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Features of lower urinary tract symptoms in patients with multiple system atrophy

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ABSTRACT

Background: Multiple system atrophy (MSA) is a fatally progressive neurodegenerative disease characterized by variable combinations of parkinsonism, cerebellar ataxia and autonomic dysfunction. Lower urinary tract dysfunction, as a manifestation of autonomic failure is one of core clinical features for a diagnosis of MSA, yet it is often underrecognized especially in the early stage of the disease.

Objective: The study aimed to describe lower urinary tract symptoms and residual urine volume in early MSA.

Subjects and methods: This was a cross-sectional study including MSA patients with disease duration of less than 5 years. Demographic and clinical characteristics were collected. All participants were assessed with UMSARS, IPSS, OABSS scores, and abdominal ultrasound was performed to measure residual urine volume.

Results: 32 MSA patients were recruited, all of whom reported lower urinary tract symptoms. Urge incontinence was the most common symptom (93.8%). Symptoms related to voiding were found in 85.7% of MSA-C patients and 88.9% of MSA-P patients. Postvoid residual urine volume (PVR) more than 100 ml was recognized in 28% of patients. There is no statistically significant difference observed in the rate of PVR abnormalities between the MSA-C and MSA-P subgroups ($p > 0.05$).

Conclusion: Lower urinary tract symptoms and abnormal residual urine volume are frequently present even in the early stage of MSA with no significant differences between different clinical subtypes.

Keywords: Lower urinary tract symptoms, residual urine volume, multiple system atrophy.

I. INTRODUCTION

Multiple system atrophy (MSA) is a fatally progressive neurodegenerative disease characterized by variable combinations of parkinsonism, cerebellar ataxia and autonomic dysfunction [1]. The prevalence of MSA is estimated to be around 2 - 5 cases per 100,000 people [2]. Abnormal accumulation of α-synuclein in the cytoplasm of glial cells and loss of neurons, mainly in the substantia nigra and the olivopontocerebellar system is the important microscopic pathological hallmark of the disease[3]. Currently, there is no cure and the treatment of MSA is mainly symptomatic.

Previous criteria for diagnosing MSA have been shown to have suboptimal accuracy (62%–79%), and low sensitivity at first clinical presentation[4,5]. Therefore, in 2022, the Movement Disorder Society developed new diagnostic criteria with improved accuracy and sensitivity, especially in the early stages of the disease. In the newly released criteria, lower urinary tract dysfunction (LUTD) is considered a core feature for early diagnosis of MSA. Indeed, a prior study reported that lower urinary tract symptoms are the sole initial manifestation of MSA in 18.2% of patients [6].

Globally, there have been many studies on LUTD in MSA. However, MSA is still an unfamiliar condition in Vietnam, and while a few studies have addressed the autonomic dysfunction in MSA, there has been no research specifically focusing on urinary symptoms - a key feature that occurs early in the disease. For these reasons, we conducted this study to explore the clinical characteristics and post-void residual urine via ultrasound inpatients in the early disease course of MSA.

II. SUBJECTS AND METHODS

This is a descriptive cross-sectional study with an analytical component conducted at the University Medical Center of Ho Chi Minh City from February 2023 to June 2023. Inclusion criteria included ones with a diagnosis of probable or definite MSA based on MDS 2022 criteria, disease duration of less than 5 years, and agreement to participate in the study. Exclusion criteria included patients with lower urinary tract symptoms caused by a specified different urological condition such as urinary tract infections or prostate disease (confirmed by clinical or laboratory findings); patients with other neurological conditions affecting urination such as brain injury, spinal cord disease, or diabetes; and patients with significant cognitive impairment or psychiatric disorders.

The sociodemographic and disease related characteristics of all participants were collected. They were then assessed with UMSARS scores, lower urinary tract symptom scores (IPSS and OABSS). Finally, abdominal ultrasound measurements for post-void residual urine were performed.

The data were analyzed using STATA 14.0 statistical software. Descriptive statistics employed frequencies and percentages of qualitative variables; means and standard deviations were used to describe quantitative variables with normal distributions; medians and interquartile ranges were used to describe variables without normal distributions. For inferential statistics, qualitative variables were analyzed using the χ^2 test or Fisher's exact test (when > 20% of cells had expected counts < 5); quantitative variables with normal distributions were analyzed using the t-test (with variance comparison); for variables without normal distributions, the non-parametric Mann-Whitney test (for two-sample comparisons) was used. A p-value < 0.05 was considered statistically significant.

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The study was approved by the Ethics Committee of Biomedical Research at the University of Medicine and Pharmacy, Ho Chi Minh City, decision number 923/HDDD-DHYD dated November 24, 2022. Patients and their families were informed about the purpose of the study, the benefits and risks of participation, their right to refuse participation, and signed informed consent forms.

III. RESULTS

32 MSA patients who met the inclusion and exclusion criteria enrolled our study. The demographic characteristics of the study sample are presented in Table 1.

***Table 1**. General Characteristics of the Study Population*

Characteristics	Value
Age	60.1 ± 6.4
Age of onset	57.6 ± 6.8
Disease duration (years)	2.5 ± 1.2 [0.2; 5]
Duration of lower urinary tract symptoms onset (months)	15.8 ± 1.6 [0; 60]
Female: male ratio	1:1
Definite/Probable Diagnosis (%)	56.2/43.8
Clinical subtype MSA-P/MSA-C	56.3/43.7
UMSARS Score - Part 1	21.9 ± 7.7 [12; 40]
UMSARS Score - Part 2	22.7 ± 8.3 [7; 42]

Among MSA patients, the most common reason for consultation was gait instability, reported by 46.9% (15/32) of patients.

3.1. Characteristics of Lower Urinary Tract Symptoms

100% (32/32) of the study participants experienced urinary symptoms, with urinary symptoms being the first manifestation of the disease, before the motor symptom onset, in 3 patients.

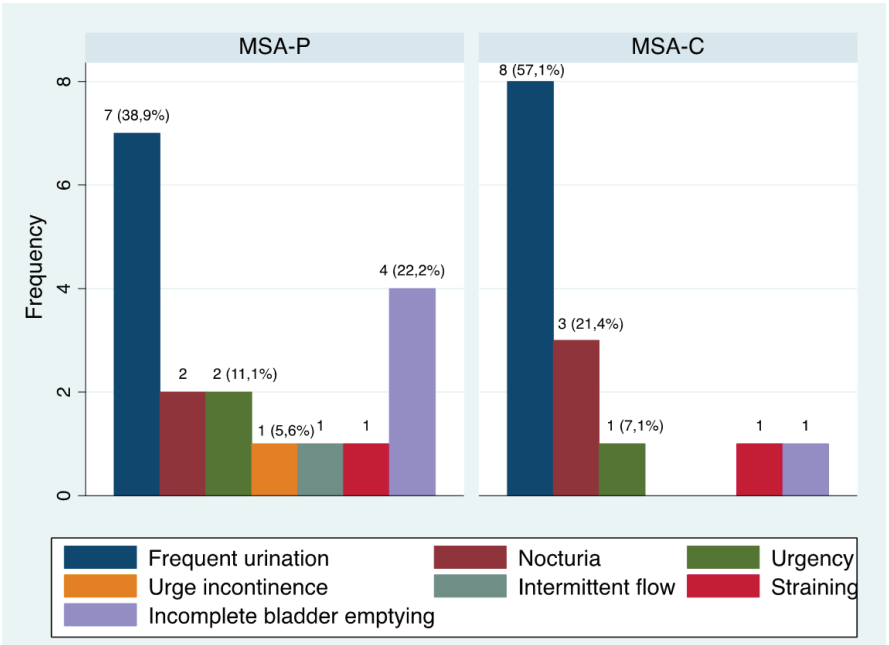

***Chart 1**. First Onset Lower Urinary Tract Symptom Type*

Frequent urination was the most frequently reported initial lower urinary tract symptom in both MSA subgroups. In the MSA-P group, the second most common symptom was the sensation of incomplete bladder emptying after urination, while it was nocturia for those in MSA-C group. Fisher's exact test showed no statistically significant difference for this symptom between the two groups (p=0.887).

3.2. Characteristics of Lower Urinary Tract Symptoms in different MSA suptypes

***Table 2**. Characteristics of Lower Urinary Tract Symptoms in the Two Subgroups MSA-P and MSA-C*

	MSA-P (N=18)	MSA-C (N=14)	P value
Storage-related urinary symptoms			
Frequent urination	16 (88.9%)	13 (92.9%)	1.000
Nocturia	15 (83.3%)	13 (92.9%)	0.613
Urgency	15 (83.3%)	14 (100%)	0.238
Urge incontinence	16 (88.9%)	14 (100%)	0.492
Control over urination	9 (50%)	11 (78.6%)	0.098*
Overall	18 (100%)	14 (100%)	
Voiding-related symptoms			
Intermittent flow	11 (61.1%)	6 (42.9%)	0.305
Weak flow	14 (77.8%)	12 (85.7%)	0.672*
Straining	8 (44.4%)	6 (42.9%)	0.928
Overall	16 (88.9%)	12 (85.7%)	1.000*
Post-voiding Symptoms			
Incomplete bladder emptying	11 (61.1%)	8 (57.1%)	0.821
IPSS score	17.1 ± 8.7 [1; 35]	17.3 ± 8 [7; 34]	0.9394'
OABSS score	18.4 ± 5.9 [4; 27]	20 ± 6 [7; 28]	0.4520'
Quality of Life (QoL)	3.3 ± 1.6 [0; 6]	3.4 ± 1.6 [0; 6]	0.8706'

**Fisher's test; **Chi-square test; 'T-test.*

Storage symptoms were observed in 100% of patients in both groups. Of all storage symptoms the most frequent one was frequent urination, followed by nocturia, urgency, and urge incontinence, with frequencies varying from 83.3% to 100%. Voiding symptoms were observed in 85.7% to 88.9% of patients in the MSA-C and MSA-P groups, respectively, with weak flow being the most common symptom in both groups. Post-voiding symptoms were more frequently noted in the MSA-P group. The severity of lower urinary tract symptoms, as assessed by the mean IPSS and OABSS scores, was moderate in both groups. The quality of life due to urinary symptoms in both groups was around the same level, ranging from mixed satisfaction to dissatisfaction. No statistically significant differences in the pattern of lower urinary tract symptoms were found between the MSA-P and MSA-C groups.

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***Table 3**. PVR Characteristics in the Two MSA Subgroups*

Characteristic	MSA-P (N=17)*	MSA-C (N=14)	P value
PVR Abnormality (%)(PVR ≥ 100 ml)	5 (27.8%)	4 (28.6%)	1.000′
PVR (ml) Median [p25; p75] (min; max)	 41 [6; 74] (2; 431)	 52 [24; 170] (3; 320)	 0,4506″

*One MSA-P patient was excluded from PVR analysis due to urinary catheterization prior to measurement. ′Fisher's test; ″Mann-Whitney test.

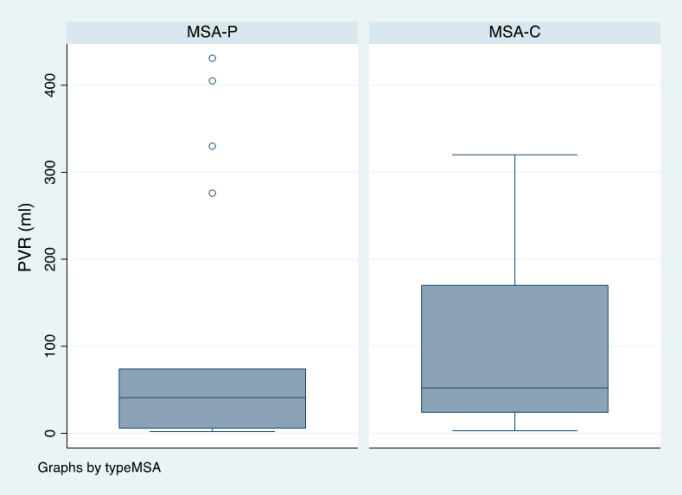

***Chart 2**. Comparison of PVR Values between the Two MSA Subgroups*

Post-void residual (PVR) volume varied widely among patients in both subgroups, from a minimum of 2 ml to a maximum of 431 ml in the MSA-P group and from a minimum of 3 ml to a maximum of 320 ml in the MSA-C group. The rate of abnormal PVR in both subgroups was approximately 28%. No statistically significant differences in PVR characteristics were observed between the two MSA subgroups ($p > 0.05$).

IV. DISCUSSION

Lower urinary tract dysfunction has long been recognized as a core clinical feature in diagnosing MSA, often appearing early in the disease course and serving as a predictor of reduced survival in MSA [7]. A prior study reported a prevalence of urinary symptoms as high as 87% in MSA patients [8]. Similarly, our study found that 100% of MSA patients had lower urinary tract symptoms, consistent with domestic research by V.N.N. Trang and international research by Ryuji Sakakibara. This result emphasizes that lower urinary tract dysfunction is common in almost all MSA patients, even in the early stage.

In our research, the average time from the onset of urinary symptoms to the motor symptom onset was 15.7 months, considerably shorter compared to a previous finding reported by Ryuji Sakakibara et al. [6] (2018), which was 2.8 years (1–7 years). Their study involved a prospective cohort of 121 MSA patients with an average follow-up period of 6.5 years. The patients were jointly monitored by experts in movement disorders, autonomic, and urology,

and the diagnosis of MSA was reconfirmed at the final visit. On the other hand, our study was a cross-sectional descriptive study, surveying patients at a single point of time by a neurologist, with symptoms collected retrospectively and a smaller sample size. Therefore, these factors may help explain the differences between the two study results.

In both MSA subgroups, frequent urination was the most frequently reported initial lower urinary tract symptom, occurring in 38.9% of MSA-P and 57.1% of MSA-C patients. Both subgroups involve degenerative damage to neurons above the pontine level, leading to storage dysfunction, reduced bladder capacity, and detrusor overactivity, manifesting as spontaneous, involuntary bladder contractions and overactive bladder symptoms. In this study of 32 MSA patients, the incidence of storage-related urinary symptoms was 100% in both subgroups, while voiding-related symptoms were 88.9% in MSA-P and 85.7% in MSA-C patients. The high rate of lower urinary tract symptoms in our MSA group is consistent with other studies from different countries, where voiding-related symptoms have been reported in up to 79% of MSA patients. Compared to the study by Sabine Eschlböck and Woosik Choi, the rate of urinary symptoms in our study is higher, which may be due to our prospective sampling design, allowing for easier symptom assessment and minimizing missed symptoms through the use of two relevant questionnaires.

When comparing the MSA-P and MSA-C subgroups, we found no significant differences in the pattern of urinary dysfunction. This finding aligns with the studies by Sabine Eschlböck and Woosik Choi, suggesting that although brain lesions causing motor symptoms differ between the two subgroups, autonomic nervous system involvement is similar in both MSA-P and MSA-C [9].

The severity of urinary symptoms, as measured by the average IPSS and OABSS scores in our study, did not differ between the two groups, with moderate severity in both MSA-P and MSA-C subgroups, scoring 17.1 and 17.3 for IPSS and 18.4 and 20 for OABSS, respectively. The quality of life due to urinary symptoms was roughly equal, around mixed satisfaction to dissatisfaction in both groups.

Similarly, the rate of PVR abnormalities in our two subgroups was around 30%, with median PVR values of 41 ml in MSA-P group and 52 ml in MSA-C group, showing no significant differences. Studies by Sabine Eschlböck and Woosik Choi also found no significant differences in PVR abnormalities between the two subgroups. However, the PVR levels in our study were significantly lower than those in the other studies. Chief among various possible reasons is that we excluded patients with comorbid conditions affecting urinary symptoms, such as diabetes, prostate enlargement, or spinal cord injury, which were not excluded in the other studies. Besides, the disease duration was shorter in this study, with 25% of patients having a disease duration of less than 2 years. Moreover, different assessment instruments were used. In more details, while we performed abdominal ultrasound measurements of RUV, the other studies used urodynamic testing via urethral catheterization. Additionally, the patients in Sabine Eschlböck and Woosik Choi's studies were subjected to invasive urodynamic testing, which may have included patients with more suggestive symptoms, possibly not representative of the entire MSA population.

In this research, when analyzing PVR results, we used the median and interquartile range because the data were skewed, with

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some patients having very low PVR (e.g., 2 ml) and others having very high PVR (>400 ml), making the mean value inappropriate for interpreting sample results. In the MSA group, the PVR levels in our study were much lower than those in previous studies, and the rate of PVR abnormalities was correspondingly lower. A study by Takashi Ito in 2006 on 245 MSA patients indicated that residual urine volume increased over the course of the disease, from 71 ml in the first year post-onset to 129 ml in the second year and 170 ml in the fifth year [10]. In the study by R. Sakakibara and T. Yamamoto, PVR measurements were performed via urethral catheterization, which is the gold standard for determining PVR, although it remains unclear whether there are differences between methods[11]. Nevertheless, this may contribute to lower sensitivity in detecting elevated PVR in our studies; additionally, the MSA disease duration in the other studies was longer.

This study has some limitations, such as a short study duration and a small sample size. Besides, the scales used in the study, IPSS and OABSS, have not been validated or widely used in neurological patients in Vietnam. Lastly, this is a cross-sectional study without a healthy control group. Future studies including control groups and double-blind designs might be necessary to provide more precise and reliable information.

V. CONCLUSION

The results of this study reveal that lower urinary tract symptoms and abnormal residual urine volume on ultrasound are frequently present even in the early stage of multiple system atrophy (MSA) regardless of different subtypes. Therefore, these symptoms should be given proper attention to aid in early diagnosis of the disease.

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