

Retrospective Study

Prolonged impacts of COVID-19-associated cystitis: A study on long-term consequences

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Abstract

BACKGROUND

The Coronavirus Disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 virus is an international health concern with substantial morbidity and mortality. COVID-associated cystitis (CAC), presents as new onset or exacerbated urinary symptoms, resembling overactive bladder (OAB) symptoms.

AIM

To examine the long-term outcomes of patients with CAC in the context of Long COVID.

METHODS

A cohort of 350 patients admitted to Detroit Hospitals with COVID-19 between May and December 2020, displaying CAC symptoms following discharge, was

prospectively followed. Initial urologic evaluations occurred at 10-14 wk and were repeated at 21-28 mo post-discharge. Symptoms were managed conservatively, employing behavioral modifications and standard OAB medications. Participants completed surveys assessing urinary symptoms and quality of life (QoL) at both time points. The primary outcome was the Urology Care Foundation Overactive Bladder Assessment Tool.

RESULTS

87% of the final cohort ($n = 310$) reported symptom improvement at 21-28 mo post-discharge. Patients with new onset CAC symptoms showed a median decrease of 9-10 points in OAB and QoL scores, while those with existing symptoms experienced a decrease of 6 points. Overall, 95.4% of patients with new onset symptoms reported symptom improvement at follow-up, contrasting with 60.7% among those with existing symptoms.

CONCLUSION

This study presents the first long-term follow-up of adult patients with CAC, revealing a promising prognosis with conservative management measures in the context of Long COVID. These findings provide reassurance to patients regarding symptom resolution and underscore the need for further research into this evolving aspect of COVID-19's impact on urological health.

Key Words: COVID associated cystitis; COVID-19; Long COVID; Overactive bladder

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Core Tip: Coronavirus disease (COVID)-associated cystitis (CAC), presents as new onset or exacerbated urinary symptoms that may resemble overactive bladder symptoms. To our knowledge, this study is the first long-term follow-up of adult patients with CAC. Our data reveals a promising prognosis with conservative management measures in the context of Long COVID. These findings provide reassurance to patients regarding symptom resolution and underscore the need for further research into this evolving aspect of COVID-19's impact on urological health.

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is an infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus which was originally identified in late 2019. There have been over 100 million reported cases and over 1 million deaths from COVID-19 in the United States since January 2020. It is clinically defined by a constellation of symptoms including fever, upper respiratory symptoms, and fatigue, among many others. While most of the symptoms associated with acute COVID-19 infection are upper respiratory in nature, numerous organ systems have been recognized to be associated with COVID-19 infection. Urologic manifestations of COVID-19 have been limited, with the coronavirus family in general causing renal and testicular dysfunction, and having only a low likelihood of being detected in the urine [1,2]. Early studies noted increases in urinary frequency, urgency, and nocturia post COVID-19 infection and termed this condition COVID-associated cystitis (CAC)[3].

The COVID-19 recovery time ranges from up to 7 days for mild illness to > 6 wk for severe cases[4]. However, approximately 80% of recovered patients will have one or more long-lasting symptoms[5]. CAC, a condition associated with new onset urinary symptoms or exacerbations of existing urinary symptoms is believed to be a manifestation of Long COVID [6]. Most commonly, patients experience new onset or exacerbation of existing symptoms consistent with overactive bladder (OAB). Clinical presentation can include urgency, frequency, nocturia, dysuria and/or urge urinary incontinence. Little is known on the management and long-term outcomes for patients diagnosed with CAC. More recently, we published OAB survey-based results of a cohort of 350 patients suffering from new or worsening OAB symptoms 10-14 weeks after their COVID-19 related hospital stay[7]. The intent of this study is to follow our cohort of 350 patients with OAB survey based results 21-28 mo after their hospitalization from COVID-19.

MATERIALS AND METHODS

This study was conducted in accordance with the Declaration of Helsinki and had full ethical approval from Wayne State University's Internal Review Board (IRB#20-04-2126-M1). Informed written consent was provided by all research participants. Discharged participants were originally admitted to one of two inner-city Detroit Hospitals for management

of COVID-19 infection between May 22, 2020 and December 31, 2020. From this group, patients who endorsed new or worsening urinary symptoms following hospital discharge were referred to a urologist. Initial urologic evaluation occurred during a scheduled appointment 10-14 wk following discharge and then was repeated at a second scheduled appointment 21-28 mo following discharge. During the interval between initial assessment and long-term follow-up, patient's symptoms were managed conservatively in a similar manner to OAB including behavioral modification and medications (anticholinergics and beta-3 agonists).

Respondents were informed that they would be asked questions regarding their urinary wellness, in addition to information regarding age, race, history of OAB or benign prostatic hyperplasia, and current medications to control urinary symptoms. When possible, the patient's hospital admission and discharge dates were confirmed to establish length-of-stay. Patients were given the option to decline participation or stop the survey at any time.

Our primary outcome variable was the American Urological Association's Urology Care Foundation Overactive Bladder Assessment Tool. The five individual symptom scores for frequency (range from 0 to 5; 0 being 'not at all' and 5 being 'almost always') of the following symptoms: Urgency, urge incontinence, incontinence, frequency, and nocturia. The total symptom score ranges from 0 (no symptoms) to 25 (most severe symptoms). Additionally, there are four QoL questions regarding symptom bother (range from 0 to 5; 0 being 'I am not bothered at all' and 5 being 'I am bothered a great deal') for urgency, urge incontinence, frequency, nocturia, and overall satisfaction with their current urinary condition. This score ranged from 0 representing "not bothered at all" to 5 representing "bothered a great deal". Patients with history of OAB symptoms were asked to score their pre-COVID-19 symptoms compared to post-COVID-19 symptoms. Lastly, a final QoL question asks, 'How have your symptoms changed your life?' Patients could then select all of the eight associated questions pertaining to specific life activities that are affected by their OAB (*e.g.* Keeping you from getting a good night's sleep?; Causing you to stay home more than you would like?; Causing you to exercise less or limit your physical activity?; Causing problems with friends or loved ones?; Keeping you from social activities or entertainment?; Keeping you from traveling, taking trips, or using public transit?; Making you plan trips around your knowledge of public restroom location?; Causing problems at work?), including a free-response option.

RESULTS

A total of 350 patients admitted with COVID-19 from May 22, 2020 and December 31, 2020 were identified with a clinical history consistent with CAC (Table 1). At initial urologic evaluation (at 10-14 wk), 250 (71%) patients were identified with new onset of symptoms, and 100 (29%) with worsening of existing symptoms. 30 of the patients with new symptoms and 10 with worsening of existing symptoms were lost to follow up. A total of 310 patients completed long-term follow up at 21-28 mo. The average age of this final cohort was 64 (range 47-82). The final cohort included 180 (58%) men and 130 (42%) women. 280 (90%) of the final cohort were black and the remaining 45 (13%) were white.

All 350 patients of the initial cohort completed the symptom score and QoL surveys at 10-14 wk post covid discharge. The median total OAB symptom score in both men and women was 18 (ranges 12-20 and 15-21, respectively). In patients with new onset OAB symptoms, the initial median symptom score was 18 (12-21). Patients with worsening OAB symptoms had an initial median symptom score of 19 (17-21) compared to a median pre-COVID-19 symptom score of 8 (4-10). The median QoL score for both men and women was 19 (16-20 and 16-21, respectively). In patients with new onset OAB symptoms, the median QoL score was 19 (16-24). In patients with worsening OAB, median pre-COVID-19 QoL score was 9 (8-10) compared to a median QoL score of 20 (19-20) at initial evaluation. Results are presented in Table 2.

All 310 patients completed the symptom score and QoL surveys at 21-28 mo post covid discharge. When compared to the initial urologic evaluation, patient reported scores at long-term follow up of 21 to 28 mo revealed decreases in median OAB and QoL scores for all groups (Table 2). Overall, 270 (87%) patients reported improved scores with conservative management. We observed a decrease in median score for both the OAB and QoL assessments from 18 (range 17-21) and 19 (range 18-20) down to 7 (range 4-20) and 8 (7-20) respectively. Of the 220 patients with new onset symptoms evaluated at the end of the study, 210 (95.4%) reported improvement in symptoms. Of the 90 patients with existing symptoms prior to COVID-19 infection and long term follow up, only 60 (66.7%) reported an improvement in their scores. In the existing symptom group, there was a decrease in median OAB and QoL scores of 6 points compared to a 9-10 point decrease in the new onset group.

DISCUSSION

Increased urinary frequency with COVID-19 was first reported in seven male patients by Mumm *et al* [8]. Despite an increasing number of subsequent studies reporting CAC, there is a paucity of long-term data regarding the prognosis and management of this condition. To our knowledge, this is the first prospective study with long-term follow up of adults with CAC. Here, we demonstrated that the majority (87%) of patients with CAC had significant improvement in their symptoms with conservative management at 21-28 mo follow up. Although our cohort only included adults, the results are consistent with a case series by Tiryaki *et al*[9] that followed 20 children (mean age 11) who developed CAC within a month of acute COVID infection. Their study reported all children eventually had complete resolution of symptoms, returning to their baseline toilet habits, within a maximum of 6 mo. The findings of a retrospective cohort study by Welk *et al*[10] cast doubt on the connection between COVID-19 and CAC. According to this study, bladder impairment after an acute COVID-19 infection may not manifest.

Table 1 Demographics of study population at 10-14 wk and at 21-28 mo, *n* (%)

	Initial urologic assessment (10-14 wk)	Follow up urologic assessment (21-28 mo)
Patients (<i>n</i>)	350	310
Age [median(range)]	64.5 (47-82)	64 (47-82)
Gender		
Female	140 (40)	130 (42)
Male	210 (60)	180 (58)
Ethnicity		
Black	305 (87)	280 (90)
White	45 (13)	30 (10)
Onset of symptoms		
New	250 (71)	220 (71)
Worsening	100 (29)	90 (29)
BPH	110 (52)	80 (44)

BPH: Benign prostatic hypertrophy.

Table 2 Outcomes assessment

	Initial urologic assessment (10-14 wk)		Follow up urologic assessment (21-28 mo)	
	OAB symptom score median (range)	QoL score median (range)	OAB symptom score median (range)	QoL score median (range)
New symptoms (<i>n</i> = 250) ^a	18 (12-21)	19 (16-24)	9 (4-21)	9 (7-20)
Worsening symptoms (<i>n</i> = 100) ^b	19 (17-21) ^c	20 (19-20) ^c	13 (5-21)	14 (6-20)
Female (<i>n</i> = 140)	18 (15-21)	19 (16-21)	8 (4-21)	7 (6-22)
Male (<i>n</i> = 210)	18 (12-20)	19 (16-20)	7 (5-20)	8 (6-23)

^a30 patients lost to follow up.

^b10 patients lost to follow up.

^cPre-COVID OAB and QoL median score: 8 (range 4-10) and 9 (8-10) respectively.

CAC: COVID-associated cystitis; OAB: Overactive bladder; QoL: Quality of life.

The primary explanation about the pathogenesis of CAC, which is still under debate, is that excessive expression of inflammatory mediators causes inflammation of the urothelium, which in turn causes bothersome lower urinary tract symptoms. Increased levels of inflammatory cytokines that are either active in the bladder or in the urine have been linked to CAC and the accompanying bladder voiding dysfunctions[7]. However, the exact pathophysiology of CAC is still under investigation and multiple studies have proposed multiple theories with supporting scientific evidences. Given that SARS-CoV-2 viral RNA has been detected in the urine sample of infected patients[11], and that ACE2 receptor is expressed on urothelial cells[12], it is proposed that SARS-CoV-2 directly invades urothelial cells *via* the ACE2 receptor ultimately leading to viral cystitis. Another theory involves the role of pro-inflammatory cytokines on the bladder mucosa as the cause lower urinary tract symptoms. These cytokines, namely IL-6, IL-8, and IP-10, were present in elevated levels in the urine of COVID-19 patients compared to the control group. Is it hypothesized that elevated levels of pro-inflammatory cytokines in contact with bladder mucosa causes changes in sensitization or function of these cells leading to lower urinary tract symptoms[3].

According to a recent study, CAC is a COVID-19 related concern that is becoming more common yet is still overlooked [13]. Considering CAC's novelty, there are no published guidelines for managing the condition, nor is there a standard test for diagnosing it. The primary objective of the symptom-based therapeutic approach for CAC is still OAB management. Given that inflammatory cascades are most likely responsible for the pathogenesis of CAC, immunomodulators that decrease pro-inflammatory cytokines and increase anti-inflammatory cytokines may hasten healing[14]. The OAB symptoms can be severe with serious quality of life implications with some patients reporting a urinary frequency of over 13 episodes per day and nocturia greater than 4 episodes a night[15]. In our cohort, most of the patients (87%)

experienced symptom relief with conservative management consisting of behavioral modification and standard OAB medications (anticholinergics and beta-3 agonists). In our cohort 40, patients continue to experience urinary frequency of over 13 episodes per day and nocturia greater than 4 episodes a night.

Our study has several limitations including the lack of objective metrics to assess urological symptoms, instead we relied on validated questionnaires which could potentially be impacted by recall bias. We also were unable to assess patient baseline symptoms prior to COVID-19 infection which makes it difficult to assess if patients has completely return to baseline at long-term follow up. Additionally, there was a long gap (21-28 mo) between the initial urologic evaluation and follow up assessment. A shorter and more frequent follow up schedule could have provided additional insight into the timeline of CAC symptoms. The strength of this study is the large cohort ($n = 310$) relative to existing studies and the representation of African American patients who traditionally have been underrepresented in medical literature[16].

CONCLUSION

We present the first long-term follow-up of adult patients who developed CAC and assessed the prognosis of CAC in Long COVID. We found that after 21-28 mo, only 13% (40/310) of patients had persistent bothersome OAB symptoms. Patients with Long COVID and CAC may be reassured that symptoms resolves in vast majority of cases through conservative management strategies.

ARTICLE HIGHLIGHTS

Research perspectives

We believe these findings can reassure patients regarding new onset or worsening urinary symptoms in the setting of long coronavirus disease (COVID). Although, additional research needs to be performed to further investigate the impact of COVID-19 on urological health.

Research conclusions

To our knowledge this is the first study to report long term follow up of patients with COVID-associated cystitis (CAC). Our results suggest a promising prognosis of these patients when managed conservatively.

Research results

Of the 350 participants included in this study, 310 patients (87%) reported improvement in their urinary symptoms at 21-28 mo following their COVID-19 hospitalization discharge. Of those, the patients with new onset CAC symptoms displayed a decrease of 9-10 points in the overactive bladder (OAB) and quality of life scores and 95.4% of these patients reported symptom improvement at follow-up. On the other hand, patients who previously experienced symptoms of OAB had a score decrease of 6 points and 60.7% of these patients had symptomatic improvement at follow-up.

Research methods

We prospectively evaluated a cohort of 350 patients who were previously hospitalized for COVID-19 between May and December 2020. These patients were included in the study if they displayed any CAC symptoms following their hospital discharge. Patients were evaluated using surveys that assessed their urinary symptoms as well as their quality of life at two time points; 10-14 wk following discharge and 21-28 wk following discharge. Their symptoms were managed using conservative measures such as behavior modification and standard OAB medications.

Research objectives

We aimed to evaluate a cohort of 350 patients for new or worsening OAB symptoms using OAB survey based results 21-28 mo following their COVID-19 hospitalization.

Research motivation

There have been early observational studies that suggest COVID-19 can manifest as urologic symptoms including urinary frequency, urgency, and nocturia which has been CAC. We recently described the results of OAB on a cohort of 350 patients who report new or worsening OAB symptoms 10-14 wk following their COVID-19 hospitalization, but there is little known regarding the management and long-term outcomes of CAC.

Research background

COVID-19 is an infection caused by the SARS-CoV-2 virus that has caused over 100 million cases and over 1 millions deaths in the United States since its identification in late 2019. There are many symptoms attributed to COVID-19 and multiple organ systems are known to be impacted including urologic manifestations. Little is known regarding long term manifestations and the impact of COVID-19 on the urologic system.

FOOTNOTES

Author contributions: Wittenberg S, Vercnocke J, Chancellor M, and Dhar S contributed to design, data collection, analysis and interpretation of results, and manuscript preparation; Liaw A and Lucas S contributed to analysis and interpretation of results and manuscript prep; Dhar N contributed to study conception, design, data collection, analysis and interpretation of results, and manuscript preparation.

Institutional review board statement: The study was reviewed and approved by the Wayne State University Institutional Review Board (Protocol Number: IRB-20-04-2126).

Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: All the authors have no relevant conflict of interests to disclose.

Data sharing statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

- 1 Wang Z, Wang D, Dai Y, Zhu S, Zeng H. Urogenital System Damaging Manifestations of 3 Human Infected Coronaviruses. *J Urol* 2021; **205**: 671-677 [PMID: [33026922](https://pubmed.ncbi.nlm.nih.gov/33026922/) DOI: [10.1097/JU.0000000000001400](https://doi.org/10.1097/JU.0000000000001400)]
- 2 Kashi AH, De la Rosette J, Amini E, Abdi H, Fallah-Karkan M, Vaezjalali M. Urinary Viral Shedding of COVID-19 and its Clinical Associations: A Systematic Review and Meta-analysis of Observational Studies. *Urol J* 2020; **17**: 433-441 [PMID: [32888186](https://pubmed.ncbi.nlm.nih.gov/32888186/) DOI: [10.22037/uj.v16i7.6248](https://doi.org/10.22037/uj.v16i7.6248)]
- 3 Lamb LE, Dhar N, Timar R, Wills M, Dhar S, Chancellor MB. COVID-19 inflammation results in urine cytokine elevation and causes COVID-19 associated cystitis (CAC). *Med Hypotheses* 2020; **145**: 110375 [PMID: [33213997](https://pubmed.ncbi.nlm.nih.gov/33213997/) DOI: [10.1016/j.mehy.2020.110375](https://doi.org/10.1016/j.mehy.2020.110375)]
- 4 Raveendran AV, Jayadevan R, Sashidharan S. Long COVID: An overview. *Diabetes Metab Syndr* 2021; **15**: 869-875 [PMID: [33892403](https://pubmed.ncbi.nlm.nih.gov/33892403/) DOI: [10.1016/j.dsx.2021.04.007](https://doi.org/10.1016/j.dsx.2021.04.007)]
- 5 Carfi A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent Symptoms in Patients After Acute COVID-19. *JAMA* 2020; **324**: 603-605 [PMID: [32644129](https://pubmed.ncbi.nlm.nih.gov/32644129/) DOI: [10.1001/jama.2020.12603](https://doi.org/10.1001/jama.2020.12603)]
- 6 Hoang Roberts L, Zwaans BMM, Peters KM, Chancellor M, Padmanabhan P. Incidence of New or Worsening Overactive Bladder Among Patients with a Prior SARS-CoV-2 Infection: A Cohort Study. *Eur Urol Open Sci* 2022; **46**: 68-74 [PMID: [36245790](https://pubmed.ncbi.nlm.nih.gov/36245790/) DOI: [10.1016/j.euro.2022.10.001](https://doi.org/10.1016/j.euro.2022.10.001)]
- 7 Lamb LE, Timar R, Wills M, Dhar S, Lucas SM, Komnenov D, Chancellor MB, Dhar N. Long COVID and COVID-19-associated cystitis (CAC). *Int Urol Nephrol* 2022; **54**: 17-21 [PMID: [34787782](https://pubmed.ncbi.nlm.nih.gov/34787782/) DOI: [10.1007/s11255-021-03030-2](https://doi.org/10.1007/s11255-021-03030-2)]
- 8 Mumm JN, Osterman A, Ruzicka M, Stihl C, Vilsmaier T, Munker D, Khatamzas E, Giessen-Jung C, Stief C, Staehler M, Rodler S. Urinary Frequency as a Possibly Overlooked Symptom in COVID-19 Patients: Does SARS-CoV-2 Cause Viral Cystitis? *Eur Urol* 2020; **78**: 624-628 [PMID: [32475747](https://pubmed.ncbi.nlm.nih.gov/32475747/) DOI: [10.1016/j.eururo.2020.05.013](https://doi.org/10.1016/j.eururo.2020.05.013)]
- 9 Tiryaki S, Egil O, Birbilen AZ, Buyukcam A. COVID-19 associated lower urinary tract symptoms in children. *J Pediatr Urol* 2022; **18**: 680.e1-680.e7 [PMID: [36153241](https://pubmed.ncbi.nlm.nih.gov/36153241/) DOI: [10.1016/j.jpuro.2022.08.018](https://doi.org/10.1016/j.jpuro.2022.08.018)]
- 10 Welk B, Richard L, Braschi E, Averbeck MA. Is coronavirus disease 2019 associated with indicators of long-term bladder dysfunction? *Neurourol Urodyn* 2021; **40**: 1200-1206 [PMID: [33942372](https://pubmed.ncbi.nlm.nih.gov/33942372/) DOI: [10.1002/nau.24682](https://doi.org/10.1002/nau.24682)]
- 11 Chan VW, Chiu PK, Yee CH, Yuan Y, Ng CF, Teoh JY. A systematic review on COVID-19: urological manifestations, viral RNA detection and special considerations in urological conditions. *World J Urol* 2021; **39**: 3127-3138 [PMID: [32462305](https://pubmed.ncbi.nlm.nih.gov/32462305/) DOI: [10.1007/s00345-020-03246-4](https://doi.org/10.1007/s00345-020-03246-4)]
- 12 Lin W, Fan J, Hu LF, Zhang Y, Ooi JD, Meng T, Jin P, Ding X, Peng LK, Song L, Tang R, Xiao Z, Ao X, Xiao XC, Zhou QL, Xiao P, Zhong Y. Single-cell analysis of angiotensin-converting enzyme II expression in human kidneys and bladders reveals a potential route of 2019 novel coronavirus infection. *Chin Med J (Engl)* 2021; **134**: 935-943 [PMID: [33879756](https://pubmed.ncbi.nlm.nih.gov/33879756/) DOI: [10.1097/CM9.0000000000001439](https://doi.org/10.1097/CM9.0000000000001439)]
- 13 Dhawan A, Ganduboina R, Dutta P, Gandrakota G, Kumar Y, Palagati K, Avvaru SN, Sreekumar A, Mylavarapu S, Nizami A, Babu AT, Alam M. COVID-associated cystitis: the culprit behind the bladder woes post-COVID infection? A review. *Int Urol Nephrol* 2023; **55**: 2367-2372 [PMID: [37410305](https://pubmed.ncbi.nlm.nih.gov/37410305/) DOI: [10.1007/s11255-023-03700-3](https://doi.org/10.1007/s11255-023-03700-3)]
- 14 Kumar R, Rathi H, Haq A, Wimalawansa SJ, Sharma A. Putative roles of vitamin D in modulating immune response and immunopathology associated with COVID-19. *Virus Res* 2021; **292**: 198235 [PMID: [33232783](https://pubmed.ncbi.nlm.nih.gov/33232783/) DOI: [10.1016/j.virusres.2020.198235](https://doi.org/10.1016/j.virusres.2020.198235)]

- 15 **Dhar N**, Dhar S, Timar R, Lucas S, Lamb LE, Chancellor MB. De Novo Urinary Symptoms Associated With COVID-19: COVID-19-Associated Cystitis. *J Clin Med Res* 2020; **12**: 681-682 [PMID: [33029276](#) DOI: [10.14740/jocmr4294](#)]
- 16 **Rochon PA**, Mashari A, Cohen A, Misra A, Laxer D, Streiner DL, Clark JP, Dergal JM, Gold J. The inclusion of minority groups in clinical trials: problems of under representation and under reporting of data. *Account Res* 2004; **11**: 215-223 [PMID: [15812967](#) DOI: [10.1080/08989620490891412](#)]



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