# Renal Stone and Patients with COVID-19 Infection: Coincidence or causality

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# **Research Article**

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# ABSTRACT

The new coronavirus disease 2019 (COVID-19) has become a disaster all over the world. The main organ infected by this virus is the respiratory system; however, various other vital systems can also be affected by potential outcomes. In the present study, we report six adult COVID-19 positive patients with new-onset renal calculi. This case series highlight the possible effects of COVID-19 infection on kidney function changes.

# INTRODUCTION

SARS-CoV and MERS-CoV, known as zoonotic coronaviruses, damage the respiratory tract and have caused severe outbreaks in the past decade. The coronavirus disease 2019 (COVID-19) virus emerged in December 2019 in Wuhan, China, and by October 23, 2020, it affected more than 42,000,000 people worldwide, causing more than 1,100,000 deaths.

The most common symptoms at the onset of the disease include fever, cough, myalgia, fatigue, dyspnea, and diarrhea. A high percentage of patients with COVID-19 show abnormalities in renal function. Presenting with the Proteinuria or elevated BUN. In this regard, several possible mechanisms such as ischemic injury, cytokine storm, and direct infection have been proposed.

In this case series, we report six cases of confirmed COVID-19 with different manifestations at initial presentation. On admission, all patients underwent initial laboratory tests including cell blood count (CBC), lactate dehydrogenase

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(LDH), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), urea and creatinine, liver function test (LFT), and coagulation tests. All of the symptoms were relieved with symptomatic therapy <sup>[1]</sup>.

# CASE PRESENTATION

A 53-year-old man referred to the emergency department with severe fatigue, chest pain, myalgia, and urticaria for two days. All vital signs including oxygen saturation (SPO<sub>2</sub>), blood pressure (BP), respiratory rate (RR), heart rate (HR), and body temperature were normal.

The initial laboratory tests showed a normal range. The patient received hydroxychloroquine, naproxen, and diphenhydramine as symptomatic treatment.

On the fourth day, he reported flank pain and urinary frequency. He also complained of sand excretion in urine three months ago. Urinary analysis (U/A) test and sonography were performed.

Sonography report showed calculus 6 mm in the inferior calyx of the right kidney and microlithiasis in the left kidney. Flank pain was relieved after naproxen and hyoscine were administered.

A 44-year-old woman referred to the emergency department with sore throat, fatigue, chest pain, myalgia, headache, dizziness, nausea, anorexia, and dyspnea for four days. The patient had a history of hysterectomy (5 years ago) and mitral valve prolapse (from 2 years ago) and used propranolol, nortriptyline, and vitamin D3.

On admission, all vital signs were normal. The initial laboratory tests showed a normal range except CRP 21, ESR 34, and lymphopenia 490/µl. Hydroxychloroquine, naproxen, diphenhydramine, and doxycycline were administered for treatment.

On the 14th day, flank pain with dysuria and discoloration of urine was reported. U/A test and sonography were performed. U/A showed microscopic hematuria, proteinuria, and bacteriuria, while sonography confirmed calculus 4-5 mm in the inferior calyx of the left kidney.

A 38-year-old woman referred to the emergency department with cough, sore throat, chest pain, and dyspnea for five days. She had a history of anemia, for which iron supplements had been administered.

On admission, all vital signs were normal. The initial laboratory tests were normal except CRP 16 and ESR 23. Hydroxychloroquine, naproxen, diphenhydramine, doxycycline, and pantoprazole were administered for treatment. On the 10th day, flank pain was reported. U/A test and sonography were performed, and the latter confirmed calculus 2-3 mm in the median calyx of the left kidney.

A 48-year-old man referred to the emergency department with cough, sore throat, headache, diarrhea, and dyspnea for five days. He had a history of hypercholesterolemia and had taken Atorvastatin.

On admission, all vital signs were normal. The initial laboratory tests were normal except serum level of CRP 28, ESR 30 and lymphopenia  $760/\mu$ l. He received hydroxychloroquine, naproxen, diphenhydramine, azithromycin, and vitamin D3.

On the 9th day, the patient reported urine discoloration, flank pain, frequent urination, and dysuria. U/A findings indicated hematuria, and sonography showed calculus 4 mm in the median calyx of the right kidney.

A 25-year-old woman referred to the emergency department with cough, sore throat, headache, myalgia, fever, fatigue, nausea, chest pain, and dyspnea for five days ago. On admission, all vital signs were normal and body temperature was 38°C.

The initial laboratory tests were normal except serum level of ESR 10. The patient was given hydroxychloroquine, naproxen, diphenhydramine, and azithromycin.

On the 3rd day, she reported fever and frequency urination. Ciprofloxacin was administered according to the results of U/A (bacteriuria and pyuria). On the 8th day, left flank pain was observed. Sonography was performed and U/A was repeated. U/A was normal, but sonography confirmed calculus 4 mm in the inferior calyx of the left kidney.

A 24-year-old woman referred to the emergency department with cough, headache, diarrhea, myalgia, fatigue, nausea, and dyspnea for three days. She had a history of anemia, for which she had taken iron supplement.

On admission, all vital signs were normal. Body temperature was 38°C. The initial laboratory tests were normal except CRP 19, ESR 29, and lymphopenia 992/µl were reported. Azithromycin, hydroxychloroquine, naproxen, diphenhydramine, and pantoprazole were administered for treatment.

At day eight, she reported right flank pain and palpitation. U/A test and sonography requested. U/A indicated pyuria, bacteriuria and hematuria.

Sonography showed calculus 2-3 mm in the inferior and median calyxes of the right kidney. Ciprofloxacin (according to urine culture results), use water frequently, diet modification recommended.

# DISCUSSION

Our case series showed that COVID-19 could affect kidneys and lead to renal calculi. Based on recent studies such as Xia et al. in China and Benedetti et al. in the United States, coronavirus can cause acute kidney injury (AKI) with varying severities and outcomes. evaluated biopsy samples of native and allograft kidneys from patients with COVID-19, and it was found that they develop a wide array of glomerular and tubular diseases. Another study noted the productive direct infection of the kidneys by SARS-CoV-2<sup>[3]</sup>.

In the present study, we reported six cases of renal calculi in patients with confirmed COVID-19 disease without any pervious history of kidney disease. Flank pain began after (on average) 15 days of symptoms onset. The risk factors for renal calculi can be divided into four major categories: dietary, genetic, environmental, and lifestyle <sup>[4]</sup>. Stone formation can be affected by demographic characteristics such as age, race, and BMI > 30 kg/m2. Thus, Shin et al. reported age older than 40 as an important risk factor. All of our cases had a BMI lower than 25 kg/m2, and three cases were under 40 years old <sup>[5]</sup>.

# CONCLUSION

Kidney stones develop about three times more frequently in individuals with positive family history. Also, comorbidities such as hypertension, diabetes, and CKD can increase this risk. In our cases, no family history of renal calculi was reported. Besides, no one had a history of comorbidities which increase the risk of stone formation.

Having examined the cases, we did not find any important risk factors for renal calculi formation. Although our data is insufficient to draw conclusions about the relationship between COVID-19 and renal calculi, it is rewarding to address the possibility of renal stone formation in the case of COVID-19 infection.

# CONTRIBUTIONS

All authors have each read and approved the contents of the manuscript. Ghazaeian and Kasiri visited the patients and participated in data acquisition and drafting the manuscript, Samaeeand Moradimajd contributed to acquisition of data and wrote the manuscript.

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# ETHICAL APPROVAL

This report was approved by the Ethics Committee of Mazandaran University of Medical Sciences (IR.MAZUMS.REC.1399.8510).

# INFORMED CONSENT AND PATIENT DETAILS

Written consent forms from all patients were obtained. All patients were assured that without mentioning their names, clinical findings of their disease would be reported.

# DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests.

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