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Original article

Clinical characteristics and risk factors associated with acute kidney injury among patients hospitalized with primary COVID-19 infection

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Abstract

Background: Coronavirus disease 19 (COVID-19) primarily affects the respiratory system with symptoms ranging from mild to severe. In addition, acute kidney injury (AKI) is an important complication of COVID-19 that causes substantially high morbidity and mortality rates. During the COVID-19 pandemic, public healthcare in Thailand experienced many cases and complications thereof.

Objective: This study aimed to establish the incidence, clinical characteristics, independent risk factors of AKI, and mortality in patients hospitalized with COVID-19 with or without AKI.

Methods: This was a retrospective; observational study performed in Lerdsin Hospital from August 2021 to August 2022. A total of 576 patients who were hospitalized with a diagnosis of COVID-19 infection were analyzed. AKI was diagnosed based on the extended Kidney Disease Global Outcomes criteria. Clinical characteristics were compared between patients with COVID-19 with or without AKI. Furthermore, independent risk factors were reported using adjusted odds ratios (aORs).

Results: One hundred and forty-five patients with COVID-19 developed AKI. The AKI group exhibited a higher proportion of male, older patients, and a higher rate of pneumonia. The independent risk factors were male gender (aOR, 1.8; 95% confidence interval (CI): 1.2–3.0), age ≥ 60 years (aOR, 2.0; 95% CI: 1.2–3.5), chronic kidney disease (aOR, 5.5; 95% CI: 2.0–14.7), coronary artery disease (aOR, 3.3; 95% CI: 1.1–9.2), pneumonia (aOR, 4.0; 95% CI: 1.5–10.5), serum potassium ≥ 4.5 mEq/L (aOR, 2.3; 95% CI: 1.1–5.0), and serum bicarbonate < 22 mEq/L (aOR, 2.4; 95% CI: 1.3–4.3). Patients with a history of COVID-19 vaccination exhibited a reduced incidence of AKI (aOR, 0.5; 95% CI: 0.3–0.8).

Conclusion: The identified independent risk factors offered predictive potential for the development of AKI. Administration of the COVID-19 vaccine in patients with COVID-19 potentially protected them against AKI.

Keywords: Acute kidney injury, clinical characteristics, COVID-19, risk factors.

During the pandemic caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which resulted in coronavirus disease 2019 (COVID-19), Thailand was one of the first countries to report cases outside of China.[1, 2] Public healthcare systems faced substantial challenges, experiencing elevated rates of COVID-19 infection and its associated complications. Among these complications, acute kidney injury (AKI) was frequently observed, and several studies have demonstrated that COVID-19–associated AKI resulted in notably high mortality rates.[3–5] However, the incidence of AKI varied widely across different regions globally.[6] Previous studies have indicated that many patients hospitalized with COVID-19–associated AKI were discharged with either partial renal recovery or ongoing reliance on dialysis.[3, 4] Factors linked to the occurrence of AKI included COVID-19 severity, underlying comorbidities, advanced age, and the patient's gender. During the initial SARS-CoV-2 outbreak in China, single-center studies and meta-analyses reported an AKI incidence rate of 0.5%–29.0% among patients hospitalized with COVID-19.[7, 8] Hospitals in Europe and the US reported notably higher rates of AKI, with incidences ranging between 30.0% and 69.0%.[9, 10] In the United

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States, the in-hospital mortality rate for patients with COVID-19 and AKI was reported to be 35.0%–41.0%. Recent meta-analyses and large-scale observational studies indicated an AKI incidence rate of 28.0%–44.0%.[11–13] Furthermore, patients with COVID-19 admitted to intensive care units (ICUs) experienced an even higher rate of AKI (46.0%–77.0%), thus reflecting the severity of their condition.[12, 14, 15] The progression of AKI was also observed among patients who were severely ill with COVID-19, with a cohort study from the UK revealing that 36% of patients in the ICU progressed from no AKI or AKI stage 1 to AKI stages 2 or 3.[14] A considerable consequence of AKI in patients with COVID-19 was an increased risk of mortality, regardless of the AKI stage.[11, 15] Moreover, the mortality rates after discharge were notably higher for patients who did not recover from AKI prior to leaving the hospital.[14] The risk factors for conventional and COVID-19–related AKI overlap, including diabetes mellitus (DM), obesity, cardiovascular disease, and chronic kidney disease (CKD). [11] In addition, risk factors that contribute to the development of COVID-19–associated AKI have been linked to poor outcomes in these patients. Furthermore, recent studies have highlighted the relationship between COVID-19 infection and kidney involvement.[16–18] Previous autopsy reports have revealed evidence of collapsed glomeruli due to ischemia, proximal tubular damage, and aggregation of red blood cells in the peritubular vessels. The proposed mechanisms for AKI development in COVID-19 infection include inflammatory and immune responses, endothelial dysfunction, coagulation pathway activation, and direct viral invasion. In addition, theories regarding hypovolemia and the interplay between lung and kidney functions have been associated with AKI in severe cases of COVID-19 infection.[19] Moreover, factors such as hemodynamic instability, hypoxemia, hypercapnia, acid-base imbalances, inflammation, and neurohormonal effects have been implicated in inducing acute respiratory distress syndrome (ARDS) in patients with severe COVID-19. Given the uncertainty surrounding the risk factors that influence the development of AKI in COVID-19 infections, this study aimed to assess the specific risk factors for AKI among patients with COVID-19 who were admitted to Lerdsin Hospital, a tertiary care facility in Bangkok, Thailand.

Materials and methods

Study population

This retrospective observational study was performed at Lerdsin Hospital from August 2021 to August 2022. A total of 576 patients with a confirmed diagnosis of COVID-19 were included in the analysis. The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Lerdsin Hospital (study no. LH651024).

Inclusion criteria

Patients were included if they had a confirmed COVID-19 diagnosis via reverse transcriptase polymerase chain reaction testing conducted on nasopharyngeal swabs, were 18 years of age or older, and were admitted to Lerdsin Hospital between August 2021 and August 2022.

Exclusion criteria

Patients were excluded from the study if they were under 18 years of age or if they had pre-existing end-stage renal disease.

Data collection

Data was extracted from the hospital's inpatient medical records. The collected demographic information included age, gender, comorbidities, COVID-19 vaccination status, and the type of COVID-19 vaccine administered. Comorbidities were classified using the International Classification of Diseases, 9th and 10th revisions (ICD-9/10-CM). The clinical data gathered during admission included vital signs, body mass index, oxygen saturation levels, diagnosis of pneumonia, prescription of antiviral medications, immunosuppressive treatment, and discharge status. Finally, laboratory test results were documented, which included the levels of serum creatinine (sCr), electrolytes, C-reactive protein, and albumin, as well as a complete blood count.

Definitions and outcomes

This research investigated the clinical characteristics and risk factors associated with AKI in patients who were hospitalized with COVID-19. AKI was diagnosed based on the extended Kidney Disease Global Outcomes (eKDIGO) criteria.[20] The baseline sCr was determined using the lowest recorded sCr level within 12 months prior to hospital admission. In cases where baseline sCr data were not available,

the sCr levels at admission were used as the reference point. It is important to note that diagnostic criteria for AKI based on urine output were not utilized in this study.

Statistical analysis

Baseline characteristics were reported as mean ± standard deviation (SD) for normally distributed data and as median with the interquartile range (IQR) for non-normally distributed data. Categorical data were presented as frequency and percentage. The chi-square test was employed for intergroup comparisons, while independent sample *t*-tests were used to assess normally distributed independent variables. For non-normally distributed data, the Mann-Whitney *U* test was applied. Univariate testing was performed to identify covariates, which were subsequently analyzed using multivariable logistic regression to determine the impact of risk factors on the development of AKI and calculate the adjusted odds ratio (aOR). Missing data were not imputed. $P < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS Statistics for Windows (version 23.0, Chicago: SPSS Inc.).

Results

Baseline characteristics

A total of 576 patients were included in this study, of whom 145 developed AKI, while the remaining 431 did not. Notable differences were observed in the baseline characteristics between the AKI and non-AKI groups. The AKI group had a significantly older average age, a higher proportion of males, and a greater prevalence of pneumonia diagnoses compared to the non-AKI group, with respective values of 68.5 ± 15.0 *vs.* 57.3 ± 19.3 years, 58.6% *vs.* 40.1%, and 93.1% *vs.* 65.9%. The sCr levels, comprising baseline sCr, sCr at admission, and sCr at one week post-admission, were significantly elevated in the AKI group compared to the non-AKI group, with respective values of 1.2 (0.9, 1.6) *vs.* 0.8 (0.6, 0.9) mg/dL, 1.5 (1.2, 2.2) mg/dL *vs.* 0.8 (0.6, 0.9) mg/dL, and 1.3 (0.9, 1.9) *vs.* 0.8 (0.6, 1.1) mg/dL. Consequently, the estimated glomerular filtration rate (eGFR) for the baseline eGFR, eGFR at admission, and eGFR one week post-admission was significantly lower in the AKI compared to the non-AKI group, with respective values of 56.5 ± 25.5 *vs.* 91.4 ± 23.7 mL/min/1.73 m², 41.1 ± 22.2 *vs.* 91.2 ± 23.6 mL/min/1.73 m², and 52.8 ± 29.9 *vs.* 83.7 ± 27.7 mL/min/1.73 m². Moreover, comorbidities such as CKD, DM, hypertension, dyslipidemia , coronary artery disease (CAD), cerebrovascular disease (CVD), and cancer were significantly more prevalent in the AKI group. In addition, a lower COVID-19 vaccination rate was observed in the AKI group. Furthermore, the AKI group exhibited decreased oxygen saturation levels and lower rates of receiving steroid and immunosuppressant treatments. Moreover, patients in the AKI group exhibited lower total lymphocyte counts, serum albumin levels, and serum bicarbonate levels **(Table 1)**.

Independent risk factors and AKI

Independent risk factors of AKI in patients who were primarily hospitalized for COVID-19 infection were male gender (aOR, 1.8; 95% confidence interval (CI): 1.2–3.0), age ≥ 60 years (aOR, 2.0; 95% confidence index (CI): 1.2–3.5), CKD (aOR, 5.5; 95% CI: 2.0–14.7), CAD (aOR, 3.3; 95% CI: 1.1–9.2), pneumonia (aOR, 4.0; 95% CI: 1.5–10.5), serum potassium ≥ 4.5 mEq/L (aOR, 2.3; 95% CI: 1.1–5.0), and serum bicarbonate < 22 mEq/L (aOR, 2.4; 95% CI: 1.3–4.3). Patients with a history of COVID-19 vaccination were less likely to develop AKI (aOR, 0.45; 95% CI: 0.3–0.8) **(Table 2, Figure 1).** The overall incidence of mortality in patients with COVID-19 was 20.8%. In addition, the in-hospital mortality of COVID-19 patients with AKI was higher compared to those without AKI (40.7% *vs.* 14.2%, $P < 0.01$).

Discussion

This study evaluated the occurrence of AKI, its clinical features, associated independent risk factors, and mortality rates among patients who were hospitalized with COVID-19. Of the 576 patients with COVID-19 who were admitted to Lerdsin Hospital, 22.7% developed AKI. Previous research has demonstrated varied rates of AKI associated with COVID-19.[6] Early studies from China reported relatively low rates of AKI among hospitalized patients, ranging from 0.5% to 29.0%, with an average of 4.5%.[7, 8] However, recent meta-analyses and observational studies have reported higher rates of COVID-19–associated AKI, ranging from 30.0% to 69.0%, which exceeded the rate observed in this study.[9, 10] The development of AKI in patients with COVID-19 is often linked to higher mortality rates. For instance, one meta-analysis of 60 studies found a 54.2% mortality rate among patients with COVID-19 and AKI compared to an overall mortality rate of 19.5%.[21] Another meta-analysis reported a 47.0% mortality rate for patients

Table 1. Baseline characteristics

Characteristics	All, n = 576	AKI, n = 145	No AKI, n = 431	*P*-value
Age, year, mean (SD)	60.2 ± 19.0	68.5 ± 15.0	57.3 ± 19.3	< 0.01**
Male, n (%)	258 (44.8)	85 (58.6)	173 (40.1)	< 0.01**
Comorbidities, n (%)				
CKD	29 (5.0)	21 (14.5)	8 (1.9)	< 0.01**
CKD stage 1	0	0	0	
CKD stage 2	1 (3.4)	0	1 (12.5)	
CKD stage 3	19 (65.5)	13 (61.9)	6 (75.0)	
CKD stage 4	7 (24.1)	7 (33.3)	0	
CKD stage 5	2 (6.9)	1 (4.8)	1 (12.5)	
Diabetes	193 (33.5)	74 (51)	119 (27.6)	< 0.01**
Hypertension	285 (49.5)	99 (68.3)	186 (43.2)	< 0.01**
Dyslipidemia	156 (27.1)	49 (33.8)	107 (24.8)	0.03*
CAD	26 (4.5)	14 (9.7)	12 (2.8)	< 0.01**
CVD	78 (13.5)	32 (22.1)	46 (10.7)	< 0.01**
Psychological disorder	9 (1.6)	3 (2.1)	6 (1.4)	0.57
Cancer	20 (3.5)	11 (7.6)	9 (2.1)	< 0.01**
Chronic lung disease	16 (2.8)	4 (2.8)	12 (2.8)	0.98
COVID vaccine, n (%)	223 (38.7)	35 (24.1)	188 (43.6)	< 0.01**
Vital signs and measurement, mean (SD)				
Body temperature, ˚C	37.0 ± 0.8	37.1 ± 1.0	37.0 ± 0.8	0.08
Heart rate, beat per min	88.0 ± 18.0	89.0 ± 20.0	87.0 ± 17.0	0.50
Respiratory rate, per min	21.0 ± 2.0	22.0 ± 3.0	21.0 ± 2.0	0.01*
Systolic BP, mmHg	131.0 ± 21.0	136.0 ± 26	130.0 ± 19.0	< 0.01**
Diastolic BP, mmHg	78.0 ± 13.0	78.0 ± 15.0	78.0 ± 12.0	0.66
Oxygen saturation, (%)	94.0 ± 4.0	93.0 ± 4.0	94.0 ± 4.0	< 0.01**
BMI, kg/m^2	25 ± 6.0	24.9 ± 6	25.1 ± 6	0.73
COVID-19 pneumonia, n (%)	419 (72.7)	135 (93.1)	284 (65.9)	< 0.01**
Laboratory results				
Baseline sCr, mg/dL, median (IQR)	0.8 (0.7, 1.1) Missing = 7	1.2 (0.9, 1.6) 56.5 ± 25.5	0.75 (0.6, 0.9) Missing = 7	< 0.01**
Baseline eGFR, mL/min/1.73 m^2, mean (SD)	82.5 ± 28.5 Missing = 7		91.4 ± 23.7 Missing = 7	< 0.01**
sCr at admission, mg/dL, median (IQR)	0.8 (0.7, 1.2) Missing = 7	1.53 (1.2, 2.3)	0.75 (0.6, 0.9) Missing = 7	< 0.01**
eGFR at admission, mL/min/1.73 m^2, mean (SD)	78.5 ± 31.9 Missing = 7	41.1 ± 22.2	91.2 ± 23.6 Missing = 7	< 0.01**
sCr at one week of admission, mg/dL, median (IQR)	1.0 (0.8, 1.6)	1.3 (0.91, 1.94)	0.83 (0.6, 1.1)	< 0.01**
eGFR at one week of admission, mlL/min/1.73 m^2, mean (SD)	64.4 ± 32.7	52.8 ± 30.0	83.7 ± 27.7	< 0.01**
Hemoglobin, g/dL, mean (SD)	12.4 ± 2.2	12 ± 2.4	13 ± 2.1	0.01**
White blood cell count, /μL, median (IQR)	7250.0 (5560, 9720)	7990.0 (6000, 11610)	7130.0 (5480, 9270)	0.01*
Total lymphocyte count, cell/mL, median (IQR)	1,149.0 (800, 1,746)	1,022.0 (612, 1,521)	1,210.0 (832, 1,814)	< 0.01**
Serum sodium, mEq/L, mean (SD)	133 ± 15	135 ± 6	133 ± 17	0.16
Serum potassium, mEq/L, mean (SD)	3.8 ± 0.6	4.1 ± 0.8	3.7 ± 0.5	< 0.01**
Serum bicarbonate, mEq/L, mean (SD)	20.5 ± 4.3	17.8 ± 4.7	21.4 ± 3.8	<0.01**
Serum albumin, g/dL, mean (SD)	3.4 ± 0.7	3.2 ± 0.7	3.5 ± 0.6	<0.01**

* indicates $P < 0.05$; ** indicates $P < 0.01$. BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes, eGFR, estimated glomerular filtration rate; IQR, interquartile range; sCr, serum creatinine.

Table 2. Unadjusted and adjusted OR of independent risk factors of AKI in hospitalized primary COVID-19-infected patients.

Independent risk factors	Unadjusted OR	Adjusted OR
Male gender	1.9 (1.2–3.0)	1.8 (1.2–3.0)
Age ≥ 60 years	2.0 (1.1–3.4)	2.0 (1.2–3.5)
CKD	5.3 (2.0–14.3)	5.5 (2.0–14.7)
CAD	3.0 (1.1–8.5)	3.3 (1.1–9.2)
Pneumonia	3.4 (1.3–9.1)	4.0 (1.5–10.5)
Serum potassium ≥ 4.5 mEq/L	2.4 (1.1–5.2)	2.3 (1.1–5.0)
Serum bicarbonate < 22 mEq/L	2.5 (1.4–4.4)	2.4 (1.3–4.2)
COVID-19 vaccine administration	0.4 (0.3–0.8)	0.5 (0.3–0.8)

AKI, acute kidney injury; CAD, coronary artery disease; CKD, chronic kidney disease; OR, odds ratios.

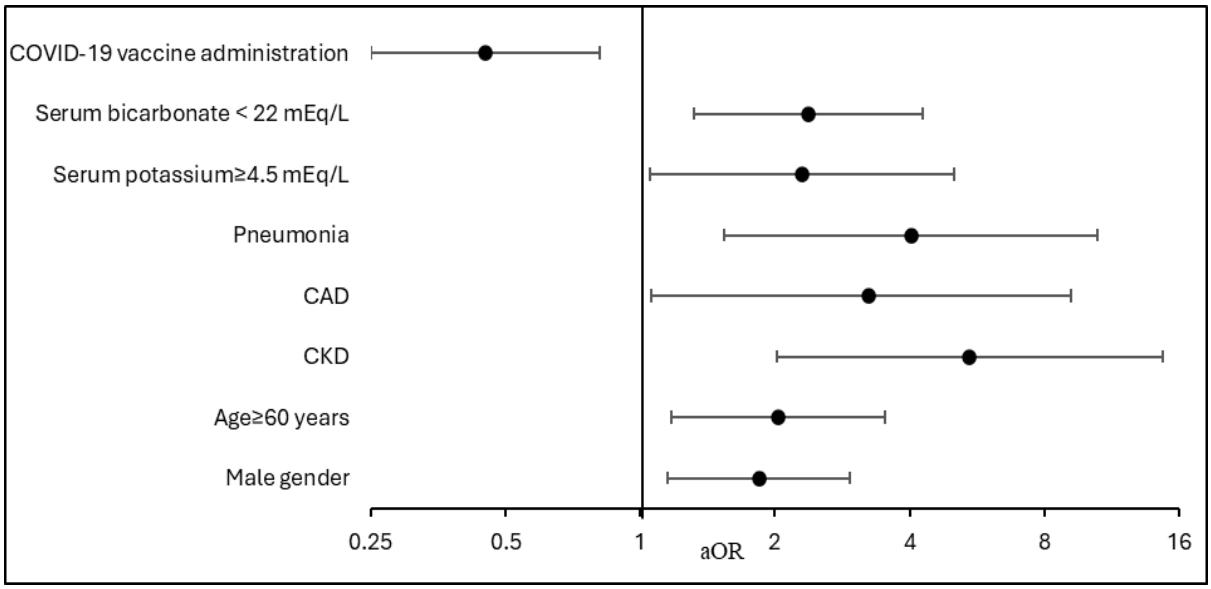

Figure 1. Adjusted OR of independent risk factors of AKI in hospitalized primary COVID-19-infected patients. AKI, acute kidney injury; CAD, coronary artery disease; CKD, chronic kidney disease; OR, odds ratios.

with COVID-19 and AKI.[22] In this study, the in-hospital mortality was significantly higher among patients with AKI compared to those without, with an overall mortality rate of 20.8%. Adherence to the Thai COVID-19 treatment guidelines and encouragement for early COVID-19 vaccination by providing any type of vaccine in Thailand might explain the lower mortality rate observed in this study.

This study identified several risk factors for AKI in hospitalized patients with COVID-19. Previous meta-analyses have linked male gender, older age, and comorbidities such as DM, hypertension, CKD, and CAD with AKI development.[11, 22, 23] This study found notable differences in the baseline characteristics of patients with and without AKI, with higher rates of male gender, older age, and COVID-19 pneumonia among the former group. In addition, patients with AKI exhibited more comorbidities, including CKD, DM, and hypertension. Laboratory results, including baseline sCr and eGFR, as well as their values at admission and one-week post-admission, were significantly higher in patients with AKI.

Furthermore, this study evaluated the independent risk factors for AKI, revealing strong associations with male gender, age over 60 years, CKD, CAD, pneumonia, serum potassium levels ≥ 4.5 mEq/L, and serum bicarbonate levels < 22 mEq/L. Research has consistently shown that male gender and older age are linked to the risk of AKI development. Recent evidence suggests that sex hormones, sex chromosomes, and genetic and epigenetic factors might influence immune responses to COVID-19.[24] In addition, socioeconomic factors such as smoking and health literacy may affect the severity of COVID-19.[25] Elderly patients, who often have multiple comorbidities and weaker immune systems, are at a higher risk of developing severe COVID-19 and AKI.[26] CKD and CAD are frequently reported as risk factors for AKI in patients with COVID-19.[11, 22, 23] This study supports previous

studies that reported that pneumonia and ARDS are associated with a higher risk of AKI.[23] Elevated serum potassium and low serum bicarbonate levels might serve as early indicators of AKI. However, patients with a history of COVID-19 vaccination were found to have a lower incidence of developing AKI **(Figure 2).** The type of vaccine varied, and therefore, the results suggested that, regardless of the vaccine type, vaccination was associated with a reduced risk of AKI. Recently, other evidence of a lower rate of AKI in patients with COVID-19 who had received COVID-19 vaccinations has been reported. A large cohort study in the US enrolled 742,799 patients with COVID-19 and demonstrated a lower rate of AKI and a reduced mortality rate in patients who were vaccinated against COVID-19.[27] A case-control study performed in Mexico also reported a lower AKI rate in patients with COVID-19 vaccination.[28] However, the potential mechanism underlying the protective effects of COVID-19 vaccination against AKI has not yet been elucidated. During the pandemic, the Thai government supported various COVID-19 vaccine types for the widespread distribution and early immunization of the Thai population. These findings indicated that COVID-19 vaccination might reduce the incidence of AKI.

The findings of this study aligned with those of previous research on the baseline characteristics, AKI incidence, mortality rates, and independent risk factors for AKI in patients with COVID-19. However, as this is a retrospective study, it is subject to biases. The lack of urine output criteria for AKI diagnosis might have resulted in an underestimation of AKI cases. Furthermore, this study used the sCr and eGFR data at admission because of the absence of baseline measurements, and the eKDIGO criteria were used to enhance diagnostic sensitivity. Long-term outcomes were not assessed because of limitations in patient follow-up. Finally, this research was performed in a public tertiary hospital during the COVID-19 outbreak in Thailand, specifically during the prevalence of the SARS-CoV-2 Alpha and Omicron variants, thus reflecting the clinical context of that period. Therefore, encouragement of COVID-19 vaccination and treatment of COVID-19 infection, along with the Thai treatment guidelines, might improve the outcomes of patients with COVID-19, especially in terms of AKI incidence and mortality.

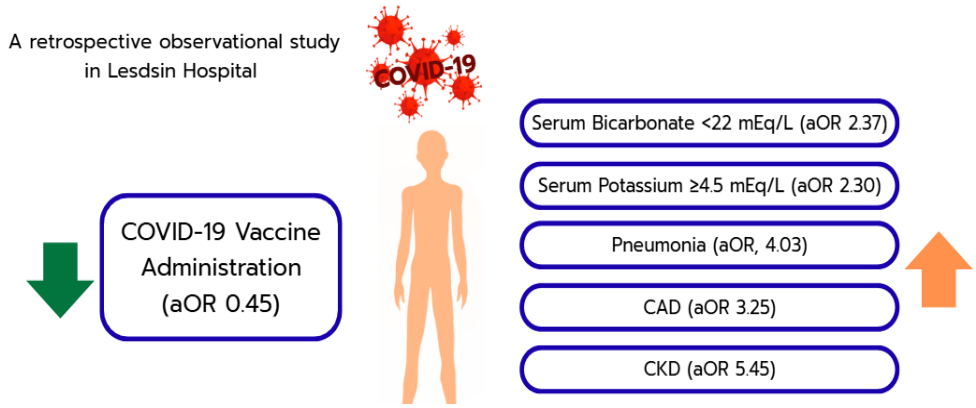

Figure 2. Summary of independent risk factors associated AKI in hospitalized primary COVID-19-infected patients. AKI, acute kidney injury.

Conclusion

This retrospective observational study was performed at a public tertiary hospital in Bangkok, Thailand. We assessed clinical baseline characteristics, AKI incidence, and mortality rates among hospitalized patients with COVID-19, as well as the independent risk factors for AKI. These findings aligned with those of previous research. This study identified male gender, advanced age, CKD, CAD, serum potassium levels ≥ 4.5 mEq/L, and serum bicarbonate levels < 22 mEq/L as independent risk factors for AKI in patients with COVID-19. Notably, this study was the first to report that COVID-19 vaccination might offer protection against the development of AKI in these patients.

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Conflicts of interest

The authors have each completed the International Committee of Medical Journal Editors Form for Disclosure of Conflicts of Interest. None of the authors has any potential or actual conflict of interest to declare.

Data sharing statement

All data generated or analyzed during the present study are included in this public article.

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