Electrolyte imbalance and clinical outcomes in hospitalized COVID-19 patients

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Abstract

***Purpose*: Electrolyte imbalance is associated with increased morbidity and mortality among critically ill coronavirus disease 2019 (COVID-19) patients. This study aimed to investigate the role of specific electrolytes in influencing patient outcomes.**

***Methods*: Retrospective analysis of COVID-19 patients who were admitted to a single center in Houston, Texas, between March 2020 and February 2022. Patients were divided into Group 1 (balanced electrolytes) and Group 2 (imbalanced electrolytes). Prevalence and outcomes of electrolyte disorders were analyzed. We defined electrolyte imbalances as sodium<135 mEq/l or sodium>145 mEq/l, or potassium<3.5 mEq/l or potassium>5.2 mEq/l, or chloride<98 mEq/l or chloride>108 mEq/l, or magnesium<1.7 mg/dl or magnesium>2.2 mg/dl, or phosphorus<2.8 mg/dl or phosphorus>4.5 mg/dl, or calcium<8.6 mg/dl or calcium>10.3 mg/dl. Data was assessed using IBM SPSS™ Statistics version 24.0 and employing descriptive statistics and chi-square tests to ascertain statistical significance.**

***Results*: A total of 953 patients were included in this analysis. The median age was 56 years (44-67), and 541 (56%) were men. The median hospitalization duration was 7 days (4-12). One hundred and seventy-nine patients (18.7%) died. The median level of sodium was 136 (133-138), potassium 3.9 (3.6-4.3), chloride 101 (98-104), calcium 8.6 (8.2-9), phosphorus 3.1 (2.6-3.7), and magnesium 2 (1.8-2.2). Ninety-four (16.5%) patients without sodium imbalance and 85 (22.2%) with sodium imbalance died (p=0.027). One hundred twenty-two (16.4%) patients without chloride imbalance and 57 (27.5%) with chloride imbalance died (p<0.001). For potassium, 153 (19.3%) patients without an imbalance died and 26 (16.1%) with an imbalance died (p=0.348). Sixty-seven (13.4%) patients without calcium imbalance and 112 (24.8%) with an imbalance died (p<0.001). Ninety-six (15.9%) without phosphorus imbalance and 83 (23.9%) patients with imbalance died (p=0.002). One hundred eleven (17%) patients without magnesium imbalance and 68 (22.7%) with imbalance died (p=0.037).**

***Conclusions*: Sodium, chloride, calcium, and phosphorus imbalances were significantly associated with higher mortality rates in COVID-19 patients. In this cohort, potassium and magnesium imbalances did not exhibit statistically significant differences in mortality rates.**

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Introduction

By the end of 2019, a new pandemic emerged from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), officially designated as coronavirus disease 2019 (COVID-19) by the World Health Organization. (1) COVID-19 manifests a wide range of clinical symptoms, spanning from mild manifestations to severe pneumonia and acute respiratory distress syndrome, with the potential for fatal outcomes. (2)

The virus enters host cells through angiotensin-converting enzyme 2 (ACE2) receptors, which are prominently found in various organs such as the heart, liver, kidneys, and lungs. These receptors play crucial roles, including the modulation of the renin-angiotensin system, blood pressure, and electrolyte balance. (2,3)

Six crucial electrolytes, namely calcium (Ca), sodium (Na), phosphorus (P), potassium (K), chloride (Cl), and magnesium (Mg), predominate in serum. (3) Apart from the potential adverse effects of SARS-CoV-2 on electrolyte equilibrium, aberrant levels of these electrolytes have been documented in other medical conditions. (4) Reduced phosphorus levels, for example, have been observed in respiratory disorders such as chronic obstructive pulmonary disease (COPD) and acute respiratory failure. (5) Similarly, instances of hypocalcemia and diminished serum magnesium levels have been associated with acute exacerbations of COPD and respiratory infections. (6)

Electrolyte disruptions in COVID-19, stem from both the virus's direct impact on infected host cells and the concurrent organ dysfunction observed during the disease course. (7) Several factors, including fever, hyperventilation, perspiration, drug-related side effects, and dietary modifications, can contribute to electrolyte imbalances in patients afflicted with COVID-19. (6)

Prior investigations have underscored that COVID-19 affected not only the respiratory system but also the nervous system, cardiovascular system, gastrointestinal (GI) tract, and urogenital system, along with their associated complications. (8) Given the significant roles played by the GI tract and kidneys in maintaining fluid and electrolyte balance within the body, disturbances in these systems can potentially lead to imbalances in fluid and electrolytes. (9)

In light of the prevalence and the impact of electrolyte imbalances on the severity of COVID-19, this study aimed to investigate the role of specific electrolytes in influencing patient clinical outcomes.

Methods

Study design and participants

A retrospective cohort analysis was conducted at a single-center hospital in Houston, Texas, from March 2020 to February 2022. Inclusion criteria included adult patients aged 18 years and above who were hospitalized for COVID-19 infection with electrolyte data on admission. Patients under the age of 18, and/or without electrolyte data were excluded.

Data collection

We used the Meditech™, an electronic medical record system at the hospital, to gather patient information for the study. This data encompassed a range of details including demographics, clinical information, laboratory tests, severity scores, imaging, treatment, duration of hospital stay, and patient outcomes.

To confirm the COVID-19 diagnosis, we utilized diverse methods such as reverse transcription polymerase chain reaction (RT-PCR), SARS antigen fluorescent immunoassay (SOFIA), or immunoglobulin G (IgG)/immunoglobulin M (IgM) rapid tests, in addition to clinical assessment and imaging. The demographic and clinical data considered factors such as age, gender, race, existing health conditions, body mass index (BMI), symptoms, vital signs at admission, and hospital treatments.

Study patients were divided into Group 1 (balanced electrolyte) and Group 2 (imbalanced electrolyte) based on the American Board of Internal Medicine laboratory test reference ranges (sodium 136-145 mEq/l, potassium 3.5-5.2 mEq/l, chloride 98-108 mEq/l, magnesium 1.7-2.2 mEq/l, calcium 8.6-10.3 mg/dl, and phosphorus 3.0-4.5 mg/dl). Hyponatremia was defined as serum sodium <135 mEq/l, and hypernatremia as >145 mEq/l. Hypokalemia was defined as serum potassium <3.5 mEq/l, and hyperkalemia as >5.2 mEq/l. Hypochloremia was defined as serum chloride <98 mEq/l, while hyperchloremia was defined as >108 mEq/l. Hypomagnesemia was defined as serum magnesium <1.7 mg/dl, and hypermagnesemia as >2.2 mg/dl. Hypocalcemia was defined as serum calcium <8.6 mg/dl, and hypercalcemia as >10.3 mg/dl. Finally, hypophosphatemia was defined as serum phosphorus <3.0 mg/dl, and hyperphosphatemia as >4.5 mg/dl. The National Institute of Health (NIH) defined critical illness as individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

The current research adhered to ethical standards and received approval from the hospital's Institutional Review Board prior to data collection. Patient data was anonymized and treated with utmost confidentiality to safeguard individual privacy.

Statistical analysis

The statistical analysis was conducted using IBM SPSS™ Statistics version 24 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean±standard deviation (SD), while categorical data were presented as frequencies and percentages. Descriptive statistics were used to summarize the demographic and clinical characteristics of both patient groups as well as the chi-square test. The data was collected and analyzed by all authors.

Results

This study included 953 patients; 412 (43.2%) were female, and 541 (56.8%) were male. The median age was 56 years (45-67). One hundred and ninety-three (20.3%) were Caucasian, 510 (53.5%) were Hispanic, 196 (20.6%) were Black, and 40 (4.2%) were from other races.

Three hundred and fifty-six (37.4%) patients had a past medical history of hypertension, 241 (25.3%) had diabetes mellitus, 27 (2.8%) had chronic obstructive pulmonary disease (COPD), 19 (2%) had myocardial infarction, 26 (2.7%) had chronic kidney disease, 25 (2.6%) had peripheral vascular disease, 22 (2.3%) had a prior stroke/transient ischaemic attack, 29 (3%) had congestive heart failure, 14 (1.5%) had liver disease, and 363 (38.1%) had other comorbidities. One patient (0.1%) used electronic cigarettes, 44 (4.6%) used tobacco, 75 (7.9 %) used alcohol, and 11 (1.2%) used illicit drugs. One hundred and fifty-four patients (16.2%) were intubated. Out of the 953 patients, only 774 (81.2%) survived.

The sequential organ failure assessment (SOFA) score during hospitalization was 2 (1-3), the median acute physiology and chronic health evaluation (APACHE) II score during hospitalization was 9 (6-13), and the median Ichikado computed tomography (CT) score on admission was 150 (120-200). Three hundred and sixty-seven patients (38.5%) had hyponatremia, 570 (59.8%) had normal levels of sodium, and 16 (1.7%) had hypernatremia. One hundred thirty-two patients (13.9%) had hypokalemia, 792 (83.1%) had normal levels of potassium, and 29 (3%) had hyperkalemia. One hundred and twenty-six (13.2%) had hypochloremia, 746 (78.3%) had normal levels of chloride, and 81 (8.5%) had hyperchloremia. Four hundred and forty-seven patients (46.9%) had hypocalcemia, 501 (52.6%) had normal levels of calcium, and 5 (0.5%) had hypercalcemia. Two hundred and eighty-one (29.5%) had hypophosphatemia, 605 (63.5%) had normal levels of phosphorus, and 67 (7%) had hyperphosphatemia. One hundred and thirty-three patients (14%) had hypomagnesemia, 653 (68.5%) had normal levels of magnesium, and 167 (17.5%) had hypermagnesemia.

An association between electrolyte imbalance and clinical outcome was found (**Table 1**). Eighty-five (47.4%) patients died and 289 (37.3%) with sodium imbalance survived (p=0.007). As for potassium imbalance, 26 (14.5%) patients died, and 135 (17.4%) patients survived (p=0.049). Among the chloride imbalance group, 57 (31.8%) patients died and 150 (19.3%) survived (p=0.001). According to magnesium imbalance, 68 (37.9%) patients died, and 232 (29.9%) patients survived (p=0.003). Concerning phosphorus imbalance, 83(46.3%) patients died and 265 (34.2%) patients survived (p<0.001). As to calcium imbalance, 112 (62.6%) patients died and 340 (43.9%) patients survived (p<0.001).

We found an association between intubated patients and phosphorus imbalance with 73 (47.4%) intubated patients with phosphorus imbalance and 81 (48.8%) intubated patients without phosphorus imbalance (p=0.024).

No statistically significant difference was found among intubated patients and sodium (p=0.866), potassium (p=0.985), chloride (p=0.147), calcium (p=0.220), and magnesium (p=0.399) imbalance. Sixty-six patients (42.9%) who were intubated had sodium imbalance and 88 (57.1%) patients that were intubated did not have sodium imbalance. Twenty-four patients (15.6%) who were intubated had potassium imbalance and 130 (84.4%) patients that were intubated did not have potassium imbalance. Regarding chloride, 49 (31.8%) patients who were intubated had chloride imbalance and 105 (68.2%) patients had chloride imbalance. Ninety patients (58.4%) who were intubated had calcium imbalance and 64 (41.6%) patients did not have calcium imbalance (p=0.220). Sixty (39%) intubated patients had magnesium imbalance and 94 (61%) without magnesium imbalance (p=0.399).

Discussion

In our cohort, patients with imbalances in sodium, potassium, and chloride exhibited a statistically significant increase in mortality and were strong indicators of COVID-19 advancing to critical illness. (10) This is a significant observation, as it suggests that maintaining proper sodium and chloride levels is crucial in the management of COVID-19 patients. (11)

Hyponatremia has emerged as the prevalent electrolyte imbalance associated with unfavorable outcomes in the last few years. (12-14)

Moutushe and co-investigators studying a connection between COVID-19 and abnormal sodium levels found that 63.50% of their cohort had hyponatremia and 15.50% had hypernatremia in moderately affected patients, and in severely affected patients, 44.40% had hyponatremia and 27.80% had hypernatremia. (15) Another similar study reported 57% of severe COVID-19 cases had hyponatremia at admission, 2% had hypernatremia on admission, and 42% developed hypernatremia after 2 weeks in the hospital. (16) Ruiz-Sanchez and associates found that 25-52% of COVID-19 patients had hyponatremia upon admission and that low sodium levels correlated with increased ventilator usage but not with mortality. (17)

In contrast, sodium, potassium, and magnesium imbalances did not show statistically significant differences in mortality rates in our cohort. This suggests that while these electrolyte imbalances may be prevalent among COVID-19 patients, they may not be as directly linked to mortality as sodium and chloride imbalances. (18,19) Electrolyte imbalances are a manifestation of the physiological derangement caused by COVID-19 infection. Our findings suggest a role for hyponatremia, hypocalcemia, and hypernatremia to be used in risk stratification, prognostication, and clinical decision-making in the treatment of patients with COVID-19.

Despite our findings, it is important to note that the clinical management of potassium and magnesium imbalances should not be overlooked, as these imbalances can still contribute to overall patient morbidity and require appropriate interventions. (19,20)

The findings regarding calcium and phosphorus imbalances are particularly noteworthy. Patients with imbalances in calcium and phosphorus exhibited significantly higher mortality rates. Hypophosphatemia is a common comorbidity but often leads to increased mortality or prolonged duration of intensive care unit stay in certain disease conditions, such as fasting, malnutrition, parenteral nutrition, metabolic or respiratory alkalosis, diabetic ketoacidosis, or alcoholism. (21) Some authors have suggested that phosphorus could serve as a reference index to determine the success of treatment in patients with acute exacerbations of chronic obstructive pulmonary disease. (22,23)

Our study underscores the importance of closely monitoring and managing these electrolytes in COVID-19 patients.

These results highlight the need for proactive monitoring and timely correction of electrolyte imbalances in critically ill COVID-19 patients. Ensuring electrolyte balance may not only improve patient outcomes but also reduce the overall burden on healthcare systems. (24) Clinical guidelines and protocols for managing electrolyte imbalances in COVID-19 patients must be available and widely implemented based on these findings.

Understanding the pathophysiological processes involved may lead to the development of more targeted interventions to improve outcomes for COVID-19 patients.

Conclusions

Our study provides important evidence that electrolyte imbalances, specifically sodium, chloride, calcium, and phosphorus, are associated with higher mortality rates in critically ill COVID-19 patients. Our findings stress the need for vigilant monitoring and intervention to maintain electrolyte balance as a key component of the clinical management of these patients.

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Table 1. Clinical outcomes in relation to electrolyte imbalance

		Clinical outcome		Total	p-value
		Dead, n (%)	Alive, n (%)		
Sodium	Hyponatremia	78 (43.6%)	289 (37.3%)	367	0.007
	Normal	94 (52.5%)	476 (61.5%)	570	
	Hypernatremia	7 (3.9%)	9 (1.2%)	16	
Potassium	Hypokalemia	17 (9.5%)	115 (14.9%)	132	0.049
	Normal	153 (85.5%)	639 (82.6%)	792	
	Hyperkalemia	9 (5%)	20 (2.6%)	29	
Chloride	Hypochloremia	32 (17.9%)	94 (12.1%)	126	0.038
	Normal	122 (68.2%)	624 (80.6%)	746	
	Hyperchloremia	25 (14%)	56 (7.2%)	81	
Magnesium	Hypomagnesemia	21 (11.7%)	112 (14.5%)	133	0.003
	Normal	111 (62%)	542 (70%)	653	
	Hypermagnesemia	47 (26.3%)	120 (15.5%)	167	
Phosphorus	Hypophosphatemia	55 (30.7%)	226 (29.2%)	281	<0.001
	Normal	96 (53.6%)	509 (65.8%)	605	
	Hyperphosphatemia	28 (15.6%)	39 (5%)	67	
Calcium	Hypocalcemia	112 (62.6%)	335 (43.3%)	447	<0.001
	Normal	67 (37.4%)	434 (56.1%)	501	
	Hypercalcemia	0 (0%)	5 (0.6%)	5	

Table 2. Gender and comorbidity data in relation to sodium

	All (n)	Hyponatremia (<135 mmol/l), n (%)	Normal range (135-145 mmol/l), n (%)	Hypernatremia (>145 mmol/l), n (%)	p-value
Male	541	239 (44.2%)	296 (54.7%)	6 (1.1%)	<0.001
Female	412	128 (31.1%)	274 (66.5%)	10 (2.4%)	
Hypertension	356	145 (40.7%)	202 (56.7%)	9 (2.5%)	0.131
Diabetes	241	108 (44.8%)	126 (52.3%)	7 (2.9%)	0.010
COPD	27	11 (40.7%)	16 (59.3%)	0 (0%)	0.777
CKD	26	6 (23.1%)	16 (61.5%)	4 (15.4%)	<0.001
Liver disease	14	6 (42.9%)	8 (57.1%)	0 (0%)	0.850

Legend: COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease.

Table 3. Gender and comorbidity data in relation to potassium

	All (n)	Hypokalemia (<3.5 mmol/l), n (%)	Normal range (3.5-5.2 mmol/l), n (%)	Hyperkalemia (>5.2 mmol/l, n (%)	p-value
Male	541	54 (10%)	469 (86.7%)	18 (3.3%)	<0.001
Female	412	78 (18.9%)	323 (78.4%)	11 (2.7%)	
Hypertension	356	43 (12.1%)	295 (82.9%)	18 (5.1%)	0.012
Diabetes	241	32 (13.3%)	193 (80.1%)	16 (6.6%)	0.001
COPD	27	6 (22.2%)	19 (70.4%)	2 (7.4%)	0.158
CKD	26	2 (7.7%)	21 (80.8%)	3 (11.5%)	0.029
Liver disease	14	1 (7.1%)	11 (78.6%)	2 (14.3%)	0.041

Legend: COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease.

Table 4. Gender and comorbidity data in relation to chloride

	All (n)	Hypochloremia (<98 mmol/l), n (%)	Normal range (98-108 mmol/l), n (%)	Hyperchloremia (>108 mmol/l), n (%)	p-value
Male	541	79 (14.6%)	422 (78%)	40 (7.4%)	0.164
Female	412	47 (11.4%)	324 (78.6%)	41(10%)	
Hypertension	356	63 (17.7%)	253 (71.1%)	40 (11.2%)	<0.001
Diabetes	241	42 (17.4%)	179 (74.3%)	20 (8.3%)	0.082
COPD	27	5 (18.5%)	20 (74.1%)	2 (7.4%)	0.708
CKD	26	6 (23.1%)	14 (53.8%)	6 (23.1%)	0.005
Liver disease	14	3 (21.4%)	10 (71.4%)	1 (7.1%)	0.657

Legend: COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease.

Table 5. Gender and comorbidity data in relation to calcium

	All (n)	Hypocalcemia (<8.6 mmol/l), n (%)	Normal range (8.6-10.3 mmol/l), n (%)	Hypercalcemia (>10.3 mmol/l), n (%)	p-value
Male	541	269 (49.7%)	270 (49.9%)	2 (0.4%)	0.112
Female	412	178 (43.2%)	231 (56.1%)	3 (0.7%)	
Hypertension	356	166 (46.6%)	188 (52.8%)	2 (0.6%)	0.985
Diabetes	241	113 (46.9%)	126 (52.3%)	2 (0.8%)	0.749
COPD	27	14 (51.9%)	13 (48.1%)	0 (0%)	0.821
CKD	26	15 (57.7%)	10 (38.5%)	1 (3.8%)	0.026
Liver disease	14	6 (42.9%)	7 (50%)	1 (7.1%)	0.003

Legend: COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease.

Table 6. Gender and comorbidity data in relation to phosphate

	All (n)	Hypophosphatemia <2.8 mmol/l), n (%)	Normal range (3.0-4.5 mmol/l), n (%)	Hyperphosphatemia (>4.5 mmol/l), n (%)	p-value
Male	541	152 (28.1%)	339 (62.7%)	50 (9.2%)	0.008
Female	412	129 (31.3%)	266 (64.6%)	17 (4.1%)	
Hypertension	356	109 (30.6%)	208 (58.4%)	39 (11%)	0.001
Diabetes	241	68 (28.2%)	143 (59.3%)	30 (12.4%)	0.001
COPD	27	6 (22.2%)	18 (66.7%)	3 (11.1%)	0.549
CKD	26	2 (7.7%)	12 (46.2%)	12 (46.2%)	<0.001
Liver disease	14	2 (14.3%)	10 (71.1%)	2 (14.3%)	0.314

Legend: COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease.

Table 7. Gender and comorbidity data in relation to magnesium

	All (n)	Hypomagnesemia (<1.7 mmol/l), n (%)	Normal range (1.7-2.2 mmol/l), n (%)	Hypermagnesemia (>2.2 mmol/l), n (%)	p-value
Male	541	64 (11.8%)	364 (67.3%)	113 (20.9%)	0.002
Female	412	69 (16.7%)	289 (70.1%)	54 (13.1%)	
Hypertension	356	64 (18%)	234 (65.7%)	58 (16.3%)	0.021
Diabetes	241	56 (23.2%)	154 (63.9%)	31 (12.9%)	<0.001
COPD	27	3 (11.1%)	21 (77.8%)	3 (11.1%)	0.560
CKD	26	3 (11.5%)	17 (65.4%)	6 (23.1%)	0.733
Liver disease	14	1 (7.1%)	10 (71.4%)	3 (21.4%)	0.736

Legend: COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease.

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