

Acute Kidney Injury in COVID-19 Pneumonia Patients Admitted to the Intensive Care Unit

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ABSTRACT

This retrospective study was conducted at the Izmir Tepecik Training and Research Hospital from January 2020 to December 2021. It aimed to determine acute kidney injury (AKI) frequency and associated factors in critically ill COVID-19 patients. Out of 177 patients, 49.7% developed AKI, with an average onset of 7.63 days. AKI stages varied, and progression occurred in 27 patients within 48 hours. ICU and hospital mortality rates were significantly higher in AKI patients (86.4% and 92%, respectively) compared to non-AKI patients (19.1% and 22.5%). The study highlights age, sequential organ failure assessment (SOFA) score, and nephrotoxic agent presence as significant factors influencing AKI development in COVID-19 patients.

Key Words: Critical care unit, COVID-19, Acute kidney failure.

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The outbreak of the COVID-19 pandemic, attributed to the novel coronavirus SARS-CoV-2, has exerted an extensive global impact, precipitating a notable surge in morbidity and mortality rates worldwide. Among the manifold complications associated with COVID-19, acute kidney injury (AKI) has emerged as a significant clinical concern, with reported incidence rates varying broadly from 0.5 to 46%.¹ Older age, male gender, comorbidities, and exposure to nephrotoxic medications are risk factors that have been identified in COVID-19 patients, including contributing to AKI's development. AKI has been associated with a significantly elevated risk of mortality and protracted hospitalisation periods.² The primary objective is understanding AKI's frequency and risk factors in COVID-19.

This single-centre retrospective cohort study investigated ICU admissions from 1st January 2020 to 31st December 2021. Inclusion criteria involved positive PCR testing, while exclusion criteria included patients under 18 years of age, chronic kidney disease, or ICU stays <48 hours. Ethical clearance was granted by the Local Ethics Committee and the Ministry of Health (ERC no: 2023/05-03). Data on demographics, disease severity, and laboratory findings were recorded.

Nephrotoxic drugs administered at admission were investigated, including intravenous contrast agents, ticlopidine, various antibiotics (colistins, vancomycin, and aminoglycosides, etc.), renin-angiotensin system blockers, diuretics, proton pump inhibitors, H2 blockers, statins, fluoxetine, calcineurin inhibitors, steroids, NSAIDs, and clopidogrel were examined for potential nephrotoxicity.³

Laboratory parameters such as whole blood count, biochemistry, and arterial blood gas were documented. AKI was defined per 2012 KDIGO criteria: A 0.3 mg/dl serum creatinine increase within 48 hours or 1.5 times the reference value within seven days. Stage 1 was 1.5-1.9 times, Stage 2 was 2.0-2.9 times, and Stage 3 was a 3 times or more increase or creatinine exceeding 4 mg/dl; renal replacement therapy patients were Stage 3. The resolution was AKI profile improvement within seven days; recovery in 48 hours was transient AKI, and 2-7 days was persistent AKI. AKI not resolving in seven days was termed acute kidney disease (AKD). AKI progression occurred with a stage increase within 48 hours. Renal recovery had a creatinine value less than 1.25 times the baseline.⁴

The collected data underwent statistical analysis using SPSS version 22. Descriptive statistics presented means, standard deviations, medians, and interquartile ranges for continuous variables. Student's t-tests or Mann-Whitney U tests based on data distribution assessed these variables. Categorical variables were analysed with Chi-square or Fisher's exact test, expressed in counts and percentages. Fisher's exact test was used if the Chi-square distribution was not feasible (more than 20% expected counts <5 or frequencies <1). Variables with

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potential associations ($p < 0.10$) post-univariate analysis underwent logistic regression analysis, presenting adjusted odds ratios with 95% confidence intervals. The significance threshold was set at $p < 0.05$.

A total of 200 patients were enrolled in the study. Fifteen were excluded due to a history of renal insufficiency, and another eight were excluded because their ICU stay was less than 48 hours. Of the remaining 177 patients, 88 (or approximately 49.7% of this cohort) developed AKI during the observation period. The average time from ICU admission to AKI onset was 7.63 ± 1.5 days.

Table I presents a comparative analysis of baseline characteristics, admission laboratory parameters, and clinical indicators between critically ill COVID-19 patients who developed AKI and those who did not.

Table I: Comparison of basal characteristics, laboratory parameters at admission, and clinical parameters among critically ill COVID-19 patients with and without AKI.

Variables	Patients with AKI n = 88 (49.7 %)	Patients without AKI n = 89 (50.3 %)	p-value
Age (year)*	70.80 ± 15.33	60.51 ± 16.87	<0.001 ^a
Gender (female)***	35 (44.9%)	43 (55.1%)	0.252 ^a
Baseline creatinine (mg/dl)**	1 (0.36)	0.9 (0.14)	0.143 ^a
APACHE II score*	18.13 ± 7.61	13.00 ± 6.74	<0.001 ^a
SOFA score**	6 (3)	4 (2)	<0.001 ^a
Need for IMV at admission***	12 (85.7%)	2 (14.3%)	<0.001 ^a
Mean arterial pressure*	71.95 ± 11.15	73.35 ± 8.85	0.380 ^a
Comorbidities***			
Obesity	3 (50%)	3 (50%)	>0.99 ^b
Hypertension	47 (59.5%)	32 (40.5%)	0.02 ^a
Coronary heart disease	26 (63.4%)	15 (36.6%)	0.04 ^a
CHF	6 (66.7%)	3 (33.3%)	0.330 ^b
Chronic AF	3 (50%)	3 (50%)	>0.99 ^b
Diabetes mellitus	25 (51%)	24 (49%)	0.99 ^a
Cerebrovascular disease	8 (50%)	8 (50%)	0.98 ^a
Asthma	7 (36.4%)	4 (63.6%)	0.34 ^a
COPD	7 (77.8%)	2 (22.2%)	0.099 ^b
Peripheral artery disease	1	0	0.497 ^b
Need for vasopressors at admission***	12 (85.7%)	2 (14.3%)	0.01 ^a
Nephrotoxic agent during ICU stay***	58 (73.4%)	21 (26.6%)	<0.01 ^a
PaO ₂ , mmHg**	60.5 (15)	65 (19)	0.134 ^a
PCO ₂ , mmHg*	38.33 ± 15.13	37.75 ± 11.25	0.83 ^a
HCO ₃ ⁻ , mmol/L*	23.99 ± 10.30	25.05 ± 5.68	0.54 ^a
Lactate, mmol/L*	1.83 ± 0.94	2.25 ± 2.78	0.37 ^a
FiO ₂ * (%)	70.98 ± 18.27	60.19 ± 22.94	0.001 ^a
PaO ₂ /FiO ₂ **	93.65 ± 58.84	107.5 ± 100.1	0.003 ^a
Haemoglobin, g/dl*	12.09 ± 2.03	12.46 ± 1.82	0.265 ^a
Platelet, 10 ³ /ml*	237.42 ± 103.75	249.98 ± 100.55	0.425 ^a
White blood cell, 10 ³ /ml**	9.600 (5.500)	9.750 (6.500)	0.179 ^a
Neutrophil, 10 ³ /ml**	8.500 (5.650)	8.150 (5.600)	0.111 ^a
Lymphocyte, 10 ³ /ml**	0.600 (0.525)	0.600 (0.675)	0.257 ^a
Albumin, g/dl**	2.95 (0.63)	3.0 (0.50)	0.732 ^a
ALT, IU/L** birim	33.00 (29.25)	28.00 (33.75)	0.622 ^a
AST, IU/L** birim	41.50 (36.25)	36.50 (26.25)	0.227 ^a
ICU mortality** (within AKI)	76 (86.4)	17 (19.1)	<0.001 ^a
Hospital mortality*** (within AKI)	81 (92.0)	20 (22.5)	<0.001 ^a

*Mean (standard deviation) Student's t-test. **Median (interquartile range) Mann-Whitney. ***Number (%) Chi-square. ^a Chi-square test. ^b Fisher's exact test.

Table II: Clinical outcome of AKI.

	Number of patients (%)
AKI	88
Stage 1 / Stage 2 / Stage 3	55 (62.5%) / 25 (28.41%) / 8 (9.09%)
Recovery from AKI	21 (23.87%)
Transient AKI	19 (21.59%)
Persistent AKI	2 (2.27%)
AKI progression	27 (30.68%)
From Stage 1 to 2 / from Stage 2 to 3	25 (28.41%) / 2 (2.27%)
AKD	19 (21.59%)
Second AKI	8 (9.09%)
After resolution of AKI / after resolution of AKD	7 (7.95%) / 1 (1.14%)

Upon conducting a logistic regression analysis, the sequential organ failure assessment (SOFA) score and exposure to nephrotoxic agents emerged as significant risk factors for AKI. The logistic regression analysis identified the SOFA score as the second considerable determinant of AKI. When subjected to a receiver operating characteristic (ROC) analysis for the SOFA score, the optimal cut-off value was 4.5. The corresponding area under the curve (AUC) was 0.729, with a sensitivity of 0.71 and a specificity of 0.62.

Out of the 177 patients, 101 were observed to have died. Intensive care unit (ICU) mortality was observed in 93 patients, and an additional eight deaths occurred post-ICU discharge (hospital mortality). The median time to mortality was 14 days, ranging from a minimum of 1 day to a maximum of 141 days.

In the AKI-developing cohort, 76 individuals (86.4%) died in the ICU, resulting in 81 hospital deaths (92%). In contrast, the non-AKI group recorded 17 ICU deaths (19.1%) and a total of 20 hospital deaths (22.5%, $p < 0.01$).

The incidence of AKI in COVID-19 patients has been a focus of investigation with varied rates reported in different studies. Advanced age, hypoxemia at admission, and the need for vasopressors were identified as potential risk factors, consistent with previous researches.⁵ Monitoring COVID-19 patients with high SOFA scores and exposure to nephrotoxic agents for AKI is crucial. Despite limitations such as the single-centre and retrospective design, the study emphasises the need for further research to comprehensively assess nephrotoxic agent exposure.

ETHICAL APPROVAL:

The study was approved by the Ethics Committee of the Izmir Tepecik Training and Research Hospital and the Ministry of Health of Turkiye (ERC no. 2023/05-03).

PATIENTS' CONSENT:

Informed consent was not sought for the present study because of its retrospective design.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

IKG: Design, acquisition and analysis of data, and writing of the manuscript.

YO: Revision of the manuscript.

AEO: Data collection.

SE: Revision and editing of the manuscript.

KR: Design and revision of the manuscript.

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