

Characteristics of and antibiotic resistance in urinary tract pathogens isolated from patients with upper urinary tract stones

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Abstract: To investigate the distribution characteristics and antibiotic resistance patterns of uropathogens in patients with upper urinary calculi and urinary tract infections, data on sex, age, positive midstream urine culture results and drug sensitivity results were collected. The statistical program SPSS 26.0 was used for statistical analysis. Among the 1414 positive urine samples, the most common pathogens were *Escherichia coli* (36.4%), *Enterococcus faecalis* (13.8%), *Staphylococcus epidermidis* (7.5%), *Klebsiella pneumoniae* (5.0%), *Streptococcus agalactiae* (3.4%) and *Enterococcus faecium* (3.3%). The incidences of *E. coli* (48.6%), *K. pneumoniae* (6.3%) and *Proteus mirabilis* (4.2%) were higher in female patients than in male patients (23.2%, 3.5%, 0.6%, respectively; $P < 0.05$). *E. faecalis* was detected more frequently in the young group (16.0%) than in the elderly group (11.2%; $P < 0.01$). Most of the isolates were resistant to levofloxacin and ciprofloxacin, while few were resistant to imipenem, meropenem, cefoperazone/sulbactam, piperacillin/tazobactam and amikacin. The bacterial spectra in patients with urinary stones varied by sex and age, which should be taken into consideration during treatment. The proportion of *E. faecium* showed an upward trend, while those of *S. epidermidis* and *S. agalactiae* demonstrated downward trends in the study period. Regardless, carbapenems, cefoperazone/sulbactam, piperacillin/tazobactam and amikacin are good choices for serious cases.

Keywords: Urinary tract infection; calculi; bacterial spectrum; antibiotic resistance.

INTRODUCTION

Urinary tract infection (UTI) and calculi are the most common diseases treated by urologists, with high incidence and recurrence rates. (Thongprayoon, *et al.* 2020, Wagenlehner, *et al.* 2020) Importantly, they always exhibit reciprocal causation. On the one hand, stones block the ureter and cause hydronephrosis, which provides favorable conditions for the growth and reproduction of bacteria. (Holmbom, *et al.* 2022) On the other hand, infection damages the urinary tract mucosa, upregulates osteopontin in renal tubular cells and changes the pH value of urine to promote the formation of urinary calculi. (Espinosa-Ortiz, *et al.* 2019) To address this problem, removing stones as completely as possible has become the foundation of treatment. Currently, minimally invasive surgeries, such as ureteroscopy and percutaneous nephroscopy, are usually performed to manage calculi.

However, perioperative infection promotes a longer treatment cycle and can even lead to serious complications, such as sepsis and infective shock. (Schnabel, *et al.* 2019, MacCraith, *et al.* 2020) Therefore, effectively controlling infection is another challenge for urologists.

According to the latest EAU Urological Infections Guidelines, appropriate antibiotic treatment depends on the detection of possible pathogens and local antibiotic resistance patterns, as well as assessment of the severity of the disease. Studies have shown that the bacterial spectrum

of urinary calculi is significantly different from that of simple UTI and the bacterial spectrum becomes more complex due to the abuse of antibiotics and the emergence of various drug-resistant bacteria. (De Lorenzis, *et al.* 2020) Given that relevant epidemiological information is relatively limited and mostly outdated in the context of increasing antibiotic resistance rate, (Asadi Karam, *et al.* 2019, Wang, *et al.* 2020) this study is devoted to analysis of the characteristics and resistance profiles of uropathogens isolated from calculi patients, with the hope of providing a basis for the management of this disease.

MATERIALS AND METHODS

Patient information

Between January 2016 and January 2020, data of 1,414 adult patients (>18 years) with upper tract urinary stones and a positive midstream urine culture were retrospectively evaluated. Patients who had chronic renal failure, kidney transplantation, immunosuppressive diseases, urine retention, spinal cord injury or confirmed pregnancy were excluded. The age, sex and diabetes status of patients were reviewed. To analyze uropathogens in patients of different ages, patients were separated into two groups: A≤60 years; B>60 years. All patients signed the study consent form for the collection and analysis of their urine. Ethical approval was No. KY2020K088 from the Ethics Committee of the Second Hospital of Tianjin Medical University.

Urine collection and culture

After instructing the patients to clean their vulva or urinary meatus, fifty milliliter of midstream urine was collected in

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sterile containers at air temperature and sent to the laboratory within two hours. All the samples were inoculated onto MacConkey agar (Oxoid, England) and blood agar (Oxoid) plates and incubated at 37°C for 18-24 hours, depending on the microorganism. When monomorphic bacterial growth was higher than 10⁵ CFU/mL, the culture was considered positive.

Drug sensitivity experiments

The identification of isolates and susceptibility tests were performed on a VITEK® 2 automated system (BioMérieux®, Marcy l'Étoile and France). The minimal inhibitory concentrations (MICs) of the antimicrobials were determined and bacterial strains were considered to be susceptible, intermediate or resistant according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) (Wayne, 2021). Intermediate and resistant isolates were grouped together at the time of the analysis.

A strain was considered highly resistant to the antibiotic when its resistance rate against the antibiotic was more than 20%. (Chen, *et al.* 2018) Quality control was assessed using *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853 and *Enterococcus faecalis* ATCC 29212. For Gram-negative bacteria, sensitivity to imipenem, meropenem, ceftazidime, cefoperazone/sulbactam, cefepime, aztreonam, piperacillin/tazobactam, amikacin, gentamicin, tobramycin, levofloxacin and ciprofloxacin was tested. For Gram-positive bacteria, sensitivity to penicillin, ampicillin, levofloxacin, ciprofloxacin, vancomycin, teicoplanin, quinupristin/dalfopristin, tigecycline, rifampicin, tetracycline, nitrofurantoin and linezolid was tested.

STATISTICAL ANALYSIS

The statistical software SPSS 26.0 for Windows was used for statistical analysis. A *P* value less than 0.05 was considered significant. Since the ages in this study did not follow a normal distribution, a nonparametric test was used to compare the age differences between men and women. The chi-square test was used to detect sex and age differences among the strains. When the chi-square test was not suitable, Fisher's exact probability test was used. The chi-square trend test was performed to analyze the changes in bacterial proportions between 2016 and 2020.

RESULTS

In this study, a total of 1414 patients with urinary stones and positive midstream urine culture were included, with an age range of 19 to 92 years. There were 730 female and 684 male patients. The median ages of the female and male patients were 60 years and 59 years, respectively (*P*=0.111).

Bacterial spectra

Of the 1414 positive urine samples, Gram-negative bacteria accounted for 60%, Gram-positive bacteria

accounted for 36.9% and fungi accounted for the remaining 3.1%. To ensure a valid sample size, the main bacteria responsible for UTIs were selected, namely, *E. coli* (36.4%), *E. faecalis* (13.8%), *S. epidermidis* (7.5%), *K. pneumoniae* (5.0%), *S. agalactiae* (3.4%), *E. faecium* (3.3%), *Staphylococcus hemolyticus* (3.3%), *Pseudomonas aeruginosa* (3.1%), *Proteus mirabilis* (2.5%) and *Acinetobacter baumannii* (2.1%). These bacteria accounted for 80.1% of the total uropathogens (table 1). Other uncommon uropathogens comprised 59 species, accounting for 19.8%, including fungi. Fungi were mostly *Candida* species, mainly *Candida albicans*.

The bacterial distribution in each sex was significantly different. Although the *E. coli* was the primary bacterial species in subjects with UTIs in both sexes, its incidence was higher in female patients (48.6%) than in male patients (23.2%; *P*<0.001). In addition, the prevalence of *P. mirabilis*, the main cause of struvite development, was higher in female patients (4.2%) than in male patients (0.6%; *P*< 0.001). This trend was similar for *K. pneumoniae*. However, *P. aeruginosa* and *A. baumannii* had higher proportions in males. Interestingly, Gram-positive bacteria were more frequently detected in men, whereas the prevalence rates of *S. agalactiae* and *E. faecium* did not differ significantly between men and women.

There was no difference in the sex ratio between the young group (M/F=0.96) and the elderly group (M/F=0.91; *P*=0.565). However, the incidence of *E. faecalis* in the young group (16.0%) was higher than that in the elderly group (11.2%; *P*<0.01). In contrast, *E. faecium* and *P. aeruginosa* were more abundant in the elderly group (*P*<0.05) (table 1).

Some noteworthy changes in the prominent bacteria responsible for UTIs were observed from 2016 to 2020 (table 2). In general, the incidence rates of *S. epidermidis* and *S. agalactiae* decreased, while the incidence rate of *E. faecium* increased (fig. 1).

In particular, the incidence rate of *E. faecalis* gradually increased in males, while there was no significant change in females (table 3). Although the compositions of uropathogens varied from year to year, *E. coli* was predominant in UTI patients throughout the study period, followed by *E. faecalis*.

Antibiotic sensitivity testing

The drug susceptibility profiles of the bacterial isolates are given in tables 4 and 5. For Gram-negative uropathogens, relatively high resistance rates to gentamicin, levofloxacin and ciprofloxacin were observed. *E. coli* also had higher resistance rates to ceftazidime, cefepime and tobramycin than the other tested antibiotics.

Table 1: Gender and age distributions of uropathogens in patients with urinary stones

Bacteria	Total	Male	Female	A	B
N (%)	N=1414	N=684	N=730	N=762	N=652
<i>Escherichia coli</i>	514(36.4%)	159(23.2%)	355(48.6%)*	268(35.2%)	246(37.7%)
<i>Enterococcus faecalis</i>	195(13.8%)	120(17.5%)	75(10.3%)*	122(16.0%)	73(11.2%) ^A
<i>Staphylococcus epidermidis</i>	106(7.5%)	70(10.2%)	36(4.9%)*	65(8.5%)	41(6.3%)
<i>Klebsiella pneumoniae</i>	70(5.0%)	24(3.5%)	46(6.3%)*	42(5.5%)	28(4.3%)
<i>Streptococcus agalactiae</i>	48(3.4%)	29(4.2%)	19(2.6%)	29(3.8%)	19(2.9%)
<i>Enterococcus faecium</i>	46(3.3%)	20(2.9%)	26(3.6%)	16(2.1%)	30(4.6%) ^A
<i>Staphylococcus haemolyticus</i>	46(3.3%)	35(5.1%)	11(1.5%)*	25(3.3%)	21(3.2%)
<i>Pseudomonas aeruginosa</i>	44(3.1%)	31(4.5%)	13(1.8%)*	17(2.2%)	27(4.1%) ^A
<i>Proteus mirabilis</i>	35(2.5%)	4(0.6%)	31(4.2%)*	24(3.1%)	11(1.7%)
<i>Acinetobacter baumannii</i>	29(2.1%)	22(3.2%)	7(1.0%)*	12(1.6%)	17(2.6%)

*Significantly different between males and females ($P < 0.05$).

^ASignificantly different between A and B ($P < 0.05$).

A: age \leq 60y; B: age $>$ 60y.

Table 2: Bacterial findings in patients with UTI and stones 2016-2020

Bacteria	2016	2017	2018	2019	2020	<i>P</i> for trend
N (%)	N=191	N=345	N=298	N=341	N=239	
<i>Escherichia coli</i>	79(41.4%)	116(33.6%)	110(36.9%)	140(41.1%)	69(28.9%)	0.212
<i>Enterococcus faecalis</i>	21(11.0%)	52(15.1%)	31(10.4%)	49(14.4%)	42(17.6%)	0.119
<i>Staphylococcus epidermidis</i>	20(10.5%)	28(8.1%)	20(6.7%)	29(8.5%)	9(3.8%)	0.031*
<i>Klebsiella pneumoniae</i>	11(5.8%)	19(5.5%)	14(4.7%)	19(5.6%)	7(2.9%)	0.238
<i>Streptococcus agalactiae</i>	6(3.1%)	20(5.8%)	14(4.7%)	1(0.3%)	7(2.9%)	0.023*
<i>Enterococcus faecium</i>	4(2.1%)	2(0.6%)	8(2.7%)	23(6.7%)	9(3.8%)	0.001*
<i>Staphylococcus haemolyticus</i>	2(1.0%)	11(3.2%)	9(3.0%)	14(4.1%)	10(4.2%)	0.066
<i>Pseudomonas aeruginosa</i>	11(5.8%)	8(2.3%)	8(2.7%)	8(2.3%)	9(3.8%)	0.420
<i>Proteus mirabilis</i>	0(0.0%)	14(4.1%)	11(3.7%)	0(0.0%)	10(4.2%)	0.625
<i>Acinetobacter baumannii</i>	4(2.1%)	6(1.7%)	7(2.3%)	10(2.9%)	2(0.8%)	0.786

*Statistically significant based on chi-square trend tests from 2016 to 2020 ($P < 0.05$).

Table 3: Bacterial findings in patients with UTI and stones 2016-2020 (grouped by gender)

Bacteria	Gender	2016 T=M+F	2017 T=M+F	2018 T=M+F	2019 T=M+F	2020 T=M+F	<i>P</i> for trend
N (%)		191=105+86	345=166+179	298=136+162	341=164+177	239=113+126	
<i>Escherichia coli</i>	Male	25 (23.81%)	41 (24.70%)	37 (27.21%)	38 (23.17%)	18 (15.93%)	0.167
	Female	54 (62.79%)	75 (41.90%)	73 (45.06%)	102 (57.63%)	51 (40.48%)	0.328
<i>Enterococcus faecalis</i>	Male	15 (14.29%)	29 (17.47%)	16 (11.76%)	32 (19.51%)	28 (24.78%)	0.044*
	Female	6 (6.98%)	23 (12.85%)	15 (9.26%)	17 (9.60%)	14 (11.11%)	0.850
<i>Staphylococcus epidermidis</i>	Male	16 (15.24%)	15 (9.04%)	13 (9.56%)	22 (13.41%)	4 (3.54%)	0.080
	Female	4 (4.65%)	13 (7.26%)	7 (4.32%)	7 (3.95%)	5 (3.97%)	0.318
<i>Klebsiella pneumoniae</i>	Male	4 (3.81%)	7 (4.22%)	6 (4.41%)	6 (3.66%)	1 (0.88%)	0.241
	Female	7 (8.14%)	12 (6.70%)	8 (4.94%)	13 (7.34%)	6 (4.76%)	0.482
<i>Streptococcus agalactiae</i>	Male	2 (1.90%)	15 (9.04%)	8 (5.88%)	1 (0.61%)	3 (2.65%)	0.074
	Female	4 (4.65%)	5 (2.79%)	6 (3.70%)	0 (0.00%)	4 (3.17%)	0.206
<i>Enterococcus faecium</i>	Male	3 (2.86%)	0 (0.00%)	3 (2.21%)	10 (6.10%)	4 (3.54%)	0.049*
	Female	1 (1.16%)	2 (1.12%)	5 (3.09%)	13 (7.34%)	5 (3.97%)	0.012*
<i>Staphylococcus haemolyticus</i>	Male	2 (1.90%)	9 (5.42%)	5 (3.68%)	12 (7.32%)	7 (6.19%)	0.108
	Female	0 (0.00%)	2 (1.12%)	4 (2.47%)	2 (1.13%)	3 (2.38%)	0.289
<i>Pseudomonas aeruginosa</i>	Male	9 (8.57%)	5 (3.01%)	5 (3.68%)	5 (3.05%)	7 (6.19%)	0.535
	Female	2 (2.33%)	3 (1.68%)	3 (1.85%)	3 (3.69%)	2 (1.59%)	0.829
<i>Proteus mirabilis</i>	Male	0 (0.00%)	2 (1.20%)	2 (1.47%)	0 (0.00%)	0 (0.00%)	0.467
	Female	0 (0.00%)	12 (6.70%)	9 (5.56%)	0 (0.00%)	10 (7.94%)	0.521
<i>Acinetobacter baumannii</i>	Male	4 (3.81%)	3 (1.81%)	5 (3.68%)	9 (5.49%)	1 (0.88%)	1.000
	Female	0 (0.00%)	3 (1.68%)	2 (1.23%)	1 (0.56%)	1 (0.79%)	0.884

*Statistically significant based on chi-square trend tests from 2016 to 2020 ($P < 0.05$). T=M+F: Total=Male + Female

Table 4: The drug resistance of Gram-negative uropathogens to commonly used antimicrobial agents

Antimicrobial agents	<i>Escherichia coli</i>	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>	<i>Proteus mirabilis</i>	<i>Acinetobacter baumannii</i>
Imipenem	1.2%	4.3%	18.6%	66.7%	6.9%
Meropenem	1.7%	—	19.2%	—	0.0%
Ceftazidime	40.7%	33.3%	7.7%	4.8%	26.3%
Cefoperazone /Sulbactam	12%	23.8%	11.5%	0%	5.3%
Cefepime	35.5%	28.6%	16.3%	11.8%	26.9%
Aztreonam	34.4%	26.5%	53.8%	0.0%	—
Piperacillin /Tazobactam	7.9%	17.1%	12.2%	0.0%	23.5%
Amikacin	4.2%	12.9%	4.7%	0.0%	7.7%
Gentamicin	52.2%	28.9%	30.8%	26.1%	36.4%
Tobramycin	48.5%	32.3%	16.3%	15.0%	27.8%
Levofloxacin	92.0%	52.9%	34.9%	76.5%	27.6%
Ciprofloxacin	88.6%	52.6%	23.3%	78.3%	31.6%

Table 5: The drug resistance of Gram-positive uropathogens to commonly used antimicrobial agents

Antimicrobial agents	<i>Enterococcus faecalis</i>	<i>Staphylococcus epidermidis</i>	<i>Streptococcus agalactiae</i>	<i>Enterococcus faecium</i>	<i>Staphylococcus haemolyticus</i>
Penicillin	4.1%	88.5%	0.0%	95.7%	93.2%
Ampicillin	3.1%	—	0.0%	91.3%	—
Levofloxacin	32.6%	49.1%	70.8%	100.0%	75.6%
Ciprofloxacin	38.3%	47.7%	—	100.0%	82.9%
Vancomycin	0.0%	0.0%	0.0%	0.0%	0.0%
Teicoplanin	0.0%	0.0%	—	3.7%	0.0%
Quinupristin /Dalfopristin	93.3%	0.0%	—	0.0%	0.0%
Tigecycline	0.0%	0.0%	0.0%	0.0%	0.0%
Rifampicin	85.4%	0.9%	—	82.8%	8.9%
Tetracycline	85.0%	19.8%	64.6%	52.2%	37.8%
Nitrofurantoin	9.4%	1.9%	—	95.7%	2.2%
Linezolid	1.1%	0.0%	0.0%	2.2%	2.2%

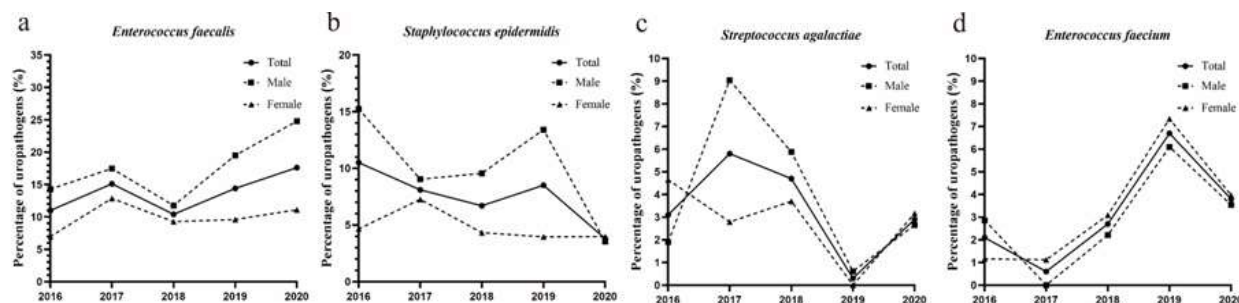


Fig. 1: The trends of uropathogens in patients with UTI and stones 2016-2020. (a) The proportion of *E. faecalis* showed an upward trend in males ($P=0.044$), while there was no significant change in females ($P=0.850$). (b) The proportion of *S. epidermidis* showed a downward trend in total ($P=0.031$). (c) The proportion of *S. agalactiae* showed a downward trend in total ($P=0.023$). (d) The proportion of *E. faecium* showed an upward trend in total ($P=0.001$).

Notably, *E. coli* displayed susceptibility to imipenem, meropenem, cefoperazone/ sulbactam, piperacillin/ tazobactam and amikacin and resistance to aztreonam. *K. pneumoniae* demonstrated multidrug resistance and only showed sensitivity to imipenem, piperacillin/tazobactam and amikacin. *P. aeruginosa* was sensitive to most antibiotics except aztreonam, gentamicin, levofloxacin and ciprofloxacin, with the highest resistance to aztreonam. *P. mirabilis* was sensitive to cefoperazone/ sulbactam, aztreonam, piperacillin/ tazobactam and amikacin, while it had high resistance to imipenem, levofloxacin and

ciprofloxacin. *A. baumannii* was sensitive to only imipenem, meropenem, cefoperazone/ sulbactam and amikacin.

Among the Gram-positive isolates, most bacteria had high resistance to levofloxacin, ciprofloxacin and tetracycline. However, vancomycin, teicoplanin, tigecycline and linezolid had good inhibitory effects on the majority of Gram-positive uropathogens. Although both *E. faecium* and *E. faecalis* were resistant to rifampicin, the resistance rates of *E. faecalis* to penicillin, ampicillin and

nitrofurantoin were much lower those of *E. faecium*. *Staphylococcus* spp. showed similar resistance to penicillin, levofloxacin and ciprofloxacin. In addition, *Staphylococcus* spp. had favorable sensitivity to vancomycin, teicoplanin, quinupristin/ dalfopristin, tigecycline, rifampicin, nitrofurantoin and linezolid. It is of great importance to note that *S. agalactiae* was sensitive to most of the antibiotics except levofloxacin and tetracycline.

DISCUSSION

In this study, the types of bacteria isolated from the urine of patients with urolithiasis varied and the proportions of bacteria differed by sex and age. Moreover, the distribution of bacteria in the population varied from year to year. Unfortunately, the phenomenon of multidrug resistance still exists.

A previous study showed that the bacterial spectrum of complicated UTIs was much wider than that of uncomplicated UTIs. (Sabih and Leslie. 2022) Baenas DF *et al.* found 13 strains in patients with uncomplicated UTIs, (Baenas *et al.* 2017) whereas Chen D *et al.* identified 42 strains of bacteria from the urine of patients with calculi and infection. (Chen, *et al.* 2018) In our study, 69 pathogens were isolated from urine, which is basically consistent with the above results. However, it is difficult to judge whether these differences were genuine epidemiological changes or resulted from the use of advanced molecular microbiological diagnostics, which needs further study.

E. coli is the most common pathogen in both uncomplicated and complicated UTIs. (Faine *et al.* 2022) In our study, *E. coli* was the major pathogen in patients with calculi, but the proportion was lower than that in patients with uncomplicated UTIs. (Kornfält Isberg, *et al.* 2019) This might contribute to the wider spectrum of bacteria in complicated UTIs. Following *E. coli*, *E. faecalis* accounted for up to 13.8% of the pathogenic bacteria in this study, similar to the findings of Ravishankar U *et al.* (Ravishankar *et al.* 2021) Regarding Enterococcus spp., there is a strong association between Enterococcus spp. and catheter-associated UTI. (Tien, *et al.* 2017) In this study, the upward trends of the prevalence of *E. faecalis* and *E. faecium* may be related to the increased use of urethral catheters.

Increasing evidence indicates that urinary catheterization can result in a robust inflammatory response (Saini, *et al.* 2017) and induce fibrinogen release, which promotes the growth of *E. faecalis* and enhances biofilm formation on the catheter. (Colomer-Winter, *et al.* 2019) Therefore, in addition to catheter, stones may stimulate the inflammatory response in the body, leading to fibrinogen secretion and providing favorable conditions for bacterial adherence and

colonization. Among the Staphylococcus species, *S. epidermidis* was predominant, accounting for 7.5%, similar to the findings of Qiao LD *et al.* (Qiao, *et al.* 2013, Huang, *et al.* 2021) However, the frequency of *S. epidermidis* decreased gradually during the observation period. It is worth mentioning that the prevalence rate of *S. agalactiae* in our study was slightly higher than that reported by De Lorenzis E *et al.* (De Lorenzis, *et al.* 2020).

This might be ascribed to the influence of diabetes mellitus, which is a known predisposing factor for *S. agalactiae* infection in adults. (Al Benwan, *et al.* 2010, Matheson, *et al.* 2021) In this study, 22.6% (320/1414) of the patients had diabetes. However, it may be due to the limitation of sample size. We still failed to find a difference in microflora between diabetic and nondiabetic patients after excluding the influence of age and sex.

The isolated strains were obviously different between males and females. The higher occurrence of *E. coli* in female patients may be related to not only a shorter urethra but also sex hormones. (Dias, *et al.* 2022) Generally, males are susceptible to infection with Gram-positive bacteria, while females tend to be infected by Gram-negative bacteria. (De Lorenzis, *et al.* 2020) Specifically, the incidence of *P. aeruginosa* in males was higher than that in females. Likewise, *P. aeruginosa* was more common in the elderly group than in the young group. (Gu, *et al.* 2022) Although increased susceptibility to *P. aeruginosa* in the elderly may due to the fact that the elderly exhibit more basic diseases and lower immunity power, the reason why young people were more susceptible to *E. faecalis* remains to be further studied.

As recommended by the latest EAU Urological Infections Guidelines, levofloxacin and ciprofloxacin are not suitable as empirical antimicrobial therapies because of their high resistance rates. In this study, all strains were resistant to levofloxacin and ciprofloxacin. Only amikacin, cefoperazone/ sulbactam, piperacillin/ tazobactam and carbapenems have relatively good therapeutic effects.

Unfortunately, *P. mirabilis* has developed resistance to imipenem. *K. pneumoniae* is not sensitive to cefoperazone/ sulbactam because of β -lactamase production, (Vachvanichsanong *et al.* 2020) and piperacillin/ tazobactam is not adequate for the treatment of *A. baumannii* infections. Similarly, there are limited options for Gram-positive bacteria: Vancomycin, teicoplanin, tigecycline and linezolid. Calculi and concomitant infection remain refractory. Given the impact on the microbiota and the persistent existence of antibiotic-resistant uropathogens, finding novel treatment strategies is becoming a pressing issue.

There are some limitations that must be mentioned. First, because of the nature of retrospective research, there may

be recall bias. Moreover, the subjects in this study were adults, so it is not known whether the results are applicable to children and adolescents. Overall, due to urinary tract obstruction in patients with urinary calculi, midstream culture may not fully represent the infection status in patients with urinary calculi. Therefore, midstream urine culture combined with stone culture may have greater value in the treatment of patients, which requires further study.

CONCLUSION

The bacterial spectrum in patients with urinary stones is complex and varies by sex and age. Due to the differences in drug resistance profiles of different pathogens, the importance of immediate urine culture and drug sensitivity tests are emphasized. However, considering that the antibiotic resistance patterns in uropathogens have not deviated significantly in recent years, carbapenems, cefoperazone/sulbactam, piperacillin/ tazobactam and amikacin can still be used as empirical drugs in the treatment of urinary calculi complicated with severe UTI when the results of bacterial culture and drug sensitivity are not yet available.

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