HSPI The Open Access Publisher

J C N JOURNAL OF CLINICAL NEPHROLOGY
ISSN 2576-9529

Research Article

Renal Manifestations in Patients with COVID-19 Admitted to the Hospital

Jawad K Manuti[1]* and Mohammed Abdul Kareem Abdi[2]

[1]Professor of Nephrology and Internal Medicine Al-Nahrain University-Medical College Department of Medicine, Al-Nahrain University, Iraq

[2]Internal Medicine Resident, Al-Imamain Al-Kadhimain Medical City, Iraq

Abstract

Objective: Renal manifestations in COVID-19 cases range from proteinuria to AKI, while COVID-19 mortality is linked to alveolar injury; renal involvement associates with diverse outcomes, including elevated mortality. The aim of this study was to compare COVID-19 infected patients with and without Chronic Kidney Disease (CKD), analyzing clinical and lab differences, acute kidney injury rates, and renal manifestations' impact on outcomes.

Methods: This prospective cohort study was conducted across three COVID-19 centers: Al-Imamain Al-Kadhimain Medical City, Al-Karamu Hospital, and Dar Al-Salam Hospital, from January to July 2021. The cohort included 100 confirmed COVID-19 infected patients, followed until discharge, recovery, or death. Two groups were defined: Group A (CKD) with documented chronic kidney disease and COVID-19, and Group B (non-CKD) without prior renal disease. Data collection encompassed demographics, medical history, radiological and biochemical data, clinical renal indicators, COVID-19 severity, urine analysis, and development of AKI.

Results: In this study involving 100 participants (33 CKD, 67 non-CKD), age differences were significant (p = 0.003), with CKD patients being older. COVID-19 severity and survival rates varied significantly (both $p < 0.001$) between study groups. Renal manifestations including proteinuria, hematuria, pyuria polyuria, oliguria, and anuria occurred more frequently in the CKD group but only proteinuria and oliguria reached statistical significance ($p < 0.05$). Male gender, proteinuria, hematuria, and AKI development were linked to heightened mortality risk. Lower hemoglobin, lymphocyte counts, and elevated D-dimer indicated CKD impact. Hypertension was significantly associated with AKI risk (p = 0.031).

Conclusion: The study highlighted that age, male gender, and comorbidities like hypertension predicted COVID-19 severity and mortality. Renal indicators, notably proteinuria, hematuria, and AKI, were significant markers of increased mortality risk.

More Information

***Address for correspondence:**
Dr. Jawad K. Manuti, F.I.C.M.S, Professor of Nephrology and Internal Medicine Al-Nahrain University-Medical College Department of Medicine, Al-Nahrain University, Iraq,
Email: drjawadkadhem@yahoo.com

https://orcid.org/0000-0001-5595-706X

Submitted: April 15, 2025
Approved: May 19, 2025
Published: May 20, 2025

How to cite this article: Manuti JK, Abdi MAK. Renal Manifestations in Patients with COVID-19 Admitted to the Hospital. J Clini Nephrol. 2025; 9(5): 056-063. Available from: https://dx.doi.org/10.29328/journal.jcn.1001156

Keywords: Severe COVID-19; Renal manifestation; Hematuria; Proteinuria

Check for updates

OPEN ACCESS

Introduction

The kidney is one of the organs notably impacted by SARS-CoV-2 infection. Research indicates that COVID-19 pneumonia patients often display various forms of kidney injury, and individuals who experience fatal outcomes frequently manifest substantial kidney damage [1]. The comorbidities that increase mortality risk in SARS-CoV-2 patients are prevalent in individuals with Chronic Kidney Disease (CKD) and End-stage Renal Disease (ESRD) [2].

Kidney injury in COVID-19 may result from direct viral invasion or systemic responses, including host immune clearance and immune tolerance disorders, endothelium-mediated vasculitis, thrombus formation, glucose and lipid metabolism disorder, and hypoxia [3].

The coronavirus is undergoing specific changes due mutations and recombination, allowing it to bind uniquely to ACE2 (angiotensin-converting enzyme 2). ACE2 is expressed in epithelial cells of the lungs, small intestine, urogenital tract, and kidney structures, and predominantly in specific kidney areas like proximal tubules, afferent arterioles, collecting ducts, and the thick ascending limb of Henle. It

is hypothesized that the virus may enter the arterioles and glomerular capillaries and initially infects the glomerular endothelial cells, potentially contributing to intrinsic renal cell damage and subsequent Acute Kidney Injury (AKI). Recent findings suggest direct infection of kidney tubules by SARS-CoV-2, potentially causing tubular necrosis [4].

Severe cases of COVID-19 infection often manifest a state of hypercoagulable state. The interaction between SARS-CoV-2 and platelets through ACE2 induces platelet activation and prompts thrombus formation. This phenomenon potentially contributes to the pathophysiology of Acute Kidney Injury (AKI) associated with COVID-19 infection [5].

The most common clinical manifestation in the renal system is proteinuria, detected either prior to or subsequent to hospital admission, present in over half of the patients, followed by hematuria, elevated blood urea nitrogen (33.7%) and serum creatinine (10.7%) were also observed. A meta-analysis further revealed that patients presented with varying extent of albuminuria (+ in 38.8% of the patients, and ++ or +++ in 10.6% of the patients). In critically ill patients with SARS-CoV-2, AKI emerged as a key predictor of mortality [3].

Nonetheless, serum Blood Urea Nitrogen (BUN) and Serum Creatinine (SCr) tests exhibited limited sensitivity in detecting early kidney impairment, despite their common use for assessing renal function. Conversely, studies have demonstrated that urine microprotein, urine IgG, and urine transferrin serve as sensitive markers for early glomerular injury, while urine α1-microglobulin may serve as an early marker of tubular injury [6]. Calculating the estimated glomerular filtration rate, endogenous creatinine clearance, and urine microalbumin/creatinine ratio may help in detecting early renal injury in infected patients [7].

Research indicates that CKD patients with COVID-19 infection experienced a higher mortality rate compared to those without the infection. This could be because CKD patients often have elevated pro-inflammatory cytokines, leading to increased oxidative stress and an inflammatory immune response. This immune system alteration might make them more susceptible to bacterial and viral infections, potentially explaining the higher mortality rate [8].

Immunosuppressive drugs are essential for effective kidney transplantation, but they could potentially increase the likelihood of complications during COVID-19 infection. Recent findings also indicate that kidney transplant recipients may experience a more severe disease progression, necessitating intensive care admission [9].

Aim of the study

The primary objective of this study is to compare the clinical characteristics and laboratory results of COVID-19 patients with a history of chronic kidney disease (CKD) and those lacking prior history of renal disease.

The secondary objective is to investigate the extent of renal system involvement in these patients and its potential significance as a prognostic indicator for monitoring disease progression and mortality.

Methods

Study design and settings

Conducted as a prospective cohort study, data were collected from patients hospitalized at three COVID-19 centers in Baghdad: Al-Imamain Al-Kadhimain Medical City, Al-Karama Hospital, and Dar Al-Salam Hospital. The study duration spanned from the outset of January to the end of July 2021. The study cohort comprised one hundred individuals with confirmed COVID-19 infection, a verification established through RT-PCR and CT chest examinations. Patients were followed-up until discharge either because of recovery or death. None of the patients had previously received COVID-19 vaccination.

Ethical issues

Ethical and scientific approval for the research was obtained from the Scientific Committee at the Department of board of health specialization. Verbal and written consent was obtained from all patients before starting data collection and after explaining the aims of the study and assuring confidentiality.

Sampling technique

One hundred samples were collected by convenience method.

Group definition: Group A (CKD) comprises individuals who have a documented history of Chronic Kidney Disease (CKD) and have contracted COVID-19. Group B (non-CKD) consists of individuals who do not have a previous history of renal disease.

Inclusion criteria: 1- Patients aged 18 years and above. 2- Patients admitted to the hospital with a confirmed COVID-19 infection by RT-PCR and CT chest. 3- Availability of clinical and laboratory data.

Exclusion criteria: 1- Patients who are lost to follow-up were excluded (discharged on their responsibility). 2- Patients with a history of malignancy. 3- Patients with a history of heart failure. 4- Patients who refused to be included in this study. 5- Cases with missing clinical and lab information. 6- Mild cases were excluded from this study.

Data collection

The data collection for this study encompassed a range of parameters related to the renal manifestation in patients admitted to the hospital with COVID-19 infection. Demographic information, including age and sex, was recorded. Anthropometric details such as weight (kg) were

documented. Additionally, patients' history of smoking, co-morbidities (including hypertension, diabetes, CKD, and ischemic heart disease), family history of renal disease, and any previous renal conditions were noted.

Clinical data pertaining to COVID-19 infection were gathered, including results of PCR tests, lung involvement as observed in CT scans, and CBC values including WBC count, hemoglobin, lymphocyte count, platelet count, and MCV. Further biochemical markers such as LDH, D-dimer, RBS, Ferritin, CPK, Troponin, and C-reactive protein were recorded.

Renal function assessment involved recording blood urea, serum creatinine, serum albumin, and serum electrolyte levels (calcium, sodium, potassium, phosphate). The presence of proteinuria and hematuria was evaluated using urine dipstick tests. The severity of COVID-19 infection was categorized, and the presence of HBV, and HCV was determined.

Clinical signs related to urine output such as polyuria, oliguria, and anuria, were documented. Urine analysis parameters including proteinuria, hematuria, and presence of pus cells were captured. Moreover, the need for dialysis during hospitalization was recorded. Finally, the outcome in terms of survival was registered.

Remdesivir is administered by intravenous infusion for approximately 30 minutes after dilution. On day 1 a loading dose of 200 mg IV is given then 100 mg IV on subsequent days. The treatment duration for Remdesivir was 5 days but if clinical improvement was not demonstrated, treatment may be extended up to 10 days. For most of the patients

Variable definition

COVID-19 severity: In the present study, participants were classified into three groups (moderate, severe, critical) according to Chinese guidelines: moderate, severe, and critical categories. Moderate cases encompassed patients displaying clinical symptoms of fever and cough, along with radiological evidence of pneumonia. A severe case was characterized by either a respiratory rate exceeding 30/min, oxygen saturation at or below 93%, or radiological evidence of ≥50% increase in pulmonary infiltrates within 24–48 hours. A critical case was identified by conditions such as respiratory failure necessitating mechanical ventilation, shock, or the presence of multiple organ failure requiring intensive care unit intervention [10].

Urine analysis: Proteinuria was identified when urinalysis indicated the presence of protein at a level of ≥ 1+. Hematuria was characterized as the detection of over four red blood cells per high-power field during urine analysis. Pyuria was designated when more than 10 pus cells per high-power field were observed on urine analysis [11].

Diagnosis of AKI: As per the KDIGO guidelines, acute kidney injury (AKI) is delineated by any of the subsequent criteria [12]:

1. A rise in serum creatinine (SCr) of ≥ 0.3 mg/dL (≥ 26.5 μmol/L) within a span of 48 hours; or
2. An elevation in SCr reaching or surpassing 1.5 times the baseline over the preceding 7 days; or
3. Urine volume remaining below 0.5 mL/kg/hour for a duration of 6 hours.

AKI severity was classified according to KDIGO guidelines as follows [12]:

A. Stage (1) increase in SCr to 1.5–1.9 times baseline or by ≥0.3 mg/dL;

B. Stage (2) increase SCr to 2.0–2.9 times baseline;

C. Stage (3) increase SCr to 3.0 times baseline or increase in serum creatinine to ≥ 4.0 mg/dL (≥ 353.6 mmol/L) or initiation of renal replacement therapy.

Statistical analysis

Continuous variables were expressed as means and standard deviations or medians with range. Categorical variables were expressed as frequency and percentages. The Welch's *t* - test was performed to test the difference in means. The difference between categorical variables was investigated using either the χ^2 test with yates' correction or Fisher's exact test, depending on the context. An unadjusted logistic regression analysis was performed to assess the risk of development of AKI and the risk of death. A *p* - value less than 0.05 was considered statistically significant. R software packages (dplyr, gt_summery and ggplot) were used for data processing, visualization, and statistical analysis ("R version 4.3.0, R Foundation for Statistical Computing, Vienna, and Austria").

Results

In this study involving a total of 100 participants, 33 with CKD and 67 without CKD, several key characteristics were evaluated. The average age of individuals with CKD was 66.6 years, whereas those without CKD had an average age of 59.2 years, showing a statistically significant difference $p = 0.003$). Gender distribution between the CKD and non-CKD groups was not significantly different ($p = 0.3$), with 69.7% of CKD patients and 58.2% of non-CKD individuals being male. Co-morbidities like hypertension and diabetes were observed in 75.8% and 72.7% of CKD patients, respectively, and in 65.7% of non-CKD participants for both conditions. The percentage of lung involvement on CT scan differed significantly between the two groups being much higher in the CKD group (68 ± 18% compared to 53 ± 15%, $p < 0.001$). The severity of COVID-19 was notably different

between the groups ($p < 0.001$), with 69.7% of CKD patients experiencing severe cases compared to 55.2% of non-CKD individuals. Survival status also differed significantly ($p = 0.026$), with 63.6% of CKD patients surviving compared to 83.6% of non-CKD individuals. Other parameters, such as weight, smoking exposure, SpO_2 with O_2 supply, and ischemic heart disease showed no statistical differences between the CKD and non-CKD groups as presented in Table 1.

In Table 2, proteinuria was observed in 90.9% of CKD patients compared to 37.3% of non-CKD individuals, with a statistically significant difference ($p < 0.001$). Hematuria was more frequent among CKD patients (33.3%) than in non-CKD individuals (17.9%), with a p - value of 0.085, although not statistically significant. Similarly, pyuria was noted in 24.2% of CKD patients and 10.4% of non-CKD individuals, with a p - value of 0.081. Oliguria was significantly more common in CKD patients (24.2%) than in non-CKD individuals (7.5%) ($p = 0.027$). Acute kidney injury (AKI) was notably more frequent in the CKD group (45.5%) than in the non-CKD group (19.4%), demonstrating statistical significance ($p = 0.006$). Among the patients with AKI, the distribution of KDIGO stages did not differ significantly ($p = 0.6$): 57.1% Stage I, 35.7% Stage II, and 7.1% at Stage III.

Table 1: Baseline Clinical Characteristics of CKD and Non-CKD Patients Describes the demographic and clinical baseline characteristics of patients, comparing those with and without chronic kidney disease (CKD).

Characteristic	Overall, N = 100[1]	CKD, N = 33[1]	Non-CKD, N = 67[1]	p - value[2]
Age (years)	61.7 ± 11.8	66.6 ± 11.2	59.2 ± 11.4	**0.003**
Sex				0.3
Male	62 (62.0%)	23 (69.7%)	39 (58.2%)	
Female	38 (38.0%)	10 (30.3%)	28 (41.8%)	
Weight (kg)	67.8 ± 9.2	66.1 ± 9.1	68.6 ± 9.2	0.2
Exposure to smoking	11 (11.0%)	2 (6.1%)	9 (13.4%)	0.3
Causes of chronic renal failure	Diabetes	45 (45%)		
	Hypertension	38 (38%)		
	Obstructive uropathy	7 (7%)		
	Systemic lupus erythematosus	5 (5%)		
	Patient on hemodialysis	18 (18%)		
Co-morbidities				
Hypertension	69 (69.0%)	25 (75.8%)	44 (65.7%)	0.3
Diabetes	68 (68.0%)	24 (72.7%)	44 (65.7%)	0.5
Ischemic heart disease	18 (18.0%)	6 (18.2%)	12 (17.9%)	> 0.9
PCR (+)	86 (86.0%)	29 (87.9%)	57 (85.1%)	> 0.9
CT scan (+)	100 (100.0%)	33 (100%)	67 (100%)	
Lung involvement on CT	65 ± 11%	68 ± 18%	53 ± 15%	< 0.001
SpO_2 with O_2 supply	94 ± 10%	91 ± 17%	96 ± 03%	0.13
Severity of COVID-19				< 0.001
Moderate	27 (27.0%)	2 (6.1%)	25 (37.3%)	
Severe	60 (60.0%)	23 (69.7%)	37 (55.2%)	
Critical	13 (13.0%)	8 (24.2%)	5 (7.5%)	
Survival status				0.026
Survived	77 (77.0%)	21 (63.6%)	56 (83.6%)	
Died	23 (23.0%)	12 (36.4%)	11 (16.4%)	

[1]Mean ± SD; n (%), [2]Welch Two Sample t - test; Pearson's Chi-squared test; Fisher's exact test.

Table 2: Renal Manifestations and Incidence of Acute Kidney Injury (AKI) in Study Group Presents renal complications observed, including proteinuria, hematuria, and AKI stages based on KDIGO criteria

Characteristic	Overall, N = 100[1]	CKD, N = 33[1]	Non-CKD, N = 67[1]	p - value[2]
Proteinuria	44 (44.0%)	30 (90.9%)	25 (37.3%)	<0.001
Hematuria	23 (23.0%)	11 (33.3%)	12 (17.9%)	0.085
Pyuria	15 (15.0%)	8 (24.2%)	7 (10.4%)	0.081
Polyuria	4 (4.0%)	2 (6.1%)	2 (3.0%)	0.6
Oliguria	13 (13.0%)	8 (24.2%)	5 (7.5%)	0.027
Anuria	1 (1.0%)	1 (3.0%)	0 (0.0%)	0.3
Acute kidney injury	28 (28.0%)	15 (45.5%)	13 (19.4%)	0.006
KDIGO stage, N = 28				0.6
Stage I	16 (57.1%)	8 (53.3%)	8 (61.5%)	
Stage II	10 (35.7%)	5 (33.3%)	5 (38.5%)	
Stage III	2 (7.1%) all of them received hemodialysis	2 (13.3%)	0 (0.0%)	

[1]n (%), [2]Pearson's Chi-squared test; Fisher's exact test

Hemoglobin levels were lower in CKD patients, and their lymphocyte counts exhibited a trend towards reduction. Inflammatory markers such as serum ferritin were significantly higher in CKD patients, likely reflecting an underlying inflammatory state. Renal function tests provided significant insights, revealing substantially elevated blood urea and serum creatinine levels in CKD patients. Serum albumin was also significantly reduced in this group, (Table 3).

Upon discharge, blood urea levels were higher in CKD patients (104.1 ± 20.0 mg/dL) compared to non-CKD individuals (40.8 ± 32.2 mg/dL) with a p - value of 0.03. Serum creatinine levels also displayed notable differences, being markedly elevated in CKD patients (2.8 ± 2.4 mg/dL) compared to non-CKD individuals (0.9 ± 0.2 mg/dL), showing statistical significance ($p = 0.001$). However, no significant differences were noted in D-dimer levels between CKD and non-CKD groups ($p = 0.6$). In terms of ferritin levels, CKD patients had higher values (455.2 ± 208.5 µg/L) compared to non-CKD individuals (340.4 ± 273.7 µg/L), demonstrating statistical significance ($p < 0.001$) as was illustrated in Table 4.

In assessing the risk factors associated with Acute Kidney Injury (AKI), several key characteristics were investigated within the study population. The odds ratios (OR) and corresponding 95% confidence intervals (CI) were computed. Increasing age showed a significant association with AKI risk, with each unit increase in age yielding an odds ratio of 1.11 (95% CI: 1.06, 1.17; $p < 0.001$). Male sex as opposed to female exhibited a higher OR of 1.79 (95% CI: 0.71, 4.80; $p = 0.2$), although not statistically significant. Weight did not have a substantial impact on AKI risk, with an OR of 0.99 (95% CI: 0.94, 1.04; $p = 0.7$). History of smoking similarly demonstrated a low OR of 0.23 (95% CI: 0.01, 1.29; $p = 0.2$). Notably, the history of hypertension was significantly associated with a higher AKI risk, with an OR of 3.60 (95% CI: 1.23, 13.2; p =

Table 3: Viral Screening and Blood Biomarkers in CKD *vs.* Non-CKD Patients Highlights blood parameters such as complete blood count (CBC), inflammatory biomarkers, and renal function test results stratified by CKD status.

Characteristic	Overall, N = 100[1]	CKD, N = 33[1]	Non-CKD, N = 67[1]	*p* - value[2]
CBC				
WBC count	13.0 ± 4.9	13.1 ± 5.6	13.0 ± 4.5	> 0.9
Hemoglobin	10.4 ± 2.3	9.8 ± 2.1	10.7 ± 2.3	0.040
Lymphocyte	6.7 ± 42.9	3.4 ± 4.9	8.3 ± 52.4	0.5
Platelets count	256.1 ± 116.7	237.0 ± 114.7	265.6 ± 117.4	0.2
MCV	85.2 ± 41.4	77.8 ± 10.0	88.8 ± 49.8	0.087
Biomarkers				
C-reactive protein	60.4 ± 43.0	67.0 ± 46.4	57.1 ± 41.2	0.3
LDH	307.8 ± 128.3	326.8 ± 140.7	298.4 ± 121.8	0.3
D-dimer	279.5 ± 630.0	597.1 ± 965.1	123.0 ± 261.6	0.009
Random blood sugar	207.4 ± 103.4	186.4 ± 95.5	217.8 ± 106.3	0.14
Ferritin	725.4 ± 405.3	911.0 ± 525.1	634.0 ± 294.9	0.007
CPK	309.0 ± 168.7	273.5 ± 152.2	326.4 ± 174.7	0.12
Troponin (+)	23 (23.0%)	5 (15.2%)	18 (26.9%)	0.2
Renal function test				
Blood urea	155.2 ± 44	218.0 ± 75.6	52.5 ± 27.8	< 0.001
Serum creatinine	4.5 ± 3.3	7.5 ± 3.2	1.2 ± 0.22	< 0.001
Serum albumin	4.2 ± 0.9	3.1 ± 1.0	4.2 ± 0.8	0.005
Serum electrolyte				
Sodium	139.8 ± 8.3	141.5 ± 8.0	136.5 ± 8.0	0.004
Potassium	4.2 ± 0.9	5.1 ± 1.2	4.0 ± 0.9	< 0.001
Calcium	10.7 ± 8.6	8.1 ± 1.2	10.1 ± 5.8	0.053
Phosphate	8.3 ± 21.2	6.9 ± 2.5	8.1 ± 4.2	< 0.001

[1]n (%); Mean ± SD, [2]Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test. Normal reference lab values: C-reactive protein (CRP) < 10 mg/L, Lactate Dehydrogenase (LDH) 140-280 U/L, D-dimer < 0.5 µg/mL, Serum Ferritin 24-336 µg/L, WBC 4.5-11.0 × 10^9/L, lymphocyte count 1-4.8 × 10^9/L, Blood Urea 6-24 mg/dL, Serum Creatinine 0.7-1.3 mg/dL

Table 4: Renal Function, D-Dimer, and Serum Ferritin Levels at Hospital Discharge Shows renal function and blood biomarker values at hospital discharge among the survived group.

Characteristic	Overall, N = 77[1]	CKD, N = 21[1]	Non-CKD, N = 56[1]	*p* - value[2]
Blood urea	97.9 ± 30.1	104.1 ± 20.0	40.8 ± 32.2	0.03
Serum creatinine	1.1 ± 11.2	2.8 ± 2.4	0.9 ± 0.2	0.001
D-dimer	112.1 ± 250.1	159.3 ± 385.9	97.4 ± 194.6	0.6
Ferritin	447.7 ± 258.0	455.2 ± 208.5	340.4 ± 273.7	< 0.001

[1]Mean ± SD, [2]Welch Two Sample *t* - test

0.031). The presence of proteinuria was associated with a significantly increased risk (OR = 23.2) (95% CI: 7.15, 106; $p < 0.001$), and hematuria similarly indicated a significant risk with an OR of 15.4 (95% CI: 3.73, 40.05; $p < 0.001$) (Table 5).

Increasing age and male sex emerged as significant predictors of higher mortality risk, with elevated Odds Ratios (ORs) observed for increasing age and male sex. A history of hypertension displayed a significant association with a greater risk of death. In contrast, variables such as weight, smoking history, and diabetes did not exhibit statistically significant associations with mortality. The presence of proteinuria, hematuria, and the development of Acute Kidney Injury (AKI) emerged as strong indicators of heightened mortality risk (Table 6).

Table 5: Risk Factors Influencing the Development of Acute Kidney Injury (AKI) Lists variables associated with an increased risk of developing AKI, including age, hypertension, and proteinuria.

Characteristic	OR[1]	95% CI[1]	*p* - value
Age	1.11	1.06, 1.17	< 0.001
Male sex	1.79	0.71, 4.80	0.2
Weight	0.99	0.94, 1.04	0.7
History of smoking	0.23	0.01, 1.29	0.2
History of hypertension	3.60	1.23, 13.2	0.031
History of DM	2.76	1.00, 8.98	0.065
Proteinuria	23.2	7.15, 106	< 0.001
Hematuria	15.4	3.73, 40.05	< 0.001

[1]OR: Odds Ratio; CI: Confidence Interval

Table 6: Risk Factors Influencing Mortality in the Study Group Identifies clinical parameters linked to an increased risk of death, such as age, male sex and presence of AKI.

Characteristic	OR[1]	95% CI[1]	*p* - value
Age	1.15	1.08, 1.23	< 0.001
Male sex	3.76	1.27, 13.9	0.026
Weight	1.01	0.96, 1.06	0.7
History of smoking	0.30	0.02, 1.73	0.3
History of hypertension	3.81	1.17, 17.2	0.044
History of DM	2.71	0.91, 10.1	0.10
Proteinuria	24.7	6.52, 162	< 0.001
Hematuria	9.4	5.34, 18.45	< 0.001
Development of AKI	22.4	11.4, 90.3	< 0.001

[1]OR: Odds Ratio; CI: Confidence Interval

Discussion

It is important to note the observed high prevalence of males and older age groups among individuals affected by COVID-19 infection in this study. This finding aligns with previous studies conducted by Wang, et al. [13] and Huang, et al. [14] both of which similarly reported a pronounced impact of COVID-19 infection on males.

Furthermore, the elevated disease prevalence among older individuals can also be linked to reduced immunity and a heightened occurrence of concurrent health conditions, particularly diabetes and hypertension. This observation is consistent with findings reported by other sources [15].

We found that proteinuria and hematuria were present in 37.3%, 17.9% in the non-CKD group. Cheng, et al. [16] conducted a prospective cohort study involving 701 COVID-19 infected patients in Wuhan, reporting a prevalence of 43.9% for proteinuria and 26.7% for hematuria. Similarly, Hirsch, et al. [4], in a cohort of 646 patients from New York City, found a proteinuria prevalence of 42.1%. Pei, et al. [17] documented higher figures, reporting proteinuria at 65.8% and hematuria at 41.7% among 333 COVID-19 infected patients. In Saudi Arabia, Allemailem, et al. [18] conducted dipstick examinations on urine samples, revealing proteinuria in 53.9% and hematuria in 22.3% of cases. Vasist, et al. [19] identified positive proteinuria in 17.6% of 75 patients and hematuria in 9.15% of 39 patients. These studies collectively underscore the substantial variability in the prevalence of proteinuria and hematuria among COVID-19 infected patients across different populations and regions.

Regarding the incidence of AKI, it was to be 19.4% in the non-CKD group. In contrast to our study, the rates of acute kidney injury (AKI) reported in other studies vary significantly. Allemailem, et al. [18] found that 23.3% of patients without prior renal disease experienced AKI, while Vasist, et al. [19] reported an occurrence of 14.8%. Cheng, et al. [17], in their study of 701 patients from Wuhan, China, documented a lower AKI rate of 5.1%. This variation may be due to differences in patient demographics, co-morbidities, and disease severity. Notably, Cheng, et al. [16] reported a lower AKI rate, possibly due to fewer co-existing conditions such as diabetes and hypertension, along with a smaller proportion of critically ill patients in their cohort (only 13.4% were critically ill).

The findings from various studies provide consistent insights into the implications of acute kidney injury (AKI), proteinuria, and hematuria on COVID-19 outcomes. In the study by Allemailem, et al. [18], patients with AKI faced a significantly higher likelihood of mortality compared to those without AKI (OR, 14.2; p = 0.003). Similarly, Vasist, et al. [19] noted that patients with AKI, proteinuria, and/or hematuria were more prone to severe COVID-19 illness. Chaudhri, et al. [22] highlighted the adverse impact of proteinuria and hematuria on clinical outcomes among hospitalized COVID-19 infected patients, both at admission and during hospitalization. Cheng, et al. [16] also reached a similar conclusion, further underscoring the consistent association between renal manifestations and adverse clinical trajectories in the context of COVID-19. These collective findings emphasize the significance of renal parameters as valuable prognostic indicators and provide valuable insights for guiding patient care and management strategies.

In the present study, individuals with CKD exhibited higher sodium (141.5 ± 8.0 *vs.* 136.5 ± 8.0, p = 0.004) and potassium (5.1 ± 1.2 *vs.* 4.0 ± 0.9, $p < 0.001$) levels compared to those without CKD. Additionally, the phosphate levels were significantly elevated in the CKD group (6.9 ± 2.5 *vs.* 8.3 ± 21.2, $p < 0.001$). However, there was no statistically significant difference in calcium levels between the two groups (8.1 ± 1.2 in non-CKD *vs.* 10.7 ± 8.6 in CKD, p = 0.053). A similar finding was observed by Guttee, et al. [20].

Existing literature underscores the relationship between CKD, AKI, and COVID-19 outcomes and reached a similar conclusion to the current study findings; for example, Filev, et al. [21] noted that at admission, CKD patients exhibited significantly higher levels of D-dimer, creatinine, and urea compared to non-CKD patients. They found that 44% (31 out of 70) of CKD patients developed AKI, which emerged as a substantial risk factor for in-hospital mortality. Similarly, Gur, et al. [22] highlighted that CKD patients experienced more AKI events and required more renal replacement therapy during hospitalization compared to control cases.

A systematic review and meta-analysis by Cai, et al. [23] found that old age, male gender, hypertension, and diabetes were significant risk factors for AKI (p - value < 0.05). Krishnasamy, et al. [24] explored the pediatric perspective, revealing that children with CKD facing moderate-to-severe COVID-19 infection or in nephrotic syndrome relapse were at risk of severe complications, including profound AKI and increased mortality. These cumulative findings underscore the intricate relationship between CKD, AKI, and COVID-19 infection, shedding light on key risk factors and potential implications for patient care and management.

Limitations

Certain limitations should be acknowledged in this study. The sample size, though substantial, could still limit the generalizability of the findings to broader populations. Additionally, the study focused on hospitalized patients, potentially excluding milder cases, which could impact the comprehensiveness of the conclusions. Moreover, the study's observational nature prevents definitive causal inferences and necessitates cautious interpretation. Also, the study does not provide insights into the longer-term renal outcomes of COVID-19 infected patients beyond the scope of hospitalization. It is crucial to acknowledge that drug-induced Acute Kidney Injury (AKI) and AKI due to dehydration could not be excluded, which may limit the generalizability of the findings on the generalizability of the findings.

Conclusion

1. Age, gender, and co-morbidities like hypertension and diabetes were notable differentiators between CKD and non-CKD groups.
2. Severity of COVID-19 infection and survival status exhibited statistically significant variations between CKD and non-CKD individuals.
3. Renal indicators such as proteinuria, hematuria, and acute kidney injury (AKI) were significantly more prevalent in the CKD group.
4. Age, proteinuria, hematuria, and history of hypertension significant risk factors for the development of AKI.

Recommendation

Based on the study's findings, several recommendations can be proposed for clinical practice and future research.

Clinicians should be vigilant about assessing renal manifestations, particularly proteinuria, hematuria, and AKI, in COVID-19 infected patients, as these factors were strongly linked to mortality. 2- Further research employing prospective and controlled designs could provide more robust evidence on the causal relationships between these renal markers and patient outcomes. 3- Additionally,

investigations into potential interventions to mitigate the impact of these renal manifestations on patient outcomes could be the way for more effective therapeutic strategies in COVID-19 management.

Declaration section

Ethics approval and consent to participate: Ethical and scientific approval for the research was obtained from the Scientific Committee at the Department of [Subject], [Category], board for medical specialization. All procedures performed in the present study involving human participants were in accordance with institutional and national ethical standards and with the 1964 Declaration of Helsinki and its later amendments. Verbal consent was obtained from all patients before starting data collection and after explaining the aims of the study and assuring confidentiality.

Consent for publication: All authors have read and approved the final version of the manuscript and have agreed to its submission for publication. No patients' identifiable information was included in this manuscript. This manuscript has not been published elsewhere and is not under consideration for publication elsewhere.

Availability of data and material: The dataset used in this study will be made available upon request. Interested readers may contact the corresponding author to request access to the data. The data are available for non-commercial purposes only and are subject to certain limitations, including restrictions on redistribution and confidentiality concerns.

Authors' contributions

Dr. Jawad K. Manuti

- Conception of design of the work
- Critical revision of the article
- Final approval of the version to be published

Dr. Mohammed Abdul Kareem Abdi

- Data collection
- Drafting the article
- Data analysis and interpretation

Acknowledgement

We would like to express our deepest appreciation to the authors, patients, and medical professionals involved in this research, and hope this study encourages further research to reduce the global impact of COVID-19.

References

1. Battle D, Soler MJ, Sparks MA, Hiremath S, South AM, Welling PA, et al. Acute kidney injury in COVID-19: Emerging evidence of a distinct pathophysiology. J Am Soc Nephrol. 2020;31:1380–3. Available from: https://doi.org/10.1681/ASN.2020040419
2. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020;97:829–38. Available from: https://doi.org/10.1016/j.kint.2020.03.005
3. Wang M, Xiong H, Chen H, Li Q, Ruan XZ. Renal injury by SARS-CoV-2 infection: A systematic review. Kidney Dis. 2021;7:100–10. Available from: https://doi.org/10.1159/000512683
4. Hirsch JS, Ng JH, Ross DW, Sharma P, Shah HH, Barnett RL, et al. Acute kidney injury in patients hospitalized with COVID-19. Kidney Int. 2020;98:209–18. Available from: https://doi.org/10.1016/j.kint.2020.05.006
5. Abou-Ismail MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. Thromb Res. 2020;194:101-115. Available from: https://doi.org/10.1016/j.thromres.2020.06.029
6. Casanova AG, Vicente-Vicente L, Hernández-Sánchez MT, Prieto M, Rihuete MI, Ramis LM, et al. Urinary transferrin pre-emptively identifies the risk of renal damage posed by subclinical tubular alterations. Biomed Pharmacother. 2020;121:109684. Available from: https://doi.org/10.1016/j.biopha.2019.109684
7. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020;395:565–74. Available from: https://www.thelancet.com/article/S0140-6736(20)30251-8/fulltext
8. Chang C-H, Fan P-C, Kuo G, Lin Y-S, Tsai T-Y, Chang S-W, et al. Infection in advanced chronic kidney disease and subsequent adverse outcomes after dialysis initiation: A nationwide cohort study. Sci Rep. 2020;10:2938. Available from: https://doi.org/10.1038/s41598-020-59794-7
9. Banerjee D, Popoola J, Shah S, Ster IC, Quan V, Phanish M. COVID-19 infection in kidney transplant recipients. Kidney Int. 2020;97:1076–82. Available from: https://doi.org/10.1016/j.kint.2020.03.018
10. Yan Y, Yang Y, Wang F, Ren H, Zhang S, Shi X, et al. Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. BMJ Open Diabetes Res Care. 2020;8:e001343. Available from: https://doi.org/10.1136/bmjdrc-2020-001343
11. Chaudhri I, Moffitt R, Taub E, Annadi RR, Hoai M, Bolotova O, et al. Association of proteinuria and hematuria with acute kidney injury and mortality in hospitalized patients with COVID-19. Kidney Blood Press Res. 2020;45:1018–32. Available from: https://doi.org/10.1159/000511946
12. Kellum J, Lameire N, Aspelin P, Barsoum R. Kidney disease: Improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012;2:124–138. Available from: https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-AKI-Guideline-English.pdf
13. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323:1061. Available from: https://doi.org/10.1001/jama.2020.1585
14. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497–506. Available from: https://doi.org/10.1016/s0140-6736(20)30183-5
15. Meng Y, Wu P, Lu W, Liu K, Ma K, Huang L, et al. Sex-specific clinical characteristics and prognosis of coronavirus disease-19 infection in Wuhan, China: A retrospective study of 168 severe patients. PLoS Pathog. 2020;16:e1008520. Available from: https://doi.org/10.1371/journal.ppat.1008520
16. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020;97:829–38. Available from: https://doi.org/10.1016/j.kint.2020.03.005
17. Pei G, Zhang Z, Peng J, Liu L, Zhang C, Yu C, et al. Renal involvement and early prognosis in patients with COVID-19 pneumonia. J Am Soc

Nephrol. 2020;31:1157–65. Available from: https://doi.org/10.1681/ASN.2020030276

18. Allemailem KS, Almatroudi A, Khan AA, Rahmani AH, Almarshad IS, Alekezem FS, et al. Manifestations of renal system involvement in hospitalized patients with COVID-19 in Saudi Arabia. PLoS One. 2021;16:e0253036. Available from: https://doi.org/10.1371/journal.pone.0253036
19. Vasist P, Yousuff M. Renal manifestations of Covid-19 and its association with severity of disease in a tertiary care hospital of south India: A retrospective study. J Assoc Physicians India. 2022;70:11–2. Available from: https://pubmed.ncbi.nlm.nih.gov/35443441/
20. Guttee V, Nie Y, Wang Y, Ding X. Impact of abnormal serum electrolyte levels and acid-base disorders on clinical outcomes among maintenance hemodialysis patients. Scient Res. 2017;4(5):1–13. Available from: https://doi.org/10.4236/oalib.1103623
21. Filev R, Rostaing L, Lyubomirova M, Bogov B, Kalinov K, Svinarov D. COVID-19 infection in chronic kidney disease patients in Bulgaria: Risk factors for death and acute kidney injury. J Pers Med. 2022;12:1676. Available from: https://doi.org/10.3390/jpm12101676
22. Gur E, Levy D, Topaz G, Naser R, Wand O, Kitay-Cohen Y, et al. Disease severity and renal outcomes of patients with chronic kidney disease infected with COVID-19. Clin Exp Nephrol. 2022;26:445–52. Available from: https://doi.org/10.1007/s10157-022-02180-6
23. Cai X, Wu G, Zhang J, Yang L. Risk factors for acute kidney injury in adult patients with COVID-19: A systematic review and meta-analysis. Front Med (Lausanne). 2021;8. Available from: https://doi.org/10.3389/fmed.2021.719472
24. Krishnasamy S, Mantan M, Mishra K, Kapoor K, Brijwal M, Kumar M, et al. SARS-CoV-2 infection in children with chronic kidney disease. Pediatr Nephrol. 2022;37:849–57. Available from: https://doi.org/10.1007/s00467-021-05218-1