganism causing urinary tract infection over the world [6-11].

In this study, in comparison to other similar studies worldwide, as follows, different resistance patterns were considered according to the local study results. The Infectious Diseases Society of America has advocated trimethoprim-sulfamethoxazole (SXT) as initial therapy for females with acute uncomplicated bacterial cystitis in settings where the prevalence of SXT resistance does not exceed 10 to 20%. The susceptibility testing data from The Surveillance Network (TSN) Database-USA (n = 286,187) from 1995 to 2001 showed the resistance rates among E. coli isolates to SXT (range, 14.8 to 17.0%), ciprofloxacin (range, 0.7 to 2.5%), and nitrofurantoin (range, 0.4 to 0.8%) [12]. In this study, the resistance of E.coli to cotrimoxazole (79%-74%) and ciprofloxacin (57%-77%) nitrofurantoin (32%-8%), was much higher, so other antibiotics should be recommended for UTI in this region. The comparison of the current study to a similar study from India indicated more similar resistance pattern to this study: ceftriaxone (60.5%), ceftazidime (57.1%), gentamicin (59.6%), nitrofurantoin (26.9%), meropenem (9.8%), ciprofloxacin (73%) and amikacin (23%) [13]. In the present study, the most important and the most prevalent co resistance phenotypes were to ceftriaxone, ciprofloxacine and trimetoprim-sulfamethoxazole (50% of isolates) then to ceftriaxone and ciprofloxacin and (aminoglycosides: gentamicine or amikacin) (33% of isolates). In the same study from USA in 2001, it was indicated that the most frequent co resistant phenotypes were resistant to ampicillin and SXT (12.0% of all isolates; 82.3% of coresistant isolates) and to ampicillin, ciprofloxacin, and SXT (1.4% of all isolates; 9.9% of coresistant isolates) [12].

The Study for Monitoring Antimicrobial Resistance Trends program collected 1643 E.coli isolates in 2009–2010 from urinary tract infection (UTI) specimens of hospitalized patients in countries around the world. Ertapenem and imipenem were the most active agents tested, inhibiting >98% of all E. coli phenotypes [14]. The data of resistance to imipenem for E.coli isolates were collected for two years (2011-2012) that showed a high resistance rate (73%-79%). In that study, Amikacin and piperacillin–tazobactam achieved 90% inhibition on E.coli isolates while in the current study, the resistance rate to amikacin (21%-13%) and pipracillin (20%-87%) was very high [15]. FQ resistance in UTI pathogens also increased globally, with the SMART study reporting the resistance rates between 6% and 75% in Gram-negative urinary pathogens isolated from hospitalized patients [14]. In this study, the resistance rate of E.coli and other uropathogens isolated from urine samples of patients for ciprofloxacin, as one of the most prescribed antibiotics for UTI in Iran , was very high and increasing (57%-77%).

Comparing this study with other similar studies from Iran, the following results were obtained. In one study, the susceptibility testing on 50 E. coli isolates showed (74%) resistance to ciprofloxacin, approximately the same rate

obtained in this study, and (36%) resistance to gentamicin which was significantly lower than the rate obtained in this study [16]. In a study conducted in northwest of Iran which took over a 14-month period, the results of antimicrobial susceptibility analysis for E. coli, as the most prevalent cause of UTI and commonly used antibiotics were: amikacin (97.8%), gentamicin (97%), ciprofloxacin (94%), nitrofurantoin (87.1%), nalidixic acid (93.7%), trimethoprim–sulfamethoxazole (48.2%), that were very different from the results of this study [7].
The resistance pattern of pathogens other than E.coli in the current study was also very high, and approximately at the same rate of resistance of E.coli except for nitrofurantoin that the resistance of E.coli was much lower.

CONCLUSION

Antibiotic resistance of uropathogens for most of the important antibiotics used empirically for UTI was very high and increasing in this hospital compared to the other hospitals Iran and also the other countries. Continuing this trend might confer a crisis in the treatment of UTI patients especially those with complicated UTIs. The results of this study indicated that more attention to antibiotic prescription and antibiotic stewardship in hospitals is urgently needed to prevent the increasing trend of antibiotic resistance and preserving the invaluable present resources of antibiotics.

Conflict of interest

It should be noted that there was no conflict of interest in this article.

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