



## Factors Affecting Mortality in COVID-19 Patients with Pre-Existing Chronic Kidney Disease

### Abstract

The emergence of COVID-19 triggered a global health crisis, sparking concerns within the medical community about its interaction with chronic kidney disease (CKD) and the heightened vulnerability of individuals with compromised renal function to severe viral infection and mortality. This retrospective study encompassed all adult patients with laboratory-confirmed COVID-19 and pre-existing CKD admitted between May 2020 and May 2023. Their demographic data, relevant clinical parameters, and laboratory values were collected. Kaplan-Meier curve analysis and Log Rank test were employed to compare survival times between CKD patients and those developing acute kidney injury (AKI), while Cox regression analyses were conducted to pinpoint factors influencing the hazard of a fatal outcome. The study, involving 150 COVID-19 patient records with pre-existing CKD, revealed that male gender, advanced age, requirement for invasive ventilation, and elevated levels of inflammatory markers such as total leukocyte count, lactate dehydrogenase, C-reactive protein, D-dimer, and IL-6 significantly increased the risk of death. These findings underscore the necessity for tailored care and meticulous management in COVID-19 patients with coexisting CKD, emphasizing the importance of addressing factors such as gender, age, and inflammatory status to mitigate mortality risks effectively.

**Keywords:** COVID-19, Renal insufficiency, Chronic, Mortality, Acute kidney injury, Risk factors

### Introduction

The emergence of COVID-19, caused by the novel coronavirus SARS-CoV-2, has triggered a global health crisis since its identification in late 2019. While primarily recognized for respiratory symptoms, the impact of the virus extends across multiple organ systems. Among these, chronic kidney disease (CKD) has surfaced as a notable risk factor for severe COVID-19 outcomes. The interaction between COVID-19 and CKD has raised concerns, as individuals with compromised renal function may face increased vulnerability to severe viral infection, and mortality necessitates a thorough investigation to guide clinical management and public health strategies.

### Materials and Methods

All patients presenting with respiratory symptoms and confirmed COVID-19 through real-time polymerase chain reaction (RT-PCR) and having pre-existing

CKD between May 2020 and May 2023 were included in the study. Patients already on maintenance hemodialysis and those having chronic heart failure or liver failure were excluded. The study was approved by the Institutional Review Board at All India Institute of Medical Sciences, Patna, number AIIMS/PAT/IEC/2021/752, dated 29/09/2021.

### Results

Of the total 150 patients included, 114 (76%) were males. The mean (SD) age of the participants was 59.9 (13.8) years with a majority, i.e., 83 (55.3%) aged more than 60 years, followed by 63 (42%) belonging to the age group of 30–60 years. One hundred and thirty five (90%) of the patients had hypertension while 110 (73.3%) had diabetes mellitus. Among the study participants, only six (4%) had a severe COVID infection. Four (2.7%) had a previous history of renal transplantation. One hundred and twenty two (81.3%) of

Shyama Shyama<sup>1</sup>,  
Harsh Vardhan<sup>2</sup> ,  
Vishnu Shankar Ojha<sup>1</sup>,  
Ratnadeep Biswas<sup>1</sup> ,  
Shamshad Ahmad<sup>3</sup>,  
Amit Kumar<sup>4</sup>

<sup>1</sup>Department of General Medicine, All India Institute of Medical Sciences, <sup>2</sup>Department of Nephrology, Patna Medical College, Departments of <sup>3</sup>Community and Family Medicine, <sup>4</sup>Nephrology, All India Institute of Medical Sciences, Patna, Bihar, India.

### Corresponding author:

Vishnu Shankar Ojha,  
Department of General Medicine, All India Institute of Medical Sciences, Patna, Bihar, India. E-mail: vsojha12@gmail.com

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the patients required hemodialysis during their hospital stay, and 83 (55.3%) developed acute kidney injury (AKI).

**Table 1: Clinicodemographic details of the study participants (n = 150)**

Variable	Categories	n (%)
Gender	Male	114 (76)
	Female	36 (24)
Age	Less than 30 years	4 (2.7)
	30–60 years	63 (42)
	More than 60 years	83 (55.3)
Comorbidities	Hypertension	135 (90)
	Diabetes Mellitus	110 (73.3)
COVID-19 severity	Severe	6 (4)
	Nonsevere	146 (96)
History of renal transplantation	Yes	4 (2.7)
	No	146 (97.3)
Dialysis requirement	Required hemodialysis	122 (81.3)
	Did not require hemodialysis	28 (18.7)
AKI on CKD	Developed AKI	83 (55.3)
	Did not develop AKI	67 (44.7)
Outcome	Discharged	46 (30.7)
	Death	104 (69.3)

AKI: acute kidney injury, CKD: chronic kidney disease

Forty six (30.7%) of the participants survived and were subsequently discharged, while 104 (69.3%) died [Table 1].

On Kaplan–Meier Curve analysis, it was seen that the median survival time in patients who developed AKI was 11 (95% CI: 8.639–13.361) days while the median survival time in patients who did not develop AKI was 12 (95% CI: 6.637–17.363) days. Although visual inspection of the curves shows a steeper curve for the patients who developed AKI [Figure 1], the Log rank test revealed that there was no significant difference between the curves [Chi-square=1.098 (at 1 degree of freedom) and P=0.30].

Univariate cox regression analyses were carried out, and it was seen that male gender, age, requirement for invasive ventilation, increase in total leukocyte count (TLC), lactate dehydrogenase (LDH), C-reactive protein (CRP), D-dimer, and IL-6 levels significantly increased the hazard of death, while the number of total hemodialysis, number of conventional hemodialysis, lymphocytosis, and increased platelet count decreased the hazard of death [Table 2].

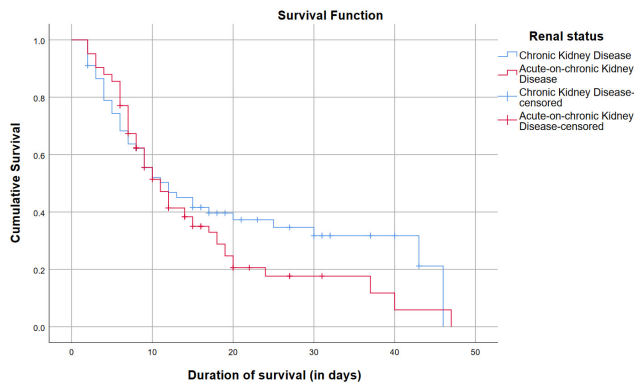
**Discussion**

In our study, there was a significant rise in D-dimer levels in nonsurvivors of COVID-19, consistent with findings reported by Tang N. *et al.*<sup>1</sup> This elevation may be attributed

**Table 2: Factors affecting mortality in COVID-19 patients with pre-existing chronic kidney disease**

Variable	Categories	Coefficient (B)	Standard Error (SE)	Hazard Ratio (HR)	95% Confidence Interval of HR		p-value*
					Lower bound	Upper bound	
Gender	Female	Ref.					
	Male	0.636	0.257	1.888	1.141	3.123	0.013*
Age (in years)		0.017	0.007	1.018	1.003	1.032	0.018*
History of renal transplantation	No	Ref.					
	Yes	-0.742	0.715	0.476	0.117	1.935	0.300
Dialysis status	No dialysis	Ref.					
	Dialysis performed	-0.076	0.251	0.927	0.567	1.516	0.762
Number of total HD		-0.217	0.044	0.805	0.739	0.877	<0.001*
Number of CHD		-0.233	0.050	0.792	0.719	0.873	<0.001*
Number of SLED		-0.133	0.238	0.875	0.513	1.493	0.625
Invasive ventilation requirement	No	Ref.					
	Yes	3.320	0.715	27.650	6.808	112.301	<0.001*
Total leukocyte count		0.020	0.010	1.020	1.001	1.040	0.042*
Lymphocytes (%)		-0.061	0.022	0.940	0.900	0.982	0.006*
Platelets		-0.003	0.001	0.997	0.994	0.999	0.019*
Albumin		-0.361	0.214	0.697	0.459	1.059	0.091
Lactate dehydrogenase		0.001	0.000	1.001	1.000	1.001	<0.001*
C-reactive protein		0.001	0.001	1.001	1.000	1.002	0.031*
D-dimer		0.019	0.009	1.019	1.002	1.037	0.028*
Procalcitonin		0.011	0.006	1.011	1.000	1.022	0.060
Serum ferritin		0.000	0.000	1.000	1.000	1.000	0.065
Serum creatinine		0.000	0.001	1.000	0.999	1.002	0.643
Interleukin 6 (IL-6)		0.000	0.000	1.000	1.000	1.001	0.012*

\*p-value less than 0.05 was considered significant., HD: Hemodialysis, CHD: Conventional hemodialysis, SLED: Sustained low efficiency dialysis Units of Total leukocyte and Platelet count: thousand cells/deciliter



**Figure 1:** Kaplan–Meier curves of patients with chronic kidney disease and acute-on-chronic kidney disease.

to disseminated intravascular coagulation (DIC) caused by sepsis. In sepsis, endothelial cells and monocytes release cytokines, causing free thrombin circulation and platelet activation, indicating activation of the common coagulation pathway.<sup>1</sup> The higher hazards ratio for invasive ventilation signified the critical status of patients necessitating invasive ventilation and increased mortality.

We observed that 55.3% of CKD patients with COVID-19 developed AKI, which may be attributed to the direct infection mechanism of the virus. SARS-CoV-2 enters cells through angiotensin converting enzyme (ACE 2), and as it circulates systemically, the kidneys—abundant in ACE 2—emerge as a potential site for viral entry, potentially causing AKI.<sup>2</sup>

In our study, older male participants faced a heightened mortality risk, potentially linked to higher ACE 2 levels in elderly males.<sup>3</sup> Notably, factors like smoking, not considered in our study, may also contribute to decreased male immunity, further escalating their risk of mortality. Age demonstrated a 1.018-fold hazard increase per year in CKD patients, which may be because of compromised viral control and prolonged proinflammatory responses.<sup>4</sup>

Interestingly, it was observed that lymphocytosis was a protective factor with a hazard ratio of 0.9,

while an increase in the TLC was found to increase the hazard of death. This may be due to the fact that lymphopenia has been frequently associated with severe COVID-19 infection.<sup>5</sup> Several potential mechanisms have been proposed to elucidate this connection. These mechanisms encompass direct lymphocyte inhibition, destruction of lymph nodes, the release of cytokines, suppression of lymphocytes due to lactic acidosis, and the attachment of the virus to the ACE 2 receptors on lymphocytes.<sup>6</sup>

## Conclusion

Factors such as male gender, advanced age, elevated inflammatory markers, and the necessity of invasive ventilation were associated with an increased risk of mortality in COVID-19 patients with coexisting CKD.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

## Conflicts of interest

There are no conflicts of interest.

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