

## Original Article

# Not the Postmenopausal Syndromes, Urinary Complaints are the Most Common Presentation of the Post-Menopausal Women

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### Abstract:

Postmenopausal estrogen deprived state causes various types of vasomotor symptoms, urogenital symptoms, and long-term health hazards. Among the postmenopausal women, this study was aimed to determine the prevalence of urogenital complaints, epidemiological studies relating with recurrent UTI, and to observe the changing pattern of bacterial resistance to commonly used antibiotics for UTI. This cross-sectional study was conducted in Faridpur, Bangladesh, from January-December 2019. Total 244 postmenopausal women attending the clinic with various complaints were selected as the study population. In-depth history, clinical examination, and relevant investigations were done. Urinary culture and sensitivity were done to isolate the causative organism and to identify the current antibiotic resistance and sensitivity pattern. Among the study population, 94.7% had urinary complaints as their first concern. However, upon query, 85.2% of them revealed that they had other postmenopausal syndromes. Among the study population, 43.4% had recurrent UTI. Burning micturition was the most common (79.2%) urinary complaint. On urinary culture, 57.5% cases had no growth; among the rest, the most common organism was *E. coli* (19.8%) followed by *Proteus* (12.3%) and *Klebsiella* (10.4%). In *Proteus* and *Klebsiella* isolates, a high number of resistances for Nitrofurantoin have been found (75% and 66.7% accordingly). Urinary complaints are the most common presentation of postmenopausal women attending the gynecology clinic. They are seeking treatment not to improve the quality of life with hormone replacement therapy (HRT), but getting rid of the pain of recurrent UTI.

**Key words:** Recurrent urinary tract infection, Postmenopausal syndrome, Bacterial resistance

### Introduction:

Urinary tract infection (UTI) is one of the most common bacterial infections worldwide with an estimated 150 million UTIs occurring annually<sup>1,2</sup>. It has been found that almost half of all women will experience at least one episode of UTI during their lifetime<sup>3,4</sup>. Almost 6-10% of girls and young women have bacteriuria and this incidence rises to 25% to as high as 50% in the case of the elderly population<sup>5</sup>. Between 8-10% postmenopausal women experience

urinary tract infection each year, and among them, more than 5% experiences a recurrence within 12 months<sup>6,7</sup>. At the same time, in some studies on Greek, Finnish and American patients, bacteriuria has been found as a cause of increased mortality in elderly individuals<sup>8-10</sup>.

Several risk factors for recurrent UTIs in postmenopausal women have been identified. Advanced age, parity, postmenopausal status, recent antimicrobial exposure, and sexual activity have been found as contributing factors to the development of UTI<sup>2,6,11-14</sup>. Different urogenital factors such as urinary incontinence, pelvic organ prolapse, cystocele, an increased postvoid residual, urinary catheterization, and urogenital surgery in postmenopausal women are also associated with increased risk of UTI<sup>5,8,11,13,15</sup>. Moreover, associated comorbidities, such as diabetes mellitus and history of a prior UTI are associated with increased risk of UTI<sup>6</sup>. Among the health behavior and epidemiological factors, genetic predisposition had been found in some cases<sup>5</sup>.

Due to increased life expectancy, a woman usually passes one-third of her life with estrogen deficiency.

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UTI is a common presentation among postmenopausal women as estrogen deficiency is one of the major causes of the development of bacteriuria. However, in the clinical setup, such women usually do not present with the complaints of postmenopausal syndromes; instead, they present with UTI and other genitourinary symptoms such as vaginal dryness, itching, irritation and dyspareunia<sup>5,16,17</sup>.

Treating women with recurrent UTI is a challenge. Nevertheless, effective treatment can minimize the burden of symptoms for patients with recurrent UTI<sup>18</sup>. It has been found that postmenopausal women using estriol orally or vaginally had a reduced rate of recurrence of UTI<sup>5,8,16,19</sup>. On the other hand, long-term, low-dose prophylactic antimicrobial therapy, specially Nitrofurantoin, has been well considered as a prophylaxis but the emergence of antimicrobial-resistant bacteria is a concern here<sup>7</sup>. Once again, a high prevalence of UTI with its inappropriate and excessive antimicrobial treatment is causing increased antibiotic resistance<sup>1</sup>.

Due to an alarming increase in multi-drug-resistant uropathogens, alternative strategies such as restoration of flora with lactobacilli using probiotics and the use of cranberry, a competitive compound that inhibits the attachment of bacteria to the uroepithelial mucosa, are being adapted to reduce the frequency of UTI<sup>8</sup>.

Despite the high prevalence of UTI in postmenopausal women, the predisposing factors have been little explored<sup>5</sup>. This study aimed to explore the epidemiological factors related to recurrent UTI in postmenopausal women. We also aimed at finding the prevalent causative organisms responsible for recurrent UTI and their antibiotic sensitivity and resistance patterns.

### Materials and Methods:

This cross-sectional study was conducted in a specialized private clinic of gynecology at Faridpur, Bangladesh, from January 2019 to December 2019. A total of 244 postmenopausal women attending the clinic with various complaints from January 2019 to June 2019 were included in the study. Recurrent UTI was defined as three or more episodes of UTI in the last year or at least two episodes in the last six months<sup>6,11</sup>. Among the patients who were diagnosed as recurrent UTI were kept in follow up for the next six months (From July 2019 to December 2019).

After taking informed consent, a detailed history of urinary complaints, other postmenopausal symptoms, familial and previous history of UTI, associated comorbidities, history of current sexual health and past

treatment history were recorded in a preformed questionnaire. At the same time, the related epidemiological status of the patients such as age, level of education, residence, parity, marital status, personal hygiene and sanitation practices were noted.

Then, a thorough clinical and gynecological examination of all the patients was done. After that, blood samples of the patients were obtained for hematologic and biochemical testing. At the same time, clean-catch midstream urine specimens were collected for urinalysis, culture and sensitivity testing.

We provided a formulated treatment approach for the 106 patients diagnosed with recurrent UTI. Firstly, we selected appropriate antibiotic based on the culture and sensitivity report. Secondly, we suggested appropriate hormone replacement therapy (HRT) after excluding all contraindications, and explaining the side effects of HRT. Thirdly, we used Cap. LUVENA as Probiotics which was first time introduced by Incepta Pharmaceuticals Limited in Bangladesh. Fourthly, we used Cap. CRANBIOTIC 400mg as cranbiotic which was first time introduced in Bangladesh by Radiant Nutraceuticals Limited. And finally, associated comorbidities were treated and the patients were advised to improve personal hygiene.

The study patients were kept in follow-up for the next 6 months at 3<sup>rd</sup> and 6<sup>th</sup> month schedule of the initiation of the treatment and the disease progress along with recurrence of UTI were recorded.

Statistical analysis was performed using GraphPad Prism version 8.4.0 for Mac (GraphPad Software, San Diego, California USA). Frequency and percentage were determined for comparative purposes. Chi-square (2) and Student's t-Test were applied to test the correlation and determine the statistical significance of patients' complaints and history concerning their diagnosis. For all analytical tests, we used 0.05 as alpha level.

Prior permission was taken from the Ethical Review Committee (ERC) of Faridpur Medical College Hospital.

### Results:

A total of 244 postmenopausal women who attended the clinic for various complaints were included in the study as the study population. Among them, 95.08% visited the clinic primarily for urinary complaints. When they were further asked for associated postmenopausal syndromes, 85.25% of them said that they had associated syndromes of postmenopausal state.

Table I shows the various presenting urinary and other postmenopausal complaints of the study population. The most common (72.5%) presenting complaint was burning micturition. In addition to that, almost half of the patients had complaints of dysuria (47.5%). Regarding associated postmenopausal complaints, 84.4% of patients had bone pain and 83.2% had a hot flush.

**Table I:** Urinary and associated postmenopausal complaints of the study population.

Presenting Complaints	Number	Percentage (%)
Urinary complaints	231	94.7
Burning micturition	177	72.5
Dysuria	116	47.5
Urgency	75	30.7
Sense of incomplete evacuation	94	38.5
Increased frequency of micturition	79	32.4
Incontinence	35	14.3
Hesitancy	54	22.1
Associated postmenopausal complaints	208	85.2
Bone pain	206	84.4
Hot flash	203	83.2
Dyspareunia	101	41.4
Vaginitis	80	32.8

Among the study population, we have found that 21.3% of patients had acute UTI and 43.4% had recurrent UTI (Table II).

**Table II:** Incidence of disease conditions among the patients (n = 244):

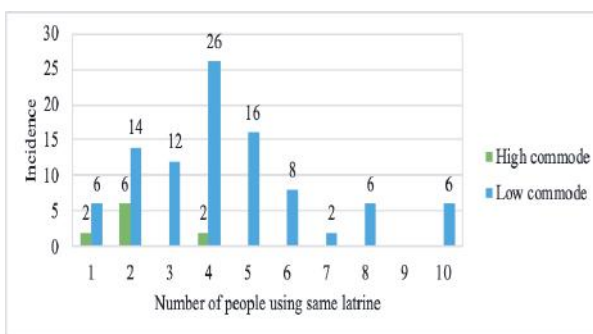
Disease condition	Number	Percentage (%)
Recurrent UTI	106	43.4
Acute UTI	52	21.3

The majority (42.5%) of the patients with recurrent UTI were between the age group of 50-59 years followed by 36.8% in the group of 40-49 years. Among them, 58.5% were from the rural area, 41.5% from the urban area and most of them (81.1%) were married at the time of diagnosis. Almost half of them were illiterate (45.3%), and most of them (90.6%) used low commode as their sanitation system. Tube well water had been found the most common (75.5%) source of water in the latrine (Table III).

**Table III:** Demographic variables of the pahegs with verweht UTI (n-106)

Traits	Number	Percentage
Age group (Years)		
30-39	6	5.7
40-49	39	36.8
50-59	45	42.5
60-69	7	6.6
70-80	6	5.7
Address		
Rural	62	58.5
Urban	44	41.5
Level of education		
Illiterate	48	45.3
Primary	20	18.9
Secondary	34	32.1
Higher secondary and above	4	3.8
Marital status		
Married	86	81.1
Widow	18	17.0
Divorced	2	1.9
Sanitation system		
Low commode	96	90.6
High commode	10	9.4
Water source in the latrine		
Tube well water	80	75.5
Supply water	20	18.9
Surface water	6	5.7

Among the respondents, most of them shared the same latrine with other members of the family and in some cases; the number of persons shared one latrine was as high as with 10 persons (Fig-1).



**Figure 1:** Bar chart of the number of people using the same latrine (n= 106)

Among the patients with recurrent UTI, approximately half of them (52.8%) were in the reference range of BMI. In case of the pattern of menopause, almost half of them (45.3%) had surgical menopause. On the other hand, more than two-thirds of the patients (64.2%) were not taking any sort of HRT (Table IV).

**Table IV:** Pattern of menopause and postmenopausal sexual and treatment history among the patients with recurrent UTI

Traits	Number	Percentage
BMI		
Underweight	6	5.7
Reference range	56	52.8
Overweight	34	32.1
Obese	10	9.4
Pattern of menopause		
Natural	58	54.7
Surgical	48	45.3
HRT		
None	68	64.2
Oral/vaginal	38	35.8

When we looked at the past and family history of the patients with recurrent UTI, we have found a statistical significance of recurrent UTI with the history of maternal UTI ( $p = <0.001$ ). We found that almost half of them had a history of antimicrobial exposure within the last year or had undergone any sort of urogenital surgery in the past. On the other hand, more than half (58.5%) of the patients with recurrent UTI had the complaint of constipation in the past (Table V).

**Table V:** Associated past and family history of the study patients (n= 106)

History of	Number	Percentage	P value
Maternal UTI	18	17.0	<0.001
Dry vagina	28	26.4	0.163
Cystocele	10	9.4	0.539
Constipation	62	58.5	0.884
Antimicrobial exposure (within last 1 year)	54	50.9	0.235
Catheterization (within last 1 year)	18	17.0	0.235
Urogenital surgery	52	49.1	0.679
Spermicidal exposure	14	13.2	0.970

On random blood sugar test of the patients with recurrent UTI, we found that most of them (84.0%) were in the normal reference range. At urine routine investigation, we found more than half of the patients (52.8%) had  $>5$  pus cells/HPF. *E. coli* was the predominant organism (26.4%) isolated in the urine culture. We also found *Proteus* and *Klebsiella* 15.1% and 11.3% cases respectively. However, in 47.2% cases, we did not find any isolate of the organism (Table VI).

**Table VI:** Investigation findings of the patients with recurrent UTI

Investigations	Number	Percentage
RBS (mmol/)		
4-6.9	89	84.0
7-9.9	11	10.4
10-12.9	3	2.8
13-18	3	2.8
Urine pus cell (/HPF)		
1-5	50	47.2
6-10	23	21.7
11-15	21	19.8
16-20	6	5.7
Plenty	6	5.7
Bacterial culture		
No growth	50	47.2
<i>E. coli</i>	28	26.4
<i>Proteus</i>	16	15.1
<i>Klebsiella</i>	12	11.3

At the antibiotic sensitivity test of the isolates, 14.3% *E. coli* were resistant to Nitrofurantoin. However, this percentage increased to 66.7% for *Klebsiella* and 75.0% for *Proteus* isolates. Among the others, Nalidixic acid, Cefuroxime, Cephalexin, Ceftriaxone, Cephadrine were found to be resistant to some degrees to the microbial isolates (Table VII).

**Table VII:** Antibiotic resistance status to the isolated organisms

Organism	<i>E. coli</i> N = 28 (%)	<i>Proteus</i> N = 16 (%)	<i>Klebsiella</i> N = 12 (%)
Nitrofurantoin	4 (14.3)	12 (75.0)	8 (66.7)
Nalidixic acid	20 (71.4)	12 (75.0)	8 (66.7)
Cefuroxime	12 (42.9)	4 (25.0)	4 (33.3)
Cephalexin	12 (42.9)	16 (100.0)	12 (100.0)
Azithromycin	8 (28.6)	0 (0.0)	0 (0.0)
Ceftriaxone	8 (28.6)	0 (0.0)	8 (66.7)
Cephadrine	8 (28.6)	0 (0.0)	12 (100.0)
Ciprofloxacin	8 (28.6)	0 (0.0)	4 (33.3)

Based on the history, clinical examination and investigation findings, Nitrofurantoin was the most common (49.1%) prescribed antibiotic. More than half of the patients (52.8%) were given estrogen as HRT. Probiotics and cranbotics were given to 60.4% and 7.5% patients respectively (Table VIII).

**Table VIII:** Treatment given to the patients with recurrent UTI ( $n = 106$ )

Treatment	Number	Percentage
Antibiotic		
None	10	9.4
Amoxicillin + clavulanic acid	4	3.8
Azithromycin	2	1.9
Cefuroxime	6	5.7
Cefuroxime + clavulanic acid	10	9.4
Moxifloxacin	22	20.8
Nitrofurantoin	52	49.1
HRT		
None	24	22.6
Estrogen	56	52.8
Tibolone	26	24.5
Probiotics	64	60.4
Cranbiotics	8	7.5

The patients were followed up during the next six months from the initiation of the treatment. Among the 106 patients with recurrent UTI, 85.8% of patients improved the symptoms and had no recurrence of UTI (Table IX).

**Table IX:** Follow-up status of the patients after treatment

Recurrence of UTI	Number	Percentage
No	91	85.8
Yes	15	14.2

### Discussion:

During the postmenopausal period, most of the women tend to ignore the PM syndromes. In a study done by Khan et al found that postmenopausal women, especially from rural areas ignore the postmenopausal syndromes and are reluctant to seek medical and psychological help. Moreover, they consider such syndromes as age-related and try to adapt with the physiological and psychological changes<sup>20</sup>. In our setting, we have found that almost all of the women attended the clinic for the relief of urinary complaints only. In a study done by Khan et al. on the Indian population, they have found that 59.6% postmenopausal women reported urinary symptoms upon query<sup>20</sup>. However, upon query, 85.2% of them said that they also had been suffering from other postmenopausal symptoms such as bone pain (84.4%), hot flash (83.2%), dyspareunia (41.4%), and others. However, they did not come to the clinic to seek help for those complaints. Rather most of the patients considered it to be normal, unavoidable age-related

complications and tried to adapt to such conditions. As a result, most of them attended the clinic in a search for the relief of the urinary complaints only.

Among the urinary complaints, we found that burning micturition was significantly associated with recurrent UTI among the postmenopausal women. Among the others, we also found dysuria, urgency, increased frequency of micturition, and other complaints. Seaberg et al, Milart et al and others have found in their study that reduced urinary flow, urinary incontinence, presence of a cystocele, and postvoiding residual urine were strongly associated with recurrent UTI<sup>11,21,22</sup>.

Although Khan et al<sup>20</sup> and others have found that rural women are less likely to seek for help, we have found that both the postmenopausal women from rural and urban area have attended the clinic; moreover, 58.4% women with postmenopausal recurrent UTI were from rural areas and 41.5% were from urban areas.

Milart et al suggested to consider the behavioral risk factors for recurrent UTI<sup>21</sup>. In case of sanitation practices, we found that most of them (90.6%) use a low commode and tube-well water is the main source of water in the latrine. Furthermore, most of the latrines are shared by many other members of the household and in many cases more than five people shared the same latrine. Maintenance proper hygiene under such circumstances may be difficult and it may be associated with recurrent UTI among the postmenopausal women.

Although the association of BMI with recurrent UTI among the postmenopausal women is inconclusive, we have found that 47.2% of women with recurrent UTI were not in their reference weight range.

While assessing the past history of the postmenopausal women with recurrent UTI, we found a significant association of recurrent UTI with a history of maternal UTI ( $p = <0.001$ ). It correlates with the study done by Hooton et al where they have found a maternal history of UTIs as a risk factor for recurrent UTI<sup>14</sup>. On the other hand, more than half of the women (58.5%) with recurrent UTI had complaints of constipation. Approximately half of them (50.9%) had antimicrobial exposure within the last 1 year, and almost half of them (49.1%) had a history of urogenital surgery.

In our study, we have found that 45.3% of women with recurrent UTI had surgical menopause. It indicates that the practice of hysterectomy and the incidence of surgical menopause is rising. Regardless of natural or surgical menopause, most of the postmenopausal women do not take any hormone replacement therapy.

When we looked at the urinary pus cells of the postmenopausal women with recurrent UTI, we have found that more than half (52.8%) of the patients had >5 pus cells/HPF. On the other hand, when we cultured the mid-stream clean catch urine, in 47.2% cases, we did not find any bacterial growth. It could be due to a large number of patients who had a recent history of antimicrobial exposure.

Among the bacterial isolates, *E. coli* was the most predominant (26.4%). Among the others, *Proteus* and *Klebsiella* were found in 15.1% and 11.3% cases respectively. Milart et al, Kodner et al and others have found that *E. coli* is the most common organism causing UTI and at the same time, *Klebsiella*, *Pseudomonas*, *Proteus*, and other in patients with risk factors for complicated UTI<sup>21,23</sup>.

Although Chu et al and others have found that most of the uropathogens still display good sensitivity to Nitrofurantoin<sup>24</sup> and we have found that this scenario might be on the verge of a drastic change. Nitrofurantoin has long been the drug of choice and the most commonly prescribed antibiotic for UTI. We found that 14.3% of isolates of *E. coli* were resistant to Nitrofurantoin. Resistance pattern is highly related to geographic variations and in a study done by Mazzulli have found that *E. coli* isolates had a 1.8% to as high as 16% resistance rate for Nitrofurantoin<sup>4</sup>. This scenario was even more alarming for *Proteus* and *Klebsiellas*, almost two-quarters of the *Proteus* isolates (75.0%) and approximately two-thirds of the *Klebsiella* isolates (66.7%) were resistant to Nitrofurantoin.

We prescribed our patients appropriate antibiotics based on the culture and sensitivity report and in more than half of the cases (52.8%), the choice of antibiotic was Nitrofurantoin. We also prescribed HRT to 52.8% of the patients.

We provided probiotics to 60.4% of our study patients. With some amount of controversy, probiotics are new approaches to prevent recurrent UTI and it has been supported by studies done by Hooton et al, Dueñas-García et al and others<sup>13,14,25</sup>.

In recent years, cranberry juice has also been suggested in some studies to reduce the recurrence of UTI and it has also been found to be an effective prophylaxis alternative<sup>25</sup>. We provided cranbotics to 7.5% of our patients.

Associated comorbidities and other complaints were treated accordingly. At the same time, we advised them to improve their personal hygiene practice.

At 3 and 6 months intervals, we followed up the study patients to understand their disease progression and get

the picture of the recurrence of UTI. Among the postmenopausal women with recurrent UTI that we treated, only a few of them (14.2%) had a recurrence and the majority (85.8%) had no recurrence of UTI during our follow-up period.

### Conclusion:

Postmenopausal women attend the gynecology clinic mainly to get relief from their urinary complaints. However, an appropriate treatment with a rational antibiotic can reduce the risk of recurrence for the majority of the patients.

**Conflict of interest:** None.

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