Original Article

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Prevalence of Hyponatremia in Patients Admitted to the Oncology Teaching Hospital

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ABSTRACT

Background: Hyponatremia is a commonly occurring electrolyte disturbance among hospitalized patients, and many studies suggest that individual serum sodium levels may have a prognostic role in assessing probability of mortality.
Aim of the study: Determination of hyponatremia prevalence in patients admitted to the Oncology Teaching Hospital.
Method: A six-month cross-sectional study of hyponatremia prevalence was conducted in the Oncology ward in Medical City. The 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, and urinary sodium (single measurement). These results were compared to the sodium levels of control of non-cancer individuals (135) selected using the same exclusion criteria.
Results: The prevalence of hyponatremia in the admitted patients was 43.7%, whereas it was 0.73% in the control group.
Conclusion: The prevalence of hyponatremia in Oncology Teaching Hospital, Medical City ward, was higher than that reported in previous studies (conducted in international cancer centers); hypoosmolar hyponatremia prevalence is almost similar to that stated in previous studies.

Keywords: Hyponatremia, Cancer patients, SIADH, Salt wasting syndrome.

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INTRODUCTION

Sodium is the major cation in the extracellular compartment in the human body. It regulates the total amount of water in the body (and hence affects blood pressure), and the movement of sodium between intracellular and extracellular compartments plays a role in critical body functions.[1] Many processes, especially in the central nervous system (CNS) and muscles, require sodium, as the movement of sodium generates electrical charges critical for their functioning. Thus, extremes in the sodium level can be fatal.[2,3] Hyponatremia is one of the most common electrolyte disturbances in cancer patients. Patients with extremely severe symptomatic hyponatremia need treatment with the administration of the hypertonic saline. Further, the syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a significant cause of cancer-related hyponatremia. Although identifying salt wasting syndrome (SWS) or SIADH as the cause of hyponatremia is difficult, the treatment strategy for SWS is different from that for SIADH. Fluid restriction is generally prescribed for the hyponatremia associated with SIADH, and fluid replacement is suggested for the volume depletion associated with SWS. Furthermore, CNS disease and cisplatin administration may cause both SWS and SIADH. This complicates the differential diagnosis, and careful management, thus, becomes necessary.[4] In acute hyponatremia, sodium levels drop rapidly, resulting in potentially dangerous effects such as rapid brain swelling which can result in coma and death.[4–6] In chronic hyponatremia, the sodium levels drop gradually over 48 hours or longer, and symptoms and complications are typically less severe.[4–6] Premenopausal women appear to be at the greatest risk of hyponatremia-related brain damage. This may be related to the effect of women's sex hormones on the body's ability to balance sodium levels.[7] The importance of measuring serum sodium level arises from its role as a prognostic factor to assess mortality. Hyponatremia is associated with poor outcomes in several medical conditions, such as liver cirrhosis,[8,9] liver cirrhosis,[10] and heart failure,[11] and infectious diseases, such 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,[15] gastric cancer,[16] and small cell lung cancer.[17] In localized renal cell carcinoma (RCC), serum sodium level below median values has recently been associated with the chances of disease-free and overall survival being poor after nephrectomy.[18] The severity of liver cirrhosis is a key component in predicting survival in patients with hepatocellular carcinoma. Serum sodium has been suggested to be incorporated into the model for end-stage liver disease to enhance its prognostic ability for cirrhosis.[9] MELD-Na was better than the model for end-stage liver disease in predicting six-month mortality, as it was an independent predictor associated with six-month mortality in multivariate logistic regression analysis. The Manchester score is an indicator of prognosis in small cell lung cancer.[19] It is calculated based on a number of physical and biochemical markers. The patients with small cell lung cancer have been scored according to serum lactate dehydrogenase, serum sodium concentration, serum alkaline phosphatase, serum bicarbonate, their performance status, and extensive stage disease.

AIM OF THE STUDY

Determination of hyponatremia prevalence in patients admitted to the Oncology Teaching Hospital.

METHOD

This was a cross-sectional study conducted from April 1, 2019, to October 1, 2019, and included 105 cancer patients admitted to the Oncology Teaching Hospital, Medical City ward. The patients were enrolled after three days of admission, with the exclusion of patients with renal disease, hypertension, and diabetes mellitus and patients on diuretic drugs. Patients' serum sodium level, random blood sugar, blood urea, and urinary sodium level were measured with single sample and analysis done by ion-selective electrode/Dimension Rxl Max along with the calculation of plasma osmolality as:

Calculated osmolality = 2[Na+] + [Glucose]/18 + [BUN]/2.8.

The control serum sodium level was measured from 136 non-cancer patients with the same exclusion criteria. Patients were categorized according to the serum sodium level into three groups: hypernatremia: > 145mEq/L; euonatremia: 135–145 mEq/L; and hyponatremia: < 135 mEq/L. Other factors considered were causes of admission, type of malignancy, type of chemotherapy (CT), and possible cause of hyponatremia, with comparison of hyponatremia prevalence between patients and the control group.

Statistical analysis

All continuous data followed normal distribution (as was ascertained using the Anderson–Darling test). Thus, we used mean and standard deviation to represent the data while describing variables presented using numbers and percentages. The Chi-square test was used to test the differences in association between various discrete variables, with t-test for two continuous variables and one-way analysis of variance (ANOVA) for three variables also being used. The Statistical Package for Social Sciences (SPSS) Version 20 was used for data entry and analysis. It was decided that graphs and tables would be used to describe the data, and suitable statistical tests were used accordingly. P-value was considered significant if less than 0.05.

RESULTS

The mean age of the patients was comparable with that of the control group (49 and 47, respectively; P-value = 0.273). Gender distribution was similar between both these groups (females were 43.8% and 44.1%, respectively and males were 56.1% and 55.8%, respectively; P-value = 0.063; Table 1).

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

Study groups	Age (years)		Gender				
	Mean	Std. Deviation	Female		Male		Total
			No.	&	No.	%	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).

Breast cancer was the most frequent type (16.2%), followed by colon cancer (13.3%) and bronchus cancer (12.4%). Together they constituted 41.9% of patients covered for the study (Table 2).

Table 2: Relative frequencies according to the site of the 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

Common causes for admission were supportive care (SC) and CT (46.7% and 44%, respectively). Other causes were chest infection (2.9%), DVT (1%), UTI (1%), and neutropenic fever (1.9%; Table 3).

Table 3: Distribution of the studied group according to the cause of admission.

Causes for Admission	No.	%
SC	49	46.7
CT	47	44.8
Other causes	9	8.5
Total	105	100.0

Most of the patients (after three days of stay) had either hyponatremia or euonatremia (Table 4).

The patient group had lower serum sodium mean level than the control group (Table 5).

Among the patients with hyponatremia, the severity of the condition was determined to be as follows: mild: 134–130 mEq/l; moderate: 129–125 mEq/l; severe: < 125 mEq/l and arranged in descending order from mild to severe (Table 6).

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 (> 145mEq/l)	2	1.9	8	5.8
Total	105	100.0	136	100

Table 5: Mean value of serum sodium level for studied groups.

	Study groups	N	Mean	Std. Deviation	P-value
Serum sodium (mEq/L)	Patients	105	134.2150	±5.87193	0.001
	Control	136	138.6185	±3.37375	

P-value ≤ 0.05 (significant).

Table 6: Relative frequency of degree of hyponatremia in the 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

There was no significant association between serum sodium status and urinary sodium loss. Only 13 patients had both hyponatremia and urinary salt wasting (Table 7).

Table 7: Association of serum sodium status and urinary loss of sodium.

			Sodium level		
			Hyponatremia	Normal	Hypernatremia
Urinary loss of sodium	Normal	Number	33	44	2
		%	71.7	77.2	100
	Renal loss > 120mEq/L	Number	13	13	0
		%	28.3	22.8	0
	Total	Number	46	57	2
		%	43.8	50.4	5.8
P-value = 0.6					

P-value ≤ 0.05 (significant).

There was no significant association between different chemotherapeutic agents and serum sodium status (Table 8).

Table 8: Association between CT group and sodium status.

			Groups			Total
			Cyclophosamide ± vincristine	Platinum-based therapy	Others	
Sodium level	Hyponatremia	Number	2	14	5	21
		%	50	46.7%	35.7%	
	Normal	Number	2	16	9	27
		%	50	53.3%	64.3%	
	Total	Number	4	30	14	48
		%				
P-value = 0.7						

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

A separate prospective cohort followed 10 patients through multiple admissions, and eight of them had a progressive decrease in serum sodium level (Table 9).

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	SC	134	129	133.5
2	HCC	SC	131	130	127.7
3	Pancreas	SC	137	136	136.5
4	Breast	Chest infection	137	133	135
5	GCT	CT	135	119	130
6	Breast	SC	136	122	129
7	CRC	CT	132	129	130
8	Pancreas	CT	138	134.5	136.2
9	Bronchus	SC	132	131	131.5
10	GCT	CT	138	136	137

DISCUSSION

After reviewing the sodium serum levels in 105 patients (i.e., those admitted to the Oncology Teaching Hospital during the said study period of six months and whose stay exceeded three days), hyponatremia was observed in 43.8% of the patients. In the case of CT-associated hyponatremia (45% of all hyponatremia cases), 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. Proper electrolytes' support with different CT compounds is difficult to administer in our hospital because of the shortage of these preparations and their high costs, causing our protocols to be delivered at a suboptimal level. This may be aggravated by the failure to follow proper infusion time because of patient noncompliance and shortage of time caused by a large number of patients. Many factors can contribute to the development of hyponatremia, especially disease burden, type of treatment, treatment-giving protocols, patient compliance, and socioeconomic status. The importance of detection of hyponatremia is that it is considered an independent prognostic factor for predicting mortality rate in admitted cancer patients. This highlights the significance of the assessment of serum sodium before, during, and after admission and management whenever appropriate. Another point to be taken into consideration is that hyposmolar hyponatremia was present in only 1% of hyponatremia patients on CT, while it was present in 52% of those admitted for SC. These two points raise the probability that the hyponatremia in the SC group was caused by disease burden in about half the cases rather than being admission-related. This explanation is supported by the progressive decrease of serum sodium level on following up with the patient through multiple admissions. This result was compared to three studies conducted to estimate the prevalence of hyponatremia in admitted cancer patients. The first study done in MD Anderson included 3357 patients admitted for treatment of variable cancers and prevalence of hyponatremia (< 135mEq\l), which was at 47% (23% at admission and 24% acquired during admission), compared to 43.8% in our study.[20] The second study conducted in the

UK included 6766 patients admitted with hematological malignancies. They were admitted to the ICU and investigated which helped detect moderate and severe hyponatremia (< 130mEq\L), which was at 4.2%, compared to 25% in our study.[21] This result may be attributed to different disease courses in hematological malignancies. The third study conducted in two Boston teaching hospitals included 6612 patients admitted with metastatic cancers, and the prevalence of hyponatremia (< 135mEq\l) was 10.8%, compared to 43.8% in this study.[22] This can be attributed to better follow-up of treatment-giving protocols. Another prospective study was carried out in a dedicated cancer hospital in Belgium for the assessment of possible causes of hyponatremia in admitted cancer patients, and the results were as follows[23]:

1. SIADH was found to be the cause in 30.4% of the cases. (Hyposmolar hyponatremia was found in 28% of the hyponatremia patients.) It might have resulted from any one of the following three factors:
   a. Ectopic ADH secretion from tumor cells as in NSCLC.
   b. Several chemotherapeutic agents (vincristine, cisplatine, ifosfamide, etc.).
   c. Stress after surgery, pain, and nausea.

2. Sodium depletion (28.7%) was found, which might be due to gastrointestinal loss (diarrhea and vomiting), and SWS, which includes both cerebral salt wasting syndrome (CSWS), which occurs with severe CNS diseases, and renal salt wasting syndrome (RSWS), which may occur with some agents such as cisplatine.[23] In a cross-sectional study of hyponatremia in patients following diagnosis with lymphoma, breast cancer (BC), colorectal (CRC), and lung cancer (both SCLC and NSCLC), hyponatremia prevalence was 60%, 37%, 64%, and 76%, respectively. Hyponatremia was negatively associated with OS in BC (HR 3.7; P = <.01), CRC (HR 2.4; P < .01), lung cancer (HR 2.4; P < .01), and lymphoma (HR 4.5; P < .01). Hyponatremia was marginally associated with shorter PFS (HR 1.3; P = .07) across cancer types.[24]

CONCLUSION

The prevalence of hyponatremia in the Oncology Teaching Hospital, Medical City ward, was found to be higher than that reported in previous studies (conducted in cancer centers in different countries); that of hyposmolar hyponatremia is almost similar, and sodium salt wasting was observed in 28% of the patients with hyponatremia.

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