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## ORIGINAL ARTICLE

# UROLOGICAL PRESENTATION OF PATIENTS WITH COVID-19 IN NINEVAH, IRAQ

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**Summary**

**Introduction:** "Corona virus-induced disease (COVID-19)" is a highly infectious respiratory disease caused by the coronavirus (SARS-COV-2). In addition to respiratory symptoms, the infected people also experience urological symptoms such as renal impairment and lower urinary tract symptoms (LUTS), which include frequency, urgency, loin pain, pyuria, and hematuria. Infertility and urolithiasis have also been detected in some patients.
**Objectives:** To evaluate the effect of the coronavirus on the urinary system and its consequences on the affected patients.
**Methods:** A prospective case series study was conducted in Mosul City, Iraq. One hundred COVID-19 patients, after a positive PCR result, confirmed their infection with the coronavirus, were evaluated clinically and sent for urine analysis and a renal function test.
**Results:** Among the 100 patients studied, more males (56%) than females (44%) were affected by COVID-19. Patients in the 51–60 age range have the highest incidence of urinary symptoms, with loin pain being the most common symptom (52%) and frequency coming in second (51%). Regarding urine analysis, pus cells, RBCs, and protein were observed in 48, 24, and 24%, respectively. Renal function tests were abnormal in 55% of infected patients.
**Conclusion:** The impact of the coronavirus on the urinary system differs from one patient to another. Patients who are elderly are severely affected, and urinary manifestations appear to be more prominent in this age group. Moreover, acute kidney injury may happen in some individuals, particularly those who are hospitalized, and the lower urinary tract infection may be accompanied by fever, dehydration, or a prolonged homestay.

*Key words: COVID-19; LUTS; AKI; SARS-COV-2; Urological diseases*

## Introduction

The coronavirus disease 2019 (COVID-19), also known as the "severe acute respiratory syndrome coronavirus (SARS-COV-2)," was first studied in Wuhan, Hubei District, China. A few months later, it had spread globally, raising the alarm of a pandemic in search of a health emergency (1, 2). The disease was then classified as mild to moderate, with severe cases requiring hospitalization and emergency care, as well as links to comorbidities or death in the elderly

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(3). The majority of the time, the coronavirus invades the respiratory tissue extensively (4), causing respiratory symptoms ranging from a cold to severe pneumonia (5). Later on, it was discovered that COVID-19 affects all organs, with the kidneys being the most severely affected and requiring medical attention (6). Due to the unavailability of clear markers of urinary symptoms, it is difficult to determine which cases require priority medical interventions (7). However, triage should be taken into consideration to determine which diseases require priority medical interventions (8). A urologist must adequately manage the urologic condition to identify the appropriate medical needs, particularly "acute kidney injury," as the pandemic's peak has affected the surgical operating rooms (9).

Hematuria, proteinuria, and pyuria are signs of kidney involvement regardless of age (11–15), but elderly males with multi-morbidity (diabetes, heart disease, kidney disease, liver disease, or other maladies) are more susceptible to this condition and its associated severe illnesses (12, 13, 15). Lower urinary tract symptoms (LUTS) in COVID-19 may be associated with frequency and dysuria, which most commonly occur in the elderly due to the presence of co-morbidities and weak immunity. Therefore, any elderly patient with unexplained LUTS should be evaluated for coronavirus infection (16, 17).

The present study was aimed at evaluating the impact of coronavirus on the urinary system and the consequences for the affected patients.

## Materials and Methods

### Study population

A prospective case series study that involves 100 COVID-19 patients who visited the Al-Salam Teaching Hospital's emergency room and outpatient urology clinic in Mosul, Iraq was conducted. The study was carried out during the period from the 1st of April 2021 to the 1st of October 2021. All of the patients in the study had COVID-19 infection, which was confirmed by a positive PCR, an increased D-dimer level, and a low serum ferritin level. The inclusion criteria include patients with a positive coronavirus infection and urological symptoms such as loin pain (unilateral or bilateral), LUTS (frequency, urgency, dysuria, incontinence), hematuria (gross or microscopic), renal impairment, or abnormal urinalysis. Patients with an existing genitourinary disease (infection, trauma, tumor, surgery, congenital anomaly), a history of neurological disease, a history of bleeding tendencies, patients taking anticoagulants, and those with any chronic diseases were all excluded from the study.

### Ethical approval and data collection

Ethical approval was obtained from the scientific committee of the hospital. Informed consent was collected from all patients in the study. A standard questionnaire that asks for the patient's personal information, such as name, age, sex, occupation, place of residence, principal complaint, and duration, was used to guide the interview with the patients. A detailed medical history that includes medical illnesses such as (hypertension, diabetes, endocrine or other diseases) and urological history that includes LUTS, loin pain, and hematuria were included in the questionnaire. Information on the nature of the drug taken, any history of trauma or surgery, and the personal history of the patient, such as smoking, alcohol intake, or drug abuse, were also obtained. A physical examination of the patient was then performed, which included a general examination for weight loss, pallor, and jaundice. This was followed by local and genital checks for any loin tenderness, mass, suprapubic mass, or scrotal swelling, and a digital rectal examination for the prostate. Urinalysis and a renal function test were performed on all patients.

### Collection and analysis of specimens

Urine specimens (midstream clean catch) were collected in a sterile plastic container using an aseptic technique. Urinalysis was carried out according to standard procedures, which included examining physical characteristics such as color, odor, pH, and specific gravity. Chemical tests were conducted by determining the levels of protein, glucose, ketone, leukocyte, nitrite, HB, bilirubin, and urobilinogen in urine specimens. Microscopic examination of urine for erythrocyte, leukocyte, bacteria, cast, crystals, and epithelial cells was made. Concerning the renal function test, blood was aspirated and the following parameters were determined: blood urea and serum creatinine (normal urea values= 3-7 Mmol, 20-45 mg/dl, and serum creatinine values= 62-124 Mmol, 0.7-1.2 mg/dl).

## Statistical analysis

Statistical analysis was performed using SPSS (IBM SPSS Statistics V22). The data were subjected to descriptive statistics. The Kruskal-Wallis test was used to compare non-parametric results. A series of comparative t-tests were employed to separate the various groups, and one-way ANOVA was utilized to compare different groups together. The results were expressed as a percentage, and a p-value of less than 0.05 is considered significant.

## Results

The results (Figure 1) showed that out of a total of 100 COVID-19 patients included in the study, males (56%) were significantly ($p<0.05$) affected than females (44%).

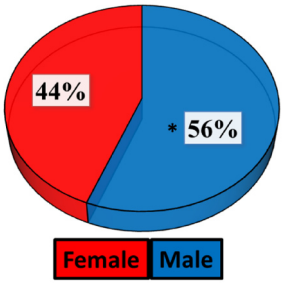


**Figure 1.** Sex distribution among the studied samples of COVID-19-positive patients. *$p<0.05$ using Chi-square test.

The average age of patients included in the study was 65 years, and patients in the age group (51-60 years) have the highest incidence of urinary symptoms (23%) as illustrated in Figure 2. However, no significant differences were observed between the groups.

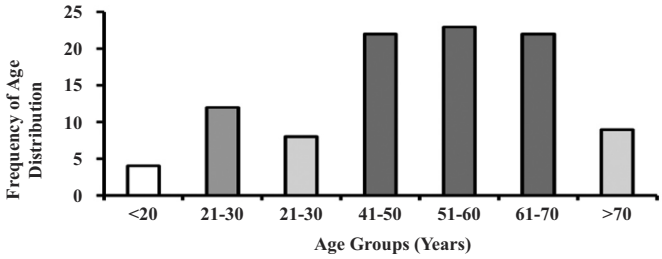


**Figure 2.** Distribution of the frequency of patients per age group in the studied samples.

In addition to fever and cough, patients with coronavirus may also experience urinary symptoms. Loin pain was the most common symptom, present in 24% of patients. Incontinence (17%) and urgency (16%) were distributed almost equally. Furthermore, hematuria and dysuria (9%) were both detected (Figure 3). However, no significant differences were found between the groups.

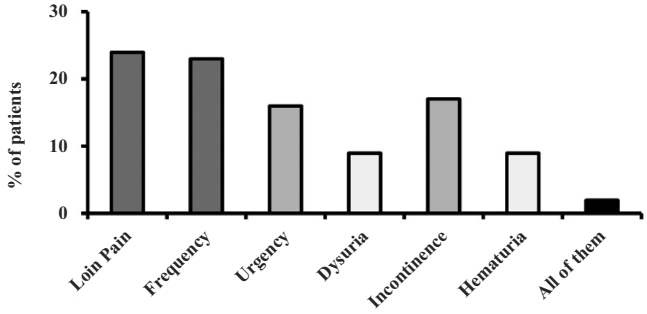


**Figure 3.** Distribution of urinary symptoms in COVID-19 patients.

Pus cells, which are present in 36% of the samples, were the most frequent abnormality in mid-stream urine analysis. Microscopic hematuria and proteinuria (at 18% each) were the next most frequent parameters obtained, with crystals making up 9% of the samples. In 3% of the samples, all symptoms were noticeable. Moreover, 16% of the total sample met the criteria for normal urine analytical results (Table 3).

**Table 3.** Outcome of the laboratory analysis of mid-stream urine.

| Laboratory urine analysis findings | Enrolled subjects (No./%) |
|---|---|
| Pus cells | 36% |
| RBC | 18% |
| Protein | 18% |
| Crystals | 9% |
| All of them | 3% |
| Normal | 16% |

Acute kidney injury can be a symptom in COVID-19 patients and is currently regarded as a common complication. In terms of renal function, 55% of the concerned patient exhibited abnormal renal function tests (Figure 4). Moreover, the GFR in the study population was estimated (eGFR) in mL/min/1.73 $m^2$ of body surface area and represented as an individual eGFR (Table 4). The status of the kidney function was taken into consideration in relation to the eGFR levels. According to eGFR, the majority of patients had mild to moderate kidney damage, and a minority had severe kidney damage. More serious cases were presented as moderate (25%) or severe (12%) cases. In none of the cases did renal failure develop.

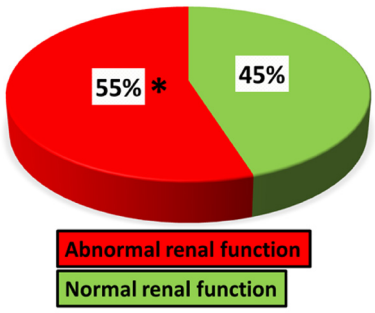


**Figure 4.** Percentage of distribution of normal versus abnormal renal functions. *P<0.05 using the Chi-square test.

The estimated glomerular filtration rate (eGFR) was calculated for all participants and was categorized in accordance with the distribution of the samples as presented in Table 4.

**Table 4.** Stages of chronic kidney disease and the frequency of distribution in urine samples.

| Normal eGFR | Kidney status | Frequency in our sample (%) |
|---|---|---|
| ≥90 | Possible kidney damage | 20 |
| 60-89 | *mild loss* of kidney function | 23 |
| 45-59 | *Mild to moderate* loss of kidney function | 20 |
| 30-44 | *Moderate to severe* loss of kidney function | 25 |
| 15-29 | *Severe loss* of kidney function | 12 |
| <15 | Kidney *failure* | 0 |
| | Total | 100 |

## Discussion

A coronavirus primarily affects the respiratory system, although other systems such as the gastrointestinal tract (GIT), cardiovascular, and urinary systems may also be affected (18). The discovery of SARS-CoV-2 in urine and/or kidneys has intensified the discussion on COVID-19's potential role in kidney damage (19-24). Therefore, this study highlighted the association of COVID-19 with urine impairments. In association with COVID-19, males have manifested more urinary deficits than females. The findings of Chaudhri *et al*. (2020), in their studied population, revealed that men (71.5%) were more involved than women (28.5%). However, the majority of the population was suffering from chronic diseases like chronic kidney injury, hypertension, and diabetes mellitus, and they were receiving chronic polytherapy (25). Also, in the study by Ouahmi *et al*. (2021) conducted on COVID-19 patients with chronic conditions, more men (68%) than women (60%) were affected (26). Most of the patients with urinary symptoms associated with COVID-19 were middle-aged adults rather than young adults. Nevertheless, the statistical analysis did not reveal any differences.

The variation in symptoms may be partially attributed to aging and associated diseases since studies on COVID-19-associated urinary symptoms (25-31) have included patients of various age groups. These range from young adults without any chronic diseases to the elderly (>75 years) with various associated chronic diseases (diabetes, hypertension, and ischemic diseases). Lower urinary tract symptoms were reported by more patients than upper urinary tract symptoms. However, urine still presented with pus cells, blood cells, and proteins in urine. Karras *et al*. (2021) did a retrospective single-center investigation on 322 patients and discovered that COVID-19 patients had excessive protein excretion in their urine despite normal renal function as indicated by a normal creatinine level (27).

The results of the present study are not consistent with the investigation of Huart *et al*. (2021), who reported that a large portion of their participants experienced either proteinuria or hematuria alone. Hematuria and proteinuria were represented as coexisting characteristics in the same individuals in the present study (31). These findings have been explained in the context of *de novo* proteinuria linked to COVID-19 (31, 32). The first kidney biopsy results indicate direct virus-mediated tubular injury (19-21). The SARS-CoV-2 virus is thought to enter cells through the tubules, where angiotensin-converting enzyme 2 is predominantly expressed (22). However, there is still debate on whether the virus may exist in the kidney (and in urine), and more research is needed (19-24). In contrast, Pei *et al*. (2020) showed that 65.8% of 333 hospitalized patients had proteinuria (33). This could be explained that most of the study participants had mild kidney disease, or other chronic illnesses (such as hypertension and diabetes), or were taking medications that could harm their kidneys on a long-term basis (such as ACE inhibitors) (34). Only 12% of individuals had severe renal disease. The majority had mild to moderate kidney damage, as shown by a decreased eGFR. In a study conducted by Huart *et al*. (2021), eGFR has been found to have decreased as early as the day of admission with a prevalence rate of 20% (31). Similarly, Ouahmi *et al*. (2021) observed that eGFR was minimally reduced reaching 87 ml/min per 1.73 $m^2$ with no differences between severely infected COVID-19 cases and non-severely affected (26).

Regarding urinary manifestation, loin pain was present in 24% of cases, making it the most frequent presenting symptom. Meanwhile, in the Can *et al*. (2021) study, the urinary frequency was the most common symptom (35). The current investigation indicated that older patients with a coronavirus infection had non-significantly higher LUTS. In addition, this study shows that renal impairment was the most common presentation when compared to other studies conducted, and it has been noticed that some patients with COVID-19 suffered from dysuria and irritant symptoms (36). Lamb *et al*. (2022) reported a significant worsening of symptoms of overactive bladder in COVID-19 patients after infection compared to before viral infection (37).

## Conclusion

Global healthcare systems are being significantly impacted by the COVID-19 pandemic. Since the virus had a wide range of impacts on the urine system related to LUTS and renal function, urology departments completely adjusted their daily practices to manage this new challenge. However, investigations are necessary to fully identify the effect of the virus on the urinary system. A more advanced investigation is needed to detect coronavirus in the urine of COVID patients.

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**Conflict of interest**

The authors declare no conflict of interest concerning the present study.

**Adherence to ethical standards**

The study was assigned a registration letter number (2856 on 02.01.2022) and submitted to the Ninevah Health Directorate.

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