



Original Article

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Level of Anxiety Shows a Positive Correlation With the Frequency of Acute Cystitis Recurrence in Women

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Purpose: Previous studies have simply confirmed recurrence of acute cystitis negatively affects a patient's psychological state. This study was performed to assess the impact of the recurrence of urinary tract infections on anxiety and depression and further assess whether there is a correlation between the number of recurrences and the degree of anxiety and depression.

Methods: This cross-sectional study enrolled patients with recurrent cystitis who visited a tertiary care center between April 2018 and June 2022. For eligible patients, depression and anxiety were assessed by the Patient Health Questionnaire-9 and State-Trait Anxiety Inventory. Among the clinical characteristics, factors that independently affected the degree of depression and anxiety were analyzed. Additionally, the relationship between the level of anxiety, depression, and the number of recurrent cystitis was assessed.

Results: A total of 112 female patients with recurrent cystitis were enrolled in this study. The proportion of patients with depression (moderate, 8%; severe, 0%) was relatively low compared with that of patients with anxiety (moderate, 22.3%; severe, 68.8%). Multivariate regression analysis showed that more recurrent episodes were significantly associated with higher anxiety scores ($P < 0.001$). It was confirmed that longer disease duration is associated with higher depression scores ($P = 0.031$). Additionally, there was a positive correlation between the number of recurrences and State-Trait Anxiety Inventory and Patient Health Questionnaire-9 scores ($r = 0.362$, $P < 0.001$ and $r = 0.248$, $P = 0.009$, respectively).

Conclusions: Our study reveals that recurrent cystitis notably increases patients' anxiety, correlating with the frequency of recurrences. Disease duration is also linked to depression. These findings emphasize the importance of preventing urinary tract infection recurrences to reduce psychological complications. To reinforce these results, larger cohort studies are necessary.

Keywords: Female; Recurrence; Cystitis; Anxiety; Depression


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INTRODUCTION


It is known that one in 2 women of all ages experience at least one episode of cystitis in their lifetime. Uncomplicated urinary tract infections (UTIs) are not life-threatening, as most cases resolve within days of treatment initiation. However, UTIs are as-

sociated with considerable morbidity and negatively affect some patients' quality of life (QoL) (time lost from daily activities) [1, 2].

Approximately one-third of female patients with UTI experience recurrence at least once [3]. Patients with recurrent UTIs experience a psychological burden because they live with the

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anxiety of sudden acute episodes and UTI symptoms [4]. Several studies have examined the psychological impact of recurrent UTIs [1, 4, 5]. The recurrence of sudden acute UTI can lead to problems such as self-devaluation or neglect, which can lead to depressive symptoms. In one study, up to 81% of women with acute or recent occurrences of UTI had a lower-than-average mental health score, and up to 71% of female patients showed depression at baseline [6].

However, previous studies have not confirmed whether the number of recurrent UTIs negatively correlates with a patient's psychological state (anxiety and depression). This study aimed to determine the impact of recurrent UTIs on patient's depression and anxiety and to assess whether there is a correlation between the degree of anxiety and depression and the number of UTI recurrences.

MATERIALS AND METHODS

Study Design and Population

This cross-sectional study enrolled patients with recurrent cystitis who visited the Urology Department of Guro Hospital, Korea University, from April 2018 to June 2022. Female patients (aged ≥ 18 years) with recurrent UTIs (defined as 2 or more acute symptomatic infections in 6 months or 3 or more infections within 1 year) were included. Patients who had urological abnormalities, systemic sepsis, an immune-compromised state, conditions that could lead to UTI-like symptoms (e.g., yeast vaginitis and interstitial cystitis), or a history of psychological disease before the history of recurrent cystitis based on a self-report or chart review were excluded. Patients who were pregnant were also excluded.

Assessment of Depression and Anxiety

Spielberger State-Trait Anxiety Inventory

The Spielberger State-Trait Anxiety Inventory (STAI) is a commonly used method for measuring anxiety levels. The STAI comprises 2 types: traits and states. Trait anxiety is a relatively stable personality characteristic, while state anxiety may vary depending on stress at a specific point in time. To measure anxiety caused by recurrent UTIs, this study assessed anxiety using the STAI-state (STAI-S). The STAI-S is a self-questionnaire comprising 20 items. The patients responded to each item on a Likert scale ranging from 1 (not at all) to 4 (very much so). The total score is the sum of responses to all 20 items and has a possible range of 20–80 points. Anxiety levels can be grouped according

to the STAI-S score as mild (≤ 39), moderate (40–45), and severe (≥ 46) [7].

Patient Health Questionnaire-9

The Patient Health Questionnaire-9 (PHQ-9) is a self-reported measure of depression consisting of 9 items that meet the criteria for diagnosis and statistics of major depression in the 4th edition (*Diagnostic and Statistical Manual of Mental Disorders, 4th ed*). Respondents could choose each item on a scale of 0 to 3 based on how much the symptoms bothered them in the past 2 weeks (0 = not at all, 1 = several days, 2 = more than half the day, 3 = nearly every day). The total score is obtained by adding the scores for the 9 items and can range from 0 to 27. Depression levels may be grouped according to the PHQ score as follows: minimal (0–4), mild (5–9), moderate (10–20), and severe (> 20) [8]. A PHQ-9 score of 10 or higher corresponds to significant depression, with 88% sensitivity and 88% specificity [9].

Clinical Data and Assessment

Data on clinical variables such as marital status, menopause, presence of comorbidities (hypertension [HTN], diabetes mellitus, history of immune-stimulating agent use, history of surgery [incontinence surgery and gynecologic surgery]), disease duration (defined as the time from the first onset of symptoms to the latest medical visit), and the number of recurrences was collected. Patients were divided into subgroups according to the number of recurrences and disease duration. Differences in the levels of anxiety and depression between these subgroups were analyzed. Among the clinical characteristics, factors that independently affected the levels of depression and anxiety were also analyzed. Also, the correlation between the number of recurrences of UTI and the level of anxiety and depression was assessed.

Statistical Analysis

Continuous variables are presented as means for parametric data and medians for nonparametric data. Categorical variables are expressed as percentages or ratios. Correlation analysis was performed on the levels of depression and anxiety based on clinical characteristics, including the number of recurrences, disease duration, and age. A t-test or 1-way analysis of variance was applied to demonstrate statistical differences.

Independent factors that affected depression and anxiety scores were determined using linear regression models. Only factors that exhibited P-values below 0.05 in the univariate

analysis were incorporated into the multivariate analysis. The regression coefficient was analyzed between depression or anxiety scores and the presence of other diseases (HTN, malignancy), disease duration, and the number of recurrences. All probabilities were 2-tailed, and the significance level was set at 0.05. Statistical analyses were performed using IBM SPSS Statistics ver. 25.0 (IBM Co., Armonk, NY, USA).

RESULTS

In this study of 112 female patients with recurrent UTIs, demographic characteristics including median age, marital status, and menopausal status are detailed in Table 1. These patients had a median age of 57 years. The majority of participants were married (89.3%). In terms of menopausal status, 74.1% were postmenopausal.

Recurrent Cystitis and Anxiety

The State-Trait Anxiety Inventory (STAI-S) revealed that a significant number of participants experienced severe (68.8%) and moderate (22.3%) anxiety, averaging a score of 56.11 ± 11.88 . The average number of recurrences was 3.64 ± 1.11 , with 46.4% experiencing 4 or more (Table 1). Multivariate linear regression analysis indicated that higher recurrence significantly predicted increased anxiety levels ($B = 6.278, P < 0.001$) (Table 2). A positive correlation was observed between the number of recurrences and STAI-S scores (Pearson correlation coefficient 0.362, $P < 0.001$) (Table 3).

Recurrent Cystitis and Depression

The PHQ-9 scores showed mild (33.9%) and moderate (8.0%) depression, with an average score of 4.12 ± 3.68 (Table 1). There were significant differences in PHQ-9 scores for 2, 3, and ≥ 4 recurrences ($P = 0.046$), and a notable correlation was found with disease duration ($P = 0.027$) (Table 2). Regression analysis revealed that higher recurrence was a predictor of increased depression ($B = 1.056, P = 0.041$), and disease duration significantly predicted the PHQ score ($B = 0.287, P = 0.031$) (Table 2). The PHQ-9 score was positively correlated with the number of recurrences (Pearson correlation coefficient 0.248, $P = 0.009$) and disease duration ($P = 0.027$) (Table 3).

DISCUSSION

Previous studies have discovered a positive correlation between

Table 1. Summary of patient characteristics (n = 112)

Variable	Value
Median age (yr)	57.00
Body weight (kg)	57.95 ± 7.60
Marital status	
Single	12 (10.7)
Married	100 (89.3)
Menopause	
Pre	29 (25.9)
Post	83 (74.1)
Immuno-stimulating agent use history (Bacterial lysate)	81 (71.7)
History of surgery	
Incontinence surgery	8 (7.14)
Gynecologic surgery	23 (20.5)
Comorbidity	
Hypertension	23 (20.5)
Diabetes mellitus	14 (12.5)
Malignancy	3 (2.7)
No. of recurrences within 1 year	3.64 ± 1.11
2 Times	18 (16.1)
3 Times	42 (37.5)
≥ 4 Times	52 (46.4)
Disease duration (mo)	
≤ 12	32 (28.5)
> 12	80 (70.8)
Psychological impact	
STAI-S ^{a)}	56.11 ± 11.88
Severe	77 (68.8)
Moderate	25 (22.3)
Mild	10 (8.9)
PHQ-9 ^{b)}	4.12 ± 3.68
Severe	0 (0)
Moderate	9 (8.0)
Mild	38 (33.9)
Minimal	65 (58.0)

Values are presented as mean \pm standard deviation or number (%). STAI-S, State-Trait Anxiety Inventory-state; PHQ-9, Patient Health Questionnaire-9.

^{a)}STAI-S mild (≤ 39), moderate (40–45), or severe anxiety (≥ 46). ^{b)}PHQ-9 minimal (0–4), mild (5–9), moderate (10–20), and severe (> 20).

the prevalence of depression and anxiety among patients with recurrent UTIs [5, 10]. In addition, Renard et al. [5] indicated that a decrease in the number of UTI recurrences was associat-

Table 2. Predictors of depression score (PHQ-9) and anxiety score (STAI-S)

Characteristic	PHQ-9					STAI-S				
	Value	Univariate		Multivariate		Value	Univariate		Multivariate	
		B	P-value	B	P-value		B	P-value	B	P-value
Age		0.028	0.505			0.088	0.077			
Menopause		0.795	0.402			2.571	0.627			
No	3.62 ± 3.19					57.03 ± 12.04				
Yes	4.29 ± 3.84					55.78 ± 11.88				
Marital status		1.126	0.438			3.621	0.231			
No	3.33 ± 3.34					60.00 ± 8.95				
Yes	4.21 ± 3.72					55.64 ± 12.13				
Diabetes mellitus		1.056	0.900			3.405	0.641			
No	4.13 ± 3.67					56.31 ± 11.86				
Yes	4.00 ± 3.86					54.71 ± 12.37				
Hypertension		0.865	0.983	0.836	0.981	2.738	0.041	2.547	0.053	
No	4.11 ± 3.39					57.27 ± 12.22				
Yes	4.13 ± 4.73					51.61 ± 9.38				
Immuno-stimulating agent use history (bacterial lysates)		-0.375	0.632			-4.401	0.079			
No	4.39 ± 3.39					59.29 ± 9.82				
Yes	4.01 ± 3.80					54.89 ± 12.42				
Incontinence surgery history		1.356	0.123			4.331	0.130			
No	55.51 ± 12.08					4.15 ± 3.77				
Yes	62.25 ± 6.39					4.25 ± 2.19				
Gynecological surgery history		0.865	0.916			2.768	0.185			
No	4.13 ± 3.64					55.35 ± 12.18				
Yes	4.04 ± 3.91					59.04 ± 10.32				
Disease duration (mo)		0.284	0.027	0.287	0.031	0.942	0.799	0.874	0.607	
≤ 12	2.85 ± 2.61					55.69 ± 11.15				
> 12	2.95 ± 1.99					57.16 ± 11.03				
Recurrent times		0.468	0.046 ^{a)}	1.056	0.041	1.442	<0.001 ^{a)}	6.278	<0.001	
2 Times	3.28 ± 2.97		-			50.06 ± 6.92		-		
3 Times	3.33 ± 3.12		0.998 ^{b)}			53.07 ± 12.15		0.603 ^{b)}		
≥ 4 Times	5.04 ± 4.14		0.063 ^{c)}			60.65 ± 11.43		0.004 ^{c)}		

Values are presented as mean ± standard deviation or number (%). STAI-S, State-Trait Anxiety Inventory-state; PHQ-9, Patient Health Questionnaire-9. ^{a)}Comparison between all groups. ^{b)}Compared to 2 times. ^{c)}Compared to 3 times.

ed with reduced anxiety and depression, but they did not present a correlation coefficient, making it impossible to determine the extent of the correlation. This study also verified that an increase in the number of recurrences leads to a heightened risk of developing anxiety and depression. We directly compared

depression and anxiety scores according to the number of recurrences and found that, even after adjusting for other factors, the number of recurrences is an independent predictor of depression and anxiety. This aspect may be considered a strength of our study in comparison to others.

Table 3. Pearson correlation analysis

Variable	STAI-S		PHQ-9	
	Coefficient	P-value	Coefficient	P-value
Age	-0.168	0.077	0.064	0.505
No. of recurrences	0.362	<0.001	0.248	0.009
Disease duration	-0.024	0.799	0.209	0.027

STAI-S, State-Trait Anxiety Inventory-state; PHQ-9, Patient Health Questionnaire-9.

Recurrent Cystitis and Anxiety

This study demonstrated that patients with recurrent UTIs frequently experience high anxiety levels, with 68.8% reporting severe and 22.3% moderate anxiety complementarily, another study found that 30% of patients with recurrent UTI suffered from anxiety, 4% from depression, and 24% from both [10]. Notably, an improvement in anxiety related to clinic visit satisfaction was observed, with STAI-S scores indicating higher anxiety in 6 patients with recurrent UTIs compared to those without, prior to their visit. The limited sample size was acknowledged as a constraint [11]. Nevertheless, our study established a positive correlation between the number of recurrences and anxiety (coefficient=0.362, $P < 0.001$), corroborating Renard et al. [5]’s findings using the Hospital Anxiety and Depression (HAD) score. Significant variations in STAI-S scores were identified across different recurrence counts ($P < 0.001$), particularly between the third and fourth recurrences, though not between the second and third, possibly due to different reference periods (6 months and 12 months). Despite these discrepancies, it was consistently evident that anxiety levels escalated with an increase in UTI recurrences.

Recurrent Cystitis and Depression

In this study, a mere 8% of patients exhibited signs of depression (moderate, 8%; severe, 0%), indicating that the incidence of depression in those with recurrent UTI is significantly lower than that of anxiety disorders (severe, 68.8%; moderate, 22.3%). A multicenter trial assessing QoL in patients with recurrent UTI using the HAD and Leicester scales found that approximately 12.9% exhibited depression initially [5]. Medina et al. [12] suggested that feelings of guilt due to restrictions in social activity or daily life among patients with recurrent UTIs might contribute to clinical symptoms of depression. Despite the low incidence, our study revealed a significant difference in PHQ-9 scores with an increase in the number of recurrences ($P = 0.046$),

supporting another study which reported decreased depression following UTI treatment and reduced incidence of UTIs, which documented significantly less depression after patients were treated for UTIs and the incidence of UTIs decreased [5]. Reflecting on the chronicity of the disease, we explored the relationship between UTI chronicity, STAI-S, and PHQ-9 scores using disease duration as a measure. Here, disease duration correlated only with PHQ-9 (correlation coefficient 0.234, $P = 0.013$), while no significant correlation was found with STAI-S. Moreover, no substantial difference was noted between PHQ-9 and STAI-S scores in relation to disease duration. Ellis and Verma [1] using the 36-item Short Form health survey (SF-36) indicated that disease duration did not markedly affect overall QoL, yet a negative correlation was observed within the SF-36 subsections (mental health section and disease duration). Given the SF-36 evaluates mental health on both depression and anxiety scales, it’s challenging to isolate the correlation specifically to depression, confirming our findings [13]. Consequently, further research is essential to elucidate the relationship between disease duration, depression, and anxiety comprehensively.

The present study is subject to several limitations. Firstly, the absence of a matched healthy control group is a notable drawback. Despite this, discerning which patients with recurrent UTIs experienced more severe psychological issues was feasible. Secondly, the potential impact of inherent personality traits on anxiety levels was not examined. For individuals predisposed to anxiety, differentiating between anxiety stemming from the disease and their baseline state is complex. This is underscored by research indicating a strong association between neurotic personality traits and symptoms of depression and anxiety, with such traits potentially leading to behaviors that increase UTI risk [14, 15]. Acknowledging depression and anxiety as secondary symptoms of recurrent cystitis is vital, along with a comprehensive understanding of the patients’ psychological profiles. Measuring STAI-T scores could have mitigated this limitation by providing a more nuanced view of the anxiety’s origin. Thirdly, the non-randomized design of the study may introduce self-selection bias, a common issue in stress-related research. This is reflected in the disproportionately high percentage of patients with severe anxiety (severe, 68.8%; moderate, 22.3%) in this study, possibly indicative of higher participation rates among those experiencing greater anxiety. Moving forward, re-evaluating the sampling method when adequate data are available will be considered to address these issues. As the fourth limitation, it should be noted that our study did not capture

comprehensive treatment histories or any data on the severity or presence of UTI symptoms. The retrospective design inherently limited the scope of information we could collect. Given the critical importance of these variables, it is crucial for future prospective studies to include such detailed data. This would allow for a more nuanced analysis of the relationships between treatment approaches, symptom details, and psychological health outcomes in patients with recurrent UTIs.

In conclusion, our study reveals that recurrent cystitis notably increases patients' anxiety, correlating with the frequency of recurrences. Disease duration is also linked to depression. These findings emphasize the importance of preventing UTI recurrences to reduce psychological complications. To reinforce these results, larger cohort studies are necessary.

AUTHOR CONTRIBUTION STATEMENT

- Conceptualization: *SBJ, MMO, STA*
- Data curation: *SBJ, MMO, HJK*
- Formal analysis: *SBJ, HJK*
- Methodology: *SBJ, MMO, STA*
- Project administration: *MMO*
- Visualization: *SBJ, MMO, STA*
- Writing - original draft: *SBJ, MMO, STA*
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