

Electrolyte Imbalances in Patients with Severe COVID-2019 admitted in ICU- A retrospective observational study

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Abstract

Early studies have reported various electrolyte abnormalities in the severe and non-severe form of COVID-19. Electrolyte imbalance may have impact on patient care but also provide information on pathophysiology of COVID-19, we aimed to analyse all early data reported on electrolytes in COVID-19 patients with non-severe and severe COVID-19 infected patients admitted in ICU. Data presented as Mean \pm SD, multiple comparison was done by Tukey's test and ANOVA for sodium, potassium, calcium and chloride, found to be significant with sodium, potassium and calcium at 95% CI, 80% power of the study with p-value=0.0001. But chloride was not significant in severe and non-severe groups. Analysis of electrolyte levels confirms that COVID-19 severity is associated with lower serum concentrations of sodium, potassium and calcium. Continuous monitoring of electrolyte levels during hospitalization in order to

establish timely and appropriate corrective actions in COVID-19 ICU admitted patients.

Keywords: Calcium, Chloride, Coronavirus, COVID-19, Sodium, Potassium, SARS-CoV-2.

Introduction

Cohort and case reports studies have described many clinical characteristics of patients with COVID-19. An infectious disease caused by novel coronavirus. Previous studies have gathered evidence on electrolyte imbalance in COVID-19. Some studies postulated the imbalance in sodium, potassium, chloride and calcium in COVID-19 patients [1] others studies linked hypokalaemia and COVID-19 they compared the base line levels with severe COVID-19 infected patients [2]. Such electrolyte imbalance has an important implication not only on patient management of diseases, but also identifying the pathophysiological mechanisms under laying COVID-19 that could drive novel therapeutic opportunities. However limited sample size and heterogeneity in electrolyte study have

limited interpretations till date. We aimed to study the impact of COVID-19 on electrolyte imbalance in ICU admitted patients.

Materials and methods

Is a retrospective observational study on severe COVID-19 infected ICU patients from September 2020 to August 2021, admitted in department of critical care medicine, Apollo health city. 100 Patients who have tested RTPCR positive with a CT cycling time score less than ≤ 18 , severely infected were considered for the study. Sample size was calculated by using fisher et;al formulae as population of infected patients were $<10,000$. Serum electrolyte levels such as sodium, potassium, calcium and chloride levels were measured by standard methods.

Laboratory investigations

Venous blood samples were collected by using vacutainers and centrifuged at 6000 rotations/minute to sperate the serum. Obtained serum was analysed immediately for the estimation of serum electrolyte sodium, potassium, chloride and calcium, analysis was performed by using The Dimension® EXL™ with LM Integrated Chemistry System. System runs up to 440 photometric, 187 IMT and 167 immunoassay tests per hour make SIEMENS.

Statistical analysis

Obtained data was analysed by using Graphpad Prism version (9.3). Data presented as Mean \pm SD, with confidence interval of 95% at 80% power of the study. Significance levels were calculated by using one-way ANOVA and Tukey's test multiple comparisons. P value <0.05 was considered to be significant. Specificity and sensitivity curve was plotted to prove the relation of electrolyte levels to COIVD-19 ICU admitted patients.

Result

The study was conducted in special ICU made for COVID-19 patients as per government protocol at department of critical care medicine, Apollo health city, Hyderabad. Out of 200 admitted patients we have randomly allocated the patients into severely infected group and non-severely infected group. Both arms had 100 patients, 50 each in one arm. Serum electrolytes were analysed by using The Dimension® EXL™ revealed in severe groups where sodium levels were 93 ± 11 (CI 95%-90-96) and in non-severe groups 131 ± 3.5 (CI 95%-130-132). Potassium levels in severe group were 2.8 ± 0.39 (CI 95% 2.7-3.0) and in non-severe groups was 3.2 ± 0.27 (CI 95% 3.2-3.3). Chloride levels in sever group was 101 ± 3.3 (CI 95% 98-101) and in non-severe group was 101 ± 3.3 (CI 95% 100-102). Chloride was not significant between severe and non-severe groups pvalue=0.4268. Calcium levels in severe group was 1.7 ± 0.25 (CI 95% 1.6-1.8) and in non-severe group was 2.1 ± 1.0 (CI 95% 2.0-2.1) for calculation purpose obtained calcium values in mg/dL was converted to mmol/L. Columns were treated with one way ANOVA showed F value of 6859 (1.796, 88.01) and p value =0.0001 and highly significant for Na^+ , K^+ and Ca^{2+} and not significant for CL^- , p=0.4268 (Table 1, Figure 1-3). Specificity and sensitivity curve showed 100% to sodium, potassium, calcium and chloride (Figure 4-7). Tukey's multiple comparisons test was performed to compare the variables of Na^+ , K^+ and Ca^{2+} was significant (p= 0.0001) but CL^- was (p=0.4268) nonsignificant in between the groups (Table 1, Figure 1).

Table 1: Levels of electrolytes in severe and non-severe COVID 19- infected patients in ICU

	Severe	Non-Severe	F value	P value
Sodium	93±11*** *	131±3.5 ****	6859	=0.0001
Potassium	2.8±0.39* ***	3.2±0.2 7****		
Calcium	1.7±0.25* ***	2.1±1.0 ****		
Chloride	99±5.5	101±3.3		=0.4268

Data presented as Mean±SD. One way ANOVA Tukey's multiple comparison tests. Treatment between columns $F(1.796, 88.01) = 6859$. $P = 0.0001$. (n= 50 in each group). * Indicates significance level.

Figure 3 - Levels of calcium in severe and non-severe COVID-19 ICU patients

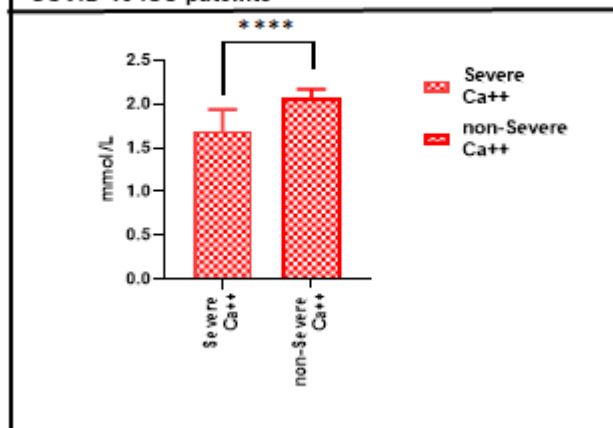


Figure 4 - ROC curve: ROC of Na^+

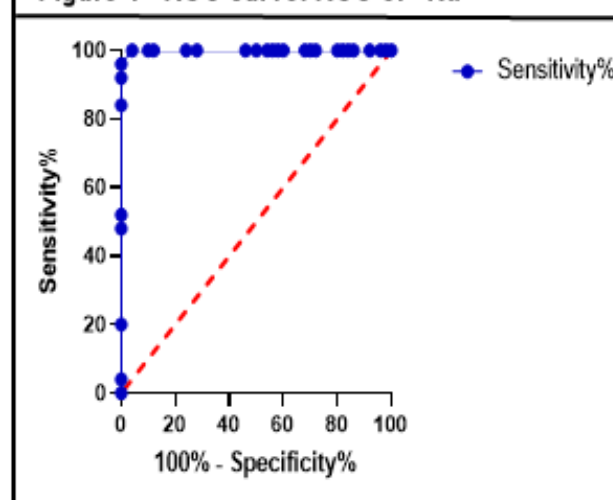


Figure 5- ROC curve: ROC of K^+

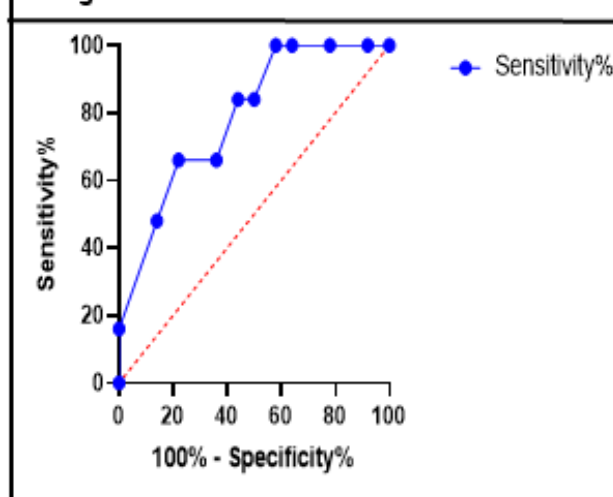


Figure 1- Electrolyte imbalance in severe and non-severe COVID-19 patients in ICU

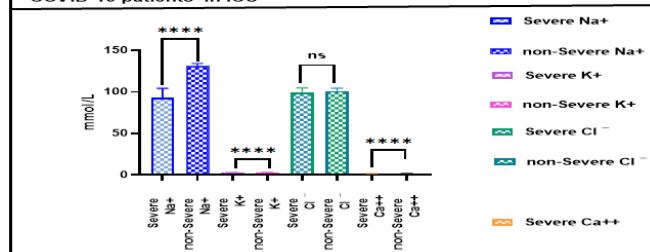
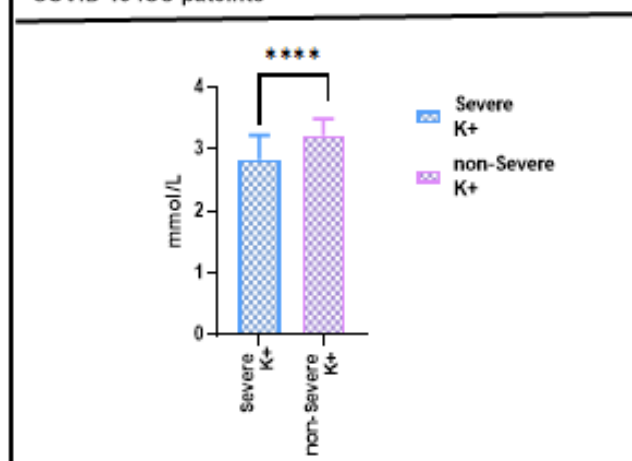
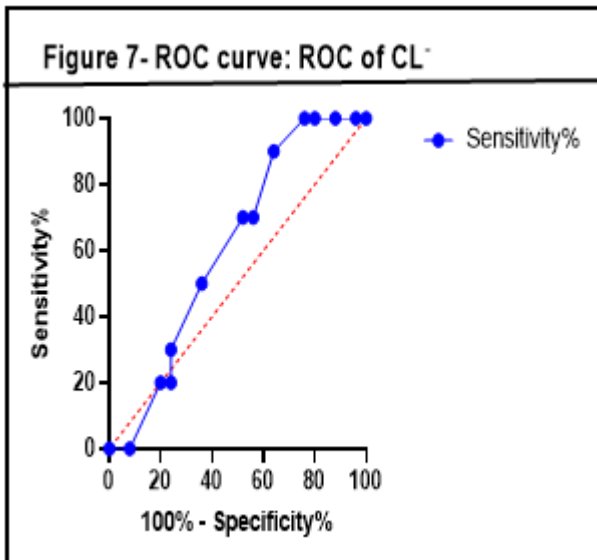
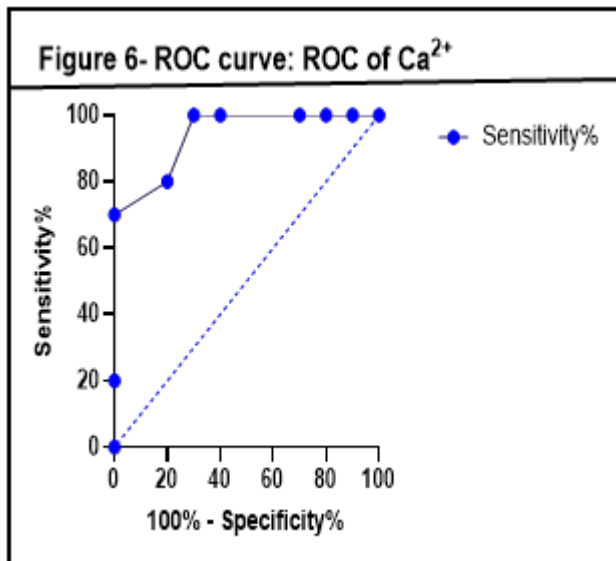


Figure 2 - Levels of potassium in severe and non-severe COVID-19 ICU patients





Discussion

In summary, confirms that COVID-19 severity is associated with lower serum concentrations of sodium, potassium and calcium. However, it is not yet known if there is a higher risk of hyponatremia or hypokalaemia. These disturbances, in particular hypokalaemia, may have clinically significant implications for COVID-19 patient management and potentially contribute to unravelling pathogenetic mechanisms underlying COVID-19. Hypokalaemia is known to exacerbate acute cardiac injury and acute respiratory distress syndrome (ARDS), which are common complications

in COVID-19 patient, especially in patients with underlying heart and lung diseases [1]. Hypokalaemia also provides an important pathophysiologic clue that the SARS-CoV-2 virus binds to its host receptor, angiotensin-converting enzyme 2 (ACE2) and reduces ACE2 receptor expression, thus leading to increased angiotensin II, which in turn can cause increased potassium excretion by decreasing the reabsorption from the kidneys, ultimately leads to hypokalaemia, maintenance of ECF potassium concentration is important for cardiac functions [2-8]. Research on animal model showed and increased plasma angiotensin II concentration, has been linked to patients with COVID-19, possibly acting as mediator of acute lung injury, as earlier confirmed in SARS-CoV [8,9]. In some COVID-19 patients' gastrointestinal loss with diarrhoea and nausea may have contribute to loss of electrolytes in as many as 34.0% and 3.9% of cases [10]. We found the same in our study. Previous researchers have reported hyponatraemia in COVID-19 [11-13]. Retrospective study by Zhang et al., noted a correlation between hyponatraemia and the severity of COVID-19 [14]. In another review study involving five studies with 1415 participants correlated the electrolyte imbalance in COVID-19 patients indicating a relationship between decreased blood sodium and disease severity [15]. Hyponatraemia may occur due to increased expression of the ACE2 receptor at proximal tubule of nephron [16]. The results of the present study show that hyponatraemia was more common in ICU admitted severely ill patients when compare to non-severe patients, above studies supports our findings. Clinical retrospective study investigated the incidence of hypocalcemia in 74.7% patients with COVID-19, with overall mortality of 4.1%, whereas the mortality of

critically ill patients was 40.0%. They also found that severely COVID-19 infected patients with lower serum calcium levels had worsen the clinical variables, higher incidences of septic shock [17] which was in agreement with our study. Hypocalcemia may be associated with imbalanced PTH in the acute phase of COVID-19. The causes of hypocalcemia include over secretion of PTH, Vitamin D deficiency, decreased dietary intake, hypoproteinemia, hypomagnesemia drug interactions [18]. Previous researchers reported that serum calcium levels less than approximately 2.0 mmol/L were associated with worse clinical outcomes in critically ill patients [19,20], these findings are more suggestive of hypocalcemia and agrees to our current study. Our study found no difference in chloride levels between severe and non-severe COVID-19 infected patients admitted in ICU. There was no study which agrees to our findings in COVID-19 patients.

Conclusions

Analysis of electrolyte levels confirms that COVID-19 severity is associated with lower serum concentrations of sodium, potassium and calcium. Continues monitoring of electrolyte levels during hospitalization in order to establish timely and appropriate corrective actions in COVID-19 ICU admitted patients. Further research, based on larger sample size, cluster-based sampling, prospective cohort studies in COVID-19 ICU patients is warranted.

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