E-ISSN 2250-0944

ISSN 2250-1150
doi: 10.48047/ijprt/15.02.434

Research Article

Interrelationship Between Lower Urinary Tract Symptoms, Diabetic Neuropathy, Early Renal Function Decline, and Psychological Distress in Adults with Metabolic Syndrome: A Cross-Sectional Study From Pakistan

Zeeshan Shaukat[1], Neesha[2], Mahboob Qadir[3], Ammad Ahmad Siddiqui[4], Shakil Asif[5], Faraz Ahmed[6]

Affiliations:

[1] Specialty Doctor Urology, Doncaster and Bassetlaw Teaching Hospitals, NHS Foundation Trust.
[2] Medical Officer, INDUS Hospital, Badin.
[3] Assistant Professor Medicine, Tertiary Care Hospital Nishtar II, Multan.
[4] Assistant Professor Urology, Sahara Medical College, Narowal.
[5] Associate Professor Psychiatry, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur AJ&K.
[6] Assistant Professor Neurology, Isra University Hospital, Hyderabad.

Corresponding author: Zeeshan Shaukat

Abstract: The growing prevalence of metabolic syndrome in South Asia has prompted concern regarding its complex multisystem consequences. Among these, lower urinary tract symptoms (LUTS), diabetic neuropathy, and early renal impairment are often underrecognized despite their substantial impact on quality of life and mental well-being. Limited regional evidence exists exploring the coexistence and interrelationship of these complications in Pakistani adults. The present study investigated the interaction between LUTS, neuropathic burden, subclinical renal decline, and psychological distress in adults with metabolic syndrome attending tertiary hospitals in Pakistan.

This cross-sectional analytical study enrolled 420 adults aged 35–70 years diagnosed with metabolic syndrome based on the International Diabetes Federation criteria. Standardized scales were employed: the International Prostate Symptom Score (IPSS) for LUTS, Michigan Neuropathy Screening Instrument (MNSI) for neuropathy, estimated glomerular filtration rate (eGFR) using CKD-EPI for renal function, and Hospital Anxiety and Depression Scale (HADS) for psychological distress. Statistical analysis revealed that moderate to severe LUTS were significantly associated with higher neuropathy scores (mean ± SD = 8.1 ± 2.9 vs. 4.3 ± 2.4; $p < 0.001$) and lower eGFR (78.2 ± 10.4 vs. 93.5 ± 11.2 mL/min/1.73 m²; $p < 0.001$). Moreover, psychological distress correlated strongly with LUTS severity ($r = 0.52$; $p < 0.001$).

The findings highlight a multidimensional interplay between peripheral nerve dysfunction, early nephropathy, and mental health burden in metabolic syndrome. Integrating urological, neurological, and psychological screening within diabetes management could enable early detection and holistic care.

Keywords: metabolic syndrome, lower urinary tract symptoms, diabetic neuropathy

Introduction: Metabolic syndrome represents a constellation of interrelated risk factors that predispose individuals to cardiovascular disease, diabetes, and chronic kidney dysfunction. With an accelerating urbanization trend, sedentary lifestyle, and dietary shifts, Pakistan has witnessed a steep rise in metabolic syndrome prevalence, now estimated to affect nearly one-third of the adult population. While metabolic syndrome is primarily considered a metabolic and cardiovascular entity, growing evidence indicates that its systemic consequences extend beyond traditional organ boundaries, affecting the nervous system, urogenital tract, and psychological health.[1-4]

Lower urinary tract symptoms are among the least discussed yet most distressing manifestations in adults with metabolic syndrome. These symptoms, including urinary frequency, urgency, nocturia, and weak stream, often arise due to autonomic and peripheral nerve dysfunction caused by chronic hyperglycemia and insulin resistance. Studies since 2022 have shown that LUTS may be an early indicator of diabetic cystopathy and emerging microvascular damage. The pathophysiological mechanism involves oxidative stress, endothelial injury, and impaired nitric oxide bioavailability, leading to bladder detrusor instability and incomplete voiding. Such changes occur early and are frequently missed in standard diabetic follow-ups.[5-8]

Diabetic neuropathy, another major complication of metabolic syndrome, is characterized by damage to somatic and autonomic nerves, affecting both peripheral sensory and motor pathways. Autonomic involvement, particularly of the sacral parasympathetic outflow, directly contributes to LUTS. Beyond motor and sensory deficits, neuropathic changes also alter renal hemodynamics through impaired vasoregulatory control. Contemporary studies have highlighted that microalbuminuria and reduced eGFR can precede overt nephropathy, emphasizing the importance of recognizing early renal decline in this population.[9-12]

Simultaneously, psychological distress has emerged as an underappreciated correlate of metabolic syndrome and its complications. Persistent symptoms such as LUTS and neuropathy contribute to anxiety, depression, and reduced quality of life. Recent research from 2023–2024 suggests a bidirectional association between psychological stress and autonomic dysfunction, creating a feedback loop that worsens somatic symptoms and metabolic control. However, limited research has examined this interrelationship comprehensively, particularly within low-resource South Asian populations where health-seeking behaviors and diagnostic resources remain constrained.

The integration of neurological, renal, and psychological perspectives is therefore essential to understanding the multifactorial burden of metabolic syndrome. The present study sought to fill this knowledge gap by investigating the interrelationship between LUTS, diabetic neuropathy, early renal function decline, and psychological distress among Pakistani adults with metabolic syndrome. The novelty of this research lies in its concurrent assessment of these domains using standardized tools and the identification of statistical correlations that reveal systemic interdependence. By characterizing these interactions, the study aims to provide evidence for a more holistic, multidisciplinary management model in metabolic syndrome care.

Methodology: A community-based cross-sectional analytical study was conducted between March and September 2024 at Nishtar II, Multan Pakistan. Using Epi Info 7.2 software, the sample size was calculated based on an expected LUTS prevalence of 35% among adults with metabolic syndrome, 95% confidence level, and 5% margin of error, yielding a minimum sample of 384; to account for non-response, 420 participants were enrolled. Adults aged 35–70 years meeting the International Diabetes Federation criteria for metabolic syndrome were included. Exclusion criteria comprised chronic kidney disease (stage 3 or above), urological malignancy, known psychiatric illness, recent urinary infection, or history of prostate surgery.

Data collection followed verbal informed consent. Sociodemographic and clinical data were recorded, including age, sex, duration of diabetes, BMI, and medication history. LUTS were assessed using the validated International Prostate Symptom Score (IPSS), neuropathy through the Michigan Neuropathy Screening Instrument (MNSI), renal function via estimated GFR (CKD-EPI equation), and psychological distress using the Hospital Anxiety and Depression Scale (HADS). Fasting blood glucose and HbA1c were measured to assess glycemic control.

Statistical analysis was performed using SPSS 26. Descriptive statistics summarized demographic and clinical characteristics. Group comparisons between mild and moderate-to-severe LUTS were analyzed using t-tests and chi-square tests. Pearson correlation coefficients evaluated relationships among LUTS, neuropathy score, eGFR, and psychological distress. A p-value < 0.05 was considered statistically significant. Ethical approval was obtained from the institutional review board, and confidentiality was maintained throughout.

Results

Table 1: Demographic and Clinical Characteristics (n = 420)

Variable	Mean ± SD or n (%)
Age (years)	54.6 ± 9.8
Male / Female	238 (56.7%) / 182 (43.3%)
Duration of diabetes (years)	8.2 ± 4.7
BMI (kg/m²)	30.4 ± 4.1
Hypertension	282 (67.1%)
HbA1c (%)	8.1 ± 1.2
eGFR (mL/min/1.73 m²)	87.8 ± 12.3
Moderate–severe LUTS	156 (37.1%)

Participants exhibited middle-aged predominance with poor glycemic control and frequent comorbid hypertension, reflecting a high-risk metabolic cohort.

Table 2: Association Between LUTS Severity and Neuropathy/Renal Function

Parameter	Mild LUTS (n = 264)	Moderate–Severe (n = 156)	p-Value
MNSI score	4.3 ± 2.4	8.1 ± 2.9	<0.001
eGFR (mL/min/1.73 m²)	93.5 ± 11.2	78.2 ± 10.4	<0.001
HbA1c (%)	7.8 ± 1.1	8.6 ± 1.2	0.002

Neuropathy severity and early renal decline showed significant worsening with LUTS progression, indicating a neuro-renal link.

Table 3: Correlation Between Study Variables

Variables	Correlation (r)	p-Value
LUTS – MNSI	0.61	<0.001
LUTS – eGFR	–0.58	<0.001
LUTS – HADS	0.52	<0.001
MNSI – eGFR	–0.49	<0.001
HADS – MNSI	0.46	<0.001

Strong positive correlations between LUTS, neuropathy, and psychological distress, and inverse associations with renal function, emphasize systemic interconnection.

Discussion: The findings demonstrate that LUTS are not isolated urological complaints but represent a broader neurovascular manifestation of metabolic syndrome. The statistically significant association between LUTS severity and diabetic neuropathy underscores the role of autonomic nerve dysfunction in bladder control impairment. Similar recent studies have documented that hyperglycemia-induced oxidative injury compromises neural transmission within the detrusor muscle, producing symptoms that parallel neuropathic burden.[13-15]

The observed decline in eGFR among participants with severe LUTS and higher neuropathy scores reveals an overlapping microvascular pathogenesis. Hyperglycemia and insulin resistance accelerate endothelial dysfunction and glomerular basement membrane thickening, which simultaneously contribute to neural ischemia. This dual vulnerability explains the synchronous emergence of bladder and renal complications in the early stages of metabolic syndrome.[16-18]

Psychological distress, found to be significantly correlated with LUTS and neuropathy, represents an emerging determinant of disease burden. The chronic discomfort and embarrassment caused by urinary symptoms exacerbate anxiety and depression, which in turn modulate autonomic balance and worsen bladder dysfunction. This bidirectional relationship between somatic symptoms and

mental health has been increasingly recognized in post-2022 research but remains underexplored in South Asian contexts.[19]

Furthermore, the gender and age distribution in this study align with regional demographic trends showing higher vulnerability among middle-aged men, possibly due to overlapping benign prostatic enlargement. However, the associations observed here persisted after adjusting for age and sex, confirming that metabolic and neuropathic factors play a dominant etiological role.

From a pathophysiological perspective, the convergence of neuropathy, nephropathy, and LUTS illustrates a systemic continuum of microvascular damage driven by chronic metabolic derangement. Each organ system reflects a facet of the same underlying process—endothelial dysfunction, oxidative stress, and low-grade inflammation. Recognizing this unified mechanism can improve multidisciplinary approaches to screening and management.[20]

The study also underscores the value of integrating psychological assessment in metabolic syndrome care. The significant correlation between HADS and both LUTS and neuropathy highlights the need for early mental health intervention to prevent a downward spiral of symptom amplification. Psychosocial support and stress-reduction strategies could complement medical treatment to improve overall patient outcomes.

Finally, the findings hold public-health implications for Pakistan, where fragmented healthcare delivery often separates endocrinology, urology, nephrology, and psychiatry services. Implementing comprehensive screening models at the primary care level could facilitate early identification of neuro-urological complications and reduce long-term morbidity.

Conclusion: This study established a statistically significant interrelationship between lower urinary tract symptoms, diabetic neuropathy, early renal function decline, and psychological distress in adults with metabolic syndrome. The results highlight the need for integrated, multidisciplinary screening in metabolic patients to address emerging neuro-urological and mental health complications. Future longitudinal research should explore causal pathways and intervention efficacy.

References

1. Ahmed N, Khan H, Javed S. Patterns of metabolic syndrome and its microvascular complications in Pakistani adults. J Clin Med. 2023;12(3):1245.
2. Alam M, Raza S, Butt H. Association of lower urinary tract dysfunction with diabetic neuropathy in South Asian populations. 2024; DOI: 10.3390/jcm1402142.
3. Bilal U, Nasir A, Tariq M. Early renal decline in metabolic syndrome: community-based observations from Lahore. 2022; DOI: 10.1016/j.dsx.2022.104856.
4. Chen Z et al. Autonomic dysfunction and bladder impairment in metabolic disorders. 2023; DOI: 10.1159/000529761.
5. Iqbal K, Siddiqui Z. Psychological distress and somatic symptom clustering in type 2 diabetes. 2023; DOI: 10.3389/fpsyt.2023.1048821.
6. Hasan S, Ali T, Rafi M. Evaluation of LUTS in metabolic syndrome: cross-sectional hospital study. 2024; DOI: 10.1007/s00404-024-07012-9.
7. Jahan F, Memon A. Impact of neuropathic pain on renal microcirculation among diabetics. 2022; DOI: 10.1016/j.diabres.2022.109020.
8. Luo C et al. Relationship between oxidative stress and urological dysfunction in metabolic disease. 2023; DOI: 10.3390/antiox12061129.
9. Maqsood A et al. Psychosomatic correlations in diabetic populations: evidence from Pakistani urban clinics. 2024; DOI: 10.1186/s12905-024-03198-5.
10. Rashid M, Farooq A. Subclinical renal dysfunction as predictor of LUTS severity. 2023; DOI: 10.1093/eururo/uead124.
11. Singh P, Reddy R. Microvascular injury and neuropathy link in metabolic syndrome. 2024; DOI: 10.3390/biomedicines12050921.
12. Qureshi S et al. Neurogenic bladder dysfunction in insulin-resistant adults. 2023; DOI: 10.1016/j.ejogrb.2023.112236.
13. Yousaf T, Iqra H. Depression and anxiety in diabetic patients with LUTS. 2023; DOI: 10.1177/20503121231108442.
14. Zhao L et al. Endothelial injury and early nephropathy pathways in metabolic syndrome. 2022; DOI: 10.3390/jcm11102873.

15. Fatima R, Hussain T. Glycemic variability and renal microcirculation changes in early nephropathy. 2024; DOI: 10.1186/s12882-024-03377-x.
16. Ali W, Kamal A. Cross-link of anxiety and urinary dysfunction in diabetics. 2023; DOI: 10.1007/s12192-023-01364-2.
17. Bukhari R, Zahra S. Community screening for metabolic syndrome complications. 2022; DOI: 10.1016/j.puhe.2022.09.016.
18. Sato K et al. Sympathetic overactivity and LUTS in insulin resistance. 2024; DOI: 10.1159/000537218.
19. Naveed M, Rehman Z. Neuropathy, nephropathy, and mental health interlink in diabetics. 2025; DOI: 10.3390/medicina61010212.
20. Kablak-Ziembicka A, Przewlocki T. Clinical significance of carotid intima-media complex assessment for prediction of systemic microvascular complications. J Clin Med. 2021;10(20):4628. DOI: https://doi.org/10.3390/jcm10204628.