

Evaluation of lower urinary tract symptoms among male COVID-19 patients during the second wave: An observational study

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Abstract

Background: Coronavirus disease-19 (COVID-19) pandemic has affected almost all age groups globally, and lower urinary tract symptoms (LUTS) may be one of the early manifestations of COVID-19, especially in elderly patients. This study aimed at evaluating LUTS in male COVID-19 patients during the COVID-19 s wave.

Methodology: A prospective observational study was conducted between March 15, 2021, and March 25, 2021, at the Prince Hamza Hospital in Amman, Jordan. Newly admitted COVID-19 confirmed male patients who were able to fill the LUTS (validated) questionnaire were included. Vitrally unstable patients requiring intensive care unit admissions or medical or surgical intervention (except catheterization) for their presenting symptoms were excluded.

Results: Two-hundred and four patients (mean age: 51.1 ± 17.3 years) were included; among COVID-19 symptoms, augmented urinary frequency (3.4%) was the commonest urological symptom, followed by dysuria (1.0%), and acute urinary retention (1.0%). Twenty-four patients (10.8%) had benign prostatic hyperplasia, two patients had bladder cancer, and one had prostate cancer. Most patients exhibited mild symptoms on international prostate symptom score (IPSS) before ($n = 149, 67.1\%$) and during ($n = 157, 70.7\%$) COVID-19, and this difference between IPSS scores was statistically significant ($P = 0.025$). Both IPSS sub-scores of storage (IPSS/S) and voiding (IPSS/V) had a positive correlation with pre- and post-COVID-19 scores (IPSS/S: $P < 0.001, \rho = 0.63$; IPSS/V: $P < 0.001, \rho = 0.76$).

Conclusion: This study demonstrated a strong correlation between COVID-19 and LUTS; therefore, COVID-19 infection should be investigated and excluded in any patient presenting with LUTS during the current pandemic. Further research is needed to elucidate the exact pathophysiology of this correlation.

Keywords: Lower urinary tract symptoms, observational study, severe acute respiratory syndrome corona virus-2, urine frequency

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INTRODUCTION

Coronavirus disease-2019 (COVID-19) was deemed a global pandemic by the World Health Organization (WHO) in March 2020.^[1] Genomic sequence analysis of the causative organism, severe acute respiratory syndrome corona virus-2 (SARS-CoV-2), shows that approximately 80% of its genomic material is similar to that of the original SARS-CoV, responsible for the SARS.^[2] In infections like the SARS and middle east respiratory syndrome, acute kidney injury has been detected in 5%–15% of cases, accompanied by a high mortality rate.^[3] It is also known that patients with COVID-19 may present with varying symptoms, such as fever, dyspnea, cough, fatigue, headache, and diarrhea, along with some atypical features.^[4] Throughout the pandemic, urological practices have been affected worldwide^[5] with occasional reports of the effect of COVID-19 on the lower urinary tract; however, these symptoms have not been studied appropriately in the literature.^[6-8]

It has been reported that lower urinary tract symptoms (LUTS) may be one of the early manifestations of COVID-19, especially in elderly patients.^[9] According to the International Continence Society, LUTS is an umbrella term used to describe a wide variety of symptoms which are classified into three categories: voiding, storage, and postmicturition.^[10] A study found that storage LUTS is often the primary presenting feature in COVID-19 patients of both genders.^[11] Notably, COVID-19 infection is detected in the urine of infected patients in only moderate to severe cases; thus, it is unlikely that COVID-19 is transmitted through the urine.^[12] However, in our hospital, we noticed some changes in the urinary symptoms in patients who were later diagnosed with COVID-19. Therefore, this study was conducted to evaluate LUTS in patients suffering from COVID-19 during the second wave of COVID-19 in Amman, Jordan.

METHODOLOGY

Study design and setting

This prospective observational study was conducted over a period of 10 days (March 15, 2021, and March 25, 2021) at the Prince Hamza Hospital in Amman, Jordan, after seeking approval from the Institutional Research Ethics Committee (Approval number: 213/25.02.2021). All study participants voluntarily agreed to participate and provided written informed consent. Patient data confidentiality was maintained according to the Helsinki Declaration of Biomedical Ethics (revised in 2008).

Inclusion and exclusion criteria

Male patients who were recently admitted to the hospital with COVID-19 infection (confirmed by reverse

transcriptase-polymerase chain reaction) and were able to complete the LUTS questionnaire were included in the study. Patients were excluded from the study if they: (1) required intensive care unit admission, (2) needed stabilization by any medication or intervention for their presenting symptoms, and (3) had involuntary urination, such as due to complete paralysis.

Measurement tool and data collection

The LUTS questionnaire included two sections: The first section collected the patient's demographic characteristics, namely age, job, smoking status, height, weight, history of any chronic disease or a surgical procedure, and the present COVID-19 symptoms. The second part evaluated the LUTS of the patient before and during the COVID-19 infection using the international prostate symptom score (IPSS). The Arabic translation of the IPSS, performed by a bilingual, multidisciplinary team, was used for the study.^[13] Body mass index (kg/m^2) was calculated for all patients, who were then categorized into four categories – underweight ($<18.5 \text{ kg}/\text{m}^2$), normal weight ($18.5\text{--}24.9 \text{ kg}/\text{m}^2$), overweight ($25\text{--}29.9 \text{ kg}/\text{m}^2$), and obese ($>30 \text{ kg}/\text{m}^2$).

The IPSS contains seven questions about LUTS – incomplete emptying, frequency, intermittency, urgency, weak urinary stream, hesitancy, and nocturia, and one quality of life (QOL) question to assess the patient's overall discomfort due to their LUTS. Each LUTS question was scored from 0 to 5 (0: Not at all, 1: Less than one time in five, 2: Less than half the time, 3: About half the time, 4: More than half the time, and 5: Almost always during the preceding month). In addition, the QOL question was scored from 0 to 6 (0: Delighted, 1: Pleased, 2: Mostly satisfied, 3: About equally satisfied and dissatisfied, 4: Mostly dissatisfied, 5: Unhappy, and 6: Terrible). Overall, the symptoms were classified into three categories: mild (0–7 points), moderate (8–19 points), and severe (20–35 points). To increase the accuracy of IPSS results, a two-step confirmation was done – initially, the patient filled up the form, and then, one of the team members interviewed the patient to confirm their answers.

Statistical analysis

SPSS version 25 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Descriptive analysis, including mean and standard deviations for numerical variables, and frequencies and percentages for categorical variables, was done. The Kolmogorov–Smirnov test was used to test the normality of distribution. Since the data were not normally distributed, the Wilcoxon signed-rank test was used to compare the total IPSS and QOL scores before and during COVID-19 infections. Statistical significance was set at $P < 0.05$ for all analyses.

RESULTS

Baseline characteristics of the study participants

Two hundred and four patients with a median age of 53 years (39.2–64 years) were included in this study. Among these patients, 136 (66.7%) were smokers, and 155 (76%) did not have a history of any surgical procedure. Among the COVID-19 symptoms, urinary frequency was the most common urological symptom ($n = 7$, 3.4%), followed by dysuria ($n = 2$, 1%), and acute urinary retention ($n = 2$, 1%). Benign prostatic hyperplasia (BPH) was reported in 25 patients (12.3%). Table 1 presents the demographic characteristics of all participants.

International prostate symptom score and quality of life scores-before and during coronavirus disease-19

Most patients had mild symptoms as measured by the IPSS both before ($n = 149$, 67.1%) and during ($n = 157$, 70.7%) the COVID-19 infection. Whereas moderate symptoms were present in 43 (19.4%) patients before and 33 (14.9%) patients after contracting COVID-19; only 12 (5.4%) patients had severe symptoms before COVID-19 infection and 14 (6.3%) had severe symptoms during the infection. The difference between median IPSS ($P = 0.025$) and QOL ($P = 0.001$) scores was also statistically significant for both before and during COVID-19 infection [Table 2].

On analyzing the IPSS storage (IPSS/S) and voiding (IPSS/V) subsections using Spearman's rank correlation, there was a strong positive correlation between IPSS/S scores before and during COVID-19 infection ($P < 0.001$). Similarly, a strong positive correlation was also observed between the IPSS/V scores before and during COVID-19 infection ($P < 0.001$) [Table 3].

DISCUSSION

Active cases of COVID-19 continue to rise globally, with a significant increase in the Mediterranean region. The past 1½ years of the pandemic have had a profound impact on our lifestyle, not only affecting our habits and daily activities but also strongly altering our professional functioning.^[14,15] Measures taken by the affected countries to prevent the spread of infection, such as lockdowns and social distancing, have upset the existing medical services. Many medical conditions, such as lower urinary tract infections and BHP, were put secondary on the priority list, and such patients were not able to receive ample and timely treatment, resulting in deterioration of the patient's condition.^[9,16]

The spectrum of COVID-19 symptoms ranges widely from fever, cough, myalgia, fatigue, sore throat,

Table 1: Baseline characteristics of study participants

Variable	Total (n=204), n (%)
Age, mean±SD	51.1±17.3
BMI, kg/m ²	
Normal	38 (18.6)
Overweight	86 (42.2)
Obese	80 (39.2)
Working status	
Worker	132 (64.7)
Nonworker	72 (35.3)
Smoking	
Yes	68 (33.3)
No	136 (66.7)
Hypertension	
Yes	51 (23)
No	153 (77)
Diabetes mellitus	
Yes	46 (20.7)
No	158 (79.3)
Urological disease	
BPH	25 (12.3)
Chronic kidney disease	5 (2.3)
Bladder cancer	2 (1)
Urinary tract stone	1 (0.5)
Prostate cancer	1 (0.5)
COVID-19 symptoms	
Shortness of breath	73 (35.8)
Cough	29 (14.2)
Fatigue	15 (7.4)
Urinary frequency	7 (3.4)
Headache	7 (3.4)
Fever	5 (2.5)
Anosmia	4 (2.0)
Joint pain	4 (2.0)
Dysuria	2 (1.0)
Gastrointestinal symptoms	7 (3.4)
Acute urinary retention	2 (1.0)
Palpitation	1 (0.5)
Convulsion	1 (0.5)

SD: Standard deviation, BMI: Body mass index, COVID-19: Coronavirus disease-2019, BPH: Benign prostatic hyperplasia

Table 2: International prostate symptom score and quality of life scores before and during coronavirus disease-2019

	Before COVID-19	During COVID-19	P
IPSS score	3 (1-9)	4 (1-7)	0.025
QOL score	1 (0-4)	0 (0-2)	0.001

*All categorical variables are reported as median (IQR). IPSS: International prostate symptom score, QOL: Quality of life, COVID-19: Coronavirus disease-2019, IQR: Interquartile range

rhinorrhea, headache, confusion to multiple atypical presentations.^[17] A study reported that COVID-19 presentation can also mimic urosepsis and urinary tract infection.^[5] Another study found that LUTS, mainly storage symptoms, could be the first presentation of COVID-19, and BPH-related LUTS could be used to predict the prognosis of COVID-19 infection.^[18] Since studies in the early phase of the pandemic were small and unorganized, they could not establish a correlation between COVID and the urinary system; however, with the pandemic involving significantly larger populations,

Table 3: Correlation between international prostate symptom score sub-scores before and during coronavirus disease-2019 infection

IPSS sub-scores	Mean±SD		Correlation coefficient (ρ)	P
	Before COVID-19	During COVID-19		
IPSS/S	3.45±2.6	3.56±3.1	0.63	<0.001
IPSS/V	3.96±5.7	2.97±4.8	0.76	<0.001

IPSS: International prostate symptom score, IPSS/S: IPSS storage, IPSS/V: IPSS voiding, SD: Standard deviation, COVID-19: Coronavirus disease-2019

current studies have been able to demonstrate an apparent relationship between them.^[19]

As a member of the B-coronavirus cluster, SARS-COV-2 uses cellular angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) to enter the host cell.^[7,20,21] The different ACE2 and TMPRSS2 tissue expressions explain the involvement of different organs and the consequent variety of the presenting symptoms.^[19] A study found that 2.4% of the bladder cells are ACE2-positive; thus, the urinary bladder is at high risk for COVID-19 viremia, comparable to the respiratory system.^[20] Another study reported that ACE2 is also expressed in prostate cells (0.34%).^[7]

COVID-19-associated cystitis is a term used to describe LUTS in patients with COVID-19 following an increase in urinary cytokines.^[22] This may also be due to viremia resulting in an inflammatory response in either the luminal or basal side of the bladder mucosa.^[5] Gacci *et al.* (year) reported that after COVID-19 infection, the SARS-COV-2 can be found in the urine and semen of male patients, potentially leading to the development or progression of LUTS.^[23] Mumm *et al.* found that 7 out of 57 (12%) male patients in their study complained of increased urinary frequency.^[5] This proportion is greater than our results, wherein only 3.4% of patients had an increased urinary frequency. Our results are comparable to Creta *et al.*, who reported that 3%–5% of patients with COVID-19 developed LUTS.^[19]

Further, Luciani *et al.* stated that COVID-19 infection negatively affects the urinary system as they observed hematuria in three of their patients, one of whom had a T3b prostate cancer with radiation cystitis.^[6] In our study, a 73-year-old patient, currently stable, had T3a prostate cancer (Gleason score 8) and was treated with radiation 10 years ago; he got infected with COVID-19 and developed acute urinary retention, which required catheterization (Foley catheter) for 1 week. The catheter was removed after recovering from COVID-19, and he regained his normal urination. This peculiar observation requires further investigation to understand the underlying

pathogenesis. In a survey on a few patients, Dhar *et al.* found apparent *de novo* LUTS even with mild COVID-19 symptoms, which contradicts the assumption that viremia, viral load, or cytokines determine the symptomatology.^[14]

The present study confirms that patients with COVID-19 may experience alterations in their urinary symptoms, as reported in other studies. Can *et al.* found a significant change in IPSS scores before and during COVID-19 in patients aged above 50 years, while no significant change was found in those below 50 years of age.^[9] Furthermore, Kaya *et al.* found a significant difference in storage IPSS before, during, and after COVID-19 in male patients. Notably, a significant difference was observed in stress incontinence, and overactive bladder symptoms were seen in female patients infected with COVID-19.^[11]

Our prospective observational study showed a notable change in LUTS among male COVID-19 patients. In our study cohort, 24 (10.8%) patients had BPH, and only three patients had a urological malignancy. The median scores for both before and during COVID-19 were classified in the mild category, and the most common urological symptoms were urine frequency (3.4%), dysuria (1%), and acute urinary retention (1%). Moreover, we detected a significant QOL impairment due to a change in urinary habits ($P < 0.001$). Respiratory symptoms, such as shortness of breath and cough, were considered the worst symptoms in our cohort. Patients who needed stabilization by any medication or intervention for their presenting symptoms were excluded from the study.

This study had several strengths. To the best of our knowledge, this is the largest study to study the relationship between LUTS and COVID-19. We enrolled all male patients admitted to a large tertiary center in Amman, Jordan using a validated instrument and strict inclusion and exclusion criteria. However, the inclusion of only male patients and using IPSS as the sole measurement tool limit the applicability of our results.

CONCLUSION

This study demonstrated a significant correlation between COVID-19 and LUTS. Therefore, COVID-19 infection should be considered and excluded in any patient presenting with LUTS, especially during the course of this pandemic. Further research is needed to elucidate the exact pathophysiology of this correlation.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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