Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
THE INCIDENCE OF NEW OR WORSENING OAB SYMPTOMS IN PATIENTS WITH PRIOR SARS COV-2 INFECTION: A COHORT STUDY

Hoang Roberts L1, Zwaans B2, Peters K3, Chancellor M4, Padmanabhan P1 1. Oakland University William Beaumont School of Medicine, Beaumont Hospital-Royal Oak, 2. Beaumont Hospital-Royal Oak

HYPOTHESIS / AIMS OF STUDY
The advent of the SARS CoV-2, or COVID-19, pandemic has spurred great research interest into this viral disease and its clinical implications. Besides the acute phase, long-term symptoms have been reported, with over 50 side effects listed thus far[1]. However, the majority of urological symptoms have been overlooked in these early studies. Given that there is extensive literature on viral etiologies causing urological conditions, such as adenovirus or BK virus in hemorrhagic cystitis, or Epstein-Barr virus in interstitial cystitis, the possibility of SARS CoV-2 causing a novel condition is not outside the realm of possibility[2,3]. Early in the pandemic, investigators from our institution were the first group to identify de novo genitourinary symptoms, such as frequency, urgency, nocturia, and pain/pressure, in individuals with prior COVID-19 infection. They termed this condition COVID-19 associated cystitis (CAC).

The aims of our study are to establish the incidence of worsening or de-novo CAC, evaluate its short-term natural progression, and to determine its correlation with serology status and antibody levels.

STUDY DESIGN, MATERIALS AND METHODS
After IRB approval, 18,785 individuals from the largest COVID-19 serology study (BLAST COVID Study Group) were invited to participate in a follow-up study, with 1,895 subsequent respondents. Demographics and serology data was obtained from the BLAST COVID Study which used the EUROMMUN serology assay to obtain SARS-CoV-2 IgG level. An antibody ratio of ≥ 1.1 is considered significant. Participants were asked to score their OAB symptoms retrospectively at three different time points - prior to the pandemic, 2 months after COVID-19 infection (if applicable), and at the present time - and prospectively at 2- and 4-months. To capture those infected after the serology studies were concluded (April to May 2020), participants were asked “Have you been diagnosed with COVID?” via a nasopharyngeal polymerase chain reaction test. If affirmative, they were prompted to evaluate their symptoms 2 months after COVID infection, and were considered PCR positive. Genitourinary symptoms were assessed using the ICIQ-OAB, a grade A validated questionnaire which assesses both symptom severity and bother. The minimal important difference (MID) of 1 is considered a significant change. Questions evaluated 4 domains: frequency (“How often do you pass urine during the day?” 0 = 1 to 6 times, 1 = 7 to 8 times, 2 = 9 to 10 times, 3 = 11 to 12 times, 4 = 13 or more times), nocturia (“During the night, how many times do you have to get up to urinate, on average?” 0 = none, 1 = 1 time, 2 = 2 times, 3 = 3 times, 4 = four or more times), urgency (“Do you have to rush to the toilet to urinate?” 0 = never, 1 = occasionally, 2 = sometimes, 3 = most of the time, 4 = all of the time), and urge incontinence (“Does urine leak before you can get to the toilet?” 0 = never, 1 = occasionally, 2 = sometimes, 3 = most of the time, 4 = all of the time). Bother score for each domain ranged from 0 (not at all) to 10 (a great deal).

Statistical analysis was conducted using IBM SPSS 28.0 and R. Categorical data (e.g. demographics) was analyzed using Pearson’s Chi Square test. Continuous data, such as the average values for the ICIQ-OAB individual and total symptom scores were calculated and the standard deviations provided. Statistical analysis was performed using 1-way ANOVA. A p-value <0.05 is considered significant. Multivariate analysis was done for co-morbidities and change in ICIQ-OAB scores based on diagnosis using 1-way ANOVA. Sample size of 618 COVID positive individuals was calculated for a power of 80% and α of 0.05 with regards to the primary objective.

Primary objective is the incidence of de novo or worsening OAB symptoms in COVID positive patients. Secondary objectives are the natural progression and the correlation between antibody levels and OAB symptoms.

RESULTS
Of the 1,895 participants, 81.7% (n = 1,548) were female, 16.5% male (n = 312), 1.9% other/unknown (n = 35). Most were Caucasian (85.8%), followed by African American (4.1%), Asian (3.8%), Hispanic (1.4%), and other/unknown (2.1%). A third of participants (n = 605) were COVID-19 positive as defined by positive serology or PCR test. Of these, 492 had 2 months post infection data with 36.4% (n = 179/492) reporting an increase of ≥ 1 unit in OAB symptom score compared to pre-pandemic. Out of these, the OAB symptoms of 22% (n = 40/179) were de novo. Comparing pre-pandemic to present symptoms, 35.7% (n = 219) of participants with prior COVID-19 infection had an increase of ≥ 1 unit on the ICIQ-OAB, compared to 15.7% (n = 202) of uninfected patients (OR: 2.99, 99.6Cl, 2.21, 4.05, p < 0.001). COVID + patients with baseline diabetes mellitus (p = 0.004), chronic steroid use (p = 0.001), or on immunosuppression (p < 0.001) were more likely to have an increase in ICIQ-OAB scores than those who were COVID – and without co-morbidities. BMI positively correlated with symptom severity in COVID + patients, so that higher BMI led to worse OAB symptoms (p = 0.213).

Approximately 40% were lost to follow up (n = 740) with 2- and 4-month data available for the remaining cohort (n = 1,155). Both COVID-19 positive (n = 192) and COVID-19 negative (n = 963) groups had significant increases in OAB symptoms from pre-pandemic to the time of study, 2- and 4-months (p < 0.001), but the difference between the two groups was only statistically significant at the time of study (3.72 vs 3.11, p = 0.003) and at 2 months (3.72 vs 3.18, p = 0.007). At 4 months follow-up, the domain with the highest average symptom severity score amongst COVID-19 positive patients was nocturia (1.21 out of 4), followed by urgency (1.04 out of 4), urinary incontinence (0.86 out of 4), and frequency (0.74 out of 4). However, participants were most bothered by urge incontinence (3.26/10), nocturia (2.96/10), and frequency (2.10/10). For participants who received a positive COVID-19 test using PCR, no correlation was found between OAB symptoms and antibody levels (r = -0.10). For participants with COVID-19 positive serology test, symptoms were weakly correlated with antibody levels (r = 0.14).

INTERPRETATION OF RESULTS
Infection with COVID-19 portends a significantly higher risk of developing de novo or worsening OAB symptoms at 2-month follow-up while OAB symptoms were increased by all participants at 4- months follow up. Of all domains, nocturia is most strongly affected, though urge incontinence was most bothersome for patients. Immunosuppression, diabetes and obesity are risk factors for CAC, though no correlation was found between antibody levels and OAB symptoms in patients with prior COVID-19 infection.

CONCLUDING MESSAGE
CAC, as a direct result of the COVID-19 pandemic, is a novel condition that may affect millions of patients worldwide. Therefore, it is imperative for practicing clinicians to be aware of this potential diagnosis. Further work evaluating the effects of available OAB treatments on CAC is in progress.

FIGURE 1
Over a third experienced worsening OAB symptoms after COVID infection. Of the total, 32% were COVID+. Out of these, 492 had 2 months post-infection data with 36.4% (n = 179/492) reporting an increase of ≥ 1 unit on the ICIQ-OAB compared to pre-pandemic.
Both symptom severity ($p=0.003$) and bother scores ($p=0.006$) were significantly higher amongst COVID positive patients at time of study than COVID negative. At 2- and 4-months symptoms remain high, but the difference was nonsignificant.

REFERENCES

1. Carfì A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. Jama. 2020;324(6):603-605.

2. Jhang JF, Hsu YH, Peng CW, Jiang YH, Ho HC, Kuo HC. Epstein-Barr Virus as a Potential Etiology of Persistent Bladder Inflammation in Human Interstitial Cystitis/Bladder Pain Syndrome. J Urol. Sep 2018;200(3):590-596. doi:10.1016/j.juro.2018.03.133

3. Winter BJ, O’Connell HE, Bowden S, Carey M, Eisen DP. A Case Control Study Reveals that Polyomaviruria Is Significantly Associated with Interstitial Cystitis and Vesical Ulceration. PLoS One. 2015;10(9):e0137310. doi:10.1371/journal.pone.0137310

Funding None
Clinical Trial No
Subjects Human
Ethics Committee Institutional Review Board at Beaumont Hospital
Helsinki Yes
Informed Consent Yes

Continence 2S2 (2022) 100364
doi: 10.1016/j.cont.2022.100364