

ORIGINAL ARTICLE

Electrolyte Abnormalities in Hospitalized COVID-19 Patients: An Observational Study

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Abstract:

Background: Coronavirus disease 2019 (COVID-19) is a potentially fatal disease with multisystem involvement. 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.

Objective: The primary objective of the present study was to evaluate the pattern of electrolyte abnormalities in hospitalized COVID-19 patients.

Methods: This retrospective study was conducted in the Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka, between January 2021 and June 2021. A total of 51 patients with COVID-19 were included in the study. Baseline levels of sodium, potassium, calcium and chloride were assessed and the effects of abnormalities in these electrolytes were evaluated. Patients demographic profile, clinical features, admission electrolyte report were documented in case record forms. Collected data were compiled and appropriate analyses were done by using computer based software. Chi-square test was used to analyse the categorical variaties. A p-value <0.05 was considered significant.

Results: In this study, total 51 hospitalized COVID-19 patients were included in the study. Majority (41.2%) patients belonged to age group 61 to 80 years with mean age 56.3±17.7 years. Two third (66.7%) patients were male with male to female ratio 2:1. Majority (31.4%) of the patients had hypertension followed by diabetes mellitus 29.4%, 23.5% had IHD, 15.7% had COPD and 35.3% were smoker. Most commonly electrolyte abnormality was hyponatraemia (56.9%) followed by hypokalemia (41.2%). Hyponatraemia was significantly higher in severe COVID-19 patient group.

Conclusion: In this study, we found that, Hyponatraemia was the most predominant electrolyte abnormality. Hyponatraemia is a sign of unfavourable prognosis in COVID-19 and baseline electrolyte assessment, even after hospitalization, would be beneficial to assess the risk for severe COVID-19.

Key words: COVID-19, Electrolyte abnormalities.

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Introduction:

Since reported in late December 2019 from the Hubei province in China, coronavirus disease 2019 (COVID-19) has spread worldwide.¹ The World Health Organization (WHO) declared COVID-19 a pandemic in mid-March 2020. Clinical presentation of COVID-19 infection is wide, from asymptomatic infection to severe viral pneumonia with acute respiratory distress syndrome (ARDS).²⁻⁴ 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.^{5,6} In a meta-analysis, lower concentrations of sodium, potassium and calcium were related to severe disease; but none of the studies included primarily evaluated the status of electrolyte imbalances and its effect on both survival and disease severity.⁶ ACE2, one of the key enzymes in the renin-angiotensin system (RAS), plays a significant role in regulating fluid and electrolyte balance.⁷ In a study including one hundred seventy-five COVID-19 patients, 18% were classified as having severe hypokalemia, 37% had hypokalemia, and 46% had normokalemia.⁸ Water excretion may also be disturbed in Coronavirus infection⁹, and hyponatremia has been reported in COVID-19 patients in a clinical case and in a small study in the United States.^{10,11} Hyponatremia and hypokalemia were reported in a series of 12 patients in China.¹² Moreno et al.¹³ described 306 COVID-19 patients in Spain with potassium measured in the first 72 h of admission. They found that hypokalemia was independently associated with requiring invasive mechanical ventilation, but mortality was not influenced by low potassium. There is a study, regarding hypocalcaemia which shows it is commonly occurred in severe COVID-19 patients and it was associated with poor outcome.¹⁴ Different electrolytes imbalance, may have important implications on management and outcome of critically ill COVID-19 patients. Earlier pool analyses suggested that electrolyte abnormalities can be a common finding in Covid-19 patients that can be an obstacle in managing these patients. So, in this study we evaluated the pattern of electrolyte abnormalities in hospitalized patients due to COVID-19 to broaden our understanding of the underlying cause of electrolyte disturbances in these patients.

Materials and methods:

This retrospective study was conducted in the Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka, between Jan 2021 and June 2021. Admission data of total 51 cases of RT-PCR positive COVID-19 patients were enrolled in this study. We collected patient demographic features (age, sex), comorbidities, history of COVID related symptoms, treatment protocol and electrolyte values including sodium, potassium and chloride were measured by ion-selective method (Auto analyzer). Other biochemical parameters including Hb, ESR, WBC, neutrophil, lymphocyte, RBS, serum creatinine, D-dimer and C-reactive protein (CRP) was also collected. The level of electrolytes were classified as normal, hypo or hyper according to laboratory reference range. Collected data were compiled and appropriate analyses were done by using computer based software. Qualitative variables were expressed in percentage. Chi-Square test was done to analyze the categorical variables, shown with cross tabulation. P value <0.05 was considered as statistically significant.

Results:

Among 51 hospitalized COVID-19 patients, majority 16(41.2%) belonged to age 61 to 80 years with mean age 56.3 ± 17.7 years. Two third (66.7%) patients were male with male to female ratio 2:1 (Table-1). Regarding co-morbidities majority 16 (31.4%) patients had hypertension followed by 15(29.4%) had diabetes mellitus, 12(23.5%) had IHD, 8(15.7%) had COPD (Table-2). Smoker was found in 18(35.3%) (Table-3). Mean Hb was found 10.6 ± 2.0 g/dl, ESR 46.7 ± 22.2 mm/hr, WBC $12.8 \pm 5.4 \times 10^9/L$, neutrophil 72.9 ± 13.4 percent, lymphocyte 20.7 ± 10.2 percent, RBS 9.0 ± 4.3 mmol/L, serum creatinine 1.16 ± 0.36 mg/dL, CRP 33.1 ± 46.9 mg/l and D-Dimer 2.1 ± 2.0 gm/dl (Table-4). More than one third (35.3%) patients moderate of severity COVID-19 (Figure 1). Regarding electrolyte imbalance, majority 29(56.9%) patients had hyponatraemia, followed by 21(41.2%) hypokalemia, 5(9.8%) hyperchloremia, 5(9.8%) hyperkalemia and 3(5.9%) hypochloremia (Table-5). Thirteen (76.5%) patients were found hyponatraemic in severe COVID-19 group and 16(47.1%) in non severe COVID-19 group which was statistically significant ($p < 0.05$) between two groups (Table-6).

Table-I*Demographic characteristics of the study patients (n=51)*

	Frequency	Percentage
Age (years)		
21-40	9	17.6
41-60	18	35.3
61-80	21	41.2
>80	3	5.9
Mean±SD	56.3±17.7	
Range (min-max)	21.0-90.0	
Sex		
Male	34	66.7
Female	17	33.3

Table-II*Co-morbidity of the study patients (n=51)*

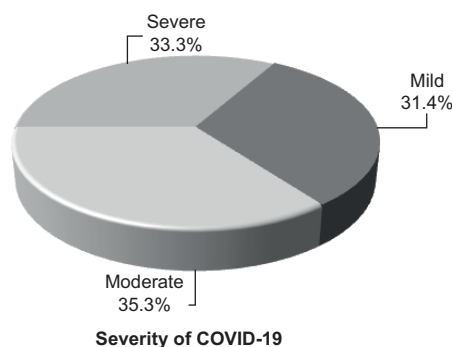
Co-morbidity	Frequency	Percentage
Hypertension	16	31.4
Diabetes mellitus	15	29.4
IHD	12	23.5
COPD	8	15.7
TB	3	5.9
Asthma	3	5.9
CKD	2	3.9
CLD	1	2.0
Malignancy	1	2.0

Table-III*Smoking status of the study patients (n=51)*

Smoking status	Frequency	Percentage
Yes	18	35.3
No	33	64.7

Table-IV*Hematological profile of the study patients (n=51)*

Investigations	Mean	±SD
Hb (g/dl)	10.6	±2.0
ESR (mm/hr)	46.7	±22.2
WBC (10 ⁹ /L)	12.8	±5.4
Neutrophil (%)	72.9	±13.4
Lymphocyte (%)	20.7	±10.2
RBS (mmol/L)	9.0	±4.3
Serum creatinine (mg/dL)	1.16	±0.36
CRP (mg/l)	33.1	±46.9
D-Dimer (gm/dl)	2.1	±2.0

**Fig.-1:** Pie chart showing severity of COVID-19 of the study patients (n=51)**Table-V***Electrolyte imbalance of the study patients (n=51)*

Electrolyte imbalance	Frequency	Percentage
Sodium		
Hyponatraemia (<135 mmol/L)	29	56.9
Normal (135-145 mmol/L)	22	43.1
Potassium		
Hypokalemia (<3.5 mmol/L)	21	41.2
Normal (3.5-5.0 mmol/L)	24	47.1
Hyperkalemia (>5.0 mmol/L)	5	9.8
Chloride		
Hypochloremia (<100 mmol/L)	3	5.9
Normal (100-108 mmol/L)	43	84.3
Hyperchloremia (>108 mmol/L)	5	9.8

Table-VI
Association between electrolyte imbalance with severity of COVID-19

Electrolyte imbalance	Severity of COVID-19		P value
	Severe(n=17)	Non Severe(n=34)	
Sodium			
Hyponatraemia	13 (76.5%)	16 (47.1%)	0.046 ^s
Normal	4 (23.5%)	18 (52.9%)	
Potassium			
Hypokalemia	8 (47.1%)	13 (38.2%)	0.741 ^{ns}
Normal	8 (47.1%)	16 (47.1%)	
Hyperkalemia	1 (5.9%)	4 (11.8%)	
Chloride			
Hypochloremia	1 (5.9%)	2 (5.9%)	0.800 ^{ns}
Normal	15 (88.2%)	28 (82.4%)	
Hyperchloremia	1 (5.9%)	4 (11.8%)	

s= significant; ns= not significant

P value reached from chi square test

Discussion

Studies on COVID-19 confirm electrolyte disturbances in patients, including sodium, potassium, chlorine, and calcium imbalances.^{2,15} One of the most common electrolyte disorders is hyponatremia, which occurs with a heightened risk of mortality in hospitalized patients.¹⁶ Some drugs previously used in the United States Food and Drug Administration's (FDA) treatment protocol for patients with COVID-19, such as chloroquine and hydroxychloroquine, can cause electrolyte imbalance.¹⁷

In this study among 51 patients with COVID-19 majority 21(41.2%) patients belonged to age 61 to 80 years with mean age 56.3±17.7 years. In a study conducted by Sultana et al.¹⁸ reported that mean age was 62.9±13.3 years. Tezcan et al.¹⁹ described that mean age was 54.3±16.3 years. Guan et al.¹⁵ observed that the median age was 47.0 years. Another study done by Zhou et al.²⁰ showed the median age of the 191 COVID patients was 56.0 years, that was almost similar with your study.

We found that male patients were predominant 34(66.7%) with male, female ratio was 2:1. De Carvalho et al.²¹ had observed that 56% patients were male and 44% were female. Sultana et al.¹⁸ demonstrated that 58.57% patients were male and 41.42% were female. Liu et al.²² described that 51.8% were male. Guan et al.¹⁵ also observed that males were more likely to be infected than females

(58.1% male and 41.9% female) that was support with my study.

Regarding co-morbidity in this study we observed that majority 16(31.4%) patients had hypertension followed by 15(29.4%) had diabetes mellitus, 12(23.5%) had IHD, 8(15.7%) had COPD, 3(5.9%) had TB, 3(5.9%) had asthma, 2(3.9%) had CKD, 1(2.0%) had CLD and 1(2.0%) had malignancy. In a study done by Tezcan et al.¹⁹ reported that 31.9% patients had hypertension followed by 23.5% had diabetes mellitus, 10.5% had coronary arterial disease, 3.2% had COPD, 7.8% had asthma, 3.9% had malignancy, 2.6% had obesity, 3.2% had chronic renal disease and 3.2% had rheumatic diseases. Malieckal et al.²³ described patients with these types of abnormalities had underlying conditions like diabetes, hypertension and coronary artery disease, which may have contributed. De Carvalho et al.²¹ showed 40.7% patients had hypertension followed by 20.2% had diabetes mellitus, 8.6% had CKD, 14.1% had CHF and 1.3% had liver cirrhosis. Zhou et al.²⁰ demonstrated that 91(48%) patients had a comorbidity, with hypertension being the most common 58(30%) patients followed by diabetes 36 (19%) and coronary heart disease 15 (8%) patients. Hu et al.²⁴ also found diabetes mellitus and hypertension were the main co morbidities related to disease severity and mortality, in their study.

This study showed 18(35.3%) patients were smoker. In a study conducted by Zhou et al.²⁰ reported 11(6%) were current smoker.

We found mean Hb was found 10.6 ± 2.0 g/dl, ESR was 46.7 ± 22.2 mm/hr, WBC was $12.8 \pm 5.4 \times 10^9/L$, neutrophil was 72.9 ± 13.4 percent, lymphocyte was 20.7 ± 10.2 percent, RBS was 9.0 ± 4.3 mmol/L, serum creatinine was 1.16 ± 0.36 mg/dL, CRP was 33.1 ± 46.9 mg/l and D-Dimer was 2.1 ± 2.0 gm/dl. Zhou et al.²⁰ had observed median WBC was $6.2 \times 10^9/L$ followed by lymphocyte count was $1.0 \times 10^9/L$ and D-Dimer was 0.8 μ g/ml.

We observed that majority (56.9%) patients had hyponatraemia, followed by 21(41.2%) was hypokalemia, 5(9.8%) was hyperchloremia, 5(9.8%) was hyperkalemia and 3(5.9%) was hypochloremia. Malieckal et al.²³ found hyponatremia was the most commonly identified disorder (37.5%) followed by hypochloremia (26.0%) and hypocalcemia (18.3%). In Turkey, in a study on 408 patients hospitalized with COVID-19 showed those with hyponatremia, hypochloremia and hypocalcemia had worse outcomes. Sultana et al.¹⁸ In their study they delayed with critically ill COVID patients total 82.85% (n= 58) had different electrolytes abnormalities and only 17.14% (n=12) had normal electrolytes level during admission period. Here most frequent electrolyte imbalance was hyponatraemia 77.1% followed by hypokalaemia 50.0%, hypocalcemia 28.6%, hypomagnesaemia 15.7%, hypermagnesaemia 7.14%. Tezcan et al.¹⁹ showed 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 hypochloreaemia were found in 28 (6.8%) patients each. Lastly, seven (1.7%) of the participants had hyperkalaemia. Duan et al.²⁵ found that sodium, potassium and chloride levels had high predictive power for COVID-19 progressing to severe disease. Liu et al.²² described that hypernatremia, hyponatremia, hyperkalemia, hypermagnesiumemia, hypocalcemia, and hypoalbuminemia were significantly more common in hospitalized patients with COVID-19. Rostami et al.²⁶ described the most common electrolyte imbalance observed in patients was hyponatremia (42%), followed by hypomagnesiumemia (35%). Another case-control study showed that hyponatremia, hypokalemia, and hypochloremia, which are electrolyte disturbances, were more common in COVID-19 patients than in controls.²¹ Hypocalcemia is also

one of the electrolyte disorders in patients with COVID-19, which can be dangerous if not controlled and can even increase the mortality rate.²⁷ In the US, Aggarwal et al.¹¹ reported that among 19 patients with COVID-19 infection admitted to the emergency department, 50% presented with hyponatremia.

The present study showed that 13(76.5%) patients had hyponatraemia in severe COVID-19 group and 16(47.1%) in non severe COVID-19 group, which was statistically significant ($p < 0.05$) between two groups. Lippi et al.⁶ reported that sodium and potassium were significantly lower in patients with severe COVID-19 patients. Previous meta-analyses have reported associations of hypocalcemia and hyponatremia with COVID-19 severity.^{28, 29}

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.

Conclusion:

In this study, we found that hyponatraemia was the most predominant electrolyte abnormality. Baseline electrolyte abnormalities, mainly hyponatraemia is 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. Hyponatraemia was significantly associated with severity of COVID-19 patients. To investigate the mechanism of electrolyte imbalance, more study of electrolytes in COVID-19 cases with multi center approach is needed.

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