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Hyponatremia Under Various Specialties

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Abstract

Purpose: Hyponatremia is frequently observed electrolytes derangement in both medical and surgical specialties with a variety of underlying illnesses. The rapidity of sodium derangement and symptoms at the time of presentation help to decide its management plan. Many times, treating primary disease specifically along with just conservative steps for hyponatremia i.e., plain water restriction, adding salt, or infusion isotonic saline help achieve desirable results.

Patients and methods: This observational study was conducted at the Indus Hospital and Health Network (IHHN) from July 2017 to April 2020 with the approval of Interactive and Research Development (IRB-IRD). All those (age >14 years) of either gender, admitted under various specialties with hyponatremia (serum sodium<135 meq/L) were enrolled after taking consent. Their history, demographics, volume status, and investigation were done and hyponatremia was categorized as mild (130 to 134 meq/L), moderate (125 to 129 meq/L), and severe (<125 meq/L). The outcome was noted on the pre-formed questionnaire as Sodium improve/unimproved, discharged, expired.

Results: Out of 262 patients with a male to female ratio of 0.8/1 (123/139), the most prevalent comorbid was hypertension 177 (67.6%), followed by CKD 171 (65.3%) and DM 142 (54.2%). The majority 102 (38.9%) had a moderate degree of hyponatremia while hypovolemia was the predominant volume status observed in 131 (50%) patients. Symptomatic hyponatremia was present in 38 (14.5%) patients. The majority of patients recovered and discharged 234 (89.3%), of which only 2 patients required hypertonic saline.

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Conclusion: Hyponatremia is frequently observed electrolyte derangement in the Tertiary Care setting, which is usually recovered with conservative treatment along with treating primary disease. The severity of hyponatremia was not seen as associated with increased mortality.

Introduction

Hyponatremia is a disorder of water balance and not derangement of sodium. The prevalence of hyponatremia has been documented as low as 6% and high as 44% [1-3]. To keep sodium in the range of 135 to 145 meq/L and osmolality 280 to 295 meq/Lin serums, water channels (aquaporin) constantly remains engaged moving water in and out of the cells [4]. This is done in addition to the thirst mechanism sensed by osmoreceptors, and antidiuretic hormone in the brain to keep osmolality maintained in this bracket [5]. When this fine balance of water and sodium is disrupted due to any reason, cells of the body come under osmotic stress, and sodium derangement occurs [6]. The manifestation of this derangement (hyponatremia) varies from mild and subtle like feeling unwell, nausea, mild unsteadiness to very ominous i.e. seizure to coma. These manifestations (symptoms) sometimes become very challenging to the clinician in differentiating them from primary disease and hyponatremia itself. The diseases like severe infection or CKD may sometimes mimic hyponatremia especially when it comes to encephalopathy [7]. When such a situation arises then clinicians find themselves challenged in opting for hypertonic saline (3%) versus managing hyponatremia conservatively and treating primary disease.

Mortality in hyponatremia has been documented in various studies between 10 to 45% [8-10]. Many clinicians think that mortality associated with hyponatremia is largely secondary to organ failure i.e. liver, kidney, and heart failure, rather than depression or anti-psychotics/diuretics medicines [11]. Deaths in these patients are related more to underlying disease than from hyponatremia causing cerebral edema [12]. Our aim in this study would remain not restricted to find the outcome i.e. Discharged or expired but at the same time to see relationship of severity of hyponatremia with its symptoms (symptomatic hyponatremia) and how conservative approach worked well towards treatment of hyponatremia. Conservative management of hyponatremia would be including plain water restriction, the addition of salts in water and diet, and use of normal saline while using hypertonic saline (3%saline) would make it aggressive approach.

Material and methods

This prospective study was conducted at the Indus Hospital and Health Network (IHHN), Karachi campus from July 2017 to April 2020 after approval of the Institutional Review Board and Interactive Research and Development (IRD_IRB_2017_03_015). All those who were of age >14 years of either gender admitted under the care of various specialties with hyponatremia (serum sodium<135 meq/L) diagnosed on the day of admission or later during the course of hospitalization were enrolled. These patients were subjected to detailed history followed by general physical examination on the day of their enrollment along with their demographic were noted. After that their relevant investigation was ordered i.e., serum urea, creatinine, blood sugar, serum and urine osmolarities, spot urine samples for sodium, chloride, potassium.

Echocardiography was done on all patients as heart failure is associated with hyponatremia and it also helps in proper assessment of volume status. Serum sodium was categorized as mild Hyponatremia (130 to 134 meq/L), moderate (125 to 129 meq/L), and severe (<125 meq/L). Spot urine sodium cut-off value was set as 20 meq/L to know the behavior of the kidney. Normal kidney behavior in face of hyponatremia is to conserve sodium provided there is no renal failure and diuretic use. In such situation urinary sodium in spot urine sample should come as <20meq/L.

Those who had a deranged renal function were further categorized into Chronic Kidney Disease (CKD) stages with the help of the "Modified of Diet and Renal Disease" (MDRD) equation. Volume status of the patient has been classified on basis of clinical examination i.e., pedal edema, jugular venous pressure, bibasilar inspiratory crepitation gallop sound, and subsequently labeled as hypovolemic, normovolemic, or hypervolemic. Apart from that neurological symptom (i.e., headache, altered mentation, ataxia, fits), any surgical procedure/Operation if done, use of hypertonic/isotonic saline (3%/0.9% saline), Diagnosis/Impression of patient and outcome i.e., those who improvement in serum sodium and symptoms, discharge and death of the patients were all noted in the pre-formed questionnaire.

Statistical analysis

The data was entered and analyzed on SPSS IBM version 21. Cleaning and coding of data were done before analysis. Mean ± STD and Median with Interquartile range were computed for continuous variables, while the frequency with percentage was calculated for categorical variables. Association between categorical variables was established by Chi-square test; on the other hand, one-way ANOVA was applied for normally distributed continuous data, while Kruskal Wallis test was executed for skewed variables. The normality of data was checked by Shapiro Wilk" s test. P-value of ≤ 0.05 was set as a significant level.

Results

There was a total of 262 patients in our study in which 123 (46.9%) were male and 139 (53.1%) were female. The mean age was 54.1 ± 16.4 years with a minimum of 15 and a maximum of 88 years. The most prevalent comorbid was HTN 177 (67.6%), followed by CKD 171 (65.3%) and DM 142 (54.2%). The majority of patients had a moderate degree of Hyponatremia 102 (38.9%), while symptomatic Hyponatremia was present only in 38 (14.5%) patients. Most of Hyponatremic patients were hypovolemic 131 (50%). The overall outcome of Hyponatremia was good as the majority of patients recovered and discharged 234 (89.3%) **Table 1.**

The description of all laboratory parameters is shown in **Table 2**.

We calculated the mean differences of patients' lab parameters according to the severity of Hyponatremia and found that serum and urine osmolality was significantly different between three degrees of Hyponatremia, as patients with mild Hyponatremia had maximum serum and urine osmolality as compared to severe Hyponatremia (p<0.001). Similarly spot urinary sodium was also high in mild and moderate Hyponatremia as compared to server Hyponatremia (p=0.017), same as serum urea was also much higher in patients with mild when compared with moderate and severe Hyponatremia (p=0.009) **Table 3**.

We have stratified patients into two groups according to presence and absence of symptoms of Hyponatremia and observed any association between Hyponatremia and volume status at the time of admission and found that hypovolemia was predominantly high in all degrees of Hyponatremia as compared to Euvolemia and hypervolemia, on the other hand in symptomatic patients, hypovolemia was dominant in patients with mild and severe Hyponatremia {6 (60%) and 8 (47.1%) respectively}, while hypervolemia was more common in moderate Hyponatremic patients 6 (54.5%) **Table 4**.

We didn't find any significant association between severity of Hyponatremia and outcome in symptomatic patients but asymptomatic patients with moderate and severe Hyponatremia more died {9 (52.9%) and 7 (41.2%) respectively} than mild Hyponatremia 1 (5.9%), on the contrary patients with mild and moderate Hyponatremia recovered the most {74 (35.7%) and 82 (39.6%) respectively} as compared to severe Hyponatremia 51 (24.6%) (p=0.038) **Table 5**.

Table 1: Characteristics of patients admitted with Hyponatremia n= 262.

Gender	n (%)
Male	123 (46.9)
Female	139 (53.1)
Comorbid	
DM	142 (54.2)
HTN	177 (67.6)
IHD	68 (26)
CKD	171 (65.3)
AKI	30 (11.5)
Severity of Hyponatremia	
Mild	85 (32.4)
Moderate	102 (38.9)
Severe	75 (28.6)
Symptoms of Hyponatremia	38 (14.5)
Volume status at admission	
Euvolemic	68 (26)
Hypovolemic	131 (50)
Hypervolumic	63 (24)
Admitting place	
Ward	212 (80.9)
ICU/CCU	50 (19.1)
Admission specialty	
Medical	196 (74.8)
Surgical	66 (25.2)
Outcome	
Discharge	234 (89.3)
Expire	28 (10.7)

Table 2: Demographic and Laboratory parameters of patients.

Laboratory parameters	Mean ± STD	Median, IQR	Minimum	Maximum
Age in Years	54.1 ± 16.4	55, 21	15	88
S. Na at admission	124.9 ± 5.9	12, 7	106	135
S. Na after Treatment	135.3 ± 5.2	136, 6	117	153
Urinary Na at admission	47 ± 26.9	42, 38	2	176
S.Osmolality at admission	295 ± 36.6	290, 52	211	412
Urine osmolality at admission	295.6 ± 130.8	285, 121	21	1018
Urinary Cl at admission	48.8 ± 28.1	41, 36	10	171
Urinary K at admission	19 ± 12.1	17, 16	2	80
S. Urea at admission	113.7 ± 70.7	107.5, 94	7	504
RBS at admission	160.1 ± 80.2	42, 38	2	176

Table 3: Mean differences of lab parameters in three classes of Hyponatremia.

Lab parameters	Hyponatremia			p value
	Mild	Moderate	Severe	
Serum Osmolality	306. ± 33.3	297.9 ± 38	278.8 ± 32.6	<0.001
Urine osmolality	310.3 ± 117.5	302.9 ± 138.5	268.7 ± 132.1	0.012
Spot urinary Na	48.6 ± 23.1	48.8 ± 29.9	40.2 ± 26.6	0.017
Sot urinary K	17.7 ± 10.5	21.2 ± 14.1	17.6 ± 10.4	0.195
Spot urinary Cl	51.8 ± 27.8	48.7 ± 29.5	45.6 ± 26.8	0.17
Serum Urea	126 ± 55.3	109.3 ± 74.9	105.7 ± 70.1	0.009

Table 4: Association of volume status of patients with severity of Hyponatremia stratified by symptoms of patients at time of admission.

Symptoms of Hyponatremia	Volume status of patients	Hyponatremia			p value
		Mild	Moderate	Severe	
Asymptomatic patients	Euvolemia	25 (33.3)	27 (29.7)	9 (15.5)	0.082
	Hypovolemia	35 (46.7)	41 (45.1)	38 (65.5)	
	hypervolemia	15 (20)	23 (25.3)	11 (19)	
Symptomatic Patients	Euvolemia	1 (10)	2 (18.2)	4 (23.5)	0.519
	Hypovolemia	6 (60)	3 (27.3)	8 (47.1)	
	hypervolemia	3 (30)	6 (54.5)	5 (29.4)	

Table 5: Association of degree of Hyponatremia with outcome of patients when stratified by symptoms.

Symptoms of Hyponatremia	Hyponatremia	Outcome		p value
		Discharged	Expired	
Symptomatic Patients	Mild	5 (18.5)	3 (45.4)	0.199
	Moderate	8 (29.6)	3 (27.3)	
	Severe	14 (51.9)	3 (27.3)	
Asymptomatic patients	Mild	74 (35.7)	1 (5.9)	0.038
	Moderate	82 (39.6)	9 (52.9)	
	Severe	51 (24.6)	7 (41.2)	

Discussion

This Prospective study conducted over 262 patients with Hyponatremia of variable degrees under medical and surgical specialties. Hypertension and CKD were the predominant comorbidities observed followed by diabetes and ischemic heart disease. Symptomatic hyponatremia (with neurological symptoms) was seen in 14.5% of cases. Near 39% of patients were of a moderate degree of hyponatremia and from volume status point, 50% of patients were hypovolemic. Death was not seen significantly among symptomatic severe hyponatremia as compared to mild and moderate hyponatremia. Apart from that, mortality was seen more in asymptomatic patients with moderate and severe Hyponatremia. The majority of patients who were recovered and discharged were of mild and moderate Hyponatremic than severe Hyponatremia. Only 2 patients out of 262 required hypertonic saline (3% saline).

If we talk about common age group suffering from hyponatremia, it comes aged group. This is most likely secondary to less optimal ability to get rid of solutes in this age group and in many of cases less efficient awareness of fluids because of high burden of comorbidity including dementia. The significant association of comorbidity i.e., diabetes and hypertension highlighted in our studied hyponatremic patients is no more surprising in this context [13,14]. Apart from this, Chronic kidney disease (CKD) and Congestive Heart Failure (CCF) have been highlighted with hyponatremia in various studies where increased volume status and use of diuretics were also noted to causing [15,16]. Apart from that, increased vasopressin level and sympathetic activity have also been implicated in CCF which marks the severity of heart failure and increases morbidity and mortality [17,18]. Most vulnerable among them developing hyponatremia with CCF is female geriatric population [19].

In normal circumstances, where there is no renal failure and no diuretics given, the kidney retains sodium as the body senses low osmolality in hyponatremia. In our studied population, mean urinary sodium was seen high although majority of our patients had hypovolemic state. The possible explanation for this is widely presence of CKD as comorbidity in our population. Other possible explanation is presence of Syndrome of Inappropriate Anti-Diuretic Hormone (SIADH) [20-22]. In both of these conditions, spot urine sodium may be found >20 meq/L because of the salt-losing phenomenon.

Symptoms of hyponatremia vary from patient to patient depending on the duration of hyponatremia, age of the patient and burden of comorbidity. Hyponatremia developed acutely (duration <48 hours) is likely to have more symptoms including neurological symptoms than chronic hyponatremia [23]. Clinicians often come under stress while choosing hypertonic saline when they encounter patients whose symptoms can be explained by hyponatremia and primary disease i.e. sepsis/Uremia [24,25]. The difficulty in choosing hypertonic saline is because of its possible fatal side effect when hyponatremia is corrected rapidly or corrected more than expected. Over correction of sodium may results into Central Pontine Myelinolysis (CPM). In such circumstances, more rational approach would be targeting primary disease at its full length and leaving hyponatremia to be managed on conservative bases. Conservative management of hyponatremia would be restriction of plain water, addition of salt in water and diet and using isotonic saline.

As far as relation of symptoms of hyponatremia with severity of hyponatremia is concerned, we don't find much literature available except few case reports, which discuss relation of symptoms with the severity of hyponatremia. Those case reports suggest a poor correlation of the severity of hyponatremia with symptoms [26,27]. We have observed the same finding in our study as no significant relationship exists between degree of hyponatremia and symptoms. In the context of suffering of patients, no matter how less symptomatic is the patient with hyponatremia, its impact towards patients and caregiver is enormous. This has been elaborated very well in the study by Decaux G et al in which, He even doubted in the existence of asymptomatic hyponatremia [28,29].

The mortality with hyponatremia has been remained under discussion for a long time. Hyponatremia leading to death or it is just the marker of severity of underlying disease, is still unresolved question. Clayton J A et al did a retrospective case note review on 105 patients with a mortality rate of around 20% [30]. He concluded in that study that mortality was more related to etiology than hyponatremia. Similarly, B Winzeler et al came up with almost the same figure of mortality, and linked mortality least connected with hyponatremia [31]. He concluded this because no one suffered brain edema or epileptic seizure, which could be attributed to hyponatremia. Baran D et al studied the general population over a three-month period with 9% mortality in which 46% were symptomatic hyponatremia [32]. We have observed in our studied population around 10% mortality, in which majority of the patients were not symptomatic. In many such studies where hyponatremia seemed least associated in terms of directly connected with mortality and found as indicator of primary disease process. With such ground, we believe hyponatremia should be taken as marker of severity of underlying disease, which should be treated vigorously, and hyponatremia conservatively until symptoms are not explained by other than hyponatremia.

Conclusion

Hyponatremia is widely prevalent in both medical and surgical specialties and often associated with comorbidities. Mortality is not significantly associated with symptomatic hyponatremia. Overall prognosis remains well when primary disease is treated hardly and managing hyponatremia conservatively.

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Disclosure

There are no conflicts of interest whatsoever in this work.

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