

# Correlation of Duration of Chemotherapy with Electrolytes in Cancer Patients: A Prospective Study Assessing the Relationship with Various Electrolytes

Ahsan Ali Siddiqui<sup>1</sup>, Reena Kumari<sup>2\*</sup>, Muhammad Khurram Zia<sup>3</sup>, Tayyaba Zubair<sup>4</sup>,

Samahir Imtiaz<sup>5</sup>, Noor ul Sahar<sup>6</sup>, Madiha Ariff<sup>7</sup> and Adnan Anwar<sup>8</sup>

<sup>1</sup>Specialist Family Medicine, Ministry of Health, Riyadh

<sup>2</sup>Resident Medical Oncology, Oncology Ward, Jinnah hospital, Pakistan

<sup>3</sup>Assistant Professor of Surgery, Liaquat College of medicine and dentistry, Pakistan

<sup>4</sup>Hamdard College of Medicine and Dentistry, Pakistan

<sup>5</sup>Medical Student, Liaquat National Medical College, Pakistan

<sup>6</sup>Medical Student, Dow University of Health and Sciences, Pakistan

<sup>7</sup>Medical Officer, Dow university of Health Sciences, Pakistan

<sup>8</sup>Assistant Professor, Department of Physiology Al Tibri Medical College Karachi, Pakistan

Received: September 17, 2018; Accepted: September 26, 2018; Published: September 27, 2018

\*Corresponding author: Reena Kumari, Resident Medical Oncology, Oncology Ward, Jinnah hospital, Pakistan, E-mail: rina\_pahuja@yahoo.com

## Abstract

**Objective:** The cancer patients are most prone to developing electrolyte abnormalities. This study aims to focus on changes in various electrolytes before and after chemotherapy in cancer patients and to establish a relationship between electrolytes with the duration of chemotherapy.

**Methodology:** This was an observational study conducted for one year in oncology ward of Jinnah Postgraduate Medical Centre, Karachi for duration of one year from April 2016 to March 2017. A total of 256 patients on chemotherapy were included in this study after getting informed consent. Patients having co morbid conditions and neurologic impairment were excluded from this study. Single or combination chemotherapy was administered to cancer patients. Data were collected through proforma and patients included in the study were followed for 3 weeks after chemotherapy course completion. The variables included were gender, body surface area, type of cancer, chemotherapy protocol, number of days on chemotherapy, electrolyte levels before and after therapy. SPSS version 20 was used to analyze the data. Data was presented as mean and standard deviation. Pearson correlation was applied to assess the relationship. P- Value of  $\leq 0.05$  was taken as significant.

**Results:** The mean electrolyte levels in serum before chemotherapy was sodium  $139.66 \pm 2.34$  mEq/L, potassium  $3.99 \pm 0.25$  mEq/L, magnesium  $2.03 \pm 0.23$  mEq/L, chloride  $102.69$  mEq/L. The total duration for which chemotherapy was given to patients was  $5.98 \pm 2.36$  days. The levels of sodium after chemotherapy with its duration showed no significant correlation (p-value=0.570,  $r = -0.036$ ). There was no significant relation between potassium levels as well (p-value=0.384,  $r = -0.055$ ).

**Conclusion:** This study predicted that there is difference in electrolyte levels before and after chemotherapy in cancer patients. Furthermore, no correlation was observed in various electrolytes with the duration of chemotherapy although the difference in electrolyte levels is not clinically significant and can be managed promptly in less time. This can prevent secondary impairment in cancer patients already undergoing chemotherapy.

**Keywords:** Electrolyte Imbalance; Chemotherapy; Correlation;

## Introduction

Electrolyte imbalance is one of the multiple issues faced by cancer patients [1], it can be associated with ongoing chemotherapy [2]. When such electrolyte imbalances occur associated with malignancy they can become life threatening and require emergency treatment modalities to prevent fatality [3]. The most prevalent electrolyte disorder in malignancy suffering patients is hyponatremia. According to one study, 14%

hyponatremic patients were having underlying malignancy [4]. Nearly half of the hyponatremia encountered were treatment acquired [5]. Potassium levels in cancer patients are usually found to be high secondary to rhabdomyolysis, tumor lysis syndrome and renal injury [6] or due to adrenal insufficiency secondary to chemotherapeutic drugs or metastatic diseases [7]. Although hypokalemia is more often documented in cancer patients than hyperkalemia [8]. The medications causing hypokalemia include certain chemotherapeutic drugs such as cisplatin, ifosfamide and

antibiotics like aminoglycoside, amphotericin B leading to renal tubular damage and/or GIT losses of potassium resulting in hypokalemia [9]. Use of diuretics in cancer patients is a major contributor to electrolyte imbalance causing hypokalemia, hyponatremia. Patients with calcium levels of 11mg/dl or greater are likely to develop hypokalemia because of diuretics [10]. There are few case reports on hypocalcemia in cancer patients [11]. The metastasis to bones can lead to calcium and magnesium abnormalities as well; hypomagnesemia is usually due to chemotherapy and rarely attributed to cancer itself [12]. The electrolyte imbalance is marked as additional risk factor causing mortality in cancer patients [13].

Electrolyte disturbances can complicate the ongoing treatment and clinical condition of the cancer patients. The etiology to these abnormalities can often be noted and managed early, establishing better chemotherapeutic compliance by the patient. The purpose of this study was to assess a correlation of various electrolyte disturbances in cancer patients undergoing treatment with the duration of chemotherapy so that effective clinical management can be proposed to such patients.

### Methodology

This was an observational study conducted using non-probability convenient sampling technique. The study was conducted for one year from April 2016 to March 2017 in Oncology Department of Jinnah Post graduate Medical Center, Karachi. A total of 256 patients on chemotherapy diagnosed with various cancers on histological basis were included in this study after getting informed consent. The ethical approval was taken from hospitals Ethical Review Committee. Patients having normal cardiac, renal, hepatic function and normal electrolyte were included in this study. Patients having co morbid

conditions, abnormal electrolyte values, neurologic impairment were excluded from this study. Patients who were non-compliant during the study were excluded from this study. patients on total parental nutrition were also excluded from this study. Single or combination of chemotherapy regime that were used included taxotere, cisplatin and fluorouracil, oxaliplatin, leucovorin, adriamycin cyclophosphamide, gemcitabine, carboplatin, paclitaxel, etoposide, daunorubicin, vincristine, prednisone, L-asparaginase, daunorubicin and cytarabine, hydroxydaunorubicin, oncovin, bleomycin, vinblastine and dacarbazine. Data were collected through proforma and patients included in the study were followed for 3 weeks after chemotherapy course completion. The variables included were age, height, weight, gender, body surface area, type of cancer, chemotherapy protocol, number of days on chemotherapy, electrolyte levels before and after therapy.

### Data Analysis

SPSS version 20 was used to analyze the data. Descriptive statistics of demographic variables was presented as mean, standard deviation and frequency in percentages. Correlation was studied in independent variables including sodium, potassium, chloride, magnesium. P-value of less than 0.05 was considered significant.

### Results

Total 256 cancer patient receiving chemotherapy were included the study having mean age of 43.24 ± 12.81 years. Mean weight of patients was 56.14 ± 11.30 kg, height was 158.43 ± 10.53 cm and body surface area was 1.56 ± 0.17 m<sup>2</sup>. The mean level of sodium before chemotherapy was 139.66 ± 2.34 mEq/L, potassium was 3.99 ± 0.25 mEq/L, magnesium was 2.03 ± 0.23, chloride was 102.69 ± 1.95 mEq/L, and creatinine was 0.60 ± 0.21 mg/dl, urea

**Table 1:** General features of the patients

Variables		Mean	Std. Deviation
Age (years)		43.24	12.81
Weight (kg)		56.14	11.30
Height (cm)		158.43	10.53
Body Surface area (m <sup>2</sup> )		1.56	0.17
Sodium (mEq/L)	Before	139.66	2.34
	After	132.27	7.26
Potassium (mEq/L)	Before	3.99	0.25
	After	3.51	0.76
Magnesium (mEq/L)	Before	2.03	0.23
	After	1.86	0.31
Chloride (mEq/L)	Before	102.69	1.95
	After	99.38	7.30
Urea (mg/dl)	Before	19.54	4.45
	After	27.09	15.24
Creatinine (mg/dl)	Before	0.60	0.21
	After	0.844	0.44
Chemotherapy (Days)		5.98	2.36

19.54±4.45mg/dl. The total duration for which chemotherapy was given to patients was 5.98±2.36days. The mean sodium levels after chemotherapy was 132.27±7.26mEq/L, potassium was 3.51±0.76mEq/L, magnesium was 1.86±0.31mEq/L, chloride was 99.38±7.30mEq/L, creatinine was 0.84±0.44mg/dl and urea was 27.09±15.24mg/dl. The total duration for which chemotherapy was given to patients was 5.98±2.36days (Table 1).

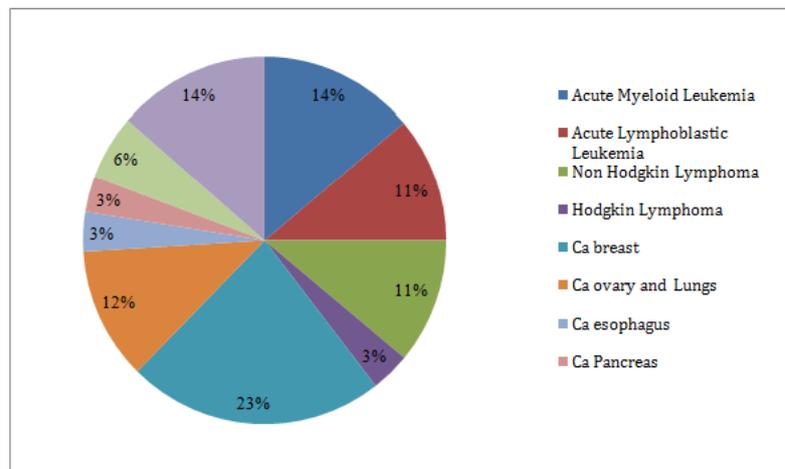
The levels of sodium after chemotherapy showed no significant correlation with duration of therapy (p-value=0.570, r = -0.036). There was no significant relation between potassium levels and duration of chemotherapy (p-value=0.384, r = -0.055). Similarly, the magnesium levels did not show significant correlation

(p-value=0.759, r = -0.019). The chloride levels remained fairly in range during the course of chemotherapy and did not show any correlation (p-value= 0.802, r = -0.016). The creatinine levels were also found to be not correlated with duration (p-value= 0.555, r = -0.037). The urea levels showed slight difference before and after chemotherapy, but it was not statistically correlated with the duration (p-value= 0.073, r = 0.112) (Table 2).

The most common group of cancer patient was breast carcinoma, number of patients was about 59(23%), 36(14%) were of acute lymphoblastic leukemia and 31(12%) patients has cancer of ovary and lungs (Figure 1).

**Table 2:** Correlation of duration of chemotherapy with electrolytes

Electrolytes	Chemotherapy (Days)	
	r-value	P-value
Sodium	-0.036	0.570
Potassium	-0.055	0.384
Magnesium	-0.019	0.759
Chloride	-0.016	0.802
Urea	0.11	0.073
Creatinine	-0.037	0.555



**Figure 1:** Frequency of different cancer in patients (n=256)

## Discussion

The data of 256 cancer patients on chemotherapy was studied to assess the changes in electrolyte levels before and after chemotherapy. In this study, the serum sodium levels didn't show much changes during the entire course of chemotherapy, prior to study they were 139.66mg/dl ±2.34 and after therapy 132.27 mg/dl±7.26, no significant difference existed (p-value=0.570, r = -0.036). Similarly, there was no significant difference found between potassium (p-value=0.384, r = -0.055), magnesium (p-value=0.759, r = -0.019) and chloride levels (p-value= 0.802, r = -0.016) before and after chemotherapy.

Overall, there is drop in sodium, potassium, chloride, magnesium levels in our study but these are not clinically significant differences (Table 1). In the previous studies, there has been increased incidence in hyponatremia seen in chemotherapy patients 47% from 4% [14, 15].The hyponatremia in patients receiving platinum-based chemotherapy is reported to be 43% [16]. In one study, a significant correlation was found in patients on chemotherapy developing blood magnesium changes (r2 = 0.7455) [17]. One study reported that hypokalemia is prevalent in 43-64% of cancer patients [18]. The management of hypokalemia is carried out in similar way as in non-cancer patients, but IV dosing are preferred in cancer patients over oral

replacement strategies and it is considered in patients having nausea or decreased appetite [19]. In case of hypomagnesemia not being treated, treatment of hypokalemia remains ineffective because of tubular cells in distal nephron not regulating potassium absorption through K1 channels (ROMK) [20]. Decrease intake and renal wasting can contribute to hypomagnesemia. The active site for magnesium reabsorption is distal nephron and it is also the site of action chemotherapeutic drugs induced renal injury [21]. Occasional hypomagnesemia, hypokalemia and hypocalcemia are reported side effects of monoclonal antibody therapy used in cancer patients [22]. In this study nearly, all patients had normal potassium, magnesium and chloride levels in serum before and after chemotherapy.

The studies mentioned above had clearly stated a variation in electrolyte imbalance in cancer patients receiving chemotherapy which is similar to our study results. The variation in electrolyte imbalance noted in our study has assured that some changes do occur in electrolytes during chemotherapy. However, the study may contain certain biases like observer bias and selection bias. There is scope to relate this electrolyte variation to different chemotherapeutic regimens used so that specific changes caused by particular drug can be known and treated promptly.

## Conclusion

This study concluded that there is difference in electrolyte levels before and after chemotherapy in cancer patients. Although the difference in electrolyte levels is not clinically significant and can be managed promptly in less time. Furthermore, no correlation was observed in electrolytes including sodium, potassium, magnesium, urea and creatinine.

## References

1. Bowman BT. Electrolyte Disorders Associated with Cancer. *Journal of Onco-Nephrology*. 2017;1(1):30-35.
2. Nriagu J, Darroudi F, Shomar B. Health effects of desalinated water: Role of electrolyte disturbance in cancer development. *Environmental research*. *Environ Res*. 2016;150:191-204. doi: 10.1016/j.envres.2016.05.038
3. Kumar RV, Bhasker S. Health-care related supportive-care factors may be responsible for poorer survival of cancer patients in developing countries. *Journal of Cancer Policy*. 2015;5:31-47.
4. Allolio B, Annane D, Ball S, Bichet D, Decaux G, Fenske W, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Eur J Endocrinol*. 2014;170(3):G1-47. doi: 10.1530/EJE-13-1020
5. Moritz ML, Ayus JC. Maintenance intravenous fluids in acutely ill patients. *N Engl J Med*. 2015;373(14):1350-1360. doi: 10.1056/NEJMr1412877
6. Lameire N, Van Biesen W, Vanholder R. Electrolyte disturbances and acute kidney injury in patients with cancer. *Semin Nephrol*. 2010;30(6):534-547. doi: 10.1016/j.semnephrol.2010.09.002
7. Carvalho F, Louro F, Zakout R. Adrenal Insufficiency in Metastatic Lung Cancer. *World Journal of Oncology*. 2015;6(3):375-377.
8. Kitai Y, Matsubara T, Yanagita M. Onco-nephrology: current concepts and future perspectives. *Jpn J Clin Oncol*. 2015;45(7):617-628. doi: 10.1093/jjco/hyv035
9. Lameire N. Nephrotoxicity of recent anti-cancer agents. *Clinical kidney journal*. 2013;7(1):11-12.
10. Latcha S. Electrolyte Disorders in Cancer Patients. *Onconephrology: Cancer, Chemotherapy and the Kidney*. 2015;7:131-162.
11. Eun JN, Choi YD, Lee JH, Jeong YA, Yoon JH, Kim HK, et al. Severe Hypocalcemia in a Patient with Recurrent Chondrosarcoma. *Intern Med*. 2017;56(14):1839-1842. doi: 10.2169/internalmedicine.56.7884
12. Fokkema MI, de Heide LJ, van Schelven WD, Hamdy NA. Severe hypocalcaemia associated with extensive osteoblastic metastases in a patient with prostate cancer. *Neth J Med*. 2005;63(1):34-37.
13. Arvind Yadav, Khodke Prasad. Status of serum electrolytes in cancer patients. *International Journal of Basic and Applied Medical Sciences*. 2015;5(1):208-211.
14. Doshi SM, Shah P, Lei X, Lahoti A, Salahudeen AK. Hyponatremia in hospitalized cancer patients and its impact on clinical outcomes. *Am J Kidney Dis*. 2012;59(2):222-228. doi: 10.1053/j.ajkd.2011.08.029
15. Berghmans T, Paesmans M, Body JJ. A prospective study on hyponatraemia in medical cancer patients: epidemiology, aetiology and differential diagnosis. *Support Care Cancer*. 2000;8(3):192-197.
16. Liamis G, Milionis H, Elisaf M. A review of drug-induced hyponatremia. *Am J Kidney Dis*. 2008;52(1):144-153. doi: 10.1053/j.ajkd.2008.03.004
17. Tsujii T, Ogaki T, Nakae K, Imai K, Kise D, Tada S, et al. Correlation between blood magnesium and calcium concentration in patients treated with an anti-EGFR antibody. *J Pharm Health Care Sci*. 2016;2:23. doi: 10.1186/s40780-016-0060-9
18. Filippatos TD, Milionis HJ, Elisaf MS. Alterations in electrolyte equilibrium in patients with acute leukemia. *Eur J Haematol*. 2005;75(6):449-460.
19. Unwin RJ, Luft FC, Shirley DG. Pathophysiology and management of hypokalemia: a clinical perspective. *Nat Rev Nephrol*. 2011;7(2):75-84. doi: 10.1038/nrneph.2010.175
20. Huang CL, Kuo E. Mechanism of hypokalemia in magnesium deficiency. *J Am Soc Nephrol*. 2007;18(10):2649-2652.
21. Groenestege WM, Thébaud S, van der Wijst J, van den Berg D, Janssen R, Tejpar S, et al. Impaired basolateral sorting of pro-EGF causes isolated recessive renal hypomagnesemia. *J Clin Invest*. 2007;117(8):2260-2267.
22. Schrag D, Chung KY, Flombaum C, Saltz L. Cetuximab therapy and symptomatic hypomagnesemia. *J Natl Cancer Inst*. 2005;97(16):1221-12214.