


ORIGINAL ARTICLE

Impact of COVID-19 pandemic on lower urinary tract symptoms in patients with benign prostatic hyperplasia and predictors of urine retention in such patients

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Abstract

Objectives: We assess the effect of coronavirus disease 2019 (COVID-19) on lower urinary tract symptoms (LUTS) of patients with benign prostatic hyperplasia (BPH). Moreover, we delineate risk factors for urine retention in such patients.

Methods: All COVID-19 infected males were expeditiously evaluated. All enrolled patients were assessed using the International Prostate Symptom Score (IPSS), uroflowmetry, and pelvi-abdominal ultrasonography for prostate volume and post-voiding residual urine (PVR) estimation.

Results: Fifty patients, who were diagnosed with BPH, were enrolled. The mean age (\pm SD) was 62.64 ± 7.69 . In the pre- and post-COVID-19 group, the mean (\pm SD) IPSS was 13.42 ± 4.32 and 26.62 ± 5.77 , respectively ($P < .001$), while PVR was 90.40 ± 32.75 and 185.42 ± 73.42 , respectively ($P < .001$), and maximum flow rate was 14.40 ± 2.75 and 10.74 ± 3.43 , respectively ($P < .004$). After infection with COVID-19, 13 (26%) patients were managed by urethral catheter fixation owing to urine retention. On bivariate analysis, age, diabetes, large prostate on digital rectal examination, alpha-blocker monotherapy, microscopic hematuria, positive urine culture, and pre-COVID-19 IPSS were significantly correlated with urine retention ($P < .001$, $P = .01$, $P < .001$, $P = .06$, $P < .001$, $P = .04$, and $P < .001$, respectively). On multivariate analysis, age, pre-COVID-19 IPSS, and positive urine culture were the independent predictors of urine retention ($P = .05$, $P < .001$, and $P = .01$, respectively).

Conclusion: LUTS in BPH patients were significantly affected by COVID-19. COVID-19 increases IPSS leading to a change in the treatment modality of BPH. On multivariate analysis, age, pre-COVID-19 IPSS, and positive urine culture were the independent predictors of urine retention post COVID-19 infection.

KEYWORDS

benign prostatic hyperplasia, COVID-19 pandemic, lower urinary tract symptoms, urine retention

1 | INTRODUCTION

Lower urinary tract symptoms (LUTS) are a term that covers a variety of symptoms that occur during storing, urination, or after urination categorized by the International Continence Society.¹ LUTS are common in adult men and are often associated with benign prostatic hyperplasia (BPH).² The prevalence of BPH increases markedly with age. In autopsy studies, it has been observed that the histological prevalence of the disease also increases with age.³

After its initial discovery in Wuhan, China, the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread throughout the world, and the consecutive coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) shortly afterward.⁴

As the pandemic is still in an early phase and many symptoms have not yet been fully described, careful clinical observation is of paramount importance.⁵ While infected individuals mostly experience mild symptoms such as fever, upper respiratory tract symptoms, shortness of breath, and diarrhea,⁶ or are asymptomatic,⁷ in severe cases, pneumonia, multiple organ failure, and death may occur.⁸ The most common comorbidities in COVID-19-positive patients are chronic lung disease, diabetes, and hypertension.⁹

Rocco et al pointed out the importance of early recognition of symptoms by urologists for proper triage of patients and to prevent missing possible SARS-CoV-2 infection because of an overlap of COVID-19 and classical urological symptoms. Additionally, fever and increased urinary frequency should be considered as important symptoms overlapping with urosepsis in the differential diagnosis of COVID-19 in ambulatory care and emergency rooms.¹⁰

Considering that the COVID-19 pandemic affects older and male patients more, it is obvious that the elderly male population with LUTS will be seriously affected by this pandemic. According to our literature review, no studies evaluate the impact of COVID-19 disease on LUTS in patients diagnosed with BPH.

2 | MATERIALS AND METHODS

After institutional board review, a cross-sectional study was carried out between May 2020 and March 2021 in a tertiary hospital. The inclusion criteria were patients who had previously been treated for BPH. Patients who had a history of previous pelvic organ surgery and/or radiotherapy, those with an active urinary system infection, or those with a history of urethral stenosis, and those diagnosed with neurogenic bladder were excluded from the study.

The patients were diagnosed with COVID-19 based on reverse transcription-polymerase chain reaction (RT-PCR) tests of oropharyngeal and nasopharyngeal swabs obtained as per the WHO guidelines. Informed consent was obtained from all patients, and the institutional ethics committee approved the study.

A pertinent medical history was obtained. The patients were evaluated using the International Prostate Symptom Score (IPSS), pelvi-abdominal ultrasonography with PVR estimation, non-contrast

computed tomography (CT) of the chest, uroflowmetry, and laboratory investigations (RT-PCR tests of oropharyngeal and nasopharyngeal swabs, urine analysis, urine culture, kidney function, complete blood count, coagulation profile, serum ferritin, interleukin-6, procalcitonin, d-dimer, C-reactive protein [CRP], and prostate-specific antigen [PSA]). IPSS before and after COVID-19 infection were compared. The evaluation time was unified on admission, during hospital stay day after day, a month, and 3 months post infection.

2.1 | Statistical analysis

Data were analyzed using SPSS 21.0 for Windows (SPSS, USA). Normality tests (Kolmogorov-Smirnov test) were performed to evaluate the distributions of numeric variables. If the distribution of numeric variables was normal, statistical analysis was performed using parametric Student *t* tests. Mann-Whitney *U* tests were used to evaluate numerical variables with a skewed distribution. Categorical variables were analyzed using chi-squared or Fisher exact tests. The level of statistical significance was set at 5% ($P < .05$). A highly significant difference was present if $P \leq .001$.

3 | RESULTS

Around 430 COVID-19 patients were screened. All 50 patients, who were diagnosed with BPH, were enrolled. The mean age (\pm SD) was 62.64 ± 7.69 . The mean body mass index ranged from 21.4 to 27.4 kg/m² with a mean of 24.11 kg/m². Diabetes, hypertension, cardiac diseases, liver, and chronic kidney disease were present in 54%, 58%, 16%, 12%, and 4% of the studied patients, respectively. Eight patients were on anticoagulant drugs. Prostate volume estimated by ultrasonography ranged from 34 to 110 g with a mean of 64.26 g. Other patient parameters are shown in Table 1.

There was a significant increase in IPSS (mean \pm SD 26.62 ± 5.77 , 25.36 ± 5.86 , 25.1 ± 6.3 during hospital stay, at 1 month, and at 3 months, respectively) in comparison with IPSS before infection (13.42 ± 4.32 ; $P < .001$). There is a statistically significant change in the IPSS on discharge and its value at 1 month ($P < .001$). Also, the IPSS 3 months after discharge significantly decreased compared with its level at 1 month ($P = .014$) (Table 2). Before COVID-19 infection, the maximum flow rate was 14.40 ± 2.75 mL/s (mean \pm SD) and significantly decreased to 10.74 ± 3.43 after infection ($P < .004$). Quality of life (QoL) deteriorated from 3.34 ± 1.0 before infection with COVID-19 to 5.3 ± 0.68 ($P < .001$). The mean (\pm SD) PVR was 90.40 ± 32.75 and 185.42 ± 73.42 in the pre- and post-COVID-19 groups, respectively ($P < .001$) (Table 3).

Thirteen patients (26%) were catheterized due to acute urine retention after being infected with COVID-19. However, none of our patients had a urethral catheter before COVID-19 infection.

Fifteen patients (30%) needed transurethral resection of the prostate (TURP) after becoming infected with COVID-19. However, all patients were on lifestyle modifications, alpha-blockers, and combined

TABLE 1 Baseline characteristics of the studied patients

Parameters	Total N = 50	
Age (mean ± SD)	62.64 ± 7.69	
BMI (mean ± SD)	24.11 ± 1.53	
Complaints before COVID-19 infection, n (%)	Obstructive LUTS	17 (34%)
	Obstructive, irritative LUTS	22 (44%)
	Irritative LUTS	11 (22%)
Hospital admission, n (%)	Ward	41 (%)
	ICU	9 (18%)
	Anticoagulant treatment, n (%)	8 (16%)
Comorbidities, n (%)	Diabetes	27 (54%)
	Hypertension	29 (58%)
	Cardiac disease	8 (16%)
	Hepatic disease	6 (12%)
	Chronic kidney disease	2 (4%)
	Preoperative BPH medications, n (%)	alpha-blockers
5-ARI ± alpha-blockers		2 (4%)
Lifestyle modifications		9 (18%)
ASA score III, n (%)	I	32 (64%)
	II	18 (36%)
DRE, n (%)	Mild	12 (24%)
	Moderate	25 (50%)
	Marked	13 (26%)
Urine culture, n (%)	Gram negative	44 (88%)
	Gram positive	4 (8%)
	Others	2 (4%)
Hematuria, n (%)	No	30 (60%)
	Microscopic	16 (32%)
	Macroscopic	4 (8%)
Preoperative prostate volume by ultrasonography (mean ± SD)	64.26 ± 18.47	
Preoperative PSA (ng/dL) (median, range)	4.15 (1.01-11)	
Hemoglobin (g/dL) (mean ± SD)	11.41 ± 1.49	
Serum creatinine (mg/dL) (mean ± SD)	1.18 ± 0.24	
White blood cell count (mean ± SD)	4.45 (2.1-12)	
Lymphocyte count (mean ± SD)	1171.72 ± 399.93	
CRP (median, range)	64.5 (18.4-186)	
Interleukin-6 (median, range)	15.25 (4-160)	
Serum ferritin (median, range)	249.8 (66-420)	
Procalcitonin (median, range)	0.64 (0.05-4.1)	
d-dimer (median, range)	70 (1.44-277)	

Abbreviations: 5-ARI, 5-alpha reductase inhibitors; ASA, American Society of Anesthesiologists; BMI, body mass index; BPH, benign prostatic hyperplasia; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; DRE, digital rectal examination; ICU, intensive care unit; LUTS, lower urinary tract symptoms; PSA, prostate-specific antigen.

treatment (alpha-blockers and 5-alpha reductase inhibitors) before infection.

No significant correlations were noticed between COVID-19 laboratory or radiologic parameters and LUTS (Table 1).

On bivariate analysis, we found that the general condition of the patients evaluated using severity assessment was not associated with urine retention post COVID-19 infection ($P = .16$). But age, diabetes, large prostate on digital rectal examination, alpha-blocker monotherapy, microscopic hematuria, positive urine culture, and pre-COVID-19 IPSS were significantly correlated with urine retention ($P < .001$, $P = .01$, $P < .001$, $P = .06$, $P < .001$, $P = .04$, and $P < .001$, respectively). On multivariate analysis, age, pre-COVID-19 IPSS, and positive urine culture were the independent predictors of urine retention after COVID-19 infection ($P = .05$, $P < .001$, and $P = .01$, respectively) (Table 4).

TABLE 2 IPSS before and after COVID-19 among the studied patients

IPSS	Mean \pm SD	P
Before COVID-19	13.42 \pm 4.32	-
During hospital stay	26.6 \pm 5.77	<.001**
At 1 mo after infection	25.36 \pm 5.86	<.001**
At 3 mo after infection	25.1 \pm 6.3	.014*

Note: P for paired sample t test.

Abbreviations: COVID-19, coronavirus disease 2019; IPSS, International Prostate Symptom Score.

* $P < .05$ is statistically significant.

**A highly significant difference was present if $P \leq .001$.

TABLE 3 Objective parameters for LUTS before COVID-19 vs after COVID-19

Parameters	Before COVID-19	After COVID-19	P value
IPSS (mean \pm SD)	13.42 \pm 4.32	26.62 \pm 5.77	<.001
Qmax (mean \pm SD)	14.40 \pm 2.75	10.74 \pm 3.43	<.004
PVR (mean \pm SD)	90.40 \pm 32.75	185.36 \pm 72.43	<.001
QoL (mean \pm SD)	3.34 \pm 1.0	5.3 \pm 0.68	<.001

Abbreviations: COVID-19, coronavirus disease 2019; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; PVR, postvoiding residual urine; Qmax, maximum flow rate; QoL, quality of life.

Parameter	OR	95% CI	P
Age	0.092	0.196-1.096	.05
IPSS before COVID-19	1.930	1.031-6.893	<.001
DM	-1.214	0.297-3.451	.725
Hematuria (microscopic)	2.086	1.373-8.055	.129
Monotherapy (alpha-blockers)	11.277	7918.190	.999
DRE	3.677	2.311-39.544	.111
Urine culture (positive)	0.686	0.504-0.950	.01
Constant	-87.125	15 836.398	.996

Abbreviations: COVID-19, coronavirus disease 2019; DM, diabetes mellitus; DRE, digital rectal examination; IPSS, International Prostate Symptom Score; OR, odds ratio.

4 | DISCUSSION

Since the report of the first cases of pneumonia of unknown cause by the WHO at the end of 2019, SARS-CoV-2 and its related disease, COVID-19, has spread rapidly all over the globe.¹¹

Gender-related COVID-19 mortality is among the most frequently reported epidemiological data.¹² Studies conducted in various countries show that males are more vulnerable to COVID-19 infections, and for this reason, the male gender is considered a poor prognostic factor by some authors.¹³

A recent review of current epidemiological studies that gathered data from 59 254 patients from 11 different countries has shown a relationship between the male gender and higher mortality rates.¹⁴ Although the question of why COVID-19 is more common and fatal in men remains a critical question awaiting an answer, recent studies have suggested that one of the reasons for the increased vulnerability of men could be androgen-mediated mechanisms.^{15,16}

BPH is one of the common causes of LUTS in older men. Age is the main factor in the development of BPH. The incidence of BPH increases from 8% in the fourth decade to over 70% in the seventh decade.¹⁷ LUTS are best assessed by approved questionnaires such as the IPSS or the American Urology Association (AUA) symptom score.¹⁸

Indeed, COVID-19 affects the general condition. The patients presented with dyspnea, tachypnea, and fever in some. All patients in our study had pneumonia confirmed by CT of the chest and were therefore admitted to the hospital.

TABLE 4 Multivariate analysis of the predictors of urine retention post COVID-19 infection

In our study, we identified that LUTS were significantly increased as we detected that there was a significant increase in IPSS (mean \pm SD 26.62 \pm 5.77) in comparison with IPSS before infection (13.42 \pm 4.32. $P < .001$), and there was a statistically significant change in IPSS on discharge and its value at 1 month. Also, IPSS 3 months after discharge significantly decreased compared with its level at 1 month. QoL of patients became worse. Also, we found that 13 patients were catheterized due to acute urine retention, and 15 patients needed TURP after being cured of COVID-19. Nine of our patients were admitted to the intensive care unit with a severe respiratory condition. Also, we noticed that they had a higher IPSS than those who were admitted to the ward.

In our study, 16 patients had microscopic hematuria and 4 had macroscopic hematuria. However, it was not statistically significant. Mumm et al, in their study, detected three patients who presented with microhematuria, which possibly further supports the hypothesis of SARS-CoV-2-induced viral cystitis on infection of urothelial cells causing the irritative LUTS.¹⁹

It is unclear whether replication of SARS-CoV-2 RNA in urothelial cells or secondary effects due to local or systemic inflammation, such as endotheliitis, are a hallmark in COVID-19 patients' symptoms as irritative symptoms of the lower urinary tract and high urinary frequency.²⁰ In our study, we found that deterioration in the general condition, especially in immuno-compromised patients, was always associated with heavy pyuria and urinary tract infection and increasing LUTS. Also, we believe that medical treatment for COVID-19 involving intravenous fluids and corticosteroids increases LUTS. Furthermore, we believe that viral cystitis induced by hematuria and replication of SARS-CoV-2 in endothelial cells causes local inflammation with increasing of irritative LUTS.

Our study found that the worse the laboratory parameters, including increase in CRP, absolute lymphopenia, d-dimer, and serum ferritin, the more deterioration in the respiratory condition. Still, there is no correlation between the differences in laboratory parameters and the higher IPSS with more deterioration in LUTS.

To the best of our knowledge, this is the first study to uncover the risk factor of urine retention in a patient with LUTS owing to BPH during the COVID-19 outbreak. One limitation of this study is the small sample size, which could be explained by the lockdown during the outbreak, hindering proper patient communication. Moreover, the study was void of a control arm, which could have provided an adequate point of reference. Thus, LUTS in BPH patients were significantly affected by COVID-19 infection. COVID-19 increases IPSS and bother scores, leading to a change in the treatment modality of BPH. Age, pre-COVID-19 IPSS, and positive urine culture were the independent predictors of urine retention post COVID-19 infection.

DISCLOSURE

There is no conflict of interest.

AUTHOR CONTRIBUTIONS

Ali Ibrahim: methodology, idea formulation, and reference collection. Diaa-Eldin Taha: review writing and revision, editing the final

draft. Mona Talaat: formal analysis and data collection. Hossam Nabeeh: supervision. Tarek Abdelbaky: data collection and final revision.

ETHICAL APPROVAL

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments.

CONSENT

Formal consent was signed by the participants for taking part in this research.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Nabeeh H, Ibrahim A, Taha D-E, Talaat M, Abdelbaky TM. Impact of COVID-19 pandemic on lower urinary tract symptoms in patients with benign prostatic hyperplasia and predictors of urine retention in such patients. *Lower Urinary Tract Symptoms*. 2022;14(1):41-46. <https://doi.org/10.1111/luts.12407>