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Research Article

RECURRENT URINARY TRACT INFECTION IN WOMEN

¹Dr Salman Hussain, ²Dr Nuzha Sajjad, ³Dr Sufyan Akram

¹MBBS, King Edward Medical University, Lahore, ²MBBS, Foundation University Medical College, Islamabad, ³MO, BHU Chechian Dittewal, Gujrat.

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Abstract:

Aim: To evaluate factors associated with recurrent urinary tract infection (UTI) in postmenopausal women.

Method: a case-control study was conducted that comparing on 149 postmenopausal women who had a history of recurrent UTI (case patients) with 53 age-matched women without a history of UTI (control patients). Questionnaire was filled by each women providing demographic data, history and clinical characteristics of prior infections, and information regarding risk factors for UTI. In addition, each patient underwent a gynecologic evaluation, renal ultrasound and urine flow studies, and blood group and secretor status testing.

Results and conclusion Three urologic factors—namely, incontinence (41% of case patients vs. 9.0% of control patients;), presence of a cystocele (19% vs. 0%; $P = .001$ $P = .001$), and postvoiding residual urine (28% vs. 2.0%;)—were all strongly associated with recurrent UTI. Multivariate analysis showed that urinary incontinence (odds ratio [OR], 5.79; 95% confidence interval [CI], 2.05–16.42;), a history of UTI before P = .0009 menopause (OR, 4.85; 95% CI, 1.7–13.84;), and nonsecretor status (OR, 2.9; 95% P = .003 CI, 1.28–6.25;) were most strongly associated with recurrent UTI in postmenopausal P = .005 women.

Corresponding author:

Dr. Salman Hussain,
MBBS, King Edward Medical University, Lahore.

QR code



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INTRODUCTION:

A recurrent urinary tract infection (UTI) is a symptomatic UTI that follows clinical resolution of an earlier UTI generally, but not necessarily, after treatment. Recurrent UTIs are frequent among young healthy women even though they generally have anatomically and physiologically normal urinary tracts. Mabeck found that nearly one-half of the women whose uncomplicated UTIs resolved spontaneously developed a recurrent UTI within the first year¹. In a recent study of college women with their first UTI, 27% experienced at least one culture-confirmed recurrence within the 6 months following the initial infection² and 2.7% had a second recurrence over this time period. In a Finnish study of women aged 17–82 years who had *Escherichia coli* cystitis, 44% had a recurrence within 1 year, 53% in women older than 55 years and 36% in younger women³. Although epidemiologic data for older women are sparse, it is estimated that 10–15% of women over age 60 have frequent recurrences⁴. No large population based studies have yet been performed to determine what proportion of women with UTI develop a pattern of high frequency recurrences. Occasionally, recurrences are due to a persistent focus of infection (relapse), but the vast majority is thought to represent re-infection. Thus, among 464 episodes of acute uncomplicated cystitis in college women treated with a variety of antimicrobials, we have found that only 26 (5.6%) had persistent infection, defined as persistence of the initially infecting species within 1 week of the start of therapy^{5–7}. In another study of 49 patients, mostly women, some of whom had ‘complicating factors’, 84% of recurrences were episodes of re-infection (as determined by bio typing), typically months apart⁸. Prospective studies have demonstrated that *E. coli* strains causing UTI may, although appropriately treated and not found in repeated urine cultures in between, cause a new UTI up to 3 years later⁹. It is not clear whether such strains persist in the fecal flora or are reacquired from another source. In a recent study of 23 women with recurrent UTI and 35 women with first episode UTI, *E. coli* strains were evaluated by chromosomal restriction fragment length polymorphism (RFLP) analysis using pulsed field gel electrophoresis¹⁰. About 30 (68%) of 44 recurrent UTIs, including several that occurred several months apart, were caused by a strain earlier identified in that individual, while 32 (91%) of the 35 strains from first episode UTIs had unique RFLP profiles.

METHOD:

Study population and subject recruitment: During the period of study, consecutive postmenopausal women with recurrent UTI (defined as >3 microbiologically documented episodes of

symptomatic UTI managed in the hospital during the last year or 2 episodes during the last 6 months) were offered enrollment in the study. All of the enrolled women (case patients) were generally healthy, and all were ambulatory and did not have indwelling catheters. To minimize the number of control patients undergoing procedures that were of no benefit to them, 1 control patient was selected for every 3 case patients enrolled. All participants provided informed consent, and the study was approved by the Review Board.

Study procedures. Evaluation of both case and control patients was undertaken when the women were asymptomatic and abacteriuric. All of the case and control patients completed a nurse administered questionnaire inquiring about their general medical history, marital status, number of pregnancies and deliveries, underlying diseases, and previous surgical procedures. They were also questioned about their history of UTIs, including age at first UTI, factors potentially related to its appearance, and urinary incontinence. Urinary incontinence was defined as follows: urinary incontinence, involuntary loss of urine that is a social or hygienic problem and is objectively demonstrable; stress incontinence, dysfunction of the bladder outlet that leads to urinary leakage when intraabdominal pressure is raised above urethral resistance during exertion, such as coughing, bending, or lifting heavy objects; and urge incontinence, the urge to void. Cystitis and pyelonephritis were defined utilizing clinical criteria, specifically dysuria; urgency and frequency (cystitis); and fever, chills, and/or loin pain (pyelonephritis). After completion of the questionnaire, the patients underwent renal ultrasonography with a post voiding step to evaluate the volume of residual urine (Diasonic, Santa Clara, CA). The post voiding renal volume was calculated automatically by the ultrasound equipment. The residual urine volume was defined as follows: mild, persistence of glutination was determined; saliva from secretors inhibited agglutination, whereas saliva from non secretors did not.

Statistical analysis. SPSS software (SPSS, Chicago) was used to determine significant differences between variables and to perform univariate and multivariate analyses for risk factors. In the univariate analysis, the χ^2 test for categorical variables and the Student’s *t* test for numerical variables were used. Logistic regression analysis was used to find out variables that were independently associated with recurrent UTI. The variables in the selected model were chosen by backward elimination. Variables included in the model were a history of UTI, urogenital interventions, secretor status, urinary flow, and age.

RESULTS AND DISCUSSION:

Comparability of Case and Control Patient: One hundred forty-nine postmenopausal women with recurrent UTI (case patients) and 53 postmenopausal women without UTI (control patients) completed the study and were included in the final study population (tables 1 and 2). The mean age (5SD) of the patients was years and that of the 65.7 5 7.2 control patients was years. The mean number 66.6 5 6.6 (5SD) of previous childbirths per patient was also similar in the 2 groups: for case patients and for con- 2.5 5 1.2 2.3 5 1.4 trol patients. Marital status and the systemic use of estrogen were proportionally similar in the 2 groups. When asked to identify factors possibly associated with their recurrent UTIs, most case patients (78%) did not relate any specific factor to the onset of recurrent UTI. However, 27 case patients (18%) believed that their UTIs started after a gynecologic surgical intervention. Only 3 case patients (2%) related their UTIs to sexual activity.

Factors Associated with Recurrent UTIs:

Underlying medical and surgical conditions: A history of UTI before menopause or in childhood was more frequent in case patients than in control patients (table 1). Thus, only 6 (11%) of 53 control patients had had at least 1 episode of UTI before menopause as compared with 44 (30%) of the case patients (OR, 3.14; 95% CI, 1.32–8.36 ;). No differences $P = .008$ were seen in the prevalence of other underlying diseases in the 2 groups, including diabetes mellitus (table 1). More case patients than control patients had undergone urogenital surgery (27% vs. 13%, respectively; OR, 2.41; 95% CI, 1.01–5.78; $P = .04$; table 2). The reasons for surgery were total hysterectomy due to myoma or uterine carcinoma in 33 case patients and 5 control patients and prolapse of the urinary bladder in 7 case patients and 2 control patients. Urologic factors. Incontinence was present in 61 (41%) of 153 case patients as compared with 5

(9%) of 53 control patients (OR, 6.65; 95% CI, 2.5–17.7; ; table 2). None of the $P ! .001$ control patients had a cystocele observed during gynecologic evaluation in contrast to 19% of the case patients (). $P ! .001$. Of the case patients, 9 (6%) had a mild cystocele, 18 (12%) had a moderate cystocele, and 2 (1%) had severe prolapse of the bladder. Residual urinary volume was considerably more common in case patients than in control patients. Thus, only 1 control patient (2%) had a measured residual urine volume as compared with 41 (28%) of the case patients (). Most case pa- $P = .0008$ tients had mild or moderate residual urine volumes; only 6 case patients had large residual urine volumes. Urinary flow was reduced in 67 (45%) of the case patients and only 12 (23%) of the control patients (OR, 2.79; 95% CI, 1.31–6.29;). $P = .004$ Most of the case patients had only mild or moderate degrees of obstruction to urine flow (table 2).

Blood group and secretor status: There were no differences between the case patients and control patients in the distribution of blood groups or Rh factor. However, 76 (51%) of the case patients were no secretors versus 16 (30.2%) of the control patients (OR, 2.41; 95% CI, 1.23–4.7; table 3). $P = .008$

Logistic regression analysis. To better define those factors independently associated with recurrent UTI in the case patients, we carried out logistic regression analysis (table 4). Even though women with either a cystocele or a residual urine volume after voiding had a very high positive predictive value for recurrent UTIs, they were excluded from the logistic regression analysis since these conditions were essentially absent in the control patients. The factors independently associated with recurrent UTIs in the multivariate analysis were urinary incontinence (OR, 5.79; 95% CI, 2.05–16.42;), a history of $P = .009$ UTI (OR, 4.85; 95% CI, 1.7–13.84;), and nonsecretor $P = .003$ status (OR, 2.9; 95% CI, 1.28–6.25;).

Table 1. Univariate analysis of demographic and historical factors associated with recurrent UTI in postmenopausal women.

Factor	Case patients (n = 149)	Control atients (n = 53)	OR (95% CI)	P
Age, y	65.7 5 7.2	66.6 5 6.6	(24.28 to 0.17)	.07
No. of children	2.5 5 1.2	2.3 5 1.4	(20.61 to 0.15)	.24
Marital status				
Married	115	41	0.9 (0.42–1.96)	.8
Divorced	10	3		
Widowed	24	9		
Current estrogen use				
Oral and/or vaginal	41 (28)	8 (15)	2.14 (0.89–5.68)	.07
None	108 (72)	45 (85)		
Diabetes mellitus	30 (20)	9 (17)	1.23 (0.54–2.8)	.62
UTI in childhood	10 (7)	0	Undefined	.06
UTI before menopause	44 (30)	6 (11)	3.14 (1.32–8.36)	.008

Table 2. Univariate analysis of urologic factors associated with recurrent UTI in postmenopausal women.

Factor	Case patients (n = 149)	Control patients (n=53)	OR (95% CI)	P
Residual urine volume	41 (23)	1 (2)	Undefined	.0008
Reduced urine flow	67 (45)	12 (23)	2.79 (1.31–6.29)	.004
Urogynecologic surgery	40 (27)	7 (13)	2.41 (1.01–5.78)	.04
Incontinence	61 (41)	5 (9)	6.65 (2.5–17.7)	!.001
Any cystocele	29 (19)	0	Undefined	!.001

Table 3. Univariate analysis of blood group and secretor status in postmenopausal women with recurrent UTI and in control patients.

Factor	Case patients (n=149)	Control patients (n=53)	OR (95% CI)	P
Blood group				
O	39 (26.5)	19 (35.8)	1	
A	65 (44.2)	20 (37.7)	0.63 (0.28–1.42)	.48
B	38 (25.5)	11 (20.8)	0.59 (0.23–1.53)	
AB	5 (3.4)	3 (5.7)	1.23 (0.71–7.1)	
Rh factor				
Positive	17 (11.6)	9 (17)	1.56 (0.65–3.76)	.31
Negative	130 (88.4)	44 (83)		
P blood group	105 (71)	32 (60.4)	1.6 (0.83–3.08)	.16
Nonsecretor	76 (51)	16 (30.2)	2.41 (1.23–4.7)	.008

Table 4: Multivariate analysis of factors predisposing postmenopausal women to UTI

Factor	OR (95% CI)	P
Urinary incontinence	5.79 (2.05–16.42)	0.0009
History of UTI	4.85 (1.7–13.84)	0.003
Nonsecretor	2.9 (1.28–6.25)	0.005

CONCLUSION:

Our data support the view that several factors importantly influence the incidence of recurrent UTI among postmenopausal women. These factors include a history of UTIs, no secretor status, and possibly other inherited predispositions, as well as urodynamic factors, especially incontinence, residual urine volume, and presence of a cystocele. These major factors predisposing to recurrent UTI in postmenopausal women differ importantly from the factors that predominate in premenopausal women with recurrent UTI.

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