

Volume Status among Hyponatremic patients admitted under Tertiary Care

Shoukat Memon, Faiza Saeed, Ashar Alam, Javeria Chughtai, Salman Imtiaz.

Department of Nephrology,
The Indus Hospital and Health Network, Karachi, Pakistan.

Abstract

Introduction: The kidneys play a vital role in the management of hyponatremic patients with fluid disturbances. This task becomes even more challenging when a patient is stricken with comorbidities like chronic kidney disease or congestive heart failure. Accurate assessment of volume status and urinary sodium excretion is essential for the right management in these patients. Both impaired renal function and compromised left ventricular function complicate the accurate evaluation of a patient's fluid status.

Method: This cross-sectional prospective study was conducted over 262 adult patients of both genders admitted with hyponatremia at The Indus Hospital, Karachi from 2017 to 2020. The patient's volume status at the time of enrollment was categorized as normovolemic, hypovolemic, or hypervolemic based on clinical examination. Spot urine sodium, chloride, potassium, urine and serum osmolality, serum urea, and Random blood sugar were all done.

Results: There was a total of 262 patients in which 123 (46.9%) were male and 139 (53.1%) were female. The mean age was 54.1 ± 16.4 years. The overall comorbid burden was high 227(86.64%), in which hypertension and CKD contributed more. Out of 262 patients, half of them suffered from hypovolemia 131(50%). Spot urine sodium (>20 meq) was found in 219(83.58%) patients, in which predominant volume status was hypovolemia 104(47.5%). Moreover, among those who could not survive were 28 (10.7%), in which hypovolemia contributed more than other volume status 12(42.85%).

Conclusion: Hypovolemia came out to be the predominant volume status among hyponatremic patients with high comorbid burden. The majority excreted more sodium in spot urine samples despite of hypovolemia.

Key words: Hypovolemia, Hyponatremia, Urinary sodium.

Corresponding Author

Dr. Shoukat Memon

Department of Nephrology,
The Indus Hospital and Health Network,
Karachi, Pakistan

Email: shoukat.memon@tih.org.pk

DOI: 10.53778/pjkd83268

Received 16 Aug, 2024 & accepted 25 Sep, 2024

PJKD 2024;8(3):29-35

Introduction:

There is a significant prevalence of hyponatremia in general and specifically in chronic kidney disease (CKD) patients including dialysis.¹⁻⁴ Its presentation and etiology is diverse both in renal and non-renal patients. Kidney plays a vital role in handling of sodium with the disturbances of volume status. Management of hyponatremic patients becomes very challenging with the progression of chronic kidney disease. Knowledge of volume status while dealing with hyponatremic patients help us both in knowing the cause and management of hyponatremia. Volume status of patients is categorized as hypovolemic, normovolemic and hypervolemic. Urinary sodium excretion in these patients further helps in overall management of these patients. A normal functioning kidney behaves differently in different volumes of

Volume status & Hyponatremia

patients through the sensors i.e., juxtaglomerular apparatus, carotid vessels, right atrium etc. A typical mechanism of the kidney is not to excrete urine sodium more than 20 meq in a patient with decreased volume status. But this normal physiology may get altered altogether once there is impairment of renal function or diuretic therapy is being instituted.⁵

Sometimes the volume status of the patient becomes quite challenging to know. A thorough physical examination, pulse, postural drop, Jugular venous pressure all help to reach exact volume status.⁶ Moreover, after devising and instituting a management plan, one changes it in another direction when expected results are not obtained. Thus, a periodic volume assessment along with serial urinary sodium in spot urine samples help to manage the patient correctly. The elderly population, often burdened with comorbidities and impaired salt excretion, frequently falls victim to this condition.⁷ Presence of CKD and congestive heart failure (CCF) further increases their susceptibility.⁸

The main objective of the current study was to explore the volume status of hyponatremic patients in Tertiary care hospital. This study aims to bridge the gap by knowing the correlation of the volume status of the patients with the excretion of urinary sodium in hyponatremic patients in the context of impaired organ and normal organ function. Additionally, this research may provide valuable insights and clinical relevance by informing precise diagnostic and management approaches tailored to the unique needs of hyponatremic patients.

Methodology:

This observational study was conducted at the Indus Hospital and Health Network Karachi campus from July 2017 to April 2020 after the approval of the Institute (Dept/Institute: Nephrology/ TIH) and Interactive Research and Development (RD-IRB Number: IRD_IRB_2017_03_015). All adults (age >16 years) of either gender admitted with hyponatremia (serum sodium <135 meq/L) with variable volume status were enrolled in this study after getting consent. These patients underwent a thorough examination of their medical history and general physical condition. Serum sodium, urea, creatinine, spot urine sodium, chloride, potassium, urine and serum osmolality, random blood sugar, lipid profile, total protein and findings regarding left ventricular functions were noted in the questionnaire.

Volume status of the patient was categorized as hypovolemic, normovolemic, and hypervolemic based on the presence or absence of pedal/sacral edema, jugular venous pressure, bibasilar inspiratory crepitation, gallop sound on auscultation at the time of enrollment. After excluding the causes of pseudohyponatremia, true hyponatremia was categorized as mild (From 130 to 134 meq/L), moderate (From 125 to 129 meq/L), and severe (<125 meq/L). Final impressions of patients, total stay at hospital, use of hypertonic saline and final outcome (sodium improved and discharge or death) were all noted in the questionnaire.

Statistical analysis:

The data underwent preprocessing and coding procedure in SPSS version 21 before analysis. Continuous variables were summarized using both mean $\pm$ standard deviation and median with interquartile range (IQR). While categorical variables were presented as frequencies and percentages. Crosstabulation (Chi-square test) was done between the volume status and comorbid, urine sodium, left

Volume status & Hyponatremia

ventricular function, neurological symptoms, and outcome of patients. For normally distributed continuous variables, one-way ANOVA was employed, while the Kruskal – Walli’ s test was utilized for the skewed data. Normality of the data was verified through the Shapiro – Wilk test. Statistical significance was determined at a level of $p \leq 0.05$.

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 overall comorbid burden was high 227(86.64%), in which hypertension was more prevalent 177 (67.6%), followed by chronic kidney disease (CKD) 171 (65.3%). A majority of patients were found to be hypovolemic 131(50%), followed by euvolemia 68(26%). Urinary sodium (>20) in spot urine ample was observed in in majority of the patients 219(83.58%), in which hypovolemia was the predominant volume status observed 104(47.5%). The mean serum sodium is 124.9 ± 5.9 . Overall, the outcome for the hyponatremia was good as the majority of patients recovered and discharged 234 (89.3%), the remaining 28 (10.7%) patients, could not survive, in which hypovolemia was the predominant volume status 12(42.85%). Table 1 and 2.

Table:1 Characteristics of 262 patients admitted with hyponatremia at a tertiary care hospital.

	n(%)
Gender	
Male	123(46.9)
Female	139(53.1)
Volume Status	
Euvolemic	68(26)
Hypovolemic	131(50)
Hypervolemic	63(24)
Comorbid	
Hypertension	177(67.6)
Chronic Kidney Disease	171(65.3)
Diabetes	142(54.2)
Ischemic Heart Disease	68(26)
Spot Urinary Sodium	
> 20 meq/l	219 (83.58)
<20 meq/L	43(16.41)
Outcome	
Discharge	234(89.3)
Expired	28(10.7)

Out of total 262 patients, 62(23.66%) were having low ejection fraction, in which majority were hypervolemic 34(54.8%). Those who had neurological symptoms were in total 38 (14.5%), where predominant volume status was hypervolemia too 17(44.7%), Table 3.

Volume status & Hyponatremia

Table:2 Demographic and Laboratory parameters of patients

Laboratory parameters	Mean $\pm$ STD	Median, IQR	Minimum	Maximum
Age in Years	54.1 $\pm$ 16.4	55 , 21	15	88
S. Na at admission	124.9 $\pm$ 5.9	126, 7	106	135
S. Na after Treatment	135.3 $\pm$ 5.2	136, 6	117	153
Urinary Na at admission	47 $\pm$ 26.9	42 ,38	2	176
S. Osmolality at admission	295 $\pm$ 36.6	290, 52	211	412
Urine osmolality at admission	295.6 $\pm$ 130.8	285, 121	21	1018
Urinary Cl at admission	48.8 $\pm$ 28.1	41 , 36	10	171
Urinary K at admission	19 $\pm$ 12.1	17, 16	2	80
S. Urea at admission	113.7 $\pm$ 70.7	107.5, 94	7	504
RBS at admission	160.1 $\pm$ 80.2	42, 38	2	176

Table:3. Distribution of Parameters by Volume Status of Patients.

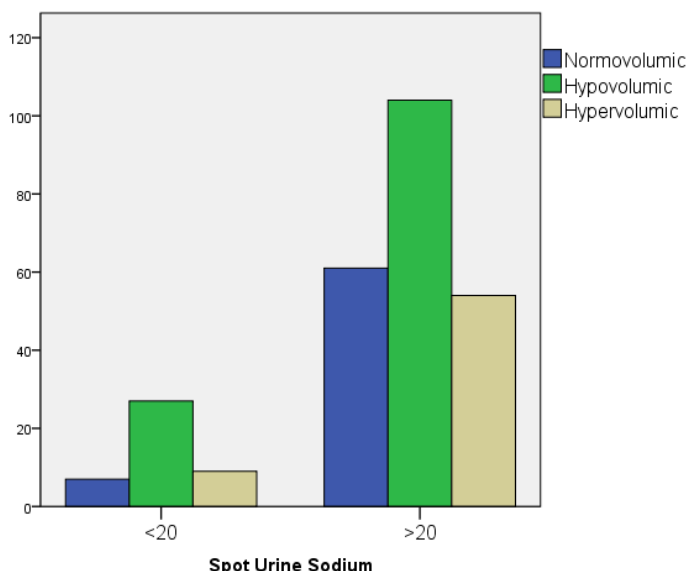
Variable	Volume Status of Patient			Total	p-value
	Normovolemic	Hypovolemic	Hypervolemic		
Comorbid					
Yes	64(90.1)	122(94.6)	59(93.7)	227(86.64%)	0.658
No	7(9.9)	7(5.4)	4(6.3)	35(13.35%)	
Total	71(100)	129(100)	63(100)	262(100)	
Neurological symptoms					
No	75(33.5%)	91(40.6%)	58(25.9%)	224(100%)	0.058
Yes	10(26.3%)	11(28.9%)	17(44.7%)	38(100%)	
Total	85	102	75	263(100%)	
LV function					
Normal'	60(30%)	111(55.5%)	29(14.5%)	200(76.33%)	
Low	8(12.9%)	20(32.3%)	34(54.8%)	62(23.66%)	
Total	85(26%)	102(50%)	75(24%)	262(100)	
Final outcome					
Discharged	79(33.76%)	90(38.46%)	65(27.77%)	234(89.3%)	0.397
Expired	6(21.42%)	12(42.85%)	10(35.71%)	28(10.7%)	
Total	68	131	63	262(100)	

Table.4: Volume Status and Urinary Sodium

	Spot urine sodium (enrollment)		Total	p-value
	≤20	>20		
Clinical volume				
Normovolumic	7(16.3)	61(27.9%)	68(26%)	0.113
Hypovolumic	27(62.8)	104(47.5%)	131(50%)	
Hypervolumic	9(20.9)	54(24.7%)	63(24%)	
Total	43(16.41%)	219(83.58%)	262(100)	

Volume status & Hyponatremia

Figure 1: Bar diagram showing patient distribution according to the urine sodium levels and volume status.



Discussion:

This study was conducted over 262 admitted cases both under medical and surgical services with low serum sodium. Majority of them were suffering from some sort of background disease, i.e., hypertension, chronic kidney disease (CKD), diabetes. The predominant volume status was found to be hypovolemia in which majority exhibited spot urine sodium(>20meq). Those who could not survive, among them hypovolemia was the predominant volume status.

Patients admitted with hyponatremia in a tertiary care hospital frequently have a high burden of comorbidities and are typically of advanced age. Older adults are more likely to suffer from chronic diseases such as heart failure, liver disease, and chronic kidney disease, all of which can contribute to the onset of hyponatremia. Additionally, polypharmacy is common among the elderly, and many of the medications they are prescribed, including diuretics, antidepressants, and antiepileptic drugs, can induce hyponatremia. In our study population, the most common comorbidities were hypertension and chronic kidney disease. The mean age was 54 years, with a significant proportion (86.64%) suffering from substantial comorbid conditions. Similarly, Estilo A et al. examined hyponatremia in approximately 265 patients, finding a high mean age of 70 years and varying volume status.⁹

Under normal circumstances, the kidneys excrete sodium based on daily intake, typically within a range of 40 to 220 meq/L.¹⁰ In cases of hypovolemia with hyponatremia, the normal response of functioning kidneys is to conserve serum sodium, resulting in low urinary sodium levels, typically below 20 meq/L in spot urine tests. However, this response can be altered by renal impairment or the use of diuretics.¹¹ In our study, a high burden of comorbidities, including hypertension and chronic kidney disease (86.64% of patients), likely contributed to urinary sodium levels exceeding 20 meq/L despite hypovolemia in the majority of our patients.

Volume status & Hyponatremia

A descriptive study conducted among hyponatremic patients in India found that the predominant volume status was euvolemia, accounting for 50.74% of the cases.¹² Serum sodium concentration is not determined by the total body sodium but rather by the ratio of total solutes in the body to total body water.¹³ When kidney function declines for any reason, the regulation of water and electrolytes is impaired. This can lead to the excessive accumulation of water, with or without accompanying electrolyte imbalances.¹⁴ With chronic kidney disease (CKD), water accumulation can occur due to impaired kidney function. However, as CKD progresses, accumulating urea exerts an osmotic effect that can lead to increased diuresis, potentially offsetting fluid retention.^{15,16} This can lead to excessive water excretion and subsequent volume depletion. This latter phenomenon was more pronounced in our studied population.

The high prevalence of hypertension in our studied population increases the risk of hyponatremia and is also linked to significant cardiovascular mortality.^{17,18} The presence of hypertension in our studied population may be multifactorial, with chronic kidney disease (CKD) being a significant contributor. Managing such patients becomes particularly challenging as CKD progresses to an advanced stage, especially when striving to maintain euvolemia.¹⁹ The risk of developing cardiovascular disease and mortality increases further in the presence of chronic kidney disease (CKD).²⁰ A substantial body of literature discusses the association between congestive heart failure (CHF) and hyponatremia.^{21,22} This occurs primarily due to elevated levels of vasopressin (AVP) and increased sympathetic activity, leading to water accumulation in the body and resulting in dilutional hyponatremia. This condition reflects the severity of heart failure and contributes significantly to both morbidity and mortality.^{23,24} In our study, we observed that one-fourth of the population had congestive heart failure (low left ventricular function), where hypervolemia was the predominant volume status. This condition contributed to mortality, with a significant association (P-value 0.03).

Major limitation of our study could be the lack of confirmation of volume status with the help of ultrasound, since such facility is not readily available in majority of the centers for point of care ultrasound, our study represents the real time clinical data among our patients.

Conclusion:

A significant number of hyponatremic patients were of advanced age in context of our region and had a high burden of comorbidities. Many of these patients exhibited a hypovolemic state but demonstrated increased urinary sodium excretion.

Acknowledgement: We gratefully acknowledge Dr. Jahanzeb Khan for the incorporation of data in SPSS.

Conflict of Interest: There is no conflict of interest in this study.

References

1. Frontera JA, Valdes E, Huang J, Lewis A, Lord AS, Zhou T, et al. Prevalence and impact of hyponatremia in patients with coronavirus disease 2019 in New York City. *Crit Care Med.* 2020;48(12):e1211-e1217.

2. Asadollahi K, Beeching N, Gill G. Hyponatremia as a risk factor for hospital mortality. *QJM*. 2006;99(12):877-80. .
3. Ravel VA, Streja E, Mehrotra R, Sim JJ, Harley K, Ayus JC, et al. Serum sodium and mortality in a national peritoneal dialysis cohort. *Nephrol Dial Transplant*. 2017;32(7):1224-33.
4. Rhee CM, Ravel VA, Ayus JC, Sim JJ, Streja E, Mehrotra R, et al. Pre-dialysis serum sodium and mortality in a national incident hemodialysis cohort. *Nephrol Dial Transplant*. 2016;31(6):992-1001.
5. Schrier RW. Diagnostic value of urinary sodium, chloride, urea, and flow. *J Am Soc Nephrol*. 2011;22(9):1610-3.
6. McGee S, Abernethy III WB, Simel DL. Is this patient hypovolemic?. *JAMA*. 1999;281(11):1022-
7. Cumming K, Hoyle GE, Hutchison JD, Soiza RL. Prevalence, incidence and etiology of hyponatremia in elderly patients with fragility fractures. *PloS one*. 2014;9(2):e88272.
8. Zhang R, Wang S, Zhang M, Cui L. Hyponatremia in patients with chronic kidney disease. *Hemodialysis International*. 2017;21(1):3-10.
9. Chen TK, Knicely DH, Grams ME. Chronic kidney disease diagnosis and management: a review. *Jama*. 2019 Oct 1;322(13):1294-304.
10. Hung SC, Kuo KL, Peng CH, Wu CH, Lien YC, Wang YC, et al. Volume overload correlates with cardiovascular risk factors in patients with chronic kidney disease. *Kidney Int*. 2014 ;85(3):703-9.
11. Yessayan L, Yee J, Frinak S, Szamosfalvi B. Treatment of severe hyponatremia in patients with kidney failure: role of continuous venovenous hemofiltration with low-sodium replacement fluid. *Am J Kidney Dis*. 2014 64(2):305-10.
12. Chatterjee N, Sengupta N, Das C, Chowdhuri AR, Basu AK, Pal SK. A descriptive study of hyponatremia in a tertiary care hospital of Eastern India. *Indian J Endocrinol Metab*. 2012 Mar;16(2):288-91.
13. Overgaard-Steensen C, Larsson A, Bluhme H, Tønnesen E, Frøkiaer J, Ring T. Edelman's equation is valid in acute hyponatremia in a porcine model: plasma sodium concentration is determined by external balances of water and cations. *Am J Physiol*. 2010 Jan;298(1):R120-9.
14. Kitiwan BK, Vasunilashorn SM, Baer HJ, Mukamal K, Juraschek SP. The association of urine osmolality with decreased kidney function and/or albuminuria in the United States. *BMC Nephrol*. 2021; 22(1):306.
15. Sands JM. Regulation of urea transporter proteins in kidney and liver. *Mt Sinai J Med*. 2000;67(2):112-9.
16. Chakraverty R, Samanta K, Mandal P, Karmakar S. Mechanism of action of diuretic and anti-diuretic drugs. In *How Synthetic Drugs Work 2023 Jan 1* (pp. 369-390). Academic Press.
17. Arima H, Barzi F, Chalmers J. Mortality patterns in hypertension. *J Hyperten*. 2011;29:S3-7.
18. Adamczak M, Surma S, Więcek A. Hyponatremia in patients with arterial hypertension: pathophysiology and management. *Arch Med Sci: AMS*. 2023;19(6):1630.
19. Horowitz B, Miskulin D, Zager P. Epidemiology of hypertension in CKD. *Adv Chronic Kidney Dis*. 2015;22(2):88-95.
20. Tonelli M, Wiebe N, Culeton B, House A, Rabbat C, Fok M, McAlister F, Garg AX. Chronic kidney disease and mortality risk: a systematic review. *J Am Soc Nephrol*. 2006;17:2034 – 2047.
21. Farmakis D, Filippatos G, Parissis J, Kremastinos DT, Gheorghiade M. Hyponatremia in heart failure. *Heart Fail Rev*. 200914(2):59-63.
22. Oren RM. Hyponatremia in congestive heart failure. *The American journal of cardiology*. 2005 May 2;95(9):2-7.
23. Ahmad F, Hadi A, Iqbal MA, ullah Khan I, Adnan Y, Haq MR, et al. Frequency of hyponatremia and in-hospital clinical outcomes in these patients hospitalized for heart failure. *J Postgrad Med Inst*. 2014;28(4).
24. Kumar S, Rubin S, Mather PJ, Whellan DJ. Hyponatremia and vasopressin antagonism in congestive heart failure. *Clin Cardiol* 2007;30(11):546-51.