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# UROLOGICAL MANIFESTATIONS OF EHLERS-DANLOS SYNDROME: A NARRATIVE REVIEW OF BLADDER DYSFUNCTION AND PELVIC FLOOR DISORDERS

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**ABSTRACT** Ehlers-Danlos Syndrome (EDS) is a hereditary connective tissue disorder that compromises the structural integrity of the urinary tract and pelvic floor. This review analyzes how collagen deficiency and associated dysautonomia lead to bladder dysfunctions (overactive bladder, urinary retention), early-onset incontinence, and pelvic organ prolapse. Patients present with complex symptoms requiring specialized diagnosis through urodynamics. Management must be multidisciplinary, prioritizing adapted pelvic floor physical therapy and surgical caution due to the high risk of recurrence caused by tissue fragility. Early recognition is fundamental to improving clinical outcomes and patient quality of life.

**KEYWORDS :** Ehlers-Danlos Syndrome; Bladder Dysfunction; Pelvic Floor Disorders; Urinary Incontinence; Collagen Deficiency.

## INTRODUCTION

Ehlers-Danlos Syndrome (EDS) encompasses a complex and heterogeneous group of heritable connective tissue disorders (HCTD) primarily defined by defects in the synthesis, processing, and structural organization of collagen (1). As the most abundant protein in the human body, collagen provides the essential framework for various organ systems, including the skin, joints, blood vessels, and the visceral organs. The 2017 International Classification recognizes 13 distinct subtypes, with the Hypermobile Ehlers-Danlos Syndrome (hEDS) being the most common, though its genetic basis remains less clearly defined compared to the classical or vascular types (2-5).

### Methods

A narrative literature review was conducted to summarize current evidence on urological manifestations of Ehlers-Danlos syndrome. A structured search was performed in four electronic databases: PubMed/MEDLINE, Scopus, Web of Science, and Embase. Search terms included combinations of "Ehlers-Danlos syndrome," "bladder dysfunction," "lower urinary tract symptoms," "pelvic floor disorders," "urinary incontinence," and "pelvic organ prolapse." Articles published in English describing urological or pelvic floor manifestations of EDS were considered. Reference lists of relevant articles were also screened to identify additional studies. After reviewing the available literature, the most relevant and informative publications were selected, and a total of 15 references were included to support this narrative synthesis.

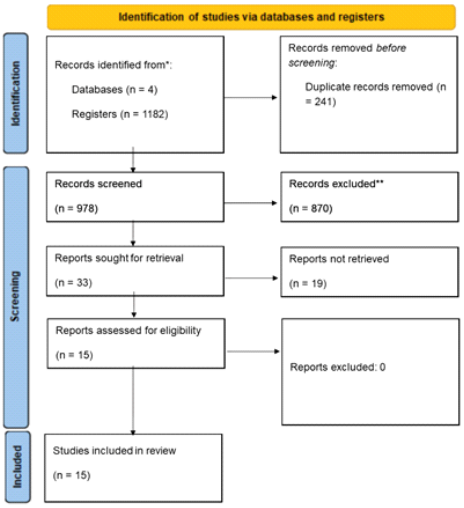


**Figure.** PRISMA.

Pathophysiological Basis of Urological Manifestations in EDS
The pathophysiology of urological manifestations in EDS is rooted in the abnormal biomechanical properties of the urogenital tissues. Collagen provides tensile strength, while elastin provides compliance. In EDS, the ratio of these proteins or their structural arrangement is altered, leading to "hyper-compliant" tissues that fail under normal physiological pressures (1,3).

Ligamentous and Fascial Laxity The pelvic floor is a dynamic diaphragm supported by the levator ani muscles and a complex network of ligaments (e.g., uterosacral, pubourethral). In EDS, these ligaments exhibit excessive elongation under tension. This laxity results in the descent of the bladder neck and urethral hypermobility, which are the primary drivers of stress urinary incontinence (SUI) (6).

Detrusor Dysfunction The bladder wall (detrusor) requires a structured collagen matrix to transmit the force of contraction effectively. In patients with EDS, the "floppy" nature of the bladder wall can lead to increased bladder compliance, where the bladder expands to large volumes without a corresponding increase in pressure. Paradoxically, this can lead to detrusor underactivity, where the muscle cannot generate enough pressure to initiate or maintain voiding, resulting in chronic urinary retention (7).

The Role of Dysautonomia A critical factor in the EDS urological profile is the high prevalence of Autonomic Nervous System (ANS) dysfunction, particularly Postural Orthostatic Tachycardia Syndrome (POTS). The bladder is under strict autonomic control (sympathetic storage, parasympathetic voiding). Dysautonomia can lead to sensory urgency, where the patient feels a constant need to void despite low volumes, or "bladder-sphincter dyssynergy," where the coordination between the bladder contraction and urethral relaxation is lost (8).

### Bladder Dysfunction in Ehlers-Danlos Syndrome

Bladder dysfunction in EDS is rarely a single symptom but rather a constellation of Lower Urinary Tract Symptoms (LUTS). The most frequently reported manifestation is Overactive Bladder (OAB), characterized by urgency, frequency, and nocturia (4). In a clinical survey of women with hEDS, nearly 70% reported significant urgency symptoms compared to less than 20% in control groups (9).

Sensory and Storage Issues Patients often describe a "hypersensitive" bladder. This may be linked to Mast Cell

Activation Syndrome (MCAS), another common EDS comorbidity. Mast cells in the bladder lining can release inflammatory mediators that irritate the sensory nerves, mimicking the symptoms of a urinary tract infection without the presence of bacteria (10).

Voiding Issues and Retention Conversely, many patients suffer from voiding difficulties. This includes a hesitant start to the stream, a weak or intermittent flow, and the sensation of incomplete emptying. Studies using urodynamic testing have identified that a significant portion of EDS patients have a "large-capacity, low-pressure" bladder (7). This "lazy bladder" phenotype is dangerous as it can lead to silent urinary retention, increasing the risk of upper urinary tract damage over time.

**Urinary Incontinence**

Urinary incontinence (UI) in the EDS population is characterized by its early onset and severity. Unlike the general population, where UI is often associated with aging or multiple childbirths, EDS patients may experience significant leakage in their teens or early twenties, even if they have never been pregnant (6,11).

Stress Urinary Incontinence (SUI) SUI is the most common form, driven by the failure of the mid-urethral support system. The "hammock hypothesis," which describes how the urethra is compressed against a stable sub-urethral layer during increased intra-abdominal pressure (like coughing), fails in EDS because the "hammock" (the endopelvic fascia) is too elastic (11).

Urge and Mixed Incontinence Urge Urinary Incontinence (UUI) is also prevalent, often exacerbated by the bladder's high compliance and sudden, uninhibited detrusor contractions. When both SUI and UUI are present (mixed incontinence), the management becomes significantly more complex, as treatments for one may exacerbate the other (12). The functional and social impact is severe, leading many young patients to limit their social interactions, physical activities, and career choices.

**Pelvic Floor Disorders**

Pelvic floor disorders (PFD) in EDS represent a major structural challenge. The most significant of these is Pelvic Organ Prolapse (POP), where the bladder (cystocele), rectum (rectocele), or uterus descends into or beyond the vaginal opening (2,13).

Premature Prolapse In the general population, POP is a condition of the elderly. In EDS, the prevalence of POP is significantly higher in young, nulliparous women. This suggests that the internal support structures are insufficient to withstand even normal daily intra-abdominal pressures (e.g., lifting, chronic constipation).

Surgical Failure and Recurrence A defining characteristic of PFD in EDS is the high rate of surgical recurrence. Standard repairs use the patient's own fascia to reinforce the support. In EDS, this "native tissue" is inherently weak and continues to stretch after surgery. Studies have shown that EDS patients have a 30-50% higher risk of needing a re-operation compared to non-EDS controls (13,14). This has led to a debate regarding the use of synthetic meshes, which provide better support but carry a higher risk of erosion and complications in fragile EDS tissues.

**Associated Urological Conditions**

The urological landscape of EDS is further complicated by several overlapping conditions:

- Recurrent Urinary Tract Infections (rUTIs): These are common and may be caused by urinary stasis from incomplete emptying or structural abnormalities like bladder diverticula, which are more common in EDS due to wall weakness (7).
- Interstitial Cystitis / Bladder Pain Syndrome (IC/BPS): Many EDS patients meet the criteria for IC/BPS. The chronic inflammation of the bladder wall is thought to be part of the systemic "allergic-inflammatory" profile of EDS/MCAS/POTS (10).
- Chronic Pelvic Pain: This is often multifactorial, involving bladder pain, pelvic floor muscle spasms (hypertonicity), and central sensitization (15).
- Functional Voiding Dysfunction: Linked to dysautonomia, where the patient cannot coordinate the relaxation of the pelvic floor muscles with a bladder contraction.

**Diagnostic Considerations**

Diagnosing urological issues in EDS requires a holistic approach that goes beyond the bladder itself.

Clinical History and Questionnaires Clinicians should use validated tools such as the International Prostate Symptom Score (IPSS) or the Overactive Bladder Questionnaire (OAB-q), even in female patients, to quantify LUTS. A specific history of joint dislocations, skin scarring, and orthostatic intolerance should be taken to confirm the EDS context.

**Physical and Specialized Exams**

- Pelvic Floor Assessment: A manual exam is crucial to assess for muscle tone (many EDS patients have paradoxically "tight" but weak pelvic floors) and the degree of prolapse (2).
- Urodynamic Studies: This is the gold standard for EDS. It can identify detrusor underactivity, overactivity, or poor compliance. It is particularly useful before considering surgery (7).
- Post-Void Residual (PVR): Every EDS patient with urinary symptoms should have a PVR check via ultrasound to rule out retention.
- Cystoscopy: Should be reserved for patients with hematuria or suspected IC/BPS to look for Hunner's lesions or structural diverticula (4).

**Management Strategies**

Management must be tiered, starting with the least invasive options, given the risks associated with surgery in this population.

**Conservative Management**

- Specialized Pelvic Floor Physical Therapy (PFPT): Standard "Kegel" exercises may be harmful if the patient has a hypertonic (overly tight) pelvic floor, which is common as the body tries to compensate for ligamentous laxity. Therapy should focus on "down-training" (relaxation) and core stability (15).
- Behavioral Modifications: Fluid management, avoiding bladder irritants (caffeine, alcohol), and "timed voiding" to prevent the bladder from overstretching (12).

**Pharmacological Treatment**

- Antimuscarinics and Beta-3 Agonists: Used for OAB. However, antimuscarinics can cause constipation and dry mouth, which can worsen EDS-related gastroparesis and POTS. Beta-3 agonists (like mirabegron) are often better tolerated (8).
- Neuromodulators: Low-dose amitriptyline or gabapentin can be effective for the neuralgic components of bladder pain.

**Surgical Management Surgery is a last resort. If required, surgeons must:**

1. Use non-absorbable sutures to account for slow wound healing.

2. Consider the use of mesh carefully, balancing the risk of recurrence vs. the risk of tissue erosion.
3. Ensure meticulous hemostasis, as EDS patients are prone to hematomas.

## CONCLUSIONS

Urological manifestations in Ehlers-Danlos Syndrome are a frequent, complex, and high-impact component of the disease. They result from a unique interplay between structural connective tissue failure and neurological (autonomic) dysregulation. Bladder dysfunction, early-onset incontinence, and recurrent prolapse are not just "comorbidities" but central features of the syndrome for many patients.

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