

Conditions Diagnosed on Bladder Biopsy in Adult Female Patients with Lower Urinary Tract Symptoms (LUTS) Refractory to Medical Treatment

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ABSTRACT

Introduction: The incidence of lower urinary tract symptoms (LUTS) as the sole presenting symptom for bladder cancer has traditionally been reported to be low. Refractory LUTS are a well-recognized initial presenting symptom in a small percentage of patients with newly diagnosed bladder cancer. Traditionally, patients who present with refractory LUTS are thought to have carcinoma in-situ (CIS) at diagnosis.

Objectives: The objective of this study was to evaluate the Conditions diagnosed on bladder biopsy in adult female patients with lower urinary tract symptoms (LUTS) refractory to medical treatment.

Materials and Methods: We queried our database of bladder cancer patients in the hospital to identify patients who presented solely with LUTS and were subsequently diagnosed with bladder cancer. Demographic, clinical, and pathologic variables were examined.

Results: 4.1% (14/340) of bladder cancer patients in our series presented solely with LUTS. Mean age and Charlson Comorbidity Index of these patients was 66.4 years. Of the 14 patients in our data presenting with LUTS, 9 (64.3%), 4 (28.6%), and 1 (7.1%) patients presented with clinical stage Ta, carcinoma in Situ (CIS), and T2 disease. At a follow up of 6 months, recurrence occurred in 7 (50.0%) patients with progression occurring in 1 (7.1%) patient. 11 (78.6%) patients were alive and currently disease free, and 3 (21.4%) patients had died, with only one (7.1%) death attributable to bladder cancer.

Practical implication: This study suggests that urologists should have a low threshold for evaluating patients with unexplained LUTS for underlying bladder cancer.

Conclusions: It is concluded that incidence of LUTS as the sole presenting symptom in patients with newly diagnosed bladder cancer.

Keywords: UTI, Bladder, Patients, Hyperplasia, LUTS, Cancer

INTRODUCTION

Lower urinary tract symptoms (LUTSs) are one of the most common clinical manifestations in men, their frequency increases with age and are often associated with prostate enlargement. Prostate, which grows macroscopically with aging, leads to bladder outlet obstruction over time¹. The clinical symptoms occurring in this picture are called LUTS. Interestingly, the number of patients diagnosed with benign prostate hyperplasia (BPH) has been increasing over the years.² In addition, there are many diseases (ureter lower end stone, urinary tract infection, bladder tumor, foreign body, urethral strictures, etc.) that cause LUTS². Therefore, the guidelines recommend that the patient presenting with LUTS should be evaluated with anamnesis, questionnaire forms (QFs), physical examination including digital rectal examination, urinalysis, prostate specific antigen (PSA), kidney function tests, uroflowmetry, and post-voiding residual urine volume³.

Urinary tract infection (UTI) is one of the most common diseases in both urology and the local primary care clinic. Although uncomplicated UTIs can usually be easily treated, recurrent UTIs (rUTIs) are common among adult women with anatomically and physiologically normal urinary tracts⁴. The pathogenesis of rUTI in humans involves bacterial factors and deficiencies in host defense. The fundamental host defense is the antibacterial adherence mechanism in the bladder urothelium⁵. We previously reported decreased E-cadherin and increased apoptotic cells in the bladder urothelium in patients with rUTI, providing evidence to support a defect in the bladder defense mechanism in human rUTI. Because rUTI might be associated with an unhealed bladder after UTI episodes, intravesical treatment to promote bladder regeneration should be a reasonable option for patients with rUTI. Platelet-rich plasma (PRP) injection has been used to treat inflammatory diseases in clinical practice, and a preclinical study also provided evidence to show that the hepatocyte growth factor in PRP mediated the anti-inflammatory effect⁶.

Several medical treatments are available to manage patients with LUTS. Alpha-adrenergic blockers (AB), 5-alpha-reductase

inhibitors (5ARI), 5-phosphodiesterase inhibitors, antimuscarinic drugs, beta-3 agonists are used to relieve LUTS, though several of them can also negatively affect sexual function and/or are associated with dizziness⁷. Phytotherapy compounds, which form a heterogeneous group that includes extracts from plants such as *Serenoa repens*, *Pygeum africanum*, *Urtica dioica*, *Cucurbita pepo* and others, are also commonly used to treat LUTS. The hexanic extract of *S. repens* (HESr) in particular has been shown to be as effective as AB and 6-month treatment with 5ARI in improving symptoms and QOL in men with LUTS, but without their negative side effects, as recently recognized in the EAU Guidelines⁸. It is frequently administered to patients with mild or moderate LUTS who wish to avoid adverse events which may be associated with other medical treatments, especially those related to sexual function⁹.

Objectives: The objective of this study was to evaluate the Conditions diagnosed on bladder biopsy in adult female patients with lower urinary tract symptoms (LUTS) refractory to medical treatment.

MATERIALS AND METHODS

This cross-sectional study was conducted in Services Institute of Medical Sciences, Lahore during June 2021 to June 2022.

Inclusion criteria

- Age > 18 years
- Patients diagnosed with LUTS

Exclusion criteria

- Patients with a known anatomical anomaly in the lower urinary tract system and neurological disease were excluded from this study.

Data Collection: The data was collected with the permission of ethical committee of hospital. All the patients were given an informed consent before the study. The data was collected through a designed questionnaire which include all the information related to age, demographic, clinical and pathological variables. Data were collected on medical conditions, history of urinary tract infections, diabetes and parity. Body mass index (BMI) was calculated using

self-reported weight and height. Lower urinary tract symptoms LUTS status was measured using the Lower Urinary Tract Symptom Tool. The LUTS Tool uses non-medical terminology and assesses the frequency and both of 18 LUTS in the past week. All LUTS symptoms are rated on a 5-point Likert scale (never, rarely, sometimes, often, or almost always) except for daytime and night time urinations. We queried our database of bladder cancer patients in the hospital to identify patients who presented solely with LUTS and were subsequently diagnosed with bladder cancer.

Statistical Analysis: All the data was analysed by SPSS (Statistical Package for social sciences release 23.0; SPSS, Inc; Chicago, IL) system for Windows. Continuous variables are expressed as mean ± SD (Standard deviation) while categorical variables will be expressed as frequencies and percentages.

RESULTS

The data was collected from 340 patients. Mean age of the patients was 42.98 ± 2.45 years. 4.1% (14/340) of bladder cancer patients in our series presented solely with LUTS. Of the 14 patients in our data presenting with LUTS, 9 (64.3%), 4 (28.6%), and 1 (7.1%) patients presented with clinical stage Ta, carcinoma in Situ (CIS), and T2 disease.

Table 1: Descriptive statistics for different variables

Features	% age
Presenting Complaint:	
Lumber pain	79.0
Hematuria	13.0
Burning micturition	8.0
LUTS	64.3
Diagnosis:	
Renal stone	63.0
Ureteric stone	21.0
Renal + Ureteric stone	10.0
Carcinoma in-situ	7.1
Recurrent stone:	
Yes	38.0
No	62.0
Family history of Urolithiasis:	
Yes	64.0
No	36.0
Stone composition on Stone analysis:	
Calcium oxalate	82.5
Calcium phosphate	2.5
Uric acid	11.5
Struvite	1.5
Cystine	2.0

Table 3: Associations between endometriosis and lower urinary tract symptoms

Lower urinary tract symptom	Participants without endometriosis		Participants with endometriosis		Crude OR (95% CI)
	No	Yes	No	Yes	
Stress urinary incontinence	44 (84.9%)	97(15.1%)	43(83.3%)	87 (16.7%)	1.13 (0.82–1.54)
Difficulty passing urine	28 (98.0%)	13 (2.0%)	47(92.1%)	41 (7.9%)	4.14 (2.19–7.80)
Blood in the urine	32 (98.6%)	9 (1.4%)	49(95.8%)	22 (4.2%)	3.10 (1.42–6.80)
Still feeling full after urination	61 (95.3%)	30 (4.7%)	42(81.2%)	98 (18.8%)	4.73 (3.08–7.25)
Having to urinate again within minutes of urinating	32 (83.0%)	109 (17.0%)	34(66.9%)	17(33.1%)	2.41 (1.83–3.18)
Pain	60(95.1%)	31 (4.9%)	39(77.0%)	11(23.0%)	5.79 (3.82–8.78)
Dysuria	59(95.1%)	31 (4.9%)	44(88.3%)	59 (11.7%)	2.55 (1.62–4.01)

DISCUSSION

Lower urinary tract symptoms (LUTS) are common among elderly people and have significant effects on individuals, caregivers, and wider health care system [9]. As the elderly population with multiple comorbidities is increasing, the burden of LUTS will increase. A number of studies have shown that LUTS cause considerable emotional distress, have a negative impact on the quality of life and can interfere with daily activities¹⁰. Social and physical activities of women with UI are often limited; they avoid participating in any activities outside the home, and this may result in social isolation and depression¹¹. In a study on the business life of women with LUTS, it has been discovered that regardless of

Table 2 shows the signs and symptoms of bladder carcinoma in selected patients.

Table 2: Patients' presenting signs and symptoms of bladder carcinoma

Clinical presentation	Patients
Rectal bleeding	99 (57)
Anemia	19 (11)
Abdominal pain	54 (31)
Bladder pain	7 (4)
Change in bowel habits	37 (21)
Weight loss	20 (11)
Bowel obstruction	16 (9)
Perforation	5 (3)
Perforated diverticulitis	1 (0.6)
Screening	5 (3)
Unknown	7 (4)

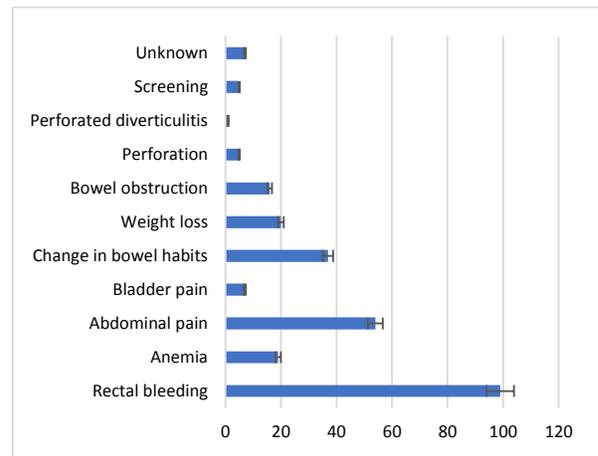


Figure 1:

Lower urinary tract symptom was common overall and was reported by 43.8% of participants. Of those with surgically confirmed endometriosis, 291 women (56%) reported any LUTS compared with 217 women (34%) of those without endometriosis. Endometriosis was associated with a statistically significantly greater odds of LUTS compared with women without endometriosis.

their urination conditions, it is more likely for women with OAB to be unemployed and that there is a decrease in the working performance of such working women. It has also been demonstrated that patients with OAB have lower quality of life scores than the patients with other chronic diseases. Sexual dysfunction is frequently seen among females with urinary symptoms¹².

Although researchers have made a great effort to investigate the pathogenesis of UTI, most studies have been carried out using various animal models, and the evidence from human bladders remains limited¹³. Recent research has suggested using intravesical PRP injection might have a therapeutic effect in

treating lower urinary tract disorders due to regenerative deficiency¹⁴.

Lower urinary tract symptoms (LUTS) such as incontinence and bladder storage or voiding issues are more likely to occur in females than males. It has been estimated that up to 80% of women experience LUTS¹⁵. However, the frequency of symptoms and their impact on women's wellbeing varies from mild to more severe. Prevalence rates also vary across the lifespan between, and within, different types of LUTS. For example, urinary incontinence, or involuntary leakage of urine, is one of the most commonly investigated sources of LUTS and reportedly affects between 13%–46% of Australian women¹⁶. However, urinary incontinence is an umbrella term which encompasses a range of leakage sub-types, such as stress urinary incontinence (SUI, leakage during physical activity), urge urinary incontinence (UUI, leakage associated with urgency) and mixed urinary incontinence¹⁷⁻¹⁹.

CONCLUSION

It is concluded that incidence of LUTS as the sole presenting symptom in patients with newly diagnosed bladder cancer. This study suggests that urologists should have a low threshold for evaluating patients with unexplained LUTS for underlying bladder cancer.

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