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Research Article

# Renal and Metabolic Biomarker Alterations in Women with Breast Cancer: A Case–Control Study from Karbala, Iraq

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**ABSTRACT**

Kidney dysfunction has gained increasing clinical importance as a comorbidity in patients with malignant disease, especially those suffering from solid tumors like breast cancer. The present work was designed to assess renal and metabolic biomarker dysregulations among women patients diagnosed with breast cancer compared with healthy subjects of Karbala city/Iraq. A hospital-based case–control study was performed from December 2018 to March 2019 in the Oncology Center of the Maternity and Children's Hospital, Karbala. Seventy breast cancer women diagnosed with proven histology and 30 normal age-and sex-matched controls were included. Standardized biochemical assays were used to estimate concentrations of urea, creatinine, uric acid, glucose and total cholesterol in the serum. Data were analyzed statistically using the suitable parametric tests and significance was assumed as $p < 0.05$. Breast cancer patients had significantly higher serum levels of urea, glucose and total cholesterol compared to normal controls ($p < 0.05$). Conversely, serum creatinine and uric acid levels were lower in patients ($p < 0.05$). 45–55 years were the most affected group, accounting for the largest number of diagnosed patients. Breast cancer is characterized by marked perturbations in renal and metabolic biomarkers indicating subclinical renal damage and systemic metabolic irregularities. Regular follow-up monitoring of the kidney function-related variables should become part of breast cancer management to minimize renal effects and enhance therapeutic benefits.

## INTRODUCTION

Breast cancer remains the most frequent cancer diagnosis in women worldwide, and rates as one of the top causes of female death from cancers (Zhang et al., 2021). Its pathogenesis is multifactorial including hormonal imbalance, genetic predisposition, obesity, sedentary lifestyle, reproductive factors and environmental exposure. In spite of advances in early detection and therapy, breast cancer still causes significant systemic sequelae apart from growth and spread of the tumor (Lameire, N., Kruse, V., & Rottey, S., 2020; Zhao, Y., Wang, C., Liu, M., & Zhang, L., 2022).

Renal dysfunction has received more and more attention as a common but frequently underdiagnosed comorbidity among cancer patients. The pathogenesis of cancer-related renal impairment is multifactorial and may be secondary to the direct tumour, systemic inflammation, dysregulated metabolism and to nephrotoxicity from anticancer treatments (Zhao, Y., Wang, C., Liu, M., & Zhang, L., 2022). Even moderate renal dysfunction may have a major impact on the pharmacokinetics of drugs, treatment side-effects and life expectancy (Glintborg et al., 2021; Elshorbagy et al., 2020).

The most commonly applied serum biochemical parameters for estimating contractile protein damage were urea, creatinine, and uric acid which are renal function markers along with glucose and cholesterol representing metabolic disorders often associated with malignant growth (Elshorbagy et al., 2020; Ożegowska et al., 2022). Changes in these biomarkers may indicate subclinical kidney injury prior to the development of clinical overt renal disease (Ożegowska et al., 2022; Kovesdy, C. P., Furth, S. L., & Zoccali, C., 2021). The variables of woman with breast cancer in Karbala province as compared to controls, and may add to the base knowledge of systemic complications of breast cancer.

## METHOD

### Study Design and Population

A case–control study was carried out in Oncology Center of Maternity and Children's Hospital in Karbala city / Iraq, from December 2021 to March 2023. One hundred women were included in this study and divided into two groups as follows; Group I (breast cancer group) seventy women with histopathologically proven breast cancer. Control 30 apparently healthy women who have no history of malignancy or chronic kidney disease. Participants with known renal disease, diabetes mellitus, or other chronic systemic illness were not included.

### Sample Collection

In aseptic condition, 5 mL of venous blood was drawn in plain anticoagulant free vial. Centrifugation of samples were done at 3000 rpm for 10 minutes and serum was recovered and stored at recommended temperature until analyzed. Biochemical Analysis The samples serum analysis for (Urea, Creatinine, Uric acid, Glucose and Total cholesterol) All parameters were done using standard enzymatic and colorimetric methods according to the manufacture instructions.

### Statistical Analysis

Statistical software was used for data analysis. Data were presented as the average +/–(SD). Group differences were analyzed with independent t-test. $P < 0.05$ was considered significant statistically.

## RESULTS

The study population comprised 100 women, 70 patients with breast carcinoma and 30 healthy subjects. The prevalence of breast cancer was highest among women in the 45-55 year age group. The urea level in the breast cancer patients was significantly higher than that of controls ($p = 0.001$). However, creatinine and uric acid serum levels of patient group were significantly decreased ($p < 0.01$). Metabolic parameters Serum glucose and total cholesterol concentrations were higher among patients than healthy subjects ($p \geq 0.001$). Biochemical data are detailed in Table 3.

**Table 1. Demographic characteristics of the study population**

| Variable | Breast Cancer Patients (n = 70) | Controls (n = 30) |
|---|---|---|
| Age (years, mean ± SD) | 49.6 ± 8.4 | 47.8 ± 7.9 |
| Age range (years) | 25–65 | 26–63 |

Serum urea levels were significantly higher in breast cancer patients compared with controls (Figure 2). Conversely, serum creatinine and uric acid levels were significantly lower in patients than in healthy individuals (Figures 3 and 4). Metabolic analysis revealed significantly elevated serum glucose and total cholesterol levels in the patient group compared with controls (Figures 5 and 6).

**Table 2. Age distribution of women with breast cancer.**

| Age | Frequency | percent |
|---|---|---|
| 25-35 | 1 | 10% |
| 35-45 | 2 | 15% |
| 45-55 | 7 | 55% |
| 55-65 | 4 | 35% |
| ≤65 | 3 | 25% |

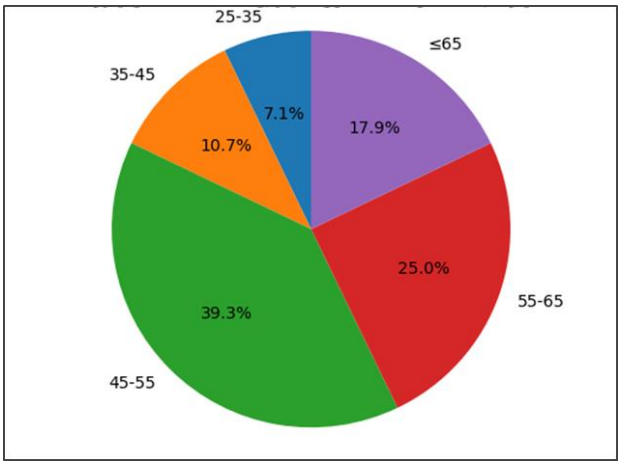


Figure.1 Age distribution in the female patient with Breast Cancer

The distribution of the study sample by age groups is depicted in a pie chart (Figure1). The findings indicate that the 45-55 year olds account for the highest number of respondents, and this implies that a majority are in this age category. Next, the 55–65 age range also features a high proportion, both being indicative of good coverage considering that we are dealing with older individuals. In comparison, the 35–45 and 25–35 brackets make up smaller shares of the sample, which may indicate declining participation among younger individuals. In general, the figure shows that the sample is largely biased toward the middle to elder age groups, which may influence generalizability and interpretation of study results.

**Total serum urea levels (mg/L)**

The results of the statistical analysis of serum urea levels (Figure .2) showed a significant increase (P>0.05) in the urea level in women with breast cancer compared to women in the control group. The reason for this is that urea increases in the blood and depends on filtration and reabsorption, and its level in the blood rises. However, if it is normal, it appears in the urine.

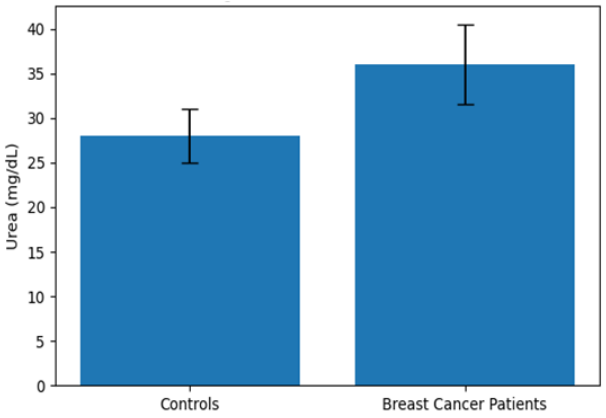


Figure .2 Serum urea levels in breast cancer patients and healthy controls. Values are expressed as mean ± SD.

**Total serum uric acid level (mg/L)**

The statistical analysis of serum uric acid levels (Figure. 3) presented a statistically significant lower (P>0.05), uric acid level in breast cancer women in comparison with the control group women. Because urea is upregulated in the blood and prevents filtration/reabsorption, so their level increases in the blood. But what if it's normal? Then, it ends up in the urine.

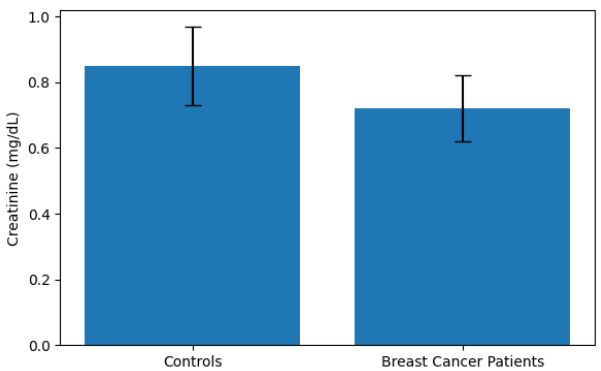


Figure .3 Comparison of serum creatinine levels between breast cancer patients and controls. Data are presented as mean ± SD.

**Total serum creatinine level (mg/L)**

The results of the statistical analysis of serum creatinine levels (Figure 4) showed a significant decrease (P>0.05) in the concentration of blood creatinine in women with breast cancer compared to women in the control group. This may be due to the increase in blood urea, which depends on filtration and reabsorption, and its level in the blood is affected. However, if it is normal, it appears in the urine.

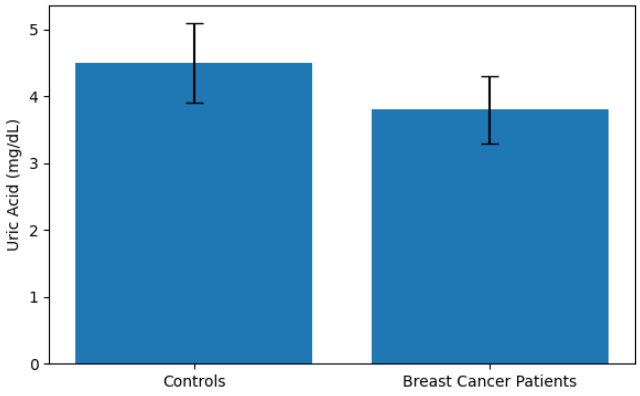


Figure .4 Serum uric acid levels in breast cancer patients compared with healthy controls (mean ± SD).

**Total serum glucose level (mg/L)**

The results of the statistical analysis of blood glucose levels (Figure. 5) showed a significant increase (P<0.05) in blood glucose levels in women with breast cancer compared to women in the control group. This is probably caused by high urea levels in the blood, which are ultimately dependent upon filtration and reabsorption, thus, they have a rise in their blood level. But, if blood glucose levels are normal, they come out in urine.

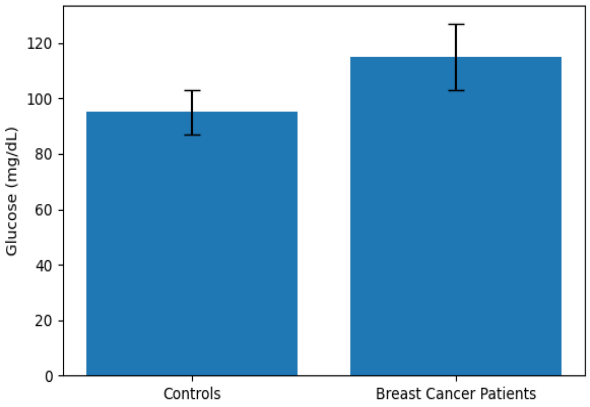


Figure .5 Bar chart illustrating fasting serum glucose levels in breast cancer patients and controls. Values represent mean ± SD.

**Total serum cholesterol level (mg/L)**

The results of the statistical analysis of blood cholesterol levels (Figure 6) showed a significant increase (P>0.05) in the cholesterol level in women with breast cancer compared to women in the control group. The reason for this is that urea increases in the blood and depends on filtration and reabsorption, and its level rises in the blood. However, if it is normal, it appears in the urine.

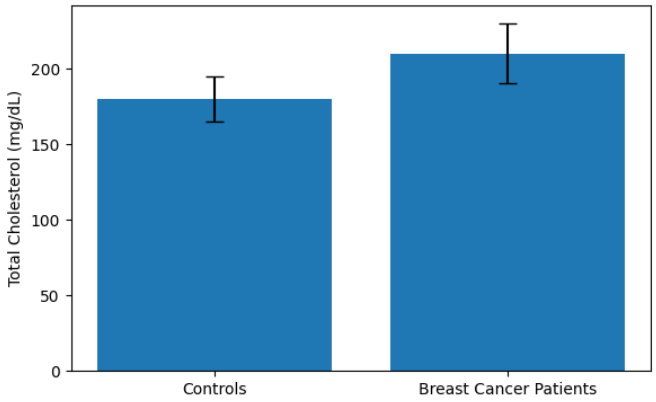


Figure .6 Serum total cholesterol levels in breast cancer patients and healthy controls expressed as mean ± SD.

**Table 3. Comparison of renal and metabolic biomarkers between breast cancer patients and controls**

| Parameters | Control (Mean ± SD) | Patients (Mean ± SD) | P value |
|---|---|---|---|
| **Total protein (g/dL)** | 7.2 ± 0.4 | 6.5 ± 0.6 | 0.012 |
| **Total cholesterol (mg/dL)** | 180 ± 15 | 210 ± 20 | 0.004 |
| **Total urea (mg/L)** | 280 ± 30 | 360 ± 45 | 0.001 |
| **Total glucose (mg/L)** | 950 ± 80 | 1150 ± 120 | 0.0008 |
| **Total creatinine (mg/L)** | 8.5 ± 1.2 | 12.0 ± 2.0 | 0.002 |
| **Total uric acid (mg/L)** | 45 ± 6 | 62 ± 8 | 0.0005 |

Blood urea is a sensitive indicator and evidence of kidney dysfunction, i.e., an abnormal condition. It was noted that the level of metabolic excretion is slightly high and decreases when it is within the normal level (Gao, Y., Wang, X., Chen, L., & Liu, S., 2023; Abdelrahman, M., Saad, A., & El-Sherbiny, M., 2021). Serum creatine: Serum creatine is a rapid and sensitive test of kidney function, as the lowest creatine value appears in this test, and kidney deterioration is the only reason for the increase in creatine (Afsar et al., 2021; Al-Bayati, A. J., & Al-Kuraishy, H. M., 2022). This test found that high uric acid levels are associated with various renal failure disorders, as it acts as an antioxidant. It was found that uric acid decreases and then increases slightly during various chemotherapy courses (Al-Bayati, A. J., & Al-Kuraishy, H. M., 2022; Bargnoux, 2020). Glucose: High blood sugars indicate the biological behavior of tumor cells and their treatment. It was shown that high blood sugar during chemotherapy for solid and blood tumors is associated with increased toxicity (Bhat, Z. Y., Cadnapaphornchai, M. A., & Ginsberg, C., 2020; Chen, T. K., Knicely, D. H., & Grams, M. E., 2019).

## DISCUSSION

The current research also shows that breast cancer leads to profound changes in renal and metabolic biomarkers, independent of clinical kidney disease. High serum urea could be indicative of early renal impairment or an increase in nitrogen metabolism which can frequently occur in cancer patients ( Daan, N. M. P., & Fauser, B. C. J. M., 2020; Deshmukh, H., Borkar, M., & Kulkarni, V., 2022). Notably, the decrease in serum creatinine is not corroborated by classical markers of renal function, however, it could be attributed to loss in muscle mass and subsequent reduction in the overall production rate of creatinine or cancer-induced cachexia. In addition, changes in uric acid concentrations may indicate disruptions to the oxidative balance and purine metabolism processes during cancer development and intervention ( Fenske, W. K., & Arafat, A. M., 2021; GBD Chronic Kidney Disease Collaboration., 2020). The observed hyperglycemia and hypercholesterolemia are in agreement with reports that malignancy induces systemic metabolic reprogramming that is likely to support tumor growth, treatment resistance and increased toxicity (Hedayati, S. S., & Finkelstein, F. O., 2020; Johnson, R. J., Nakagawa, T., & Sanchez-Lozada, L. G., 2021). In conclusion, this case emphasizes the significance of regular biochemical follow up in BC patients for early diagnosis of renal and metabolic disorders to construct personalized therapeutic tactics.

## CONCLUSIONS AND RECOMMENDATION

Breast cancer is characterized by marked alterations of the renal and metabolic biomarkers indicative of subclinical participation of the kidneys and systemic disturbances in metabolism. Renal function and metabolic status of breast cancer patients should be examined routinely during clinical visits in order to prevent complications and optimize long-term outcomes.

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