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Antibiotic Resistance Pattern Among Isolated Bacteria from Urinary Tract Infection Patients in the Intensive Care Unit

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ABSTRACT

Background: Urinary tract infection (UTI) is one of the most important health care issues with a major role in occurrence of nosocomial infections. Rise in antibiotic resistance rate by UTIs not only lead to morbidity and mortality, but also impose a remarkable financial burden on health care infrastructure. This study was undertaken to evaluate the prevalence of UTIs and identify common microorganisms responsible for infection and their antibiotic resistance profile in our Intensive Care Unit (ICU).

Methods: In this perspective cross-sectional study, data from patients admitted to the ICU of two main referral hospitals in Yasouj, Southern-west Iran from 2015- 2016 was collected. Patients were selected in a subsequent manner and were asked to provide a midstream urine sample. Positive cultures were subsequently placed in differential culture medium for the diagnosis of the causative pathogen, while also evaluating with Muller Hinton Agar culture for antibiogram through disc diffusion method, to evaluate the pathogens sensitivity and resistance towards the tested antibiotics.

Results: Based on bacterial culture results among a total of 112 obtained urine samples, 100 (89.2%) were negative while 12 (10.8%) were positive, in which the majority were gram-negative (6.25%) and the most frequent pathogen was Escherichia coli (5.3%). All cases of UTI in our population were fully resistant to cephalexin, ampicillin, and amoxicillin. Also, all gram-negative cultures were sensitive to amikacin. There was also no significant association between the antibiogram results with age, gender, and gram results.

Conclusion: we report actual data on the resistance patterns of uro-pathogens in a public hospital in Iran. Escherichia coli showed a high prevalence among all UTIs with lower resistance rates to the antibiotics. Resistance to nalidixic acid and trimethoprim-sulfamethoxazole were significantly lower than other oral antibiotics, making both a suitable and cheap alternative for the empirical treatment.

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Introduction

Urinary Tract Infection (UTI) is one of the most common bacterial infections among inpatients and out-patients' settings. Noteworthy, it has been claimed to involve 150 million people around the world each year, leading to remarkable morbidity and mortality (1). Recurrent UTIs have emerged as a burdensome challenge on healthcare systems as the point of causing roughly 10 million office visits per year and the most common cause of eighter community-acquired and nosocomial infections of admitted patients at hospitals in the United State (2, 3). Particularly, UTI is one of the major complications in intensive care patients (ICPs). Statistical analyses have been revealed that world widely this condition accounts for approximately 40% of the 2 million nosocomial infections each year (4). Moreover, about 80% of hospital-related UTIs are contributed to urinary catheter insertion. The occurrence of a catheter-associated UTI has directly been rising with the duration of insertion in about 5% per day, and even up to 100% after 28 days of catheterization (5).

The diversity of bacterial uro-pathogens that cause UTI extremely differs based on sex, race, and underlying disease (6). On the other hand, the gradual acceleration in antibiotic resistance is a crucial issue in many countries like Iran, as the great proportion of antibiotics therapy followed by self-prescription accounts for one of the main leading causes. Inadequate information, lack of regulating policies, easy availability, and low cost have all ascribed to self-prescription (7, 8).

Another notable aspect is improper and unreasonable over-use of antibiotics based on clinician order. Hence, society should strive to conserve the use of this invaluable resource through education and regulation (9, 10). Meanwhile, the most significant criteria for eligible antibiotic prescription are appropriate dose and route of administration, many studies in Iran have suggested that 30%–60% of the antibiotics prescribing has been incorrect (11). Haphazard antibiotic resistance is affecting the health care system with poorer outcomes including delayed symptom resolution, repeated medical consults, and disease progression due to ascending infection (12).

Despite effortless treatment of UTI, recent unreasonable use or prescription of antibiotics have posed some obstacles. Analysis of antibiotic susceptibility causing UTIs especially in the high-risk immunosuppressed ICPs is a huge assessment to diminish morbidity and mortality. Therefore, this study aims to determine antibiotic resistance patterns in isolated bacterial strain from UTI patients admitted in the ICU of two main referral hospitals in Yasuj, southern west Iran.

Materials and Methods

In this perspective, descriptive, cross-sectional study, data from patients admitted to the ICU of two main referral hospitals (Emam Sajjad and Shahid Beheshti Hospital) in Yasouj, Kohgiluyeh and Boyer-Ahmad Province, Southern-west Iran from 2015- 2016 were collected. The sample size was calculated based on a prevalence of UTI of 0.15, and a α=0.05 and d=0.1, reaching an ultimate sample size of 112 patients. The inclusion criteria consisted of all adult patients who were admitted to the hospital's ICU during the study period. The exclusion criteria consisted of unwillingness to participate in the study or provide informed consent, in which in these cases the patients were amended from the study and the next admitted patient full-field their spot. Also, samples in favor of contamination were repeated. Patients were selected in a subsequent manner, in which patients who fulfilled the inclusion criteria were asked to provide a midstream urine sample. Samples were then transferred to the microbiology lab, in which cultures (e.g., EMB Muller Hinton agar, Blood Agar) were obtained. The cultures were placed in autoclaves at 37 degrees for 24 hours. Positive cultures were subsequently placed in differential culture medium (e.g., Urea, citrate, SH2 Indole

Motility (SIM), triple sugar Iron Igar (TSI)) for the diagnosis of the causative pathogen, while also evaluating with Muller Hinton Agar culture for antibiogram through disc diffusion method, to evaluate the pathogens sensitivity and resistance towards the tested antibiotics.

Data regarding the patients' culture results, along with their age and gender were obtained and analyzed accordingly with SPSS version 22.0. Data are presented as frequency and percentage (%) or mean and standard deviation (SD). A Chi-square test was used to evaluate the association among variables and a P-value of under 0.05 was considered statistically significant.

Result

Among a total of 112 obtained urine samples, 39 (34.8%) were male and 73 (65.2%) were female. Also, 46 (41%) were under 50 years of age and 66 (59%) were 50 years and above. Based on bacterial culture results, 100 (89.2%) were negative while 12 (10.8%) were positive, in which the majority were gram-negative (6.25%) and the most frequent pathogen was *Escherichia coli* (5.3%). In other words, Gram-negative was 7/12 in positive urine cultures in which *E. coli* was 6/12. Table 1 demonstrates the results of bacterial culture among our population.

Antibiogram assays to evaluate the sensitivity and resistance of the positive cultures were performed, which the results are demonstrated in table 2. As demonstrated in table 2, all cases of UTI in our population were fully resistant to cephalexin, ampicillin, and amoxicillin. Also, all gram-negative cultures were sensitive to amikacin. There was also no significant association between the antibiogram results with age, gender, and gram results.

Discussion

The burdensome effect of antibiotic-resistant healthcare-associated UTIs (HAUTI) has become a growing public health threat globally. Differences in antimicrobial susceptibility contributes to numerous factors including endemic resistant pathogens, over-prescription of antibiotics, irregular use of antibiotics, the severity of the underlying disease and length of hospitalization (13). Investigating the prevalence of these bacteria alongside focusing on antibiotic resistance pattern among ICUPs can be helpful to diminish health and cost burden.

At first glance, total prevalence of UTIs in our study was 10.8%, this fraction was variable between 15.1% to 18.2% in other studies surveyed in various parts of Iran.(14) Whereas our findings has to correspond with previous surveys from three European countries (including Slovenia, Italy, and Norway) revealed UTIs occurrence rate roughly 1-10% (15). Another study of ICPs in France showed close enough results to the current one with 9.6% (16). In addition, a notable wide survey conducted in the Calgary health region of Canada reported total incidence density of ICU-acquired UTIs of 9.6 per 1000 ICU days (17). Declining rate in the current study compared to previous ones conducted in Iran may suggest an impressive healthcare performance improvement over time particularly during catheter insertion.

To date, the most culpable organisms responsible for uro-pathogens documented to be similar to other geographical areas, a greater dominance of gram negatives bacteria, mainly *E. coli* accounted for 50% of samples followed by 8.3% *Pseudomonas*, while *Acinetobacter* was completely absent. Earlier papers also reported *E.coli* as the largest proportion compare to other microorganisms, for instance: 69% (uncomplicated UTIs) and 70% (complicated UTIs) in Denmark, (18) 93.55% (for children), 60.24% (for adult), and 45.83% (for elderly) in Saudi Arabia (19), 41% in Somalia (20), 76.7% mean prevalence for Germany, Italy, Russia, Switzerland and Poland (21), 32.9% in India (22), 76.5% in Brazil (23), and 38.7% from 17 Asian countries were positive for *E. coli* (24). Besides, Mortazavi-Tabatabaei et al.

report in a similar same geographical region, claimed *E. coli* with 62% incidence rate as the most prevalent etiology of uro-pathogens (25). Due to the presence of these bacteria in the digestive tract system, poor hygiene can potentially pose a risk to fecal-perineal-urethral contamination therefore this will be the most probable explanation for UTIs caused by Enteric bacteria (26).

Considering gram-positive bacteria were accounted for 41.7% of isolated samples (consisting of *Staphylococcus epidermidis*, *Staphylococcus aureus* both were 16.7% and *Staphylococcus saprophyticus* 8.3%). Similar to current study, a study conducted in France, after *E. coli*, Gram-positive cocci was the most common cause of infection (27). This situation can be explained by the fact that the streptococcal family is widely assumed to be a noticeable group of normal flora, hence they can cause contamination particularly during catheterization. Another reason on the same side of this statement was the low amount of colony counts (<100000) (28).

Emerging of resistance among uro-pathogens is increasingly reported within a variety of resistant patterns. Result of antibiogram test from isolates *E. coli* revealed significant resistance rate to amino-penicillin (amoxicillin and ampicillin) and first generation of cephalosporines (cephalexin). Compare to our observation, an earlier meta-analysis survey conducted by Mihankhah et al (11), also confined remarkable resistance rates toward these antibiotics. This high resistance trend is express of enormous antibiotic selection pressure widely due to the inexpensive and readily accessibility of these agents, mostly used as first line or common choices in many healthcare settings. Additionally, a study from other part of Iran the highest resistance rate of *E. coli* samples was reported toward third generation of cephalosporines and gentamicin (14), while in our survey the degree of resistance to third generation of cephalosporines were varied (cefixime (14.2%), ceftriaxone (71.4%). Moreover, highest susceptibility rate to aminoglycosides observed, was consistent with other studies conducted by Eslami et al. (29), from Iran, Bean et al from England and Peterson et al from United States (30, 31). Since these antibiotics are used as last resort in treatment of serious infections.

Similar to *E. coli* samples, all *Staphylococcus* isolates were resistant to aminopenicillins and first generation of cephalosporins. They exhibited total resistance to fluroquinolones, 60% to sulfonamide, 40% to aminoglycosides, 40%. This finding is in agreement with the previous study conducted in Iran (32). However sulfonamides are broadly prescribed for treatment of upper and lower UTIs in recent years, we found an acceptable susceptibility rate of uro-pathogens towards them.

In our study, age and sex were not significantly associated with the development of UTIs in ICPs; a similar picture has been observed by Adukauskiene et al and Agarwal et al (33, 34). Noteworthy there are some conflicting ideas on the higher occurrence of catheter-associated urinary tract infections (CAUTIs) among females (35, 36). In addition, the risk factors which were considerably linked with CAUTIs might include duration of catheter insertion, diabetes, previous catheterization, and length of ICU stay. Various authors have cited these as being important reasons for the development of infection (36, 37).

Our study highlights the prevalence of UTI and emergence of drug resistance pattern within the tertiary hospital among critical ill patients. It is claimed that infections caused by antibiotic-resistant pathogens causes higher mortality and morbidity (38). In our findings, even though it appeared patients were more resistant against oral antibiotics as a result of over-prescription, still therapeutic outcomes with sulfonamide and quinolone are sustainable. Considering the nephrotoxic effect of aminoglycosides, the priority for treatment of hospitalized UTI patient were third generation of cephalosporines. Probably at this juncture, a local antibiogram has to be asses in every ICU set up in order to achieve better clinical decision-making regarding initiation of empirical-

Table 1. Microbiological results of urinary tract infection among intensive care patients.

Culture result		Frequency; N=12	Percentage (%)
Pathogen	*Escherichia coli*	6	50
	Staphylococcus epidermidis	2	16.7
	Staphylococcus aureus	2	16.7
	Staphylococcus saprophyticus	1	8.3
	Pseudomonas	1	8.3
Count	≤3000	2	16.7
	6000	1	8.3
	100,000	9	75
Gram	Positive	5	41.6
	Negative	7	58.4

Table 2. Antibiogram assay of urinary tract infection among intensive care patients.

Antibiogram		**Total**	**Age**; (%)		**Gender**; (%)		**Gram**; (%)	
			< 50	≥ 50	Female	Male	Positive	Negative
Gentamycin	Sen	10 (83.5)	5 (100)	5 (71.4)	5 (100)	5 (71.4)	3 (60)	7 (100)
	Res	2 (16.6)	0 (0)	2 (28.6)	0 (0)	2 (28.6)	2 (40)	0 (0)
Nitrofurantoin	Sen	5 (71.4)	2 (100)	3 (60)	3 (75)	2 (66.6)	-	5 (71.4)
	Res	2 (28.6)	0 (0)	2 (40)	1 (25)	1 (33.4)	-	2 (28.6)
Cephalexin	Sen	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Res	12 (100)	6 (100)	6 (100)	4 (100)	8 (100)	5 (100)	7 (100)
Ciprofloxacin	Sen	6 (50)	3 (50)	3 (50)	4 (57.1)	2 (40)	2 (40)	4 (57.1)
	Res	6 (50)	3 (50)	3 (50)	3 (42.9)	3 (60)	3 (60)	3 (42.9)
Cefixime	Sen	1 (14.2)	1 (33.4)	0 (0)	1 (25)	0 (0)	-	1 (14.2)
	Res	6 (85.7)	2 (66.6)	4 (100)	3 (75)	3 (100)	-	6 (85.8)

Ampicillin	Sen	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Res	12 (100)	7 (100)	5 (100)	6 (100)	6 (100)	5 (100)	7 (100)
Trimethoprim sulfamethoxazole	Sen	9 (75)	5 (83.4)	4 (66.6)	3 (75)	6 (75)	3 (60)	6 (85.7)
	Res	3 (25)	1 (16.6)	2 (33.4)	1 (25)	2 (25)	2 (40)	1 (14.3)
Amikacin	Sen	7 (100)	4 (100)	3 (100)	3 (100)	4 (100)	-	7 (100)
	Res	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ceftriaxone	Sen	5 (71.4)	2 (100)	3 (60)	1 (50)	4 (80)	-	5 (71.4)
	Res	2 (28.6)	0 (0)	2 (40)	1 (50)	1 (20)	-	2 (28.6)
Amoxicillin	Sen	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Res	12 (100)	5 (100)	7 (100)	5 (100)	7 (100)	5 (100)	7 (100)
Nalidixic acid	Sen	6 (85.7)	3 (75)	3 (100)	3 (100)	3 (75)	-	6 (85.7)
	Res	1 (14.3)	1 (25)	0 (0)	0 (0)	1 (25)	-	1 (14.3)
Neomycin	Sen	8 (66.6)	5 (83.3)	3 (50)	2 (50)	6 (75)	2 (40)	6 (85.7)
	Res	4 (33.4)	1 (16.7)	3 (50)	2 (50)	2 (25)	3 (60)	1 (14.3)

antibiotic and will remove hurdles in empirical therapy. Most importantly such a de-escalating program prevents outsourcing antibiotics and minimizes collateral damage to current and future patients.

Among the limitations of our study, detailed evaluation of the resistance pattern based on species in our study was not performed. The result of this study was only limited to one hundred and twelve samples in two hospitals in one of the southwest provinces in the country and a national antibiotic resistance surveillance of this organism is recommended for further study.

Conclusion

Our study highlights the prevalence of UTI and emergence of drug resistance pattern within the tertiary hospital among critical ill patients. Studies addressing on regional differences of antibiotic resistance pattern are becoming crucial particularly with detailed focus on UTIs as one of the major nosocomial infections. Additionally, the main role of this issue in bringing preventive strategies for ICPs has been moved it to the forefront.

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Ethics approval and consent to participate

The present study was approved by the Medical Ethics Committee (Yasuj University of Medical Sciences Ethics committee) of the academy and all experiments were performed in accordance with relevant guidelines and regulations.

Conflict of interest

The authors declare that they have no competing interests.

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