

# To evaluate the changes in Biochemical parameters of Breast cancer patients' during treatment at Larkana Sindh.

Sikandar Khatoon Seelro<sup>1</sup>, Mahak Memon<sup>2</sup>, Afsheen Shah<sup>3\*</sup>

## ABSTRACT:

**Objective:** To evaluate the changes in blood chemistry of breast cancer patients while under treatment at Larkana Institute of Nuclear Medicine and Radiotherapy (LINAR) Larkana, Sindh, Pakistan.

**Methodology:** The present study was conducted on the two hundred Breast cancer patients and divided them in four groups on the basis of their treatment; age ranges between 20-70 years. Demographic characteristics of patients and blood samples were collected for biochemical parameters i.e., Electrolytes (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, HCO<sub>3</sub><sup>-</sup>), Calcium, Urea and Creatinine. Patients' data was divided in groups on the basis of their treatment.

**Results:** Present study focused on analysis of biochemical parameters of breast cancer patients during treatment. 36% of patients suffering from Breast cancer have been belonging to age group 41-50 years; whereas 11% risk was also found in age group 20-30 years which is highly alarming. Urea & Creatinine was found highly significantly increased in all groups; this is indication of poor blood flow to kidneys and threat of renal failure.

**Conclusion:** Hyponatremia, hyperkalaemia, hypochloreaemia and hypercalcemia was found in patients. Increased level of urea & creatinine is a big threat for renal failure in breast cancer patients. Chemotherapy with Radiotherapy and Surgery group was more prone to electrolytes imbalance.

**Keywords:** Breast cancer, Chemotherapy, Radiotherapy, Electrolytes, Treatment.

## Introduction:

Breast cancer is a major health risk and might cause death of women.<sup>1</sup> It is increasing in developing countries specially in Pakistan.<sup>2,3</sup> Different treatments i.e., Chemotherapy, Radiotherapy, Surgery and combination of all; are administered to the patient depending upon stage of disease.<sup>1-5</sup> All types of therapies are aggressive in nature and have serious side effects which are occasionally reversible and sometimes irreversible.<sup>5</sup> These therapies alter the biochemical parameters and effect vital organs of the body. Chemotherapy is the mixture of specific medicines which is meant to target cancerous cells that are dividing and mutating at an abnormal rate to shrink or slow down their growth. This is systematic therapy and effects electrolytes, Calcium, Urea and Creatinine.<sup>6,7</sup> Radiotherapy is a treatment which uses low level of radiations like x-rays thrown on target mass to kill cancerous cells. Radiotherapy is an external cancer treatment.<sup>8</sup> Radiotherapy causes vomiting and diarrhoea which creates electrolytes imbalance whereas prolonged Radiotherapy might cause Comorbid Cancer like Lungs cancer etcetera. Surgery is the process of removal of tumour or excessive mass or carcinogenic material. Surgery causes blood loss and increases weakness of patient which would certainly affect biochemical parameters i.e., electrolytes and Urea. Radiotherapy and surgery also change the concentration of biochemical parameters like electrolytes, urea and creatinine and effects on concentration of calcium. All treatment modalities may change level of serum calcium and further complicate the illness and make patient venerable to diseases of liver and kid-

neys.<sup>9</sup> Whichever type of treatment is administered to the patient, all blood parameters should be focused and minor changes addressed during the treatment.<sup>10</sup>

## Objective:

To analyse the variations in biochemical parameters of breast cancer patients during chemotherapy, radiotherapy and surgery being done at LINAR (Larkana Institute of Nuclear Medicine and Radiotherapy), Larkana, Sindh, Pakistan.

## Methodology:

This study conducted at Department of Oncology, LINAR, Larkana during period from August 2022 to Feb 2023 after approval by ethical committee vide Reference no. IOB/294.b/2022, dated 13.06.2022. During study period, 200 consecutive female patients hospitalized at Department of Oncology, Larkana Institute of Nuclear Medicine and Radiotherapy Hospital (LINAR), Larkana, Sindh were enrolled by using convenience sampling. Based upon treatment modality i.e., chemotherapy (CT n=53), chemo and radiotherapy (CT & RT n=44), surgery (SG n=57) and combination of all three types of treatment (CRS n=46); for study purpose each modality was considered as separate group. Patients hospitalized for treatment of other type of cancer were excluded from the study. Data collected using a self-designed Questionnaire in Sindhi/Urdu. This questionnaire consists of 20 questions regarding demographic characteristics of patients that includes age, gender, and marital status, literacy rate, number of children, occupation, diet, medical assessment, supplementary medication, family history, general information of hospital. Blood samples collected for biochemical analysis that includes serum electrolytes (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, and HCO<sub>3</sub><sup>-</sup>), calcium, urea and creatinine. Electrolytes and calcium (Ca<sup>+</sup>) were analysed by Ion-Selective Electrode method on Electrolyte analyser as reported by Vázquez et al.<sup>11</sup> Urea & Creatinine were analysed by as reported by de Almeida et al.<sup>12</sup> For study purpose, data analysis performed using IBM SPSS (version 22). Data presented as mean, standard deviation. Student t test used for difference between bio-

1. PhD Scholar, Institute of Biochemistry, University of Sindh, Jamshoro Pakistan.
2. Assistant Professor, Peoples University of Medical and Health Sciences, Shaheed Benazirabad
3. Professor; Institute of Biochemistry; University of Sindh; Jamshoro.

\*=corresponding author :

Email: [afsheen.shah@usindh.edu.pk](mailto:afsheen.shah@usindh.edu.pk)

chemical changes between treatment modalities and 0.05 consider as significant.

**Results:**

All hospitalized female breast cancer patients were from adjoining areas of the Larkana, however 4% were from Baluchistan.

**Table no 1: Demographic characteristics.**

n=200	
<b>Age</b>	
20-30	11%
31-40	26%
41-50	36%
51-60	16%
Above 60	11%
<b>Presenting feature</b>	
Tumour	58%
Swelling	9%
Pain	28%
Infection	13%
Skin Allergy	2%
<b>Management at LINAR Hospital</b>	
Daily OPD	30%
Daily Chemotherapy	20%
Daily Radiations	30%
Daily Surgery	10%
Daily Admit	10%
<b>Family history of Breast Cancer</b>	
Yes	34.2%
No	65.8%
<b>Breast feeding</b>	
Yes	67.1%
No.	32.9%
<b>History of Birth control pills used</b>	
Yes	22%
No	78%
<b>Stage of Carcinoma</b>	
Stage 0	20%
Stage 1&II	30%
Stage III 50%	60%
<b>Grade of Cancer</b>	
Grade I	28.5%
Grade II	58.5%
Grade III	13%

For study purpose serum level of Na<sup>+</sup>, K<sup>+</sup> and Ca<sup>2+</sup> were considered as follows. Serum Na<sup>+</sup> when below normal is considered as mild, moderate and severe hyponatremia with serum level of 130-134 mEq/L, 125-129 mEq/L, and < 125 mEq/L respectively. For K<sup>+</sup>, hypokalaemia is considered as mild and severe when serum K<sup>+</sup> is < 3.5 mEq/L, < 2.5 mEq/L respectively. Hyperkalaemia is considered when serum K<sup>+</sup> is > 5.5 mEq/L. For serum Ca<sup>2+</sup>, hypercalcemia was considered mild, moderate and hypercalcaemic crisis

when serum Ca<sup>2+</sup> found between 10.5 to 11.9 mg/dL, 12.0 to 13.9 mg/dL and 14.0 to 16.0 mg/dL respectively. Among all patients only 7% were educated, 97% were married and 83% were housewives. According to history menstrual cycle was regular in 40% cases and right breast affected in 57.1%. Other characteristics are shown in table no1.

Table no 2 shows Mean ±SD and p value of electrolytes (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, HCO<sub>3</sub><sup>-</sup>), serum calcium, urea and creatinine in patients receiving different treatment. T-test have been used to compare p value of each group with control. Significant level used has been <0.05.

**Table 2: Serum Electrolytes, Urea, Creatinine, and Calcium levels in all groups during different treatments.**

Parameters N=200	HC Mean ±SD n=50	CT Mean ±SD n=53	CT & RT Mean ±SD n=44	SG Mean ±SD n=57	CRS Mean ±SD n=46	Normal Ranges
Sodium	138.20 ±2.6	134.33 ±2.6 p =0.02	123.94 ±2.5 p =0.04	137.10 ±1.90 p =0.005	131.80 ±1.53 p =0.03	135-145 mEq/L
Potassium	4.02±1.2	4.51±1.42 p =0.07	5.8±2.10 p =0.04	4.40±0.64 p =0.05	5.55±1.82 p =0.04	3.5-5.2 mEq/L
Chloride	101.33 ±045	86.63±2.4 p =0.05	97.83±4.32 p =0.05	100.27 ±3.10 p =0.07	97.40±5.15 p =0.06	96-106 mEq/L
Bicarbonate	23.73±3.31	23.17±3.13 p =0.49	22.97±3.057 p =0.35	25.50±2.28 p =0.31	23.3±2.52 p =0.61	23-30 mEq/L
Urea	6.20±1.290	8.53±1.61 p <0.000	7.20±1.3 p =<0.000	7.12±0.44 p <0.000	6.81±1.3 p <0.001	3.3-6.7 mmo/l/L
Creatinine	74.33±20.181	97.90±2.2 p =<0.000	87.03±4.0 p =0.02	82.77±3.9 p =0.01	75.63±1.9 p =0.07	80-115 mmo/l/L
Calcium	9.36±1.561	11.79±0.68 p =<0.000	11.96±0.34 p =<0.000	6.78±1.34 p =<0.000	12.28±2.2 p =<0.000	8.5-10.2 mg/dl

Healthy Control (HC), Chemotherapy (CT), Chemotherapy & Radiotherapy (CT & RT), Surgery Group (SG) and Chemotherapy, Chemotherapy & Radiotherapy, Surgery (CRS). P is significant level.

**Discussion:**

Breast cancer is increasing day by day among women in Pakistan<sup>1-4</sup> as well as within developed countries. Present study focuses on analysis of biochemical parameters of breast cancer patients during treatment. 36% of patients suffering from Breast cancer have been belonging to age group 41-50 years,<sup>6</sup> whereas 11% from early age group 20-30 years which is quite concerning. Normalcy of menstrual cycle is mandatory for regulation of hormones, proper func-

tioning of ovaries and regulation of breast cell metabolism. 60% women have been found with irregular menstrual cycles which might be one of the major risk factors for development of tumour. During interview; majority of females complained about extensive labour specially while using manual Sewing Machines; thereby contributing to their breast issues. Other women attributed the risk to minor accidents i.e., jerk/ shock/ strike/ pressing of breast; which aggravated due to continuous negligence and converted to breast cancer. 93% of females have been uneducated and 83% have been housewives (Table No. 1). Late diagnosis and continuous negligence aggravated their disease. Saeed et al;<sup>5</sup> reported that fear of cancer therapies is main cause of delayed treatment. Resultantly they reach to advance stage where they are administered multiple aggressive therapies for immediate relief. These therapies alter the biochemical parameters of blood and increase other complications. 34.2% Patients had positive family history (Table No. 1); which merits early diagnosis and counselling of their close family members. During study it has also been assessed that nutritive care of patient was being ignored. Hypernatremia has been found in Surgery group (SG) whereas Hyponatremia has been observed in all other three groups such as CT, CT & RT and CRS groups. Sodium is major cation of blood, both hypo and hyper conditions increase the complications in patients. Severe Hyponatremia have been observed in CT&RT group whereas Mild Hyponatremia has been observed in all other groups.<sup>13</sup> Potassium is needed for proper functioning of heart and other body tissues. Hyperkalaemia has been found in all groups and its increased level may affect respiratory and cardiovascular functioning, Tadesse & Laminie<sup>10</sup> also reported that sodium reduces and potassium increases after the treatment. Chloride has been significantly low in CT and CT&RT groups. Low level of chloride strongly warrants evaluation of acid base balance. There was no significant change in bicarbonate in all groups. Serum urea and creatinine is used to evaluate the renal functions of normal person and excretion of these factors indicate lean body mass. Higher level of creatinine causes renal impairment. In this study; Urea & Creatinine has been found highly significantly increased in all groups which is indication of poor blood flow to kidneys and may cause renal failure. Van et al;<sup>11</sup> and Statlender et al;<sup>12</sup> reported same findings. Calcium was found low in Surgery group (SG), a finding in agreement with other studies,<sup>13,14</sup> but significantly high in all other three groups i.e., CT, CT&RT and CRS groups, almost identical figure reported by others.<sup>15</sup> Slight increase in calcium level has been observed in all types of treatments except surgery patients in which hypocalcaemia,<sup>16,17</sup> has been found mostly at stage I and stage III of this study. Hypocalcaemia has been found clearly linked with chemotherapeutic drugs and had direct effect on parathyroid hormone suppression or change in calcium sensing.<sup>18</sup> Balanced diet including use of vegetables and fruits; and improved water intake is essential for quality of life of breast cancer patients.<sup>19,20</sup>

#### Conclusion:

Biochemical abnormalities are not uncommon in breast cancer patients who are under active treatment by any modality. Notably, the group undergoing chemotherapy in conjunction with radiotherapy and surgery exhibited a greater susceptibility to electrolyte imbalances. It is advisable to

monitor biochemical abnormalities in all breast cancer who are under active treatment.

**Acknowledgement:** The authors are thankful to the administration of LINAR Hospital Larkana for their profound cooperation during collection of data of subjects for the study.

**Funding and Conflict of Interest:** None.

**Author's Note:** This is M.Phils. Study of 1st Author.

#### References:

- Zaheer S, Yasmeen F. Historical trends in breast cancer presentation among women in Pakistan from joint-point regression analysis. *Pak J Med Sci.* 2024 Jan;40 (1Part-I):134-9. doi: [10.12669/pjms.40.1.7123](https://doi.org/10.12669/pjms.40.1.7123). PMID: [38196449](https://pubmed.ncbi.nlm.nih.gov/38196449/). PMCID: [PMC10772447](https://pubmed.ncbi.nlm.nih.gov/PMC10772447/).
- Ahmad S, Ur Rehman S, Iqbal A, Farooq RK, Shahid A, Ullah MI. Breast cancer research in Pakistan: A bibliometric analysis. *SAGE Open.* 2021 Sep;11 (3):21582440211046934. doi: [10.1177/21582440211046934](https://doi.org/10.1177/21582440211046934).
- Kim PP, Kim SH, Gomez NR. Fluids, Electrolytes, and Nutrition. In *The Vascular Surgery In-Training Examination Review (VSITE) 2023* Mar 3 (pp. 25-46). Cham: Springer International Publishing. [https://doi.org/10.1007/978-3-031-24121-5\\_3](https://doi.org/10.1007/978-3-031-24121-5_3).
- Wang J, Wu S-G. Breast cancer: an overview of current therapeutic strategies, challenge, and perspectives. *Breast Cancer (Dove Med Press).* 2023, 31 Dec;15:721-30. doi: [10.2147/BCTT.S432526](https://doi.org/10.2147/BCTT.S432526). PMID: [37881514](https://pubmed.ncbi.nlm.nih.gov/37881514/). PMCID: [PMC10596062](https://pubmed.ncbi.nlm.nih.gov/PMC10596062/).
- Saeed S, Asim M, Sohail MM. Fears and barriers: problems in breast cancer diagnosis and treatment in Pakistan. *BMC Womens Health.* 2021 Dec;21(1):151. doi: [10.1186/s12905-021-01293-6](https://doi.org/10.1186/s12905-021-01293-6). PMID: [33853583](https://pubmed.ncbi.nlm.nih.gov/33853583/).
- Traves KP, Cokenakes SEH. Breast cancer treatment. *Am Fam Physician.* 2021 Aug;104(2):171-8. PMID: [34383430](https://pubmed.ncbi.nlm.nih.gov/34383430/).
- Turcotte A, Achi S, Mamlouk O, Mandayam S. Electrolytes disturbances in cancer patients. *Curr Opin Nephrol Hypertens.* 2022 1 Sep;31(5):425-34. doi: [10.1097/MNH.0000000000000819](https://doi.org/10.1097/MNH.0000000000000819). PMID: [35894276](https://pubmed.ncbi.nlm.nih.gov/35894276/).
- Ferreira A, da Silva JB, Chuva MT, Costa JM, Pereira D, Brito-da-Silva J. Challenges of renal function assessment in breast cancer patients treated with abemaciclib: A case report. *Cureus.* 2024 25 Aug;16 (8). doi: [10.7759/cureus.67714](https://doi.org/10.7759/cureus.67714).
- Berardi, R., Torniai, M., Lenci, E., Pecci, F., Morgese, F. & Rinaldi, S. Electrolyte disorders in cancer patients: A systematic review. *Journal of Cancer Metastasis and Treatment*, 2019, 79. DOI: [10.20517/2394-4722.2019.008](https://doi.org/10.20517/2394-4722.2019.008).
- Tadesse FA, Leminie AA. Effects of Adriamycin-cytosin chemotherapy on hematological and electrolyte parameters among breast cancer patients. *Front Oncol.* 2023 2 May; 13:1103013. doi: [10.3389/fonc.2023.1103013](https://doi.org/10.3389/fonc.2023.1103013). PMID: [37205205](https://pubmed.ncbi.nlm.nih.gov/37205205/).
- Vázquez, M., Mikhelson, K., Piepponen, S., Rämö, J., Sillanpää, M. et al. Determination of Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, and Cl<sup>-</sup> ions in wood pulp suspension using ion-selective electrodes. *Electroanalysis*, Sep 2001; 13 (13), 1119-1124. DOI: [10.1002/1521-4109\(200109\)13:13<1119::AID-ELAN1119>3.0.CO;2-M](https://doi.org/10.1002/1521-4109(200109)13:13<1119::AID-ELAN1119>3.0.CO;2-M).
- de Almeida, M.L., Saatkamp, C.J., Fernandes, A.B., Pinheiro, A.L.B. & Silveira, L., Jr. Estimating the concentration of urea and creatinine in the human serum

- of normal and dialysis patients through Raman spectroscopy. *Lasers in Medical Science*, 2016 Sep;31(7), 1415-1423. DOI: [10.1007/s10103-016-2003-y](https://doi.org/10.1007/s10103-016-2003-y). Epub 8 July 2016. PubMed: [27393683](https://pubmed.ncbi.nlm.nih.gov/27393683/).
13. Alem A, Edae CK, Kelta Wabalo E, Abera Tareke A, Ayalew Bedanie A, Reta W et al. Factors influencing the occurrence of electrolyte disorders in cancer patients. *SAGE Open Med*. 2021 Oct; 9: 20503121211052861. doi: [10.1177/20503121211052861](https://doi.org/10.1177/20503121211052861). PMID: [34691474](https://pubmed.ncbi.nlm.nih.gov/34691474/). PMCID: [PMC8532243](https://pubmed.ncbi.nlm.nih.gov/PMC8532243/).
  14. Van der Slikke, E.C., Star, B.S., de Jager, V.D., Leferink, M.B.M., Klein, L.M., Quinten, V.M., Olgers, T.J., Ter Maaten, J.C. & Bouma, H.R.A high urea-to-creatinine ratio predicts long-term mortality independent of acute kidney injury among patients hospitalized with an infection. *Scientific Reports*, 2020; 10, 15649. DOI: [10.1038/s41598-020-72815-9](https://doi.org/10.1038/s41598-020-72815-9), PubMed: [32973256](https://pubmed.ncbi.nlm.nih.gov/32973256/).
  15. Statlender, L., Shochat, T., Robinson, E., Fishman, G., Hellerman-Itzhaki, M., Bendavid, I., Singer, P. & Kagan, I. Urea to creatinine ratio as a predictor of persistent critical illness. *Journal of Critical Care*, 2024; 83, 154834. DOI: [10.1016/j.jcrc.2024.154834](https://doi.org/10.1016/j.jcrc.2024.154834), PubMed: [38781812](https://pubmed.ncbi.nlm.nih.gov/38781812/).
  16. Yanase, Y., Bando, H., Sato, R., Matsuo, T., Ueda, A., Okazaki, M., Hashimoto, S., Iguchi-Manaka, A. & Hara, H. Recurrent severe hypocalcemia following chemotherapy regimen changes in advanced breast cancer: Two case reports. *Journal of Medical Case Reports*, 2024; 18, 150. DOI: [10.1186/s13256-024-04478-3](https://doi.org/10.1186/s13256-024-04478-3), PubMed: [38523303](https://pubmed.ncbi.nlm.nih.gov/38523303/).
  17. Lumachi, F. & Basso, S.M. Cancer and hypercalcemia. In *Handbook of Cancer and Immunology* (2023, 29 Jan), (pp. 1-23). Springer International Publishing: Cham, Germany. DOI: [10.1007/9](https://doi.org/10.1007/9).
  18. Majeed I, Ammanuallah R, Anwar AW, Rafique HM, Imran F. Diagnostic and treatment delays in breast cancer in association with multiple factors in Pakistan. *East Mediterr Health J*. 2021 Jan 23;27(1):23-32. doi: [10.26719/emhj.20.051](https://doi.org/10.26719/emhj.20.051). PMID: 33538316.
  19. Košec A, Hergešić F, Matovinović F, Rašić I, Vagić D, Bedeković V. Identifying early postoperative serum parathyroid hormone levels as predictors of hypocalcaemia after total thyroidectomy: A prospective non-randomized study. *Am J Otolaryngol*. 2020 May-Jun;41(3):102416. doi: [10.1016/j.amjoto.2020.102416](https://doi.org/10.1016/j.amjoto.2020.102416), [10.1016/j.amjoto.2020.102416](https://doi.org/10.1016/j.amjoto.2020.102416). Epub 2020 Feb 4. PMID: [32046865](https://pubmed.ncbi.nlm.nih.gov/32046865/)
  20. Armenta-Guirado BI, González-Rocha A, Mérida-Ortega Á, López-Carrillo L, Denova-Gutiérrez E. Lifestyle Quality Indices and Female Breast Cancer Risk: A Systematic Review and Meta-Analysis. *Adv Nutr*. 2023 Jul;14(4):685-709. doi: [10.1016/j.advnut.2023.04.007](https://doi.org/10.1016/j.advnut.2023.04.007), [10.1016/j.advnut.2023.04.007](https://doi.org/10.1016/j.advnut.2023.04.007). Epub 2023 Apr 20. PMID:[37085092](https://pubmed.ncbi.nlm.nih.gov/37085092/). ; PMCID: [PMC10334144](https://pubmed.ncbi.nlm.nih.gov/PMC10334144/)