

**ORIGINAL RESEARCH**

# Renal Consequences of COVID-19: A Tertiary Care Hospital Perspective

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**ABSTRACT**

**Introduction:** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing COVID-19, extends its impact beyond the respiratory system, often affecting the kidneys. Understanding the mechanisms of renal involvement is vital for effective management. This study explores how SARS-CoV-2 induces Acute Kidney Injury (AKI) and its implications, aiming to bridge gaps in Central data. **Material and Methods:** Conducted at NSCB Medical College, Jabalpur, from January 1, 2021, to June 30, 2022, this prospective study screened 2,830 COVID-19 patients. Ethical approval was obtained, and 200 AKI cases were identified based on RT-PCR confirmation. Inclusion criteria comprised age > 18 years and positive RT-PCR results. Data included demographic profiles, medical history, and various investigations, with follow-up after 90 days. **Results:** The cohort's mean age was  $59.38 \pm 15.2$  years, with a predominant male representation (74%). Incidence of AKI was 7.07%, revealing significant insights into COVID-19-associated renal complications. Proteinuria (55%) and hematuria (39.50%) were common on admission, persisting in survivors after 90 days (17.44% and 8.14%, respectively). Hemodialysis was administered in 2% of cases, with notable challenges. In-hospital mortality was 57%, with mortality associations identified for various factors, including inotropic support, oxygen requirement and inflammatory markers. **Conclusion:** This study underscores the prevalence of AKI in COVID-19 patients, emphasizing its association with increased mortality and persistent renal damage post-discharge. Regular follow-up for potential CKD development is crucial. Mortality risk factors, including inotropic support and heightened inflammatory markers, necessitate a multidisciplinary approach for immediate and long-term patient well-being. The findings contribute valuable insights into the complex interplay between COVID-19 and renal health, guiding future research and clinical management strategies.

**Key words:** COVID-19, Acute Kidney Injury, Proteinuria, Hematuria

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**INTRODUCTION**

SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2), the virus responsible for COVID-19, is not limited to causing respiratory issues; it can also have a significant impact on the kidneys, giving rise to renal complications. Understanding how the virus interacts with the kidneys and the resulting consequences is crucial for managing and treating COVID-19-related kidney problems.

SARS-CoV-2 can induce AKI through various mechanisms. Firstly, there are nonspecific causes, such as hypovolemia (reduced blood volume), nephrotoxic medications, excessive positive end-expiratory pressure (PEEP) in mechanical ventilation, and right heart failure. The virus's ability to enter podocytes (specialized cells in the kidney) via ACE2 and CD147 and proximal tubule cells through ACE2 is significant. This invasion can lead to acute proximal

tubular injury resulting in tubular necrosis and dysfunction of podocytes, potentially causing glomerular disorders like focal segmental glomerulosclerosis (FSGS). It can also leads to an unbalanced activation of the renin-angiotensin-aldosterone system (RAAS), an increase in proinflammatory cytokines and a procoagulant state are also contributors to AKI, thrombotic microangiopathy and various glomerulonephritis.(1–3)The virus has occasionally been detected in urine samples from COVID-19 patients, hinting at the possibility of a renal reservoir for the virus. However, the communicability of the virus through urine requires further investigation.(4,5) Sometimes drugs used in treatment of COVID-19 responsible for Acute kidney injury directly or indirectly.

Considering wide spectrum of renal manifestation of COVID-19 and lack of data regarding same in Central

study we conducted prospective study at our tertiary care centre.

## AIMS AND OBJECTIVES

### Primary Objective

To determine incidence of Acute Kidney Injury in COVID-19 patients at a tertiary center.

### Secondary Objective

To assess the effects of Acute Kidney Injury on: a) Proteinuria/Haematuria b) Progression to CKD after 90 days follow up c) Requirement of Haemodialysis d) Mortality

## MATERIAL AND METHODS

**Study Location:** This prospective observational study took place at NSCB Medical College, Jabalpur, Madhya Pradesh.

**Ethical Approval:** Approval from the institutional ethics committee at NSCB Medical College was secured before initiation, ensuring strict adherence to ethical standards and guidelines.

**Study Period:** The investigation spanned from January 1, 2021, to June 30, 2022, during which comprehensive data collection and analysis were conducted.

**Participant Screening:** A meticulous screening process was implemented, involving the evaluation of 2830 patients seeking medical attention at the tertiary care teaching hospital.

### Inclusion Criteria

Patients confirmed positive for COVID-19 by RT-PCR.

Age group included in the study > 18 years.

### Exclusion Criteria

Patients with negative RT-PCR results, even in cases where a high suspicion was present based on radiological imaging.

**Identification of Renal Manifestations:** Patients presenting with renal manifestations, including conditions such as Acute Kidney Injury (AKI) as defined by KDIGO, hematuria, or proteinuria, were identified among the screened individuals. A total of 200 patients met these criteria.

**Informed Consent:** Prior to inclusion, informed consent was obtained either from the patients or their relatives. Follow-up with the 200 eligible patients was conducted telephonically after 3 months, and the required data were collected.

**Data Collection at Enrollment:** Demographic data, medical history, and a battery of investigations, including RT-PCR for COVID-19, complete blood count, renal function test, liver function test, urine

routine and microscopic examination, inflammatory markers (D-Dimer, Serum Ferritin, Serum LDH, C Reactive Protein), chest X-ray (PA view), and ultrasound of the KUB region, were collected at the time of patient enrollment.

**Management of Patients:** Patients were managed according to the ICMR PROTOCOL FOR COVID-19.

**Data Analysis:** All data were meticulously entered into an Excel Spreadsheet, and a descriptive analysis of demographic and clinical profiles was performed using mean, range, and cumulative frequency as a percentage.

## RESULTS

### Demographic Profile

In the cohort of 200 COVID-19 positive patients with Acute Kidney Injury (AKI) enrolled in this study, the age distribution revealed notable patterns. A substantial portion, specifically 28.50%, fell within the age group of 61-70 years, with 75% of the total population being above 50 years. The age spectrum of the entire population (n=200) ranged from a minimum of 20 years to a maximum of 87 years, demonstrating a diverse demographic. The mean age was calculated at  $59.38 \pm 15.2$  years.

Gender distribution among the AKI patients exhibited a predominance of males, constituting 74.00% (148 patients), while females accounted for 26.00% (52 patients). (Table 1)

### Primary Objective

In our study, we screened 2,830 COVID-19 patients to specifically identify cases of Acute Kidney Injury (AKI). Following a comprehensive examination, we identified 200 cases of AKI, resulting in an overall incidence rate of 7.07%. This finding provides important insights into the prevalence of AKI within our studied group, offering valuable information about kidney health in the context of COVID-19.

### Secondary Objectives

#### Proteinuria

Proteinuria was observed in 110 study patients (55%) upon admission, with 1+ proteinuria being the most prevalent. Of these, 65 subjects exhibited simultaneous hematuria. Upon reassessment after 90 days, using the Dip-stick Method, 15 patients (17.44%) among 86 survivors still showed urine protein loss. Among these, 5 patients presented with both proteinuria and hematuria, while 10 patients manifested proteinuria alone.

#### Hematuria

At admission, 79 study patients (39.50%) displayed hematuria, primarily 1+. Additionally, 65 subjects presented with hematuria concurrent with proteinuria, while only 14 exhibited hematuria alone. After 90

days, among 86 survivors, 7 patients (8.14%) continued to show urine blood loss. Of these, 5 patients displayed both proteinuria and hematuria, while 2 patients exhibited hematuria alone.

### Dialysis Modality

Hemodialysis was the chosen method for renal replacement therapy in our study. Notably, alternative methods such as peritoneal dialysis and continuous renal replacement therapy (CRRT) were not utilized at our center.

**Implementation and Outcomes:** Among our study participants, 4 subjects (2%) received timely hemodialysis. Unfortunately, two of these patients faced in-hospital mortality, while the remaining two survived and underwent a 30-day follow-up. Impressively, both survivors exhibited complete recovery, reflected in serum creatinine values of 0.85 and 0.76 mg/dl, respectively, with no evidence of protein or red blood cell loss.

### Challenges in Hemodialysis Implementation

Despite recommendations for hemodialysis in 8 additional subjects, the procedure could not be carried out due to high doses of dual inotropic support (both nor-adrenaline and dopamine). Regrettably, these individuals succumbed to their illnesses. Additionally, 4 subjects relying on BiPAP support experienced deterioration and passed away before transitioning to hemodialysis.

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### Mortality

In-hospital mortality affected 114 patients (57%), while 83 patients were discharged (41.50%), and 3 patients (1.50%) left against medical advice. Age-specific analysis revealed the highest mortality (50.88%) in the age group of 61 to 70 years. Among the deceased, 75.43% were males, and 24.56% were females. Significant associations with mortality were identified for inotropic support, oxygen requirement, BiPAP support, synchronized intermittent mechanical ventilation, D-Dimer, LDH, CRP, and GGT, with p-values <0.05.(Table2) These findings underscore the multifaceted clinical considerations influencing outcomes in COVID-19 patients with AKI.

## DISCUSSION

**Gender Disparity:** Our findings revealed a substantial gender disparity among the studied population, with 74% (148 patients) being males and 26% (52 patients) females. This aligns with similar observations in regional and international studies, such as those conducted by Sindhu et al (6) in South India (81.6% males), Lumlertgul et al (7) in London (70% male subjects), and Fisher et al (8) in New York, all underscoring a male predominance in COVID-19 cases.(Table 3)

**Age Dynamics:** The mean age at presentation in our study was  $59.38 \pm 15.2$  years, indicating a notable prevalence of Acute Kidney Injury (AKI) among older COVID-19-positive patients. This finding resonates with other Indian studies, reinforcing the association between age and AKI manifestation in the context of COVID-19.

Our primary objective was to determine the incidence of Acute Kidney Injury (AKI) in COVID-19 positive patients admitted to our tertiary care center between January 1, 2021, and June 31, 2022. Among the 2,830 subjects screened in our study, 200 patients were identified with AKI, resulting in a calculated total incidence of 7.07%. This finding aligns with a study conducted in South India by Sindhu et al (18) in 2020, where 7.2% incidence of AKI was reported among 2650 hospitalized patients. However, our study contrasts with the work of Sundaram et al (19) in South India, which reported a higher incidence of 28.2%, possibly attributed to the smaller sample size (n=110) in that study and also that AKI incidence was among the patients with urinary abnormalities. In North India, Sharma et al's(9) study on 3010 patients observed a higher AKI incidence of 31.5%. International comparisons reveal variations. Studies in the United States by Chan et al(10), Hirsch et al (11), and Fischer et al (8) demonstrated even higher rates of AKI incidence, ranging from 36.6% to 56.9%.(Table 3) In the United Kingdom, studies by Kolhe et al ((12)and Lumlertgul et al (7)reported disparate incidences of 36.2% and 76.7%, respectively. The differences in these UK studies, which included 4,759 and 313 patients, may contribute to the variance from our findings. Notably, these Western studies incorporated chronic kidney disease patients, a group excluded from our study. Furthermore, the use of KDIGO criteria for AKI definition was consistent across all Western studies. Beyond methodological disparities, genetic factors, race, and ethnicity might influence AKI susceptibility, potentially explaining the consistently high incidences observed in Western studies.

Among the study subjects diagnosed with Acute Kidney Injury (AKI), an assessment of proteinuria and hematuria was conducted using the dip-stick method. On admission, 55% of AKI patients exhibited proteinuria, and 39.50% had hematuria. The most prevalent finding was 1+ proteinuria, observed in 26% of AKI patients, while 1+ hematuria was the most common, noted in 22.50% of AKI patients. These findings align with similar Indian studies, such as Bansode et al (13), reporting proteinuria and hematuria incidences of 66% and 41%, respectively, and Sampathkumar et al (14) with incidences of 46% and 34%, respectively. However, Vashisht and Yousuf (15) found lower incidences of proteinuria (17.6%) and hematuria (9.15%). In a New York study by Chan et al (10), a notably high percentage of AKI patients, 84%, exhibited proteinuria, and 81% had hematuria. A systematic review by Raina et al (16) reported an

overall incidence of proteinuria and hematuria in AKI patients as 52.47% and 35.89%, respectively.

Among the 86 survivors in our study, follow-up after discharge revealed 17.44% continued to have urine protein loss, and 8.14% continued to have hematuria after 90 days, indicative of progression to Chronic Kidney Disease (CKD). Among them, 5 patients showed both proteinuria and hematuria, 10 patients showed proteinuria alone, and 2 patients showed hematuria alone. For 69 patients with available serum creatinine data, levels remained within normal limits.

Comparatively, studies by Bansode et al (13) and Sharma et al (9) in India reported CKD progression rates of 49% and 30.3%, respectively, after 90 days follow-up. In the Western context, Lumlertgul et al (7) demonstrated that 16.5% of AKI survivors developed CKD (eGFR < 60 ml/min/1.73 m<sup>2</sup>) after 90 days of follow-up. Our findings contribute to the understanding of AKI's lasting impact on renal function, emphasizing the importance of extended monitoring for potential CKD progression.

Within our study cohort of 200 subjects, 4 patients (2%) required hemodialysis as part of their treatment. Of these, 2 patients experienced in-hospital mortality, while the remaining 2 were discharged and followed up 90 days later, demonstrating complete recovery with serum creatinine values of 0.85 and 0.76 mg/dl, respectively. Notably, 8 additional subjects were advised hemodialysis but could not undergo the procedure due to the reasons detailed above. Comparisons with other studies provide insights into the variability in hemodialysis requirements among COVID-19 patients with AKI. Mogga et al (17) reported a lower dialysis requirement of 0.7%, while Banerjee et al (18) documented a 3.5% requirement. In contrast, higher rates were observed in studies by Bansode et al (12) and Sampathkumar et al (14), reporting requirements of 40.5% and 23%, respectively, showcasing the diversity in clinical presentations.

Internationally, Western studies demonstrated elevated hemodialysis needs. Hirsch et al (11) reported a requirement of 14.3% among admitted AKI cases, while Lumlertgul et al (7) indicated that 32% of AKI patients needed hemodialysis. A systematic review by Raina et al (16), encompassing 60 studies, revealed a hemodialysis requirement in 39.04% of AKI patients with COVID-19. These varying rates may stem from differences in patient demographics, comorbidities, healthcare infrastructure, and the severity of COVID-19 cases across different regions.

Within our study encompassing 200 COVID-19 patients with Acute Kidney Injury (AKI), a significant portion, 57%, experienced in-hospital mortality. This rate aligns with mortality findings in other Indian studies, where Bansode et al (13) reported a mortality rate of 55.85%, Sampathkumar et al (14) noted 44%, and Sharma et al (9) recorded 42.3%. Divergent mortality rates were observed in studies conducted by Sindhu et al (6) and Sundaram et al (5), where mortality rates were 22.1% and 24.5%, respectively. Sindhu et al's (6) study demonstrated a particularly high ICU mortality of 74.5%, emphasizing the severity of cases in the intensive care setting. Sundaram et al's (19) lower mortality rate could be attributed to the smaller sample size (n=110) used in the study. In Western studies, mortality rates were comparable to our findings. Chan et al (21), Raina et al (16), and Kolhe et al (12) reported mortality rates of 50%, 54.24%, and 60.5%, respectively. Conversely, Hirsch et al (11) and Fisher et al (8) from New York, U.S.A., demonstrated lower mortality rates of 35% and 33.7%, respectively. The discrepancy may be linked to larger sample sizes (5449 and 3345 patients) in the U.S. studies, the use of continuous renal replacement therapy (CRRT) for hemodialysis in unstable patients (not employed in our study due to non-availability), and variations in genetic factors, race, and ethnicity.

**Table 1-Baseline characteristics of hospitalised COVID-19 patients with AKI**

Baseline Lab Parameter	Mean ± SD
Hemoglobin (gm/dl)	12.57 ± 2.36
Total Leucocyte Count (per cubic mm)	11439.8 ± 6100.15
Serum urea(mg/dL)	80.21 ± 57.98
Serum creatinine(mg/dL)	2.2 ± 0.7
SGPT (U/L)	63.28 ± 92.35
SGOT (U/L)	111.04 ± 297.49
Total bilirubin(mg/dL)	0.89 ± 0.61
Total protein(g/dL)	6.75 ± 0.78
Albumin(g/dL)	3.56 ± 0.52
Globulin(g/dL)	3.19 ± 0.62
Serum sodium(mEq/L)	139.03 ± 7.49
Serum potassium(mEq/L)	4.71 ± 0.85
D dimer(mcg/mL)	4.54 ± 7.31
LDH(U/L)	811.92 ± 412.86
Ferritin(ng/mL)	488.88 ± 419.94
CRP(mg/L)	67.16 ± 76.55

**Table 2-Comparison among survivors and non-survivors among Study cohort**

Parameters	Non survivors(n=114)	Survivors(n=86)	Total	P value
Age	59.5	59	-	0.843‡
Male: Female	3.07	2.58	-	0.593†
Inotropic support	18 (100%)	0 (0%)	18 (100%)	<.0001*
Hemodialysis	2 (50%)	2 (50%)	4 (100%)	1*
Inj. Remedesivir	31 (57.41%)	23 (42.59%)	54 (100%)	0.944†
Diabetes mellitus	31 (67.39%)	15 (32.61%)	46 (100%)	0.105†
Hypertension	21 (51.22%)	20 (48.78%)	41 (100%)	0.402†
Patients on Room Air	5 (12.20%)	36 (87.80%)	41 (100%)	<.0001†
Oxygen support required	109 (68.55%)	50 (31.45%)	159 (100%)	<.0001†
BiPaP	32 (78.05%)	9 (21.95%)	41 (100%)	0.002†
SIMV	21 (100%)	0 (0%)	21 (100%)	<.0001*
NRM	31 (56.36%)	24 (43.64%)	55 (100%)	0.911†
HFNC	8 (88.89%)	1 (11.11%)	9 (100%)	0.081*
MASK	15 (48.39%)	16 (51.61%)	31 (100%)	0.292†
T-PIECE	2 (100%)	0 (0%)	2 (100%)	0.507*
Inflammatory markers				
D dimer (mcg/mL)	5.59 ± 7.57	3.19 ± 6.8	4.54 ± 7.31	0.0001§
LDH(U/L)	939.45 ± 448.75	634.81 ± 273.92	811.92 ± 412.86	<.0001‡
Ferritin(ng/mL)	472.6 ± 375.27	512.3 ± 479.5	488.88 ± 419.94	0.585‡
CRP(mg/L)	86.09 ± 83.06	41.73 ± 58.28	67.16 ± 76.55	<.0001§

† Chi square test; \* Fisher's exact test; ‡ Independent t test; § Mann Whitney test

**Table 3 -Comparison of renal profile and outcome among different studies**

Name of Study	Chan et al(10)	Fischer et al(8)	Hirch et al(11)	Sindhu et al(6)	Sundaram et al(5)	Sharma et al(9)	Our study
Incidence of AKI	46%	56.9%	36.6%	7.2%	28.2%	31.5%	7.07%
No of patients Screened	3993	3345	5449	2650	110	3010	2830
M:F Ratio	1.5	1.34	1.76	4.42	2.67	2.9	2.85
Mean Age	71	67.1	69	62.6	61.2	59	59.38
Associated with Diabetes	31%	29.9%	41.6%	72.1%	52.7%	50.4%	23%
Associated with Hypertension	45%	-	64.8%	66.8%	47.3%	52%	20.5%
Hemodialysis Requirement	19%	8.61%	14.3%	4.2%	6.36%	18.7%	2%
Proteinuria on admission	84%	62.43%	42.1%	38.7%	58.1%	76%	55%
Microscopic Hematuria on admission	81%		46.1%	8.4%	32.3%	67%	39.5%
Mortality	50%	33.7%	34.8%	22.1%	24.5%	42.3%	57%
Mode of Dialysis	-	HD,CRR T,PIRRT	HD,CRR T	SLED,H D	CRRT	-	HD,SLE D

## CONCLUSION

AKI is prevalent in COVID-19 hospitalized patients, elevating mortality risk. Residual kidney damage after three months post-discharge raises concerns, prompting nephrologists to advocate regular follow-up for potential CKD development. Mortality risk factors in AKI patients encompass inotropic support, oxygen reliance, and heightened inflammatory markers. Survivors often exhibit acute kidney disease at discharge, emphasizing the lasting impact. This underscores the imperative for vigilant post-discharge monitoring and comprehensive care to address persistent renal issues. The study underscores the critical link between AKI and COVID-19 outcomes, necessitating a proactive and multidisciplinary

approach for both immediate and long-term patient well-being.

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