Prevalence, risk factors and microorganisms of urinary tract infections in patients with type 2 diabetes mellitus: a retrospective study in China

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**Background:** Urinary tract infections (UTIs) occur more frequently in diabetic patients. This study was conducted to investigate the prevalence, risk factors and microorganisms of UTIs in Chinese patients with type 2 diabetes (T2D).

**Patients and methods:** A total of 3,652 Chinese inpatients with T2D were reviewed and data on their clinical characteristics, symptoms of UTIs, random blood glucose, HbA1c, glutamic acid decarboxylase antibody, insulin autoantibody, albumin excretion rate in 24-hour urine, urine culture and susceptibility to antibiotics, and so on were collected. Binary logistic analysis was performed to look for risk factors of UTIs.

**Results:** There were 409 (11.2%) patients suffering from UTIs. Gender, age, random blood glucose, insulin autoantibody and albumin excretion rate in 24-hour urine were the risk factors of UTIs in diabetic patients. The percentage of positive urine cultures was higher in the asymptomatic bacteriuria patients than in symptomatic patients (P<0.001). The incidence of septicemia was considerable in the UTIs and asymptomatic bacteriuria groups. Escherichia coli was the most common pathogenic microorganism isolated in diabetic patients with UTIs, and one-half of the E. coli infections were multidrug resistant. Furthermore, meropenem was the most effective antibiotic on E. coli.

**Conclusion:** We suggest that a routine urine analysis or urine culture should be conducted in patients with T2D diabetes who have the identified risk factors. The UTIs might affect the islet function or blood glucose control in patients with T2D. Before a doctor decides to prescribe antibiotics to a diabetic patient with UTIs, the drug sensitivity test should be performed.

**Keywords:** urinary tract infections, asymptomatic bacteriuria, diabetes, multidrug resistant

**Introduction**

Patients with diabetes are susceptible to infections (about four times more than non-diabetics), which might be ascribed to their abnormalities in immune function. Among the infections, urinary tract infections (UTIs) occur more frequently in diabetic patients because of urine glucose excretion and chronic neurologic bladder dysfunction. Furthermore, the prevalence of asymptomatic bacteriuria (ASB) in diabetic patients is three times higher than in normal people; however, whether the symptomatic UTIs are preceded by ASB is unknown.

UTIs may cause serious complications in diabetic patients, such as emphysematous cystitis, renal failure, bacteremia and papillary necrosis. UTIs can also cause systemic inflammation and oxidative stress that elevate blood glucose and increase insulin resistance. Although the incidence of UTIs is higher and the severity of UTIs is more than anyone thought of previously, less than half of the UTI patients seek treatment in Asia.

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Escherichia coli is the frequent uropathogen in UTIs. However, the incidences of UTIs in different races and ethnicities are different. In previous studies, it was reported that the isolation of E. coli in European patients with UTIs was decreasing in the past 15 years.13,14 The isolation rate of E. coli was 26% in Japanese patients with UTIs and 55.1% in Indian patients. Both these studies were published in 2014.15,16

In this study, we reviewed 3,653 Chinese patients with type 2 diabetes (T2D) and studied the prevalence and characteristics of UTIs. The objective of this study is to find the risk factors and responsible pathogenetic microorganisms of UTIs in Chinese patients with T2D.

Patients and methods
Patient selection
The study protocol and patient consent forms were approved by the Institutional Ethical Committee of Nanjing First Hospital, Nanjing Medical University. All patients gave written informed consent to participate in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The methods were carried out in accordance with the Declaration of Helsinki guidelines, including any relevant details.

A total of 3,652 Chinese patients with T2D, who were hospitalized in the Department of Endocrinology, Nanjing First Hospital, Nanjing Medical University between March 2013 and July 2016, were included in this retrospective study. All of the patients were diagnosed with diabetes mellitus according to the American Diabetes Association diabetic definition standard by the admitting physician in our department before hospitalization. The exclusion criteria for patient selection were pregnancy and use of antimicrobial drugs in the last 14 days.

Patients were diagnosed as having UTIs if they met one of the following criteria or both: 1) pyuria (a leukocyte count of >10/mm² in clean-voided midstream urine specimen) in routine urine analysis of two urine samples, accompanied by symptoms of UTIs (including dysuria, pollakiuria, urgency, dysuria and fever) or not and 2) two positive midstream urine cultures (presence of at least 10³ colony forming units/mL of Gram-negative bacteria or 10⁴ colony forming units/mL of Gram-positive bacteria) with the same microorganism. Four hundred and nine of the patients were diagnosed with UTIs according to the criteria, and 388 patients who had other infections (such as respiratory tract infections, skin and mucus membrane infections, digestive tract infections) were excluded.

Data collection
The patients’ age, gender, height, weight, presence or absence of symptoms of UTI, and the type, duration and treatment of diabetes were recorded. Measurements of random blood glucose (RBG; measured when they began hospitalization), HbA1c, fasting and 2-hour post-meal serum c-peptide, glutamic acid decarboxylase antibody (GAD-Ab), insulin autoantibody (IAA), total cholesterol, high-density lipoprotein cholesterol, triglycerides, low-density lipoprotein cholesterol, albumin excretion rate in 24-hour urine (UAHb), blood leukocyte count (total leukocytes and percentage of band forms), blood creatine (Cr), glutamate-pyruvate transaminase, potassium concentration, blood albumin and uric acid (measured during the first 3 days of hospitalization) were collected. The initial body mass index (BMI) of the patients was calculated as weight in kilograms divided by height in meters squared. Out of the total studied population, 345 patients underwent positive urine cultures and tests for susceptibility to antibiotics, and the results were recorded. An isolate was considered as multidrug resistant (MDR) if found resistant to three or more antimicrobials belonging to different classes/groups of antimicrobials.

Statistical analysis
Analyses were performed using the SPSS 16.0 (SPSS Inc., Chicago, IL, USA) statistical package. All variables were tested for normal distribution of the data. Data are presented as means ± standard error or percentages. Differences between UTIs and non-UTIs were examined using the Student’s unpaired t-test for parametric data or the Mann–Whitney U test for nonparametric data. The categorical data were examined with chi-square test. Binary logistic analysis was performed to look for the risk factors of UTIs in the sample population.

Results
Characteristics of the UTI patients
Of the 3,652 patients with T2D in the study, aged between 18 and 94 years (mean age, 59.32±14.13), 409 patients were diagnosed as having UTIs. Among the 409 (11.2%) UTI patients, 221 patients had no UTI symptoms and 9 patients had urethral catheters. Eleven patients had bloodstream infections accompanying UTIs and among them, six had...
no UTI symptoms. One of the patients died of serious infections. The incidence of UTIs was higher in female than in males (24.13% vs 3.67%; P < 0.0001). Patients with UTIs were older and had longer duration of diabetes mellitus than non-UTI patients (P < 0.0001). Blood leukocyte count, Cr and UAlb increased in UTI patients, while uric acid, glutamate–pyruvate transaminase and blood albumin decreased (all with P < 0.005). There were no differences in BMI and serum potassium between the two groups (Table 1). RBG, GAD-Ab and IAA increased in patients with UTIs (P < 0.001), while HbA1c, blood lipids and C-peptide were similar in patients with UTIs to those of non-UTI patients (P > 0.05; Table 1).

**Risk factors of UTIs**

Risk factors for UTIs were examined in stepwise binary logistic regression model. All factors associated with UTIs at P < 0.5 in unadjusted analyses were included in the backward selection regression model and odds ratios and 95% CI were derived. Gender, age, duration of diabetes, BMI, HbA1c, fasting and 2-hour post-meal serum c-peptide, RBG, IAA, GAD-Ab, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, total cholesterol and UAlb were entered in the logistic regression model, and gender, age, RBG, IAA and UAlb were identified as significant risk factors for UTIs (P < 0.05; Table 2).

**Urine cultures**

One hundred and fifty-two patients with symptoms of UTI and 193 patients without the symptoms of UTI had efficient midstream urine culture. Among the 193 patients with asymptomatic UTI, 136 (70.47%) were positive in midstream urine culture and diagnosed as ASB, and 67 (44.08%) patients were positive in midstream urine culture among the 152 patients symptomatic of UTI. There were significant differences in positive rate of urine culture between the two groups (P < 0.0001; Figure 1).

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**Table 1** Characterization of patients with T2D

| Characteristics | Non-UTIs | UTIs | P-value |
|-----------------|----------|------|---------|
| Gender (male/female) | 1.783/1.072 | 0.704 | <0.001 |
| Age (years) | 57.43±0.26 | 64.28±0.64 | <0.001 |
| Duration of DM (years) | 6.09±0.12 | 7.66±0.36 | <0.001 |
| BMI (kg/m^2) | 24.46±0.07 | 24.33±0.18 | 0.257 |
| WBC (<10^9/L) | 6.35±0.06 | 7.28±0.20 | 0.001 |
| N (%) | 59.85±0.33 | 64.67±0.65 | <0.001 |
| L (%) | 32.51±0.31 | 28.65±0.59 | <0.001 |
| Cr (µmol/L) | 74.66±1.56 | 81.89±2.46 | <0.001 |
| UA (µmol/L) | 332.46±4.04 | 320.55±7.64 | <0.001 |
| ALT (IU/L) | 31.39±0.94 | 27.39±1.41 | <0.001 |
| Alb (g/L) | 41.5±0.15 | 38.82±0.26 | <0.001 |
| Blood K⁺ (mmol/L) | 3.93±0.01 | 3.91±0.03 | 0.279 |
| UAlb (mg/g) | 66.40±3.48 | 104.85±14.66 | 0.001 |
| RBG (mmol/L) | 11.71±0.14 | 13.03±0.40 | 0.003 |
| HbA1c (%) | 9.48±0.04 | 9.54±0.13 | 0.952 |
| FC-P (ng/mL) | 1.77±0.03 | 1.86±0.06 | 0.256 |
| 2hC-P (ng/mL) | 4.01±0.06 | 4.07±0.17 | 0.792 |
| GAD-Ab (IU/mL) | 20.99±0.57 | 23.95±1.47 | <0.001 |
| IAA (%) | 5.95±0.19 | 7.41±0.58 | <0.001 |
| TG (mmol/L) | 2.10±0.04 | 1.92±0.09 | 0.105 |
| TC (mmol/L) | 5.10±0.03 | 5.12±0.07 | 0.957 |
| HDL-c (mmol/L) | 1.37±0.01 | 1.40±0.02 | 0.063 |
| LDL-c (mmol/L) | 2.95±0.12 | 2.80±0.04 | 0.617 |

**Table 2** Risk factors for UTIs in diabetic patients

| Risk factors | OR | 95% CI | P-value |
|-------------|----|--------|---------|
| Gender (female) | 10.665 | 7.016–16.211 | <0.001 |
| Age | 1.019 | 1.006–1.032 | 0.005 |
| RBG | 1.034 | 1.013–1.055 | 0.001 |
| IAA | 1.015 | 1.002–1.028 | 0.022 |
| UAlb | 1.001 | 1.001–1.002 | <0.001 |

**Abbreviations:** IAA, insulin autoantibody; OR, odds ratio; RBG, random blood glucose; UAlb, albumin excretion rate in 24-hour urine; UTI, urinary tract infection. 

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**Figure 1** Urine cultures in diabetic patients.

**Notes:** Exactly 84.9% patients with positive UTI symptoms underwent positive urine cultures and 44.08% of them were positive. Also, 87.33% patients without UTI symptoms underwent positive urine cultures and 70.47% were positive. The percentage of positive urine cultures in the two groups was similar; however, the rate of positive urine cultures was significantly higher in symptom (+) group than in symptom (-) group (P < 0.0001).

**Abbreviation:** UTI, urinary tract infection.
The distribution of the microorganisms that caused UTIs is shown in Table 3. There was no difference between patients with and without UTI symptoms in the distribution of the urine microorganism ($P>0.05$). Both the patients in ASB group and in the symptom group showed high prevalence of *E. coli* infections (85.29% and 83.58%, respectively). There were 26 male and 177 female among the patients with positive urine cultures. The positive rate of urine cultures in male UTI patients was lower than in female patients (38.24% vs 51.91%, $P<0.05$). With respect to bacterial infection, male patients had less Gram-negative bacterial infection (53.85% vs 89.27%, $P<0.00001$) and more Gram-positive bacterial infection (30.77% vs 9.04%, $P<0.01$) than female patients. Analysis of the pathogenetic microorganisms responsible for infection showed that *E. coli* infection was more common in female patients than in male, while *Klebsiella pneumoniae*, *Enterococcus*, and *Staphylococcus* infections were more common in male patients than in female (all with $P<0.05$; Table 3).

### Drug sensitivity test

The drug resistance pattern of the most popular microorganisms is summarized in Figure 2. *E. coli* and *K. pneumoniae* exhibited high resistance to amoxicillin; the resistance rates were 71.6% and 100%, respectively. However, meropenem was effective for all the microorganisms. *Staphylococcus* was resistant to penicillin (88.8%), tetracycline (77.8%) and erythromycin (77.8%), but exhibited no resistance to nitrofurantoin and vancomycin. *Enterococcus* was resistant to tetracycline (66.7%) and sensitive to chloramphenicol (0% resistance). The incidences of MDR isolates in *E. coli*, *K. pneumoniae*, *Staphylococcus* and *Enterococcus* were 50.0%, 41.7%, 33.3% and 66.7%, respectively. There was no significant difference in MDR occurrence among these four microorganisms ($P>0.05$).

### Discussion

In this study, the prevalence of UTIs in diabetic patients was 11.2%, which was similar to that reported in Asia in other...
The authors report no conflicts of interest in this work.

Disclosure

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The different incidences of MDR E. coli infections might be due to the racial differences and overuse of antibiotics in some countries.

The most effective antibiotics on Gram-negative bacterial infections were meropenem and amikacin in our study, which is similar to that reported in a study in Bangladesh. Vancomycin and nitrofurantoin proved to be effective drugs against Gram-positive bacterial infections. Chloramphenicol is a very old drug; however, it was still effective on Staphylococcus infection and no resistant isolate was found.

Enterococcus showed 25% resistance to nitrofurantoin. Because of the prevalence of extended-spectrum beta-lactamases produced by bacterial pathogens, amoxicillin showed 100% resistance to E. coli and 71.6% resistance to K. pneumoniae. Furthermore, penicillin and ampicillin also showed high resistance to Gram-positive bacteria. The resistance of E. coli to cephalosporins, including cefotaxim, cefepime, cefuroxime, cephalothin, varied from 17.2% to 58.2%. These antibiotics were commonly used in our hospital. Although the resistance rates in diabetic patients were similar to non-diabetic patients, our results suggest cautious use of these antibiotics for the treatment of UTIs.

The limitation of this study is that of the total studied population, only 345 patients underwent positive urine cultures and susceptibility test for antibiotics. In future, we will further expand the sample size of patients with T2D if possible.

In summary, our study suggested that female gender, old age, microalbuminuria, high RBG and IAA were risk factors for UTIs in diabetic patients. The UTIs might affect the islet function or blood glucose control in patients with T2D. The rate of positive urine cultures was higher in asymptomatic patients than in symptomatic patients, and the severity of ABS and symptomatic UTIs was similar in patients with T2D. We suggest that a routine urine analysis or urine culture should be conducted in diabetes patients who have the identified risk factors. E. coli was the most common pathogenic microorganism isolated from diabetic patients with UTIs, and meropenem was the most effective antibiotic on E. coli that was resistant to amoxicillin. When a doctor decides to prescribe antibiotics to a diabetic patient with UTIs, drug sensitivity test should be performed.

The authors report no conflicts of interest in this work.
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