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PREVALENCE AND PATTERN OF HYPONATREMIA AND HYPOMAGNESEMIA IN CRITICALLY ILL PATIENTS

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ABSTRACT

Electrolyte disturbances are important determinant of outcome in ICU admitted patients with multi-organ dysfunction. This study is conducted in a ICU setup of a referral hospital. 100 critically ill patients are taken as study subjects. Mean age of study population range from 22- 90 years. 58% of study population are males. Common electrolyte abnormality observed in present study are hyponatremia (65%) followed by hypomagnesemia. Mortality is highest in severe hyponatremia (83.3%) group followed by hypomagnesemia (66.7%).

KEYWORDS: Hyponatremia, Hypomagnesemia.

INTRODUCTION

Intensive care unit (ICU) services require expensive technology, and account for as much as 10 percent of all health care costs. The outcome of critically ill patients is therefore of importance not only to the patients and their families, but also to the society. After admission to the ICU, the outcome is dependent upon both the diagnosis and management of the primary illness and, in many cases, the presence or absence of multi-organ involvement.[1]

On the other hand, electrolytes such as potassium, sodium, magnesium, calcium and phosphate play important roles in cellular metabolism and energy transformation, and in the regulation of cell membrane potentials, especially those of muscle and nerve cells, which demonstrate their important role in the outcome of critically ill patients. Depletion of these electrolytes can induce a wide range of clinical disorders, including neuromuscular dysfunction and severe arrhythmias. The risk for these disorders increases significantly when more than one electrolyte is deficient.[2]

It is well known that hypokalemia can induce cardiac arrhythmias (especially in patients with ischemic heart disease and left ventricular hypertrophy), and that it is associated with other adverse effects such as muscle weakness, rhabdomyolysis, renal failure and hyperglycemia. Additionally, hyperkalemia may cause symptoms such as severe muscle weakness or paralysis

and cardiac conduction abnormality which may lead to adverse outcomes in ill ICU patients.[3-6] Moreover, hyponatremia is a common electrolyte abnormality in critically ill patients.[6-9] The risk of hyponatremia among hospitalized patients is influenced by the underlying disease state and clinical circumstances. The symptoms directly attributable to hyponatremia primarily occur with acute and marked reductions in the plasma sodium concentration and reflect neurologic dysfunction induced by cerebral edema. In this setting, the associated fall in plasma osmolality creates an osmolal gradient that favors water movement into the cells, leading in particular to brain edema.[6,10,11]

Another sodium disturbance, hypernatremia, is basically a mirror image of hyponatremia.[6,10,11,12] The rise in the plasma sodium concentration and osmolality causes acute water movement out of the brain; this decrease in brain volume can cause rupture of the cerebral veins, leading to focal intracerebral and subarachnoid hemorrhages and possible irreversible neurologic damage. The clinical manifestations of this disorder begin with lethargy, weakness, and irritability, and can progress to twitching, seizures, and coma.[6,10]

Thus, the importance of regulating potassium and sodium levels is well recognized in most intensive care units (ICUs). On the other hand, the development of many electrolyte disturbances in the ICU can be prevented by attention to the usual intravenous fluids and

nutrition. Most studies on this subject are focused on the incidence and prevalence of these electrolyte disturbances among ICU patients. Therefore, the aim of this study was to evaluate the prevalence and pattern of hyponatremia and hypomagnesemia in order to assess their effects on patient outcome in an ICU setting.

MATERIAL AND METHODS

Study design and setting
This was a longitudinal, observational study carried out in the in-patient of the Department of General Medicine of a tertiary care teaching hospital during the period from October 2016 to July 2017. The source population was the patients admitted to the ICU and the General Medicine ward. Only patients with an APACHE II score ≥ 4 and more than 15 years of age were included in the study. Patients with an age less than 15 years, alcoholics, smokers, post-operative critically ill, with pseudo-hyponatremia, hypertriglyceridemia were excluded to minimize the effect of confounders.

Sample size calculation and sampling technique
The study was carried out on a convenience sample of 100 patients admitted to the ICU and General Medicine ward. Studies have reported the occurrence of hyponatremia and hypomagnesaemia in critically ill ICU admitted patients to be between 16-29% and 14-70% respectively.[13,14] Assuming a prevalence of electrolyte imbalance in ICU patients to be 70% from available literature, at a two sided confidence level of 95% and an absolute precision of 10, the sample size was calculated to be 81 using nMasters software. To account for loss to follow up the sample size was further increased by 10%. Finally 100 patients were included in the study.

Ethical considerations
The study protocol was approved by the Institutional Ethics Committee of M.K.C.G. Medical College. Written informed consent was obtained from the patient or their attendants prior to their inclusion in the study. The implication of their participation in the study was thoroughly explained to the study participants.

Data collection and study parameters
The patient data was collected by the investigators themselves in a predesigned case record form. The case record form captured data on patient age, gender, diagnosis at admission, association with hypertension and diabetes mellitus, duration of hospital stay, outcome like mortality or survival at discharge. APACHE II, presence of multi-organ dysfunction, fluid status was assessed for each patient. Serum sodium and magnesium as well as other routine investigations were done.

Study definitions
For the present study multi-organ dysfunction was defined as dysfunction of more than one organ and requiring intervention to maintain homeostasis. A serum sodium level of 130-134 mEq/L, 125-129mEq/L and ≤ 124 mEq/L were considered as mild, moderate and severe hyponatremia respectively. A serum magnesium level of ≤ 1.4mEq/L was considered hypomagnesemia.

Statistical analysis
Descriptive analytical statistics was used to interpret the data collected. Continuous variables were presented as mean ± SD and categorical variables were presented as proportions. A p value of ≤ 0.05 was considered as statistically significant. All the statistical analysis were done using the Graph Pad Prism 6.0 trial version.

RESULTS

The present study included 100 critically ill patients with an APACHE II score of ≥ 4. The mean age of the study population was 58.5±16.26 years with a range of 22-90 years. 58% of the participants ware males. At admission the most common presentation was coma (15%), followed by seizures (14%), confusion (13%) and dyspnea (11%). With respect to diagnosis at admission hyponatremia was mostly associated with acute stroke (18.4%) whereas hypomagnesaemia was mostly associated with COPD (33.3%). [Table 1]Among the study participants with hyponatremia 60% were male. Hypomagnesaemia was equally prevalent in the either gender. Electrolyte imbalance was more common in patents > 60 years of age. The distribution of hyponatremia and hypomagnesaemia according to age is represented in Table 2. Majority of the cases (43%) were having moderate hyponatremia. Only 22% of the study participants had severe hyponatremia. It was observed that 16% patients had the co-existance of hyponatremia and hypomagnesaemia. Both hypomagnesesmia and severe hyponatremia was seen in 43.5% of patients. [Table 3] The association of hyponatremia and hydration status is depicted in Table 4The associated electrolyte imbalances, comorbidity like diabetes mellitus, hypertension, multi-organ dysfunction syndrome is presented in Table 5.

In the present study majority of the patients (38.3%) had an APACHE II score of 25-35. [Table 6] The mean duration of hospital stay was maximum for hypomagnesemia (10.33±3.14 days). [Table 7] Ventilator requirement was maximum for patients with hypomagnesemia (83.3%) and severe hyponatrimea (83.3%). Mortality was highest in patients with severe hyponatremia (83.3%) followed by hypomagnesemia (66.7%). [Table 8].

Table 1: Diagnosis at admission with regard to hyponatremia, hypomagnesemia, both and control in the study participants.

Diagnosis	Hyponatremia	Hypomagnesemia	Both	Control	Total
Multilobar pneumonia	3(8%)	xx	1(6%)	2(5%)	6%
Severe malaria	1(3%)	xx	xx	5(13%)	6%
Pyogenic meningitis	xx	1(7%)	xx	1(3%)	2%
Complicated UTI	2(5%)	xx	1(6%)	2(5%)	5%
Myocarditis with CCF	3(8%)	xx	xx	1(3%)	4%
Sepsis	1(3%)	xx	xx	Xx	1%
Dissiminated TB	1(3%)	1(17%)	1(6%)	Xx	4%
AGE with AKI	2(5%)	xx	1(6%)	Xx	3%
AMI	xx	1(17%)	3(19%)	4(10%)	8%
HHS/DKA	2(5%)	xx	3(19%)	2(5%)	7%
OP poisoning	2(5%)	xx	Xx	2(5%)	6%
Snake bite	4(11%)	xx	Xx	2(5%)	2%
Decompensated cirrhosis	5(13%)	xx	1(6%)	6(15%)	12%
COPD with corpulmonale	4(11%)	2(32%)	2(13%)	5(13%)	12%
Acute stroke	7(18%)	xx	2(13%)	3(8%)	12%
CKD with complications	3(8%)	1(17%)	2(13%)	4(10%)	10%
Total	38(100%)	6(100%)	16(100%)	40(100%)	100%

Table 2: Prevalence of hyponatremia, hypomagnesemia, both in elderly.

Age Group	Hyponatremaia		Hypomagnesemia		Both		Control	
	N	%	N	%	N	%	N	%
< 60 years	14	36.8	1	16.7	5	31.25	28	70
>60 years	24	63.2	5	83.3	11	68.75	12	30
P value	0.006		0.0205		0.0035			

Table 3: Association of hyponatremaia with hypomagnesemia.

	Mild Hyponatremaia		Moderate Hyponatremaia		Severe Hyponatremaia	
	N	%	N	%	N	%
Hypomagnesemia	4	25	5	31.25	7	43.75
P value	1.00		0.1065		0.0038	

Table 4: Type of hyponatremia according to hydration status.

Hydration	Mild		Moderate		Severe	
	N	%	N	%	N	%
Euvolumeic	12	66.7	14	60.9	8	61.5
Hypovolumeic	2	11.1	4	17.4	2	15.4
Hypervolumeic	4	22.2	5	21.7	3	23.1
Total	18	100	23	100	13	100

Table 5: Association of hypertension, diabetes mellitus and multi-organ dysfunction syndrome with hyponatremia, hypomagnesemia, both in elderly.

Parameters	Hypertensive		Non-hypertensive		P value
	N	%	N	%	
Hyponatremia	18	47.4	20	52.6	0.247
Hypomagnesemia	4	66.7	2	33.3	0.174
Both	10	62.5	6	37.5	0.069
Control	13	32.5	27	67.5	0.125
	With DM		With DM		P value
	N	%	N	%	
Hyponatremia	18	47.4	20	52.6	0.058
Hypomagnesemia	5	83.3	1	16.7	0.010
Both	14	87.5	2	12.5	0.001

Control	10	25.0	30	75.0	0.001
	With MODS		With MODS		P value
	N	%	N	%	
Hyponatremia	20	59.9	18	42.1	0.009
Hypomagnesemia	5	83.3	1	16.7	0.010
Both	11	68.8	5	31.2	0.005
Control	10	25.0	30	75.0	0.002

Table 6: Association of hyponatremia, hypomagnesemia, both and control with APACHE II in elderly.

APACHE II	Hyponatremaia		Hypomagnesemia		Both		Control	
	N	%	N	%	N	%	N	%
5-15	5	13.1	1	16.7	5	12.5	16	40.0
15-25	15	39.5	1	16.7	4	25.0	13	32.5
25-35	14	36.9	2	33.3	7	43.7	7	17.5
>35	4	10.5	2	33.3	3	18.7	4	10.0
Total	38	100	6	100	16	100	40	100

Table 7: Association of hyponatremia, hypomagnesemia, both and control with mean duration of hospital stay in elderly.

Duration of hospital stay	< 5 days		5-10 days		> 15 days		Total number of patients	
	N	%	N	%	N	%	N	%
Hyponatremia	5	13.2	26	68.4	7	18.4	38	100
Hypomagnesemia	1	16.7	5	83.3	xx	xx	6	100
Both	5	31.2	10	62.5	1	6.25	16	100
Control	16	40.0	24	60.0	xx	xx	40	100

Table 8: Association of hyponatremia, hypomagnesemia, both and control with outcome.

	Death		Discharge		P value
	N	%	N	%	
Hyponatremia					
Mild	3	21.4	11	78.6	0.734
Moderate	8	44.5	10	55.5	0.003
Severe	5	83.3	1	16.7	0.009
Hypomagnesemia	4	66.7	2	33.3	0.022
Both	9	56.2	7	43.8	0.007
Control	7	17.5	33	82.5	0.0006

DISCUSSION

In the present study 38%, 6%, 16% patients had hyponatremia, hypomagnesaemia and both respectively. 40% patients had neither. Benanai et al, their study on 2188 patients and De Vita et al have observed prevalence of hyponatremia in ICU patients to be 16% and 29.6% respectively.[13,14] Since this was a study carried out in a tertiary care referral hospital we observed a higher prevalence. Ryzen et al have observed the prevalence of hypomagnesemia to be 51%.[15] In the present study the mean age was 58.5±16.26 years. In a study by Limaye et al the mean age was 67 years.[16] Anomg the patients with hyponatremia 60.5% were males and 39.5% were females. Subba Rao et al have also observed that males had an higher incidence of electrolyte imbalance.[17] In the present study hyponatremia at admission was observed maximally in patients with acute stroke followed by COPD and organophosphorous poisoning whereas hypomagnesemia was most prevalent in COPD patients. AMI and HHS/DKA group of patients had maximum number of patients with both the kind of electrolyte imbalances. They had observed that circulatory and respiratory diseases formed the major group. Mandal et al have also found that 41.4% cases of electrolyte imbalance were suffering from CNS diseases.[18] Similar to the findings of the present study Hochman et al have observed that increasing age was associated with electrolyte imbalance. 22%, 43% and 35% had severe, moderate and mild hyponatremia respectively.[19] In the study by Hochman et al 39% had mild hyponatremia and 61% had moderate to severe hyponatremia. In the hyponatremia group 47.4% had hypertension whereas 66.7% with hypomagnesemia had hypertension.[19] Similar were the observations by Mohan S et al.[20] They have reported a prevalence of 4.5% of hypomagnesemia in ambulatory hypertensive patients. In hyponatremia group 47.4 had Diabates Mellitus where as the incidence was 83.3% in those with hypomagnesesmia. Limaye et al have also observed that hypomagnesemaia was more common among diabetics.

APACHE II score is one of the various ICU scoring systems available to prognosticate the patients condition. In this study maximum number of cases were having an APACHE II score of 25-35.[16] The mean score was highest for hypomagnesemia 26.6±10.43 followed by 23.39±7,34 for hyponatremia and 24.06±9.6 for both. Safavi et al have found a statistically significant higher mean APACHE II score in hypomagnesemia patients.[21] The mean duration of hospital stay was longest for hypomagnesemia being 10.33±3.14 days and shortest for severe hyponatremia 8.2±1.78 days. In a study by Soliman et al there was no difference in the length of ICU stay between such patients.[22] In the presentstudy the shorter duration of hospital stay in cases of severe hyponatremia may be due to increased mortality. This study observed the highest mortality in severe hyponatremia group. Chernow et al have observed a higher mortality in hypomagnesemia group.[23] Other studies have observed a 60 fold increase in the mortality in hyponatremic patients.[24,25]

Some of the major limitations of the present study were that it was carried out on a small sample of ICU patients. Alcoholics and smokers were excluded. Outcome was not adjusted for confounders like age, disease etiology, severiety of illness, APACHE II score etc.

CONCLUSION

There was no gender variation in the prevalence of hyponatremia and hypomagnesemia in critically ill patients. When there was an association of hypomagnesemia with severe hyponatremia the prognosis was poor. There was a distinctive relationship between comorbidities like hypertension and diabetes mellitus and electrolyte imbalances. Case fatality was highest for severe hyponatremia followed by hypomagnesemia.

REFERENCES

1. Viktoria D Mayr, Martin W Dünser, VeronikaGreil, Stefan Jochberger, Günter Luckner, Hanno Ulmer, Barbara E Friesenecker, JukkaTakala, Walter R Hasibeder. Causes of death and determinants of outcome in critically ill patients. Critical Care, 2006, Volume 10, Number 6, Page 1.
2. Marshall DC, Salciccioli JD, Goodson RJ, Pimentel MA, Sun KY, Celi LA, Shalhoub J.J Crit Care., 2017 Aug; 40: 63-68.
3. Lee JW. Fluid and electrolyte disturbances in critically ill patients. Electrolyte Blood Press, 2010 Dec; 8(2): 72-81.
4. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med, 2001; 345: 1368–1377.
5. Sakr Y, Vincent JL, Reinhart K, et al. High tidal volume and positive fluid balance are associated with worse outcome in acute lung injury. Chest., 2005; 128: 3098–3108.
6. Bouchard J, Soroko SB, Chertow GM, et al. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Int., 2009; 76: 422–427.
7. Payen D, de Pont AC, Sakr Y, Spies C, Reinhart K, Vincent JL. A positive fluid balance is associated with a worse outcome in patients with acute renal failure. Crit Care, 2008; 12: R74.
8. Schetz M. Critical Care Nephrology. 2nd ed. Philadelphia: Saunders, 2009. Assessment of volume status; pp. 499–504.
9. Funk GC, Lindner G, Druml W, et al. Incidence and prognosis of dysnatremias present on ICU admission. Intensive Care Med, 2010; 36: 304–311.
10. Stelfox HT, Ahmed SB, Khandwala F, Zygun D, Shahpori R, Laupland K. The epidemiology of intensive care unit-acquired hyponatraemia and hypernatraemia in medical-surgical intensive care units. Crit Care, 2008; 12: R162.
11. Buckley MS, Leblanc JM, Cawley MJ. Electrolyte disturbances associated with commonly prescribed medications in the intensive care unit. Crit Care Med, 2010; 38(6 Suppl): S253–S264.
12. Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med, 2000; 342: 1581–1589.
13. Bennani SL, Abouqal R, Zeggwagh AA et al. Incidence, causes and prognostic factors of hyponatremia in an intensive care unit. Rev Med Interne, 2003 Apr; 24(4): 224-9.
14. DeVitaMV, Gardenswartz MH, Konecky A, Zabetakis PM. Incidence and etiology of hyponatremia in an intensive care unit. Clinical Nephrology, 01 Oct 1990; 34(4): 163-166.
15. Ryzen E, Wagers PW, Singer FR, Rude RK. Magnesium deficiency in a medical ICU population. Crit Care Med., 1985 Jan; 13(1): 19-21.
16. Limaye CS, Londhey VA, Nadkart MY, Borges NE. Hypomagnesemia in critically ill medical patients J Assoc Physicians India, 2011 Jan; 59: 19-22.
17. Subba Rao SD, Thaoma B. Electrolyte abnormalities in children admitted to intensive care. Indian Pediatrics, 2000; 37: 1348-1353.
18. Mandal AK, Saklayan MG, Hillman NM, Market RJ. Predictive factors for high mortality in hypernatremic patients. Am J Emerg Med, 1997; 15: 130-132.
19. Hochman I, Cabili S, Peer G. Hyponatremia in internal medicine ward patients, Isr J Med Sci., 1989; 35: 73-76.
20. Mohan S, Gu S, Parikh A, Radhakrishnan J. Prevalence of hyponatremia and association with mortality: results from NHANES. Am J Med, 2013 Dec; 126(12): 1127-37.
21. Safavi M, Honarmand A. Admission hypomagnesemia--impact on mortality or morbidity in critically ill patients. Middle East J Anaesthesiol, 2007 Oct; 19(3): 645-60.
22. Soliman HM, Mercan D, Lobo SS, Mélot C, Vincent JL. Development of ionized hypomagnesemia is

associated with higher mortality rates. Crit Care Med, 2003 Apr; 31(4): 1082-7.

23. Chernow B, Bamberger S, Stoiko M, Vadnais M, Mills S, Hoellerich V, Warshaw AL. Hypomagnesemia in patients in postoperative intensive care. Chest, 1989 Feb; 95(2): 391-7.

24. Charles BS, Menon I, Girish TS, Cherian AM. Hypomagnesemia in the ICU - Does Correction Matter? JAssoc Physicians India, 2016 Nov; 64(11): 15-19.

25. Jiang P, Lv Q, Lai T, Xu F Does Hypomagnesemia Impact on the Outcome of Patients Admitted to the Intensive Care Unit? A Systematic Review and Meta-Analysis. Shock, 2017 Mar; 47(3): 288-295.