

# The natremia in the oncology wards: a hospital-based combine study

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ABSTRACT

Imbalance in natremia is a common electrolyte disturbance in patients' bodies, and it may play important roles in prognosis or mortality outcomes. This study aims to estimate, determine, and assess the imbalance in sodium concentration in cancer patients. It is a hospital-based combined cross-sectional-case-control study conducted at an oncology ward. The serum levels of sodium and urinary sodium were measured using a single sample, and the analysis was performed using the Ion selective electrode/dimension RXL/MAX device (ACCU, China). One-hundred control serum sodium levels were measured from non-cancer patients who met the same exclusion criteria. Patients were categorized into three groups based on their serum sodium levels. The most frequent cancer type observed was breast cancer, followed by colorectal cancer. The main reasons for admission were supportive care (48.8%) and chemotherapy (51.2%). The mean age of the patients was comparable to that of the control group, with  $47.58 \pm 12.88$  years and  $48.25 \pm 11.9$  years, respectively. Most patients (after 3 days of admission) exhibited euonatremia. Only six out of 250 cancer cases and four out of 100 healthy subjects had hypernatremia. The cancer group had a lower mean serum sodium level than the healthy group. A significant association was found between different chemotherapeutic agents and serum sodium status. The prevalence of hyponatremia is higher in cancer cases, and the prevalence of hypo-osmolar hyponatremia can be detected. Hyponatremia is common in the supportive care group due to the disease burden. Sodium salt wasting can be observed in cases of hyponatremia.

**Key words:** hyponatremia, SIADH, salt wasting syndrome, hypo-osmolar

## INTRODUCTION

Sodium is the primary extracellular cation in the human body, regulating the total body water [1]. Various processes, particularly in the central nervous system and muscles, rely on sodium as it generates critical electrical charges necessary for their function [2, 3]. Hyponatremia is a frequent electrolyte disturbance observed in cancer patients. The Syndrome Of Inappropriate Antidiuretic Hormone secretion (SIADH) is a significant cause of cancer-related hyponatremia [1]. Acute untreated hyponatremia can lead to morbidity and mortality due to osmotically induced cerebral edema, while overly rapid correction of chronic hyponatremia can result in severe neurological impairment and osmotic demyelination-related death [4].

Furthermore, hyponatremia has been linked to poor overall survival in various cancer types, including hepatocellular carcinoma [5], gastric cancer [6], small-cell lung cancer [7], and localized renal cell carcinoma [8]. Early management of hyponatremia, involving fluid restriction and sodium replacement, has shown promise in minimizing adverse effects on patient survival [9, 10].

This study aims to estimate, determine, and assess the imbalance in sodium concentration in patients with cancer.

## METHODS

### Study design and setting

This combined study was conducted from April 1, 2020, to October 1, 2021, and included 250 cancer patients and 100 individuals without cancer at the oncology ward.

### Exclusion criteria

Patients were enrolled 3 days after admission, excluding those with renal disease, hypertension, diabetes mellitus, and those taking diuretic drugs.

### Samples collection

Serum sodium levels, RBS (random blood sugar), blood urea, and urinary sodium were measured using a single sample. The analysis was performed using the Ion selective electrode/dimension RXL/MAX device (ACCU, China). Additionally, plasma osmolarity was calculated.

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

Approximately 100 control subjects' serum sodium levels were measured from non-cancer patients who met the same exclusion

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criteria. Patients were categorized into three groups based on their serum sodium levels: hypernatremia (>145 mEq/L), euonatremia (135 mEq/L – 145 mEq/L), and hyponatremia (<135 mEq/L). The study also analyzed the causes of admission, type of malignancy, type of chemotherapy, and potential causes of hyponatremia, comparing the prevalence of hyponatremia between patients and controls.

### Statistical analysis

Data entry and analysis were performed using SPSS version 24 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics such as

mean and standard deviation were utilized to represent the data, while categorical variables were presented using their numbers and percentages. The chi-square test was employed, and a p-value of less than 0.05 was considered statistically significant.

### RESULTS

Breast cancer was the most frequent type, accounting for 41.2% of cases, followed by colorectal cancer at 18.4%. The common reasons for admission were supportive care (48.8%) and chemotherapy (51.2%) (Table 1). The mean age of patients was nearly comparable to that of the control group, with 47.58 ± 12.88 years versus 48.25

**Tab. 1.** Baseline distribution in this study

Variables		No.	%
Tumor types	Breast	103	41.2
	Colorectal	46	18.4
	Lung	34	13.6
	Bladder	30	12
	GIT	9	3.6
	Soft tissue sarcoma	11	4.4
	Lymphoma	7	2.8
	Gliomas	10	4
Admission reasons	Supportive	122	48.8
	Administer of anti-cancer	128	51.2

**Tab. 2.** Analysis between groups of the study

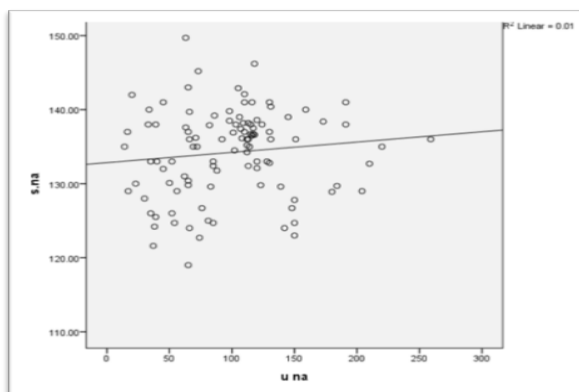
Variables	Patients (n=250)		Control (n=100)		P-value	
	%	n	%	n		
Age (years) mean±SD	47.58±12.88		48.25±11.9		0.06	
Male Female	Gender	62	155	60	60	0.73
		38	95	40	40	
Hyponatremia (<135) Normal (135-145) Hypernatremia (>145)	Sodium level (mEq/l)	35.2	88	3	3	0.01
		62.4	156	93	93	
		2.4	6	4	4	
Serum sodium (mEq/L) mean±SD	133.22±6.58		135.44±6.88		0.01	

**Tab. 3.** Association of serum sodium with chemotherapy protocols

Sodium level	Regimens			P-value
	Cyclophosamide	Platinum-based	Others	
	n (%)			
Hyponatremia	33 (37.5)	31 (35.2)	24 (27.3)	0.01

**Tab. 4.** Association of serum sodium status and urinary loss

Sodium level	Urinary loss of sodium [n (%)]		P-value
	Normal	Renal loss >120mEq/L	
Hyponatremia	56 (22.4)	32 (12.8)	0.06
Normal	149 (59.6)	7 (2.8)	
Hypernatremia	6 (2.4)	0	



**Fig. 1.** Scatter plot of the correlation between urinary and serum sodium

$\pm 11.9$  years, respectively ( $p=0.06$ ). The gender distribution was similar in both groups, with females comprising 38% and 40% and males comprising 62% and 60%, respectively ( $p=0.73$ ).

After 3 days of admission, most of the patients were found to have euonatrnia. Only six out of 250 cancerous cases and four out of 100 healthy subjects exhibited hypernatremia. The cancer group had a lower mean serum sodium level than the healthy group (Table 2). There was a significant association between different chemotherapeutic agents and serum sodium status (Table 3). However, no significant association was observed between serum sodium status and urinary sodium loss (Table 4 and Figure 1).

## DISCUSSION

After reviewing the sodium serum levels of 250 cancerous patients, it was found that 35.2% of them had hyponatremia. Among the cases of chemotherapy-associated hyponatremia, cyclophosphamide and platinum compounds were the most commonly implicated drugs. These anti-cancer medications typically necessitate special electrolyte and fluid replacement measures before, during, and after chemotherapy administration.

The administration of appropriate electrolyte support in conjunction with different anti-cancer treatments poses challenges due to the scarcity of these preparations and their high cost, resulting in suboptimal delivery of our protocols. This issue may be further exacerbated by non-compliance cases, leading to failure in adhering to proper infusion times and time constraints caused by the large number of cases.

Several factors can contribute to the development of hyponatremia, including the burden of the disease, the type of treatment, specific chemotherapy protocols, individual compliance, and socioeconomic status [3].

Detecting hyponatremia is of significant importance as it serves as an independent prognostic factor for predicting mortality in hospitalized cancer patients. These findings underscore the significance of assessing serum sodium levels before, during, and after admission and appropriately managing any imbalances that may arise.

Another noteworthy observation is that hypo-osmolar hyponatremia was found in only 1% of hyponatremic cases undergoing chemotherapy, whereas it accounted for 52% of cases admitted for supportive care [4]. These findings suggest a higher likelihood that hyponatremia in the supportive care group was predominantly caused by the disease burden in approximately half of the cases rather than reasons related to admission. This explanation is further supported by the progressive decline in

serum sodium levels observed in patients throughout multiple admissions. To validate this result, a comparison was made with three studies conducted to estimate the prevalence of hyponatremia in hospitalized cancer patients [11-13].

Other studies conducted to assess potential causes of hyponatremia in hospitalized patients identified SIADH as the cause in 30.4% of cases (with hypo-osmolar hyponatremia found in 22.4% of hyponatremic patients in this study). Sodium depletion (12.8%) was another identified cause, which could be attributed to gastrointestinal losses such as diarrhea and vomiting, as well as salt wasting syndromes, including cerebral salt wasting and renal salt wasting syndromes, which may occur with certain agents like cisplatin [13]. Hyponatremia was observed in many patients, primarily those receiving chemotherapy with platinum compounds and chelating agents.

In conclusion, it is imperative to include routine measurement of serum sodium levels during the initial evaluation and admission of cancer patients. Close adherence to chemotherapy protocols and the provision of necessary medical and pharmacological support during administration is crucial. Prompt management of hyponatremia upon detection is essential and should not be delayed.

## CONCLUSION

Cancer patients need special electrolyte and fluid support before, during, and after administration. Hyponatremia can be induced by various factors, including the disease burden, type of treatment, treatment protocols, patient compliance, and socioeconomic status. In the supportive care group, hyponatremia is more commonly associated with the disease burden rather than admission-related factors. Furthermore, hyponatremia can be accompanied by sodium salt wasting.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study approved by Department of Medicine, College of Medicine, and University of Basrah (ID: # 34). All individuals signature the written inform consent to enrolled in this study.

## COMPETING INTERESTS

None.

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