Original
ISSN 2521-8492

Prevalence of Hyponatremia in Admitted Patients in Oncology Teaching Hospital

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(Submitted: 23 February 2021 – Revised version received: 02 March 2021 – Accepted: 28 March 2021 – Published online: 26 June 2021)

Abstract
Objective This study aimed to investigate determination of hyponatremia prevalence in admitted patients in Oncology teaching hospital.
Methods 6 months cross sectional study of hyponatremia prevalence done in Oncology ward in Medical city, patients (105) who were admitted for more than three days with different types of malignancies, and causes of admission, were investigated for serum sodium, Blood urea, random blood sugar, urinary Na. (single measurement) and compared to S. Na level of control (135) of non-caner individuals with same exclusion criteria.
Results The prevalence of hyponatremia in admitted patient was 43.7%, compared to 0.73% in control group.
Conclusion The prevalence of hyponatremia in Oncology Teaching Hospital / Medical city ward was higher than previous studies (done in international cancer centres), hyposmolarhyponatremia prevalence is almost similar to previous studies.
Keywords Hyponatremia, cancer patients, SIADH, salt wasting syndrome.

Introduction

Sodium is the major cation in the extracellular compartment in human body, it regulates the total amount of water in the body (and hence affecting blood pressure), and the movement of sodium between intracellular and extracellular compartments plays role in critical body functions.[1] Many processes especially in CNS and muscles require sodium, as the movement of sodium generates electrical charges critical for their function, so extremes in sodium level can be fatal.[2,3] Hyponatremia is the most common electrolyte disorders in carcinogenic patients. Patients with very severe hyponatremia requisite management with hypertonic saline. "Syndrome of inappropriate antidiuretic hormone secretion" (SIADH) is an important reason of hyponatremia leading cancer. Fluid restriction is usually recommended for the hyponatremia related with SIADH, and fluid additional is designated for the volume reduction related with "Salt wasting syndrome" (SWS). Moreover, central nervous system illness and cisplatin management may cause together "SWS and SIADH". This confounds the differential diagnosis, and careful treatment is essential.[4] Sodium levels decrease quickly lead to dangerous effects in acute hyponatremia, like quick brain bulge, that lead to coma and death.[4-6] While in chronic hyponatremia, sodium levels decrease slowly over 48 hours or more, symptoms besides complications are usually less sever.[4-6] Premenopausal females seem to be at the utmost danger of brain damage due to hyponatremia. This associated to the consequence of females' sexual hormones on the body's capability to equilibrium level of sodium.[7] The importance of measurement of serum sodium level came from its role as prognostic factor to assess mortality. Hyponatremia is associated with poor outcome in several medical conditions, such as liver cirrhosis,[8,9] liver cirrhosis,[10] heart failure,[11] and infectious diseases as pneumonia,[12] childhood meningitis,[13] and necrotizing soft-tissue infection.[14] Moreover, hyponatremia has recently been associated with poor overall survival in hepatocellular carcinoma,[8] gastric cancer,[15] and small cell lung cancer.[16] In localized RCC, serum sodium level below median values has recently been associated with poor disease free and overall survival after nephrectomy.[17] The severity of liver cirrhosis is a key component to predict survival in patients with hepatocellular carcinoma. Serum sodium has been suggested to incorporate into the model for end-stage liver disease to enhance its prognostic ability for cirrhosis.[9] The MELD-Na was better than model for end-stage liver disease in predicting 6-month mortality, it was an independent predictor associated with 6-month mortality in multivariate logistic regression analysis. Manchester score is an indicator of prognosis in small cell lung cancer,[18] It is calculated from a number of physical and biochemical markers. A patients with small cell lung cancer were scored according to, Serum lactate dehydrogenase, serum sodium concentration, serum alkaline phosphatase, serum bicarbonate, performance status, and extensive stage disease. This study aimed the determination of hyponatremia prevalence in admitted patients in Oncology teaching hospital.

Method

This is across sectional study conducted in the period from April to October 2019, included cancer patients (105) admitted in Oncology teaching hospital/medical city ward. Patient enrolled after three days of admission, with exclusion of patient with renal disease, hypertension, diabetes Mellitus, and patient on diuretic drugs. Patient's serum level of Sodium, RBS, blood urea, and urinary Sodium level were measured with single sample and analysis done by Ion selective electrode/ dimension RXL/MAX device, along with calculation of plasma osmolality,

$$\text{Calculated Osmolality} = 2[Na^+] + [\text{Glucose}]/18 + [\text{BUN}]/2.8.$$

Controls serum Sodium (total no. 136) were measured from non-cancer patient with same exclusion criteria. Patient were categorized according to serum sodium level to three groups (hypernatremia >145 mEq/L, euonatremia 135–145 mEq/L, and hyponatremia <135 mEq/L), causes of admission, the type of malignancy, type of chemotherapy, and possible cause of hyponatremia, with comparison of hyponatremia prevalence between patients and control.

Statistical Analysis

All continuous data follow normal distribution (using Anderson darling test) thus we use mean and standard deviation to represent the data, while describe variables presented using their numbers and parentage. Chi square test used to test the differences in association between various discrete variables, while either *t*-test for 2 continuous variables and one way ANOVA for 3 variables. The Statistical Package for Social Science (SPSS) version 20 was used for data entry and analysis. Graphs and tables were used to describe the data and suitable statistical tests were used accordingly. *P*-value was considered significant if less than 0.05.

Results

Mean age of patients was comparable with control (49 and 47 respectively) (*P* value = 0.273), also gender distribution was similar between both group (females were 43.8% and 44.1% respectively, and males were 56.1% and 55.8% respectively), (*P* value = 0.063). (Table 1).

Breast cancer was the most frequent type with 16.2%, followed by colon cancer 13.3% and bronchus CA 12.4% (collectively they constitute 41.9% of the study). As in Table 2.

Common causes for admission were supportive are and chemotherapy (46.7% and 44% respectively), other causes of admission were (with chest 2.9% infection, DVT 1%, UTI 1% and neutropenic fever 1.9%). (As in Table 3).

Most of the patients (after 3 days of admission) were either hyponatremia or euonatrmia. (As in Table 4).

The patient group had lower serum sodium mean level than the control group. As in Table 5.

Among patients with hyponatremia the severity (Mild 134–130 mEq/l, Moderate [(129–125 mEq/l, Severe (<125 mEq/l)] was arranged in descending order from mild to severe. As in Table 6.

No significant association between serum sodium status and urinary sodium loss, only 13 patients had both hyponatremia and urinary salt wasting. As in Table 7.

Table 1. **Mean age and sex distribution of studied groups**

Study groups	Age/years		Gender				
	Mean	Standard deviation	Female		Male		Total
			No.	Percentage	No.	Percentage	No.
Patients	49	±14	46	43.8%	59	56.1%	105
Control	47	±14	60	44.1%	76	55.8%	136
P-value	0.273		0.063				

P-value ≤0.05 (significant).

Table 2. **Relative frequencies according to site of tumor**

Tumors	No.	%
Breast	17	16.2
Colon	14	13.3
Bronchus	13	12.4
Bladder	10	9.5
Germ cell	7	6.7
Pancreas	7	6.7
Gastric	6	5.7
HCC	5	4.8
STS	4	3.8
Granulosa cell tumor	3	2.9
Others	19	18.1
Total	105	100

Table 3. **Distribution of studied group according to cause of admission**

Variables	No.	%
Supportive care	49	46.7
Chemotherapy	47	44.8
Others	9	8.5
Total	105	100.0

No significant association between different chemotherapeutic agents and serum sodium status. As in Table 8.

Separated prospective Cohort followed ten patients through multiple admissions, and eight of them had progressive decrease in serum sodium level. (Table 9).

Discussion

After reviewing sodium serum level in 105 patients (those were admitted to Oncology teaching hospital in period of six months, and whom admission was more than 3 days), hyponatremia was observed in 43.8% of them. In case of chemotherapy associated hyponatremia (45% of all hyponatremia), platinum compounds and chelating agents were the most common drugs associated with hyponatremia, and these agents usually need special electrolytes and fluid support before, during and after administration. The proper electrolytes support with different chemotherapy is difficult to apply in our hospital because of shortage of these preparations and their cost making our protocols being delivered in suboptimal level. This may be aggravated by the failure to follow the proper infusion time because of patient noncompliance, and shortage of time caused by large number of patients. Many factors can contribute to development of hyponatremia above all the disease burden, type of treatment, treatment giving

Table 4. **Sodium level**

	Patients		Control	
	No.	%	No.	%
Hyponatremia (<135 mEq/l)	46	43.8	1	0.73%
Normal (135–145 mEq/l)	57	54.3	127	93.3%
Hypernatremia (>145 mEq/l)	2	1.9	8	5.8%
Total	105	100.0	136	100%

Table 5. **Mean value of serum sodium according to studied groups**

	Study groups	*N*	Mean	Std. deviation	*P*- value
Serum sodium mEq/l	Patients	105	134.2150	±5.87193	0.001
Total	Control	136	138.6185	±3.37375	

P-value ≤0.05 (significant).

Table 6. **Relative frequency of degree of hyponatremia in patients group**

	No.	%
Mild (134–130 mEq/l)	19	41.3
Moderate (129–125 mEq/l)	17	37.0
Severe (<125 mEq/l)	10	21.7
Total	46	100.0

protocols, patient compliance and socioeconomic status. The importance of detection of hyponatremia is that it is considered as independent prognostic factor for predicting mortality rate in admitted cancer patients. All that highlights the importance of assessment of serum sodium before, during and after admission, and management whenever appropriate. Another point to be taken in consideration was that hyposmolarhyponatremia was only present in 1% of hyponatremia patients on chemotherapy, while it was present in 52% of those admitted for supportive care. These two points raise the probability that the hyponatremia in supportive care group was caused by disease burden in about half the cases rather than admission related. This explanation is supported also by the progressive decrease of serum sodium level on following patient through multiple admissions. This result was compared to three studies done to estimate the prevalence of hyponatremia in admitted cancer patients. 1st study done in M D Anderson and it included 3357 admitted patients with variables cancers, prevalence of hyponatremia(<135 mEq\l) was 47% (23% at admission and 24% acquired during admission), compared to 43.8% in our study.[19] 2nd study done in UK included 6766 admitted patients with hematological malignancies, they were admitted to ICU, they were investigated to detect moderate and severe hyponatremia (<130 mEq\L) and it was 4.2% compared to 25% in our study.[20] This result may be attributed to different disease course in hematological malignancies. 3rd study done in two Boston teaching hospitals and included 6612 admitted patients with

Table 7. **Assocciation of serum sodium status and urinary loss of sodium**

			Sodium level		
			Hypon-atremia	Normal	Hyperna-tremia
Uranary loss of sodium	Normal	Number	33	44	2
		Percentage	71.7%	77.2%	100%
	Renal loss >120 mEq/L	Number	13	13	0
		Percentage	28.3%	22.8%	0%
	Total	Number	46	57	2
		Percentage	43.8%	50.4%	5.8%

P value = 0.6. *P*-value ≤0.05 (significant).

Table 8. **Assocciation of chemo group and S. sodium status**

			Groups			Total
			Cyclopho-samide ± Vincristine	Platinum based therapy	Others	
Sodium level	Hypon-atremia	Number	2	14	5	21
		Percent-age	50%	46.7%	35.7%	
	Normal	Number	2	16	9	27
		Percent-age	50%	53.3%	64.3%	
	Total	Number	4	30	14	48
		Percent-age				

P value = 0.7. *others include (Gemzarnavilbine, taxter, ABVD, 5FU, and zometa). *P*-value ≤0.05 (significant).

Table 9. **Follow up of sodium level in patients with multiple admissions**

Patient	Diagnosis	Cause of admission	1st S. Na level	Last S. Na level	Mean S. Na level
1	Bladder ca	S C	134	129	133.5
2	HCC	S C	131	130	127.7
3	Pancreas	S C	137	136	136.5
4	Breast	Chest infection	137	133	135
5	GCT	CT	135	119	130
6	Breast	S C	136	122	129
7	CRC	CT	132	129	130
8	Pancreas	CT	138	134.5	136.2
9	Bronchus	S C	132	131	131.5
10	GCT	CT	138	136	137

metastatic cancers and prevalence of hyponatremia (<135 mEq\l) was 10.8% compared to 43.8% in this study.[21] This can be attributed to better follow up of treatment giving protocols. Another prospective study that was done in dedicated cancer hospital in Belgium for assessment of possible causes of

hyponatremia in admitted cancer patients and the results were:[22]

1. SIADH found to be the cause in 30.4% (hypos molar hyponatremia found in 28% of hyponatremia patients in this study), it may be resulted from;
   A. Ectopic ADH secretion from tumor cells as in NSCLC.
   B. Several chemotherapeutic agents (vincristine, cisplatine, ifosfamide, ect.)
   C. Stress after surgery, pain and nausea.
2. Sodium reduction (28%) because gastrointestinal loss (diarrhea besides vomiting), and "salt wasting syndrome" (SWS), include together "cerebral salt wasting" (CSWS) that occur with severe central nervous system illnesses, and "renal salt wasting syndrome" (RSWS) occur with cisplatin.[22] "Hyponatremia prevalence is (76%) in Lung cancer, (37%) in Breast cancer, (64%) in Colorectal cancer, and 60% in lymphoma". Hyponatremia was slightly related with smaller "Progression free survival (HR 1.3, $P = .07$)" crossways cancer kinds.[23]

Conclusion

The prevalence of hyponatremia in Oncology teaching hospital/Medical city ward was higher than previous studies (conducted in international cancer centres), hypos molar hyponatremia is almost similar and sodium salt wasting observed in 28% patients with hyponatremia.

Acknowledgments

We would like to acknowledge everyone who played a role in my academic activities.

Conflicts of Interest

None.

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