

SJMLS - 7(2) - 009

Anti-tumour therapy and renal-associated derangements among Breast Cancer Patients attending University of Calabar Teaching Hospital, Calabar NigeriaUdosen, J.E.¹, Akwiwu, E.C.^{2*}, Akpotuzor, D.U.², Akpotuzor, J.O.²Department of Surgery, University of Calabar, Calabar, Nigeria¹, Department of Haematology and Blood Transfusion Science, University of Calabar, Calabar, Nigeria².Author for Correspondence *: ecakwiwu@gmail.com/ +234-803-677-7296/ORCID Number: 0000-0001-6097-557X. <https://dx.doi.org/10.4314/sokjmls.v7i2.9>**Abstract**

Among the different biomedical derangements that have been observed in breast cancer, renal function parameters are considered quite important. Renal-associated derangements are part of the critical aspects in the management of cancer patients. These morbidity indicators could find usefulness in determining the dynamics of genetic and pharmacologic interplay with regards to anti-tumour agents. The present study therefore focused on women of Southern Nigerian descent who had been diagnosed with breast cancer and receiving chemotherapy after surgical removal of the breast tumour. The study was conducted in University of Calabar Teaching Hospital, Calabar. It included 36 cases of pathologically diagnosed breast cancer (BC) patients as well as 36 apparently healthy females drawn from the general population who served as control group. Ethical approval and informed consent were duly sought from the Health and Research Ethics Committee (HREC) of University of Calabar Teaching Hospital. Standard colorimetric methods were used to determine all the parameters (Sodium, Potassium, Chloride, Bicarbonate, Urea and Creatinine) among the BC patients who were receiving adjuvant 5-fluorouracil, epirubicin, cyclophosphamide (FEC) chemotherapy and the control group. The data obtained were analyzed in Statistical Package for Social Sciences (SPSS) using students t-test at 95% confidence level with p-value of 0.05. Breast Cancer patients had significantly lower mean value of Chloride compared to control subjects ($p = 0.022$). In terms of derangements, this study recorded higher proportions of hyponatremia (42%), hypokalemia (33%) and hypochloremia (42%) alongside hypercreatininemia (33%). The observed

hyponatremia and hypokalemia were mainly mild-moderate (31% and 33% respectively) in terms of severity. In conclusion, this study observed renal-associated derangements among breast cancer patients on treatment, mainly in the form of hyponatremia, hypokalemia, hypochloremia and hypercreatininemia.

Keywords: Breast cancer, chemotherapy, renal function tests,

Introduction

Breast cancer management in resource-poor settings including Nigeria remains challenging owing in part to inadequate health infrastructure in terms of availability and accessibility as well as deficit in health-seeking behaviours of the populace (Adesunkanmi *et al.*, 2006; Anyanwu, 2000). More sensitive, however, is the aspect of management of the condition and its toll on the financial and social wellbeing of affected persons. Breast cancer has been reported as the world's most prevalent cancer affecting mainly women (WHO, 2021). The vulnerability of women in developing regions apparently extends to maternal health which has necessitated deliberate effort at investigating healthcare delivery in medical conditions peculiar to women particularly breast cancer (Udosen *et al.*, 2022; Akwiwu *et al.*, 2021; Akpotuzor *et al.*, 2011). Quality of life and overall survival among other factors are critical in the journey of breast cancer management (de Jong *et al.*, 2006; Sadler *et al.*, 2001). Among the different biomedical derangements that have been observed in breast cancer, renal function parameters are considered quite important. Monitoring and prompt correction of renal-

associated morbidity indicators are crucial in assessing and adjusting drug options in the management of cancer patients (Berardi *et al.*, 2019). Extreme values of blood electrolytes, urea and creatinine are associated with life-threatening outcomes, hence the routine assessment of these parameters.

Renal-associated derangements are part of the critical aspects in the management of cancer patients. Among the contributing factors are cancer physiopathology, anti-tumor treatments, concomitant clinical conditions, or therapies (Berardi *et al.*, 2016). It is interesting that overtime, these renal-associated morbidity indicators could find usefulness in determining the dynamics of genetic and pharmacologic interplay with regards to anti-tumour agents (Ingles-Garces *et al.*, 2018; Liamis *et al.*, 2016). Apart from integrating these parameters in the assessment tools during clinical trials for emerging therapies, there might be need for continuous evaluation of existing therapies (such as adjuvant 5-fluorouracil, epirubicin, cyclophosphamide (FEC) chemotherapy) across different populations. This could contribute to review of anti-tumour agents/ therapies with regards to defined populations. The present study therefore focused on women of Southern Nigerian descent who had been diagnosed with breast cancer and receiving FEC chemotherapy after surgical removal of the breast tumour.

Materials and Methods

The study was conducted in University of Calabar Teaching Hospital, Calabar. It included 36 cases of pathologically diagnosed breast cancer (BC) patients as well as 36 apparently

healthy females drawn from the general population who served as control group. Ethical approval was obtained from the Health and Research Ethics Committee (HREC) of University of Calabar Teaching Hospital. Written informed consent was obtained from each participant enrolled in the research and confidentiality was maintained.

Standard colorimetric methods were used to determine all the parameters among the BC patients who were receiving adjuvant 5-fluorouracil, epirubicin, cyclophosphamide (FEC) chemotherapy and the control group. The electrolytes consisting of sodium, potassium, chloride and bicarbonate were assayed using kits from Teco Diagnostics, USA. Urea and Creatinine levels were determined using kits from Randox Laboratories Limited, UK. The data obtained were analyzed in Statistical Package for Social Sciences (SPSS version 22.0) using students t-test at 95% confidence level with p-value of 0.05.

Results

Table 1 shows the comparison of mean values of Sodium, Potassium, Chloride, Bicarbonate, Urea and Creatinine between Breast Cancer patients and control subjects. Breast Cancer patients had significantly lower mean value of Chloride compared to control subjects ($p = 0.022$).

Proportions of Breast Cancer Patients with derangement in the measured parameters is shown in Table 2. The study recorded more of hyponatremia, hypokalemia and hypochloremia alongside hypercreatininemia. The observed hyponatremia and hypokalemia were mainly mild-moderate in terms of severity (Table 3).

Table 1: Selected renal function Parameters of Breast Cancer (BC) Patients and Controls

Parameter	BC patients n=36	Control group n=36	p-value
Sodium (135-144 mmol/l)	134.14±10.76	137.28±4.72	0.113
Potassium (3.6-5.5 mmol/l)	4.04±1.20	4.05±0.52	0.934
Chloride (98-106 mmol/l)	96.00±11.63	100.67±2.87	0.022
Bicarbonate (23-34 mmol/l)	26.33±2.61	26.14±2.13	0.738
Urea (1.7-9.1 mmol/l)	3.49±1.61	3.39±0.72	0.721
Creatinine (44-80 µmol/l)	67.69±17.68	61.67±10.66	0.085

Table 2: Proportions of Breast Cancer Patients with derangement in measured parameters

Parameter	Below Range	Within Range	Above Range
	n (%)	n (%)	n (%)
Sodium (135-144 mmol/l)	15 (42)	17 (47)	4 (11)
Potassium (3.6-5.5 mmol/l)	12 (33)	23 (64)	1 (3)
Chloride (98-106 mmol/l)	15 (42)	18 (50)	3 (8)
Bicarbonate (23-34 mmol/l)	2 (6)	34 (94)	0 (0)
Urea (1.7-9.1 mmol/l)	2 (6)	34 (94)	0 (0)
Creatinine (44-80 µmol/l)	5 (14)	19 (53)	12 (33)

Table 3: Severity of Sodium and Potassium derangements within the studied population

Parameter	Number	Percent
	n = 36	100%
Sodium		
Severe Hyponatremia (<125 mmol/l)	4	11
Mild-moderate Hyponatremia (125-134 mmol/l)	11	31
Normal Sodium range (135-144 mmol/l)	17	47
Mild-moderate Hypernatremia (145-154 mmol/l)	3	8
Severe Hypernatremia (>155 mmol/l)	1	3
Potassium		
Severe Hypokalemia (<2.5 mmol/l)	0	0
Mild-moderate Hypokalemia (2.5-3.5 mmol/l)	12	33
Normal Potassium range (3.6-5.5 mmol/l)	23	64
Mild-moderate Hyperkalemia (5.6-6.5 mmol/l)	0	0
Severe Hyperkalemia (>6.5mmol/l)	1	3

Discussion

This study on anti-tumour therapy and renal-associated derangements was carried out among breast cancer patients accessing care at University of Calabar Teaching Hospital, Calabar Nigeria. A comparison of mean values of sodium, potassium, chloride, bicarbonate, urea and creatinine between breast cancer patients and control subjects revealed no significant differences except for the chloride that was significantly lower among breast cancer patients compared to control subjects. Chloride channels and associated transporters, known to facilitate pH balance among other roles, are in recent times

appreciated for their participation in cell proliferation. Thus, gaining attention in the field of cancer research (Kim *et al.*, 2022). The finding of lower chloride mean level may therefore be the result of direct antiproliferative effect of chemotherapy, albeit with the potential of adverse renal involvement. The observed comparable values of measured parameters between breast cancer patients and control subjects may have been due to small sample size. However, to appreciate the pattern of renal-associated derangements encountered during breast cancer treatment, it was necessary to go beyond comparison of mean values between test

and control groups. Thus, proportions of breast cancer patients with values below and above established reference ranges were determined.

The present study recorded more of hyponatremia, hypokalemia and hypochloremia alongside hypercreatininemia. The observed hyponatremia and hypokalemia were mainly mild-moderate in terms of severity; a pattern in concordance with earlier reports (Berardi *et al.*, 2015; Doshi *et al.*, 2012). At the extremes of blood sodium levels, hyponatremia occurs more often than hypernatremia. In fact, the former is reportedly the commonest blood electrolyte derangement in cancer (Castilo *et al.*, 2012). Similarly, hypokalemia is quite common in cancer relative to the upper extreme values. Blood electrolyte imbalance in cancer has been linked to expression of trans-membrane proteins involved in the transfer of these ions. Abnormal expressions of Nav 1.5 (one of the voltage-gated sodium channels) and KCN (potassium channels) have been implicated as seeming promoters of tumour progression in breast cancer (Haren *et al.*, 2010; Fraser *et al.*, 2005). The goal of treatment is to address underlying cause of disease and correct derangements. However, chemotherapeutic agents have been reported to contribute to electrolyte imbalance. Diuretic mechanism of some of these agents in addition to vomiting and diarrhoea as adverse effects of chemotherapy in general may lead to hypernatremia and hypokalemia, while treatment-induced renal injury, redistribution as well as reduced thirst stimulation secondary to vomiting and diarrhoea are capable of causing hyponatremia and hyperkalemia (Berardi *et al.*, 2019; Kozłowska *et al.*, 2019). The finding of higher proportions of hypercreatininemia and hypochloremia within the studied population appears to support the mechanism of treatment-induced renal complication. It is however not unlikely that more than one mechanism could be driving the pattern of derangements observed in the present study. In conclusion, this study observed renal-associated derangements among breast cancer patients on treatment, mainly in the form of hyponatremia, hypokalemia, hypochloremia and hypercreatininemia.

Conflict of interest

All Authors declare no conflict of interest

References

- Adesunkanmi, A.R., Lawal O.O., Adelusola, K.A., Durosimi, M.A. (2006). The severity, outcome and challenges of breast cancer in Nigeria. *Breast*; **15(3)**:399-409.
- Akpotuzor, J.O., Akwiwu, E.C., Okpokam, D.C., Keunmoe, P. (2011). Analyses of haematological malignancies records from University of Calabar Teaching Hospital Calabar, Nigeria (1983-2008). *International Journal of Natural and Applied Sciences*; **7(1)**: 133-136.
- Akwiwu, E.C., Okafor, A.O., Akpan, P.A., Akpotuzor, J.O., Asemota, E.A., Okoroiwu, H.U., Anyanwu, S.O. (2021). Serum P53 Protein Level and Some Haematologic Parameters among Women of Reproductive Age Living with HIV Infection. *Nigerian Journal of Physiological Science*; **36(1)**: 85–89.
- Anyanwu, S.N. (2000). Breast cancer in eastern Nigeria: a ten-year review. *West African Journal of Medicine*; **19(2)**:120-125.
- Berardi, R., Caramanti, M., Castagnani, M., Guglielmi, S., Marcucci, F., Savini, A., *et al.* (2015). Hyponatremia is a predictor of hospital length and cost of stay and outcome in cancer patients. *Support Care Cancer*; **23**:3095–3101.
- Berardi, R., Rinaldi, S., Caramanti, M., Grohè, C., Santoni, M., Morgese, F., *et al.* (2016). Hyponatremia in cancer patients: time for a new approach. *Critical Review in Oncology/Hematology*; **102**:15-25.
- Berardi, R., Torniai, M., Lenci, E., Pecci, F., Morgese, F., Rinaldi, S. (2019). Electrolyte disorders in cancer patients: a systematic review. *Journal of Cancer Metastasis and Treatment*; **5**:79.
- Castillo, J.J., Vincent, M., Justice, E. (2012). Diagnosis and management of hyponatremia in cancer patients. *Oncologist*; **17**:756-765.
- de Jong, N., Candel, M.J., Schouten, H.C., Abu-Saad, H.H., Courtens, A.M. (2006). Course of the fatigue dimension "activity level" and the interference of fatigue with daily living activities for patients with breast cancer receiving adjuvant chemotherapy. *Cancer Nursing*; **29(5)**: E1-13.

- Doshi, S.M., Shah, P., Lei, X., Lahoti, A., Salahudeen, A.K. (2012). Hyponatremia in hospitalized cancer patients and its impact on clinical outcomes. *American Journal of Kidney Diseases*; **59**:222–228.
- Fraser, S.P., Diss, J.K., Chioni, A.M., Mycielska, M.E., Pan, H., *et al.* (2005). Voltage-gated sodium channel expression and potentiation of human breast cancer metastasis. *Clinical Cancer Research*; **11**:5381-5389.
- Haren, N., Khorsi, H., Faouzi, M., Ahidouch, A., Sevestre, H., *et al.* (2010). Intermediate conductance Ca^{2+} activated K^{+} channels are expressed and functional in breast adenocarcinomas: correlation with tumour grade and metastasis status. *Histology and Histopathology*; **25**:1247-1255.
- Ingles-Garces, A.H., Ang, J.E., Ameratunga, M., Chénard-Poirier, M., Dolling, D., *et al.* (2018). A study of 1088 consecutive cases of electrolyte abnormalities in oncology phase I trials. *European Journal of Cancer*; **104**:32-38.
- Kim, H.J., Lee, P.C., Hong, J.H. (2022). Chloride Channels and Transporters: Roles beyond Classical Cellular Homeostatic pH or Ion Balance in Cancers. *Cancers (Basel)*; **14**(4):856.
- Kozłowska, K., Kozłowski, L., Małyszko, J. (2019). Hypertension prevalence in early breast cancer patients undergoing primary surgery. *Advances in Medical Sciences*; **64**(1):32-36.
- Liamis, G., Filippatos, T.D., Elisaf, M.S. (2016). Electrolyte disorders associated with the use of anticancer drugs. *European Journal of Pharmacology*; **777**:78-87.
- Sadler, I.J., Jacobsen, P.B. (2001). Progress in understanding fatigue associated with breast cancer treatment. *Cancer Investigation*; **19**(7):723-731.
- Udosen, J.E., Akwiwu, E.C., Akpotuzor, D.U., Akpotuzor J.O. (2022). Some Haematological Parameters of Breast Cancer Patients accessing therapy at University of Calabar Teaching Hospital, Calabar Nigeria. *Sokoto Journal of Medical Laboratory Science*; **7**(1): 89-93.
- World Health Organization (2021). Fact sheets on cancer. <https://www.who.int/news-room/fact-sheets/detail/breast-cancer>. Accessed May 4, 2022.

Citation: Udosen, J.E., Akwiwu, E.C., Akpotuzor, D.U., Akpotuzor, J.O. Anti-tumour therapy and renal-associated derangements among Breast Cancer Patients attending University of Calabar Teaching Hospital, Calabar Nigeria. *Sokoto Journal of Medical Laboratory Science*; **7**(2): 80 - 84. <https://dx.doi.org/10.4314/sokjmls.v7i2.9>

Copyright: This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.