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An Investigation of Subsequent Lower Urinary Tract Symptoms in Patients With a History of Infection of COVID-19 at Tadbir Clinic in Urmia City During the Period From December 2020 to July 2021

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Abstract**Introduction**

More associated symptoms have been reported with the increasing number of COVID-19 cases worldwide. However, the precise impact of the disease on the urinary system and related urinary symptoms has yet to be adequately evaluated. The present study aims to investigate the subsequent lower urinary tract symptoms in patients attending Tadbir Clinic in Urmia City who have a history of infection due to COVID-19 within less than two months.

Methods

This study evaluated patients referred to the Urology Department of Tadbir Clinic in Urmia City between December 2020 and July 2021 who had tested positive for COVID-19 by RT-PCR within the past two months. The patient's hospitalization history and the occurrence or exacerbation of urinary symptoms were recorded, and they completed the International Prostate Symptom Score (IPSS) questionnaire.

Results

This study included 150 patients with a mean age of 44.12 years, including 80 males and 70 females. None of the patients had severe urinary symptoms. 92.7% of the patients had mild urinary symptoms, and 7.3% had moderate urinary symptoms. The prevalence of moderate urinary symptoms was significantly higher in females than in males (P -value = 0.04). Individuals with moderate urinary symptoms had a higher mean age than those with mild urinary symptoms (P -value = 0.03). Among patients with or without a history of hospitalization, including those with a history of intensive care unit (ICU) admission, there was no significant difference in the severity of urinary symptoms (P -value = 0.5). Nocturia was the most common symptom reported by patients after the COVID-19 infection.

Conclusion

The severity of urinary symptoms was higher in females than males, and individuals with more severe urinary symptoms were generally older. There was no significant difference in terms of hospitalization history or the occurrence of severe urinary symptoms. Nocturia and frequency were the most prevalent symptoms among the patients.

Keywords: infection, subsequent lower urinary tract symptoms, COVID-19

Introduction

Subsequent lower urinary tract infections (UTIs) are common among individuals seeking urological care. These infections are often caused by bacterial agents such as *E. coli* and *Enterococcus* [1]. Viruses, as infectious agents, have a lower prevalence and are primarily observed in individuals with immunodeficiency.

UTIs include cystitis, prostatitis, seminal vesiculitis, and urinary tract inflammation. Symptoms such as hematuria, genital and suprapubic pain, urgency, urinary frequency, nocturia (urinating more than three times during the night), purulent discharge, hematospermia, and, in rare cases, prostatic abscess, urinary retention, and urinary incontinence can be

observed in UTIs [1]. According to the Baltimore classification, the most common viral agents causing subsequent lower UTIs are classified into seven groups. HSV (Herpes Simplex Virus), CMV (Cytomegalovirus), and BKV types 1 and 2 are among the most identified agents. In this classification, coronaviruses and SARS fall under group 4 (positive-sense single-standard RNA) [2]. SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), the causative agent of COVID-19, has been recognized as the pandemic of the century since December 2019 [4, 3]. SARS-CoV-2 attaches to ACE2 receptors through its spike protein, which is present in a wide range of cells in the body, such as lung epithelial cells, endothelial cells, the gastrointestinal system, kidneys, and the urinary tract, leading to various symptoms [5]. The most common renal involvement in these patients is observed in the form of acute kidney injury (AKI) [6]. Several studies indicate that the mortality rate is 5.3 times higher in COVID-19 patients with AKI than in those without renal involvement [7]. Research has shown that the highest distribution of ACE2 receptors is found in the basal and intermediate layers of the bladder, predominantly expressed in urothelial cells. Since ACE2 acts as the receptor for SARS-CoV-2, COVID-19 can render patients susceptible to symptoms and complications related to the urogenital system [8]. The coronavirus can induce non-degenerative damage to mucosal bladder cells, followed by the release of increasing levels of cytokines during inflammation and severe involvement, leading to the onset of irritative urinary symptoms [7]. Lower urinary tract symptoms (LUTS) were assessed in patients diagnosed with COVID-19 within the past two months and presented to the intervention clinic in Urmia City using the IPSS questionnaire.

Method

The present study is cross-sectional, and its population consists of patients who, without any prior symptoms of the lower urinary tract system, have visited the clinic and stated that their recent COVID-19 infection had exacerbated such symptoms in their lower urinary tract system. Patients with a history of recurrent urinary tract infections, positive urine cultures, or recent use of diuretic medication were excluded from the study population. Relevant information regarding the period of COVID-19 infection and hospitalization was collected based on the patient's medical records. After providing sufficient explanations regarding the purpose of the questionnaire and the confidentiality of information, the patients completed the IPSS1 questionnaire, which contained questions about urinary symptoms. Subsequently, based on the scores obtained from the questionnaire, patients were classified into three groups: mild symptoms (0–7), moderate symptoms (8–19), and severe symptoms (20–35). Patients with moderate to severe symptoms

were referred to a urology specialist for further evaluation and treatment interventions. The Urmia University of Medical Sciences Ethics Committee approved the present study under the ethics code IR.UMSU.REC.1400.065. After obtaining permission from the ethics committee, data collection was conducted. Throughout the research process, the researchers adhered to the principles of the Declaration of Helsinki and the Medical Ethics Declaration of the Ministry of Health. Patient information remained confidential, and no costs were imposed on the individuals under investigation.

Data Analysis

The data analysis method involved converting the defining features of patients (lower urinary tract symptoms) into numerical indices using plenty of tables, graphs, and descriptive statistics, including mean values and standard deviations. The Chi-Square Test was used to examine the frequency of lower urinary tract symptoms based on age groups, hospitalization history, and gender. The presence or absence of lower urinary tract symptoms was evaluated through multivariable logistic regression analysis. A significance level of less than 0.05 was considered statistically significant.

Results

In this study, the study population consisted of 150 patients who had visited the clinic with a history of COVID-19 infection in the past two months. The mean age of the patients was 44.12 ± 14.26 , and the gender distribution included 120 males (80%), and the rest were females. Based on the patients' responses to the IPSS1 questionnaire, 92.7% of the patients (139 individuals) had mild urinary symptoms, while the remaining had moderate urinary symptoms. None of the patients had severe urinary symptoms. Furthermore, it was found that urinary frequency and nocturia were more common than other urinary symptoms, and urinary incontinence was less frequently reported by the patients (Table 1).

Statistical analysis revealed a significant difference in the prevalence of moderate urinary symptoms between individuals over 50 and those under 50 (P -value = 0.04). Furthermore, the statistical analysis regarding the evaluation of gender showed that moderate urinary symptoms were more common in women than men (P -value = 0.04) (Table 2). A comparison of individuals with different degrees of urinary symptoms regarding hospitalization history did not demonstrate a significant difference between individuals with and without a history of hospitalization in the urology department (P -value = 0.67). Additionally, no significant relationship was found between hospitalization in the intensive care unit and non-hospitalization in this department (P -value = 0.08) (Table 2).

Urinary symptom		Percentage
Incomplete Bladder Emptying	It didn't exist at all	82.7
	Less than once every 5 times	7.3
	Less than half the time	4.7
	About half the time	5.3
	More than half the time	0
Intermittent Urination	It didn't exist at all	90.7
	Less than once every 5 times	5.3
	Less than half the time	4
	About half the time	0
	More than half the time	0
Urgency	It didn't exist at all	74
	Less than once every 5 times	12.7
	Less than half the time	12
	About half the time	0
	More than half the time	0
Poor flow of urine	It didn't exist at all	90
	Less than once every 5 times	2.7
	Less than half the time	5.3
	About half the time	2
	More than half the time	0
Frequent Urination	It didn't exist at all	47.3
	Less than once every 5 times	13.3
	Less than half the time	26.7
	About half the time	19
	More than half the time	2.7
Nocturia	It didn't exist at all	42.7
	Less than once every 5 times	13.3
	Less than half the time	20.7
	About half the time	22
	More than half the time	0
Dysuria	It didn't exist at all	92
	Less than once every 5 times	2
	Less than half the time	4.7
	About half the time	1.3
	More than half the time	0
Almost always	It didn't exist at all	0
	Less than once every 5 times	0
	Less than half the time	0
	About half the time	0
	More than half the time	0

Table 1: Frequency of severity of urinary symptoms of patients

		Urinary symptoms (percentage)	
		Mild	Moderate
Age	Under 50 years	97.9	2.1
	Over 50 years	83.6	16.4
Sex	Male	95	5
	Female	83.3	16.7
Had a history of hospitalization	ICU	3.6	18.2
	Ward	96.4	81.8
Had no history of hospitalization		79.9	81.8

Table 2: Frequency and distribution of sex, age and history of hospitalization

Discussion

The average age of patients in the present study was 44.12 years, and most of the study population consisted of males. In the study conducted by Sheikhi et al. on the impact of COVID-19 on lower urinary tract symptoms, a higher percentage of male patients were reported, and the average age was 61.6 years. These findings are consistent with the present study [9]. On the other hand, Kaya et al. identified that most patients with COVID-19-related lower urinary tract symptoms were female [10]. The results of this study were contradictory to the present study. Additionally, the average age of patients in this study was 30 years, approximately 14 years lower than the average age in the present study [10]. In the study by Nikpouraghdam et al., the average age of patients was 57.5 years [11].

In the present study, individuals with moderate urinary symptoms were older than those with mild symptoms. The average IPSS score of individuals over 50 was also higher. In the study conducted by Nikpouraghdam et al., it was determined that the average IPSS score in individuals over the age of 50 was significantly higher than in those under 50 years old. These results are consistent with the present study's findings [11]. Furthermore, the study by Nikpouraghdam et al. revealed that the average IPSS score of individuals over 50 increased during the COVID-19 pandemic compared to the pre-pandemic period [11].

The present study's findings indicated that urinary frequency and nocturia were more common than other urinary symptoms in patients. Moreover, women had higher LUTS scores than men. Additionally, individuals with severe urinary symptoms were older than those with mild symptoms. In the study by Mumm et al., urinary symptoms were more prevalent in patients with COVID-19, which were considered signs of COVID-19 [12]. In the study by Kaya et al., patients experienced storage symptoms such as urinary frequency and nocturia at the onset of COVID-19, and these urinary symptoms significantly improved after recovery [10]. In the study by Sheikhi et al., the most common LUTS in patients with COVID-19 were urinary frequency, dysuria, urinary urgency, and hesitancy [9]. Zhai et al. reported three COVID-19 patients with evident hematuria [13]. Zheng et al. also observed a higher prevalence of glucosuria and proteinuria in COVID-19 patients, which

could be contributing factors to disease severity [14].

The increased prevalence of urinary problems, especially symptoms like urinary frequency and nocturia, classified as storage symptoms, can be attributed to psychological factors related to the disease. Stress and depression in patients can excessively stimulate the bladder, leading to urinary symptoms [15]. Additionally, coughing can also play a role as a common sign in COVID-19 patients in exacerbating urinary symptoms associated with the disease. Increased coughing episodes in patients can exert pressure on the bladder, resulting in urinary symptoms such as incontinence. However, in the present study, there was no significant difference in symptom severity between individuals with and without a history of hospitalization or those in specialized care units, indicating a muted influence of psychological conditions and anxiety related to hospitalization on post-COVID-19 patients. Studies have shown that over time, urinary symptoms decrease in patients with COVID-19 [10].

Conclusion

COVID-19 can contribute to the development of underlying urinary symptoms in patients. The present study demonstrated that subclinical urinary symptoms, particularly nocturia, and frequency, are more prevalent in women, especially older individuals.

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