


Behavioral and dietary risk factors of recurrent urinary tract infection in Chinese postmenopausal women: a case–control study

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Abstract

Objective: The present study aimed to examine the behavioral and dietary risk factors of recurrent urinary tract infection (RUTI) in postmenopausal patients in China.

Methods: We performed a population-based case–control study with 193 postmenopausal women with RUTI and 193 age-matched healthy female controls with no history of RUTI. The study was conducted between January 2016 and June 2018 in Changzhou, China. Data were collected using an interviewer-based questionnaire, including information on demographics, lifestyle behavior, and habitual diet. Conditional logistic regression analysis was conducted to examine the risk factors associated with RUTI.

Results: Wiping from back to front after toilet use, sedentary behavior >6 hours/day, delayed voiding, and chronic constipation were associated with an increased risk of RUTI. Drinking more than three cups of green tea per month showed an inverse association with RUTI.

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However, there was no evidence of dose dependency for overall consumption. Additionally, the three-cup association involved a small proportion of cases and may reflect statistical artifact.

Conclusions: Wiping from back to front after toilet use, sedentary behavior, delayed voiding, and chronic constipation are associated with an increased risk of RUTI in postmenopausal women.

Keywords

Postmenopause, recurrent urinary tract infection, risk factor, toileting habit, sedentary behavior, chronic constipation

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Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections that is globally encountered by women.^{1,2} Approximately 50% of women have reported at least one episode of UTI in their lifetime.³ A recent study indicated that, apart from lower respiratory tract infection, UTI accounts for 11.29% of infections, and is the second most frequent type of healthcare-associated infection in mainland China.⁴ Recurrent urinary tract infection (RUTI) is frequently defined as more than two episodes in the last 6 months or more than three episodes in the last 12 months.⁵ The prevalence of UTI increases with age, such that the prevalence rate increases to 8% to 10% in postmenopausal women, and of these, 5% of UTIs will recur within 1 year.⁶ Postmenopausal women are more likely to have anatomical and physiological risk factors, such as cystocele, incontinence, incomplete bladder emptying, and estrogen deficiency, predisposing them to RUTI, compared with premenopausal women.

Antibiotics can alleviate the symptoms of UTI, but cannot reduce the recurrence rate and improve the outcome. Moreover, antibiotic resistance has become an increasing concern, and it is attributed to the increased use of a post-coital or long-term,

low-dose, daily antibiotic regimen administered as prophylaxis against RUTI.⁷ Recent studies have suggested that cranberry products, probiotics, the bacterial vaccine Uromune, D-mannose powder, and vitamin D have a role in preventing RUTI.^{8–13} However, the evidence for these non-antibiotic products are weak, and more studies on this issue are required.

RUTI leads to various negative effects on the quality of life and imposes a significant economic burden upon public healthcare.^{14–16} At present, China has a population of 1.34 billion, which is steadily increasing and rapidly aging at the same time.⁴ Therefore, RUTI is an important issue in the increasingly aging population in China. However, the risk factors associated with RUTI in postmenopausal women have not been widely described in China. Therefore, this study aimed to evaluate behavioral and dietary risk factors associated with RUTI in postmenopausal women, and to provide a basis of designing preventative strategies.

Material and methods

Study population

A total of 5867 postmenopausal women with suspected UTI who presented at

the outpatient clinics of the Nephrology Department at Changzhou Affiliated Hospital of Nanjing University of Chinese Medicine between January 2016 and June 2018 were prospectively recruited. Individuals were included if they were women, menopausal (without menstruation for at least 12 months), and had a documented history of two or more culture-confirmed symptomatic episodes of uncomplicated UTI in the previous 6 months or three or more during the previous year. UTI was defined as major bacteriuria established by a urine culture $\geq 10^5$ CFU/mL, and with the presence of at least two of the following clinical symptoms: frequency, urgency, and dysuria. Uncomplicated UTI was defined as normal anatomical function of the urinary system when UTI occurred, and there were no complications. Complicated UTI was defined as the presence of anatomical or functional abnormalities in the urinary system, such as urinary tract obstruction, an operation history of the urinary system, indwelling catheter, diabetes mellitus, and immune system diseases.

The exclusion criteria were patients aged >80 years, functional or anatomical abnormalities of the genitourinary tract, neurogenic bladder, interstitial cystitis, asymptomatic bacteriuria, an indwelling urinary catheter, hormone replacement therapy, diabetes mellitus, stroke, heart disease, respiratory disease, and tumors.

Controls were age-matched healthy postmenopausal women with no history of RUTI who attended the Hospital Healthy Examination Center at the same time interval as cases. Control subjects were subjected to urine culture and, if sterile, they were included in this study.

Urinalysis and clinical examination

Urinalysis and urine cultures were collected at enrollment in the study. All of the participants were routinely instructed on the

proper collection technique for midstream clean-catch urine specimens, including cleansing of the external female genitalia two to three times with a prepackaged wipe and spreading the labia before voiding to reduce contamination of the specimen. Physical measurements, including body weight and height, were collected by standardized methods for anthropometrics. Body weight without heavy clothing to the nearest 0.05 kg was measured using a body fat and weight measurement device (GL-150P; G-Tech international Co. Ltd., Uijeongbu, Korea). Height was measured without shoes to the nearest 0.1 cm. Additionally, a thorough physical examination was performed by a clinician, and genitourinary ultrasonography was performed by an ultrasonologist using a color Doppler ultrasound diagnostic apparatus (Philips IU22; Philips, Amsterdam, Holland).

Questionnaire survey

Information on demographics, lifestyle behavior, and dietary behavior was collected face-to-face by trained interviewers using a self-made, structured questionnaire. Demographic data included age, body mass index (BMI), time since the last menstrual period, marital status, education levels, and number of deliveries. Information of lifestyle behavior during the previous year included smoking habits, sedentary behavior, wiping from front to back or back to front after toilet use, delayed voiding, and having a bath by standing or sitting. Bathing practice meant the women's typical bathing behavior. Data on dietary behavior during the previous year were collected by using a validated food frequency questionnaire according to local dietary preference. The diet included fresh fruits, fresh vegetables, green tea, liquid, dairy products, soy bean products, spicy foods, and fatty foods.

Ethics statement

All participants fully understood the research contents and provided written informed consent for participation in the registry. This study was approved by the Ethics Committee of Changzhou Affiliated Hospital of Nanjing University of Chinese Medicine (Jiangsu, China).

Definitions

Smoking habit. Smoking habit was categorized into three groups of never, former (cessation of smoking, ≥ 6 months), and current (daily smoking, ≥ 6 months).

Delayed voiding and chronic constipation. Delayed voiding behavior was defined as behavior in which individuals inhibited the voiding urge and delayed voiding. Determination of delayed voiding behavior was achieved with the following question: "During the past year, have you delayed voiding when busy or in public?" Delayed voiding behavior was grouped into the three categories of never/rarely, sometimes, and always/often. Constipation was defined as infrequent defecation (less than three bowel movements per week), and/or the presence of frequent (more than twice a week) passage of hard stools and/or need to strain and/or sensation of incomplete evacuation. Participants were asked: "Have you had any of the following problems in the previous year?" Response options were listed as "never/rarely", "sometimes", or "frequent".

Sedentary behavior. Self-reported sedentary behavior was measured using the following question: "During the past year, what was the average time per day you spent at the following types of activities: sitting, reclining, lying, watching TV, and spending time on the internet?" Sedentary behavior was classified into the following four groups: < 2 hours/day, 2 to 4 hours/day, 4 to 6 hours/day, and > 6 hours/day.

Dietary habits. The question "During the past year, did you eat fresh fruit?" pertaining to fruit intake included the following choices of answers: "never/rarely", "1 to 2 times/week", "3 to 4 times/week", and " ≥ 5 times/week". The question pertaining to vegetable intake was "During the past year, did you eat fresh vegetables?" and the choice of answers included " < 500 g/day" and " ≥ 500 g/day". Information on drinking green tea was obtained with the question "During the past year, did you consume green tea, and how often?" The choices of answers to this question were classified into the following five categories: never, 1 to 3 cups/month, 1 to 3 cups/week, 1 to 2 cups/day, and ≥ 3 cups/day. Liquid consumption was classified into the following four groups: ≤ 0.5 L/day, > 0.5 L/day and ≤ 1.0 L/day, > 1.0 L/day and ≤ 1.5 L/day, and > 1.5 L/day. Liquid consumption included daily intake of green tea and other liquid consumption, such as water, coffee, and juice. Older people are accustomed to using "jin" (approximately 500 mL) as a common liquid measure of intake. We chose 0.5 L/day increments for liquids to make their choices more intuitive. The question pertaining to dairy products (e.g., milk, yogurt, and powdered milk) and soy bean products (e.g., soybean milk and tofu) was "During the past year, how often did you consume this food?" The participants were instructed to select from four consumption frequency categories (never/rarely, 1–2 times/week, 3–4 times/week, and ≥ 5 times/week). The question "How often did you eat this food?" was asked for eating spicy foods (e.g., hot peppers, dried chilies, pointed peppers, and chili sauce) and fatty foods (e.g., red meat, animal fats, and processed meat). The choices of answers included "never/rarely", "1 to 2 times/month", "3 to 4 times/month", "2 to 3 times/week", and "almost every day".

Statistical analysis

Statistical analyses were performed using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). Categorical variables are shown as number and percentage. Univariable conditional logistic regression models were initially used to estimate the associations of lifestyle behavior and dietary behavior on the risk of RUTI, with adjustment for BMI, time since the last menstrual period, marital status, education level, and number of deliveries. Associations were determined by calculating the odds ratios (ORs) and 95% confidence intervals (CIs). Variables with $P \leq 0.2$ in this analysis were further subjected to multivariable conditional logistic regression models, and their associations with RUTI were estimated by additionally adjusting for smoking and liquid consumption. A two-sided $P < 0.05$ was considered significant.

Results

Characteristics

Of the 5867 female patients who were invited to participate in the study, 1065 were diagnosed as having UTIs. The remaining 4802 patients had negative urinalysis and urine culture results. They were diagnosed with lower urinary tract symptoms (e.g., overactive bladder, incomplete bladder emptying), neurogenic bladder, pelvic organ prolapse, and pelvic infection. Among the 1065 (18.15%) patients with UTI, 862 were not eligible for the study because they had no recurrent history of UTIs ($n = 732$), diabetes ($n = 104$), ureteral calculi ($n = 9$), stroke ($n = 6$), heart disease ($n = 8$), and hormone replacement therapy ($n = 3$). We also excluded 10 individuals because of missing data of height ($n = 2$), weight ($n = 4$), and the time since the last menstrual period ($n = 4$). Over the 30-month study period, 193 cases and 193

controls were included in the final analysis (Figure 1).

More than 60% of the participants were >60 years old and 75.39% did not have menstruation for >5 years. The mean age of cases was 61.61 ± 9.57 years and that in the controls was 62.93 ± 9.17 years, with no significant difference in age between cases and controls. Characteristics of the participants are shown in Table 1. There were no significant differences in age, marital status, time since the last menstrual period, education level, number of deliveries, and smoking habits between cases and controls. However, mean BMI was significantly higher in cases than in controls (26.64 ± 3.02 vs. 24.96 ± 3.26 kg/m², $P = 0.02$) (Table 1).

Clinical symptoms and distribution of organisms

In this study, the predominant clinical presentations in postmenopausal patients were frequency, urgency, painful voiding, and difficulty in emptying the bladder. Other generalized unspecific symptoms, such as lower abdominal pain, low back pain, and genital discomfort, were also observed. Among postmenopausal patients with a total of 193 pathogens, 162 Gram-negative bacteria, 27 Gram-positive bacteria, and four fungi were isolated. Among these women, the proportion of *Escherichia coli* was the largest (61.66%), followed by *Klebsiella pneumoniae* (15.03%) and *Proteus mirabilis* (7.25%) (Table 2).

Lifestyle and dietary behavior

There was a small number of current and former smokers (3.37% of the total women), with no significant difference between cases and controls (Table 3).

In univariable conditional logistic regression analysis, wiping from back to front after toilet use was a risk factor for RUTI

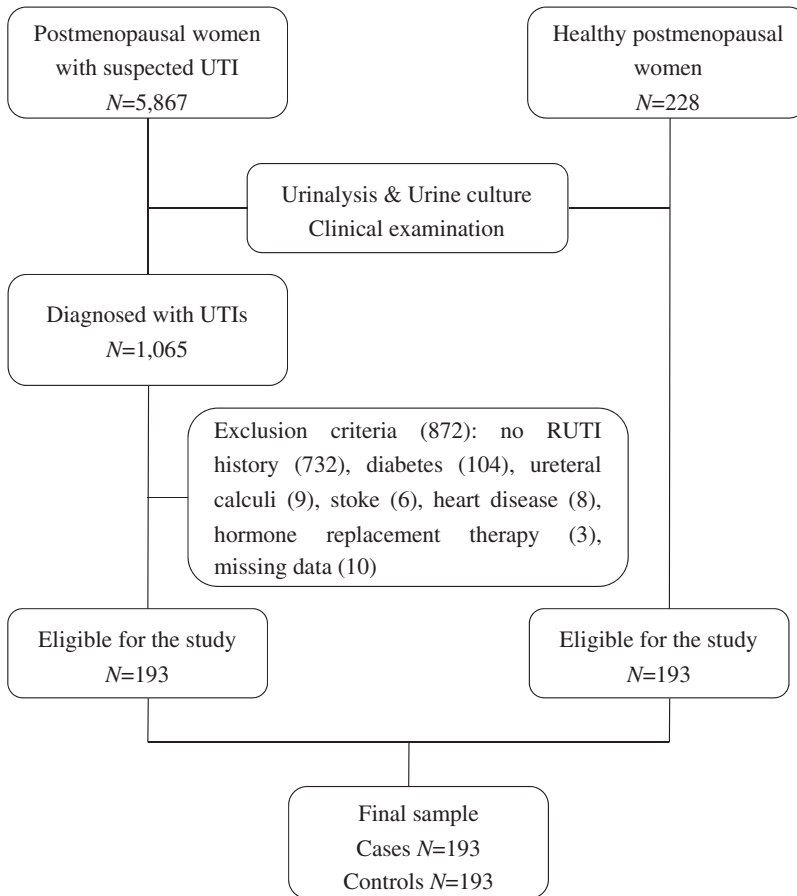


Figure 1. Flowchart of the study population.

(adjusted OR = 4.35, 95% CI = 2.38–7.94, $P < 0.001$). A significantly higher proportion of cases reported sedentary behavior ≥ 2 hours/day than did controls (41.97% vs. 26.42%, $P < 0.001$). A significantly higher rate of cases was more likely to delay voiding compared with controls (60.10% vs. 18.13%, $P < 0.001$). Chronic constipation was observed significantly more frequently in cases than in controls (82.90% vs. 46.63%, $P < 0.001$). The proportions of having a bath by standing or sitting were not statistically significant between cases and controls.

No significant differences in the consumption of fruits, vegetables, liquid, dairy products, soy bean products, spicy foods, and fatty foods were observed between cases and controls (Table 4). At baseline, 21.76% of controls reported consuming ≥ 1 cup/day of green tea and 88.08% of cases reported never/rarely consuming green tea. Because of the infrequency of green tea consumption of more than one to three cups per month in cases, we consolidated the three groups (1–3 cups/week, 1–2 cups/day, and ≥ 3 cups/day) of green tea drinking. Green tea drinking of > 3 cups/month was observed more

Table 1. Characteristics of cases and controls.

Characteristics	Controls (n = 193)	Cases (n = 193)	OR (95% CI)	P value
Age (years)				
40–49	19 (9.84)	12 (6.22)	Matched	
50–59	57 (29.53)	63 (32.64)		
60–69	68 (35.23)	65 (33.68)		
70–80	49 (25.39)	53 (27.46)		
BMI				
<25 kg/m ²	95 (49.22)	68 (35.23)	Ref	0.020
≥25 and <30 kg/m ²	83 (43.01)	104 (53.89)	1.78 (1.15–2.74)	
≥30 kg/m ²	15 (7.77)	21 (10.88)	2.15 (1.00–4.65)	
Time since the last menstrual period (years)				
1–5	52 (26.94)	43 (22.28)	Ref	0.475
6–10	44 (22.80)	50 (25.91)	1.44 (0.78–2.66)	
>10	97 (50.26)	100 (51.81)	1.32 (0.76–2.27)	
Marital status				
Single	6 (3.11)	5 (2.59)	Ref	0.937
Married	146 (75.65)	151 (78.24)	1.24 (0.38–4.10)	
Divorced/separated	25 (12.95)	23 (11.92)	1.09 (0.29–4.15)	
Widowed	16 (8.29)	14 (7.25)	1.04 (0.27–3.93)	
Education level				
Illiteracy	32 (16.58)	40 (20.73)	Ref	0.268
Primary school	89 (46.11)	97 (50.26)	0.86 (0.49–1.50)	
Middle school	55 (28.50)	37 (19.17)	0.55 (0.29–1.03)	
High school	13 (6.74)	12 (6.22)	0.72 (0.29–1.77)	
College and above	4 (2.07)	7 (3.63)	1.35 (0.36–5.10)	
Number of deliveries				
0–2	146 (75.65)	138 (71.50)	Ref	0.671
3–5	35 (18.13)	41 (21.24)	1.22 (0.75–1.98)	
≥6	12 (6.22)	14 (7.25)	1.23 (0.56–2.69)	

Values are shown as n (%). OR, odds ratio; CI, confidence interval; BMI, body mass index; Ref, reference.

Table 2. Pathogens detected in patients with recurrent urinary tract infection.

Microorganism	Number of patients (%)
Gram-negative	
<i>Escherichia coli</i>	119 (61.66)
<i>Klebsiella pneumoniae</i>	29 (15.03)
<i>Proteus mirabilis</i>	14 (7.25)
Gram-positive	
<i>Streptococcus agalactiae</i>	12 (6.22)
<i>Enterococcus faecalis</i>	9 (4.66)
<i>Staphylococcus epidermidis</i>	6 (3.11)
Fungus	
<i>Candida albicans</i>	4 (2.07)

frequently in controls than in cases (29.53% vs 3.62%, $P < 0.001$).

Multivariable conditional logistic regression analysis was adjusted for BMI, the time since the last menstrual period, marital status, education level, number of deliveries, smoking, and liquid consumption. The significant independent risk factors for RUTI were wiping from back to front after toilet use ($P < 0.001$), sedentary behavior >6 hours/day ($P < 0.05$), delayed voiding ($P < 0.001$), and chronic constipation ($P < 0.001$). In contrast, drinking >3 cups/month of green tea was

Table 3. Comparison of lifestyle behavior and chronic constipation between cases and controls.

Variables	Controls n (%)	Cases n (%)	OR (95% CI)	Adjusted OR ^a (95% CI)	P value
Smoking					
Never	186 (96.37)	187 (96.89)	Ref	Ref	0.780
Former	5 (2.59)	4 (2.07)	0.80 (0.22–2.98)	0.68 (0.16–2.84)	
Current	2 (1.04)	2 (1.04)	1.00 (0.14–7.10)	1.72 (0.18–16.06)	
Wiping after toilet use					
Front to back	155 (80.31)	109 (56.48)	Ref	Ref	<0.001
Back to front	38 (19.69)	84 (43.52)	3.71 (2.17–6.33)	4.35 (2.38–7.94)	
Sedentary behavior					
<2 hours/day	142 (73.58)	112 (58.03)	Ref	Ref	<0.001
2–4 hours/day	36 (18.65)	37 (19.17)	1.39 (0.80–2.41)	1.20 (0.66–2.16)	
4–6 hours/day	9 (4.66)	30 (15.54)	4.02 (1.81–8.92)	4.67 (2.01–10.87)	
>6 hours/day	6 (3.11)	14 (7.25)	2.90 (1.07–7.87)	2.90 (1.01–8.36)	
Delayed voiding					
Never/rarely	158 (81.87)	77 (39.90)	Ref	Ref	<0.001
Sometimes	25 (12.95)	70 (36.27)	5.91 (3.07–11.40)	5.63 (2.83–11.20)	
Always/often	10 (5.18)	46 (23.83)	7.18 (3.25–15.88)	7.78 (3.34–18.12)	
Chronic constipation					
Never/rarely	103 (53.37)	33 (17.10)	Ref	Ref	<0.001
Sometimes	56 (29.02)	82 (42.49)	4.61 (2.55–8.33)	4.47 (2.39–8.36)	
Frequent	34 (17.62)	78 (40.41)	7.56 (3.91–14.63)	8.98 (4.32–18.63)	
Having a bath					
By standing	154 (79.79)	161 (83.42)	Ref	Ref	
By sitting	39 (20.21)	32 (16.58)	0.78 (0.46–1.32)	0.86 (0.49–1.50)	0.591

^aOR: adjusted for body mass index, time since the last menstrual period, marital status, education level, and number of deliveries. OR, odds ratio; CI, confidence interval; Ref, reference.

associated with a decreased risk of RUTI ($P < 0.001$) (Table 5).

Discussion

Postmenopausal women are biologically, physiologically, and behaviorally exposed to an increased risk of developing UTI. UTI is a common genitourinary tract complaint in postmenopausal women with a high rate of recurrence after menopause.^{17,18} The prevalence of RUTI significantly increases with age. UTI is often overdiagnosed in postmenopausal women, and a positive urine culture often leads to initiation of antibiotic treatment, regardless of the presence or absence of symptoms referable to infection.¹⁹ Asymptomatic bacteriuria (ASB) is

common in postmenopausal women, without symptoms or signs of UTI. Treatment of asymptomatic bacteriuria is usually futile, and it increases the risk of subsequent symptomatic UTI episodes, and is thus not recommended for this patient group.²⁰ The criteria used to diagnose symptomatic UTI or ASB are problematic. A quantitative count of $\geq 10^5$ CFU/mL is appropriate for symptomatic UTI and ASB.¹⁹

In our study, the majority of patients had their RUTI caused by *E. coli*. *E. coli* is believed to cause 80% to 90% of all UTIs, and it ascends the urethra to the bladder causing cystitis, or even up the ureters into the kidneys, leading to pyelonephritis.^{21,22} Other pathogens that we identified were *Klebsiella pneumoniae* (15.03%),

Table 4. Comparison of dietary behavior between cases and controls.

Variables	Controls n (%)	Cases n (%)	OR (95% CI)	Adjusted OR ^a (95% CI)	P value
Fresh fruits					
Never/rarely	35 (18.13)	30 (15.54)	Ref	Ref	0.535
1–2 times/week	29 (15.03)	25 (12.95)	0.99 (0.48–2.06)	0.74 (0.33–1.66)	
3–4 times/week	114 (59.07)	118 (61.14)	1.20 (0.69–2.07)	1.09 (0.60–1.98)	
≥5 times/week	15 (7.77)	20 (10.36)	1.54 (0.68–3.46)	1.48 (0.61–3.59)	
Fresh vegetables					
<500 g/day	52 (26.94)	60 (31.09)	Ref	Ref	0.446
≥500 g/day	141 (73.06)	133 (68.91)	0.80 (0.50–1.27)	0.82 (0.50–1.36)	
Green tea drinking					
Never	129 (66.84)	170 (88.08)	Ref	Ref	<0.001
1–3 cups/month	7 (3.63)	16 (8.29)	1.38 (0.53–3.62)	1.18 (0.40–3.46)	
>3 cups/month	57 (29.53)	7 (3.62)	0.06 (0.02–0.19)	0.05 (0.01–0.16)	
Liquid consumption					
≤0.5 L/day	44 (22.80)	47 (24.35)	Ref	Ref	0.815
>0.5 and ≤1.0 L/day	51 (26.42)	56 (29.02)	1.00 (0.58–1.71)	0.93 (0.52–1.64)	
>1.0 and ≤1.5 L/day	72 (37.31)	68 (35.23)	0.88 (0.52–1.50)	0.83 (0.46–1.49)	
>1.5 L/day	26 (13.47)	22 (11.40)	0.79 (0.38–1.63)	0.71 (0.33–1.53)	
Dairy products					
Never/rarely	33 (17.10)	29 (15.03)	Ref	Ref	0.960
1–2 times/week	37 (19.17)	43 (22.28)	1.35 (0.68–2.71)	1.16 (0.55–2.42)	
3–4 times/week	66 (34.20)	70 (36.27)	1.21 (0.67–2.19)	1.03 (0.54–1.95)	
≥5 times/week	57 (29.53)	51 (26.42)	1.03 (0.55–1.92)	0.98 (0.50–1.90)	
Soy bean products					
Never/rarely	23 (11.92)	22 (11.40)	Ref	Ref	0.954
1–2 times/week	76 (39.38)	79 (40.93)	1.08 (0.54–2.17)	1.01 (0.47–2.17)	
3–4 times/week	54 (27.98)	55 (28.50)	1.07 (0.51–2.24)	0.98 (0.43–2.21)	
≥5 times/week	40 (20.73)	37 (19.17)	0.97 (0.44–2.13)	0.86 (0.36–2.01)	
Spicy foods					
Never/rarely	98 (50.78)	101 (52.33)	Ref	Ref	0.964
1–2 times/month	26 (13.47)	23 (11.92)	0.86 (0.46–1.61)	0.87 (0.45–1.72)	
3–4 times/month	37 (19.17)	41 (21.24)	1.06 (0.62–1.80)	0.93 (0.52–1.67)	
2–3 times/week	21 (10.88)	19 (9.84)	0.87 (0.45–1.68)	0.96 (0.46–2.03)	
Almost every day	11 (5.70)	9 (4.66)	0.76 (0.29–2.00)	0.68 (0.24–1.95)	
Fatty foods					
Never/rarely	133 (68.91)	126 (65.28)	Ref	Ref	0.763
1–2 times/month	14 (7.25)	21 (10.88)	1.50 (0.76–2.96)	1.59 (0.75–3.35)	
3–4 times/month	20 (10.36)	22 (11.40)	1.11 (0.60–2.08)	1.09 (0.55–2.13)	
2–3 times/week	19 (9.84)	17 (8.81)	0.95 (0.48–1.85)	0.89 (0.43–1.83)	
Almost every day	7 (3.63)	7 (3.63)	1.02 (0.35–2.96)	0.80 (0.25–2.54)	

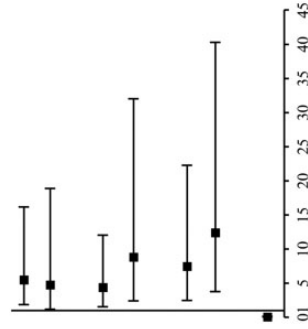
^aOR: adjusted for body mass index, time since the last menstrual period, marital status, education level, and number of deliveries. OR, odds ratio; CI, confidence interval; Ref, reference.

Proteus mirabilis (7.25%), *Streptococcus agalactiae* (6.22%), *Enterococcus faecalis* (4.66%), *Staphylococcus epidermidis* (3.11%), and *Candida albicans* (2.07%).

These results are similar to those of other studies conducted in China.²³ Treatment of *E. coli* with antibiotics is often ineffective because of acquisition of drug-resistant

Table 5. Attributable risk factors associated with recurrent urinary tract infection in multivariable analysis.

Variables	OR (95% CI)	Adjusted OR ^a (95% CI)	P value
Wiping from back to front	3.86 (1.68–8.83)	5.46 (1.84–16.20)	<0.001
Sedentary > 6 hours/day	4.59 (1.03–20.34)	4.68 (1.16–18.89)	<0.05
Delayed voiding			
Sometimes	4.85 (2.01–11.69)	4.35 (1.57–12.04)	<0.001
Always/often	7.22 (2.29–22.75)	8.78 (2.41–32.00)	<0.001
Chronic constipation			
Sometimes	4.91 (2.14–11.26)	7.43 (2.48–22.26)	<0.001
Frequent	6.88 (2.78–17.04)	12.36 (3.80–40.26)	<0.001
Drinking green tea			
> 3 cups/month	0.06 (0.01–0.28)	0.02 (0.01–0.15)	<0.001



^aOR: adjusted for body mass index, time since the last menstrual period, marital status, education level, number of deliveries, smoking, and liquid consumption. OR, odds ratio; CI, confidence interval. In the chart, symbols represent ORs and bars represent the 95% CIs.

genes by the bacteria. Li et al.⁸ reported that more than 45% of *E. coli* isolated from UTIs were resistant to wide-spectrum antibiotics. Chen et al.²⁴ demonstrated that *E. coli* strains harboring class 1 integron showed high resistance towards tobramycin.

The incidence of UTI might be higher in patients with diabetes because of multiple mechanisms, such as genetic susceptibility and a damaged immune response.²⁵ In our study, patients with diabetes were excluded because their eating behavior and dietary patterns are influenced by this disease. These patients often consume a low-carbohydrate, low-fat diet for achieving tight control over blood glucose levels.

Estrogen deficiency in postmenopausal women has a strong association with RUTI.^{1,26} Lüthje et al.²⁷ found that estrogen induced expression of antimicrobial peptides and promoted expression and redistribution of cell-cell contact-associated proteins. Postmenopausal women are more predisposed to RUTI because of their decreased production of antimicrobial peptides and diminished integrity of the urothelial lining. The available evidence suggests that estrogen is effective in reducing UTI episodes in some patients as a prophylactic therapy;^{27,28} however, this evidence is controversial.²⁹ In contrast, supplementation with estrogen significantly increased the susceptibility of surgically menopausal mice to ascending UTI.³⁰ In our study, the proportion of postmenopausal patients with RUTI who received estrogen therapy was limited. Generally, prescriptions for hormone replacement therapy for Chinese women are lagging behind those for Caucasian women in the postmenopausal period.

We observed that wiping from back to front after toilet use was associated with an increased risk of RUTI. Some studies have shown that wiping habits from back to front after a bowel movement or urination are associated with an increased risk of

UTI.^{31,32} In women, the urethra is close to the genitalia and anus. The fecal microbiota is a primary source of *E. coli* causing UTIs via the fecal-perineal-urethral route. Whole-genome phylogenetic analysis of bacterial strains that were isolated from the same female vagina and bladder showed highly similar *E. coli*, suggesting an interlinked female genitourinary tract microbiota.³³ Therefore, improving hygiene behavior after using the toilet is thought to reduce the risk of contaminating the urethra with *E. coli*.

In our study, the mean BMI of cases was significantly higher than that in controls. A significantly higher proportion of cases reported a sedentary behavior ≥ 2 hours/day than did controls. Sedentary behavior is associated with a greater increase in BMI in postmenopausal women.³⁴ A recent cross-sectional study showed that obesity (BMI ≥ 30 kg/m²) was a risk factor for UTI, and the incidence of UTI was correlated with increasing degrees of BMI.³⁵ In multivariable conditional regression analysis, sedentary behavior > 6 hours/day was found to be associated with RUTI. We speculate that sedentary behavior might have a cause and effect relationship with elevated BMI and delayed voiding behavior.

We identified the toileting behavior of delayed voiding as a risk factor for RUTI, which is consistent with a previous study.³⁶ Not emptying the bladder frequently enough can cause bacteria to accumulate inside the urinary tract. Furthermore, delayed voiding combined with the Valsalva maneuver can aggravate the bladder neck's descent in women, leading to lower urinary tract symptoms.³⁷ Emptying the bladder regularly helps flush away any bacteria.

In our study, the rate of chronic constipation in cases was significantly higher than that in controls. Retrospective and prospective studies in children and adults have suggested that constipation plays an etiological

role in UTI.^{38,39} Compression of the bladder by the rectum or sigmoid colon loaded with feces may cause stimulation of stretch receptors. This results in uninhibited bladder contractions, which are common to vesico-ureteral reflux, RUTI, and enuresis.⁴⁰ Clinicians should consider the use of stool softeners or a soluble fiber because of the high incidence of constipation and association with RUTI.

Interestingly, we found that drinking green tea was observed less frequently in cases than in controls. Green tea is derived from the leaves of *Camellia sinensis*, and has been consumed with a history of thousands of years in China. Green tea has a high quantity of tea polyphenols, and has an inhibitory effect on the growth of *E. coli* strains and a synergistic effect with antibiotics in *in vitro* experimental studies.^{41–44} We found that drinking >3 cups/month of green tea decreased the risk of RUTI. Notably, green tea was associated with a decreased risk of RUTI, but not fresh fruits or vegetables, which also contain plant polyphenols. An example of this situation is that strawberry and lemon extracts show an inhibition zone against bacteria causing UTI.⁴⁵ Additionally, different green teas have varying polyphenol content and brewing conditions are known to affect phenolic content.⁴⁶ These various factors of green tea need to be further studied.

The present study has several limitations. First, this was a single-center study and the sample size was small. Second, sexual intercourse was not queried. However, a previous study suggested that behavioral risk factors, such as sexual activity and contraceptive use, do not play a large role in RUTI after menopause as in premenopausal women.⁴⁷ Third, internet use may not have been sedentary if people were accessing the internet on their mobile devices, which is frequently performed while standing or ambulatory. Fourth, with regard to the query of wiping practices

after toilet use, only two modes of wiping were queried and the approach of dabbing was assumed to fall into the front to back wiping. Fifth, the food frequency questionnaire is not a broadly comprehensive reflection of diet because it does not include snack foods, carbohydrates, seafood, poultry, or alcohol. Additionally, although drinking more than three cups of green tea per month showed an inverse association with case status, there was no evidence of green tea dose-dependency for overall consumption. Furthermore, the three-cup association involved a small proportion of cases and may reflect statistical artifact. Sixth, many genetic associations and comorbid host factors that are thought to be risk factors for RUTI were not included in the survey. Liu et al.⁴⁸ showed that the Ala19Val polymorphism of the SP-A1 gene and Lys223Gln polymorphism of the SP-A2 gene may be genetic factors that affect susceptibility of RUTI in Chinese women. The final limitation is recall bias in this case-control study, which is especially common in self-reporting and retrospective cohort studies.

Conclusion

Our study shows that postmenopausal women with chronic constipation and poor hygiene behavior or urination habits are at high risk of developing RUTI. Therefore, postmenopausal women with RUTI should undergo a comprehensive assessment to identify possible risk factors to reduce the incidence of RUTI. The inverse association of drinking more than three cups of green tea per month with RUTI could have been affected by the small proportion of cases.

Declaration of conflicting interest

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