

# Effect of Chemotherapy on Liver and Kidney Functions in Breast Cancer Patients in Western Libya

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**Abstract: Background:** Chemotherapy targets rapidly dividing cells. While effective against cancer, it inadvertently damages healthy cells, leading to various systemic side effects. **Objectives:** This study evaluated changes in biochemical variables including liver enzymes (ALT, AST, ALP), renal markers (urea, creatinine, uric acid), and electrolytes in breast cancer patients at the National Cancer Institute of Sabratha. **Materials and Methods:** A comparative analysis was conducted involving 150 patients undergoing treatment and 100 healthy controls. Data were extracted from medical records and analyzed using SPSS to determine statistical significance. **Results:** Post-chemotherapy data revealed a significant increase ( $P < 0.01$ ) in liver enzyme activities, concentrations of serum urea, creatinine, and uric acid. Additionally, sodium and chloride levels decreased significantly, while potassium levels rose. **Conclusions:** Chemotherapy induces marked biochemical alterations. These changes are significantly more pronounced following treatment compared to pre-treatment levels, highlighting the drug's impact on hepatic and renal functions.

Keywords—Chemotherapy; Liver function; Kidney function; Breast cancer; National Oncology Institute in Sabratha; Western Libya

## 1. INTRODUCTION (Heading 1)

Despite significant advances in diagnostic and treatment methods, chemotherapy remains a cornerstone of many breast cancer cases, whether as adjuvant therapy after surgery, neoadjuvant therapy before surgery, or palliative care in advanced stages [1]. Chemotherapy works by targeting rapidly dividing cells, including cancer cells, but it also affects rapidly dividing healthy cells in the body, leading to a wide range of side effects [2]. Doxorubicin and cyclophosphamide are among the most important drugs recently used to treat patients with advanced breast cancer [3]. Cancer drugs target and precisely destroy cancer cells, which is the majority of anticancer therapies. However, this treatment also destroys precursor cells for healthy blood cells in the bone marrow [4, 5]. The combined treatment of breast cancer with doxorubicin and cyclophosphamide affects various biological parameters, leading to physiological abnormalities [3]. Chemotherapy can affect the functions of other vital organs, such as the liver and kidneys, due to their role in the metabolism and excretion of chemotherapy drugs. These effects can range from a transient increase in liver enzymes or creatinine to severe organ damage in some cases [6, 7]. Chemotherapy has clear effects on liver and kidney function in women with breast cancer. However, further research is needed to evaluate these effects in different geographic and population contexts, identify factors influencing the severity of these complications, and develop effective intervention strategies to improve patient outcomes and quality of life [8].

A study involving 178 participants at the Felege-Hiwot Comprehensive Specialist Hospital, including 66 women with benign breast tumors, 23 with malignant tumors, and 89 healthy women, showed that patients with breast cancer had significantly higher serum uric acid concentrations ( $6.84 \pm 2.54$ ) ( $p < 0.05$ ). Compared to healthy women, patients with malignant tumors had a 5.53-fold higher risk of hyperuricemia and a 4-fold higher risk of uremia Values [9]. Siriwardana *et al.* [10] and Lin *et al.* [11] studied the effect of modified typical chemotherapy doses in Sri Lanka on liver and kidney function in breast cancer patients was investigated. Seventy-five breast cancer patients with normal liver and kidney function were examined who were treated with doxorubicin, cyclophosphamide, and paclitaxel chemotherapy at the Oncology Clinic of UHKDU University. Mean serum sAST, sALT, and creatinine levels were 27.57 U/L, 31.32 U/L, and 0.71 mg/dL, respectively, before the start of 16 cycles of chemotherapy. Mean sAST and sALT levels increased significantly over the course of treatment ( $p < 0.05$ ), while mean creatinine levels did not change significantly from baseline ( $p > 0.05$ ). The study found a significant positive correlation between the chemotherapy cycle and serum sAST, sALT, and creatinine levels.

A study by Lin *et al.* [11] found that elevated liver enzymes were common after chemotherapy for breast cancer and that some Chemotherapy drugs carry a higher risk of liver damage. The results of Wang *et al.* [12] indicated that some chemotherapy protocols can lead to a decline in kidney function, necessitating close monitoring.

The results of the study by Tadesse & Leminie [13] showed a significant decrease in mean serum sodium ( $\text{Na}^+$ ) concentration and a significant increase in mean serum

potassium (K<sup>+</sup>) concentration in patients treated with Adriamycin-Cytosin compared to untreated patients.

Given the prevalence of breast cancer and the increasing use of chemotherapy in its treatment, understanding the effects of this treatment on liver and kidney function has become crucial. Therefore, this study aims to evaluate these effects in breast cancer patients receiving chemotherapy, with the goal of improving care and developing strategies to mitigate these side effects.

**2. Objectives**

Due to the scarcity of studies demonstrating the effect of chemotherapy on biochemical variables in breast cancer patients in the Western region, and the current limited published studies on the effects of chemotherapy on these variables in breast cancer patients, this study was conducted. At the National Cancer Institute in Sabratha, this study aimed to investigate the effect of chemotherapy on serum levels of liver enzymes, urea, creatinine, uric acid, sodium, potassium, and chloride ions in breast cancer patients undergoing chemotherapy at the institute.

**3. Materials and Methods**

**3.1. Study Design**

This study was conducted on 150 breast cancer patients undergoing chemotherapy at the National Cancer Institute in Sabratha, and 100 healthy women without any chronic diseases served as a control group. The ages of the participants ranged from 25 to 80 years. Ethical approval was obtained from the National Cancer Institute in Sabratha to conduct the study.

**3.2. Blood Test Collection**

Blood tests were collected from the patient records of the participating patients undergoing chemotherapy. These tests included measuring serum levels of urea, creatinine, uric acid, and liver function enzymes (ALT, AST, and ALP).

**3.3. Statistical Analysis**

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS) (version 25) via one-way analysis of variance (ANOVA). Results are expressed as mean ± standard error. The probability level ( $P < 0.05$ ,  $P < 0.01$ ) is considered significant in all statistical tests.

**4. Results**

**4.1. Effect of Chemotherapy on the Activities of Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and Alkaline Phosphatase (ALP) in Blood Serum**

The results shown in Table 1 & Figure. 1 illustrate the effect of chemotherapy on the activities of ALT, AST, and ALP in blood serum. A significant increase ( $P < 0.01$ ) was observed in ALT activity before chemotherapy ( $23.29 \pm 0.11$ ) and after chemotherapy ( $29.8 \pm 0.19$ ) compared to the control group ( $18.5 \pm 0.14$ ). ALT activity was significantly increased ( $P < 0.01$ ) after chemotherapy ( $23.29 \pm 0.11$ ) compared to before chemotherapy ( $23.29 \pm 0.11$ ).

We also observed a significant increase ( $P < 0.01$ ) in serum AST activity before chemotherapy ( $24.81 \pm 0.15$ ) and after

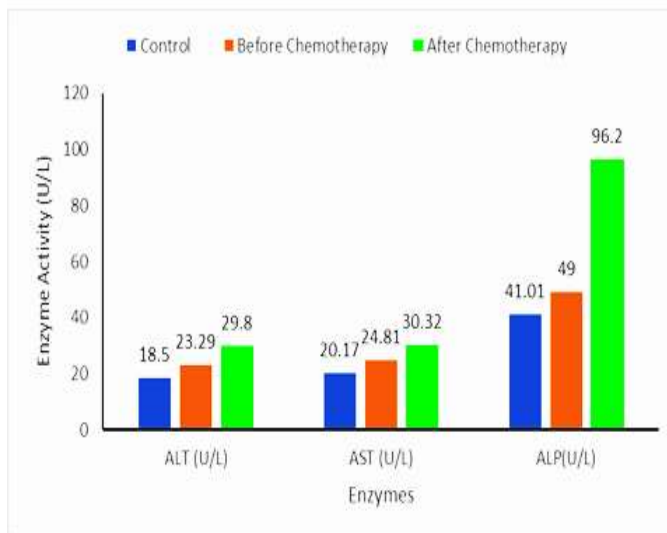
chemotherapy ( $30.32 \pm 0.10$ ) compared to the control group ( $20.17 \pm 0.12$ ). Serum AST activity also increased significantly ( $P < 0.01$ ) after chemotherapy ( $30.32 \pm 0.10$ ) compared to before chemotherapy ( $23.29 \pm 0.11$ ) (Table 1 & Figure. 1).

Furthermore, a significant increase ( $P < 0.01$ ) was observed in serum alkaline phosphatase activity before chemotherapy ( $49.00 \pm 0.23$ ) and after chemotherapy ( $96.2 \pm 0.21$ ) compared to the control group ( $41.01 \pm 0.15$ ). Serum alkaline phosphatase activity increased significantly ( $P > 0.01$ ) after chemotherapy ( $96.2 \pm 0.21$ ) compared to before chemotherapy ( $49.00 \pm 0.23$ ) (Table 1 & Figure. 1).

**Table 1. Effect of chemotherapy on activities of serum ALT , AST, and ALP**

Groups	Control	Before Chemotherapy	After Chemotherapy
	Mean ± SE	Mean ± SE	Mean ± SE
ALT (U/L)	18.5± 0.14	23.29 ± 0.11**	29.8±0.19###**
AST (U/L)	20.17± 0.12	24.81 ± 0.15**	±0.10###** 30.32
ALP(U/L)	41.01±0.15	49.00±0.23**	96.2 ±0.21###**

*\*\**: Significant at  $P < 0.01$  compared with the control; *##*: Significant at  $P < 0.01$  compared before Chemotherapy.



**Figure 1. Effect of chemotherapy on activities of serum ALT , AST, and ALP**

**4.2. Effect of Chemotherapy on Serum Urea, Creatinine, and Uric Acid Concentrations**

The results indicate a significant increase ( $P < 0.01$ ) in serum urea concentration (mg/dL) before chemotherapy ( $20.12 \pm 0.09$ ) and after chemotherapy ( $26.3 \pm 0.10$ ) compared to the control group ( $12.5 \pm 0.16$ ). Serum urea concentration

increased significantly ( $P < 0.01$ ) after chemotherapy ( $26.3 \pm 0.10$ ) compared to before chemotherapy ( $20.12 \pm 0.09$ ) (Table 2 & Figure 2).

We observed a significant increase ( $P < 0.01$ ) in serum creatinine concentration (mg/dL) before chemotherapy ( $0.9 \pm 0.06$ ) and after chemotherapy ( $2.27 \pm 0.12$ ) compared to the control group ( $0.6 \pm 0.02$ ). Serum creatinine concentration (mg/dL) also increased significantly ( $P < 0.01$ ) after chemotherapy ( $2.27 \pm 0.12$ ) compared to before chemotherapy ( $0.9 \pm 0.06$ ) (Table 2 & Figure 2).

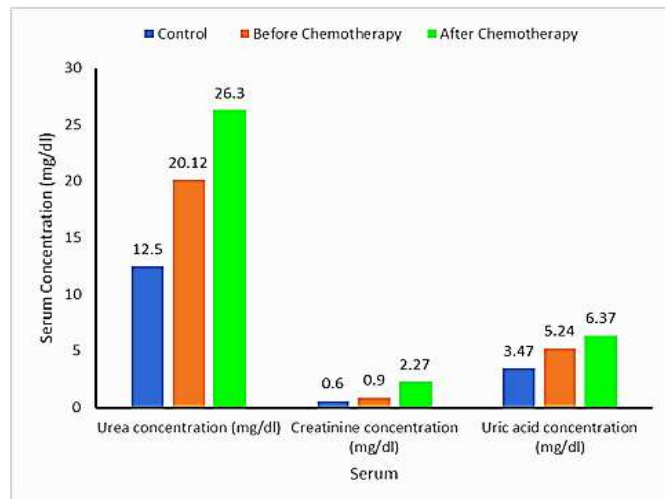
Also, Table 2 & Figure 2 show a significant increase ( $P < 0.01$ ) in serum uric acid concentration (mg/dL) before chemotherapy ( $5.24 \pm 0.10$ ) and after chemotherapy ( $6.37 \pm 0.16$ ) compared to the control group ( $3.47 \pm 0.14$ ). Serum uric acid concentration (mg/dl) increased significantly ( $P < 0.01$ ) after chemotherapy ( $6.37 \pm 0.16$ ) compared to before chemotherapy ( $5.24 \pm 0.10$ ).

**Table 2. Effect of chemotherapy on concentrations of serum urea , creatinine, and uric acid**

Parameters	Control	Before Chemotherapy	After Chemotherapy
	Mean ± SE	Mean ± SE	Mean ± SE
Urea concentration (mg/dl)	12.5 ± 0.16	20.12 ± 0.09**	26.3 ± 0.10###**
Creatinine concentration (mg/dl)	0.6 ± 0.02	0.9 ± 0.06**	2.27 ± 0.12###**
Uric acid concentration (mg/dl)	3.47 ± 0.14	5.24 ± 0.10**	6.37 ± 0.16###**

**4.3. Effect of Chemotherapy on Serum Sodium, Potassium, and Chloride Ion Concentrations**

Statistical analysis of the results showed a significant decrease ( $P < 0.01$ ) in serum sodium and chloride ion concentrations (mEq/L) before chemotherapy ( $138 \pm 0.26$ ,  $103 \pm 0.08$ ) and after chemotherapy ( $134 \pm 0.21$ ,  $100 \pm 0.06$ ) compared to the control group ( $141 \pm 1.08$ ,  $105.8 \pm 0.25$ ), respectively. The significant decrease ( $P < 0.01$ ) in serum sodium and chloride ion concentrations (mEq/L) after chemotherapy ( $134 \pm 0.21$ ) and ( $100 \pm 0.06$ ) compared to before chemotherapy ( $138 \pm 0.26$ ) and ( $103 \pm 0.08$ ), respectively (Table 3). Conversely, serum potassium ion concentration (mEq/L) increased significantly ( $P < 0.01$ ) before chemotherapy ( $4.4 \pm 0.01$ ) and after chemotherapy ( $4.99 \pm 0.03$ ) compared to the control group ( $4.1 \pm 0.05$ ). The significant increase ( $P < 0.01$ ) in serum potassium ion concentration (mEq/L) after chemotherapy ( $4.99 \pm 0.03$ ) compared to before chemotherapy ( $4.4 \pm 0.01$ ) (Table 3).



**Figure 2. Effect of chemotherapy on concentrations of serum urea , creatinine, and uric acid**

**Table 3. Effect of chemotherapy on concentrations of serum Na+ , K+, and Cl-**

Parameters	Control	Before Chemotherapy	After Chemotherapy
	Mean ± SE	Mean ± SE	Mean ± SE
Na+ concentration (mEq/L)	141 ± 1.08	138 ± 0.26**	134 ± 0.21###**
K+ concentration (mEq/L)	4.1 ± 0.05	4.4 ± 0.01**	4.99 ± 0.03###**
Cl- concentration (mEq/L)	105.8 ± 0.25	103 ± 0.08**	100 ± 0.06###**

\*\* : Significant at  $P < 0.01$  compared with the control; #: Significant at  $P < 0.01$  compared before Chemotherapy .

**5. Discussion**

Chemotherapy is an important treatment method used in the management of breast cancer patients. Blood biochemical variables show the chemicals secreted or produced during metabolic processes in the body, and these substances provide vital information about the functions of various organs. Numerous studies have demonstrated that chemotherapy has both short-term and long-term effects on organ function [10, 14, 15]. Chemotherapy remains the preferred treatment for hundreds of thousands of patients diagnosed with cancer annually [16]. During chemotherapy, all blood biochemistry tests are routinely performed, along with other breast cancer treatments, to check for chemicals that are released or produced from body tissues during the breakdown

(metabolism) of certain substances [17-19]. This study was conducted on a sample of breast cancer patients undergoing chemotherapy at the National Cancer Institute in Sabratha. Data were collected from the patient records of those receiving chemotherapy, including biochemical measurements (urea, creatinine, uric acid, and liver function enzymes (ALT, AST, and ALP) in serum) to assess the effect of chemotherapy on serum biochemical variables.

Blood chemistry analysis provides valuable information about the function of the kidneys, liver, and other organs. Abnormal blood chemistry results can indicate the spread of breast cancer to the bones, kidneys, or liver [19-21]. Liver function tests primarily rely on the enzyme levels of aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase [19, 22, 23].

The results of the current study showed a significant increase ( $P < 0.01$ ) in the activities of the ALT and AST enzymes, and ALP enzymes before and after chemotherapy compared to the control group. The ALT and ALP enzyme activities were significantly increased ( $P < 0.01$ ) after chemotherapy compared to before. These results are consistent with those of a cross-sectional study by Siriwardana *et al.* [10] on 75 breast cancer patients who received a chemotherapy regimen of doxorubicin, cyclophosphamide, and paclitaxel, with normal liver function at the start of treatment, at the Oncology Clinic of the University of Hong Kong. Before the start of the 16-cycle chemotherapy, the mean serum AST and ALT levels were 27.57 U/L and 31.32 U/L, respectively. A statistically significant increase ( $P < 0.05$ ) in the mean AST and ALT levels was observed. Compared to pre-chemotherapy levels, elevated serum sAST and sALT levels indicated a statistically significant short-term effect on liver function after standard chemotherapy of choice, similar to other studies. However, this effect was not clinically significant [24].

Several studies have found significant differences in kidney function after chemotherapy [25, 26]. Chemotherapy regimens used to treat breast cancer, including cyclophosphamide, adriamycin, and methotrexate, have been shown to be nephrotoxic [27-29].

The results of the current study show a significant increase ( $P < 0.01$ ) in serum urea, creatinine, and uric acid concentrations before and after chemotherapy compared to the control group. Urea concentrations were particularly high. Serum creatinine and uric acid levels were significantly increased ( $P < 0.01$ ) after chemotherapy compared to before treatment. These findings are consistent with the study by Hurria *et al.* [30], which demonstrated elevated creatinine levels after chemotherapy in elderly breast cancer patients, and that this increase was associated with increased hematologic toxicity due to decreased chemotherapy clearance. Similarly, the study by Obadipe *et al.* [31] showed a significant increase in mean creatinine and urea levels recorded after chemotherapy, indicating nephrotoxicity resulting from cancer chemotherapy. It is known that chemotherapy drugs such as cyclophosphamide, adriamycin, and 5-fluorouracil (CAF) negatively affect biochemical variables, causing hyperuricemia [32]. Hyperuricemia can

lead to renal dysfunction due to increased cell turnover (tumor lysis syndrome) in cancer treatment [33].

Many side effects, including Kidney toxicity and electrolyte imbalances remain a serious clinical challenge. Given the kidneys' essential roles in the normal functioning of body systems and the maintenance of electrolyte balance, assessing kidney function and electrolyte levels before each chemotherapy cycle will aid in the early detection of kidney toxicity and electrolyte imbalance [31].

The current study recorded a significant decrease ( $P < 0.01$ ) in serum sodium and chloride ion concentrations before and after chemotherapy compared to the control group. The significant decrease ( $P < 0.01$ ) in serum sodium and chloride ion concentrations was even greater after chemotherapy compared to before chemotherapy, while serum potassium ion concentrations were significantly higher ( $P < 0.01$ ) both before and after chemotherapy compared to the control group. The significant increase ( $P < 0.01$ ) in serum potassium ion concentration was even greater after chemotherapy compared to before chemotherapy. This finding is consistent with previous studies [13, 34]. The study of Obadipe *et al.*, [31] demonstrated a significant decrease in sodium and chloride ion levels following chemotherapy, indicating disturbances in sodium, potassium, and chloride ion levels caused by chemotherapy in cancer treatment participants. Serum sodium levels were significantly reduced in breast cancer patients treated with AC in this study [13].

This decrease in electrolyte levels after chemotherapy suggests electrolyte imbalance or a chemotherapy-associated disturbance in the study participants. The observed decrease in serum electrolyte levels following chemotherapy may be due to increased renal loss, commonly known as electrolyte wastage. The kidneys are a key organ involved in electrolyte balance. Impairing the kidney's functional units through chemical agents negatively affects critical kidney processes, including glomerular filtration, which in turn disrupts electrolyte balance [31, 35]. Electrolyte imbalance is a common problem in cancer patients and may be associated with ongoing chemotherapy [31, 36]. The development of these chemotherapy-associated disorders can lead to dysfunction in multiple organs if not promptly addressed [31, 37]. Therefore, early detection and management of these disorders are crucial in the comprehensive care of cancer patients [31]. Decreased serum sodium levels may be attributed to the effect of chemotherapy drugs that impair the kidney's ability to regulate sodium balance. A previous study revealed that oxidative stress induced by chemotherapy was the cause of decreased serum sodium levels [38]. Adriamycin has an anthracycline structure and produces reactive oxygen species (ROS), leading to DNA damage in renal epithelial cells responsible for electrolyte processing [39, 40]. These anticancer drugs often cause a variety of side effects and stimulate ROS production [41]. Oxidative stress inhibits sodium ion channels ( $\text{Na}^+/\text{K}^+$  ATPase) and sodium ion channels in the apical membrane of renal tubular epithelial cells [42]. The kidneys may be susceptible to the development of drug toxicity due to their role in the metabolism and

excretion of toxic substances. The proximal portion of the nephron, in particular, has a high capacity for drug uptake via phagocytosis or transport proteins [39, 43]. This high rate of conduction and uptake leads to high intracellular concentrations of drug metabolites and to renal expression of tumor necrosis factor A (TNF-A), resulting in the formation of potentially toxic metabolites and reactive oxygen species [39]. Oxidative stress also causes mitochondrial dysfunction, decreased adenosine triphosphate (ATPase) activity, impaired solute transport, and cation imbalance [43]. Consequently, sodium and water reabsorption decreases, while salt and water excretion increases, leading to polyuria [39, 43].

The proximal portion of the nephron is highly receptive to drugs via phagocytosis or transport proteins [39, 43]. The results of the current study indicate a significant increase in mean serum potassium levels in breast cancer patients following chemotherapy, consistent with a previous study [34]. Chemotherapy-induced tumor lysis syndrome may also contribute to the elevated serum potassium levels. Chemotherapy-induced tumor lysis is characterized by hyperkalemia and hyperuricemia [44, 45] (Lofterod et al., 2018). A possible explanation for the increased serum potassium levels in chemotherapy-treated breast cancer patients is decreased urinary potassium excretion [13].

## 6. Conclusion

This study concludes that there is a significant increase ( $P < 0.01$ ) in the activities of the ALT and AST enzymes, and ALP enzyme, both before and after chemotherapy compared to the control group. The activities of ALT and AST enzymes, and ALP, were significantly increased ( $P < 0.01$ ) after chemotherapy compared to before. Similarly, there is a significant increase ( $P < 0.01$ ) in serum urea, creatinine, and uric acid concentrations before and after chemotherapy compared to the control group. Serum urea, creatinine, and uric acid concentrations were significantly increased ( $P < 0.01$ ) after chemotherapy compared to before. Serum potassium concentration increased significantly ( $P < 0.01$ ) both before and after chemotherapy compared to the control group. The significant increase ( $P < 0.01$ ) in serum potassium concentration was even greater after chemotherapy compared to before. Conversely, serum sodium and chloride concentrations decreased significantly ( $P < 0.01$ ) both before and after chemotherapy compared to the control group. The significant decrease ( $P < 0.01$ ) in serum sodium and chloride concentrations was even greater after chemotherapy compared to before. Therefore, continuous monitoring of liver enzyme activity (ALT, AST, ALP) and kidney function (urea, creatinine, and uric acid) is essential before and during treatment. Regular monitoring of serum electrolyte balance (sodium, chloride, and potassium) is also necessary, along with appropriate measures to correct sodium and chloride deficiency and potassium excess. Significant biological and laboratory changes (such as elevated kidney and liver function markers) may necessitate adjustments to chemotherapy doses or protocols to reduce toxicity and improve patients' quality of life. Long-term follow-up studies are essential to assess the

impact of chemotherapy-induced changes in liver and kidney function and electrolyte balance on prognosis and long-term patient quality of life.

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