International Journal of Research in Medical Sciences
Raza U et al. Int J Res Med Sci. 2025 Oct;13(10):3968-3971
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20253132

Original Research Article

Increased blood level of urea and creatinine after chemotherapy in breast cancer patients

Uzma Raza[1], Ali Iftikhar[2], Aziza Khanam[3]*, Sidra Rizwan[4]

[1]Department of Biochemistry, Hamdard College of Medicine, Karachi, Pakistan
[2]Karachi Institute of Medical Sciences, Karachi, Pakistan
[3]A1-Tibri Medical College, Isra University Karachi Campus, Karachi, Pakistan
[4]Department of Oncology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan

Received: 03 July 2025
Revised: 05 August 2025
Accepted: 11 September 2025

***Correspondence:**
Dr. Aziza Khanam,
E-mail: azizqadeer@yahoo.com

ABSTRACT

Background: Breast cancer is treated with surgery and often combined with chemotherapy, radiotherapy and or hormonal therapy or both. The treatment has some side effects such as hair loss, nausea, fatigue peripheral neuropathy, nephropathy etc. The objective of the study was to assess the nephrotoxic effects after treatment of breast cancer.
Methods: The infiltrating ductal carcinoma patients were treated with surgery, chemotherapy, with or without radiotherapy and hormonal therapy. The non-diabetic, non-cardiac post-menopausal breast cancer patients were further subdivided on the basis of nodes histopathology, with or without lymph node metastasis. Patients were subjected to different combination of disciplines of therapy including radiotherapy, chemotherapy and hormonal therapy. The blood samples were collected before and after chemotherapy. The blood was analyzed for urea and creatinine to assess the nephrotoxicity.
Results: There was a significant increase in blood urea and creatinine levels after the treatment as compared to before the start of therapy.
Conclusions: It is concluded that treatment of cancer (with chemotherapy, radiotherapy, hormonal therapy) lead to nephrotoxicity.

Keywords: Breast cancer, Chemotherapy, Creatinine, Nephrotoxicity, Treatment, Urea

INTRODUCTION

Breast cancer occurs twenty five percent of the women worldwide and is responsible for one in six deaths among women.[1] The cancer treatment depends on size, grade, involvement of lymph nodes and histopathology of tumor. Breast cancer treatment includes surgery, chemotherapy, radiation and hormonal therapy etc.[2]

Chemotherapy toxicity is increased when given adjuvant radiotherapy or hormone therapy. The toxicity includes dermatological side effects, nausea, vomiting, anorexia, constipation, dehydration, diarrhea, weight loss, anemia, low neutrophil counts, dyslipidemia, hyperglycemia and nephrotoxicity etc.[3]

Cancer therapy is associated with adverse effects such as nephrotoxicity which affects the quality of life.[2] Antimetabolites of anticancer drugs have shown to cause renal inefficiency.[4] The normal kidney function in these subjects is altered and may lead to kidney failure due to para neoplastic syndromes, hypercalcemia, and in rare cases tumor lysis syndrome.[1] The earlier reported work stated that nephrotoxicity is one of the toxic effects produced by chemotherapy radiotherapy/hormonal therapy, which may lead to permanent renal failure.[5]

Blood creatinine and breakdown products of creatinine phosphate and urea are widely used to assess the function of kidney.[6]

In current study blood creatinine and urea were estimated to assess the kidney function. The different disciplines of treatment combinations were surgery, chemotherapy and hormonal therapy with or without radiation.

METHODS

The study included 220 adult female control subjects having no signs and symptoms of cancer. Total 177 post-menopausal pre-diagnosed, non-diabetic, non-cardiac, breast infiltrating ductal carcinoma female patients were included out of which 116 patients were with lymph node metastasis and 61 breast cancer patients were without lymph node metastasis only.

The patients who underwent modified radical one breast mastectomy were included in the study. Patients and control subjects using contraceptive and hormonal therapy were excluded from the study. The control and patients' demographic data was collected before the start of the study.

The experimented comparative study was performed from January 2018 to December 2019 at Al-Tibri Medical College and ethical approval was given by the institute. Breast cancer patients suffering from diabetes or heart disease were excluded from the study.

The blood of control and breast cancer patients were collected from the oncology department of the Hospital. The data analysis, was done by social sciences version 11, p value <0.05 was considered significant.

The treatment plan was based on the histopathology reports. The treatment was initiated by chemotherapy or surgery depending on the tumor size, sometimes radiotherapy is also included hormonal therapy was given to hormone receptor positive patients. The chemotherapeutic disciplines included were 5-flourouracil - adriamycin - cyclophosphamide (FAC), cyclophosphamide - adriamycin - 5-fluorouracil. (CMF), adriamycin cyclophosphamide (AC), adriamycin cyclophosphamide paclitaxel (ACT). One of these combinations of drugs were given to patients on the basis of histopathology of tumor. For hormone receptor positive patients, hormonal therapy tamoxifen was suggested for 5 years.

The blood samples of control normal subjects and breast cancer patients were collected and analysed for blood urea (by Roche diagnostic kit) and creatinine (Roche Diagnostics GMBH kit) before the start of treatment. The blood sample of breast cancer patients was collected second time, fourteen weeks after the last chemotherapy dose. During these fourteen weeks radiotherapy treatment and 8 weeks of tamoxifen treatment were completed.

The patients were divided into two groups, one having lymph node metastasis and another without metastasis. The breast cancer patients were treated with different combinations of surgery, chemotherapy, radiotherapy and hormonal therapy.

RESULTS

Table 1 shows the demographic data of control and cancer patients, which shows that the breast cancer patients having children were lower as compared to control subjects, whereas percentage of subjects having abortion was high as compared to control subjects. No comparative significant change in BMI was observed in the two groups.

Table 1: History of control and breast cancer female subjects.

Subjects	Age (years)	Age at marriage (years)	Percentage having children	Percentage having abortions	BMI (kg/m^2)
Control	58.98±0.78 (220)	30.90±0.40 (220)	90.20 (180)	15.0 (33)	23.80±2.50 (220)
Breast cancer patients	64.60±6.92 (177)	29.44±0.52 (177)	80.01 (177)	60.10 (120)	25.0±0.50 (177)

Age and body mass index of control and breast cancer patients are expressed as mean±SEM

Table 2: Variation of blood creatinine and urea in control and breast carcinoma patients without lymph node metastasis.

Non diabetic non cardiac breast carcinoma patients							
Renal function test	**Control**	**Surg + chemo + hormone therapy with or without radiotherapy**		**Surg + chemo + radiotherapy**		**Surg + hormone therapy + radiotherapy**	
		Before	**After**	**Before**	**After**	**Before**	**After**
Creatinine mg/dl	0.60±0.01 (220)	0.70±0.01 (38)	0.96±0.01* (38)	0.62±0.02 (17)	1.31±0.06* (17)	0.62±0.01 (6)	0.85±0.06 (6)
Urea mg/dl	23.04±0.17 (220)	28.61±0.50 (38)	36.04±0.49* (38)	22.53±0.77R (17)	41.40±0.64* (17)	28.17±0.75 (6)	31.0±0.04* (6)

The blood creatinine and urea concentration of control and breast carcinoma patients without lymph node metastasis before treatment and after treatment are tabulated. Treatment includes surgery (surg), chemotherapy (chemo) hormonal therapy (tamoxifen) and radiotherapy. Chemotherapy included different combinations of 5-flurouracil (F). Adriamycin (A) cyclophosphamide (C) methotrexate (M) and paclitaxel (T) as FAC, CMF, AC and AC-T. *Statistically significant p<0.05.

Table 3: Variation of blood creatinine and urea in control and breast carcinoma patients with lymph node metastasis, before and after treatment.

Non diabetic non cardiac breast carcinoma patients											
Renal function test	**Control**	**Surgery + chemo + with or without radiotherapy**		**Surgery + chemo + radiotherapy**		**Surgery + hormone therapy + radiotherapy**		**Chemo + surgery + hormone therapy + radiotherapy**		**Chemotherapy + surgery + chemo + with or without radiotherapy**	
		Before	**After**	**Before**	**After**	**Before**	**After**	**Before**	**After**	**Before**	**After**
Creatinine mg/dl	0.58±0.02 (220)	0.61±0.01 (39)	0.96±0.01* (39)	0.62±0.02 (36)	1.28±0.02 * (36)	0.65±0.05 (9)	0.85±0.05* (9)	0.63±0.03 (11)	1.00±0.02 * (11)	0.70±0.02 (21)	1.10±0.02* (21)
Urea mg/dl	23.6±0.17 (220)	21.30±0.3 5 (39)	29.40±0.44 * (39)	21.86±0.6 1 (36)	33.0±0.64 * (36)	22.11±1.6 1 (9)	27.30±1.09* (9)	25.80±0.8 0 (11)	35.0±0.80 * (11)	24.80±0.7 5 (21)	36.10±0.7) * (21)

The blood creatinine and urea in control and breast carcinoma patients with lymph node metastasis are tabulated before and after treatment. Treatment includes surgery (surg) chemotherapy (chemo), hormonal therapy (tamoxifen) and radiotherapy. Chemotherapy included different combinations of 5-flurouracil (F), adriamycin (A) cyclophosphamide (C), methotrexate (M) and paclitaxel (T) as FAC, CMF, AC and AC-T. * Statistically significant $p<0.05$.

The patients who were suffering from breast cancer, either with lymph node metastasis or without metastasis, were treated with different combinations of therapy which includes surgery, chemotherapy, hormonal therapy and with or without radiotherapy. All breast cancer patients (with or without lymph node metastasis) had shown a high level of blood creatinine and urea after therapy as compared to before therapy (Tables 2 and 3).

DISCUSSION

The histopathological characteristic of tumors decide the pattern of treatment. Effective and least toxic treatment were selected by the physicians.[7] The invasive breast cancer patients were treated with chemotherapy, surgery, radiotherapy and hormone therapy.[8] In some cases, radiotherapy in addition to surgery and chemotherapy improved the disease free survival.[9] Hormonal therapy is beneficial for hormone receptor positive patients. Forty-four breast cancer patients without lymph node metastasis and twenty patients with lymph node metastasis were treated with hormonal therapy (Tables 2 and 3).

Chemotherapeutic agents produce toxicities which include hematological, dermatological, gastrointestinal and nephrotoxicity.[10] Renal insufficiency is common in patients with cancer and dose adjustment and number of cycles of neoplastic drug adjustment might be needed.[11]

In non diabetic and non cardiac breast cancer patients, the blood creatinine and urea concentrations were significantly high after treatment (chemotherapy, radiotherapy and hormonal therapy) as compared to before treatment in both with or without lymph nodes metastasis (Tables 2 and 3). Earlier studies reported that methotrexate, cyclophosphamide and 5-fluorouracil administration produces nephrotoxicity.[12] Methotrexate is eliminated by kidney and produces nephrotoxicity at the dose of 500 mg/m^2.[13] Cyclophosphamide an alkylating agent produces nephrotoxicity through oxidative stress.[14] cisplatin is another antineoplastic agent, which produce toxic effects on the renal function, and an increased in blood creatinine.[15,16] Tamoxifen given to hormone receptor positive patients also altered the renal function parameters.[17] So a number of clinical factors may cause nephrotoxicity due to cytotoxic drugs.

In old women the decreased total body water leads to an increase in free fraction of drugs in blood. In this way, the kidney is exposed to a high concentration of drugs which accumulate in the medulla of the kidneys leading to kidney failure.[18] The amount of creatinine also depends on age, body weight and sex. In patients with chronic renal failure, high concentrations of malondialdehyde (MDA) and low activity of superoxide dismutase (SOD) were correlated with diminished renal function.

The limitation of the study was that only smaller number of patients were selected from only one hospital. Another limitation was that the second blood samples were collected after 14 weeks of last chemotherapy and after 8 weeks of hormonal therapy whereas hormonal treatment is usually given for 5 years, but it was not possible for us to take the blood sample after 5 years.

CONCLUSION

The study characterized the burden of chemotherapy induced nephrotoxicity which is indicated by increased levels of blood urea and creatinine after treatment of breast cancer patients. The dose adjustment and management of side effects is very necessary to tackle/manage nephrotoxicity. The study suggested further research on factors related to chemotherapy induced toxicity.

ACKNOWLEDGEMENTS

We are thankful to the doctors and staff of Liaquat National Hospital for allowing to collect the blood samples from the breast cancer patients.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Moradi N, Izadi S, Hemmati HR. Renal insufficiency in breast cancer patients; a review study. J Nephropharmacol. 2024;13(2):e11659.
2. Shen G, Zhao F, Huo X, Ren D, Du F, Zheng F, et al. Meta Analysis of HER 2-enrieched subtype predicting the pathological complete response with in HER 2-positive Breast cancer in patients who received neoadjuvant treatment. Front Ocncol. 2021;11.
3. Horie S, Oya M, Nangaku M, Yasuda Y, Komatsu Y, Yanagita M, et al. Guidelines for treatment of renal injury during cancer chemotherapy 2016. Clin Exp Nephrol. 2018;22(1):210-44.
4. Boeno FP, Patel J, Montalro RN, Lapierre Nguyen Schreiber CM, Smuder AJ. Effect of exercise preconditioning on Doxorubicin induced liver and kidney Toxicity in male and female Rats. Int. J Mol Sci. 2023;24(12):10222.
5. Chen C, Xie D, Gewirtz DA, Li N. Nephrotoxicity in cancer Treatmen: An update. Adv. Cancer Res. 2022;155:77-129.
6. Kamal A. Estimation of blood urea and serum creatinine level in patients of renal disorder. IJFALS. 2014;4(4)199-202
7. Fang CY, Lou DY, Zhou LQ, Wang JC, Yaug B, He QJ, et al. Natural products: potential treatments for as platin induced nephrotoxicity. Acta Pharmacol Sinica. 2021;42(12):1951-69.
8. Korde LA, Somerfield MR, Carey LA, Crews JR, Denduluri N, Hwang ES, Khan SA, Loibl S, Morris EA, Perez A, Regan MM. Neoadjuvant chemotherapy, endocrine therapy, and targeted therapy for breast cancer: ASCO guideline. J Clin Oncol. 2021;39(13):1485-505.
9. Rajan KK, Fairhurst K, Birkbeck B, Novintan S, Wilson R, Savovic J, et al. Overall survival after mastectomy Vevsus breast-conserving surgery with adjuvant radiotherapy for early stage breast cancer Meta-analysis. BJS Open. 2024May 17;8(3):Zrae040.
10. Nguyen SUI, Phan AT, Nguyen LM, Cai H, Tran TV, Shu XO, et al. Chemotherapy induced toxicities and their association with clinical and non-clinical factors among Breast Cancer Patients in Vietnam. Curr Oncol. 2022;29(11):8269-84.
11. Kitai Y, Matsubara T, Funakoshi T, Horimatsu T, Muto M, Yanagita M. Cancer screening and treatment in patients with end-stage renal disease: remaining issues in the field of onco-nephrology. Ren Replace Ther. 2016;2(1):33.
12. Obadipe JA, Samuel TA, Jimoh MA, Folorunso SA. Chemotherapy induced electrolyte disorders, nephrotoxicity in cancer patients from selected Nigerian tertiary care hospital. Niger Med J. 2022;63(3):1196-203.
13. Hamed KM, Dighriri IM, Baomer AC, Alhar-Thy BT, Alenazai FE, Alali GH, et al. overview of methotrexate toxicity. A comprehensive literature, review. Cureus. 2022;14(9):e29518.
14. Cai Z, Samdelov S, Kullak Ublick G, Visentin M. Molecular mechanisms of Colistin induced nephrotoxicity. Molecules. 2019;24(3):653.
15. Griffein BR, Faubel S, Edelstein CL. Biomarkers of drug induced kidney toxicity. Ther Drug Monit. 2019;41:213-26.
16. Zazuli Z, Vijverberg S, Slob E, Liu G, Carleton B, Veltam J, et al. Genetic variation and cisplatin Nephrotoxicity. A systemic reviews. Front Pharm. 2018,27;111.
17. Alshanwani AR, Mohamed AM, Faddah LM, Shaheen S, Arafah MM, Hagar H, et al. Cyanocobalamin and/or calcitriol mitigate renal damage-mediated by tamoxifen in rats: Implication of caspase-3/NF-κB signaling pathways. Life Sci. 2021;277:119512.
18. Halka J, Spaleniak S, Kade G, Antosieioic S, Signorshi D. The nephrotoxicity of drugs used in causal oncological therapies. Curr Oncol. 2022;8:29(12):9681-94.

Cite this article as: Raza U, Iftikhar A, Khanam A, Rizwan S. Increased blood level of urea and creatinine after chemotherapy in breast cancer patients. Int J Res Med Sci 2025;13:3968-71.