

## Risk factors for recurrent cystitis following acute cystitis in female patients

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**Abstract** We conducted a retrospective analysis of acute cystitis (AC) patients to evaluate the risk factors of recurrent cystitis (RC) patients following AC. The clinical records of 254 subjects with a confirmed diagnosis of AC and 90 healthy subjects who visited the Health Promotion Center between 2008 and 2012 were reviewed. A patient was diagnosed with RC if she was treated for three or more symptomatic episodes of cystitis over a 12-month period. Results were analyzed according to three groups: normal control (group A,  $n = 90$ ), AC (group B,  $n = 121$ ), and RC (group C,  $n = 133$ ). Women in the cystitis groups (groups B and C) were more likely to have diabetes, be menopausal, have a history of catheterization or sexually transmitted infections (STI), have a low daily water intake, have frequent sexual intercourse, and to use contraception more frequently than the normal control group ( $P < 0.05$ ). In groups B and C, *Escherichia coli* was the most common uropathogen, followed by *Staphylococcus saprophyticus*, *Enterococcus* species, and *Klebsiella* species. There were no differences between groups in the detection rates of these uropathogens. Factors that affected progression to RC were diabetes, catheterization history, STI history, sexual intercourse more than four times per month, sexual intercourse in the last month, and the use of contraceptives ( $P < 0.05$ ). The identification of these factors may help develop preventive, diagnostic, and therapeutic strategies for treating RC that has progressed from AC.

**Keywords** Cystitis · Recurrent · Factor

### Introduction

Urinary tract infections (UTIs) are among the most common infections, with an estimated annual global incidence of at least 250 million cases, and are costly both to patients and to healthcare funding systems [1]. Uncomplicated cystitis accounts for the greatest number of UTIs, particularly in women. It is estimated that one-half of all women will have at least one episode of acute uncomplicated cystitis during their lifetime [2]. Foxman et al. [3] reported that as many as 10 % of women experience at least one episode of acute uncomplicated cystitis per year, and 60 % have at least one episode during their lifetime. Among the 6–8 million young women estimated to contract acute cystitis each year, most have only single or sporadic episodes [4].

Recurrent UTI is a symptomatic UTI that follows the clinical resolution of an earlier UTI generally, but not necessarily, after treatment. Recurrent UTIs are common among young healthy women, even though they generally have anatomically and physiologically normal urinary tracts. Mabeck [5] found that nearly one-half of women whose uncomplicated UTIs resolved spontaneously developed a recurrent UTI within the first year.

Bacteriuria is defined as the presence of bacteria in the urine. If the patient is symptomatic, the presence of 100 colony-forming units (CFU)/ml is enough to diagnose bacteriuria. If asymptomatic, the presence of 100,000 CFU/ml is required for diagnosis [6]. Recurrent UTI refers to a symptomatic UTI that follows the resolution of a previous UTI [7] with three or more symptomatic episodes over a 12-month period [8].

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Common risk factors for recurrent UTI are well established and include sexual intercourse, genetics, the distance of the urethra from the anus, and the use of contraceptives, antimicrobials, or estrogen [9]. This study investigated the risk factors for recurrent cystitis following acute cystitis in female patients.

## Materials and methods

Two hundred and fifty-four female patients between 18 and 65 years of age who received treatment for cystitis in a urology office and 90 patients who visited the Health Promotion Center (HPC) between January 2008 and February 2012 were included in this study. All enrolled subjects with cystitis had undergone urine analysis and urine culture. Patients were divided into three groups: normal control (group A,  $n = 90$ ), acute cystitis (AC) (group B,  $n = 121$ ), and recurrent cystitis (RC) (group C,  $n = 133$ ).

Clinical variables such as marital status, menopausal status, catheterization history, history of sexually transmitted infections (STI), presence of diabetes or hypertension, daily water intake, and sexual behavior were analyzed, as were microbiological variables (urine culture). Clinical variables that were not described in medical records were obtained by calling the patient, with their consent.

Clean-catch midstream urine samples were tested for the presence of leukocytes by microscopy, and a dip-slide was prepared and sent to a central laboratory for culture. A positive test was defined as a urine sample containing  $\geq 10^3$  CFU/ml and the presence of pyuria ( $>5$  white blood cells in a high-power field in a centrifuged sample) [10]. All isolates with bacterial counts  $\geq 10^3$  CFU/ml were identified and tested.

Urinary tract infection was defined as  $>10^3$  CFU/ml uropathogen in the midstream urine culture from a woman experiencing more than two symptoms of cystitis (dysuria, urgency, frequency, suprapubic pain, or hematuria). Recurrent cystitis was diagnosed in patients who were treated for three or more symptomatic episodes of cystitis over a 12-month period.

Episodes of asymptomatic bacteriuria and symptomatic episodes that failed to meet these criteria were excluded. The study protocol was first approved by a central ethical committee (Catholic Medical Centre, The Catholic University of Korea College of Medicine, Seoul, Korea, no. SC12RISI0169), and then by the respective local ethics committees.

### Statistical analysis

Variables were characterized using Student's  $t$  test,  $\chi^2$  test, and multiple logistic regression analysis.  $P$  values  $< 0.05$  were considered statistically significant.

## Results

Tables 1 and 2 show the clinical and sexual behavior characteristics of all patients according to group.

Compared with the normal control group (group A), patients in the cystitis groups (group B and C) were older ( $56.7 \pm 14.8$  and  $54.6 \pm 15.0$  years old in groups B and C, respectively, vs.  $50.1 \pm 16.9$  years old in group A), had higher rates of diabetes (16.5 and 26.3 % in groups B and C, respectively, vs. 8.8 % in group A), menopause (65.2 and 55.6 vs. 45.5 %), catheterization history (11.5 and 18.8 vs. 5.5 %), history of STI (13.2 and 25.5 vs. 6.6 %), frequent sexual intercourse (5–8 times/month: 18.8 and 24.0 vs. 11.1 %;  $>9$  times/month: 15.7 and 20.3 vs. 11.1 %), sexual intercourse in the last month (50.4 and 61.6 vs. 38.8 %), contraceptive use (20.6, 33.8 vs. 10.0 %), and had a tendency to drink less water per day ( $P < 0.05$ ). Hypertension, marital status, and type of contraception were not different between the normal control group and the cystitis groups (Tables 1, 2).

Compared to the AC group (group B), the RC group (group C) had higher rates of diabetes (26.3 vs. 16.5 %), catheterization history (18.8 vs. 11.5 %), STI history (25.5 vs. 13.2 %), frequent sexual intercourse (5–8 times/month: 24.0 vs. 18.8 %;  $>9$  times/month: 20.3 vs. 15.7 %), and contraceptive use (33.8 vs. 20.6 %) ( $P < 0.05$ ). There were no differences between the AC and RC group in terms of hypertension, marital status, menopause, daily water intake, contraceptive use, or type of contraception (Tables 1, 2).

The most frequently observed pathogen in groups B and C was *E. coli*, followed by *Staphylococcus saprophyticus*, *Enterococcus* species, and *Klebsiella* species. No significant differences were found between groups regarding the spectrum and distribution of the isolated pathogens (Table 3).

In multivariate hazard regression analysis, variables related to sexual behavior (STI history, frequency of intercourse, history of intercourse in the last month, use of contraceptives) were strongly associated with risk of RC following AC. Patients who had sexual intercourse more than nine times per month were most strongly associated with risk of RC (HR, 2.715). Diabetes (HR, 1.729) and a history of catheterizations (HR, 2.142) were also associated with risk of RC following AC ( $P < 0.05$ ) (Table 4).

## Discussion

Recurrent UTI is defined as a symptomatic UTI following the resolution of an earlier episode, usually after appropriate treatment [11], with three or more symptomatic episodes of symptomatic UTIs over a 12-month period [8]. Recurrent UTIs include relapses (symptomatic recurrent

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