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Evaluation of Interleukin-1β and Renal Function Parameters in Women with Breast Cancer in Kirkuk City

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Abstract

This study aimed to determine the serum levels of Interleukin-1β and kidney function parameters (urea and creatinine) among women who were diagnosed with breast cancer. A total of 90 samples with a mean age of 54.86 years were included. Sixty-nine women with breast cancer were performed in the current study and were recruited from the patients who attended Kirkuk Oncology and Hematology Specialized Center from the beginning of October 2024 to the end of January 2025. The patients were classified into three groups: the first group included 23 women with stage I, the second group included 23 women with stage II and the last group comprised 23 women with stage III. Also, twenty-one healthy women reported as controls were enrolled. As a result, significant levels increased in Interleukin-1β and the parameters of kidney function urea and creatinine have been reported in breast cancer women compared with healthy ones. When a comparison of the three clinical stages of cancer was made, significant levels increased were observed in parameters of kidney function urea and creatinine, while it was observed the absence of a statistical level increase in Interleukin-1β. Finally, it is to be concluded that the Interleukin-1β, urea, and creatinine have a statistical level increase in breast cancer women compared with healthy ones.

Keywords: Breast cancer, Interleukin-1β ،Renal Function, Creatinine, Urea

تقييم إنترلوكين-1 β ومعايير وظائف الكلية لدى النساء المصابات بسرطان الثدي في مدينة كركوك

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الخلاصة

هدفت الدراسة إلى تقييم مستويات Interleukin-1β و ووظائف الكلى بما في ذلك اليوريا والكرياتينين، في مصل الدم لدى النساء المصابات بسرطان الثدي. تضمنت الدراسة (90) عينة بمتوسط أعمار بلغت (54.86 سنة)، شملت تسعة و ستون (69) امرأة مصابة بسرطان الثدي راجعن

مركز كركوك التخصصي للأورام وأمراض الدم خلال المدة من بداية تشرين الاول 2024 إلى نهاية كانون الثاني 2025، وزعت على ثلاث مجاميع، المجموعة الأولى تتكون من (23) أمرأة في المرحلة الأولى والمجموعة الثانية (23) أمرأة في المرحلة الثانية ومجموعة تتكون من (23) أمرأة في المرحلة الثالثة. بالإضافة إلى واحدة وعشرون (21) امرأة سليمة بوصفهن مجموعة سيطرة.اظهرت النتائج وجود ارتفاعا معنويا ($p \leq 0.05$) في تركيز Interleukin-1β واليوريا و الكرياتينين وعند المقارنة بين مراحل الإصابة وجد فروق معنوية ($p \leq 0.05$) في مستويات وظائف الكلى اليوريا والكرياتينين،، فضلاً عن عدم وجود فروق معنوية في مستويات Interleukin-1β نستنتج من الدراسة ارتفاعًا معنويًا في مستويات Interleukin-1β وUrea وCreatinine لدى النساء المصابات بسرطان الثدي مقارنةً بالأصحاء، مما يشير إلى وجود اضطراب فسيولوجي ناتج عن التأثيرات الالتهابية المرتبطة بالمرض. كما بيّنت النتائج وجود فروق معنوية في مستويات Urea وCreatinine بين المراحل السريرية لسرطان الثدي، مما قد يعكس تزايد العبء الالتهابي والخلوي مع تقدم المرض، في حين لم تُسجَّل فروق معنوية في مستويات Interleukin-1β وهو ما قد يدل على ثبات نسبي في هذه المؤشر عبر المراحل المختلفة.

الكلمات المفتاحية:سرطان الثدي، Interleukin-1β ، وظائف الكلى ، الكرياتينين ، اليوريا

1-Introduction

Breast cancer represents a group of malignant diseases that are mainly caused by genetic disorder or disordered cell growth in the breast tissues, in specific, the epithelium cells linings either the milk ducts or lobules. These changes cause the affected cells to lose self-regulation and normal division and to form masses that can invade the neighboring tissue or disseminate to other parts through the bloodstream or lymph (1,2). Epidemiology studies indicate that breast cancer is the top most frequent cancer among women worldwide and a key cause of cancer deaths in women as shown from a recent publication published in Nature Medicine. In 2022, there were 2.3 million new breast cancer cases reported and 0.67 million deaths, the trends are expected to increase with the 5% annually to new cases 3.2 million and 1.1 million deaths annually by 2050 on the same patterns (3).this indicates that the disease is becoming a great health burden globally especially in countries with poor access to cancer care. Chronic inflammation encourages the DNA mutations necessary for the growth of various types of cancer, including breast cancer, to occur. During chronic inflammation, macrophages release cytokines and growth factors that create free radicals and noxious molecules that continually promote genetic damage. These hazardous molecules cause normal cells to turn cancerous by increasing cell proliferation and sprouting, inhibiting apoptosis, and stimulating tumor formation and metastasis. Immune cells and macrophages interact to create a setting for a pro-carcinogenic joust in the tumor microenvironment, where immune responses that secure tumor growth and development.(4) Interleukin 1-beta is the major pro-inflammatory cytokine whose major source is the macrophages elicited by immune stimuli, and the major saint cytokine that mediates inflammatory responses in that the inflammatory signaling pathways are mediated by activation of the nuclear

factor kappa B. Given the rising importance of all Parnell markers in malignant tumors particularly in breast cancer, there is need for site-specific study to analyze these markers in their native ecosystems and communities(5). Thus, the current study investigates the analysis of serum levels of IL-1β, urea, and creatinine in women with breast cancer in Kirkuk city to determine their correlation if any with the pathological features of the disease.

2-Materials and Methods

Study Desing

The experiment, or the practical section of the conducted study, lasted from the start of October 2024 to the end of December 2025. In total, 90 blood samples were gathered, which were divided into two prominent groups: the first one made up 69 samples of 40-80-year-old women with a diagnosis of breast cancer and, based on the stage of the development of clinical manifestations of the disease, the samples were further classified into three subgroups, each consisting of 23 samples: 23 samples of the second stage, 23 of the third stage, and 23 of the fourth stage; the second group was composed of 21 healthy women without breast cancer, which served as a control group for further biochemical and physiological measurements and tests..

Blood Samples

Colon blood samples were taken from women; 4 mL of venous blood was taken after processing the puncture site with disinfectant. Next, the samples were placed in a glass tube and left 30 minutes at room temperature, allowing it to clot. The serum was separated and analyzed by centrifugation at a speed of 3000 revolutions per minute for 15 minutes.

Biochemical Analysis

Thus, the levels of several biochemical markers were defined for the study groups. Serum Interleukin-1β concentrations were detected using commercially available ELISA kits from Sunlong, China, according to the enzyme-linked immunosorbent assay ELISA procedure recommended by the manufacturer(6). Serum urea and creatinine levels were determined with commercially available kits from Biolis 30i, Japan, according to the enzymatic chemical method(7) .

Statistical Analysis

Statistical analysis; the data analysis was done by SPSS version 18 through T-test to compare the mean values between patients and controls, then using the P-value at ≤ 0.05 for significance and ANOVA test was obtained for the different stages and P-value ≤ 0.05 for significant comparison and the quantitative variables will be revealed by mean ± SD (Mean ± SD) (8).

3 - Results and Discussion

Serum Interleukin-1β Concentration in Women with Breast Cancer and Controls

The results of the study, as depicted in Table (1), showed a significant increase at ($P \leq 0.05$) in serum lnterleukin-lβ levels observed among women with breast cancer when compared to healthy individuals, with the patients' results being at a mean concentration of (170.55 ± 18.25pg/mL), while the control group showed the following results at a mean level of (71.76 ± 10.17 pg/mL). This result describes a probable relationship between high-level lnterleukin-lβ and the existence of malignancy, as it usually acts as a pro-inflammatory cytokine and rises during chronic inflammation conditions as mentioned in other study results(9) . When analyzed by the disease stage, no significant disparities were observed at ($P \leq 0.05$), as per Table (2), with mean values of (170.88 ± 1.42 pg/mL) for stage II, (169.97 ± 1.86 pg/mL) for stage III, and (170.81 ± 4.76 pg/mL) for stage IV. These results are similar to previous findings which concluded that lnterleukin-lβ mainly indicates the general inflammatory status or the immune reaction independently from the tumor' cancer stage and other findings suggested that its changes may more actuated by other determinants such as tumor tissue or premedication process rather than disease stage itself(10). The cause of the high levels of lnterleukin-lβ in these participants was the activation of the innate immune system, which responded to inflammatory signs released by the developing tumor. Leaking pro-inflammatory molecules like prostaglandins, cancer cells enhanced the inflammatory response, which, in turn, increased lnterleukin-lβ serum levels(11). The beneficial microenvironment caused by the growing tumors went beyond the action of lnterleukin-lβ cells themselves.IRECT Evidence of activation was the expression of IL-1 receptor type I on the surface of tumor cells, which played a role in causing their growth. The binding to this receptor activated numerous internal signaling pathways, such as NF-κB and MAPK, which stimulated the genes responsible for the inflammatory action(12). Additionally, some cancer cells, particularly in multifaceted subtypes such as triple-negative breast cancer, might produce lnterleukin-lβ on their own. This self-production establishes an inflammatory microenvironment that promotes tumor cell survival and metastatic potential, indicating that Interleukin-1β acts not only as an inflammatory marker but also as an active contributor to tumor progression (13).

Serum Creatinine concentration in women with breast cancer and Controls

Significant differences ($p \leq 0.05$) were observed in serum creatinine levels among women with breast cancer compared to healthy controls, as shown in Table (1) . Mean creatinine concentrations in patients were (0.81 ± 0.43 mg/dL) ,compared to (0.48 ± 0.20 mg/dL) in the control group. These findings are

consistent with previous reports (14), indicating that elevated creatinine levels in breast cancer patients may result from metabolic alterations, such as increased protein catabolism, as well as potential effects of chemotherapy on liver function. Furthermore, analysis by clinical stage revealed significant differences ($p \leq 0.05$) in creatinine levels among stages of breast cancer , as shown in Table (2) , with mean values of (0.69 ± 0.11 mg/dL) for stage II, (0.77 ± 0.17 mg/dL) for stage III, and (0.97 ± 0.06 mg/dL) for stage IV, indicating a progressive increase with disease advancement. These results align with previous studies (15), which reported that creatinine levels tend to rise as breast cancer progresses.

The elevated serum creatinine levels observed in women with breast cancer may be attributed to renal dysfunction caused by the direct effects of the tumor on kidney tissue. Tumor cells and tumor-associated immune cells release pro-inflammatory cytokines, which can induce vascular constriction, reducing glomerular filtration rate and consequently increasing creatinine levels (16). Chemotherapy also plays a role in impairing renal function, particularly nephrotoxic drugs, which can directly damage renal tubular cells through oxidative stress and decreased renal blood perfusion. This ultimately leads to reduced glomerular filtration, accumulation of creatinine, and renal functional disturbances (17).

Serum Urea Concentration in Women with Breast Cancerand Controls

The study recorded a significant increase ($p \leq 0.05$) in serum urea levels in women with breast cancer compared to healthy controls, with (31.20 ± 1.82 mg/dL) in patients versus (28.50 ± 4.91 mg/dL) in the control group , as shown in Table (1). Furthermore, the finding is in agreement with previous studies (18) that found out that the levels of urea in the blood remains elevated in breast cancer patients compared to the population mean. A comparison of urea levels between clinical stages two and three and stage four reveals a statistically significant $p \leq 0.05$ difference as presented in Table 2 above, stage two, 27.58 ± 2.56 mg/dl, stage three, 30.62 ± 3.26 mg/dl and stage four 35.39 ± 3.09 mg/dl. According to an earlier finding (19), the values increase progressively with advancing disease reflect the continued damage of renal function as a result of tumor progression and the increased metabolic load. Elevation may also result from the inflammatory response of the tumor. One –time –chronic inflammation affects renal function; it leads to an increased level of nitrogenous content leading to increased accumulation in the urea from the blood flow. Consequently, metabolic pathways are triggered, and pro- inflammatory transmitters release from the blood pool reduce the efficiency of filtration (20). Chemotherapy aggravates elevated urea levels. It acts on renal cells, causing partial tissue destruction, which enhances cellular filtration and metabolism

increases renal filtration pressure, thus promoting enhanced metabolic accumulation (21) (22) .

Table (1) concentration Interleukin-1β, Creatinine, urea among women with breast cancer and controls

*The values in the table indicate to (Mean ± S.D)

*Different letters Horizontally indicate significant differences at ($P \leq 0.05$)

Table (2) concentration Interleukin-1β, Creatinine, urea among women with Breast Cancer according to the clinical stage of the disease

Groups / Variable	Stage 2	Stage 3	Stage 4
Interleukin-1β (pg/mL)	170.88 ± 1.42 (a)	169.97 ±1.86 (b)	170.81 ± 4.76 (a)
Urea (mg/dl)	27.58 ± 2.56 (c)	30.62 ± 3.26 (b)	35.39 ± 3.09 (a)
Creatinie (mg/dl)	0.69 ± 0.11 (c)	0.77 ± 0.17 (b)	0.97 ±0.06 (a)

Groups / Variable	Control	Patients
Interleukin-1β (pg/ml)	71.76 ±10.17 B	170.55 ± 18.25 A
Urea (mg/dl)	28.50 ± 4.91 B	31.20 ±1.82 A
Creatinie (mg/dl)	0.48 ± 0.20 B	0.81 ± 0.43 A

*The values in the table indicate to (Mean ± S.D)

*Different letters Horizontally indicate significant differences at ($P \leq 0.05$)

Concolusion

Based on the findings of the current study, the levels of Interleukin-1β, creatinine, and urea are believed to have a statistically significant increase $P \leq 0.05$ in women suffering breast cancer compared to the values established in the control group. There was no statistically significant difference observed $P \leq 0.05$ in the Interleukin-1β concentration concerning the clinical stages in breast cancer patients. However, statistically meaningful values were observed regarding the levels of creatinine and urea across the clinical stages.

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