

Urinary Symptoms and Bladder Dysfunction in Patients with Neuromyelitis Optica Spectrum Disorders: Evaluation with Urodynamics and Management

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Abstract

Objective To assess lower urinary tract symptoms (LUTSs) in patients with neuromyelitis optica spectrum disorders (NMOSDs) and bladder dysfunction through urodynamics (filling and voiding phase of cystometrography) and management based on findings.

Patients and Methods The study included 42 (34 females) patients admitted to the rehabilitation department. Neurologic evaluation was performed and severity of myelitis was assessed using the American Spinal Injury Association Impairment Scale. All patients underwent urodynamics, and management was based on the findings.

Results Mean age was 34.5 years (range: 11–64 years; standard deviation: 13.1). Twenty-three (54.8%) patients had a first episode of myelitis, whereas 19 patients had relapses (number of episodes varying from 2 to 7). Eleven (26%) patients had increased frequency, 16 (37%) had urgency, 12 (28%) had urge incontinence, 8 (18.6%) had stress incontinence, 22 (52.4%) had nocturia, 31 (72%) had retention of urine, 22 (52.4%) had incomplete evacuation, and 14 (33.3%) patients had mixed urinary complaints. The common urodynamic findings were neurogenic detrusor overactivity (NDO) with detrusor-sphincter dyssynergia (DSD) in 14 (33.3%) patients, NDO without DSD in 8 (19%), and acontractile detrusor in 20 (47.6%). Pharmacotherapy was advised to 22 (52.4%) patients, whereas clean intermittent catheterization (CIC)/self-catheterization was advised to 39 (92.9%) patients.

Conclusions Urinary retention was observed to be the most common urinary complaint in patients with NMOSD followed by NDO with or without sphincter dyssynergia. Urodynamics should be performed in all patients with LUTSs for best management. CIC remains the gold standard for the management of neurogenic bladder dysfunction.

Keywords

- ▶ neuromyelitis optica spectrum disorders
- ▶ neurogenic bladder dysfunction
- ▶ urinary symptoms
- ▶ urodynamics

Introduction

Neuromyelitis optica spectrum disorder (NMOSD), also known as Devic's disease, is an idiopathic demyelinating disease involving the optic nerve/s, spinal cord, and periventricular areas of the brain. It has a poorer prognosis as compared with the other demyelinating diseases of the central nervous system, notably multiple sclerosis (MS).^{1,2}

The diagnosis consensus criteria for NMOSD includes at least one core clinical characteristic (optic neuritis or longitudinally extensive transverse myelitis), a positive test for aquaporin 4 antibody (AQP4) immunoglobulin G (IgG) or for IgG against myelin oligodendrocyte glycoprotein (MOG), and exclusion of alternative diagnosis.^{3,4}

AQP4 antibody positivity is more commonly associated with female gender and older age. Patients with MOG antibodies have better outcomes from the episode and a lower risk for visual and motor disability. In MOG-positive NMOSD, there are more chances of conus involvement; hence, the urodynamic presentation may be different than aquaporin-positive NMO.⁴

The typical peak age at onset is between 35 and 45 years, but it may manifest in children and the elderly also. Female preponderance is substantially higher in seropositive (~9–10:1) than in seronegative patients (~2:1). The majority of NMO cases are sporadic, but rare familial cases indistinguishable from the former with respect to clinical presentation, age, and sex distribution have been reported.^{5–10}

Predictors of a worse prognosis are number of relapses in the first 2 years of disease activity, the severity of the first attack, male sex, Afro-Caribbean or Asian ethnicity, young age at onset, and incidence of autoimmune disorders such as thyroiditis, systemic lupus erythematosus, and Sjogren's syndrome.^{11–14}

The incidence of lower urinary tract symptoms (LUTS) in NMOSD is approximately 80%.¹⁵ As there is a predilection for longitudinally extensive transverse myelitis and central cord lesions, the chances of bladder dysfunction are very high.¹⁴ LUTS are more frequent and more severe in NMOSD as compare with patients with MS.¹¹ Patients with NMOSD showing sensorimotor recovery from a particular episode may continue to have urinary symptoms, which underlines the importance of managing bladder dysfunction. Moreover, urinary complications significantly increase the economic burden on the patient and caregivers due to prolonged hospital stay and pharmacological treatment.

The objective of this prospective study was to assess the LUTS through urodynamics (UDS; filling and voiding phase of cystometrography) in patients with NMOSD with neurogenic bladder dysfunction who were admitted for inpatient rehabilitation. The management of bladder dysfunction was based on the UDS findings.

Materials and Methods

This cross-sectional study was conducted in the Department of Neurological Rehabilitation of a university tertiary research hospital between September 2017 and May 2019. The diagnosis of neuromyelitis optica was made in the Department of Neurology after the patients fulfilled the clinical, diagnostic, and laboratory work-up and imaging criteria.⁴ NMOSD patients with neurogenic bladder dysfunction with varying urinary complaints who were admitted to the department for inpatient rehabilitation were included in the study. The project was approved by the Institute's Ethics Committee, and informed consent was obtained from the patients before recruiting for the study. Patients with MS, myelopathies with ethiopathological diagnosis other than NMOSD, a history of pelvic or prostate surgery, previous pelvic radiotherapy, no urinary complaints, and genital prolapse were excluded from the study.

A detailed clinical and neurologic examination was performed after admission. Their neurologic status and recovery

(admission and discharge) were recorded using the American Spinal Injury Association Impairment Scale (AIS). Urinary symptoms were recorded in all the patients. At least 72 hours of bladder diary was maintained to note down urinary symptoms and for understanding bladder pattern. Transabdominal and pelvic ultrasonography (for the evaluation of the kidneys, ureter, bladder, prostate status in men, and postvoiding residual urine) was performed in the patients enrolled in the study before conducting UDS.

UDS (filling and voiding phase cystometrography) was performed using multichannel pressure recording technology with Primus (Life-Tech). The urodynamic studies were performed according to the "Good Urodynamic Practice" recommended by the International Continence Society. All definitions used were in accordance with the International Continence Society Report.^{16,17} Filling cystometry was performed with patients in the supine position on the urodynamic table. Bladder filling performed with normal saline at medium fill rate (10–50 mL/minute). Patients were asked to report the events during the filling phase, such as first desire, normal desire, strong desire, painful sensation, and urge to pass urine. When patients were not able to hold urine or having pain or when bladder cystometric capacity was reached, they were asked to void. Recordings were made during the procedure (both filling and voiding phases). Sphincter electromyography was performed to observe sphincter activity and possible synergic/detrusor sphincter dyssynergic pattern. Complete data were captured by the software, and final urodynamic diagnosis was made following the analysis of graph produced by the equipment. Patients were advised management based on UDS findings, which included pharmacotherapy, and supportive and behavioral measures.^{16,18}

Statistical Analysis

Data were analyzed using Statistical Package for Social Science (SPSS), version 22.0 (IBM Corp., Armonk, New York, United States). Descriptive statistics included frequency, mean, and standard deviation (SD) for quantitative variables such as age, duration of illness, duration of urinary complaints, and illness severity scores. It also included detrusor characteristics and management advised. Spearman's correlation coefficient was used to correlate between severity of illness and UDS findings. *p*-Value of <0.05 was considered statistically significant.

Results

The study included 42 patients (34 females and 8 males) with NMOSD, with a mean age of 34.5 years (range: 11–64 years; SD: 13.1). Twenty-three (54.8%) patients had a first episode of illness, whereas 19 patients had relapses (number of episodes varying from 2 to 7). The mean length of stay in the rehabilitation unit was 33 days (range: 10–78 days; SD: 17). The topographical clinical presentation was as follows: tetraplegia in 12 (28.5%) and paraplegia in 30 (71.4%). At admission, 8 patients had complete sensorimotor impairment (AIS-A), 16 had complete motor impairment (AIS-B), and 18 had incomplete motor impairment (AIS-C or D). Patients

Table 1 Urodynamic characteristics of bladder in patients with paraplegia and tetraplegia

Clinical diagnosis	Bladder characteristics based on UDS			
	Neurogenic detrusor overactivity with DSD	Neurogenic detrusor overactivity without sphincter dyssynergy	Acontractile/hypocontractile detrusor	Total
Paraplegia	8	5	17	30
Tetraplegia	6	3	3	12
Total	14	8	20	42

Abbreviations: DSD, detrusor-sphincter dyssynergia; UDS, urodynamics.

Table 2 Correlation between the neurologic status of the patients (using the admission ASIA impairment scale) and urodynamic findings

Neurologic status as per the ASIA impairment scale	Urodynamic findings				Total	p-Value
	Neurogenic detrusor overactivity without dyssynergia	Neurogenic detrusor overactivity with DSD	Acontractile detrusor	Normal study		
A	1	3	4	0	8	>0.05
B	5	2	9	0	16	
C	2	6	4	0	12	
D	0	3	3	0	6	
E	0	0	0	0	0	
Total	8	14	20	0	42	

Abbreviations: ASIA, American Spinal Injury Association; DSD, detrusor-sphincter dyssynergia.

showed significant neurologic recovery during rehabilitation, and there was significant improvement in grades in the AIS scale. At discharge, only four patients were AIS-A grade and five patients were AIS-B grade. Thirty-four (80%) patients were AIS-C or D, implying incomplete motor impairment and significant neurologic recovery. Eleven (26%) patients had increased frequency, 16 (37%) had urgency, 12 (28%) had urge incontinence, 8 (18.6%) had stress incontinence, 22 (52.4%) had nocturia, 31 (72%) had retention of urine, 22 (52.4%) had incomplete evacuation, and 14 (33.3%) patients had mixed urinary complaints.

More than 52% (22/42) patients had neurogenic detrusor overactivity (NDO) with or without detrusor-sphincter dyssynergia (DSD), and all the 22 (52.3%) patients were started on medications (antimuscarinic such as tolterodine/solifenacin or selective β -3 adrenoceptor agonist such as Mirabegron). Five patients having DSD were started on imipramine (tricyclic antidepressant) for nonrelaxing sphincter/dyssynergia, with varying results. None of the patients had normal UDS findings, but as three of the patients were having insignificant post void residual consistently, which was confirmed both clinically (with voluntary void followed by clean intermittent catheterization [CIC]) and with pre- and postvoid USG of the abdomen, they were advised to continue voluntary micturition with regular USG screening in the follow-up period. Thirty-nine (92%) patients were advised timed voiding with CIC/clean intermittent self-catheterization (CIC/CISC), which remains the gold standard for the management of neurogenic bladder along with fluid restriction measures to manage neurogenic bladder. DSD was seen in 14 patients, and very high

peak detrusor pressures were noted. Acontractile detrusors were seen in 46% ($N = 20$) patients who were advised timed voiding (4–6 hourly) with fluid restriction (► **Tables 1** and **2**).

Discussion

Management of neurogenic bladder dysfunction is important to prevent recurrent urinary tract infection, preserve renal function, and manage urinary incontinence/retention in most of the spinal cord lesions as well as NMO spectrum disorders.

Nineteen (45.2%) patients had relapsed, and all these patients had urinary symptoms during previous episodes also. Only three of these underwent UDS during the previous episode and were managing bladder appropriately based on the advice of a urologist. The remaining 16 patients had never consulted any urologist or visited a rehabilitation department with UDS facility. They were managing bladder with either indwelling catheter with continuous drainage or diaper use or were having reflex void with multiple leak episodes. This is unfortunate as bladder management should be an integral part of comprehensive rehabilitation and suggests an important gap that needs to be filled by the treating neurologists or the rehabilitation physician. Six patients had pressure ulcers at the sacral region/ischial tuberosity, and poor bladder management and leaking of urine might have contributed to these occurrences.

More than half of the patients (22/42) had NDO on UDS with or without dyssynergia, which is on the expected

line and has been abundantly reported in the literature in patients with NMOSD.¹⁸⁻²¹ UDS was performed in 23 patients with a first episode of illness and urinary symptoms only when the patients were out of spinal shocklike picture and had more “definitive” bladder dysfunction symptoms such as increased frequency, urgency, or incontinence after 4 to 6 weeks of illness. During the initial phase, the patients have the inability to void, with urinary retention as a predominant complaint. As with other myelopathies, UDS performed after 4 to 6 weeks of insult would give a more accurate status of bladder dysfunction and help in managing bladder better in the longer term. Our experience with both traumatic and nontraumatic myelopathies yielded similar results in the past.^{19,20}

No significant correlation was observed between the neurologic statuses of the patients (AIS) with bladder characteristics based on UDS. This has been observed and reported in the literature while studying patients with long-segment myelitis (transverse myelitis) and trying to observe a “set pattern” or correlation between UDS findings and severity of neurologic lesions (AIS).^{16,22}

This study underlines the importance of performing UDS in all NMOSD patients irrespective of the extent of sensorimotor recovery for the management of LUTS as the patients can have both LMN and UMN types of bladder, which can only be understood clearly with a properly written bladder diary and objectively by doing UDS.

Only one patient had complete motor recovery and was AIS-E grade at the time of discharge. Although patients had neurologic and functional recovery, none of the patients had normal UDS finding, which underlines the fact that there is no definitive correlation between sensorimotor recovery and recovery of autonomic dysfunction.^{23,24} NMOSD patients who retain independent ambulatory status may continue to have urinary complaints and have to be managed based on UDS findings with CIC or CISC. This usually is associated with timed voiding and fluid restriction, with or without medications.

The limitation of the study was the lack of follow-up, which would have provided more information about changing bladder pattern, compliance of patient, and need to stick to a fixed program versus dynamic management program based on urinary symptoms. The strength of the study is that homogeneous population with other demyelinating illness (MS and acute transverse myelitis) was excluded from the study to have a better understanding of bladder dysfunction in NMOSD.

Conclusions

This study suggests that LUTSs are very common in NMOSD. Neurogenic bladder in NMOSD showed a mixed picture, with both overactive and acontractile detrusors in almost equal proportions among the patients. None of the patients was found to have normal urodynamic study. We observed that patients showing good neurologic and functional recovery continue to have urinary symptoms

and need to manage the bladder as advised by the treating team based on UDS findings.

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None.

Conflict of Interest

None declared.

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