JMSR
Journal of Medical and Scientific Research

ORIGINAL RESEARCH

Role of electrolytes in determining severity in COVID-19

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Abstract

Introduction: Coronavirus disease 2019 (COVID-19) is a viral disease which originated in the city of Wuhan (China) and progressively spread to all the continents and brought the world to a standstill. Various severity markers have been seen to play a role in the COVID-19. International studies have demonstrated role of serum electrolyte in COVID-19 as a potential severity marker. Hence, this study was undertaken in Indian patients.

Material and methods: 100 COVID-19 reverse transcription polymerase chain reaction (RT-PCR) positive patient of non-severe and severe disease of either gender getting admitted to hospital and above 18 years were enrolled in the month of August to September 2020. The mean values of electrolytes and high-sensitivity C-reactive protein (HsCRP) in non- severe and severe disease were compared and correlated.

Results: 100 patients including 70 of non-severe and 30 of severe disease were evaluated. The mean sodiumwas 134.03±6.77mEq/L and 135.5± 6.77mEq/l in the non-severe and the severe groups respectively (p value=0.91); potassium was 4.24±0.61mEq/l and 4.52±0.80 mEq/l respectively (p value=0.75); corrected serum calcium was 8.38±0.74 mg/dl and 8.48±0.74mg/dl respectively (p value = 0.95); phosphorus levels was 3.66±1.99mg/dl and 3.45±1.63 respectively (p value = 0.52); and serum magnesium level was 2.15±0.3 mEq/l and 2.03±0.56 mEq/l (p value = 0.18). The mean level of HsCRP was 30.95±49.41 mg/L in non- severe while 94.78±79.62 mg/L in severe infection (p value=0.03). In the severe group, the electrolyte values were found to be poorly correlated with the hsCRP levels.

Conclusion: Electrolytes does not serve as severity markers in COVID-19 in an Indian population.

Keywords: electrolytes; COVID-19; RT-PCR corona positive

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Received 2 December 2020; *Revised* 21 December 2020; *Accepted* 26 December 2020; *Published* 31 December 2020

Citation: Anita R, Omkar KC, Rohit K, Rakesh KB. Role of electrolytes in determining severity in COVID-19. J Med Sci Res. 2021; 9(1):18-23. DOI: http://dx.doi.org/10.17727/JMSR.2021/9-4

Introduction

While the world is still fighting the coronavirus disease 2019 (COVID-19) with the best possible way and a beam of hope of many vaccines reaching the market in upcoming months, the role of physicians meanwhile has not reduced and still cases of severe COVID-19 admitting to hospitals have high mortality [1]. COVID-19 is a viral disease manifested with fever, cough, anosmia, diarrhoea, breathlessness and acute respiratory distress syndrome, whilea substantial population of patients being asymptomatic [2]. The disease was originated in the city of Wuhan (China) and progressively spread to all the continents and bring the world to a standstill [3]. It's been a year now since the first case was reported but the death tally is still continuously increasing however recovery rates have improved over time and India have one of the finest recovery rates despite infecting over 10 million population and bringing serious social and economic consequences [3, 4].

The pathogenesis of the disease starts from attachment of the virus via Angiotensin converting enzyme2 (ACE2) receptor as the entry point into the cell. Attachment of SARS-CoV-2 pathogen modulates this receptor leading to a decreased expression which leads to accumulation of angiotensin I (ATI), due to decrease in the alternate pathway of AT II stimulation via ACE 2 and overstimulation of ATI receptor leading to raised blood pressure, hypokalaemia, sodium retention due to increase in aldosterone bringing electrolyte abnormalities in COVID-19 [5, 6].

Various severity markers have been seen to play a role in the COVID-19. Studies have demonstrated the role of interleukin-6 (IL-6), C-reactive protein (CRP), lactate dehydrogenase (LDH), procalcitonin level as severity markers of the disease [7, 8]. A few studies have also revealed an association of level of electrolytes with the severity of the infection [9]. In non-COVID-19 setting as well, electrolyte imbalance has temporal relationship with the severity of disease and its prognosis [10, 11]. Hence, serum electrolyte level in COVID-19 non-severe and severe patients need to bestudiedto elucidate whether this relationship exists in the Indian population of patients.

Material and methods

A single centred observational study was done in the Department of Biochemistry and Department of Respiratory Medicine,Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi from August 2020 to September 2020. 100 COVID-19 reverse transcription polymerase chain reaction (RT-PCR) positive patient of non-severe and severe disease of either gendergetting admitted in hospital and above 18 years were taken as cases. Severe COVID-19 was defined as a patient hospitalised with admission in ICU or requiring intubation or mechanical ventilation [12]; all other cases managed in the ward were considered non-severe.

Inclusion criteria: The study population comprised non-severe and severe COVID-19 patients who gave written consent. Patients not willing to give written consent were excluded. Patients demographic profile, co-morbidities, times since onset of symptomsalong with baseline biochemical profile including serum sodium, potassium, calcium, phosphorus, magnesium and HsCRP were done at the time of admission (onetime assessment only). The levels of serum calcium was corrected for the corresponding serum albumin levels.

The biochemical parameters were analysed by using fully automatic analysers Beckman Coulter AU-680 with maintenance of requisite internal and external quality controls. The normal reference levels for electrolytes for electrolytes were 135-145mEq/L for serum sodium, 3.5-5.5 mEq/L for serum potassium, 9-11 mg/dl for serum calcium, for serum phosphorus 2.5-4.5 mg/dl, for serum magnesium 2.5-3.5 mEq/L and HsCRP<1 mg/L. Hyponatremia was defined as serum sodium level below 135mEq/l.

The study was approved by Institutional Ethics Committee.

Statistical analysis

All the data was collected in a predesigned proforma and analysed. Parametric data was represented as mean and standard deviations or median and Interquartile range (IQR) and categorical data was presented as percentage. The electrolyte levels in non-severe and severe groups were compared using the T test. In the severe group, the electrolyte levels were correlated with their corresponding HsCRP levels. A two tailed 'P value' of less than 0.05 was considered significant. All data were analysed by SPSS 21.0 (USA).

Results

Total 100 patients were taken for the study. 70

patients were of non- severe disease and 30 were of severe disease on admission. The mean age of participants was 47.65±8.35 years in non- severe and 56.35±7.15 years in severe disease group. The base line characteristics of participants are shown in Table 1.

Table 1: Baseline and clinical profile of patients infected with COVID-19.

Parameters	*Non severe disease N(%)*	*Severe disease N(%)*
Age		
18-40 years	35 (50%)	2 (6.66%)
40-60 years	25 (35.71%)	12 (40.0%)
≥60 years	10 (14.28%)	16 (53.33%)
Sex		
Male	45 (64.28%)	25 (83.33%)
Female	25 (35.71%)	5 (16.66%)
Smokers	15 (21.42%)	18 (60.00%)
Alcohol intake	21 (30%)	7 (23.33%)
History of comorbidities		
Hypertension	41 (58.57%)	17 (56.66%)
Diabetes mellitus	32 (45.71%)	12 (40%)
Coronary artery disease	22 (31.42%)	7 (23.33%)
Symptoms		
Fever	57 (81.42%)	27 (90.00%)
Cough/ expectoration	65 (92.85%)	29 (96.66%)
Diarrhoea	7 (10.00%)	2 (06.66%)
Malaise	65 (92.85%)	30 (100%)
Sore throat	49 (70.00%)	21 (70.00%)
Anosmia	5 (07.14%)	1 (03.33%)
Laboratory findings		
White blood cell count, $\times 10^9$L	6.7 (5.5-8.3)	7.1 (5.9-8.7)
Neutrophil count,%	55.35 (49.7-62.45)	63.54 (53.45-70.60)
Lymphocyte count, %	25 (23-33)	22 (17.75-27.30)
Hemoglobin, g%	11.4 (10.3-12.5)	10.7 (10.0-13.7)
Platelet count, $\times 10^9$L	190 (168-220)	176 (145-190)

Data are mentioned as median and IQR or N (%).

The mean sodium level among non-severe disease was 133.03± 6.77mEq/Lwhile in severe disease it was 135.5±6.77mEq/l. The mean serum potassium level was 4.24±0.61 mEq/l in non-severe group and 4.52±0.80 mEq/l in severe group. The adjusted serum calcium levels were 8.38±0.74 mg/dl in non -severe and 8.48±0.74mg/dl in severe disease. The mean level of serum phosphorus was 3.66±1.99mg/dl in non-severe disease while 3.45±1.63mg/dl in severe disease. The mean serum magnesium level was 2.15±0.3mEq/l in non-severe while 2.03±0.56 mEq/l in severe disease. The mean level of high-sensitivity C-reactive protein (HsCRP) was 30.95±49.41 mg/L in non-severe while 94.78±79.62 mg/L in severe infection (Table 2).

The regression analysis among non-severe and severe group in serum sodium was p=0.91, serum potassium p=0.75, calcium p=0.95, phosphorus p=0.52, magnesium p=0.12, HSCRP=0.03 (P<0.05). Correlation analysis between serum electrolyte levels in severe disease and their corresponding HsCRP levels reveals r= 0.14 for sodium (p=0.43), r=-0.10 for potassium (p=0.57), r=0.05 for calcium (p=0.78), r=0.24 for phosphorus (p=0.40), r=-0.28 (p=0.12) for magnesium (Table 3).

Discussion

At the cell level, extra and intracellular electrolyte balance is strictly maintained and their imbalance leads to array of clinical manifestation. Role of electrolytes in patients admitted in intensive care unit (ICU) is seen in many studies and has been used as severity marker or in prognosis [10, 11]. On-going COVID-19 pandemic causes significant mortality in patients with comorbidities and mortality rate in ICU is seen in up to 77% of cases in a study [1]. Baseline electrolyte measurement could detect early subclinical deterioration and early intervention could reduce mortality.

In our study, we have taken 100 COVID-19 RT-PCR positive patients. 30 patients were of severe disease and required ICU admission. When the serum electrolytes of non- severe and severe disease compared, the differences were not statistically significant however, the difference in HsCRP levels of non-severe and severe COVID-19 infection was statistically significant (p<0.05) as also seen in other studies revealing HsCRP as a reliable marker of severity in COVID-19 infection [7].

Table 2: Biochemical profile of non-severe and severe COVID-19 patients.

Serum electrolytes/ Inflam. marker	*Non severe disease N=70*	*Severe disease N=30*	*Normal range*	*P value*
Serum sodium (mEq/l)	133.03±6.77	135.5±6.77	135-145	0.91
Serum potassium (mEq/l)	4.24±0.61	4.52±0.80	3.5-5.5	0.75
Serum calcium (mg/dl)	8.38±0.74	8.48±0.74	9.0-11.0	0.95
Serum phosphorus (mg/dl)	3.66±1.99	3.45±1.63	2.5-4.5	0.52
Serum magnesium mEq/l)	2.15±0.39	2.03±0.56	2.5-3.5	0.18
HsCRP (mg/l)	30.95±49.41	94.78±79.62	<1.0	0.03

Data are mentioned as Mean ± Standard deviation, p<0.05 - significant

Table 3: Correlation of electrolyte levels in severe COVID-19 with their corresponding HsCRP levels.

	SerumNa (mEq/l)	*Serum K (mEq/l)*	*SerumCa (mg/dl)*	*SerumPO4 (mg/dl)*	*Serum Mg (Eq/l)*
Correlation coefficient (R)	0.14	-0.10	0.05	0.24	-0.28
P value	0.43	0.57	0.78	0.40	0.12

Hyponatremia has been associated with the poor prognosis in many ICU based study [10]. Sodium, an extracellular ion maintains the internal milieu with Na-K pump and affects extra cellular fluid volume and maintains blood pressure required for normal functioning of cellular environment [13]. In ICU, most common cause of hyponatremia is syndrome of inappropriate anti diuretic hormone secretion (SIADH) causing hyponatremia leading to neurological deterioration, seizures, coma [14]. In our study, we did not find statistically significant difference in serum sodium in between non severe and severe COVID-19 patients in contrary to other studies and a meta-analysis showing low sodium level association with the disease severity [15, 16].

Over stimulation ATI causes increase in aldosterone, a potent vasoconstrictor along with loss of potassium and increase level of serum sodium by increased reabsorption. In our cases, serum potassium level when compared with non-severe disease and severe disease, had negative insignificant correlation and with no significance when serum potassium in severe disease is compared with HsCRP. Though these findings are not consistent with the previous findings where Chen D and colleagues showed hypokalaemia associated in significant number of patients with COVID-19 disease [17].

Serum calcium exists in two forms in the human beings. One is total calcium and other is ionised calcium. It is always ionised calcium whose deficiency or excess exhibit clinical manifestation. We have taken corrected calcium in our patient for study which also revealed no statistical difference either in non- severe versus severe group nor when compared with HsCRP (Severe Group). Hypocalcaemia and hypophosphatemia is associated with the decrease in probability of patient in invasive ventilation to wean off. Its low level causes diaphragm depression and inability to spontaneous ventilation leading to increased dependence on mechanical ventilation and morbidity [18-20]. Our study findings were not consistent with the international observation mentioning serum calcium as severity predictor in COVID-19 [21].

Magnesium level plays important role in neuromuscular excitability and diaphragmatic coordination during respiration [22, 23]. Its deficiency causes diaphragmatic dysfunction in the background of sepsis apart from fatal cardiac arrhythmias [24]. In our study, we did not find any difference in serum levels of magnesium in non-severe and severe COVID-19 patients moreover, with the HsCRP levels in severe disease in contrary to previous study revealing temporal relationship of serum magnesium level with the severity of the disease in ICU setting [25].

HsCRP is a systemic inflammatory marker and its prognostic value is seen in the community acquired

pneumonia and cardiovascular morbidity [26, 27]. In clinical scenario, patient may not present with the signs of sepsis and HsCRP help to predict the underlying severity of the disease and accordingly treatment along with monitoring the therapy corresponding to its levels [28]. In our study, HsCRP was significantly higher in severe COVID-19 disease suggesting a reliable marker of severity of this infection and few other studies also echoed our findings [29, 30]. However our study showed poor correlation of electrolytes in severe disease with their corresponding HsCRP levels.

Hence, all the above mentioned observations did not signify electrolyte as a severity markers. It is possibly due to the small sample size not reflecting data from population as seen in many Chinese population studies revealing strong association of electrolyte abnormalities with severity of the COVID-19 despite of same Asian ethnicity. Another possibility was ACE gene polymorphism among Asian ethnicity which does increases the susceptibility to various diseases but resist conformational changes at the receptor site and hence no electrolyte changes are observed however, this need to be confirmed with large population to come to conclusion [31-33].

Conclusion

Electrolytes do not serve as severity markers in COVID-19 in an Indian population.

Conflicts of interest

Authors declare no conflicts of interest.

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