

CASE REPORT

Urodynamically proven lower urinary tract dysfunction in children after COVID-19: A case series

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Abstract

Case: Since the declaration of COVID-19 as a pandemic, other unexpected symptoms related to the infection besides the respiratory system have been reported. Although a few case reports have revealed that adult patients with COVID-19 also complained of urinary frequency and nocturia, the exact pathophysiology is still unclear. In this case series, we present three children aged 14 to 17 years with urodynamically proven lower urinary tract dysfunction (LUTD) following COVID-19.

Outcome: None of the patients had constipation or bowel disorder before the diagnosis of COVID-19. In addition, neurological examination and related imaging revealed no signs of etiological factors. The median time from diagnosis of COVID-19 infection to the onset of lower urinary tract symptoms was 3 months. Incomplete bladder emptying/urinary retention supported by increased bladder compliance, high post-micturition residual urine volumes, and absence of detrusor pressure increase during the voiding phase in the pressure flow study (acontractile detrusor in two patients and hypocontractile detrusor in one patient) were observed.

Conclusion: We observed that LUTD (eg, incomplete bladder emptying, urinary retention) can be prominent some time after the diagnosis of COVID-19. Even though psychogenic or neurogenic causes may not be excluded completely, clinicians should be aware of a recent COVID-19 infection in children with sudden-onset LUTD.

KEYWORDS

COVID-19, detrusor hypocontractility, lower urinary tract dysfunction, pediatric, SARS-CoV-2, urinary retention

1 | INTRODUCTION

It has been almost 2 years since the rapid spread of SARS-CoV-2 and the announcement of COVID-19 as a pandemic by the World Health Organization. The respiratory system is the main affected site attacked by this virus. However, numerous reports indicated other system involvement such as neurological and hematopoietic systems in patients diagnosed with COVID-19.¹ On the other hand, there have been growing data on the effects of COVID-19 on the genitourinary system.² “COVID-19-associated cystitis” has been defined for adult patients who have had COVID-19 with complaints of urinary frequency and nocturia.^{3,4}

To our knowledge, lower urinary tract dysfunction (LUTD) associated with COVID-19 in the pediatric population has not been reported in the literature. We present three pediatric cases with urodynamically proven LUTD following COVID-19.

2 | CASE SERIES

Toilet-trained children under the age of 18 who were admitted to our pediatric urology department with various lower urinary tract symptoms (LUTS) between June 2020 and September 2021 were retrospectively evaluated. Children who were not neurologically intact and

TABLE 1 Demographic and clinical data of patients

Pt #	Age (y)/gender	LUTS	Time to symptom onset after COVID-19 diagnosis (mo)	DVSS ^a	GFR (CKD-EPI)	Urinary tract imaging	Cystometry results	Neurological assessment	Treatment
1	17, F	Incomplete bladder emptying, frequency, constipation	4	9/2	145 mL/min	No dilation	DOA: (-) EBC: 350-500 mL Cystometric capacity: 431 mL (normal for age) Compliance: 62.7 mL/cmH ₂ O Hypocontractile detrusor PMR: 431 mL	NNE ^b spinal MRI: normal	CIC
2	14, F	Urinary retention	3	10/2	145 mL/min	US: L-grade 2 HN, R-grade 1 HN	DOA: (-) EBC: 350-500 mL Cystometric capacity: 650 mL (increased for age) Compliance: 100 mL/cmH ₂ O Acontractile detrusor PMR: 657 mL	NNE ^b spinal MRI: normal	CIC
3	15, M	Incomplete bladder emptying, intermittency, hesitancy, constipation	3	13/2	147 mL/min	US: L-grade 1 HN, R-grade 1 HN	DOA: (-) EBC: 350-500 mL Cystometric capacity: 450 mL (normal for age) Compliance: 119.5 mL/cmH ₂ O Acontractile detrusor PMR: 450 mL	NNE ^b spinal MRI: normal	CIC

Abbreviations: CIC, clean intermittent catheterization; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; DOA, detrusor overactivity; DVSS, dysfunctional voiding symptom score; EBC, estimated bladder capacity for age; F, female; GFR, glomerular filtration rate; HN, hydronephrosis; L, left; LUTS, lower urinary tract symptoms; M, male; MRI, magnetic resonance imaging; NNE, normal neurological evaluation; PMR, post-micturition residual; Pt, patient; R, right; US, ultrasound.

^aDVSS consists of 13 questions about daytime and nighttime urinary symptoms, voiding and bowel habits, and 1 item for quality of life.⁶ The total score ranges from 0 to 35. A score above 8.5 indicates voiding abnormalities. According to this tool, our patients had the following symptoms:

Question 5. How many times does your child urinate? More than seven times/day (1).

Question 6. My child strains during voiding. No (0), Yes (4).

Question 7. My child feels pain during voiding. No (0), Yes (1).

Question 8. My child voids intermittently. No (0), Yes (2).

Question 9. My child needs to go back to the bathroom soon after he/she finishes. No (0), Yes (2).

Question 11. My child holds by crossing his/her legs. No (0), Yes (1).

Question 13. My child does not have a bowel movement daily. No (0), Yes (1).

Quality of Life: If your child experiences the symptoms mentioned above, does it affect his/her family, social, or school life? No = 1, Yes = 2. Seriously affects = 3.

Pt#1: 5, 6, 7, 9, 13; Quality of Life: 2.

Pt#2: 5, 6, 7, 9, 11; Quality of Life: 2.

Pt#3: 5, 6, 7, 8, 9, 11, 13; Quality of Life: 2.

^bNormal neurological examination includes intact perineal sensation and anal tone, normal muscle mass and strength sensation of the lower extremities, normal deep tendon reflexes, normal gait, and absence of skin lesions overlying the sacrum.

had any anatomical urological pathology were excluded. Among them, three children with urodynamically proven LUTD following the diagnosis of COVID-19 were included in this study.

All patients had positive nasopharyngeal swab results for SARS-CoV-2 and findings of pulmonary involvement detectable on thoracic imaging by computed tomography. Although all patients had fever, shivering, abdominal pain, and cough at the time of positive nasopharyngeal swab, none of them had LUTS at that time. None of the patients had a serious infection, so they received only supportive therapy for their symptoms. None of them required hospitalization or admission to the intensive care unit. Since severe infection or persistent fever was not observed, therapeutic agents (eg, steroids) that could cause neuroinflammation symptoms were not used in any of them according to the multicenter initial guidance recommendations for children.⁵

Presence of LUTD was initially evaluated using dysfunctional voiding symptom score (DVSS),⁶ while noninvasive studies, including uroflowmetry, electromyogram, and post-micturition residual (PMR) urine measurement, were performed on all patients. PMR was considered as abnormal if greater than 10% of the expected bladder capacity [$30 \times (\text{age in years} + 1)$]. In addition, video-urodynamic studies were performed in all patients due to abnormal uroflowmetry curve shape, PMR, and DVSS.

Demographic and clinical data of these patients are shown in Table 1. Incomplete bladder emptying/urinary retention supported by increased bladder compliance, high PMR volumes, and absence of detrusor pressure increase during the voiding phase in the urodynamics study (acontractile detrusor in two patients and hypocontractile detrusor in one patient) were observed in all patients. None of the patients had a previous history of constipation or bowel disorders. Neurological examination revealed no upper neuron signs suggestive of myelitis (eg, paraparesis, exaggerated deep reflexes, positive extensor plantar reflexes, decreased pin prick sensation, and decreased position sensation below T5) or lower neuron signs suggestive of conus/cauda equina lesion or peripheral neuropathy (eg, paraparesis, loss of deep reflexes, and unilateral/bilateral loss of sensation). In addition, related neurological imaging revealed no signs of etiological factors.

3 | DISCUSSION

Recent studies have reported irritative urinary symptoms, particularly frequency and nocturia, as a result of COVID-19 in adult patients, although strong evidence has not been provided.^{3,4} Mumm et al⁴ hypothesized that the expression of the receptors for cell surface protein angiotensin-converting enzyme 2 (ACE2), also described as the receptor for SARS-CoV-2, in the luminal or basal urothelial cells may lead to endotheliitis and the local inflammation of the bladder. On the other hand, elevated levels of inflammatory cytokines (interleukin-6 [IL-6], IL-8, and IP-10) in urine were demonstrated by Lamb et al³ who suggested the view of bladder inflammation associated with COVID-19. In reports supporting these views, SARS-CoV-2 is held responsible for the development of neuroinflammation, which causes neuronal demyelination in the central and peripheral nervous system. It has been reported that the exaggerated release of pro-inflammatory

molecules also known as “cytokine storm” can cause demyelinating diseases in a similar way as in viral diseases.⁷ Based on this mechanism, it is also argued that the inflammation and demyelination of the pudendal nerve can cause bladder and bowel incontinence.⁸ In contrast, it has been reported that demyelination of the nervous system can also lead to urinary and fecal retention through not completely understood mechanisms.⁹

Acute urinary retention, another endpoint of LUTD, is an extremely rare entity in childhood compared to adults.¹⁰ The most common causes reported in the literature are balanoposthitis, acute constipation/fecal impaction, trauma, urinary tract infection, and idiopathic and neurological events. Moreover, it has been noted that urinary retention may be originating from febrile systemic infections (eg, viral, enteric, and non-urogenital), albeit to a lesser extent.⁹ In this context, some studies in the adult literature report COVID-19 may cause exacerbation of LUTS in patients with benign prostatic hyperplasia and may even be a predictor of urinary retention.¹¹ Even an occult meningeal reaction has been reported in an elderly patient, independent of COVID-19, on the basis of urinary retention of undetermined etiology.¹² This shows that every possibility should be considered in the differential diagnosis. On the other hand, we have not yet come across a report directly associating the development of nonneurological urinary retention with COVID-19 in the pediatric literature.

Some viral diseases have been accused of causing transient LUTD development through neurological involvement. These diseases include polioviruses, Coxsackievirus type A7, echoviruses, enterovirus type 71, and West Nile virus. It has been reported that these viruses can cause acute flaccid paralysis and detrusor areflexia by affecting the motor or sensorial tracts.^{9,13} In a rare case of pediatric “post-COVID-19 transverse myelitis,” the authors associated SARS-CoV-2, which causes the multisystem inflammatory syndrome, with the subsequent development of urinary and fecal retention.¹³ In contrast, in our study, neurological imaging, including magnetic resonance imaging (MRI) of the brain and the spinal cord, showed no pathological signs that could lead to the symptoms of these patients. Although previous reports have associated certain coronavirus genotypes with neurological events (eg, encephalomyelitis, seizure, and Guillain-Barre),^{9,13} different signs of LUTD can be observed even as a consequence of nonneuropathic virus variants.

Since the median time to symptom onset after diagnosis of COVID-19 is 3 months in our patients, it can be considered that LUTD can begin even after the resolution of pulmonary findings. Therefore, we think that LUTS do not occur as a result of a direct viral effect that exists only in the acute COVID-19 period. An immune process following the acute period might have possibly played a role in the pathogenesis. However, the exact pathophysiology of LUTS related to COVID-19 is still unclear, although the increased expression of inflammatory cytokines (eg, IL-6, IL-8, IP-10) in the bladder and the expression of ACE2 receptors on urothelial cells have been demonstrated.^{3,4} Even though some studies indicate urological problems related to COVID-19, contrary data exist. A recent study conducted with a large patient population over 66 years of age has found no significant increase in the development of urinary storage symptoms, medication due to overactive bladder, or the need for urological intervention during the first 5 months after diagnosis of COVID-19.¹⁴

LUTS developing on the background of depression, anxiety, or other stress symptoms (insomnia, etc.) without a neurologic or organic etiology has been defined as bladder somatic symptom disorder.¹⁵ Specific features observed in this disorder are urodynamically increased bladder sensation, hypersensitivity, and the findings of underactive bladder without PMR.¹⁵ Therefore, we think that LUTD observed in our patients differed from bladder somatic symptom disorder or a transient psychogenic disease due to their decreased/normal bladder sensation and increased PMR. However, post-COVID-19 urinary retention still might have a psychogenic cause since our case series include only three patients which limits extrapolation.

Supportive therapy forms the basis of medication in children with COVID-19, so it is a priority to determine the respiratory status, oxygen, and fluid/electrolyte needs.⁵ If necessary, it is recommended to start empirical antibiotic therapy for possible community-acquired infections.⁵ Glucocorticoids are recommended in cases of persistent fever, severe disease, or development of the multisystemic inflammatory syndrome.⁵ Since therapeutic agents (eg, steroids) that could cause neuroinflammation symptoms were not used in any of our patients, the possibility of an etiological factor related to therapeutic agents were excluded.

Since autoimmune antibodies or inflammatory cytokines in urine or blood were not evaluated, we cannot propose a clear hypothesis regarding the molecular pathogenesis. However, we observed that LUTD (eg, incomplete bladder emptying, urinary retention) can be prominent some time after the diagnosis of COVID-19. Based on our findings, clinicians should be aware of a recent COVID-19 infection in children with sudden-onset LUTD. Although it is difficult to comment on whether post-COVID-19 urinary retention has psychogenic or neurogenic origins, these factors should also be considered in the differential diagnosis.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Selvi I.: Acquisition of data, analysis and interpretation of data, literature search, and drafting of the manuscript. Dönmez M.İ.: Analysis and interpretation of data and critical revision of the manuscript for important intellectual content. Ziylan O.: Administration, critical revision of the manuscript for important intellectual content and supervision. Oktar T.: Conception and design, administration, critical revision of the manuscript for important intellectual content, technical and material support, and supervision.

ETHICS STATEMENT

All procedures performed in our study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT

Informed written consent was obtained from the patients for publication of this case report without revealing their names and identities.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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