

# Assessment of renal function among covid-19 patients admitted to the intensive care unit

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**Abstract:** Severe acute respiratory viral infections are frequently associated with multiple organ failure, including acute kidney damage. The present study aimed to investigate the associated influence of COVID-19 on renal function in patients admitted to the intensive care unit in Asir region, Saudi Arabia. Thirty patients infected with COVID-19 who were referred to the intensive care unit during November and October 2020 at Asir central hospital, Asir region, Saudi Arabia were recruited. The age of patients ranged between 30 and 90 years old. Renal function tests exhibited dramatic changes in the renal biomarkers in patients with COVID-19. Blood urea levels in COVID-19 patients were significantly higher than in the control group. In addition, significantly lower albumin levels with abnormally decreased total protein levels were found in COVID-19 patients. Among the different electrolytes analyzed, a significantly lower calcium level was observed in COVID-19 patients' groups than in the controls. Renal function tests for COVID-19-infected ICU patients revealed significant changes, indicating the major impact of COVID-19 on kidney function. Monitoring renal function tests may assist in the early prognosis of COVID-19 patients. It is, therefore, crucial to increase the understanding of renal function tests in COVID-19 patients who were admitted to the hospital before their condition deteriorated.

**Keywords:** COVID-19, kidney function tests, intensive care unit (ICU), renal functions, SARS-CoV-2.

## INTRODUCTION

A novel third virus belongs to coronaviruses that have emerged in the last 20 years was first identified in Wuhan, China in December 2019. The virus has spread worldwide and led to high morbidity and mortality (McMichael *et al.*, 2020). The rapidly spread coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has become a world health emergency encompassing mild upper respiratory tract illness with symptoms including fever, cough, and difficulty breathing while the severe complications include respiratory failure and death (Benedetti *et al.*, 2020). Although respiratory failure is the main feature of COVID-19, the influence of the virus on other body organs, such as kidneys, has also been explored, as these organs showed a common extrapulmonary target of the virus (Huang *et al.*, 2020; Su *et al.*, 2020).

Kidneys play a significant role in the regulation of blood fluid and pressure as well as hematopoiesis by producing erythropoietin and thrombopoietin hormones (Jelkmann *et al.*, 2011; Kazama *et al.*, 2011). The evaluation of biochemical profile is a significant assessment of the functional capacity of several critical organs and systems

including kidneys. It is essential to illustrate that more than 40% of COVID-19 patients who are admitted to the hospital have abnormal renal function tests including albuminuria or hematuria (Cheng *et al.*, 2020; Ronco *et al.*, 2020). Interestingly, hospitalized patients with SARS-CoV-2 infection are at a high risk of mortality (Gross *et al.*, 2020; Uribarri *et al.*, 2020). Additionally, a study demonstrated that chronic renal failure patients are prone to be infected with COVID-19 infection (Uribarri *et al.*, 2020). Thus, those patients require high care and well isolation.

Renal function tests revealed an elevation in serum creatinine and blood urea nitrogen during the COVID-19 infection period (Hong *et al.*, 2020). Specifically, this increase in serum creatinine and blood urea nitrogen was significant in the COVID-19 peak when compared to the recovery period suggesting that SARS-CoV-2 infection has a high impact on renal function. In this study, we investigated the effect of COVID-19 on renal function among hospitalized patients admitted to the intensive care unit (ICU) in Asir region, Saudi Arabia.

## MATERIALS AND METHODS

### *Covid-19 patients*

The present study has been carried out in the Department of Clinical Laboratory Sciences, Faculty of Applied

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Medical Sciences, King Khalid University, Saudi Arabia. The study has included results of 30 patients infected with COVID-19 receiving treatment in the ICU, Asir Central Hospital, Asir Region, Saudi Arabia, and then compared to selected healthy individuals. The age of patients ranged between 30 and 90 years old.

#### Ethical consideration

Ethical approval {REC - No: (REC-11-10-2020)} for this study was obtained from the Regional Committee for Research Ethics, Directorate Health Affairs - Asir Region, Ministry of Health, Saudi Arabia.

#### Sample collection of healthy individuals

Blood samples were collected from vein puncture of selected healthy participants and placed in a plain tube without any anticoagulant for several biochemical tests. The serum was separated from the clot by centrifugation at 3000 rpm for 10 minutes at room temperature. The clear supernatant was immediately transferred to another test tube and used for serum biochemical analysis.

#### Patient data collection

We obtained patients data from the Laboratory Information System (LIS) exclusively, which provided information on the age, gender, ethnicity, and results of each patient.

#### Biochemical analysis

Evaluation of kidney function tests (KFT) was analyzed using a fully automated biochemical analyzer (Autoanalyser, Bechman DXC 600). Serum creatinine, serum uric acid, serum urea, serum albumin, serum total protein, serum sodium, serum magnesium, serum chloride, serum calcium, and serum potassium were measured.

### STATISTICAL ANALYSIS

For statistical analysis, GraphPad Prism was used for analyses (GraphPad Prism version 9.00 for Mac, GraphPad Software, San Diego CA). Mann–Whitney U test was applied to compare COVID-19 patients with normal healthy individuals. To evaluate the degree of association between two variables, Spearman’s correlation was used. A significant P value was considered when it is less than 0.05.

### RESULTS

Laboratory findings of ICU COVID-19 patients for kidney function tests indicated several differences compared to healthy controls. Serum creatinine level in COVID-19 patients and the control group were compared and the results showed a slight increase in creatinine level in the COVID-19 patients’ group (Fig. 1; controls, M = 0.85 mg/dL; COVID-19 patients, M = 1.01 mg/dL, P =

0.1141). However, when the Mann–Whitney U test was used, the results revealed that the difference between the two groups was insignificant.

Furthermore, the median of uric acid of COVID-19 ICU patients did not differ statistically from that of non-COVID-19 controls when Mann–Whitney U test was used to compare the medians of the two groups (Fig. 2; controls, M = 5.00 mg/dL; COVID-19 patients, M = 4.55 mg/dL, P = 0.5565). In contrast, blood urea level revealed a roughly 2-fold significant increase in the subjected group in comparison with controls (Fig. 3; controls, M = 25.00 mg/dL; COVID-19 patients, M = 60.90 mg/dL, P = <0.0001).

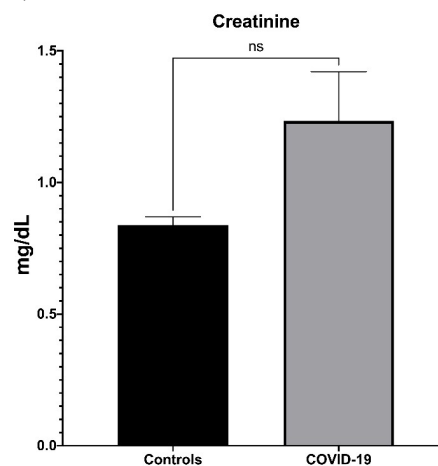


Fig. 1: Comparison of creatinine levels between intensive care unit (ICU) COVID-19 patients and healthy controls. Samples from COVID-19 ICU patients (n = 30) and normal controls (n = 40) were collected to measure the creatinine levels.

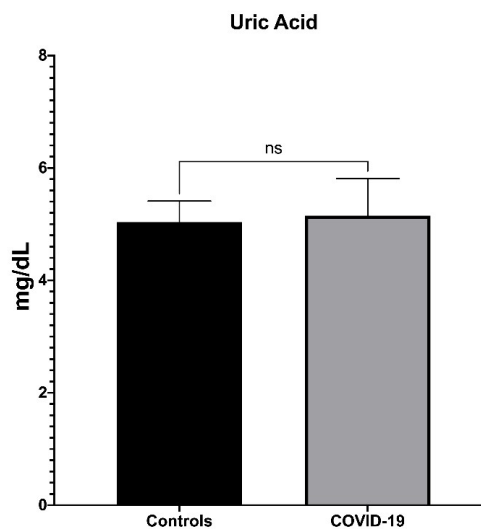
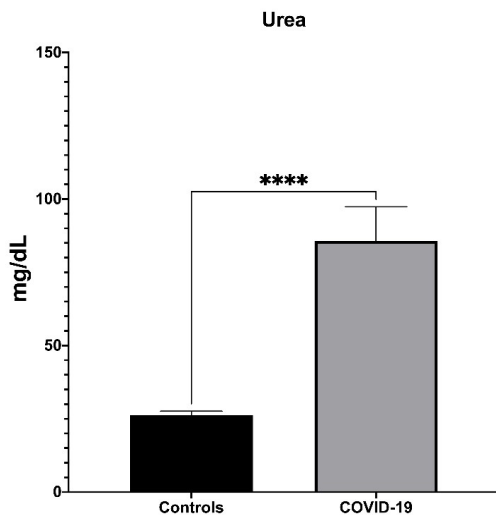
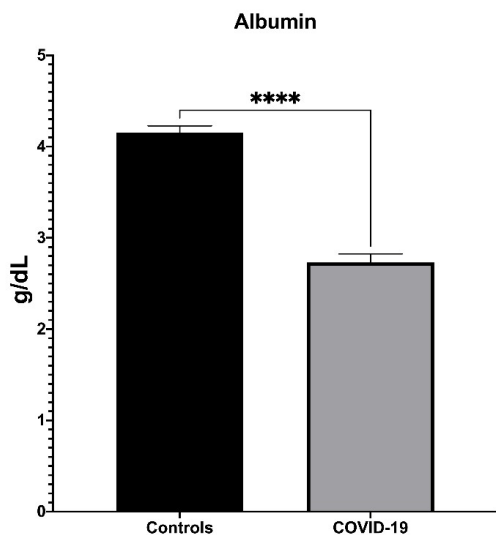


Fig. 2: Comparison of uric acid levels between intensive care unit (ICU) COVID-19 patients and healthy controls. Samples from COVID-19 ICU patients (n = 30) and normal controls (n = 40) were collected to measure the uric acid levels.

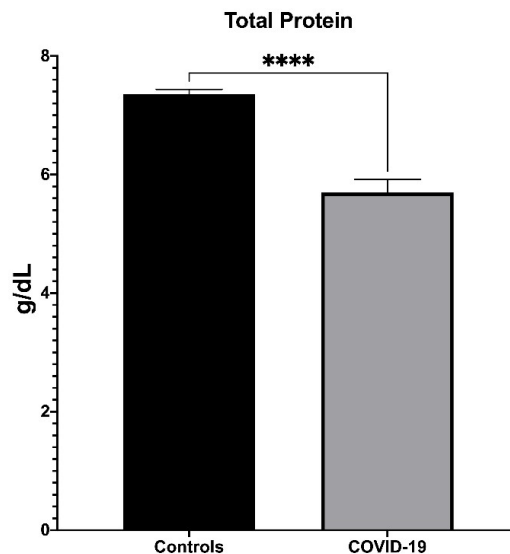
Moreover, the median of the albumin in the control and COVID-19 groups was compared using Mann–Whitney U test at  $P < 0.05$ . The results showed significantly lower albumin levels in COVID-19 ICU patients than that of the controls (Fig. 4; controls,  $M = 4.18$  g/dL; COVID-19 patients,  $M = 2.61$  g/dL,  $P = <0.0001$ ). Similarly, a comparison of the median of total protein values in the two groups was statistically measured using Mann–Whitney U test at  $P < 0.05$ . Total protein level in the patients' group was significantly less than those in the control group (Fig. 5; controls,  $M = 7.34$  g/dL; COVID-19 patients,  $M = 5.98$  g/dL,  $P = <0.0001$ ).



**Fig. 3:** Comparison of urea levels between intensive care unit (ICU) COVID-19 patients and healthy controls. Samples from COVID-19 ICU patients ( $n = 30$ ) and normal controls ( $n = 40$ ) were collected to measure the urea levels. \*\*\*\* $p < 0.0001$



**Fig. 4:** Comparison of albumin levels between intensive care unit (ICU) COVID-19 patients and healthy controls. Samples from COVID-19 ICU patients ( $n = 30$ ) and normal controls ( $n = 40$ ) were collected to measure the albumin levels. \*\*\*\* $p < 0.0001$



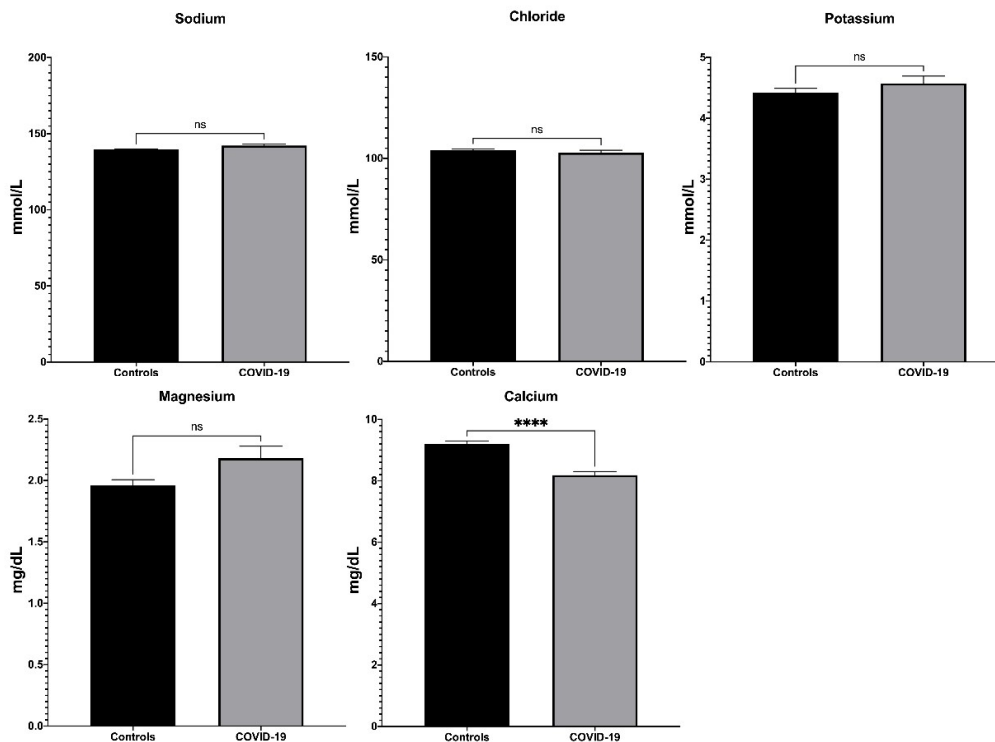
**Fig. 5:** Comparison of total protein levels between intensive care unit (ICU) COVID-19 patients and healthy controls. Samples from COVID-19 ICU patients ( $n = 30$ ) and normal controls ( $n = 40$ ) were collected to measure the total protein levels. \*\*\*\* $p < 0.0001$

The differences in electrolyte panel including serum sodium, serum magnesium, serum chloride, serum calcium, and serum potassium were analyzed in COVID-19 ICU patients and the healthy controls. Though, Mann–Whitney U test at  $P < 0.05$  was used to compare the medians of the two groups, and no statistical differences ( $P > 0.05$ ) were observed (Fig. 6). However, calcium level in ICU COVID-19 patients was significantly lower than that in the control (controls,  $M = 9.29$  mg/dL; COVID-19 patients,  $M = 8.30$  mg/dL,  $P = <0.0001$ ).

## DISCUSSION

Several studies have illustrated the detrimental impact of SARS-CoV-2 infection on hospitalized patients (Cheng *et al.*, 2020; Uribarri *et al.*, 2020; Hong *et al.*, 2020). Herein, we investigated the effect of COVID-19 on renal function among 30 hospitalized patients being admitted to the ICU in Asir region, Saudi Arabia. Abnormal renal function markers may indicate loss of kidney function that could lead to acute kidney injury (Cheng *et al.*, 2020).

Our findings indicated abnormal renal function tests in the ICU COVID-19 patients. While there was a slight increase in serum creatinine (not statistically significant), significant abnormal levels of blood urea, albumin, and total protein were observed in COVID-19 patients indicating the possible causal relation between COVID-19 infection and acute deterioration of kidney functions. The observed increase in serum creatinine and blood urea is consistent with the other studies (Cheng *et al.*, 2020; Gross *et al.*, 2020). These abnormal levels reflected the possible renal dysfunctions.



**Fig. 6:** Comparison of electrolytes (sodium, potassium, magnesium, chloride, and calcium levels in intensive care unit (ICU) COVID-19 patients and healthy controls. Samples from COVID-19 ICU patients (n = 30) and normal controls (n = 40) were collected to measure the electrolytes levels. \*\*\*\*p<0.0001

Moreover, albumin and total protein exhibited remarkably low abnormal levels, which is consistent with other studies that reported decreased albumin, and total protein levels in COVID-19 patients (Hong *et al.*, 2020; Zhao *et al.*, 2020). The possible explanation is that protein levels indicate the nutritional status of the patient and therefore the decreased levels of the protein may be due to long hospitalization (Zhao *et al.*, 2020). Reduced level of proteins in the body indicates the poor nutritional status of the patient, leading to decreased immunity to infection. Reduced albumin has been attributed to mortality with patient's severe renal disease, reflecting the effect of the infection on kidneys (Li *et al.*, 2020).

Abnormal electrolytes have also been reported to be associated with the severity of the SARS-CoV-2 infection. Our finding shows a significant decrease in Ca levels. This observation supports other studies that have shown a significantly low serum Ca level in severely ill COVID-19 patients (Zhou *et al.*, 2020; Cappellini *et al.*, 2020). Serum Ca is involved in several biological functions such as hormonal regulation, and blood coagulation (Peacock, 2010). Hypocalcemia has been reported to be associated with multiple organ dysfunction in COVID-19 patients (Peacock, 2010). Moreover, changes in Ca level could promote the activation of inflammatory reactions (Zhou *et al.*, 2020; Cappellini *et al.*, 2020). IL-6, a pro-inflammatory cytokine, is an important factor in

triggering the cytokine storm. IL-6 has been found significantly activated in critically ill COVID-19 patients with low Ca concentrations (Zhou *et al.*, 2020). An interesting point highlighted by another study was that IL-6 could cause a decrease in Ca level by up-regulating the calcium-sensing receptor gene (Hendy *et al.*, 2016). We, therefore, support the speculation by Zhou *et al.* (2020) that the cytokine storm may be associated with the viral load leading to low serum Ca, so the use of IL-6 inhibitors could be a good therapeutic approach.

COVID-19 may be a major cause of kidney injury resulting in an abnormal renal function test, as it has been documented to affect kidney tissues directly (Cheng *et al.*, 2020). This effect might be a progress of inflammatory reaction to kidney tissue after lung dysfunction, or it might be that renal failure accelerates the lung and other organ impairment as a result of abundant inflammatory cytokines. The interaction between virus and high rate of angiotensin-converting enzyme 2 receptor on kidney cell surface might be speculated and may cause kidney disease (Cheng *et al.*, 2020; Li *et al.*, 2020).

## CONCLUSION

This is the first reported study assessing the kidney markers and electrolytes in severe COVID-19 ICU patients in Asir Region. Significant abnormal levels of

blood urea, albumin, total protein, and calcium were found in COVID-19 patients compared to the controls. Monitoring renal function tests will indeed help in the early prognosis of COVID-19 patients. It is, therefore, crucial to increase the understanding of renal function tests in COVID-19 patients who were admitted to the hospital before their condition deteriorated. Nevertheless, due to the small sample size and limited observation time, additional studies from the same region are needed to confirm these findings.

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