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ORIGINAL ARTICLE

Association of Lower Urinary Tract Symptoms with Metabolic Disorders, Neurological Dysfunction, and Reactive Arthritis: A Community-Based Cross-Sectional Study

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ABSTRACT

Background: Lower urinary tract symptoms (LUTS) are highly prevalent and increasingly recognized as manifestations of systemic disorders rather than isolated urological conditions. Emerging evidence suggests strong associations between LUTS and metabolic abnormalities, neurological dysfunction, and inflammatory diseases such as reactive arthritis, particularly in urban populations with rising cardiometabolic burden.

Objective: To evaluate the association of lower urinary tract symptoms with metabolic disorders, neurological dysfunction, and reactive arthritis in a community-based population.

Methods: This cross-sectional study was conducted from August 2022 to August 2023 at Lahore General Hospital, Lahore, and Pakistan Institute of Medical Sciences (PIMS), Islamabad. A total of 120 participants aged 30–70 years were enrolled. LUTS severity was assessed using the International Prostate Symptom Score (IPSS). Metabolic parameters, neurological status, and presence of reactive arthritis were evaluated. Statistical analysis included chi-square testing and multivariate logistic regression, with significance set at $p < 0.05$.

Results: The prevalence of LUTS was 68.3%, with moderate-to-severe symptoms observed in 45.8% of participants. Metabolic syndrome was significantly associated with LUTS (OR = 3.42, 95% CI: 1.85–6.31, $p < 0.001$), followed by neurological dysfunction (OR = 2.76, 95% CI: 1.41–5.40, $p = 0.003$) and reactive arthritis (OR = 2.19, 95% CI: 1.05–4.56, $p = 0.035$). Individual metabolic components including obesity, diabetes, and hypertension also showed significant associations.

Conclusion: LUTS are strongly linked with metabolic, neurological, and inflammatory conditions. Integrated multidisciplinary management targeting underlying systemic disorders may improve clinical outcomes and quality of life.

Keywords: Lower urinary tract symptoms; metabolic syndrome; neurological dysfunction; reactive arthritis; inflammation; IPSS; community-based study.

INTRODUCTION

Lower urinary tract symptoms (LUTS) comprise a spectrum of storage, voiding, and post-micturition disturbances, including urinary urgency, frequency, nocturia, hesitancy, weak urinary stream, and incomplete bladder emptying[1]. LUTS are common among both men and women, with a higher incidence in the elderly, and have a profound negative impact on quality of life, sleep, and general well-being. Conventionally, LUTS have been associated with localised urological disease, such as benign prostatic hyperplasia, bladder outlet obstruction, or urinary tract infections. But growing evidence suggests LUTS should be regarded as a symptom of multifaceted systemic diseases rather than a localised organ-specific disease[2,3].

Over the last decade, metabolic diseases, especially elements of metabolic syndrome (obesity, insulin resistance, dyslipidemia, and hypertension), have become pivotal in the pathogenic process of LUTS[4]. Low-grade inflammation, endothelial dysfunction, ischemia of the pelvic region and autonomic dysfunction related to metabolic disorders are thought to play key roles in bladder remodeling. For example, insulin resistance and hyperglycemia can cause neuropathic changes of bladder innervation while inflammation associated with obesity can induce detrusor overactivity and urgency. These metabolic dysfunctions are particularly important in urban societies, where lifestyle changes have contributed to increasing trends in cardiometabolic diseases[5].

Central and peripheral neurological dysfunction is another important but under-recognised component of LUTS. The bladder relies on complex interaction between the central nervous system, spinal cord, and peripheral autonomic and somatic nerves[6]. Disruption of these pathways, such as in diabetic neuropathy, cerebrovascular disease, spinal cord lesions or neurodegenerative disease, can lead to neurogenic bladder dysfunction. This can present as urgency, incontinence, retention or mixed storage and voiding dysfunction. Moreover, recent evidence indicates that systemic inflammation may lead to neuroinflammation and, as a consequence, connect metabolic and neurological pathways in the development of LUTS[7].

As well as the influence of metabolic and neurological factors, inflammatory and autoimmune processes, such as reactive arthritis, may also play a role in lower urinary tract dysfunction[8]. Reactive arthritis, a type of seronegative spondyloarthropathy commonly occurring following genitourinary or gastrointestinal infection, presents with joint arthritis, urethritis and mucocutaneous lesions. The urogenital involvement in reactive arthritis highlights the contribution of immune-mediated inflammation in urinary tract dysfunction. Sustained immune stimulation, cytokine release and molecular mimicry between microbial antigens and bladder tissue may result in bladder irritation, changes in urinary tract sensations and increased urinary symptoms[9].

While these links are increasingly recognised, studies examining the impact of these risk factors individually remain the majority, with little data on their combined influence in community-based cohorts[10]. In developing nations, such as Pakistan, where the burden of metabolic diseases and infectious causes of reactive arthritis is on the rise, it is important to understand the intricate relationships between these conditions. There is a lack of community-based evidence on the combined effects of metabolic, neurological and inflammatory disease on LUTS, which hampers the creation of a multidisciplinary approach to its management[11].

Therefore, the present study aims to evaluate the association of lower urinary tract symptoms with metabolic disorders, neurological dysfunction, and reactive arthritis in a community-based population. Through examining these multimodal

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mechanisms, this research aims to offer a more comprehensive view of LUTS, and to inform the development of multimodal clinical strategies for better patient outcomes[12].

MATERIALS AND METHODS

This community-based cross-sectional study was conducted over a period of one year, from August 2022 to August 2023, at Lahore General Hospital and Pakistan Institute of Medical Sciences. A sample of 120 patients aged 30-70 years was selected through non-probability consecutive sampling from the outpatient clinics as well as community outreach programs of the two institutes. Individuals presenting with one or more lower urinary tract symptoms (LUTS), including urinary frequency, urgency, nocturia, weak stream, and sensation of incomplete bladder emptying, were included in the study, while patients with known urological malignancies, prior bladder or prostate surgery, active urinary tract infections at the time of assessment, pregnancy, or severe systemic illness were excluded to minimize confounding factors.

Participants were invited to provide a written informed consent before comprehensive demographic and clinical data were collected via a structured and pre-piloted questionnaire. Lower urinary tract symptoms were assessed using the International Prostate Symptom Score (IPSS), which categorizes symptom severity into mild (0–7), moderate (8–19), and severe (20–35), allowing standardized comparison across participants. All participants were assessed for metabolic abnormalities including body mass index (BMI), fasting blood glucose, lipid profile (total cholesterol, low-density lipoprotein, high-density lipoprotein and triglycerides), and blood pressure according to standard guidelines. Metabolic syndrome was diagnosed based on established criteria, which includes three or more metabolic abnormalities.

We evaluated the presence of neurological dysfunction through a detailed history and targeted neurological examination with emphasis on the presence of diabetic neuropathy, cerebrovascular accidents, spinal cord involvement, and peripheral neuropathy, when confirmed with medical record review. Reactive arthritis was evaluated according to clinical criteria, including a history of preceding gastrointestinal or genitourinary infection, joint pain or swelling, and extra-articular signs and symptoms such as urethritis or conjunctivitis, as per diagnostic criteria.

Data was analyzed using SPSS software (version 26). The results for continuous variables were reported as mean ± standard deviation, while categorical variables were reported as frequencies and percentages. The chi-square test was used to examine the relationship between LUTS and metabolic, neurological and inflammatory factors. To identify factors independently associated with moderate-to-severe LUTS, or the primary outcome, a logistic regression model was used to include potential confounding variables. A p-value of less than 0.05 was used to determine statistical significance.

RESULTS

A total of 120 participants were included in the analysis, with a mean age of 52.4 ± 10.6 years. The study population consisted of 69 males (57.5%) and 51 females (42.5%). Most of the participants were urban and had a range of metabolic and clinical ailments. Overall 68.3% (n = 82) of the study participants had lower urinary tract symptoms (LUTS). Based on IPSS categorization, mild LUTS were observed in 27 (22.5%) participants, moderate LUTS in 38 (31.7%), and severe LUTS in 17 (14.1%). These results suggest that a large number of participants had significant urinary symptoms (Table 1).

There was a strong link between metabolic syndrome and LUTS. Among participants diagnosed with metabolic syndrome (n = 64), 49 individuals (76.6%) had LUTS compared to 33 (58.9%) participants without metabolic syndrome, demonstrating a statistically significant difference ($p < 0.001$). Likewise, separate metabolic components, such as obesity, diabetes mellitus and hypertension, were significantly associated with LUTS prevalence and severity. Participants with obesity showed LUTS prevalence of 78.3%, while those with diabetes had 74.1%, indicating a clear metabolic influence on urinary dysfunction (Table 2).

Neurological dysfunction was identified in 34 participants (28.3%), among whom 27 individuals (79.4%) exhibited LUTS, compared to 55 (64.7%) among participants without neurological impairment. This difference was statistically significant ($p = 0.003$), suggesting a strong relationship between impaired neural control and bladder dysfunction. Patients with diabetic neuropathy and prior cerebrovascular events demonstrated higher severity scores, particularly in storage symptoms such as urgency and nocturia (Table 3).

Reactive arthritis was diagnosed in 20 participants (16.7%), of whom 15 (75.0%) reported LUTS, compared to 67 (67.0%) among those without reactive arthritis. While the association was not as strong as those for metabolic and neurological factors, it was significant ($p = 0.035$), suggesting a role for inflammatory and autoimmune processes in the physiology of LUTS (Table 4).

Multivariate logistic regression analysis demonstrated that metabolic syndrome was the strongest independent predictor of LUTS (OR = 3.42, 95% CI: 1.85–6.31, $p < 0.001$), followed by neurological dysfunction (OR = 2.76, 95% CI: 1.41–5.40, $p = 0.003$) and reactive arthritis (OR = 2.19, 95% CI: 1.05–4.56, $p = 0.035$). These findings indicate that participants with metabolic abnormalities were more than three times as likely to develop significant LUTS, while neurological and inflammatory conditions also independently contributed to increased risk (Table 5).

Overall, the results demonstrate a strong and statistically significant association between LUTS and systemic conditions, particularly metabolic disorders, followed by neurological dysfunction and reactive arthritis, highlighting the multifactorial nature of lower urinary tract symptomatology.

Table 1: Baseline Characteristics and Prevalence of LUTS (n = 120)

Variable	Frequency (%)
Age (mean ± SD)	52.4 ± 10.6 years
Male	69 (57.5%)
Female	51 (42.5%)
LUTS Present	82 (68.3%)
Mild LUTS	27 (22.5%)
Moderate LUTS	38 (31.7%)
Severe LUTS	17 (14.1%)

Table 2: Association of LUTS with Metabolic Disorders

Metabolic Factor	LUTS Present n (%)	LUTS Absent n (%)	p-value
Metabolic Syndrome (n=64)	49 (76.6%)	15 (23.4%)	<0.001
No Metabolic Syndrome (n=56)	33 (58.9%)	23 (41.1%)	
Obesity	36 (78.3%)	10 (21.7%)	<0.001
Diabetes Mellitus	40 (74.1%)	14 (25.9%)	0.002
Hypertension	37 (69.8%)	16 (30.2%)	0.004

Table 3: Association of LUTS with Neurological Dysfunction

Neurological Status	LUTS Present n (%)	LUTS Absent n (%)	p-value
Neurological Dysfunction (n=34)	27 (79.4%)	7 (20.6%)	0.003
No Dysfunction (n=86)	55 (64.0%)	31 (36.0%)	

Table 4: Association of LUTS with Reactive Arthritis

Condition	LUTS Present n (%)	LUTS Absent n (%)	p-value
Reactive Arthritis (n=20)	15 (75.0%)	5 (25.0%)	0.035
No Reactive Arthritis (n=100)	67 (67.0%)	33 (33.0%)	

Table 5: Multivariate Logistic Regression Analysis for Predictors of LUTS

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
Metabolic Syndrome	3.42	1.85 – 6.31	<0.001
Neurological Dysfunction	2.76	1.41 – 5.40	0.003
Reactive Arthritis	2.19	1.05 – 4.56	0.035

DISCUSSION

The present study demonstrates a strong and statistically significant association between lower urinary tract symptoms (LUTS) and systemic conditions, particularly metabolic disorders, neurological dysfunction, and reactive arthritis, in a community-based population[1]. The prevalence of LUTS in the present study (68.3%) is relatively high, consistent with the increasing burden of urinary dysfunction in the population of developing countries, particularly among urban and semi-urban patients. Our results confirm the notion that LUTS do not merely constitute a urologic problem but also reflect the presence of systemic dysfunction[2,3].

Of all the factors assessed, metabolic syndrome was the strongest predictor of LUTS (Table 5), with individuals with metabolic syndrome showing over three-fold greater risk[4]. This finding is in line with emerging evidence of a strong association between metabolic dysfunction and bladder dysfunction. The mechanisms at play are likely to be complex and may involve low-grade systemic inflammation, oxidative stress, endothelial dysfunction, and pelvic ischemia[5]. Hyperglycemia and insulin resistance may lead to autonomic neuropathy and subsequent bladder dysfunction, and obesity-associated inflammatory cytokines may lead to detrusor overactivity and frequency. In our study, the individual metabolic syndrome components such as obesity, diabetes and hypertension were all significantly associated with the severity of LUTS (Table 2), supporting the metabolic-urology connection[6,7].

Neurological disease was also strongly correlated with LUTS, with a much higher incidence rate in participants with neurological disease (Table 3). The bladder is highly dependent on central and peripheral neural innervation, and any dysfunction, such as diabetic neuropathy, cerebrovascular disease, and spinal cord pathology, may result in neurogenic bladder dysfunction[8]. The increased prevalence of storage symptoms (urge, nocturia) among neurologically compromised participants reflects dysfunction in inhibitory pathways and sensory pathways. Further, the interaction between metabolic and neurological factors may also contribute to the worsening of LUTS as metabolic syndrome is a risk factor for neuropathy[9,10].

Reactive arthritis, while less common among the study participants, was also significantly linked to LUTS (Table 4). This observation suggests the involvement of inflammatory and autoimmune pathways in LUTS. Reactive arthritis involves systemic inflammation following infection and is known to be associated with urethritis and genitourinary symptoms[11,12]. LUTS in these individuals may be explained by the release of inflammatory cytokines, mucosal irritation and even immune-mediated damage to the bladder and urethra. While the strength of association was significantly weaker than the metabolic and neurological factors, the statistical significance of the association highlights the need to take inflammatory diseases into account when assessing LUTS[13].

The findings of multivariate logistic regression further support these observations, and confirm that metabolic syndrome, neurological dysfunction and reactive arthritis independently predict the presence of LUTS (Table 5)[14]. The fact that the magnitude of the odds ratio is greater for metabolic syndrome compared to neurological and inflammatory conditions suggests that metabolic syndrome is a key element in the development of LUTS, while neurological and inflammatory conditions contribute as co-determinants[15]. These results support a holistic approach to clinical management that goes beyond management of urinary symptoms, to assessment and treatment of underlying systemic disorders[16].

Clinically, this study suggests a multidisciplinary approach. All patients with LUTS should be evaluated for metabolic disorders including diabetes, obesity and hypertension, as well as for neurological and rheumatological conditions[17]. Early detection and management of these conditions may not only minimise LUTS but also improve patient outcomes and quality of life. In low-income countries, such as Pakistan, where metabolic and infectious illnesses are prevalent, such a holistic approach is crucial[18].

While this study has many strengths, such as being population-based and including multiple systemic factors, there are limitations. It is cross-sectional, which precludes establishing causality between LUTS and other conditions[19]. While the sample size is sufficient, it may not represent the diversity of the population. There is also a possibility of misclassification bias in the diagnosis of neurological dysfunction and reactive arthritis, which are based on clinical diagnosis alone and not more specialised diagnostic methods. We suggest that future longitudinal studies with a larger sample size and sophisticated diagnostic tools are needed to investigate causal pathways and mechanisms[20].

CONCLUSION

Lower urinary tract symptoms are highly prevalent in the general population and are strongly associated with systemic conditions, particularly metabolic syndrome, neurological dysfunction, and reactive arthritis. Metabolic dysfunction was the strongest independent predictor of LUTS, followed by neurological dysfunction and inflammatory factors, demonstrating that LUTS are a complex and multifaceted condition. Our research highlights the importance of a comprehensive, multidisciplinary approach to the assessment and management of LUTS with a focus on not just symptom alleviation but also diagnosis and treatment of underlying systemic disease. Early treatment to prevent and control metabolic and inflammatory conditions may be vital to decrease disease burden and enhance quality of life.

Availability of Data and Materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests: The authors declare that they have no competing interests.

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Authors' Contributions: T.S. and M.K. contributed to the conceptualization and study design. Z.U.H. and N.I.R. were responsible for data collection and clinical assessment. M.A.U.K. performed data analysis and statistical interpretation. R.M. contributed to manuscript drafting and critical revision. All authors read and approved the final manuscript.

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