

Evaluation of Urea, Creatinine, and Total Protein in Iraqi Women with Breast Cancer Patients in Pre- and Postmenopausal

Evaluation of Urea, Creatinine, and Total Protein in Iraqi Women with Breast Cancer

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ABSTRACT

Objective: To evaluate the relationship between Iraqi women subjected to breast cancer and their serum levels of urea, creatinine, total protein and body mass index.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Anbar Cancer Center, Iraq from 1st October 2023 to 30th June 2024.

Methods: One hundred women's (60 women's with breast cancer and 40 women healthy) were enrolled. They were divided in to two groups (pre-menopausal and post-menopausal). Concentration of serum urea, creatinine and total protein were determined by enzymatic colorimetric method using Semi-Auto Analyzer instrument (spectrophotometry).

Results: The Urea and creatinine concentrations showed significant differences between the breast cancer patients and healthy controls, while total protein and body mass index did not show a significant difference compared to the control group at premenopausal. At post-menopausal all parameter showed a significant difference compared to the control groups. The parameters were compared based on the body mass index and significant differences were observed compared to the control group in pre- and post-menopausal status.

Conclusion: Renal functions test can be considered as risk factors for women's with breast cancer.

Key Words: Serum urea, Serum creatinine, Serum total protein, Breast cancer, Body mass index

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INTRODUCTION

Breast cancer (BC) is the most prevalent malignancy among women and one of the leading causes of cancer-related mortality in Iraq.¹ Breast cancer is the second most common cancer globally, after lung cancer.² Tumors come in two primary varieties: benign and malignant.³ Metastasis is the process by which malignant tumors spread to other parts of the body. This method allows tumors to spread to different areas of the body. Another name for tumours that are cancerous is malignant tumours.

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Unlike many other malignancies, blood cancers like leukemia typically do not develop into solid tumors. Noncancerous tumors don't invade other tissues which are known as metastasis.⁴ Cancer cells that enter the blood or lymphatic system have the potential to metastasis, or spread, to other areas of the body. One component of the immune system in your body is the lymphatic system. Lymph nodes are microscopic glands about the size of beans that are a part of a system of tubes and organs that collect and move clear lymph fluid from the body's tissues into the bloodstream. Waste materials from tissues and immune system cells are present in the clear lymph fluid that fills the lymphatic tubes. The breast is drained of extra lymph fluid by the lymph vessels. Breast cancer may result from the facilitation of cell entrance and proliferation in lymph nodes by lymph veins.⁵

In 2016, about 650 million adults were obese and approximately 1.9 billion were overweight. Obesity and the risk of breast cancer are significantly correlated. Because adipose tissue serves as the primary reservoir for estrogen production after menopause, premenopausal obesity and premature menopause reduce the risk, whereas postmenopausal obesity increases it. In postmenopausal women who are overweight, elevated blood estrogen levels and

enhanced peripheral estrogen generation have been identified as important risk factors for breast cancer.⁶ The blood chemistry panel (BCP) is a routine test used to assess a range of chemical components created during the breakdown or metabolism of certain substances or discharged from bodily tissues. The BCP quantifies the blood's concentrations of chemicals, enzymes, and organic waste products. It assesses the condition and appropriate operation of different organs throughout chemotherapy. According to the aberrant blood chemistry results, breast cancer may have progressed to the liver, kidney, or bone. Few studies have examined the relationships between kidney function tests (KFTs) and liver function tests (LFTs) and breast cancer mortality.⁷

A patient with BC who has normal kidney function runs the risk of developing renal failure because of hypercalcemia, tumor lysis syndrome (TLS), and paraneoplastic syndromes.⁸

Many chemotherapy drugs must be metabolized and eliminated by the kidneys in good functioning order.⁹ A common consequence for patients with solid tumors is renal impairment. Approximately 50-60% of individuals with solid tumor malignancies are thought to have a glomerular filtration rate (GFR) that is below normal, with creatinine clearance typically falling between 60 and 90 mL/min.¹⁰

Breast cancer may have a variety of effects on renal function. These processes are closely linked to paraneoplastic syndrome. Antigen antibody complex accumulation in tubular and glomerular structures, fluid and electrolyte imbalance, and ectopic hormone release can all contribute to renal impairment in paraneoplastic disorders.¹¹

Proteins are known to be the fundamental building blocks of all living cells and to be present in a wide range of chemicals, such as hormones, enzymes, and antibodies. Serum protein concentration variations have been linked to the progression of cancer and may be a sign of health issues that could yield crucial diagnostic data.¹² The equilibrium between the rates of protein synthesis and catabolism or loss determines the amount of protein in the serum. The amount of albumin, globulin, fibrinogen, and total protein in the plasma are all measured by a total plasma protein test¹³, which also demonstrates how an organism is really operating.¹⁴

The body mass index (BMI) is a measurement of body fat based on height and weight. According to the International Association for the Study of Obesity, the International Obesity Task Force, and the regional office of the World Health Organization for the Western Pacific Region, normal weight for Asian adults is defined as BMI 18.5 to 22.9 kg/m², overweight as BMI 23 to 24.9 kg/m², and obesity as BMI 25 kg/m² or higher.¹⁵ Mortality increases by 20% for males and 10% for women when body weight is more than 20% over average. Compared to non-obese people, obese

individuals with a BMI of more than 30 kg/m² are more likely to die young.¹⁶ Globally, being overweight or obese ranks as the fifth most common preventable cause of death.¹⁷ According to WHO estimates, problems from overweight and obesity were responsible for 4.5 million deaths globally in 2013.¹⁸

METHODS

This descriptive study was conducted at Anbar Cancer Center, Iraq from 1st October 2023 to 30th June 2024 vide letter 43egr/QM/Approval/rgEEUI3 date 24th September 2023. One hundred women (60 patients and 40 healthy) divided into two groups: group 1 (premenopausal) comprised 25 patients and 23 healthy; and group 2 (postmenopausal) comprised 35 patients and 17 healthy. The venous blood sample was collected and placed in a gel tube for the serum separation (centrifugation at 3000 rpm for 10 min.). Serum samples were stored in the freezer at -20°C until use. Serum urea, creatinine, and total protein were measured using a Semi-Auto Analyzer kit (AGAPPE, Switzerland). The data was analyzed through SPSS-26. A p-value <0.05 was considered significant.

RESULTS

There was a significant increase in serum levels (urea and creatinine) in BC pre- and post-menopausal women as compared to controls ($p \leq 0.001$). There was also an increase in serum level of total protein in BC pre-menopausal but no significant difference ($p > 0.05$), while serum level of total protein in BC post-menopausal showed a significant increase as compared with controls ($p \leq 0.01$). For BMI, there was no significant difference in both pre- and post-menopausal stages compared to the control group ($p > 0.05$) [Table 1].

There was a significant increase in serum levels (urea and creatinine) in BC post-menopausal women as compared to BC pre-menopausal women ($p \leq 0.001$ and $p \leq 0.05$, respectively), while there was an increase in serum levels of total protein in BC post-menopausal women but no significant difference compared to BC pre-menopausal women ($p > 0.05$). Regarding BMI, no significant difference was observed between the two states ($p > 0.05$) [Table 2].

There was a significant increase in serum levels (urea, creatinine, and total protein) in BC premenopausal women as compared to controls ($p \leq 0.05$, $p \leq 0.001$, and $p \leq 0.05$, respectively). Also, there was a significant increase in serum levels (urea and creatinine) in BC postmenopausal women as compared to controls ($p \leq 0.01$, $p \leq 0.05$, respectively), while serum total protein levels showed an increase but no significant difference compared to controls ($p > 0.05$) at BMI 18-24 kg/m². At BMI of 25-29 kg/m², there was a significant increase in serum levels (urea, creatinine, and total protein) in BC premenopausal women as compared to

controls ($p \leq 0.001$, $p \leq 0.001$, and $p \leq 0.05$, respectively), while serum levels (urea and creatinine) showed a significant increase in BC postmenopausal women as compared to controls ($p \leq 0.001$ and $p \leq 0.05$, respectively), except serum total protein level showed an increase compared with the control but was not significant ($p > 0.05$). At BMI of 30-40 kg/m², there was a significant increase in serum levels (urea and

creatinine) as compared to controls ($p \leq 0.001$ and $p \leq 0.05$, respectively), while serum total protein levels showed an increase compared with control but without significance ($p > 0.05$). In BC pre-menopausal women and in BC post-menopausal women, all parameters showed a significant increase as compared to controls ($p \leq 0.001$, $p \leq 0.001$, and $p \leq 0.01$, respectively) [Table 3].

Table No. 1: Comparison of serum of pre- and post-menopausal patients with control group

Groups		Urea (mg/dL)	Creatinine (mg/dL)	Total protein (g/dL)	BMI (kg/m ²)	Age
Pre-menopausal	Control (n=23)	21.870±2.321	0.804±0.114	6.354±0.436	28.458±5.063	37.80±5.12
	Case (n=25)	31.346±8.634	1.158±0.174	6.576±0.481	27.948±4.332	38.42±5.20
	P-Value	0.000***	0.000***	0.10 ^{NS}	0.71 ^{NS}	0.11 ^{NS}
Post-menopausal	Control (n=17)	30.167±3.974	1.00±0.118	6.844±0.564	27.832±5.231	56.12±7.33
	Case (n=35)	42.800±6.676	1.304±0.264	7.490±0.623	27.840±5.048	57.50±8.18
	P-Value	0.000***	0.000***	0.00**	1.00NS	0.244NS

*P<0.05, **P<0.01, ***P<0.001, NS = Not-significant (P>0.05)

Table No. 2: The differences between studied parameters in premenopausal and postmenopausal states

Groups	Urea (mg/dL)	Creatinine (mg/dL)	Total protein (g/dL)	BMI (Kg/m ²)	Age
Pre-menopausal (n=25)	31.346±8.634	1.158±0.174	6.576±0.481	27.948±4.332	38.42±5.20
Post-menopausal (n=35)	42.800±6.676	1.304±0.264	7.490±0.623	27.840±5.048	57.50±8.18
P-Value	0.000***	0.017*	0.930NS	0.33NS	0.000***

*P<0.05, **P<0.01, ***P<0.001, NS = Not-significant (P>0.05)

Table No. 3: The serum parameters in pre- and post-menopausal patients and the control group according to body mass index

BMI (kg/m ²)	Groups		Urea (mg/dL)	Creatinine (mg/dL)	Total protein (g/dL)
18 – 24	Pre-menopausal patients	Control (n=7)	21.428±2.070	0.857±0.097	6.147±0.434
		Case (n=8)	33.125±11.494	1.225±0.138	6.698 ±0.534
		P-Value	0.020*	0.000***	0.046*
	Post-menopausal patients	Control (n=6)	32.333±1.861	1.050±0.083	6.908±0.502
		Case (n=11)	45.090±9.016	1.313±0.289	7.214±0.512
		P-Value	0.004**	0.048*	0.251NS
25 – 29	Pre-menopausal patients	Control (n=7)	22.285±2.058	0.814±0.089	6.554±0.446
		Case (n=9)	31.555±7.535	1.122±0.192	6.742±0.558
		P-Value	0.000***	0.000***	0.03*
	Post-menopausal patients	Control (n=6)	32.1667±4.262	1.066±0.121	7.333±0.294
		Case (n=12)	44.666±4.559	1.341±0.227	7.604±0.774
		P-Value	0.000***	0.014*	0.426NS

30 – 40	Pre-menopausal patients	Control (n=9)	21.888±2.842	0.775±0.133	6.336±0.257
		Case (n=9)	29.555±7.333	1.258±0.290	6.351±0.399
		P-Value	0.01*	0.007**	0.928NS
	Post-menopausal patients	Control (n=6)	26.000±0.894	0.883±0.040	6.290±.274
		Case (n=12)	38.833±4.108	1.133±0.187	7.629±0.512
		P-Value	0.000***	0.000***	0.002**

*P<0.05, **P<0.01, ***P<0.001, NS = Not-significant (P>0.05)

DISCUSSION

According to the current study, premenopausal and postmenopausal BC women had significantly higher urea levels than healthy women. The results of the current study are consistent with those of Al-Hussein¹⁹ and Chauhan et al²⁰, whose results showed a significant rise in the concentration of urea in BC, and urea is an important chemical parameter for cancer monitoring, while the results of the current study disagreed with Al-Saeedi et al²¹ and Devi et al²², who indicated that there was no difference in urea concentrations when comparing women with breast cancer with healthy people where they are within the normal range, as shown by the results of the study by Abou Zaid et al²³ a small increase in urea concentration in the affected group compared to the healthy group. One possible explanation for the higher urea levels in BC compared to the healthy group is an increase in cellular protein metabolism brought on by chemotherapy's increased death of cancer cells and some healthy cells.²¹ Serum creatinine levels are thought to be a more sensitive indicator of renal function than urea. Since elevated creatinine can only be caused by renal dysfunction. In this study, creatinine levels throughout premenopausal and premenopausal status were found to be statistically significantly higher in BC women than in healthy women. Devi et al²² found that creatinine levels between 1.0 and 2.0 mg/dl were higher than the typical reference range; this finding is consistent with our study. In contrast to our investigation, Abdallah et al²⁴ discovered that BC cases had lower creatinine levels when compared to control. Creatinine levels rise in BC patients in both pre-menopausal and post-menopausal states, according to several studies.²⁵ The glomerulus mostly filters creatinine, although between 10% and 40% of creatinine clearance depends on active tubular secretion that is mediated by several solute-carrier transporters, including MATE2-K, organic cation transporter (OCT2), and multidrug and toxin extrusion protein MATE1. The proximal tubule cells' basolateral membrane contains an organic cation transporter that takes up cations from the blood and transports them into the cells. On the other hand, MATE1 and MATE2-K are located on the apical membrane and mediate the efflux of organic

compounds, including toxins and drugs, from the cells to the urine.²⁶ Inhibition of these particular solute-carrier transporters can therefore result in a substantial reduction in creatinine clearance, which will raise serum creatinine levels.²⁷

However, our research revealed that premenopausal and postmenopausal BC women had significantly higher levels of total protein than the control group. The present study is consistent with a Jordanian study that found elevated serum total protein in BC²⁸ and with multiple investigations that found elevated serum total protein in brain tumors.²⁹ The fact that albumin and other proteins, collectively referred to as globulins, make up total serum protein may be the cause of this rise in concentration. It is well known that oxidative stress, such as that caused by cancer, can alter the concentration of serum albumin.³⁰

The findings demonstrated that postmenopausal women had considerably greater levels of urea, creatinine, and total protein than premenopausal women. These findings concurred with those of Omon et al.³¹ For both pre-menopausal and post-menopausal women with BC, there was a significant correlation between increased BMI and elevated levels of urea, creatinine, and total protein. The increased BMI might affect metabolic indicators and renal function in this patient population, our study points to a connection between obesity, metabolic dysfunction, and BC. These results are consistent with literature.^{32,33}

CONCLUSION

The difference in the levels of urea, creatinine, and total protein between women before and after menopause, as the levels of urea, creatinine, and total protein in women after menopause were higher than before menopause and found differences in urea, creatinine, and total protein level based on BMI in women with BC who were premenopausal and postmenopausal.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Nasr Afit Alobaidy, Zaid Ahmed Hameed
Drafting or Revising Critically:	Nasr Afit Alobaidy, Baraa Qassim Dawood
Final Approval of version:	All the above authors

Agreement to accountable for all aspects of work:	All the above authors
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