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Evaluation Of The Serum Levels Of Interleukin-6, Interleukin-10, And C-Reactive Protein In Iraqi Women With Breast Cancer

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Abstract: Breast cancer is the most prevalent form of cancer in women and is the leading cause of global cancer-related mortality. The study aimed to assess the changes in some serum biomarkers linked to immunity responses in Iraqi breast cancer patients and understand their multifaceted role in the disease's progression. The current investigation comprised a cohort of 55 women diagnosed with breast cancer and a control group of 45 healthy participants. The levels of interleukin-6 (IL-6), interleukin-10 (IL-10), and Creactive protein (CRP) were estimated in the serum of breast cancer patients. The results showed that patients with breast cancer had a significant increase (p<0.05) in IL-6, IL-10, and CRP serum concentrations as compared to healthy women. These findings give support to the evidence suggesting that these markers may play an essential role in the progression of breast cancer.

Keywords: Biochemical parameters, Immunity response, Breast cancer, Iraqi patients.

1.Introduction

Breast cancer is the most common form of cancer among women globally, with 2 million new cases reported in 2018. It is the primary cause of global mortality, resulting in 626,700 fatalities in 2018 [1]. Numerous modifiable and non-modifiable risk factors, can either cause or facilitate the growth of breast cancer [2].

Cytokines can induce the synthesis of hepcidin in the liver. Furthermore, the proinflammatory cytokines have the effect of reducing the production of ferroportin in enterocytes located in the duodenum, impeding the transportation of iron from these enterocytes to transferrin [3]. Serum inflammatory cytokines, such as interleukin-6 (IL-6) and interleukin-10 (IL-10), have been suggested as potential tumor indicators to diagnose various types of malignancies [4,5].

C-reactive protein (CRP) is a protein that may rise by a factor of 1,000 in response to an infection or inflammation [6]. Within 24 to 72 hours of severe tissue injury, such as trauma and progressive cancer, CRP levels in the plasma rise from 1 g/ml to over 500 g/ml [7].

CRP can rise to varying degrees in the peripheral blood of various cancer patients. El-Abd *et al.* (2017) found a correlation between the fluctuation of CRP in peripheral blood and

the onset and development of breast cancer [8]. As a non-specific protein with multiple functions and a straightforward detection method, CRP may play a role in predicting and assessing the survival of cancer patients [9].

This study aims to assess alterations in the serum levels of IL-6, IL-10, and CRP in women with breast cancer. Additionally, this research aims to evaluate the potential prognostic value of these biomarkers in the early detection of breast cancer.

2.Methodology

Experimental design:

The study involved samples from patients admitted to the Al-Furat Al-Awsat Center for Tumors in Al-Najaf City from February 1 to May 1, 2023, for breast cancer checkups and treatment. This study included only female breast cancer patients, who were divided into subgroups.

The study enrolled Iraqi breast cancer patients and healthy participants, with a total of 55 patients and 45 healthy participants. The participants were informed about the study's objectives and provided informed consent, and the project received approval from the scientific ethical committee.

Estimation of biochemical criteria:

To conduct biochemical analyses, a volume of 5 ml of blood was collected from resting patients and the control group. To measure the levels of IL-6, IL-10, and CRP in the serum, the samples were transferred into Eppendorf containers after separation by centrifugation. The samples were stored at -20 °C until analysis [10]. The levels of IL-6, IL-10, and CRP in the blood were found using an enzymelinked immunosorbent assay (ELISA). These kits facilitate the precise measurement of the levels of these parameters in humans. The tests were carried out according to the manufacturer's instructions.

Statistical analysis:

The study used the statistical package for social sciences (SPSS, version 23) for statistical analyses. For comparisons between groups, the independent t-test and standard deviation were used. All statistical tests were thought to be significant at a level less than <0.05.

3.Results and Discussion

The statistical analysis in this study revealed that IL-6 and IL-10 in the serum were significantly elevated (p<0.05) between patients and the control groups. Figures (1&2). Consequently, our findings confirmed the findings of prior studies [11,12,13].



Figure (1): Interleukin 6 value in the breast cancer patients and control group.

- Values are means ± SD. Independent t-test.

- (*) =Significant differences exist at the p < 0.05.



Figure (4-11): Interleukin 10 value in the breast cancer patients and control group. - Values are means ± SD. Independent t-test.

- (*) =Significant differences exist at the p<0.05.

Cytokines are 5-70 kDa protein molecules that control the immune system's responses and normal function [14]. Cytokines and receptors play diverse roles in immune homeostasis, influencing autoimmunity, metabolic and endocrinologic disorders, cardiovascular diseases, and cancer pathophysiology [15].

The roles and biomarker potentials of IL-6 and IL-10 in women with breast cancer have been reviewed in several recent reports [4, 16, 17, 5, 18].

IL-6 is a key factor in chronic inflammation, autoimmune diseases, and cancer, promoting angiogenesis and metastasis, and serving as an autocrine and paracrine growth factor [19].

A study on 87 hormone-refractory metastatic breast cancer patients found that high levels of IL-6 were linked to poor survival [20]. Higher circulating IL-6 levels may serve as an independent prognostic marker, as they correlate with the disease's stage [11]. Furthermore, higher circulating IL-6 levels in untreated metastatic breast cancer patients at diagnosis are associated with lower survival rates [21].

IL-6 triggers chronic inflammation, leading to cancer and a poor prognosis. Combining

inhibitors and target blockage drugs may be a novel treatment strategy for IL-6-mediated immune diseases and human cancers [5].

The study reveals that high IL-6 and IL-10 levels in breast cancer tissues reduce migration but don't affect cell adhesion. High expression is associated with clinicopathological criteria and improved DFS and BCSS [22]. IL-6 and IL-1 β mRNA expression increased significantly in malignant breast cancer patients compared to benign tumors, potentially contributing to cancer development [23].

IL-10, a cytokine produced by immune cells like macrophages, T lymphocytes, and natural killer cells, has both immunosuppressive and anti-angiogenic functions, promoting tumor cell proliferation and metastasis [4].

Kozłowski *et al.* (2003) found in a previous study that elevated blood levels of IL-6, IL-8, and IL-10 have a strong connection with breast cancer, potentially aiding diagnosis and aggressive management [11].

Concerning C-reactive protein (CRP), Figure (3) shows a significant increase (p<0.05) in serum CRP concentration in patients with breast cancer. This is consistent with previous research [24, 25, 26].



Figure (4-12): C-reactive protein level in the breast cancer patients and control group. - Values are means ± SD. Independent t-test.

[38]

- (*) =Significant differences exist at the p<0.05.

CRP is produced predominantly by liver hepatocytes but also by macrophages, smooth muscle cells, endothelial cells, lymphoid cells, and adipocytes [6]. Furthermore, CRP serves as a reliable indicator of IL6 activity, as its production by hepatocytes is entirely dependent on IL6 [27].

CRP is a protein that may rise by a factor of 1,000 in response to an infection or inflammation [6]. Within 24 to 72 hours of severe tissue injury, such as trauma and progressive cancer, CRP levels in the plasma rise from 1 g/ml to over 500 g/ml [7].

CRP can rise to varying degrees in the peripheral blood of various cancer patients. El-Abd *et al.* (2017) found a correlation between the fluctuation of CRP in peripheral blood and the onset and development of breast cancer [8]. As a non-specific protein with multiple functions and a straightforward detection method, CRP may play a role in predicting and assessing the survival of cancer patients [9].

4.Conclusion

In conclusion, the current study demonstrates a noteworthy association between heightened concentrations of interleukin-6, interleukin-10, and C-reactive protein in the bloodstream and their role in breast cancer pathogenesis and immune response. Additional research using a substantial cohort is necessary to gain further insights and validate the usefulness of these criteria in combination with other tumor markers.

Ethical approval

This study was conducted under approval by the medical ethics committee at the University of Kufa (2017). Verbal and written consent was provided by parents and agreement for publication was obtained from both participants and researchers.

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