Original Article

Pattern of electrolytes in a cohort of critically ill COVID-19 patients

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ABSTRACT

Background: *Coronavirus disease 2019 (COVID-19) is a potentially fatal disease with multisystem involvement. Several studies have reported various electrolyte abnormalities at admission in patients who progress to the severe form of COVID-19. This study evaluated the electrolyte pattern in confirmed and critically ill COVID-19 patients.*

Methods: *This cross sectional study was carried out in the department of critical care medicine of BIRDEM General Hospital, Dhaka, Bangladesh, from 1st July to 10th November, 2020. Total 70 RT-PCR positive, critically ill COVID-19 patients, were enrolled. Patients' demographic profile, clinical features, admission electrolyte report, length of ICU stay and outcome were documented in case record forms.*

Results: *In this cohort, total 70 RT-PCR positive COVID-19 cases (male 41, female 29, mean age 62.9 ± 13.3years) were enrolled. Fifty eight (82.85%) patients had different electrolytes abnormalities including hyponatraemia (54, 77.1%), hypokalaemia (35, 50%), hypocalcaemia (20, 28.6%) and hypomagnesaemia (11,15.7%). Regarding clinical symptoms, 98.6% (n=69) had respiratory distress, 97.1% (n=68) had cough, 94.3% (n= 66) had history of fever and 10.0 % (n=7) presented with unconsciousness. Diabetes mellitus (DM) was the most common co morbidity (94.3%).Mean length of ICU stay were 6.4 ± 3.4 days, where 48.57% (n=34) survived and 51.42% (n=36) died. Among 36 death cases, 33 patient (91.7%) had hyponatraemia (p value=0.003), which was statistically significant.*

Conclusion: *In this study, we found that, hyponatraemia was the most predominant electrolyte abnormality. Among 36 death cases, around 92% had hyponatraemia. Like other studies, it showed that various electrolyte imbalances seem to have an impact on disease process. So, base line electrolyte assessment would be beneficial for evaluating the risk of severity of COVID-19. So, more study of electrolytes in COVID-19 cases with multi center approach is needed.*

Key words: *COVID-19, electrolyte imbalance, hyponatraemia, outcome.*

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INTRODUCTION

An ongoing outbreak of pneumonia associated with the severe acute respiratory corona virus 2 (SARS-CoV-2) started in December, 2019, in Wuhan, China. Information about critically ill patients with SARS-CoV-2 infection is limited.[1]The disease is designated as COVID-19, which stands for corona virus disease 2019.[2] 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. Furthermore, the disease may have an impact on various parts of the body including the cardiac, nervous, renal, gastrointestinal and coagulation systems.[3]

In early COVID-19 studies, some evidence has been provided that electrolyte disorders may also be present

upon patient's presentation, including sodium, potassium, chloride and calcium abnormalities. [1]

SARS-CoV-2 invades human cells through binding angiotensin I converting enzyme 2 (ACE2) on the cell membrane. ACE2 is widely distributed in many types of human tissues, especially in the vital organs, such as heart, liver, kidney, and lungs. ACE2 is viewed as the principal counter-regulatory mechanism for the main axis of renin–angiotensin system (RAS) that is an essential player in the control of blood pressure and electrolyte balance. SARS-CoV-2 binds ACE2 and enhances the degradation of ACE2, and thus decreases the counter-act of ACE2 on RAS. The final effect is to increase reabsorption of sodium and water, and thereafter increase blood pressure and excretion of potassium (K+). Besides, patients with COVID-19 often had gastrointestinal symptoms such as diarrhea and vomiting. Collectively, the impacts on RAS and gastrointestinal system by COVID-19 probably lead to disruptions of homeostasis of electrolytes and pH.[4]

Hyponatraemia is frequently associated with atypical pneumonia and increased the risk of ICU admission, prolonged length of stay, higher hospital cost, and increased mortality rates.[5-10] Moderate and severe hyponatraemia have been described in case reports of severe COVID-19 infection. The authors of these studies have suggested that hyponatraemia at admission may serve as an indicator of potential corona virus disease 2019 (COVID-19) infection. However, data on the prevalence, severity, and impact of hyponatraemia in the context of a large COVID-19 cohort is lacking.[11] There is a study, regarding hypocalcaemia which shows it is commonly occurred in severe COVID-19 patients and it was associated with poor outcome. [12] Different electrolytes imbalance, may have important implications on management and outcome of critically ill COVID-19 patients. So, in this study, we aimed to analyze the electrolytes pattern of severe COVID-19 infection and there outcome.

METHODS

This cross sectional study was carried out in the department of critical care medicine (ICU) of BIRDEM General Hospital from 1st July to 10th November, 2020.

Admission data of total 70 cases of RT-PCR positive COVID-19 patients, who were critically ill were enrolled in this study. We collected patients demographic features (age, sex), comorbidities, history of COVID related symptoms, treatment protocol, requirements of mechanical ventilation, length of ICU stay, electrolyte values including sodium, potassium, chloride, magnesium and corrected calcium. Other biochemical parameters including aspartate aminotransferase, alanine aminotransferase, s.creatinine, creatine kinase, lactate dehydrogenase (LDH), D-dimer, albumin, ferritin, C-reactive protein (CRP) and blood counts also collected. The level of electrolytes were classified as normal, hypo or hyper according to laboratory reference range. Here normal reference values of different electrolytes are Sodium: 135-145 mmol/L, Potassium: 3.5-5 mmol/L, Chloride: 95-105 mmol/L, Magnesium: 1.5-2 mmol/L and total calcium: 8.5 – 10.2 mg/L. we calculated the corrected calcium levels based upon serum albumin levels. The outcome was defined as survival (transferred or discharged) and death at ICU.

Statistical analysis were carried out using SPSS version 19. We included the variables -age, gender, comorbidities, length of ICU stay in multivariate analysis. Results are given as Mean ± Standard Deviation. A value of $p < 0.05$ was considered statistically significant.

RESULTS

A total 70 critically ill, RT-PCR positive for COVID-19 patients were included in this study. Among them, 58.57 % (n= 41) were male and 41.42% (n=29) were female, mean age was 62.9 ± 13.3.years, other age distribution shown in table I. 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%, n=54) and other electrolytes abnormalities were shown in table II. Regarding clinical symptoms, 98.6% (n=69) had respiratory distress, 97.1% (n=68) had cough, 94.3% (n= 66) had history of fever and 10.0 % (n=7) presented with unconsciousness. Different types of co-morbidities are shown in a tabulated form (Table III).

Table I Distribution of COVID-19 positive cases according to age (N=70)

Age group (years)	Frequency	Percentage
<50	7	10.
51 - 60	22	31.42
61 - 70	24	34.3
71 - 80	14	20.0
>80	3	4.3

Table II Individual electrolyte imbalance among COVID-19 positive cases (N=70)

	Frequency	Percentage
Hyponatraemia	54	77.1
Hypokalaemia	35	50.0
Hypocalcemia	20	28.6
Hypomagnesaemia	11	15.7
Hypermagnesaemia	5	7.14

Table III Co morbidities among the study subjects (N=70)

Co morbidity	Frequency	Percentage
DM	66	94.3
HTN	60	85.7
Asthma	13	18.6
COPD	10	14.3
IHD	16	22.9
CKD	10	14.3
ESRD	6	8.6
CLD	4	5.7

*Multiple responses

Mean length of ICU stay were 6.4 ± 3.4 days (Table IV). Among 70 COVID patients, 48.57% (n=34) were transferred to the isolation ward or discharged at home, who were considered as survival and 51.42% (n=36) died at ICU. Among48.57% (n=34) survival cases, we found, 61.8% (n=21) had hyponatraemia, 44.1% (n=15) had hypokalaemia, 23.5% (n=8) had hypocalcaemia and 8.8% (n=3) had hypomagnesaemia. Among 51.42% (n=36) death cases, we found, 91.7% (n=33) had hyponatraemia, 55.6% (n=20) had hypokalaemia, 33.35 (n=12) had hypocalcaemia and 22.2% (n=8) had hypomagnesaemia. (Table V)

Table IV Distribution of COVID-19 positive cases according to length of ICU stay (N=70)

Length of ICU stay (days)	Frequency	Percentage
1 - 5	28	40.0
6 - 10	34	48.6
11 - 15	6	8.6
16 - 20	2	2.9

In this study p-value is significant in case of hyponatraemia in terms of outcome. Here showed hyponatraemia is associated with poor outcome in COVID 19 patient. (Table V)

Table V Outcome comparison in relation with individual electrolyte imbalance (N=70)

	Survived	Death	p-value
Hyponatraemia	21 (61.8)	33 (91.7)	0.003
Hypokalaemia	15 (44.1)	20 (55.6)	0.339
Hypocalcaemia	8 (23.5)	12 (33.3)	0.522
Hypomagnesaemia	3 (8.8)	8 (22.2)	0.225
Hypermagnesaemia	2 (5.9)	3 (8.3)	1.000

DISCUSSION

In this study we found that male were more infected than female by COVID 19. Here 58.57 % (n= 41) were male and 41.42% (n=29) were female. Our result consistent with a study performed by Gaung et al in China.Their results showed that males were more likely to be infected than females (58.1% male and 41.9% female).[13]

In our study, age distribution shows <50 years (10%), in 51 -60 years(31.42%), in 61-70 years (34.3%), in 71-80 years (20%) and > 80 years (4.3%).The age group were mostly affected in this study, were 61–70 years (n=24, 34.3 %) and Mean age ±SD was 62.9 ± 13.3 years. In a study at Wuhan shows the median age of the 191 COVID patients was 56.0 years (IQR 46.0–67.0), ranging from 18 years to 87 years median age was 63 years and inter quartile range, (50-72 years).[14]

In this study we showed respiratory distress (98.6%, n= 69) was the most dominating symptom than fever (94.3%, n=66). Fever was also a dominant symptom seen by Guan et al,[13] Wang et al [15], Zangh et al.[16] Regarding co morbidity, DM is more common than others. We found 94.3% were diabetic. Hu Y et al also found diabetes mellitus and hypertension were the main co morbidities related to disease severity and mortality, in their study.[17]

In a study, Tezcan ME et al 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 hypochloraemia were found in 28 (6.8%) patients each. Lastly, seven (1.7%) of the participants had hyperkalaemia. None of the patients in their cohort had hypernatraemia, hyperchloraemia or hypercalcaemia at baseline.[3] In our study we found only 5 cases of hypermagnesaemia. Here we found that, 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 hyponatremia (77.1%, n=54), 50% (n=35) had hypokalaemia, 28.6% (n=20) cases had hypocalcemia,15.7%(n=11) had hypomagnesaemia and hypermagnesaemia was found in 5 (7.14%) cases.

Moreover, Duan J et al found that sodium, potassium and chloride levels had high predictive power for COVID-19 progressing to severe disease.[18] Another study by Tezcan ME et al showed that low baseline sodium, chloride and calcium levels related to higher frequency of mortality, higher ICU and MV requirement and longer hospital stays.[3] However, hyponatraemia was the common electrolyte abnormality related to unfavorable outcome in these studies, which also comparable to our study, that showed hyponatraemia was most frequent electrolyte abnormality and also associated with poor outcome.

Limitations

We had some limitations in our study. First here we evaluated only a limited number of electrolyte influences on disease prognosis in a single center. To get more information, multi centered analysis should be done. Second, we did not assess the etiology of electrolyte abnormalities. Third here we evaluated only critically ill COVID -19 patient. So, these data does not represent the all COVID -19 patient. Fourth, this study was conducted in a tertiary care hospital where most of the patient populations were diabetic and having pre-existing multiple co-morbidities.

Conclusion

Here, we found that, Hyponatraemia was the most predominant electrolyte abnormality. Among 36 death cases, around 92% had Hyponatraemia. In 34 survived cases, nearly 62% had Hyponatraemia. So, from our study, it showed that hyponatraemia also associated with poor outcome in critically ill COVID-19 patients. So, base line electrolyte assessment would be beneficial for evaluating the risk of severity of COVID-19. So, more study of electrolytes in COVID-19 cases with multi center approach is needed. Serial electrolyte analysis throughout the course of illness in COVID may give more information about the disease progression.

Authors' contribution: RS designed the study, drafted manuscript. ASMAA was overall supervisor. NM, EA collected data. All authors were involved in patient management, read and approved the final manuscript for submission.

Conflicts of interest: Nothing to declare.

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