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HYPONATREMIA AS A PROGNOSTIC FACTOR IN COVID-19

Emergency Medicine

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ABSTRACT

Introduction: Hyponatremia has already been described in sever acute respiratory syndrome (SARS) which was associated with poor outcome. This is also seen in sars-cov-2 for the most part with moderate to severe infection. Thus, hyponatremia can be taken as a prognostic factor. Severe hyponatremia has long been recognized as a direct cause of death or permanent neurological alterations. Patients with Coronavirus disease 2019 (COVID-19), caused by SARS-COV2 infection, can develop a potentially fatal rapid-onset pneumonia.
Aim: To describe the impact of hyponatremia on COVID-19 patient outcome.
Material and methods: It is a retrospective study on the patient admitted in Peerless Hospital and diagnosed COVID 19 positive, confirmed by RT-PCR or Gene – X pert. Data of the serum sodium concentrations of patients with COVID19 infection after admission and analysed the relationship between the serum sodium and severity of the illness and its outcome. 320 participants were taken.
Result: In our study, 131(40.9%) COVID-19 patients were in Hyponatremic and 189(59.1%) COVID-19 patients were in Normonatremic group. High Systolic blood pressure, High Diastolic blood pressure, low SPO2 and high Respiratory rate was observed in Hyponatremic COVID-19 patients which were statistically significant. 272 (85.0%) patients were Alive and 48 (15.0%) patients were Death.
Conclusion: Our study showed an independent relationship between 131 Hyponatremic COVID-19 patients at admission and transfer to ICU, use of mechanic ventilation or death. Our results support the test sodium in hospitalized COVID-19 patients as another bedside screening tool for early identification of patients at high risk of poor outcome.

KEYWORDS

Hyponatremia, COVID-19, SARS-COV-2, Sever acute respiratory syndrome

INTRODUCTION

As COVID 19 infection has spread around the world, the search of prognostic components is essential to provide adapted care and improve patient survival.

Hyponatremia has already been described in sever acute respiratory syndrome (SARS) which was associated with poor outcome. This is also seen in sars-cov-2 for the most part with moderate to severe infection. Thus, hyponatremia can be taken as a prognostic factor.

Both hyponatremia and hypernatremia have been found to be associated with expanded mortality in hospitalized patients in general, as well as particularly in patients admitted with community-acquired pneumonia (CAP) [1]. Studies have reported a prevalence of hyponatremia at admission with CAP extending from 8 to 28% [1,2], when hyponatremia is well-defined as a serum sodium level (SNa) <135 mmol/L. On the other hand, the prevalence of hypernatremia in these patients, as defined by a SNa >145 mmol/L, is much lower, with a prevalence of 5.3% [3].

Severe hyponatremia has long been recognized as a coordinate cause of death or permanent neurological alterations. The most important risk factors for death in patients admitted with SNa <115 mmol/L have been found to be hypoxia and sepsis [4], both of which can be caused by pneumonia.

However, in CAP, hyponatremia is generally mild [1]. However mild/moderate admission hyponatremia has moreover been related with an increased mortality rate in hospitalized patients, and specifically in those with CAP. Mild hyponatremia may be an indicator of underlying disease severity instead of a direct causal agent, in contrast to what can occur in severe hyponatremia. Indeed, Cuesta et al. found that not all serum sodium levels are alike in patients with CAP, with a higher mortality rate for patients with hypervolemic hyponatremia than for those with euvolemic hyponatremia induced by the Syndrome of Inadequate Antidiuresis (SIAD) [5].

The connection between sepsis and hyponatremia is unclear. Hyponatremia has been considered to be a risk factor for infection, particularly for Staphylococcus aureus bacteremia [6]. Pro-inflammatory cytokines such as IL-1b and IL-6 can fortify hypothalamic Arginine Vasopressin secretion. In fact, in a small retrospective study, Berni et al. found that IL-6 levels were inversely proportional to SNa, with the lowest SNa in patients exhibiting the highest IL-6 levels in patients with SARS-COV2 (severe-acute-respiratory syndrome caused by Coronavirus-type 2) and hyponatremia [7]. Patients with severe hyponatremia and sepsis display a higher mortality rate than those with severe hyponatremia alone [4]. But no such relationship has been portrayed in patients with mild/moderate hyponatremia.

In contrast with hyponatremia, baseline hypernatremia has been appeared to be directly related with the diagnosis of sepsis at admission. Additionally, patients showing both hypernatremia and sepsis are recognized to have a higher mortality rate than those presenting sepsis alone [8].

Patients with Coronavirus disease 2019 (COVID-19), caused by SARS-COV2 infection, can develop a hypothetically fatal rapid-onset pneumonia. In reality, mortality in patients hospitalized with COVID-19 can be as high as 20.3–27.9% [9,10]. Whether hyponatremia and hypernatremia are related with a poor prognosis in patients admitted with CAP due to COVID-19 remains to be illuminated. The essential objective of this study was to find out whether dysnatremia at admittance is associated with disease severity in patients hospitalized with COVID-19 CAP, assessing mortality, sepsis, hypoxia, and intensive therapy (IT) with mechanical ventilation (MV) or admittance to an intensive care unit (ICU).

AIMS AND OBJECTIVES

The aim of the study is to describe the impact of hyponatremia on COVID-19 patient outcome.

MATERIALS AND METHODS

It is a retrospective study on the patient admitted in Peerless Hospital and diagnosed COVID 19 positive, confirmed by RT-PCR or Gene – X pert.

Data of the serum sodium concentrations of patients with COVID19 infection after admission and analysed the relationship between the serum sodium and severity of the illness and its outcome.

Sample size: was around 320.
Proposed analysis: Hyponatremia had already been described as a prognostic factor in SARS pulmonary infection. Here we were analyse if hyponatremia in Covid19is associated with severe consequences like I.C.U transfer, use of NIV, mechical ventilation or death.

Outcome: Identification of prognostic factors for COVID19 remains essential to provide the proper care and discuss associated medication and administration. Hyponatremia can be used as another screening tool for early identification of patients at high risk of poor outcome. Can early detection reduce the hospital stay?

Timeline: May 2020 to September 2020 –data collecting. October 2020 to January 2021-thesis writing, statistical analysis, discussion and conclusion.

Status: On the process of collecting data.

STATISTICALANALYSIS:

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 24.0. and GraphPad Prism version 5. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.p-value ≤ 0.05 was considered for statistically significant.

RESULT AND DISCUSSION

In our study out of 320 (100.0%) patients, 28(8.8%) patients were ≤30 years old, 48(15.0%) patients were 31-40 years old, 79(24.7%) patients were 41-50 years old, 90(28.1%) patients were 51-60 years old and 75(23.4%) patients were 61-70 years old. The mean Age (mean± s.d.) of patients was 48.7938 ± 12.8700 years.

In our study, 272 (85.0%) patients were Alive and 48 (15.0%) patients were Death. Survivability rate was higher in Normonatremic group patients [173 (91.5%)] compared to Hyponatremic group patients [99(75.6%)]. 32 (24.4%) Hyponatremic patients and 16 (8.5%) Normonatremic patients were died which was statistically significant (p<0.0001).

DE CARVALHO H et al [11](2020) found that hyponatremia was generally mild. There were more male patients in the hyponatremic group (p = 0.005).

We found that 144(45.0%) patients were Female and 176(55.0%) patients were Male. In Hyponatremic group, 51 (38.9%) patients were Female and 80 (61.1%) patients were Male. In Normonatremic group, 93 (49.2%) patients were Female and 96 (50.8%) patients were Male which was not statistically significant (p=0.0692). In Hyponatremic group of patients the survivability and mortality rate both were higher in male patients [59 (59.6%) and 21 (65.6%) respectively] compared to female patients [40(40.4%) and 11 (34.4%) respectively] which was not statistically significant (p=0.5431).

Frontera JA et al [12](2020) found that among 4,645 patient encounters, hyponatremia (sodium < 135 mmol/L) occurred in 1,373 (30%) and 374 of 1,373 (27%) required invasive mechanical ventilation. Mild, moderate, and severe hyponatremia occurred in 1,032 (22%), 305 (7%), and 36 (1%) patients, respectively.

In our study, higher number of Normonatremic patients [189(59.1%)] were present compared to Hyponatremic patients [131(40.9%)].

We found that most of the Hyponatremic patients were 51-60 years old [36 (27.5%)]. Rest of 21 (16.0%) Hyponatremic patients were ≤30 years old, 7 (5.3%) Hyponatremic patients were 31-40 years old, 34 (26.0%) Hyponatremic patients were 41-50 years old and 33 (25.2%) Hyponatremic patients were 61-70 years old. Most of the Normonatremic patients were also 51-60 years old [54 (28.6%)]. Rest of 30 (15.9%) Normonatremic patients were ≤30 years old, 18 (9.5%) Normonatremic patients were 31-40 years old, 45 (23.8%) Normonatremic patients were 41-50 years old and 42 (22.2%) Normonatremic patients were 61-70 years old. Association of Age in group vs Group was not statistically significant (p=0.6991). The mean Age (mean± s.d.) of Hyponatremic patients was [49.2901± 12.7945 years] higher than the mean Age (mean± s.d.) of Normonatremic patients [48.4497 ± 12.9448 years] which was not statistically significant (p=0.5666).

It was found that, In Hyponatremic group, survivability rate was higher in the patients of age group 51-60 years [36 (27.5%)] and rest 19 (14.5%) patients were ≤30 years old, 9 (6.9%) patients were 31-40 years old, 34(26.0%) patients were 31-40 years old and 33 (25.2%) patients were 61-70 years old all survived. Mortality rate was found in the age group of 51-60 years age group [21(65.3%)] and 61-70 years age group [11 (34.4%)]. Association of Age in group vs Outcome in Hyponatremic was statistically significant (p<0.0001). In Hyponatremic group of patients the mean Age (mean± s.d.) of survived patients was 46.6544± 12.6350 years and expired patients was 60.9167± 5.2098 years. It was statistically significant (p<0.0001).

We found that out of 320 (100.0%) patients, 41(12.8%) patients had Diabetes, 30(9.4%) patients had Hypertension (HTN), 23(7.2%) patients had Congestive heart failure, 16(5.0%) patients had Coronary artery disease, 9(2.8%) patients had Cirrhosis, 14(4.4%) patients had Active neoplasia, 25(7.8%) patients had the current habit of smoking, 190 (59.4%) patients had Body temperature, 122 (38.1%) patients had Diarrhea, 221 (69.1%) patients had a problem of Vomiting, 278 (86.9%) patients had Agueusia, 268 (83.8%) patients had Anosmia, 38 (11.9%) patients had Neurologic involvement.

Our study showed that the number of diabetic patients were higher in Hyponatremic group [26 (19.8%)] compared to Normonatremic group patients [15 (7.9%)]. Association of Diabetes vs Group was statistically significant (p=0.0017). In Hyponatremic group of patients, mortality rate was higher [20 (62.5%)] in diabetic patients compared to survivability rate [6 (6.1%)]. It was statistically significant (p<0.0001). 25 (19.1%) Hyponatremic patients and 5 (2.6%) Normonatremic patients had Hypertension (HTN) which was statistically significant (p<0.0001). In Hyponatremic group of patients, all 25 (78.1%) patients with Hypertension (HTN) were died. Association of HTN vs Outcome in Hyponatremic was statistically significant (p<0.0001).

We found that 19(14.5%) Hyponatremic patients had Congestive heart failure and only 4 (2.1%) Normonatremic patients had Congestive heart failure which was statistically significant (p<0.0001). In Hyponatremic group of patients the rate of survivability was higher [11 (11.1%)] in Congestive heart failure patients compared to mortality rate [8 (25.0%)] and this was not statistically significant (p=0.0524). 10 (7.6%) Hyponatremic patients and 6 (3.2%) Normonatremic patients had Coronary artery disease which was not statistically significant (p=0.0719). In Hyponatremic patients, all 10 (31.3%) patients with Coronary artery disease were died and it was statistically significant (p<0.0001).

It was found that Only 9 (6.9%) Hyponatremic patients had Cirrhosis and in Normonatremic group, no patients had Cirrhosis which was statistically significant (p=0.0002). In Hyponatremic group of patients, 5 (5.1%) patients with Cirrhosis were survived and 4 (12.5%) patients with Cirrhosis were expired which was not statistically significant (p=0.1475). 9 (6.9%) Hyponatremic patients and 5 (2.6%) Normonatremic patients had Active neoplasia. Association of Active neoplasia vs Group was not statistically significant (p=0.0692). In Hyponatremic patients, rate of mortality was higher [7 (21.9%)] in patients with Active neoplasia compared to survivability [2 (2.0%)] which was statistically significant (p<0.0001).

We found that 9 (6.9%) Hyponatremic patients and 16 (8.5%) Normonatremic patients had a current habit of smoking. Association of Current smoker vs Group was not statistically significant (p=0.6010). In Hyponatremic group of patients, mortality rate was higher [6 (18.8%)] in patients who had a habit of smoking compared to survivability rate [3 (3.0%)] which was statistically significant (p=0.0022). 79 (60.3%) Hyponatremic patients and 111 (58.7%) Normonatremic patients had Body temperature which was not statistically significant (p=0.7778). In Hyponatremic group of patients, 57 (57.6%) patients with Body temperature were survived and 22 (68.8%) patients with Body temperature were expired which was not statistically significant (p=0.2613).

In our study 50 (38.2%) Hyponatremic patients and 72 (38.1%) Normonatremic patients had Diarrhea which was not statistically significant (p=0.9894). In Hyponatremic group of patients, 37(37.4%) patients with Diarrhea were survived and 13(40.6%) patients with Diarrhea were expired which was not statistically significant (p=0.7420). Most of the Normonatremic patients [130 (68.8%)] had a problem of Vomiting compared to Hyponatremic patients [91 (69.5%)]. Association of Vomiting vs Group was not statistically

significant (p=0.8966). In Hyponatremic group of patients, survivability rate was higher [72(72.7%)] in patients with symptom of Vomiting compared to mortality rate [19(59.4%)] which was also not statistically significant (p=0.1539).

We found that 114 (87.0%) Hyponatremic patients and 164 (86.8%) Normonatremic patients had Agueusia which was not statistically significant (p=0.9479). In Hyponatremic group of patients, 86(86.9%) patients with Agueusia were survived and 28(87.5%) patients with Agueusia were expired. It was not statistically significant (p=0.9263). 110 (84.0%) Hyponatremic patients and 158 (83.6%) Normonatremic patients had Anosmia which was not statistically significant (p=0.9294). In Hyponatremic patients, 81(81.8%) patients with Anosmia were survived and 29(90.6%) patients with Anosmia were expired. It was not statistically significant (p=0.2378).

It was found that 34 (26.0%) Hyponatremic patients and 4 (2.1%) Normonatremic patients had Neurologic involvement. Association of Neurologic involvement vs Group was statistically significant (p<0.0001). In Hyponatremic group of patients, 16(16.2%) patients with Neurologic involvement were survived and 18(56.3%) patients with Neurologic involvement were expired. It was also statistically significant (p<0.0001).

DE CARVALHO H et al [11] (2020) found that ICU admission, mechanic ventilation or death were significantly higher in hyponatremic compared to normonatremic patients (34 versus 14%; p < 0.001; 16% versus 5%; p = 0.002; 19 versus 9%, p = 0.021, respectively). Hyponatremia was an independent predictor of poor outcome (adjusted Odds-ratio: 2.49 [1.18–5.33, p = 0.017]).

We found that 48 (15.0%) patients need to Transferred in ICU. 31 (23.7%) Hyponatremic patients and 17 (9.0%) Normonatremic patients were Transferred in ICU. Association of Transfer in ICU vs Group was statistically significant (p=0.0003). All 31(96.9%) Hyponatremic patients who need to Transfer in ICU were expired which was statistically significant (p<0.0001). 53 (16.6.0%) patients were in Mechanic ventilation. 31 (23.7%) Hyponatremic patients and 22 (11.6%) Normonatremic patients were in Mechanic ventilation which was statistically significant (p=0.0044). All 31(96.9%) Hyponatremic patients who moved to Mechanic ventilation were expired which was statistically significant (p<0.0001).

In our study the mean Systolic blood pressure (mean± s.d.) of patients was 100.1125 ± 9.6983. The mean Diastolic blood pressure (mean± s.d.) of patients was 77.0375 ± 12.2410. The mean SPO2 (mean± s.d.) of patients was 93.1188 ± 13.0176. The mean Respiratory rate (mean± s.d.) of patients was 23.2375 ± 2.9764 /min.

It was found that the mean Systolic blood pressure (mean± s.d.) of Hyponatremic patients was 102.4275 ± 11.7356 and Normonatremic patients was 98.5079 ± 7.6183 which was statistically significant (p=0.0003). The mean Diastolic blood pressure (mean± s.d.) of Hyponatremic patients was 79.7405 ± 13.9921 and Normonatremic patients was 75.1640 ± 10.5002. This was also statistically significant (p=0.0009). The mean SPO2 (mean± s.d.) of Hyponatremic patients was 91.4427 ± 14.4468 and Normonatremic patients was 94.2804± 11.8281 which was not statistically significant (p=0.0551). The mean Respiratory rate (mean± s.d.) of Hyponatremic patients was 23.8092± 3.4264 /min and Normonatremic patients was 22.8413± 2.5550 /min which was statistically significant (p=0.0041).

We found that in Hyponatremic group of patients, the mean Systolic blood pressure (mean± s.d.) of survived patients was 99.6364± 8.1334 and an expired patient was 111.0625± 16.3272. Difference of mean Systolic blood pressure with both Outcome in Hyponatremic was statistically significant (p<0.0001). The mean Diastolic blood pressure (mean± s.d.) of survived patients was 76.4040± 11.2267 and expired patients was 90.0625± 16.6442 which was statistically significant (p<0.0001).

We also found that in Hyponatremic group of patients, the mean SPO2 (mean± s.d.) of survived patients was 76.4040± 1.2771and expired patients was 90.0625± 17.3493. It was statistically significant (p<0.0001). The mean Respiratory rate (mean± s.d.) of survived patients was 22.1919± 1.7652/min. and expired patients was 28.8125± 2.2781/min. which was statistically significant (p<0.0001).

Table: Difference of mean Age, systolic blood pressure, Diastolic blood pressure, SPO2, Respiratory rate (/min): Group

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Age	Hyponatremic	131	49.2901	12.7945	23.0000	68.0000	52.0000	0.5666
	Normonatremic	189	48.4497	12.9448	23.0000	68.0000	51.0000	
Systolic blood pressure	Hyponatremic	131	102.4275	11.7356	90.0000	140.0000	98.0000	0.0003
	Normonatremic	189	98.5079	7.6183	90.0000	136.0000	98.0000	
Diastolic blood pressure	Hyponatremic	131	79.7405	13.9921	60.0000	114.0000	78.0000	0.0009
	Normonatremic	189	75.1640	10.5002	60.0000	114.0000	72.0000	
SPO2	Hyponatremic	131	91.4427	14.4468	45.0000	100.0000	97.0000	0.0551
	Normonatremic	189	94.2804	11.8281	45.0000	100.0000	98.0000	
Respiratory rate (/min)	Hyponatremic	131	23.8092	3.4264	20.0000	32.0000	24.0000	0.0041
	Normonatremic	189	22.8413	2.5550	20.0000	32.0000	22.0000	

Table: Difference of mean Age, Systolic blood pressure, Diastolic blood pressure, SPO2 and Respiratory rate (/min): Outcome in Hyponatremic

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Age	Alive	272	46.6544	12.6350	23.0000	68.0000	47.0000	<0.0001
	Death	48	60.9167	5.2098	51.0000	68.0000	62.5000	
Systolic blood pressure	Alive	99	99.6364	8.1334	90.0000	130.0000	98.0000	<0.0001
	Death	32	111.0625	16.3272	90.0000	140.0000	106.0000	
Diastolic blood pressure	Alive	99	76.4040	11.2267	60.0000	114.0000	74.0000	<0.0001
	Death	32	90.0625	16.6442	66.0000	114.0000	88.0000	
SPO2	Alive	99	76.4040	1.2771	96.0000	100.0000	98.0000	<0.0001
	Death	32	90.0625	17.3493	45.0000	98.0000	70.0000	
Respiratory rate (/min)	Alive	99	22.1919	1.7652	20.0000	25.0000	22.0000	<0.0001
	Death	32	28.8125	2.2781	22.0000	32.0000	30.0000	

CONCLUSION

In our study, 28(8.8%) patients were ≤30 years old, 48(15.0%) patients were 31-40 years old, 79(24.7%) patients were 41-50 years old, 90(28.1%) patients were 51-60 years old and 75(23.4%) patients were 61-70 years old.

Poor outcome was found in higher age group in Hyponatremic COVID-19 patients which was statistically significant.

In our study, 131(40.9%) COVID-19 patients were in Hyponatremic and 189(59.1%) COVID-19 patients were in Normonatremic.

It was found that Hyponatremic COVID-19 patients were significantly associated with Diabetes, HTN, Cirrhosis, Neurologic involvement and Congestive heart failure but Hyponatremic COVID-19 patients were not significantly associated with Coronary artery disease, Active neoplasia, Current smoker, Body temperature, Diarrhea, Vomiting, Agueusia, Anosmia .

High Systolic blood pressure, High Diastolic blood pressure, low SPO2 and high Respiratory rate was observed in Hyponatremic COVID-19 patients which were statistically significant.

In Hyponatremic COVID-19 patients, Diabetes, HTN, Coronary artery disease, Active neoplasia, Neurologic involvement, Current smoker and Congestive heart failure were significantly associated with poor outcome but Cirrhosis, Body temperature, Diarrhea, Vomiting, Agueusia, Anosmia were not significantly associated with poor outcome.

We found that 48 (15.0%) patients were Transfer in ICU, 35(10.9%) patients were in Mechanic ventilation, 272 (85.0%) patients were Alive and 48 (15.0%) patients were Death.

Poor outcome was observed in Hyponatremic COVID-19 patients compared to Normonatremic COVID-19 patient which was statistically significant.

In Hyponatremic COVID-19 patients, High Systolic blood pressure, High Diastolic blood pressure, low SPO2 and low Respiratory rate was significantly related to poor outcome.

In 320 patients with COVID-19, our study showed an independent relationship between 131 Hyponatremic COVID-19 patients at admission and transfer to ICU, use of mechanic ventilation or death. Our results support the test sodium in hospitalized COVID-19 patients as another bedside screening tool for early identification of patients at high risk of poor outcome.

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