

Baseline electrolyte abnormalities would be related to poor prognosis in hospitalized coronavirus disease 2019 patients

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Abstract

Electrolyte abnormalities are not uncommon in coronavirus disease 2019 (COVID-19). Several studies have suggested that various electrolyte imbalances seem to have an impact on disease prognosis. However, no study has primarily focused on the effect of baseline electrolyte abnormalities on disease outcome. In this study, we assessed the validity of the hypothesis that baseline electrolyte imbalances may be related to unfavourable outcomes in hospitalized COVID-19 patients. Design of the study was retrospective and observational. We included 408 hospitalized individuals with COVID-19 over 18 years old. Baseline levels of sodium, potassium, calcium and chloride were assessed and the effects of abnormalities in these electrolytes on requirement for intensive care unit and mechanical ventilation, hospitalization duration and treatment outcome were evaluated. Patients were clustered based on electrolyte levels and clusters were compared according to outcome variables. Frequency of other severe disease indices was compared between the clusters. Lastly, we evaluated the independent factors related to COVID-19-associated deaths with multivariate analyses. In all, 228 (55.8%) of the patients had at least one electrolyte imbalance at baseline. Hyponatraemia was the most frequent electrolyte abnormality. Patients with hyponatraemia, hypochloreaemia or hypocalcaemia had, respectively, more frequent requirement for intensive care unit and mechanical ventilation, higher mortality rate and longer hospitalization. The clusters associated with electrolyte abnormalities had unfavourable outcomes. Also, Clinical and laboratory features associated with severe disease were detected more often in those clusters. Hyponatraemia was an independent factor related to death from COVID-19 (OR 10.33; 95% CI 1.62–65.62; p 0.01). Furthermore, baseline electrolyte imbalances, primarily hyponatraemia, were related to poor prognosis in COVID-19 and baseline electrolyte assessment would be beneficial for evaluating the risk of severe COVID-19.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of the developing worldwide health problem, coronavirus disease 2019 (COVID-19), which was first

reported in December 2019, in the Chinese province of Wuhan [1]. It is a potentially fatal disease with multisystem involvements. However, its primary target is the human respiratory system. In the pulmonary system, SARS-CoV-2 induces severe pneumonia and causes acute respiratory distress syndrome [2]. Furthermore, the disease may have an impact on various parts of the body including the cardiac [3], nervous [4], renal [5], gastrointestinal [6] and coagulation [7] systems.

Several demographic, clinical and laboratory parameters correlate with prognosis and severity of COVID-19. Hypertension and diabetes mellitus are the most prevalent comorbidities associated with disease severity [8]. Likewise, lower lymphocyte and platelet counts; increased serum ferritin,

interleukin-6 (IL-6) and IL-10 levels; abnormalities in coagulation parameters such as increased D-dimer levels; alterations in cardiac and muscle injury parameters; and abnormalities in liver and kidney function biomarkers were found to be related to severe disease and unfavourable outcome in COVID-19 [9].

More than three-quarters of hospitalized individuals with COVID-19 had some renal involvement during the course of the disease [5]. Most frequent forms of renal involvement in COVID-19 are acute kidney injury, proteinuria, haematuria and electrolyte imbalances [5,10]. In a meta-analysis, lower concentrations of sodium, potassium and calcium were related to severe disease [10]; but, none of the studies included primarily evaluated the status of electrolyte imbalances and its effect on both survival and disease severity.

In this study, we evaluate the validity of the hypothesis that was developed within the scope of our observations: ‘The electrolyte imbalances at the first visit, even before treatments, may be related to unfavourable outcomes; higher frequency of intensive care unit (ICU) and mechanical ventilation (MV) requirement and increased inpatient days in the hospitalized COVID-19 patients.’

Materials and methods

All 408 individuals with COVID-19 over 18 years old who were hospitalized in one of the pandemic clinics of a tertiary health-care facility were retrospectively taken into the study. We diagnosed COVID-19 through two different approaches. First, all individuals with a positive PCR test for SARS-CoV-2 were accepted as having COVID-19. Moreover, those individuals with a negative PCR test were given a COVID-19 diagnosis if they fulfilled all three clinical criteria: (a) having fever and/or respiratory symptoms, (b) having compatible chest imaging findings [11] and (c) having decreased lymphocyte count while the white blood cell count was normal or decreased [12]. All individuals with possible COVID-19 were first sent to the pandemic outpatient clinics of the same tertiary health-care facility. Then, those individuals who fulfilled the Turkish Health Ministry COVID-19 Guidelines criteria for hospitalization were transferred to pandemic clinics. According to these criteria, COVID-19 patients with any of four conditions were hospitalized. These conditions were having any co-morbidity, radiological features compatible with pneumonia, age >50 years and having clinical features including respiratory distress, tachypnoea, oxygen saturation (SpO₂) <93% and tachycardia [13]. Patient discharge was decided according to same guidelines. Among the individuals with COVID-19 who were treated as inpatients, those who had no fever and no need for oxygen within the previous 48–72 hours were discharged [13].

TABLE 1. Demographic and disease-related features of the COVID-19 patients

	Patients (n = 408)
Age (years), mean ± SD	54.3 ± 16.3
Gender (M/F)	188/220
Positive PCR test, n (%)	267 (65.4)
Pulmonary involvement, ^a n (%)	380 (93.1)
SpO ₂ <92%, ^b n (%)	121 (29.7)
Fever, ^c n (%)	102 (25.0)
Electrolyte abnormalities, ^d n (%)	228 (55.8)
Time between onset of symptoms and hospitalization (days), mean ± SD	3.3 ± 1.4
Disease severity (NEWS score), mean ± SD	2.0 ± 2.28
Presenting symptoms, n (%)	
Cough	235 (57.6)
Shortness of breath	151 (37.0)
Fever	151 (37.0)
Musculoskeletal	46 (11.3)
Headache	16 (7.0)
Nasal discharge	2 (0.5)
Sore throat	27 (6.6)
Loss of taste or smell	11 (2.7)
Malaise	127 (31.1)
Diarrhoea	21 (5.1)
Nausea/vomiting	32 (7.8)
Loss of appetite	20 (4.9)
Co-morbidities, n (%)	
Diabetes mellitus	96 (23.5)
Hypertension	130 (31.9)
Coronary arterial disease	43 (10.5)
COPD	13 (3.2)
Asthma	32 (7.8)
Malignancy	16 (3.9)
Obesity ^e	6 (2.6)
Chronic renal disease	13 (3.2)
Rheumatic diseases	13 (3.2)
Treatment, n (%)	
Hydroxychloroquine	404 (99.0)
Azithromycin	376 (92.2)
Favipiravir	85 (20.8)
Other antibiotics	301 (73.8)
Tocilizumab	8 (2.0)
Lopinavir–Ritonavir	10 (2.5)
Primary end points, n (%)	
Deceased	26 (6.4)
Discharged	382 (93.6)
Length of hospitalization (days), mean ± SD	7.2 ± 5.9
Requirement for ICU	37 (9.1)
Requirement for MV	29 (7.1)

Abbreviations: COPD, chronic obstructive pulmonary disease; F, female; ICU, intensive care unit; M, male; MV, mechanical ventilation PCR, polymerase chain reaction test for SARS-CoV-2; SpO₂, saturation of oxygen.
^aPulmonary involvement at any chest imaging.
^bDuring hospitalization.
^cFever >38.0°C during hospitalization.
^dAny electrolyte abnormalities in the levels of sodium, potassium, calcium or chloride.
^eObesity, body mass index ≥30 kg/m².

We collected the patients' demographic features (age, gender), co-morbidities, presenting COVID-19-related symptoms, results of SARS-CoV-2 PCR test, treatment history for COVID-19 during hospitalization, outcome, requirement for ICU, requirement for MV, duration of hospitalization, measurements of fever and SpO₂ during hospitalization, time between disease onset and hospitalization, baseline disease severity (measured by National Early Warning Score—NEWS) [14] and baseline laboratory values (blood levels of electrolytes including sodium, potassium, chloride, corrected calcium; other biochemical parameters including aspartate aminotransferase, alanine aminotransferase, creatinine, creatine kinase, lactate dehydrogenase (LDH), D-dimer, albumin, ferritin, C-reactive protein (CRP) and blood counts). All the study

TABLE 2. Baseline electrolyte abnormalities' effect on primary endpoints

		OR	95% CI	p
Requirement for ICU, n (%)				
Hyponatraemia	25/146 (17.1)	3.73	1.93–7.21	<0.001
Hypokalaemia	5/28 (17.8)	2.48	0.88–7.0	0.08
Hyperkalaemia	2/7 (28.5)	4.18	0.78–22.35	0.09
Hypochloraemia	11/28 (39.2)	8.81	3.74–20.74	<0.001
Hypocalcaemia	11/39 (28.2)	5.18	2.32–11.57	<0.001
Requirement for MV, n (%)				
Hyponatraemia	18/146 (12.3)	3.20	1.47–6.99	0.003
Hypokalaemia	4/28 (14.2)	2.32	0.74–7.2	0.14
Hyperkalaemia	0/7 (0.0)	N/A	N/A	N/A
Hypochloraemia	9/28 (32.4)	6.23	2.58–15.04	<0.001
Hypocalcaemia	9/39 (23.0)	5.23	2.19–12.5	<0.001
Mortality, n (%)				
Hyponatraemia	19/146 (13.0)	5.40	2.21–13.20	<0.001
Hypokalaemia	2/28 (7.1)	1.15	0.25–5.14	0.85
Hyperkalaemia	0/7 (0.0)	N/A	N/A	N/A
Hypochloraemia	6/28 (21.4)	5.08	1.84–14.00	0.001
Hypocalcaemia	8/39 (20.5)	5.14	2.06–12.80	<0.001
Duration of hospitalization (days) ^a				
Hyponatraemia	8.72 ± 5.74	1.06	1.03–1.12	0.001
Hypokalaemia	7.51 ± 4.64	0.98	0.93–1.06	0.80
Hyperkalaemia	9.24 ± 4.40	1.02	0.95–1.12	0.40
Hypochloraemia	12.75 ± 6.79	1.09	1.04–1.14	<0.001
Hypocalcaemia	11.35 ± 9.36	1.08	1.04–1.12	<0.001

Abbreviations: ICU, intensive care unit; MV, mechanical ventilation.

parameters were obtained retrospectively from the hospital's medical records.

COVID-19 treatments were administered based upon the Turkish Health Ministry COVID-19 Guideline [13]. Furthermore, requirement for ICU or MV were decided by the ICU specialist in reference to same guideline [13]. Patient outcome was classified as deceased or discharged. The levels of electrolytes, aspartate aminotransferase, alanine aminotransferase, creatinine, creatine kinase, LDH, albumin and CRP were classified according to the laboratory reference ranges as normal, low or high. However, ferritin and D-dimer levels were classified based upon their levels related to unfavourable prognosis in COVID-19. These cut-off levels were specified as 300 mg/mL for ferritin and 1000 mg/L for D-dimer [15]. Also, we focused on white blood cell, platelet and lymphocyte counts at blood count. Platelet levels $<100 \times 10^9/L$ and lymphocyte levels $<1 \times 10^9/L$ were accepted as cut-off values for severe disease [16]. The calcium levels were corrected based upon serum albumin levels [17].

Primary end points were patient outcome, requirement for ICU, requirement for MV and duration of hospitalization. Patients were clustered by baseline electrolyte levels, and these clusters were compared according to those primary end points. We assessed the independent factors related to deaths from COVID-19.

This study was approved by both the Local Research Ethics Committee and the Turkish Health Ministry before data collection and was carried out in compliance with the Helsinki Declaration.

Statistical analyses

Statistical analyses were carried out using SPSS Version 17.0 (SPSS Inc., Chicago, IL, USA). To determine if the data were

normally distributed, the Kolmogorov–Smirnov test was performed. None of the parameters was distributed normally so comparisons of the continuous variables and categorical variables were performed using Mann–Whitney *U* test and χ^2 test, respectively. For classifying the patients in accordance with electrolyte levels, we implemented two-step cluster analyses. Sodium, potassium, chloride and calcium levels were included in the analyses. Then, we compared the clusters for primary end points. We also evaluated the independent factors related to mortality from COVID-19 by multivariate analysis using binary logistic regression. We included the variables age, gender, disease severity, time between disease onset and hospitalization, electrolyte abnormalities, co-morbidities, pulmonary infiltration, fever and hypoxaemia during hospitalization in the multivariate analysis. Results are given as mean \pm standard deviation. A value of $p < 0.05$ was considered statistically significant.

Results

We included 408 hospitalized individuals with COVID-19 in the study. In the COVID-19 cohort, 220 (53.9%) of the patients were women. Mean age was 54.3 ± 16.3 years and 267 (65.4%) were SARS-CoV-2 PCR-positive. The most frequent presenting symptoms were cough, fever and shortness of breath, and the most frequent co-morbidities were diabetes mellitus, hypertension and coronary arterial diseases. Thirty-seven (9.1%) of the patients were transferred to the ICU and 29 (7.1%) needed MV during their hospitalization. Furthermore, 26 (6.4%) of the 408 patients died (Table 1).

We found that 228 (55.8%) of the patients had an electrolyte abnormality at baseline. Hyponatraemia was the most frequent baseline electrolyte abnormality (146; 35.8%). Thirty-nine (9.5%) had hypocalcaemia, and hypokalaemia and hypochloraemia were found in 28 (6.8%) patients each. Lastly, seven (1.7%) of the participants had hyperkalaemia. None of the patients in our cohort had hypernatraemia, hyperchloraemia or hypercalcaemia at baseline. Frequency of ICU requirement, MV requirement and mortality were higher, and duration of hospitalization was longer in patients with hyponatraemia, hypochloraemia and hypocalcaemia compared with patients without individual electrolyte abnormalities (Table 2).

We classified individuals based upon electrolyte abnormalities. After administering two-step cluster analyses, the patients were divided into two clusters. All studied electrolytes (sodium, potassium, calcium and chloride) made significant contributions to both clusters. Herein, in both clusters, sodium levels were the most significant variable (Fig. 1a). All patients in cluster 1 had normal levels of sodium, chloride, potassium and calcium. Those in cluster 2 were mainly hyponatraemic, normokalaemic,

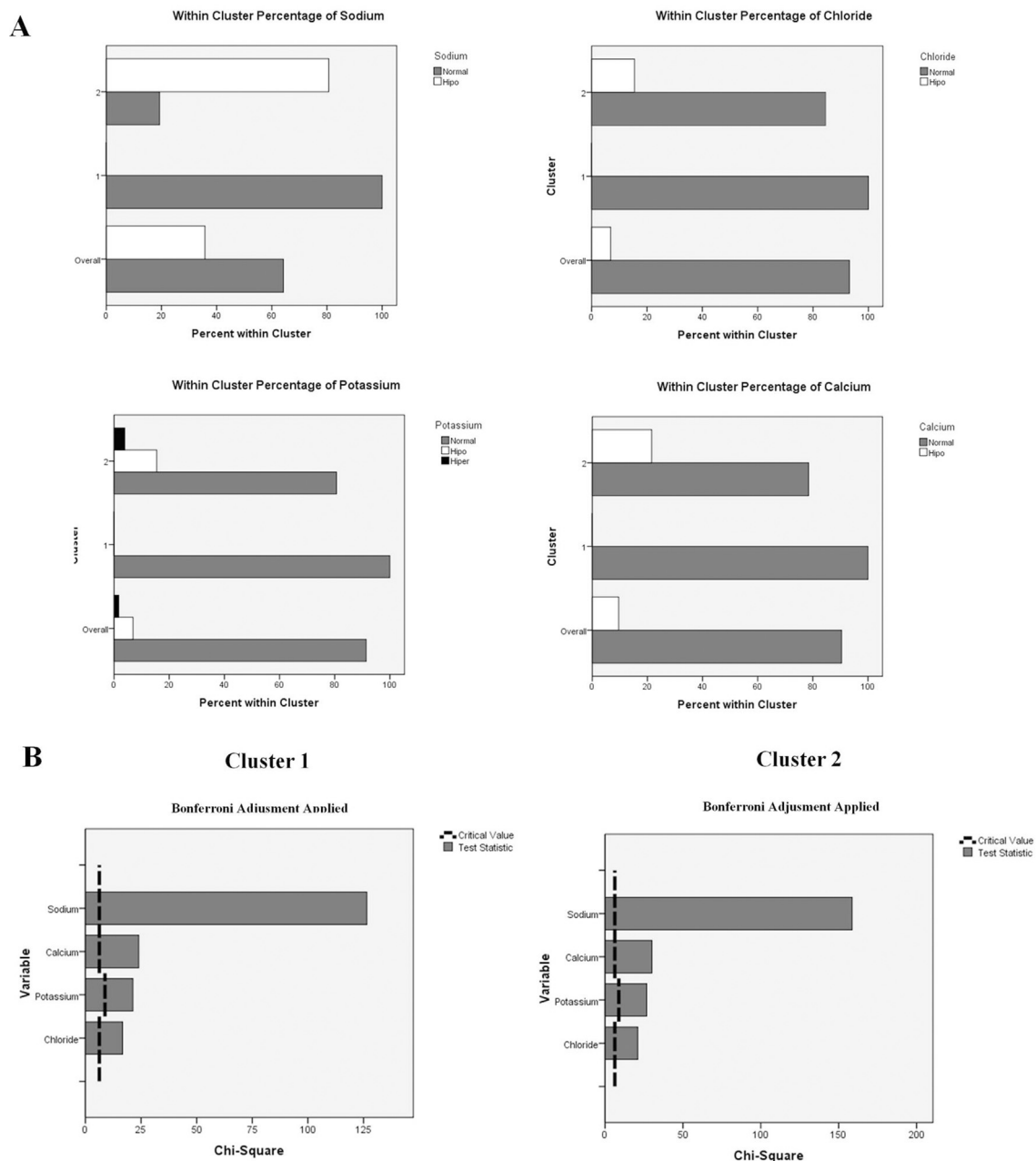


FIG. 1. (a) Percentage of electrolyte abnormalities within clusters; (b) significance of the electrolyte abnormalities in the clusters.

normocalcaemic and normochloreaemic. However, all patients with abnormal levels of potassium, sodium, calcium and chloride aggregated in cluster 2 (Fig. 1b). Cluster 1 contained no individuals with electrolyte abnormalities, and even though all patients with electrolyte abnormalities were in cluster 2, the main difference between the two clusters was sodium levels.

Patients in cluster 2 were older, and had higher frequencies of hypoxaemia and fever during hospitalization. Moreover, only fever and musculoskeletal findings as presenting symptoms were different between groups. Both those presenting

symptoms were more frequent in cluster 2. Diabetes mellitus, hypertension and coronary arterial diseases were more often found in cluster 2. Lastly, baseline COVID disease severity scores were higher in cluster 2 (Table 3).

C-reactive protein, LDH, D-dimer, creatinine and ferritin levels of the patients in cluster 2 were more frequently higher than cut off values compared with cluster 1 patients. Also, more patients in cluster 2 had low levels of lymphocyte counts (Table 4).

In terms of outcome parameters, cluster 2 patients had worse prognosis compared with those in cluster 1. More patients in

TABLE 3. Demographic and disease-related features of the patients in the different clusters

	Cluster 1 (n = 227)	Cluster 2 (n = 181)	p
Age (years), mean ± SD	51.5 ± 15.5	57.8 ± 16.6	<0.001
Gender (M/F)	90/137	98/83	0.004
Positive PCR test, n (%)	143 (63.0)	124 (68.5)	0.25
Pulmonary involvement, ^a n (%)	207 (91.2)	173 (95.6)	0.08
SpO ₂ ≤ 92%, ^b n (%)	45 (19.8)	76 (42.0)	<0.001
Fever, ^c n (%)	41 (18.1)	61 (33.7)	<0.001
Time between onset of symptoms and hospitalization (days), mean ± SD	3.5 ± 1.4	3.0 ± 1.3	0.06
Disease severity (NEWS score), mean ± SD	1.4 ± 1.8	2.8 ± 2.5	<0.001
Presenting symptoms, n (%)			
Cough	139 (61.2)	96 (53.0)	0.10
Shortness of breath	78 (34.4)	73 (40.3)	0.21
Fever	65 (28.6)	86 (47.5)	<0.001
Musculoskeletal	32 (14.1)	14 (7.7)	0.04
Headache	16 (7.0)	17 (9.4)	0.38
Nasal discharge	2 (0.9)	0 (0.0)	0.20
Sore throat	16 (7.0)	11 (6.1)	0.69
Loss of taste or smell	5 (2.2)	6 (3.3)	0.54
Malaise	72 (31.7)	55 (30.4)	0.77
Diarrhoea	10 (4.4)	11 (6.1)	0.44
Nausea/vomiting	15 (6.6)	17 (9.4)	0.29
Loss of appetite	9 (4.0)	11 (6.1)	0.36
Co-morbidities, n (%)			
Diabetes mellitus	43 (18.9)	53 (29.3)	0.01
Hypertension	63 (27.8)	67 (37.0)	0.04
Coronary arterial disease	14 (6.2)	29 (16.0)	0.001
COPD	4 (1.8)	9 (5.0)	0.06
Asthma	23 (10.1)	9 (5.0)	0.05
Malignancy	6 (2.6)	10 (5.5)	0.13
Obesity ^d	6 (2.6)	6 (3.3)	0.68
Chronic renal disease	3 (1.3)	10 (5.5)	0.01
Rheumatic diseases	6 (2.6)	7 (3.9)	0.48
Treatment, n (%)			
Hydroxychloroquine	226 (99.6)	178 (98.3)	0.32
Azithromycin	207 (91.2)	169 (93.4)	0.41
Favipiravir	32 (14.1)	53 (29.3)	<0.001
Other antibiotics	159 (70.0)	142 (78.5)	0.05
Tocilizumab	3 (1.3)	5 (2.8)	0.47
Lopinavir–Ritonavir	3 (1.3)	7 (3.9)	0.11
Primary end points, n (%)			
Deceased	5 (2.2)	21 (11.6)	0.001
Discharged	222 (97.8)	160 (88.4)	
Length of hospitalization, mean ± SD	6.1 ± 5.3	8.6 ± 6.4	<0.001
Requirement for ICU	8 (3.5)	29 (16.0)	<0.001
Requirement for MV	7 (3.1)	22 (12.2)	<0.001

Abbreviations: COPD, chronic obstructive pulmonary disease; F, female; ICU, intensive care unit; M, male; MV, mechanical ventilation PCR, polymerase chain reaction test for SARS-CoV-2; SpO₂, saturation of oxygen.
^aPulmonary involvement at any chest imaging.
^bDuring hospitalization.
^cFever >38.0°C during hospitalization.
^dObesity, body mass index ≥30 kg/m².

cluster 2 died and requirement for ICU and MV was more frequent in cluster 2. Lastly, patients in cluster 2 had longer hospitalization duration with regard to cluster 1 (Table 3).

Lastly, we conducted multivariate analyses to evaluate the risk factors associated with COVID-19-related deaths. Hyponatraemia, age, disease severity, fever during hospitalization and having at least one of the co-morbidities were independent variables for death from COVID-19 (Table 5).

Discussion

We evaluated the effect of electrolyte imbalances on frequency of ICU and MV requirement, hospitalization length and

treatment outcome; it was found that sodium, chloride and calcium abnormalities were related to unfavourable outcome. Furthermore, after clustering patients based upon electrolyte imbalances, they were divided into two different groups. The main difference between the groups was frequency of sodium abnormalities. Patients aggregated in the cluster with electrolyte imbalances had worse prognosis compared with patients with normal electrolyte levels. Furthermore, hyponatraemia was independently related to death from COVID-19.

There were several clinical and laboratory features related to severe disease in COVID-19. In one study, levels of sodium, CRP and pre-albumin, the platelet count and pCO₂ had the highest predictive power for severe disease [18]. Also, in hospitalized patients, older age, D-dimer and high SOFA scores were relevant to mortality [15]. In blood counts, increased white blood cell counts, and low lymphocyte and platelet counts were more often found in individuals who died [9]. Diabetes mellitus and hypertension were the main co-morbidities related to disease severity and mortality [8]. In a meta-analysis, abnormalities in coagulation parameters such as increased D-dimer levels, alterations in cardiac and muscle injury biomarkers, and liver and kidney function tests were related to severe disease and unfavourable outcome in COVID-19 [9]. Risk factors for hospitalization and prolonged hospitalization were also studied. High CRP, older age and low lymphocyte counts were related to hospitalization [19] and hypoalbuminaemia, increased levels of ferritin and LDH were correlated to prolonged hospitalization [20]. Several cytokines contribute to the pathogenesis of the disease; high levels of IL-6, IL-10 and tumour necrosis factor were correlated with disease severity [21,22]. Likewise, serum electrolyte abnormalities may be relevant to severe disease. In a meta-analysis, sodium and potassium levels were significantly lower in severe COVID-19 [10]. Moreover, it was found that sodium, potassium and chloride levels had high predictive power for COVID-19 progressing to severe disease [18]. In our study, we showed that low baseline sodium, chloride and calcium levels related to higher frequency of mortality, higher ICU and MV requirement and longer hospital stays. In the studies described above, various electrolyte abnormalities were found to be relevant to severe disease or poor prognosis. However, hyponatraemia was the common electrolyte abnormality related to unfavourable outcome in these studies. Therefore, assessing baseline electrolyte levels, primarily sodium status, would help physicians perform a risk evaluation for COVID-19 severity.

One study showed that sodium and IL-6 levels were inversely correlated and, as in other studies, sodium levels were associated with more severe outcome [23]. As IL-6 is one of the key cytokines for cytokine storm and poor prognosis [24], it could be speculated that low sodium levels would be an indirect sign of increased IL-6

TABLE 4. Baseline laboratory abnormalities of the patients in the different clusters

	Cluster 1 (n = 227)	Cluster 2 (n = 181)	p
Sodium, <135 meq/L	0 (0.0)	146 (80.7)	<0.001
Potassium			
<3.5 meq/L	0 (0.0)	146 (80.7)	<0.001
>5.5 meq/L	0 (0.0)	7 (3.9)	0.003
Chloride, <97 meq/L	0 (0.0)	28 (15.5)	<0.001
Calcium, <8.5 mg/dL	0 (0.0)	39 (21.5)	<0.001
CRP, >10 mg/L	114 (50.2)	146 (80.7)	<0.001
ALT, >35 IU/L	32 (14.1)	28 (15.5)	0.68
AST, >35 IU/L	33 (14.5)	41 (22.7)	0.32
Creatinine, >1.2 mg/dL	16 (7.0)	25 (13.8)	0.02
LDH, >240 U/L	72 (31.7)	91 (50.3)	<0.001
CK, >185 U/L	25 (11.0)	32 (17.7)	0.07
D-dimer, ≥1000 ng/mL	54 (23.8)	67 (37.0)	0.001
Platelet, <100 × 10 ⁹ /L	2 (0.9)	3 (1.7)	0.47
Lymphocyte, ≤1 × 10 ⁹ /L	54 (23.8)	75 (41.4)	<0.001
White blood cell			
≤4 × 10 ⁹ /L	25 (11.0)	30 (16.6)	0.10
>10 × 10 ⁹ /L	18 (7.9)	24 (13.3)	0.07
Ferritin, ≥300 mg/mL	11 (4.8)	24 (13.3)	0.02
Albumin, <3.5 g/L	42 (18.5)	56 (30.9)	0.002

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CRP, C-reactive protein; LDH, lactate dehydrogenase.

levels and may be related to severe disease phenotype. Furthermore, hyponatraemia was the most prominent electrolyte abnormality that increased the likelihood of mortality in hospitalized patients [25]. Therefore, low sodium levels would also be accepted as a risk factor for mortality in hospitalized COVID-19 patients, as for other diseases.

There may be several causes for electrolyte abnormalities in COVID-19. Kidney involvement and inappropriate anti-diuretic hormone syndrome [26] would be the key pathogenesis for electrolyte imbalance. Endotheliitis [27], proximal tubule injury, up-regulated angiotensin-converting enzyme 2 in kidney tissue, renal hypoxia and abnormal coagulation could account for electrolyte abnormalities related to kidney injury [28].

In our study, all patients with abnormal electrolyte levels aggregated in cluster 2. Also, the prominent electrolyte imbalance in cluster 2 was hyponatraemia. Several demographic features

TABLE 5. Multivariate analyses of the factors related to mortality from COVID-19

	OR	95% CI	p
Hyponatraemia	10.33	1.62–65.62	0.01
Potassium abnormality	5.11	0.56–46.14	0.14
Hypochloraemia	2.60	0.28–23.54	0.39
Hypocalcaemia	2.32	0.74–7.2	0.14
Age	1.05	1.03–1.09	0.03
Pulmonary involvement ^a	0.99	0.97–2.34	0.99
SpO ₂ ≤92% ^b	0.24	0.16–3.72	0.31
Fever ^c	8.42	1.43–49.52	0.01
Disease severity	3.44	1.67–5.1	<0.001
Male gender	0.91	0.21–3.86	0.99
Time between onset of symptoms and hospitalization	1.71	0.98–2.87	0.06
Co-morbidities	6.66	1.12–26.65	0.004

^aPulmonary involvement at any chest imaging.

^bDuring hospitalization.

^cFever >38.0°C during hospitalization.

(older age), biochemical abnormalities (alterations in CRP, LDH, D-dimer, creatinine, ferritin and lymphocyte counts) and co-morbidities (diabetes mellitus, hypertension and coronary arterial diseases) relevant to severe COVID-19 [9] were also more frequent in cluster 2. Electrolyte abnormalities were detected together with some of the variables associated with poor prognosis, so they may be a strong indicator of severe disease.

There were some limitations of the study. First, we evaluated only a limited number of electrolyte influences on disease prognosis. Furthermore, we did not assess the aetiology of the electrolyte abnormalities. Only hospitalized individuals were included in the study. Therefore, the data did not represent all COVID-19 patients. Lastly, as the study was of a retrospective and observational design, we evaluated only the baseline electrolyte levels. As a result, the data did not show the effect of subsequent electrolyte abnormalities developed during hospitalization on outcome.

Baseline electrolyte abnormalities, mainly hyponatraemia are a sign of unfavourable prognosis in COVID-19 and baseline electrolyte assessment, even after hospitalization, would be beneficial to assessing the risk for severe COVID-19.

Conflict of interest

The authors declare that they have no conflicts of interest.

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Authors' contributions

MET wrote the paper and contributed to the conception of design of the study. GDG contributed to the acquisition, analysis and interpretation of data for the work and to drafting the article; NS made important contributions to conceptual and planning stages of the study. NZK contributed to the collection and processing, analysis and interpretation of the data. RSO drafted and critically revised the article for important intellectual content. All authors have approved the final version of the manuscript.

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