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Effect of Electrolyte Imbalance on Mortality and Late Acute Kidney Injury in Hospitalized COVID-19 Patients

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Introduction. As a multisystem illness, Coronavirus disease 2019 (COVID-19) can damage different organs. This study investigated the effect of electrolyte imbalance (EI), with or without concomitant renal dysfunction, on the prognosis of COVID-19 in hospitalized patients.

Methods. We evaluated 499 hospitalized patients with confirmed COVID-19, without a history of chronic kidney disease. The patients' demographic data, laboratory values, and outcomes were retrospectively collected from the hospital information system. Serumelectrolytes including sodium, potassium, magnesium, calcium, and phosphorus abnormalities were analyzed on admission and during the hospitalization period. The outcomes of this study were the occurrence of acute kidney injury (AKI) after the first week of hospitalization and in-hospital mortality rate. Multivariate analyses were carried out to obtain the independent risk of each EI on mortality, by adjusting for age, gender, and AKI occurrence.

Results. Among the 499 COVID-19 patients (60.9% male), AKI occurred in 168 (33.7%) and mortality in 92 (18.4%) cases. Hypocalcemia (38%) and hyponatremia (22.6%) were the most prevalent EIs, and all EIs were more common in the AKI group than in the non-AKI group. Hyponatremia (Adjusted Odds ratio [AOR] = 2.34, 95% CI: 1.30 to 4.18), hypernatremia (AOR = 8.52, 95% CI: 1.95 to 37.32), and hyperkalemia (AOR = 4.63, 95% CI: 1.65 to 13) on admission were associated with poor prognosis. Moreover, hyponatremia (AOR = 3.02, 95% CI: 1.28 to 7.15) and hyperphosphatemia (AOR = 5.12, 95% CI: 1.24 to 21.09) on admission were associated with late AKI occurrence.

Conclusion. This study highlights the role of hyponatremia, hypernatremia, hyperkalemia, and hyperphosphatemia in poor prognosis of COVID-19. According to the independent effect of EI on late AKI and mortality, we recommend physicians to raise awareness to closely monitor and correct EI during hospitalization.

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INTRODUCTION

In March 2020, the World Health Organization (WHO) declared Coronavirus Disease 2019 (COVID-19) a pandemic.[1] Over time, an extensive range of clinical characteristics has been reported in patients with COVID-19.[2] Although initially known

as a lower respiratory tract infection, COVID-19 has proved to cause multiorgan involvement.[3] Renal involvement is one of the known extrapulmonary manifestations of COVID-19, which can be manifested as acute kidney injury (AKI), electrolyte imbalance (EI), and metabolic acidosis.[4] Possible mechanisms of renal involvement in COVID-19 are immune-mediated hemodynamic disturbances, endothelial cell damage, impairment of the renin-angiotensin-aldosterone system, and the direct viral infection of glomerular or tubular cells.[5] The percentage of COVID-19 patients, developing AKI, ranges from 0.5%, in mild disease, to more than 50%, in severe cases.[6-9] Electrolyte imbalance (EI) also appears to be common, as reported in a recent study on 11635 cases, in which, only 32.7% of admitted COVID-19 patients had normal electrolyte values.[10]

COVID-19 cases complicated with AKI, have significantly high mortality rates.[11,12] Studies show that EIs, such as hyponatremia and hypokalemia, are prevalent among COVID-19 patients, particularly in severe cases.[13, 14] Moreover, COVID-19 cases complicated with one or more EIs have a poorer prognosis compared with cases with normal electrolytes.[15] However, the impact of EI in prognosis of the COVID-19 patients can be defined as a mediator variable or an independent factor. Few research has focused on kidney function among COVID-19 patients with EI. This study investigated the association between EI and the prognosis of COVID-19 in patients with and without AKI to evaluate the relationship between electrolyte imbalance and prognosis.

MATERIALS AND METHODS

Study Population

This retrospective study enrolled 567 patients with positive COVID-19 reverse transcription polymerase chain reaction (RT-PCR) tests between 20 February and 20 March, 2021, in the Imam Hossein Hospital, a tertiary healthcare center in Tehran. On the first day of admission, nasopharyngeal and/or oropharyngeal swab samples were used to confirm COVID-19 cases. The criteria for hospitalization were in concordance with the National COVID-19 guideline, which were SPO2 < 90%, RR > 30, or conmupted tomographic (CT)-scan involvement ≥ 50%.[16] A total number of 68 patients were excluded due to transfer to other hospitals (n = 9) or a history of chronic kidney disease (CKD) (n = 59).

Variables and Definitions

Serum levels of sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), and phosphorus (P) were evaluated in this study. Electrolyte imbalances were defined as follows: hyponatremia (Na < 135 mEq/L), hypernatremia (Na > 145 mEq/L), hypokalemia (K < 3.5 mEq/L), hyperkalemia (K > 5.1 mEq/L), hypomagnesemia (Mg < 1.6 mg/dL), hypermagnesemia (Mg > 2.4 mg/dL), hypophosphatemia (P < 2.5 mg/dL), and hyperphosphatemia (P > 4.5 mg/dL). The corrected total calcium level was calculated with serum albumin, by using a conventional calcium correction formula (Payne formula).[17] Thus, total calcium levels of less than 8.5 mg/dL and higher than 10.1 mg/dL were considered as hypocalcemia and hypercalcemia, respectively.

Patients with CKD were excluded from the study, and the remainings were assessed regarding kidney function. According to the Kidney Disease Improving Global Outcomes (KDIGO) criteria, AKI was defined as an increase of 0.3 mg/dL in serum creatinine within 48 hours or a 50% increase of serum creatinine in last 7 days. The most recent serum creatinine level 7 to 365 days prior to admission, or the lowest creatinine level during hospitalization was considered the baseline for each patient. Stages of the AKI and its initiation time were also defined based on the KDIGO criteria.[18] Occurrence of AKI in the first 7 days of admission was considered early, and if happened after the seventh day, was defined as late AKI. In-hospital mortality was assessed in this study and referred to as "mortality" in the paper.

Data Collection

In this retrospective study, medical records and patients' information, including demographic data, signs and symptoms on admission, medical history, hospitalization length, outcome (died vs. survived), and laboratory values for the first nine days of hospitalization, if available, were collected using the hospital's electronic information system, by the medical team to the electrolyte values on admission, any EI at any time during hospitalization was also evaluated.

Statistical Analysis

Baseline patients' characteristics and variables were reported as mean (± standard deviation) for continuous variables and number (percentage) for categorical variables. The normality of data distribution was assessed. For comparison between the groups, independent sample t-test or Man-Whitney U test and Chi-square or Fisher's exact test were used, for continuous and categorical variables, respectively. We ran the multivariate analysis using binary logistic regression, to obtain the independent risk of each electrolyte abnormality, by adjusting age and gender, as potential confounders, and calculated the adjusted odds ratio (OR) for late AKI occurrence. We also evaluated the independent risk of each electrolyte abnormality on mortality, by adjusting potential confounders, including age, sex, AKI, and presence of diabetes, hypertension, and cardiovascular disease. The case fatality ratio was defined as the fraction of patients dying from a specific condition/disease.[19] In this study we investigated case fatality ratio of COVID-19 in patients with EI. Statistical analyses were performed using the IBM SPSS statistics, version 26. All statistical analyses were two-sided, and a *P* value of less than .05 was considered statistically significant.

Ethical Consideration

The study obtained approval from the Institutional Review Board (IRB) of the Shahid Beheshti University of Medical Sciences. Data were anonymized before analysis, and patient confidentiality and data security were concerned at all levels. The study was completed under the Helsinki Declaration (2013) guidelines.

RESULTS

Baseline Characteristics

Four hundred and ninty-nine patients (60.9% male gender) with a mean age of 59.3 ± 17.9

Table 1. Baseline Characteristics of Patients on Admission

	AKI Patients (n = 168)	Non-AKI Patients (n = 331)	Total (n = 499)	*P*
	Count/mean (%SD)	Count/mean (%SD)	Count/mean (%SD)	
Age, y	67 (17)	56 (17)	59.3 (17.9)	< .001
Male	112 (66.7)	192 (58)	304 (60.9)	> .05
Hospital Stays, d	9 (7.7)	5.7 (4.38)	6.8 (6)	< .001
BMI, kg/m^2	26.89 (3.76)	26.66 (3.90)	26.72 (3.85)	> .05
Presenting Symptoms				
Dyspnea	100 (59.5)	189 (57.1)	289 (57.9)	> .05
Cough	79 (47)	216 (65.3)	295 (59.1)	< .001
Fever	84 (51.2)	145 (43.8)	229 (46.3)	> .05
Chills	54 (32.1)	126 (38.1)	180 (36.1)	> .05
Fatigue	59 (35.1)	142 (42.9)	201 (40.3)	> .05
Anosmia	10 (6)	84 (25.4)	94 (18.8)	< .001
Diarrhea	17 (10.2)	48 (14.8)	65 (13.2)	> .05
Constipation	5 (3.7)	20 (6.5)	25 (5.7)	> .05
Nausea	30 (19.5)	52 (21.8)	82 (20.9)	> .05
Vomiting	38 (22.8)	71 (21.5)	109 (21.9)	> .05
Rectorrhagia	3 (2.3)	2 (0.7)	5 (1.2)	> .05
Headache	9 (5.5)	55 (17.4)	64 (13.4)	< .001
Myalgia	24 (14.6)	84 (26.4)	108 (22.4)	< .05
Medical History				
Diabetes	35 (21.5)	67 (21.1)	102 (21.3)	> .05
Hypertension	52 (31.9)	73 (23)	125 (26)	< .05
Respiratory	15 (9.2)	29 (9.1)	44 (9.1)	> .05
Cardiovascular	32 (19.6)	41 (12.9)	73 (15.2)	> .05
Neurologic	28 (17.2)	29 (9.1)	57 (11.9)	< .05
Immunodeficiency	4 (2.6)	4 (1.7)	8 (2)	> .05
Cancer	17 (10.4)	21 (6.6)	38 (7.9)	> .05
Rheumatologic	1 (0.6)	4 (1.3)	5 (1)	> .05

Table 1. Continued

	AKI Patients (n = 168)	Non-AKI Patients (n = 331)	Total (n = 499)	*P*
	Count/mean (%SD)	Count/mean (%SD)	Count/mean (%SD)	
AKI				
Occurrence	168		168 (33.7)	
Early	143 (85.1)		143 (85.1)	
Late	25 (14.9)		25 (14.9)	
Stage 1	115 (68.4)		115 (68.4)	
Stage 2	29 (17.3)		29 (17.3)	
Stage 3	24 (14.3)		24 (14.3)	
Outcomes				
Mechanical Ventilation	28 (18.2)	15 (6.3)	43 (10.9)	< .001
ICU	20 (11.9)	22 (6.6)	42 (8.4)	< .05
Death	55 (32.7)	37 (11.2)	92 (18.4)	< .001
Electrolyte on admission				
Na				
Hyponatremia	48 (28.7)	56 (19)	104 (22.6)	< .05
Hypernatremia	8 (4.8)	4 (1.4)	12 (2.6)	< .05
Normal	111 (66.5)	234 (79.6)	345 (74.8)	
K				
Hypokalemia	14 (8.4)	20 (6.8)	34 (7.4)	> .05
Hyperkalemia	13 (7.8)	7 (2.4)	20 (4.3)	< .05
Normal	140 (83.8)	266 (90.8)	406 (88.3)	
Mg				
Hypomagnesemia	18 (13.2)	15 (7.3)	33 (9.7)	> .05
Hypermagnesemia	6 (4.4)	3 (1.5)	9 (2.6)	> .05
Normal	112 (82.4)	188 (91.3)	300 (87.7)	
Ca				
Hypocalcemia	50 (36.5)	84 (39.1)	134 (38)	> .05
Hypercalcemia	8 (5.8)	7 (3.3)	15 (4.3)	> .05
Normal	79 (57.7)	124 (57.7)	203 (57.7)	
P				
Hypophosphatemia	19 (16.2)	31 (17.3)	50 (16.9)	> .05
Hyperphosphatemia	28 (23.9)	8 (4.5)	36 (12.2)	< .001
Normal	70 (59.8)	140 (78.2)	210 (70.9)	

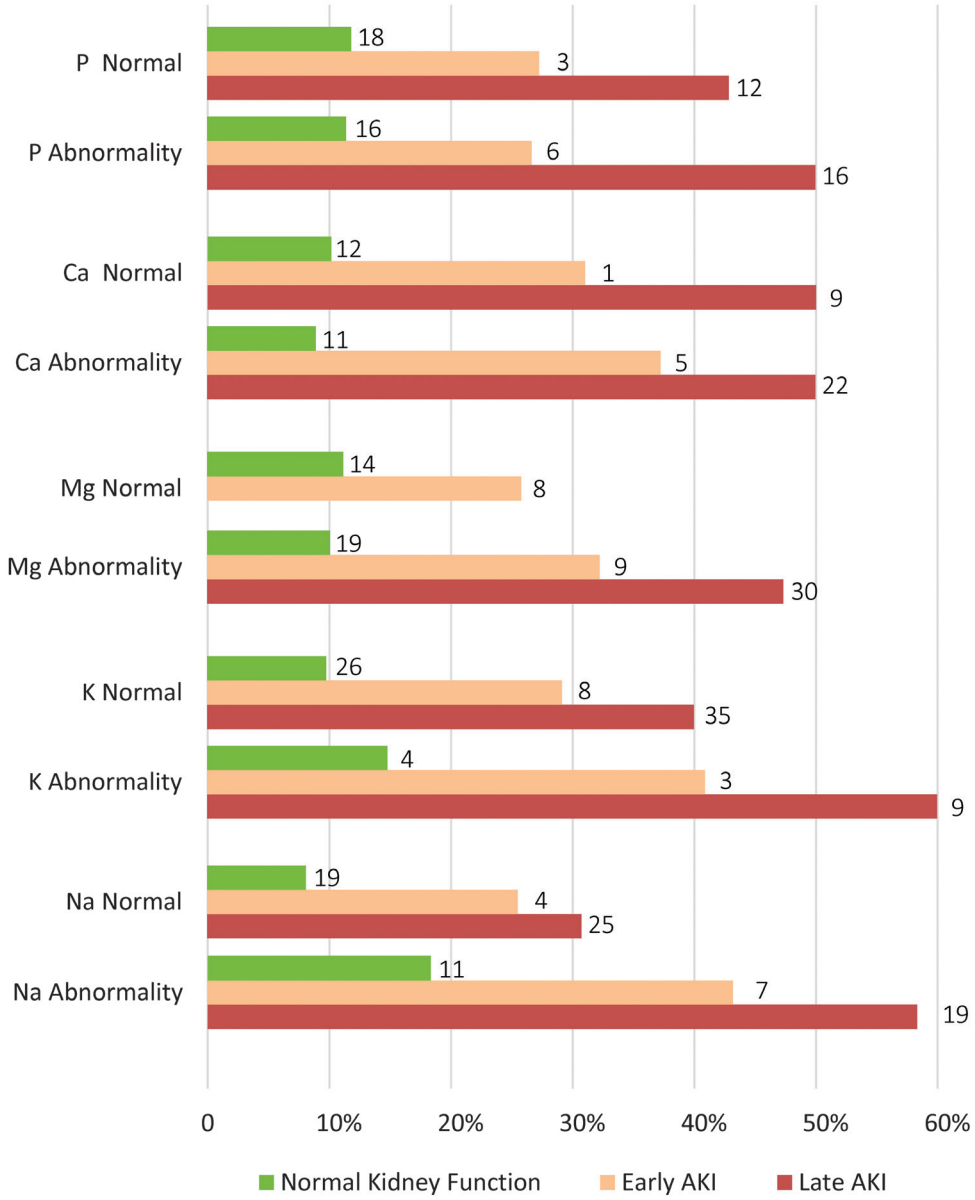
years were enrolled in this study (Table 1). The most common clinical presentations on admission were cough (59.1%), dyspnea (57.9%), and fever (46.3%), and the most frequent comorbidities were hypertension (26%) and diabetes mellitus (21.3%). EI on admission was observed in 55.7% of the patients, with hypocalcemia (n = 134; 38%) being the most frequent abnormality, followed by hyponatremia (n = 104; 22.6%). A total of 42 patients (8.4%) were admitted to the intensive care unit, and 92 patients (18.4%) died.

Acute Kidney Injury and Prognosis

One hundred and sixty-eight patients (33.7%) experienced AKI with a mean age of 67 ± 17, which was higher than patients with normal kidney function ($P < .001$). The mean days of hospital stay were 9 ± 7.7 in patients with AKI and 5.7 ± 4.4 in non-AKI patients ($P < .001$). Patients complicated with AKI had also a higher mortality rate than the non-AKI group (32.7% vs. 11.2%, $P < .001$). Comorbidities and electrolyte abnormalities on the first day are shown in Table 1. The proportion of patients with history of hypertension and neurologic disease was more common in the AKI group than in the non-AKI group (31.9% vs. 23%, $P < .05$; 17.2% vs. 9.1%, $P < .05$; respectively). Regarding electrolytes, sodium level abnormality, hyperkalemia, and hyperphosphatemia were significantly more common in the AKI group than in the non-AKI group (Table 1).

Electrolyte Imbalance and Prognosis

As depicted in Figure, patients with COVID-19



Case fatality ratio and electrolyte imbalance among early acute kidney injury (AKI), late AKI, and normal kidney function COVID-19 inpatients.

and concomitant Na and K abnormalities on admission, had a higher case fatality ratio in both AKI and non-AKI groups. Table 2 describes age, sex, comorbidities, and the AKI adjusted odds ratio for mortality in AKI and patients with normal kidney function. Admittance hyponatremia, hypernatremia, and hyperkalemia were associated with poor prognosis (adjusted OR of 2.34, 8.52, and 4.63, respectively; $P < .05$). Patients were also assessed regarding the presence of each electrolyte abnormality at any time during hospital stay (individuals with a high and low level of a specific electrolyte were considered in both groups). Serial laboratory test results throughout hospitalization were reviewed and, Na imbalance (adjusted OR = 3.27, $P < .001$ for hyponatremia, and adjusted OR = 4.07, $P < .001$ for hypernatremia), hyperkalemia (adjusted OR = 7.74, $P < .001$), hypermagnesemia (adjusted OR = 4.31, $P < .05$), and hyperphosphatemia (adjusted OR = 2.24, $P < .05$) were associated with higher mortality rates. No significant association was found between low levels of other electrolytes and mortality, except for hyponatremia .

Table 2. Mortality of Patients Based on Electrolyte Abnormalities on Admission and During Hospitalization

	AKI Patients	Non-AKI Patients	Total	Adjusted Odd Ratio*	*P*
	Death Count (%)	Death Count (%)	Death Count (%)		
Sodium on Admission					
Hyponatremia	19 (39.6)	9 (16.1)	28 (26.9)	2.34 (1.30 to 4.18)	< .05
Hypernatremia	7 (87.5)	2 (50)	9 (75)	8.52 (1.95 to 37.32)	< .05
Normal Sodium Level§	29 (26.1)	19 (8.1)	48 (13.9)		
Potassium on Admission					
Hypokalemia	4 (28.6)	2 (10)	6 (17.6)	0.65 (0.22 to 1.91)	> .05
Hyperkalemia	8 (61.5)	2 (28.6)	10 (50)	4.63 (1.65 to 13.00)	< .05
Normal Potassium Level§	43 (30.7)	26 (9.8)	69 (17)		
Magnesium on Admission					
Hypomagnesemia	5 (27.8)	3 (20)	8 (24.2)	1.34 (0.53 to 3.41)	> .05
Hypermagnesemia	3 (50)	1 (33.3)	4 (44.4)	1.75 (0.41 to 7.43)	> .05
Normal Magnesium Level§	39 (34.8)	19 (10.1)	58 (19.3)		
Calcium on Admission					
Hypocalcemia	12 (24)	14 (16.7)	26 (19.4)	1.01 (0.55 to 1.87)	> .05
Hypercalcemia	4 (50)	1 (14.3)	5 (33.3)	1.32 (0.32 to 5.39)	> .05
Normal Calcium Level§	29 (36.7)	11 (8.9)	40 (19.7)		
Phosphorus on Admission					
Hypophosphatemia	6 (31.6)	3 (9.7)	9 (18)	1.13 (0.47 to 2.71)	> .05
Hyperphosphatemia	13 (46.4)	0 (0)	13 (36.1)	1.44 (0.60 to 3.43)	> .05
Normal Phosphorus Level§	21 (30)	16 (11.4)	37 (17.6)		
Sodium During Hospitalization					
Hyponatremia	24 (38.7)	14 (17.7)	38 (27)	3.27 (1.78 to 6.01)	< .001
Hypernatremia	22 (55)	7 (17.5)	29 (36.3)	4.07 (2.02 to 8.17)	< .001
Normal Sodium Level§	15 (19.5)	13 (6.9)	28 (10.6)		
Potassium During Hospitalization					
Hypokalemia	9 (22.5)	10 (21.3)	19 (21.8)	1.46 (0.75 to 2.86)	> .05
Hyperkalemia	22 (71)	4 (26.7)	26 (56.5)	7.74 (3.54 to 16.95)	< .001
Normal Potassium Level§	26 (25.7)	18 (7.6)	44 (13)		
Magnesium During Hospitalization					
Hypomagnesemia	8 (27.6)	4 (16.7)	12 (22.6)	1.16 (0.53 to 2.53)	> .05
Hypermagnesemia	10 (76.9)	3 (30)	13 (56.5)	4.31 (1.63 to 11.38)	< .05
Normal Magnesium Leve§	32 (32.3)	17 (9.5)	49 (17.6)		
Calcium During Hospitalization					
Hypocalcemia	24 (32)	15 (13.9)	39 (21.3)	1.46 (0.8 to 2.66)	> .05
Hypercalcemia	6 (54.5)	1 (14.3)	7 (38.9)	2.29 (0.68 to 7.79)	> .05
Normal Calcium Level§	18 (30.5)	10 (9.3)	28 (16.9)		
Phosphorus During Hospitalization					
Hypophosphatemia	11 (39.3)	3 (8.8)	14 (22.6)	1.63 (0.75 to 3.55)	> .05
Hyperphosphatemia	18 (52.9)	0 (0)	18 (35.3)	2.24 (1.00 to 4.99)	< .05
Normal Phosphorus Level§	14 (23.3)	16 (12.3)	30 (15.8)		

*The odd ratio was adjusted by age, sex, AKI presence, existing diabetes, hypertension, and cardiovascular disease.
§Reference Group

Electrolyte Imbalance and Late Acute Kidney Injury

Twenty-five patients developed late AKI, among all participants. The case fatality rate of late AKI (44%) was higher than that of early AKI (30.7%) and normal kidney function (11.1%). Late AKI occurred more frequently in patients with admittance hyponatremia (n = 12; 17.6%) than in patients with normal sodium levels (n = 13; 5.3%), with an age-gender-adjusted OR of 3.02 ($P < .05$). Hyperphosphatemia was also an important predictive factor for mortality with age-gender-adjusted OR = 5.12 ($P < .05$) (Table 3).

Table 3. Electrolyte Abnormality on Admission and Occurrence of Late AKI Among Patients with Normal Kidney Function in the First Week

Electrolyte	Late AKI Occurrence Count (%)	Adjusted OR (CI)*	*P*
Sodium			
Hyponatremia	12 (17.6)	3.02 (1.28 to 7.15)	< .05
Hypernatremia**	0 (0)	N/A	N/A
Normal Sodium Level§	13 (5.3)		
Potassium			
Hypokalemia	3 (13)	1.9 (0.49 to 7.32)	> .05
Hyperkalemia	2 (22.2)	3.02 (0.55 to 16.52)	> .05
Normal Potassium Level§	20 (7)		
Magnesium			
Hypomagnesemia	2 (11.8)	1.27 (0.26 to 6.18)	> .05
Hypermagnesemia	3 (50)	5.38 (0.94 to 30.62)	> .05
Normal Magnesium Level§	19 (9.2)		
Calcium			
Hypocalcemia	10 (10.6)	1.12 (0.44 to 2.89)	> .05
Hypercalcemia	2 (22.2)	2.91 (0.48 to 17.46)	> .05
Normal Calcium Level§	11 (8.1)		
Phosphorus			
Hypophosphatemia	4 (11.4)	1.69 (0.48 to 5.94)	> .05
Hyperphosphatemia	4 (33.3)	5.12 (1.24 to 21.09)	< .05
Normal Phosphorus Level§	10 (6.7)		

*Adjusted by age and sex
**No patient experiencing hypernatremia developed late AKI during hospitalization.
§Reference Group.

DISCUSSION

COVID-19 is a viral disease, affecting respiratory tract and has many extrapulmonary manifestations.[4] The kidney, an organ with high Angiotensin-converting enzyme 2 (ACE2) concentration, can be damaged by COVID-19 since COVID-19 pathology is linked to Interleukin-6 (IL-6) and ACE2.[20] Previous studies showed that EI and AKI were associated with poor prognosis in COVID-19 patients.[11,12,15,21] However, it is not clearly known whether the effect of EI on mortality results from AKI, or it has an independent association with mortality. We evaluated the role of EI on mortality and occurrent late AKI in COVID-19 cases. Patients with hyponatremia, hypernatremia, and hyperkalemia on admission, had a high risk for mortality, even after adjustment with AKI occurrence, age, sex, and comorbidities. Moreover, AKI occurring after seven days of hospitalization, were highly evident in cases with hyponatremia and hyperphosphatemia.

Direct viral infection of kidneys, inflammation, microthrombi, and immune cell infiltration can cause AKI in COVID-19 patients.[5] In line with previous literature, we found that 33% of hospitalized COVID-19 patients experienced AKI, with three times higher mortality rate.[11, 12, 22] In addition, we noticed that 15% of AKI cases occurred after the first week of hospitalization (late AKI). Hyponatremia (adjusted OR = 3.02) and hyperphosphatemia (adjusted OR = 5.12) on admission, are shown to predict late AKI. Early studies on non-COVID 19 patients, also support the role of hyponatremia and hyperphosphatemia in occurrence of AKI.[23, 24] Although further investigations are needed in this regard, we recommend physicians to be aware of EI during hospitalization, to prevent mortality and late AKI.

Hyponatremia is one of the most prevalent EIs in COVID-19 cases, probably due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), high sodium excretion, or low sodium intake.[20,25] In addition, low serum sodium levels may cause upregulation of ACE2s and higher entry of coronavirus into cells.[20] Inconsistent with previous studies, our findings suggested that sodium abnormality on admission was of high importance in predicting mortality.[15, 21] In addition, hyponatremia or hypernatremia, occuring during hospitalization, were correlated with a higher

mortality rate.[26] Therefore, correction of sodium abnormalities in COVID-19 patients is essential for prevention of poor outcome.

We found no correlation between hypokalemia on admission and death, while hyperkalemia, either on admission or during hospital stay, was associated with higher mortality, which was consistent with the result of the study by Alfano *et al.*[27] Liu *et al.* disclosed that high average potassium levels during hospitalization, were significantly correlated with 30 days mortality. The underlying pathophysiology of this relationship is unknown, although the role of potassium in electrophysiology of myocardium, presence of concomitant multiorgan dysfunction, and the effect of acid-base disturbance, may explain this association to some extent.[28]

Hypocalcemia is highly prevalent in severe COVID-19 cases.[29,30] It was found in 38% of our hospitalazied COVID-19 patients. However, in our study, hypocalcemia on admission or its occurrence during hospitalization, did not correlate with late AKI or mortality. This finding, contradicts a number of preliminary works in this field, which showed a relationship between hypocalcemia and mortality.[31, 32] In a letter, Siniorakis *et al.*, pointed out that previous studies mainly focused on total calcium, and few studies assessed corrected calcium concentration, considering albumin levels. Moreover, ionozed, rather than total Ca^{2+} has essential effects on viral internalization, replication, and virions budding.[33] Hence, further investigations are necessary to assess the effect of ionized calcium levels on mortality in COVID-19.

Magnesium and phosphorus are involved in some immune functions, Adenosine triphosphate (ATP) production, and acute respiratory syndrome.[20, 34] In this regard only hypermagnesemia and hyperphosphatemia were found to be associated with mortality during hospitalization. Similarly, a recent study on 1685 patients showed that hypermagnesemia, either on admission or during hospitalization, was associated with higher death rates.[35] It is noteworthy that, all hyperphosphatemia-associated mortality in our study was observed in the AKI group. Therefore, hyperphosphatemia might predict poor outcome, only in patients with concomitant AKI. However, there is a lack of evidence in this regard, and the available literature is controversial.

There are some limitations in our research that should be considered. As we analyzed the serum electrolyte levels retrospectively, some values were unavailable or were not checked, especially calcium, magnesium, and phosphorus levels. Another limitation of this study is unavailability of the data regarding patients' medication history, which could be associated with the occurance of AKI. . As we only enrolled patients with known outcome and excluded the patients who were transferred to other hospitals or discharged against medical advice, out-of-hospital mortality was unknown. Many other factors influence electrolyte levels, and the COVID-19 effect is one of the potential influencers. For example, medications used to treat COVID-19 and other comorbidities can affect electrolyte levels. However, we tried to minimize other confounders by excluding CKD patients and providing age, gender, comorbidities, and the AKI adjusted odds ratio.

CONCLUSION

Hyponatremia, hypernatremia, and hyperkalemia are associated with poor prognosis in COVID-19 patients, regardless of their kidney function. Moreover, late AKI is more prevalent in patients with admittance hyponatremia or hyperphosphatemia. Since EI may be predictive of late AKI and poor prognosis, we recommend physicians to be sensitive to this entity and correct any EI that is present on admission or occurs during hospitalization.

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