ADVANCES IN NEPHROLOGY

# Metabolic Cystopathy: An umbrella for Diabetic cystopathy and the Obese bladder

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## Abstract

Metabolic syndrome (MetS) is a group of interconnected conditions that include central obesity, insulin resistance, dyslipidaemia, and hypertension. Although the cardiovascular and endocrine effects of this syndrome are well-recognized, its impact on the function of the lower urinary tract is often overlooked. Bladder dysfunction- often presenting as diabetic cystopathy in diabetes- may stem from the wider metabolic environment of MetS. In this review, we propose the term Metabolic Cystopathy. We detail the pathophysiological connections, clinical manifestations, diagnostic methodologies, and treatment options. We stress the importance of multifactorial management approach, including urology, endocrinology, nephrology, dietetics and physiotherapy, to effectively address this condition.

**Keywords:** Diabetes, diabetic cystopathy, lifestyle disorders, metabolic syndrome, obesity

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## Introduction

The increasing incidence of MetS has become a significant global health issue, impacting approximately 25% of adults around the world.[1] Defined by central obesity, insulin resistance, hypertension, and dyslipidaemia, MetS increases the risk of various chronic conditions, particularly type 2 diabetes mellitus (T2DM), cardiovascular diseases, and kidney disease (CeReMe diseases).[1,2] At the same time, its effects on the lower urinary tract and bladder function continue to be an area of evolving interest.

Historically, bladder issues related to diabetes have been referred to as "diabetic cystopathy," a condition initially described by Frimodt-Møller more than four decades ago.[3] It is characterized by reduced bladder sensation, increased bladder capacity, and diminished detrusor contractility. However, recent research indicates that individuals with MetS, regardless of their glycaemic status, often encounter lower urinary tract symptoms (LUTS). These include urinary urgency, frequent urination, nocturia, and difficulties with voiding. This broadening range of symptoms and conditions calls for a reassessment of the causes of bladder dysfunction in metabolic disorders.[4,5]

The term "obese bladder" acts as both a clinical term and an effective communication mechanism during patient consultations. It allows individuals to connect their bladder issues with metabolic and weight-related causes, emphasizing the necessity of making lifestyle adjustments. Presenting the condition in this manner improves comprehension, and motivates adherence to non-drug treatments like weight reduction and changes in diet. We propose the term "metabolic cystopathy" to refer to bladder dysfunction linked to MetS, irrespective of glycaemic or adiposity status. By comparing and contrasting this condition with diabetic cystopathy and utilizing findings from recent studies, this review seeks to offer a thorough understanding of the pathogenesis, clinical characteristics, diagnostics, and multidisciplinary treatment of metabolic cystopathy.

### Pathophysiology

Bladder dysfunction in MetS is the result of a complicated interaction among metabolic, inflammatory, neurogenic, and vascular changes. In contrast to the clearer mechanisms observed in diabetic cystopathy, the development of metabolic cystopathy is influenced by multiple factors and often occurs gradually. Table 1 depicts the etiological framework of metabolic cystopathy.

A. Visceral Obesity and Inflammatory Cytokines Visceral adipose tissue functions like an endocrine organ by releasing pro-inflammatory cytokines such as IL-6, TNF-α, and resistin. These lead to systemic inflammation, which negatively impacts the contractility of bladder detrusor smooth muscle and causes dysfunction in the urothelium. Additionally, ongoing low-grade inflammation heightens the sensitivity of afferent bladder nerves, resulting in increased urgency and frequency of urination.[5-7]

B. Insulin Resistance and Autonomic Dysfunction Insulin resistance hinders glucose absorption and results in

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elevated insulin levels, which may damage autonomic nerve fibres. This subtle form of autonomic neuropathy affects both the sensory and motor regulation of the bladder, causing inconsistent detrusor reactions that can vary from overactivity to underactivity.[5-7]

**Table-1:** Etiological Framework of Metabolic Cystopathy.

| Pathogenic Factor | Mechanism | Effect on Bladder |
|---|---|---|
| **Visceral Adiposity** | Pro-inflammatory cytokine release | Sensory nerve sensitization, detrusor overactivity |
| **Insulin Resistance** | Autonomic nerve dysfunction | Bladder hypoactivity, incomplete emptying |
| **Hypertension** | Vascular remodelling, ischaemia | Fibrosis, poor compliance |
| **Dyslipidaemia** | Endothelial dysfunction | Microvascular compromise |
| **Urothelial Dysfunction** | Altered receptor expression | Sensory/motor signalling errors |
| **Mechanical Obesity Impact** | Increased intra-abdominal pressure | Stress incontinence, detrusor-sphincter dyssynergia |

**Table-2:** Stages of metabolic cystopathy.

| Early (Compensated Stage) | Intermediate | Late (Decompensated Stage) |
|---|---|---|
| • Increased urinary frequency and urgency | • Mixed LUTS: urgency, frequency, hesitancy, weak stream | • Poor bladder emptying, overflow incontinence |
| • Nocturia and mild urge incontinence | • Emerging detrusor underactivity with rising post-void residual (PVR) | • Atonic bladder and high PVR |
| • Preserved detrusor function with signs of overactivity | | • Risk of upper urinary tract involvement (hydronephrosis, infections) |

**Table-3:** Comparative Features of Diabetic and Metabolic Cystopathy.

| Feature | Diabetic Cystopathy | Metabolic Cystopathy |
|---|---|---|
| **Primary Aetiology** | Chronic hyperglycaemia | Insulin resistance, obesity, hypertension |
| **Bladder Sensation** | Decreased | Variable: often preserved early |
| **Detrusor Function** | Underactive (late) | Mixed: overactive (early), underactive (late) |
| **Autonomic Neuropathy** | Prominent | Subclinical or emerging |
| **Vascular Component** | Moderate | Prominent (hypertension-induced ischaemia) |
| **Urothelial Changes** | Altered ATP, prostaglandin signalling | Similar but earlier onset |
| **Inflammation** | Moderate | High-grade systemic |
| **Progression** | Predictable stages | Variable, multifactorial |

**Table-4:** Diagnostic Algorithm.

| Diagnostic Modality | Utility |
|---|---|
| Detailed History | Evaluate LUTS, dietary/lifestyle factors, comorbidities |
| Physical Exam | Assess abdominal/pelvic tone, signs of obesity-related complications |
| Laboratory Tests | Fasting glucose, HbA1c, lipid profile, CRP, Kidney function test |
| Urinalysis | Rule out infection, microscopic or macroscopic haematuria, Casts |
| Uroflowmetry | Detect flow abnormalities, hesitancy, intermittent stream |
| Post-Void Residual (PVR) | Quantify incomplete emptying |
| Bladder Diary | Identify patterns in urgency, frequency, incontinence |
| Urodynamic Studies | Confirm detrusor overactivity/underactivity, compliance |
| Pelvic USG | Assess bladder wall thickness, structural anomalies |

C. Hypertension and Vascular Insufficiency Chronic hypertension results in impaired function of the endothelium and arteriosclerosis. In the bladder, decreased blood flow leads to ischaemia, low oxygen levels, and ultimately fibrosis of the detrusor muscle, which affects bladder compliance and ability to contract.[5]

D. Urothelial Dysfunction The urothelium plays a crucial role in the sensory signalling of the bladder, but it can become dysfunctional in MetS. Research indicates that there is an elevated expression of M2 and M3 muscarinic receptors, along with changes in ATP and prostaglandin signalling. These alterations can lead to detrusor overactivity and a decrease in bladder compliance.[8]

E. Pelvic Floor Alterations and Increased Intra-abdominal Pressure Obesity increases intra-abdominal pressure, which negatively affects the functionality of the pelvic floor. This results in stress urinary incontinence, difficulty in fully emptying the bladder, and worsening of LUTS.[9]

## Clinical Spectrum

Patients may present with storage symptoms, voiding symptoms, or both, which may evolve over time. Recognition of this spectrum is crucial for prompt diagnosis and early management. Evolution of metabolic cystopathy can be divided into three stages, as depicted in Table 2. The comparative features of diabetic and metabolic cystopathy have been framed in Table 3.

## Management

For timely diagnosis, a stepwise approach incorporating clinical, biochemical, urological, and radiological assessment is essential (Table 4). Effective management lies in a multidisciplinary, stage-specific, and symptom-driven approach (Table 5). Due to the systemic involvement of MetS and its significant effects on bladder and kidney health, a multidisciplinary strategy is crucial for effective management.

Urologists play a key role in identifying and managing LUTS. Nephrologists are involved in tracking kidney function, addressing associated CKD, and ensuring that treatments do not negatively impact renal health, particularly in patients with elevated post-void residuals or repeated urinary tract infections. Endocrinologists are essential in enhancing glycaemic control and providing insulin sensitizers or other medications that target the metabolic issues related to MetS. Physiotherapists support the implementation of pelvic floor muscle exercises and

**Table-5:** Summary of Management Options.

| Treatment Modality | Indications | Role |
|---|---|---|
| Lifestyle Measures | All stages | First-line; symptom relief and metabolic control |
| Antimuscarinics/β3-Agonists | Storage symptoms | Reduce urgency/frequency |
| Alpha-Blockers | Voiding symptoms | Facilitate emptying |
| CIC | Decompensated bladder | Prevent retention, protect renal function |
| Neuromodulation | Refractory LUTS | Modulate nerve activity |
| Surgery | BOO or failed other measures | Address anatomical/functional obstruction |

bladder training programmes, which are especially helpful for patients experiencing detrusor underactivity or stress incontinence. Dietitians provide customized advice on weight management, anti-inflammatory diets, and fluid management strategies, all of which help to ease metabolic issues and bladder symptoms. Psychologists focus on addressing mental health challenges such as anxiety and depression that often occur with chronic illness and can exacerbate LUTS or impede adherence to treatment. This collaborative, cross-discipline approach not only boosts patient engagement and symptom management but also improves long-term results and decreases recurrence rates.

**Lifestyle and Behavioural Interventions**

- Weight reduction (5-10% can reduce LUTS by 50%)
- Dietary changes (low salt, controlled fluid intake, avoidance of bladder irritants)
- Pelvic floor exercises and bladder training
- Timed voiding and double voiding techniques

**Pharmacological Therapies**

- Storage Symptoms: Antimuscarinics (e.g., solifenacin), β3-agonists (e.g., mirabegron)
- Voiding Symptoms: Alpha-blockers (e.g., tamsulosin)
- Metabolic Control: Metformin, SGLT2 inhibitors (for weight loss and glucose control)
- Inflammation: Statins, ACE inhibitors (reduce endothelial dysfunction)

**Interventional Procedures**

- Clean intermittent catheterization for high PVR
- Intravesical botulinum toxin for refractory detrusor overactivity
- Sacral neuromodulation for chronic LUTS unresponsive to medications

**Surgical Interventions**

- Urethral dilatation or transurethral resection of prostate (TURP) (if bladder outlet obstruction present)
- Bladder augmentation or diversion in extreme cases

## Conclusion

Metabolic cystopathy is an emerging concept which highlights the urological effects of the MetS. Although its underlying mechanisms are similar to those of diabetic cystopathy, it is also mediated by factors such as visceral obesity, vascular issues, systemic inflammation and autonomic dysfunction. Early identification and collaborative treatment can greatly enhance the quality of life for those affected. Epidemiological research, establishment of standardized management guidelines, and studies evaluating new treatment options, particularly those targetting urothelial inflammation and regulating autonomic function, are required. Incorporating urological health into metabolic care is not merely advantageous- it is vital.

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