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Original Article

Patterns of etiology and antibiotic resistance of bacteria causing urinary tract infections in the Anhui Provincial Hospital

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Abstract: This study aimed to investigate the distributions and changing trends of pathogens of urinary tract infection in recent years in order to provide a theoretical basis for the rational clinical application of antibiotics. We collected 182 strains of pathogens isolated from patients with urinary tract infection for identification and drug-susceptibility analysis. Among all the pathogens isolated, 107 cases (58.8%) were *Escherichia coli*, with 100% sensitivity to carbapenems. The gram-positive bacteria exhibited a penicillin resistance rate of up to 90% and a vancomycin sensitive rate of 100%. Among the gram-negative bacteria causing urinary tract infections, the *E. coli*-produced extended-spectrum beta-lactamase strain exhibited the highest detection rate (49.5%). Currently, *E. coli* remains the main pathogen of urinary tract infections. The resistance rates of pathogens toward different antibiotics have been increasing, and clinicians should refer to local drug susceptibility test results when choosing the most rational antibiotics.

Keywords: Urinary tract infection, etiology, antibiotic resistance, extended-spectrum β-lactamase

Introduction

Urinary tract infection (UTI) is an extremely common community- and hospital-acquired infection, with a high incidence rate and annual cost of treatment [1-4]. Related studies on etiology and antibiotic susceptibility of UTIs had led to widespread concern globally. The changes in the distributions and drug resistance of pathogens exhibited an important role in clinical UTI treatment [5-7]. Owing to the increasing cases of antibiotic administration, the number of drug-resistant pathogens had increased year after year, thus presenting great challenges to clinical treatment [8-10]. In order to understand the distribution, drug susceptibility, and drug resistance of UTI inpatients at our hospital and to guide the clinical application of antibiotics, 182 UTI patients with positive urine culture results were selected from among the inpatients at our hospital in the past 3 years. Then, pathogens and antibiotic susceptibility test results were retrospectively analyzed.

Methods

Materials

From August 2010 to December 2013, 182 UTI patients with positive urine culture results were selected from among the inpatients at Anhui Provincial Hospital, including 159 women (87.4%) and 23 men (12.6%). This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Anhui Medical University. Written informed consent was obtained from all participants.

Diagnostic criteria

All the selected cases were consistent with the following diagnostic criteria for UTI [11]: for women, having acute uncomplicated urinary symptoms (dysuria, urinary frequency, and bladder discomfort), bacterial colony count of ≥103/mL in cultured specimens from clean middle part of urine, and only a single bacterial

Table 1. Age distributions of UTI patients

Age (years)	19-34	35-64	≥65	Sum
Cases	40	64	78	182
Percentage (%)	22.0	35.2	42.8	100

Table 2. Distribution percentages of pathogens in UTI (%)

Pathogens	Number of stain	Percentage
Gram-negative bacilli	158	86.8
E. coli	107	58.8
Klebsiella pneumoniae	31	17.0
Pseudomonas aeruginosa	7	3.8
Proteus mirabilis	6	3.3
Enterobacter cloacae	3	1.6
Other Gram-negative bacilli	4	2.2
Gram-positive cocci	20	11
Enterococcus faecalis	11	6.0
Staphylococcus aureus	4	2.2
Feces Enterococcus	3	1.6
Staphylococcus epidermidis	2	1.1
Fungi	4	2.2
Sum	182	100

strain; and for men, having acute uncomplicated pyelonephritis symptoms (fever, chills, back pain, with or without urinary frequency, and dysuria) and a bacterial colony count of ≥104/mL in cultured specimens from clean middle part of urine.

Specimen collection

All the urine samples were collected from the clean middle part of the first morning urine under the guidance of clinicians, placed into sterilized containers, and immediately submitted for detection.

Isolation and culture

Urine specimens of 10 μL were aseptically sampled and inoculated onto blood agar plates for culture for 18 to 24 hours at 35-37°C. Colony morphology was observed, and gram staining and colony counting were performed. A positive specimen was defined as containing gram-negative bacteria with a colony count of ≥105/mL, gram-positive bacteria with a colony count of ≥104/mL, and the same pathogen appearing in more than two cultures of the same specimen.

Identification and susceptibility of pathogens

Pathogens were identified by using the Vitek AMS pathogen identification system and ancillary reagents (bioMérieux, France). Susceptibility testing was performed by using the KB paper-diffusion method, with the drug selection rules, interpretation criteria, and quality control requirements of the national Committee for Clinical Laboratory Standards (USA, 2003). The standard strains were *Escherichia* coli ATCC 25922, *Staphylococcus aureus* ATCC 25923, and *Pseudomonas aeruginosa* ATCC 27853, which were all purchased from the National Institutes for Food and Drug Control of the Health Ministry of China.

Results

Age distribution of the UTI patients

Among the 182 UTI patients with positive urinary culture results, 40 (22.0%) were in the young age group (19-34 years old), 64 (35.2%) were in the middle-and-older age group (35-64 years old), and 78 (42.8%) were in the older age group (over 65 years old; **Table 1**).

Distributions of pathogens

Among the 182 cases, 178 (97.8%) were bacterial infections and 4 (2.2%) were fungal infections. Among the bacterial pathogens, 158 (86.8%) were gram-negative bacteria and 20 (11.0%) were gram-positive bacteria. Among the isolated pathogens, the top 5 bacteria were *E. coli* (107 cases, 58.8%), *Klebsiella pneumoniae* (31 cases, 17.0%), *Enterococcus faecalis* (11 cases, 6.0%), *Pseudomonas aeruginosa* (7 cases, 3.8%), and *Proteus mirabilis* (6 cases, 3.3%; **Table 2**).

Susceptibility test results

The gram-negative bacteria showed various degrees of antibiotic resistance toward different antibiotics. *E. coli* exhibited a resistance rate as high as 86.9% to ampicillin and 61.7% to quinolones such as ofloxacin. It was much more sensitive to third-generation cephalosporins, such as ceftazidime and sodium ceftriaxone, with resistance rates of 23.4% and 46.7%, respectively. Its susceptibility to carbapenems was 100%. The susceptibility of *K. pneumoniae* to carbapenems remains high at 100%, while

Table 3. Drug resistance rates of main pathogens towards the antibiotics in UTI (%)

Antibiotics	E. coli (n=107)				Klebsiella pneumonia (n=31)				Gram positive cocci (n=20)			
	Resistance		Sensitivity		Resistance		Sensitivity		Resistance		Sensitivity	
	Stain number	Resistance rate	Stain number	Sensitivity rate	Stain number	Resistance rate	Stain number	Sensitivity rate	Stain number	Resistance rate	Stain number	Sensitivity rate
Amikacin	32	29.9	75	70.1	3	9.7	28	90.3	-	-	-	-
Aztreonam	66	61.7	41	38.3	9	29.0	22	71.0	-	-	-	-
Ceftazidime	25	23.4	82	76.6	7	22.6	24	77.4	-	-	-	-
Ceftriaxone	50	46.7	57	53.3	10	32.3	21	67.7	-	-	-	-
Cefepime	35	32.7	72	67.3	10	32.3	21	67.7	-	-	-	-
Cefotetan	52	48.6	55	51.4	11	35.5	20	64.5	-	-	-	-
Cefazolin	53	49.5	54	50.5	12	38.7	19	61.3	-	-	-	-
Ertapenem	0	0.0	107	100.0	0	0.0	31	100.0	-	-	-	-
Imipenem	0	0.0	107	100.0	0	0.0	31	100.0	-	-	-	-
Nitrofurantoin	20	18.7	87	81.3	7	22.6	24	77.4	-	-	-	-
Compound Sulfamethoxazol	60	56.1	47	43.9	10	32.3	21	67.7	-	-	-	-
Tobramycin	66	61.7	41	38.3	11	35.5	20	64.5	-	-	-	-
Piperacillin tazobactam	15	14.0	92	86.0	6	19.4	25	80.6	-	-	-	-
Ampicillin	93	86.9	14	13.1	31	100.0	0	0.0	14	70.0	6	30.0
Ciprofloxacin	86	80.3	21	19.6	13	41.9	18	58.1	13	65.0	7	35.0
Gentamicin	60	56.1	47	43.9	10	32.3	21	67.7	10	50.0	10	50.0
Levofloxacin	66	61.7	41	38.3	12	38.7	19	61.3	12	60.0	8	40.0
Erythromycin	-	-	-	-	-	-	-	-	14	70.0	6	30.0
Penicillin	-	-	-	-	-	-	-	-	18	90.0	2	10.0
Tetracycline	-	-	-	-	-	-	-	-	15	75.0	5	25.0
Vancomycin	-	-	-	-	-	-	-	-	0	0	20	100.0

Table 4. Detection rates of ESBL-producing gram negative bacilli

Pathogens	Stain number	EBSL-producing stain number	Detection rate
E. coli	107	53	49.5
Klebsiella pneumoniae	31	4	12.9
Pseudomonas aeruginosa	7	0	0.0
Proteus mirabilis	6	0	0.0
Enterobacter cloacae	3	0	0.0
Other Gram-negative bacilli	4	1	25.0

the resistance of the bacteria to other kinds of antibiotic drugs was of different levels.

The gram-positive bacteria exhibited resistance to penicillin at a rate as high as 90% and to ampicillin at 70%. Their resistance rates to quinolones were also high, such as 60% to levofloxacin and 65% to ciprofloxacin, while their susceptibility to vancomycin remained high at 100% (**Table 3**).

Test results for extended-spectrum beta-lactamases produced by gram-negative bacteria strains

Among the 158 UTI cases caused by gram-negative bacteria, the extended-spectrum beta-lactamase (ESBL)-producing *E. coli* strain exhibited the highest detection rate (49.5%), followed by *K. pneumonia* (12.9%). By contrast, no ESBL-positive strains were detected from the UTI cases caused by *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Enterobacter cloacae* (**Table 4**).

Discussion

UTI is clinically considered as a common infectious disease. Women account for most of the patients because their urethra is closer to the anus and vagina. Thus, the female urethra is vulnerable to contamination by vaginal secretions and feces. Moreover, it is short and wide, which makes it easy for pathogens to invade the bladder. By contrast, in men, the urethra is slender. Meanwhile, prostatic fluid contains antimicrobial substances; therefore, men are less prone to develop UTI [12]. UTI often occurs in older women. This is related to the facts that after menopause, women experience a decrease in estrogen levels, systemic and/or local immune dysfunction, and some alterations in renal physiology and anatomy.

With the widespread administration of antibiotics, the cure rate of UTI has greatly increased. However, at the same time, antibiotic abuse also caused an increase in drug resistance of pathogens. Studies have shown that the changes in the distribution and drug resistance of UTI pathogens were associated with time and geographical factors [13]. Therefore, analysis of the distributions and drug resistance of local UTI pathogens could effectively help to guide the clinical application of antibiotics.

The comparison between the statistical results of this study and those conducted at our hospital in 2006 [14] revealed that the distribution of UTI pathogens in our hospital was still mainly *E. coli*, consistent with the results reported in the literature abroad [15], which exhibited significantly increased resistance to third-generation cephalosporins and quinolones while maintaining high sensitivity to carbapenems. The drug resistance of other kinds of pathogens also exhibited a significant increase.

In this study, the drug resistance rates of gram-negative bacilli and gram-positive cocci toward the ampicillin were higher, consistent with the reports of foreign literature [16, 17]. This finding suggests that ampicillin was not available for the treatment of partial UTI or should be applied in combination with other drugs [15]. In clinical application, quinolones such as ofloxacin are much more common. The present study showed that the gram-negative bacilli and gram-positive cocci exhibited higher resistance rates toward quinolones, with significant cross-resistance. Therefore, quinolones should not be recommended as the preferred therapy without obtaining susceptibility test results [18].

The resistance of gram-negative bacilli toward third-generation cephalosporins was gradually increased. Furthermore, their resistance to fourth-generation cephalosporins emerged, which was considered to be related with the clinical abuse of antibiotics. The gram-negative bacilli maintained high sensitivity to carbapenems in this study, and their sensitivity rates to

E. coli and *K. pneumoniae* were both 100%. However, previous studies reported that gram-negative bacilli with antibiotic resistance were found in some areas [19]. Noteworthy is the finding that the resistance rate of gram-negative bacilli toward nitrofurantoin was always low, consistent with the results in other regions [20]. The proposed reason for the hypersensitivity toward this drug is inconclusive, which might be related to the different mechanisms of action and few clinical applications.

Gram-positive cocci accounted for a relatively small proportion of the UTI pathogens, among which *E. coli* was the most prevalent. Gram-positive cocci exhibited a high resistance rate to penicillin, reaching up to 90%. Their resistance rate to quinolones and macrolides were also high, but it maintained 100% sensitivity to vancomycin. For clinical therapeutic application, it could be appropriately combined with other antibiotics according to susceptibility test results.

ESBLs could decompose penicillins, cephalosporins, aztreonam, and other antibacterial drugs, making them ineffective against the bacteria or making these bacteria resistant to these drugs. The results of this study showed that ESBLs were most commonly produced by *E. coli* and *K. pneumoniae*. Results of in vitro antibiotic susceptibility testing for ESBL-producing strains sometimes show partial or complete sensitivity to third-generation cephalosporins or aztreonam, among other drugs, while showing actual resistance in patients. Studies showed that the preferred treatment for ESBL-producing strains should be imipenem or a complex preparation that includes enzyme inhibitors [21]. Therefore, ESBL detection for identifying gram-negative bacilli strains has important significance toward the clinical treatment and rational use of antibiotics.

In summary, the main pathogen of the UTI cases in our hospital was still *E. coli*, whereas gram-positive cocci accounted for a small proportion of cases. Gram-negative bacilli had increasing resistance to penicillins, quinolones, and cephalosporins but maintained a high sensitivity to carbapenems, but the generation of resistance should be wary of. The resistance rates of gram-positive cocci to penicillins, quinolones, and macrolides were all high. However, some drugs are not suitable as monotherapies for UTI and should be combined with appropriate antibiotics according to susceptibility test results. The ESBL-producing gram-negative bacilli strains, namely *E. coli* and *K. pneumonia*, had higher detection rates. In clinical application, the rational choice of antibiotics should be based on susceptibility test results.

Disclosure of conflict of interest

None.

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