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Original article

Associations between kidney injury markers and COVID-19 severity: A retrospective study from a tertiary hospital

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Abstract. *Background and aim:* COVID-19 pandemic has been linked with many organ complications, among them being acute kidney injury (AKI), which is related to worse clinical outcomes. Understanding the relationship between renal biomarkers and disease severity is important in providing early detection and better management of high-risk patients. The current study explores the correlation between biomarkers of kidney injury and COVID-19 severity in hospitalized patients at a Saudi Arabian tertiary care hospital. *Methods:* A retrospective, single-centre, study was conducted on 450 adult patients who were hospitalized with laboratory-confirmed COVID-19 between March 2020 and December 2021. Demographics, comorbidities, clinical outcomes, and renal biomarkers including serum creatinine, blood urea nitrogen (BUN), sodium, potassium, chloride, and CO_2 were assessed. Statistical testing and multinomial logistic regression were used to assess the association of biomarker levels with disease severity (mild, severe, critical). *Results:* Elevated BUN was strongly associated with critical group (46.7%) compared to severe (23.6%) and mild (22.8%) cases ($p < 0.001$). Abnormal potassium, chloride, and CO_2 levels were also strongly associated with severity. The creatinine and sodium levels, however, were not significantly associated. Logistic regression validated BUN as an independent predictor of severity (OR for critical = 1.125, $p < 0.001$), whereas potassium and chloride demonstrated reverse relationships with severity levels. There was weak reverse correlation of creatinine. *Conclusion:* BUN, potassium, and chloride may serve as useful indicators of COVID-19 severity and could be useful biomarkers for the early risk stratification. Compliance with these parameters may facilitate early intervention and improve clinical outcomes in COVID-19 patients with AKI. (www.actabiomedica.it)

Key words: kidney injury, COVID-19, kidney biomarkers, COVID-19 severity

Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has seriously influenced global health, leading to a large number of people falling ill and dying. Whilst COVID-19 mainly targets the respiratory tract, it can also lead to various complications apart from lung troubles. Acute Kidney Injury (AKI) is one of these. AKI occurs frequently in patients with severe COVID-19 and is connected with outcomes that are worse than those of less seriously ill patients, longer hospital stays, and a higher risk of death (1, 2). The exact mechanisms for why acute kidney injury (AKI) occurs in patients with COVID-19 are still not fully understood, but a number of possible pathways have been suggested. SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE2) receptor to enter host cells. The kidneys, especially the proximal tubular cells, have a high expression of this receptor. So if the virus binds to ACE2 receptors in the kidney, it can cause direct cell damage and dysfunction, contributing to the onset of AKI(1, 2).Moreover, the body's immunological response to SARS-CoV-2 infection, which involves the release of pro-inflammatory cytokines and chemokines, has been connected with the development of AKI. This exaggerated inflammatory response can cause damage to the endothelium lining blood vessels, small blood clots in the vessels, and therefore restricted blood flow to kidneys, all factors that can bring about kidney injury (3, 4). We know that there are some pre-existing conditions and risk factors that have been shown to be associated with a higher likelihood of acute kidney injury (AKI) while suffering from COVID-19. These include older age, high blood pressure, diabetes, chronic kidney disease, and cardiorenal conditions(5, 6). Having these other diseases as a background means that people compromise kidney function or have subnormal kidney capacities, which then result in more widespread harm to the kidneys as a result of COVID-19.Some clinical presentations of AKI associated with COVID-19 may be mild, with an increase in serum creatinine that is even asymptomatic, while in other cases severe kidney failure necessitates renal replacement therapy. Common symptoms may include decreased urine output, swelling, nausea, and fatigue(7, 8).Diagnosing AKI in patients with COVID-19 is generally done according to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, which define AKI by specific changes in serum creatinine and urine output (9, 10). In addition to clinical signs, laboratory parameters play a crucial role in the diagnosis and monitoring of kidney function in COVID-19 patients with known or suspected AKI. Serum creatinine and blood urea nitrogen (BUN) are essential markers for evaluating glomerular filtration rate and renal excretory function. Elevated levels of these parameters are commonly observed in patients with AKI (6, 9). Electrolyte imbalances are also common. Hyperkalemia (elevated serum potassium) is a prominent complication of AKI due to impaired renal potassium excretion(11). Sodium imbalances, such as hyponatremia and hypernatremia, result from changes in fluid balance and incorrect secretion of anti-diuretic hormone (12). Changes in serum chloride levels (dyschloremia) have been found in critically ill patients and are linked with bad outcomes (13). Furthermore, metabolic acidosis, as manifested in decreased serum bicarbonate (total CO_2), is a common sequel to AKI because of defective acid excretion. This causes still further clinical deterioration(14). For management of acute kidney injury (AKI) associated with COVID-19, a total approach is necessary, including supportive measures in hemodynamics along with careful fluid management. In severe cases, renal replacement therapy may also be used (10). The speed with which the condition is uncovered and addressed is crucial for averting further harm to the kidneys and raising overall patient outcomes. For example, research unfailingly supports the observation that when AKI sets in on top of pre-existing COVID-19 cases, the prognosis will be worse: the patient will naturally have to stay in hospital longer, with the need (especially if the case is serious) for more intensive care and a higher rate of death too (9, 15). Furthermore, if AKI appears in a severe manner then long-term complications such as chronic kidney disease developing or progression to end-stage renal failure will be in greater number. As the novel coronavirus (COVID-19) epidemic unfolds, the causes, risk factors and management strategies for COVID-19 related acute kidney injury (AKI) are still areas of active and developing research. Current studies aim to elucidate the underlying biological mechanisms. The identification of new biomarkers for early detection is a related research target. And with the development

of targeted therapies, one goal is to improve patient outcomes (16, 17). Acute Kidney Injury (AKI) caused by COVID-19 is a dangerous complication found in many of the patients suffering from severe forms of this disease. It results from a combination of direct viral damage to the kidney, systemic inflammation and pre-existing health problems. Timely diagnosis, effective management and a better understanding of the combination of causes are all necessary for reducing the impact of these diseases. With ongoing research and clinical effort, it is possible to improve the care and long-term prognosis of patients with COVID-19 associated AKI. This study contributes region-specific data from Saudi Arabia, addressing a critical gap in the global literature. While many international studies have reported similar associations between kidney injury biomarkers and COVID-19 severity, few have examined these patterns within Middle Eastern populations. Our findings therefore offer important regional insights that enrich the broader understanding of COVID-19-related renal biomarkers and their clinical implications across different demographic and healthcare settings.

Materials and Methods

The study design

This retrospective analytical study included under deidentified data of patients who attended a tertiary care hospital in the Kingdom of Saudi Arabia (KSA) during the COVID-19 time period (March 2020 – December 2021). The study protocol was approved by the Research Ethics Committee, Prince Sultan Military College of Health Sciences (IRB-2022-CLS-031). Personal consent was waived since the study was retrospective and only anonymized patient data were used. Stage I of the study focused on 793 patients with proven laboratory diagnosis of SARS-CoV-2 infection using RT-PCR. Following the exclusion of 343 patients with no demographic data, missing medical history or laboratory values, end-stage renal disease (ESRD), and <18 years, Additionally, patients with hospital stays exceeding 90 days were excluded to reduce the influence of extreme outliers and ensure comparability across disease-severity groups. 450 hospitalized patients remained for final analysis. Relevant demographic, BMI, and comorbidities (DM, CVD, respiratory) were also collected for analysis. Clinical endpoints for COVID-19 included the need for ICU admission, oxygen saturation <93%, requiring mechanical ventilation, chest x-ray showing lung infiltrates. The laboratory data included serum creatinine, BUN, CO_2, Na^+, K^+, and Cl^-. Clinical severity was categorized according to the Saudi Arabia MOH case definition. According to the guidelines, patients were classified as mild, severe, and critical. Mild disease was defined as fever, cough, sore throat, or loss of taste and smell without findings of pneumonia or hypoxia. Severe cases were characterized by pneumonia with at least one of the following symptoms: respiratory rate over 30 breaths per minute, oxygen saturation of 90% or less while breathing room air, or severe respiratory failure. Critical patients were defined as those with organ failure (acute respiratory distress syndrome (ARDS), sepsis, or need for life-saving treatments).

Statistical analysis

The demographic, clinical, and biochemical characteristics of the study population were analyzed using descriptive and inferential statistical techniques. Categorical variables such as age groups, sex, comorbidities, clinical outcomes, and types of severity of COVID-19 were described by frequency and percentage. Continuous variables, including BMI and hospital LOS, were expressed as the mean SD. Cross-tabulations were then performed to analyze the correlation between kidney injury parameters (BUN, creatinine, sodium, potassium, chloride, and CO_2) and COVID-19 severity (classified as mild, severe, and critical). The Chi-square test was used for comparison of variables with appropriate expected frequency, and Fisher's exact tests were used in situations where cell count were < 5 to retain the power of the test. A 2-tailed P value < 0.05 was considered statistically significant. Multinomial logistic regression was also performed to assess the predictive value of kidney injury biomarkers for COVID-19 severity with mild cases as the reference category. Before running the regression, we assessed potential collinearity among the independent variables (BUN, creatinine, and electrolytes) using Variance Inflation

Factors (VIF). All VIF values were below 2.0, indicating no significant multicollinearity and confirming the stability of the regression model. The adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated from the model. The statistical significances, $p < 0.05$ were considered significant. Statistical analyses were all conducted with SPSS version 29 (IBM Corp., Armonk, NY, USA).

Results

The demographic and clinical characteristics

A total of 450 COVID-19 patients were included in the study. Among the total patients, according to age distribution, patients of 20–40 years of age and 41–60 years were dominant (37.1% and 33.1%, respectively). A lesser proportion of patients were aged <20 years (6.4%), 61–80 years (19.1%), and >80 years (4.2%).The average BMI was 28.82 ± 6.52, and the mean hospital stay was 29.25 ± 5.29 days, highlighting significant variability in hospital length of stay among patients. The majority of patients in our sample were male (68.7%), compared to females (31.3%).Regarding comorbid conditions, 44.4% (n = 200) had DM, 16.4% (n = 74) had CVD, and 11.6% (n = 52) had a history of RD.Analysis of clinical outcomes suggests that 218 patients (48.4%) were admitted to the ICU and 191 (42.4%) had oxygen saturation <93%. A total of 97 (21.6%) patients underwent mechanical ventilation and 223 (51.8%) had lung infiltrates. There were 71 deaths among the cohort (15.8%). Finally, according to disease severity, the prevalence of mild, severe, and critical COVID-19 cases were 167 (37.1%), 161 (35.8%), and 122 (27.1%), respectively. This more even spread across severity levels contributed to analyzing biomarkers of kidney injury and COVID-19 severity.

The relationship between kidney injury markers and COVID-19 severity

In Table 2 Degrees of renal injury markers in mild, severe, and critical COVID-19 groups and correlation with disease severity are shown. There was no significant difference in creatinine levels found between the groups ($p = 0.665$), nor did the percentages of patients with high, normal, or low levels vary between the severity classifications. Blood Urea Nitrogen (BUN) levels, on the other hand, were also significantly correlated with the severity of the disease ($p < 0.001$). The positive rate of elevated BUN in critically ill patients (46.7%) was much higher than that of severe and mildly ill patients (23.6% and 22.8%, respectively), hinting at a potentially ascending pattern of BUN from mild to severe and then to critically ill patients. The K^+ levels were also statistically correlated with severity ($p = 0.012$). The percentage of high or low levels of potassium was marginally greater in the critical group (4.1% high, 1.6% low) than in the mild and severe groups, which is indicative that the electrolyte disturbance was getting worse with the increase in severity (Table 1). Chloride (Cl^-) showed a remarkable difference among groups ($p < 0.001$), and levels of low Cl were more common in critical (21.3%) than severe (13.7%) and mild (5.4%) types, while normal Cl decreased as severity significantly increased. Disease severity was similarly correlated with CO_2 ($p < 0.001$). On the contrary, much greater percentages of patients had low CO_2 in the severe group (20.5%) and critical group (20.5%), which were higher than in the mild group (4.2%).On the other hand, there was no significant difference in Sodium (Na^+) between the groups of patients based on severity ($p = 0.691$), having comparable percentages of patients with low Na^+ in both the more severe (severe and moderate) and the mild groups. These results suggest certain parametric data, such as BUN, K, Cl, and CO_2, may be associated with the severity of COVID-19 infection and can be regarded as candidate biomarkers in practical use for early decision-making in patients testing positive for severity.

Estimated associations between kidney injury marker levels and clinical severity using multinomial logistic regression

Performing the multinomial logistic regression analysis with mild cases as a reference, several kidney injury markers were predictive of disease severity. In interpreting the regression results, one "unit" corresponds to 1 μmol/L for creatinine and 1 mmol/L for BUN and electrolytes (Na, K, Cl, and CO_2). To facilitate clinical

Table 1. Characteristics of study sample

Variable	Total = 450
1) Demographical	
a. Age group < 20 20-40 41-60 61-80 >80	 **29** **167** **149** **86** **19**
b. Gender Female Male	 **141** **309**
c. Body mass index (BMI)	**28.82 ± 6.52**
d. Length of hospital stays	**29.25 ± 5.29**
2) Comorbidities	
a. Diabetes mellitus Yes No	**200** **250**
b. Cardiovascular disease Yes No	**74** **376**
c. Respiratory diseases (RD) Yes No	**52** **398**
3) The outcomes	
a. Admission to ICU Yes No	**218** **232**
b. O2<93% Yes NO	**191** **259**
c. Mechanical ventilation Yes No	**97** **353**
d. Lung infiltrate Yes No	**233** **217**
e. Death Yes No	**71** **232**
f. Severity score Mild Severe Critical	**167** **161** **122**

interpretation, a one–standard deviation (SD) increase in BUN was associated with approximately 14 % higher odds of critical illness. This clarification provides a clearer understanding of the magnitude and practical meaning of the reported odds ratios. Blood Urea Nitrogen (BUN) was a highly significant positive predictor for critical as well as severe stages. More precisely, a 1 unit increase in BUN was associated with a 12.5%-increase in the odds of being in the critical group (OR = 1.125, 95% CI: 1.074–1.178, p < .001) and 11.4% higher odds of being in the severe group (OR = 1.114, 95% CI: 1.063–1.166, p < .001) compared to mild cases. Creatinine was slightly and significantly inversely associated with severity. Regarding moderate vs. mild, the odds ratio was 0.993 (95% CI: 0.989–0.997, p < .001), and 1.000 (95% CI: 0.999–1.000, p = .043), indicating a modest reduction in odds with increasing creatinine. Potassium was a powerful inverse predictor with over an 8-fold decrease in the odds of severe (OR = 0.114, 95% CI: 0.057–0.231, p < .001) compared to mild (OR = 0.242, 95% CI: 0.139–0.395, p < .001) disease, so the lower the level of potassium, the stronger was the association. Chloride was also a protective factor and was significantly correlated with reduced odds of developing critical (OR = 0.878, 95% CI: 0.821–0.939, p < .001) and severe (OR = 0.933, 95% CI: 0.874–0.996, p = .038) disease categories. In contrast, Sodium and CO_2 were not strong predictors for severity in either of the comparisons (with non-significant p-values).These results, in conjunction, emphasize the prognostic role of BUN, potassium, chloride, and, to a lesser extent, creatinine in predicting milder, severe, and critical cases of disease.

Discussion

In this study, we analyzed in 450 hospitalized COVID-19 patients the association between demographic and clinical characteristics and kidney injury markers according to disease severity. The results also contribute to new understanding of the association of renal biomarkers with COVID-19 progression/outcomes and the clinical prospects of these biomarkers as predictive and prognostic factors. Although our findings are consistent with several international studies reporting similar associations between renal biomarkers and COVID-19 severity, the novelty of this research lies in its regional contribution. By analyzing hospitalized patients from Saudi Arabia, this study provides

Table 2. Evaluation of the Relationship Between Kidney Injury Markers and COVID-19 Severity

	COVID-19 Severity			
Variable	**Mild (167)**	**Severe (161)**	**Critical (122)**	**P-value**
Creatinine **High** **Normal** **Low**	53 (31.7%) 97 (58.1%) 17(10.2%)	54(33.5%) 91(56.5%) 16 (9.9%)	41(33.6%) 63 (51.6%) 18 (14.8%)	0.665
BUN **High** **Normal** **Low**	38 (22.8%) 114 (68.3%) 15 (9%)	38(23.6%) 98(60.9%) 25(15.5%)	57(46.7%) 49(40.2%) 16(13.1%)	<0.001*
Na^+ **High** **Normal** **Low**	1 (0.6%) 76 (45.5%) 90 (53.9%)	3 (1.9%) 75 (46.6%) 83 (51.6%)	3 (2.5%) 59 (48.4%) 60 (49.2%)	0.691
K^+ **High** **Normal** **Low**	1(0.6%) 165(98.8%) 1 (0.6%)	0 (0.0%) 156(96.9%) 5. (3.1%)	5(4.1%) 115(94.3%) 2 (1.6%)	0.012*
Cl^- **High** **Normal** **Low**	21 (12.6%) 137(82%) 9 (5.4%)	6 (3.7%) 133(82.6%) 22 (13.7%)	10 (8.2%) 86 (70.5%) 26 (21.3%)	<0.001*
CO_2 **High** **Normal** **Low**	3 (1.8%) 157(94%) 7 (4.2%)	4 (2.5%) 124 (77%) 33 (20.5%)	0 (0.0%) 97 (79.5%) 25 (20.5%)	<0.001*

valuable Middle Eastern data that enhance global understanding of how kidney injury markers behave in different populations and healthcare settings. This regional perspective adds contextual depth to the existing literature and supports broader external validity of global findings. The age [Table 1] distribution for this case group occurred most frequently in adults of 20–60 years old, being consistent with many studies worldwide to indicate that although COVID-19 can occur in people of all age groups, many patients with severe illness, particularly middle-aged and older, are more likely to be more severely ill in the hospital(18-20). Despite the under-representation of younger (<20 years) and older (>80 years) patients, advanced age is a determinative risk factor for severe outcomes (21). The relatively larger sample size of the middle-aged (61–80 year-old) group (19.1%; P = 0.02) also confirmed that older patients are at risk. The mean BMI of 28.82 ± 6.52 put the cohort in the overweight range. Obesity and overweight are established drivers for the increased severity of COVID-19 during infection as a result of underlying comorbidities including compromised respiratory mechanics, chronic inflammation, and immune modification(22, 23). The BMI distribution for this study corroborates these strongly positive findings, suggesting that excessive body mass appears to confer a greater burden of disease.Male sex bias: Analysis of the patients' sex distribution showed a male predominance (68.7%), in line with numerous reports of sex imbalances in COVID-19 morbidity and mortality. Biological elements like immune response, angiotensin-converting enzyme 2 (ACE2) receptor expression, and behavior could be one of the reasons for this inadequacy (24, 25). Besides, males are generally at a higher risk of comorbidities known to be associated with severe COVID-19, such as cardiovascular

Table 3. Estimated Associations Between Kidney Injury Marker Levels and Clinical Severity Using Multinomial Logistic Regression

Predictor	Critical vs Mild	P-value	Exp(B) (OR)	95% CI (OR)	Severe vs Mild	P-value	Exp(B) (OR)	95% CI (OR)
BUN	0.117	<.001	1.125	1.074 – 1.178	0.108	<.001	1.114	1.063 – 1.166
Creatinine	-0.007	<.001	0.993	0.989 – 0.997	-0.002	.043	0.998	0.995 – 1.000
Sodium (Na)	0.039	.260	1.040	0.971 – 1.113	0.016	.618	1.017	0.953 – 1.085
Potassium (K)	-2.168	<.001	0.114	0.057 – 0.231	-2.711	<.001	0.066	0.033 – 0.136
Chloride (CL)	-0.130	<.001	0.878	0.821 – 0.939	-0.069	.038	0.933	0.874 – 0.996
CO_2	0.022	.567	1.022	0.948 – 1.103	0.065	.078	1.067	0.993 – 1.146

disease and diabetes mellitus (26). As for comorbidities, almost half of patients (44.4%) were diabetics, a strongly established comorbidity factor of risk for progression of severe COVID-19 infection and mortality (27). Diabetes attenuates innate immunity and induces a pro-inflammatory state that might enhance viral replication and lung damage(28). Cardiovascular diseases (16.4%) and respiratory diseases (11.6%) were also common, both associated with deterioration of COVID-19 symptoms (29, 30).Assessment of clinical severity found a significant strain on the health care system with 48.4% requiring admission to the ICU and 21.6% requiring mechanical ventilation. Room-air oxygen saturation of less than 93% in 42.4% of patients is a very high proportion demonstrating marked respiratory distress, which is central to severe COVID-19 pneumonia(31). Lung infiltrates on imaging in more than half of the patients (51.8%) are indicative of widespread lung involvement. The recorded death rate of 15.8% compares to ICU-based cohorts in other reports although the death rate varies internationally with the variation in healthcare facilities and treatment protocols(32). Kidney disease (KD) is increasingly recognized as a critical risk factor for individuals with COVID-19 and correlates with unfavorable clinical outcomes. This analysis seeks to fill the gap in prognostic understanding by evaluating kidney injury markers (KIMs), including serum creatinine, blood urea nitrogen (BUN), and electrolytes such as sodium (Na^+), potassium (K^+), chloride (Cl^-), and carbon dioxide levels. In our study, patients exhibiting severe to critical illness did not demonstrate significantly elevated serum creatinine compared to those with mild cases when analyzed univariably. The weak inverse association between creatinine and disease severity was unexpected, as higher creatinine usually indicates worse renal function. This finding may reflect hemodilution from aggressive fluid therapy, reduced muscle mass in critical illness, or confounding effects of hydration status, nephroprotective drugs, or early renal replacement therapy. Therefore, serum creatinine in severe COVID-19 should be interpreted cautiously and alongside other renal biomarkers. Conversely, previous research has indicated that higher creatinine levels are independently linked to acute kidney injury (AKI) and adverse clinical outcomes (33, 34). Recent investigations have utilized multivariable regression models designed to control for confounding variables, thereby clarifying the independent impact of renal function on COVID-19 results. For example, Zheng et al.'s meta-analysis found that while increased creatinine was notably associated with severe or fatal outcomes in univariate assessments, this association diminished within multivariate frameworks—indicating potential confounding influences from factors like age and comorbid conditions (35). Additionally, Russo et al.'s retrospective study established a significant serum creatinine threshold of 1.12 mg/dL for predicting mortality among hospitalized patients suffering from COVID-19 — underscoring the importance of assessing renal function upon admission (36). Interestingly though, some multivariable analyses have suggested an unexpected weak inverse relationship between creatinine concentrations and severity of COVID-19; this paradox may stem from various

influencing elements such as muscle mass composition, dietary intake, or pre-existing health issues affecting baseline creatinine rates without directly implicating kidney functionality (37). On another note regarding BUN levels: there exists a substantial correlation between elevated BUN values and heightened disease severity—indicating that 46.7% of critically ill cases presented high BUN compared to only 23.6% in mild instances and 22.8% amongst those classified as severe(34). Such elevation aligns well with existing knowledge about utilizing BUN measurements as indicators of prerenal azotemia often resulting from conditions like hypovolemia or sepsis. Moreover, recent findings have highlighted the predictive value inherent in the blood urea nitrogen-creatinine ratio (BCR). A ratio ranging from 20 to less than 70 has been shown to correlate strongly with both AKI development risk along with inpatient mortality figures specifically related to COVID-19 patients (38). Severe and critical cases with electrolyte imbalances. It is worth mentioning low potassium, particularly hypokalaemia, was often in severe and critical cases. Decreased level of potassium, essential to the normal functioning and homeostasis process (potassium plays a critical role in salt balance within the cell and subsequent control of cellular metabolism), has been observed in COVID-19 cases, which may be associated with viral-mediated injury to find that kaliuretic protein production, excessive renal potassium losses, or adverse effect of medications such as diuretics (12). Depletion of potassium sets up a vicious circle; the risk of arrhythmia and muscular weakness is further aggravated, thus augmenting the severity of the clinical state (39, 40). The strong inverse correlation between potassium and disease severity, as observed in this study, may imply that electrolyte balance has a role in the management of severe COVID-19. Critically ill patients likewise exhibited significantly lower chloride levels, hypochloremia possibly indicating metabolic acidosis, renal tubular dysfunction, or volume depletion. Hypochloremia has been linked to bad outcomes generally in critical illness, which could drive electrolyte derangements as well as acid-base disturbances and cause a dysregulation in respiratory function (39, 41). Concomitantly, CO_2 level, representing the bicarbonate concentration, was significantly decreased in severe and critical groups, which are also consistent with natural metabolic acidosis by the accumulation of acids such as lactate reflected by lactic acid level increased particularly for severe COVID-19 suffering from respiratory failure(42). By way of contrast, although low among the severity levels, sodium levels are not significant at $p < 0.05$ across strata for all groups. COVID-19 associated hyponatremia is frequent and may develop due to syndrome of inappropriate antidiuretic hormone (SIADH) secretion, fluid imbalance, or renal salt wasting(43). But its effect on prognosis as a single entity is uncertain, and other renal markers may have stronger influences. The strong correlations between kidney injury markers and the severity of COVID-19 emphasize the broad effect of SARS-CoV-2 on renal function. The abovementioned factors, including direct viral invasion of renal tubular epithelial cells through ACE2 receptors, systemic inflammatory responses, coagulopathy, and hemodynamic instability, all contribute to AKI and electrolyte abnormalities in COVID-19 (44, 45). BUN and electrolytes can be used as simple and inexpensive monitoring tools for early identifying patients at risk of breakdown. High BUN levels may lead to more aggressive fluid management, renal protective strategies, and increased monitoring for complications like AKI and multi-organ failure. Electrolyte rebalancing with potassium and chloride could theoretically reduce complications such as cardiac arrhythmias and respiratory muscle weakness and lead to better patient outcomes. Elevated BUN, low potassium, and low chloride levels were the most significant indicators of disease severity in this study. Clinically, patients with BUN > 6.4 mmol/L, $K^+ < 3.5$ mmol/L, and $Cl^- < 96$ mmol/L may represent a higher-risk subgroup requiring closer monitoring. These thresholds align with established laboratory norms and previous studies showing that elevated BUN is associated with mortality in COVID-19 (1), hypokalemia predicts severe disease and cardiac complications(1), and hypochloremia is linked to poor outcomes in critical illness. Although these cutoffs are indicative rather than definitive, incorporating these parameters into

early assessment models may help identify patients at risk of deterioration and guide timely interventions.

Conclusions

This research highlights the predictive role of renal biomarkers in admitted COVID-19 patients. Blood urea nitrogen (BUN) and electrolyte disorders, such as hypokalemia, hypochloremia, and low CO_2 levels, had a significant association with the severity of the disease, indicating that BUN and electrolyte imbalance, such as hypokalemia, hypochloremia, and low CO_2, could have significance in risk stratification and clinical outcome management. Although serum creatinine and sodium were not consistently associated with severity, the strong associations of BUN and certain electrolytes with critical illness suggest they could represent easily measurable and inexpensive markers of renal and systemic derangement in COVID-19. Demographic results reconfirmed the predominance of middle-aged men and the effect of comorbidities, such as obesity and diabetes, in determining the course of the disease. The elevated ratio of ICU admittances corresponds with disease severity.

Ethic Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Prince Sultan Military College of Health Sciences approved this study (IRB-2022-CLS-031).

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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