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Letter to the Editor

LETTER TO THE EDITOR

Electrolyte abnormalities in patients hospitalized with COVID-19

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) worldwide pandemic and the disease it inflicts, coronavirus disease 2019 (COVID-19), has been found to impact multiple organ systems, including pulmonary, cardiovascular, neurologic and kidney. In particular, while acute kidney injury (AKI) has been widely reported, other manifestations including electrolyte disturbances have been less well described [1, 2]. Early studies suggested that changes in serum sodium, potassium, chloride and calcium may be associated with infection and could be associated with disease severity [3]. At a large New York health system, we assessed data from >10 000 patients hospitalized with COVID-19 to evaluate the prevalence at hospital presentation of the full spectrum of electrolyte disorders.Detailed methods of the study can be found in the Supplementary Material.

Between 1 March 2020, and 27 April 2020, 11 635 patients were hospitalized for COVID-19, of which 10 385 were included in our final cohort. While for most serum electrolytes, overall missingness was ≤0.1%, serum magnesium and serum phosphorus had a substantial missingness (28.5% and 39.8%, respectively). Overall, hyponatremia was the most commonly identified disorder (37.5%), followed by hypochloremia (26.0%) and hypocalcemia (18.3%) (Table 1; see Figure 1B). Among patients with an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2, 30.3% had hyponatremia, 11.1% had hyperkalemia and 19.7% had hypochloremia (Table 1 and Figure 1A). Hypocalcemia was seen in 19.2% of patients. Hyperphosphatemia (13.9%) and hypermagnesemia (12.2%) were seen in a minority; however, there was a significant amount of data missing (37.4% and 26.2%, respectively) for this group.

Kidney transplant patients most commonly had hyponatremia (42.4%), hyperkalemia (16.7%) and hypochloremia (19%) (Table 1 and Figure 1A). In this group, hypophosphatemia (16.7%), hypomagnesemia (15.2%) and hypocalcemia (12.1%) were common, although many patients did not have these electrolytes checked (25.8%, 19.7% and 1.5%, respectively).

Patients with end-stage kidney disease (ESKD) were most commonly found to have hyponatremia (40.9%), hyperkalemia (23.4%) and hypochloremia (62%). Hyperphosphatemia (45.7%), hypermagnesemia (8.4%) and hypocalcemia (27.8%) were also seen (missingness of 26.8%, 23.2% and 0.2%, respectively) (Table 1 and Figure 1A).

Many patients had multiple co-occurring electrolyte disorders at presentation. Examining only electrolytes with ≤0.1% missingness (excluding magnesium and phosphorus), only 3393 (32.7%) had completely normal electrolytes on admission. For patients with electrolyte abnormalities, the most common

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Table 1. The proportion of electrolyte disorders by admission eGFR and dialysis status

Electrolyte categories	eGFR >60 mL/min/1.73 m^2	eGFR <60 mL/min/1.73 m^2	Kidney transplant	ESKD on dialysis	Total
Sodium, *n* (%)					
High	162 (2.7)	684 (17.9)	3 (4.5)	11 (2.6)	860 (8.3)
Low	2526 (41.7)	1161 (30.3)	28 (42.4)	171 (40.9)	3886 (37.5)
Normal	3365 (55.6)	1980 (51.7)	34 (51.5)	235 (56.2)	5614 (54.1)
Missing	0 (0.0)	6 (0.2)	1 (1.5)	1 (0.2)	8 (0.1)
Potassium, *n* (%)					
High	147 (2.4)	427 (11.1)	11 (16.7)	98 (23.4)	683 (6.6)
Low	822 (13.6)	351 (9.2)	7 (10.6)	28 (6.7)	1208 (11.7)
Normal	5082 (84.0)	3047 (79.5)	47 (71.2)	290 (69.4)	8466 (81.7)
Missing	2 (0.0)	6 (0.2)	1 (1.5)	2 (0.5)	11 (0.1)
Chloride, *n* (%)					
High	184 (3.0)	643 (16.8)	6 (9.1)	6 (1.4)	839 (8.1)
Low	1674 (27.7)	753 (19.7)	13 (19.7)	259 (62.0)	2699 (26.0)
Normal	4194 (69.3)	2432 (63.5)	46 (69.7)	152 (36.4)	6824 (65.8)
Missing	1 (0.0)	3 (0.1)	1 (1.5)	1 (0.2)	6 (0.1)
Phosphorus, *n* (%)					
High	149 (2.5)	533 (13.9)	10 (15.2)	191 (45.7)	883 (8.5)
Low	723 (11.9)	354 (9.2)	11 (16.7)	9 (2.2)	1097 (10.6)
Normal	2612 (43.2)	1512 (39.5)	28 (42.4)	106 (25.4)	4258 (41.1)
Missing	2569 (42.4)	1432 (37.4)	17 (25.8)	112 (26.8)	4130 (39.8)
Calcium, *n* (%)					
High	36 (0.6)	63 (1.6)	6 (9.1)	7 (1.7)	112 (1.1)
Low	1039 (17.2)	734 (19.2)	8 (12.1)	116 (27.8)	1897 (18.3)
Normal	4978 (82.2)	3034 (79.2)	51 (77.3)	294 (70.3)	8357 (80.6)
Missing	0 (0.0)	0 (0.0)	1 (1.5)	1 (0.2)	2 (0.0)
Magnesium					
High	213 (3.5)	467 (12.2)	1 (1.5)	35 (8.4)	716 (6.9)
Low	228 (3.8)	194 (5.1)	10 (15.2)	9 (2.2)	441 (4.3)
Normal	3771 (62.3)	2167 (56.6)	42 (63.6)	277 (66.3)	6257 (60.3)
Missing	1841 (30.4)	1003 (26.2)	13 (19.7)	97 (23.2)	2954 (28.5)

presentation was hyponatremia and hypochloremia together [1289 (12.4%)], followed by hyponatremia alone [1150 (11.1%)]. Many other combinations of electrolyte abnormalities were seen, as demonstrated in Figure 1B.

This is the first and largest study to evaluate all electrolyte disorders noted in hospitalized patients with COVID-19. Hyponatremia was the most prevalent electrolyte abnormality, followed by hypochloremia and hypocalcemia. In Turkey, in a study of 408 patients hospitalized with COVID-19, those with hyponatremia, hypochloremia and hypocalcemia had worse outcomes [4]. Patients with these types of abnormalities had underlying conditions like diabetes, hypertension and coronary artery disease, which may have contributed. In our population, it appears that overall low sodium, chloride and calcium levels were evident regardless of kidney function, kidney transplant or dialysis status.

We have previously demonstrated that ESKD and AKI in the setting of COVID-19 infection is associated with poor prognosis and death [2, 5]. It is likely that electrolyte abnormalities further contributed to the severity of these conditions. Surprisingly, patients with a lower eGFR had fewer electrolyte abnormalities, although missing data were common. Even in this cohort, hyponatremia was the most commonly encountered finding, which was seen in kidney transplant recipients as well. These latter patients also had a fair amount of magnesium- and phosphate-based disorders, likely a result of calcineurin inhibitor use. In ESKD patients, sodium-related disorders and hyperkalemia along with hyperphosphatemia prevailed, which may simply be a result of dialysis status rather than specifically related to COVID-19.

This study focused on the prevalence at admission of electrolyte disorders seen with COVID-19 patients, without a focus on mortality and other outcomes. Thus no causal relationship can be assigned to COVID-19 and any electrolyte disorder, as either the disease, other comorbid conditions or medications could account for the electrolyte changes. In summary, this study highlights the various electrolyte disorders in hospitalized COVID-19 patients. Overall, hyponatremia was the most commonly identified disorder, followed by hypochloremia and hypocalcemia. A majority of patients had at least one electrolyte abnormality on admission and several had multiple abnormalities. Further studies are needed to look at mortality outcomes related specifically to each electrolyte disorder.

SUPPLEMENTARY DATA

Supplementary data are available at ckj online.

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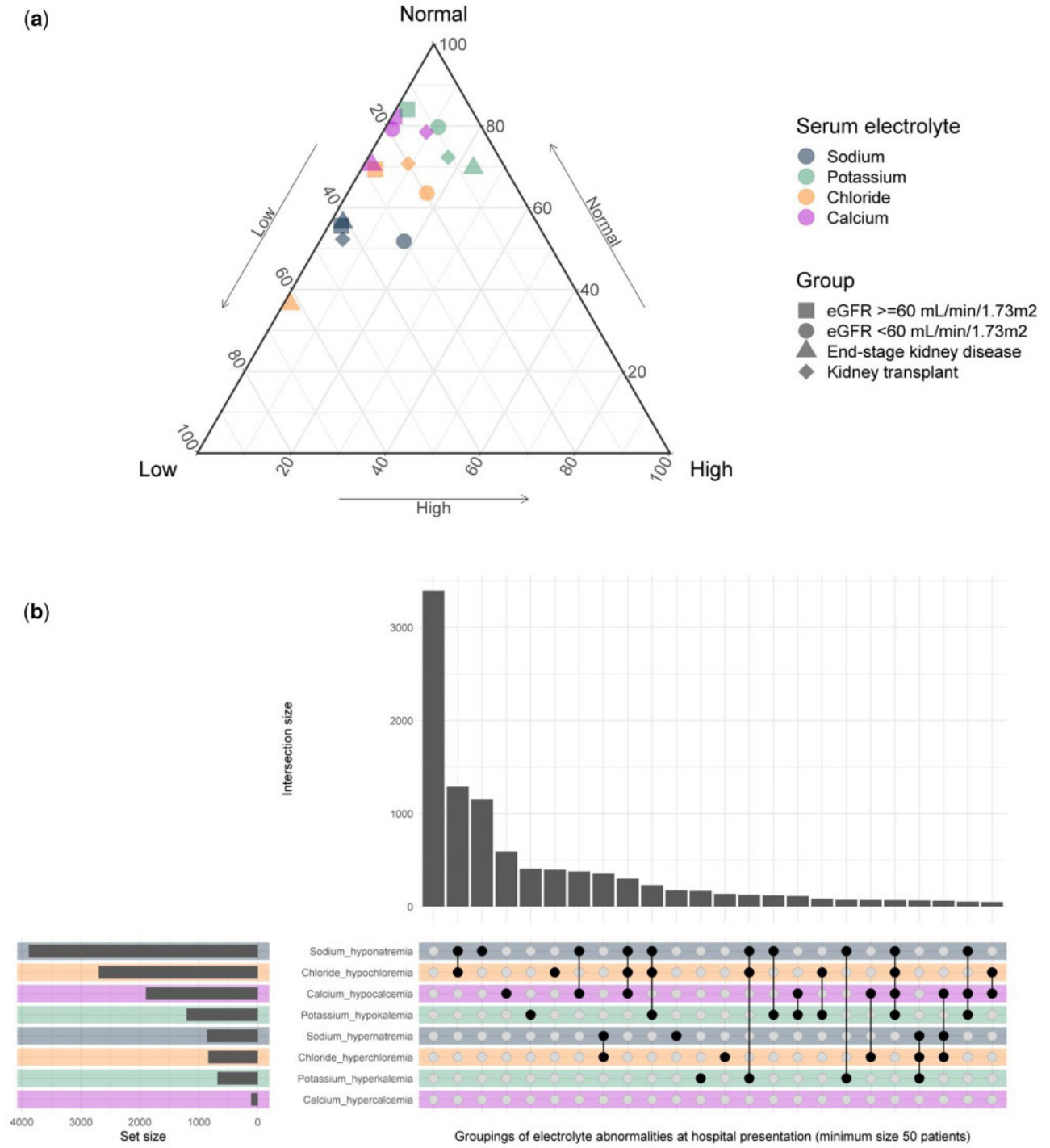

FIGURE 1: Electrolyte disorders at admission for patients hospitalized with COVID-19, with breakdown of (A) electrolytes by category (normal, high, low) for subgroups and (B) co-occurrence of electrolyte disorders. Panel A shows a ternary plot with balance of normal, high and low levels for each of four serum electrolytes (sodium, potassium, chloride and calcium), stratified by kidney group (normal eGFR, eGFR <60 mL/min/1.73 m^2, ESKD and kidney transplant). The three axes show the percent breakdown for each individual electrolyte group dyad and the clustering of points in the upper left of the triangle indicates that most electrolytes were normal, while low levels were seen next most commonly. Elevated electrolyte levels were least common, although 18% of patients with an eGFR <60 mL/min/1.73 m^2 had high sodium/hypernatremia (blue–gray circle) and 23% of those with ESKD had high potassium/hyperkalemia (green triangle). Panel B shows electrolyte abnormalities and their co-occurrence. Horizontal bars ('set size') show the prevalence of specific individual electrolyte abnormalities, while vertical bars ('intersection size') show the co-occurrence. Overall, hyponatremia was the most common electrolyte disorder, followed by hypochloremia, hypocalcemia and hypokalemia. Hypercalcemia was the least common electrolyte abnormality overall. Of the cohort, only 3393 (32.7%) had completely normal electrolytes on admission (first vertical bar, with no electrolyte abnormalities selected in the grid). The most common presentation of abnormality was hyponatremia and hypochloremia together (second vertical bar and selected in the grid) in 1289 (12.4%), followed by hyponatremia alone (third vertical bar and selected in the grid) in 1150 (11.1%). Colors in both panels encode specific electrolytes. These figures include only patients without missing values ($n = 10\,366$) and exclude serum magnesium and phosphorus, as these electrolytes had a significant amount of missingness.

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