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Evaluation of immunological factors (IL-23, IL-27) and the TLR3 receptor in women with breast cancer

Ahmed Mahdi Hassan

Department of Biology , College of Science , University of Kirkuk , Iraq

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Abstract

Objective: What distinguishes breast cancer in women is the abnormal proliferation of cells. Moreover, it is widespread among women worldwide, but understanding its basic causes remains complex. It has been found to have a close relationship with the immune system, namely interleukins (IL) and Toll receptors (TLRs), with the spread and development of cancer among women affected around the world. The aim of this study is to assess the levels of IL-23, IL-27, and TLR3 to determine their roles in pathological processes

Methods: Sixty blood samples were These samples were taken from women with this disease, and the same number of samples were also taken from healthy women who did not have breast cancer In the city of Kirkuk. All of them were between 22 and 48 years old, and we measured some immune indicators, including IL-23, IL-27, and TLR3.

Result: This study showed a significant increase in interleukinin concentrations (23, 27) in addition to elevated Toll-3 receptors For women with breast cancer. The results indicate the importance of these immunological markers in women with breast cancer, and suggest their use as indicators of disease progression or as potential tools in developing treatments for breast cancer.

Conclusion: Breast cancer development is linked to changes in IL-23 and IL-27 levels, as well as TLR3. Evidence suggests that these cytokines contribute significantly to tumor growth and spread, and that TLR3 helps the immune system fight cancer cells. These cytokines may represent a therapeutic strategy for controlling breast cancer in advanced ways.

Keywords: Interleukin , Breast cancer

Introduction

Cancer is one of the deadliest diseases, and breast cancer is one of its most common forms, affecting many adult women. Every year, there are a significant number of deaths from breast cancer; in 2020 alone, an estimated 685,000 deaths worldwide were attributed to this disease (1). All available evidence suggests that cultural factors, such as beliefs and values, influence breast cancer screening and detection among women in some communities where these factors are prevalent, leading to higher mortality rates in those communities(2).

Low rates of breast cancer screening and diagnosis lead to late detection, resulting in diagnosis at later stages or failure to recognize symptoms. This, in turn, leads to worse outcomes and higher mortality rates compared to cases diagnosed early. Many social beliefs passed down from generation to generation negatively influence the diagnosis of various medical conditions, especially gynecological diseases. Therefore, it is crucial to change these beliefs and raise awareness within communities to enable early diagnosis and reduce mortality rates(3).

Cultural beliefs have a significant impact on breast cancer cases and are among the main factors influencing women's decisions regarding early breast cancer screening practices in some societies(4).

Interleukins It plays a key role in the spread and progression of breast cancer. Most interleukins are produced and secreted by immune cells, and they are also produced by bone cells and cancer cells. Interleukins are secreted in response to both para- and auto-secreting signals. Furthermore, their effects on tumor growth are not uniform(5).

Interleukin-23 (IL-23), discovered in 2000, is an inflammatory promoter produced by antigen-producing cells. Active IL-23 consists of two subunits, p19 and p40, and its levels are elevated in most human malignancies, including breast cancer(6).

Interleukin-27 (IL-27) is discovered in 2002, consisting of an alpha (α) subunit and a beta (β) subunit. IL-27 is secreted by , including macrophages and monocytes, and its levels are elevated in several cancers, including esophageal, gastric, and breast cancer patients (7). Immunotherapy is a new and advanced strategy for treating breast cancer. (8).

TLR3 receptors are essential innate immune proteins found within cell endosomals and play a crucial role in virus detection by recognizing double-stranded RNA (dsRNA) (9). Activation of TLR3 leads to the production of type I interferons and inflammatory cytokines to combat viral infections. It also serves as a link between innate and adaptive immunity. TLR3 differs from other receptors in that it is located inside cells (in endosomals) rather than on their surface, and it is specialized for detecting dsRNA(10).

This receptor recognizes double-stranded RNA and stimulates of the therapeutic efficacy of dsRNA in breast cancer Activation of the TLR3 receptor When activated, TLR3 plays a key role in enhancing and amplifying the effects of anticancer agents; this receptor acts as a suppressor gene, leading to an overall reduction in the incidence of breast cancer (11).

Materials and methods

We obtained 60 blood samples from women aged 22 to 48 years Injuries, and 60 blood samples from women who were not infected in the same age group, In the city of Kirkuk . The immunological variants (IL-23, IL-27, TLR3) were measured in both groups above using ELISA technology.

Statistical analysis In the city of Kirkuk

The statistical analysis was performed using SPSS version 26. The t-test was used to calculate the mean and standard deviation, and a value of $P \leq 0.01$ was considered statistically significant.

Results

Interleukin 23

IL-23 levels were measured in groups of BC patients and a healthy control. The results were reported as mean ± standard deviation (219.21 ± 65.33 and 48.98 ± 16.48) pg/ml, respectively. Illustrated in figure below, the t-test made a remarkably higher IL-23 level in the BC patients than in the control group ($P \leq 0.01$).

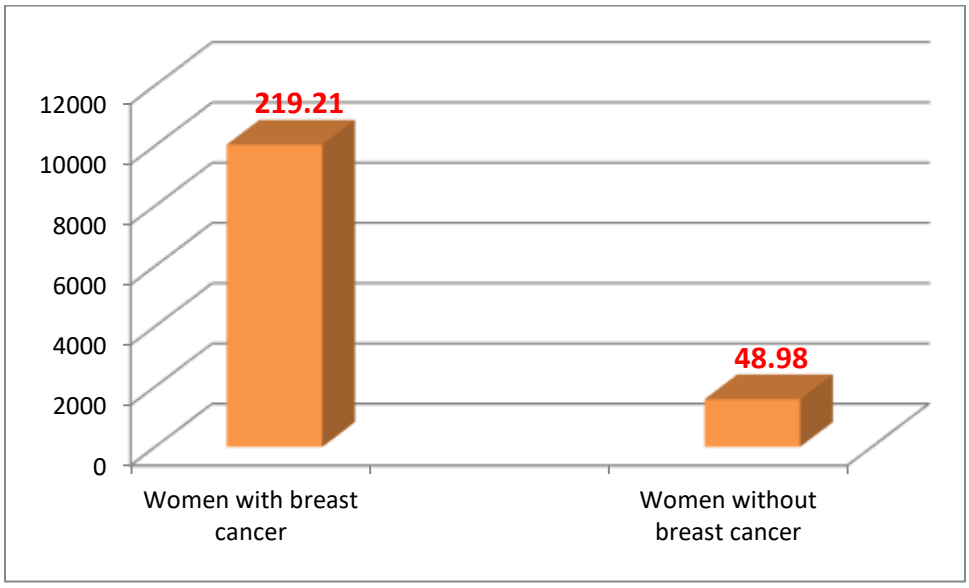

Fig. 1 Interleukin 23 Interleukin 27

IL-27 levels were measured in groups of BC patients and a healthy control. The results were reported as mean ± standard deviation (1133.01 ± 81.76 and 381.42 ± 74.22) pg/ml, respectively. The t-test showed that compared to the control group, the BC patients had a substantially higher IL-27 level ($P \leq 0.01$), Illustrated in figure below.

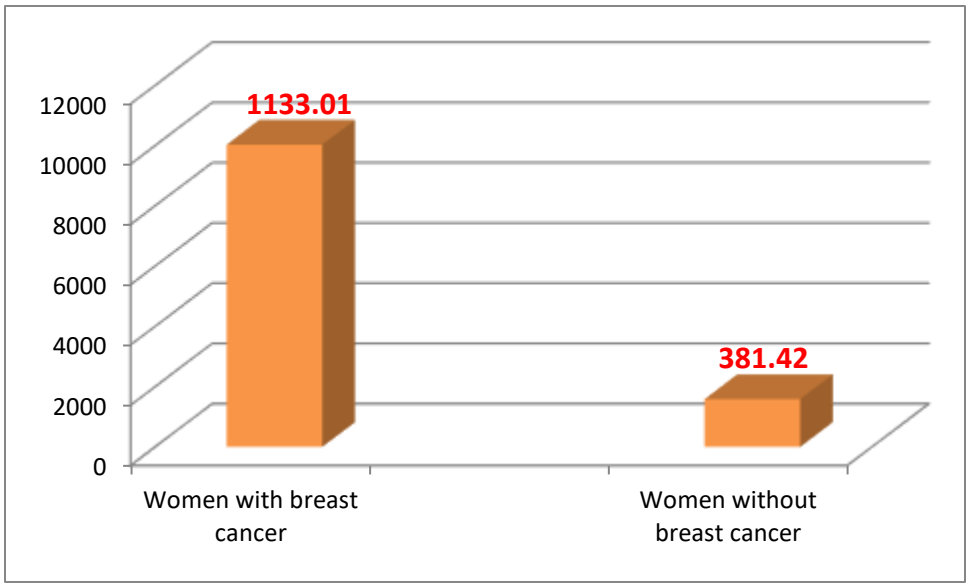

Fig. 2 Interleukin 27

Toll-like receptors 3

TLR3 levels were measured in groups of BC patients and a healthy control. The results were reported as mean ± standard deviation (10033.07 ± 562.40 and 1583.98 ± 278.25) ng/L, respectively. The t-test demonstrated that the TLR3 level in the BC patients was substantially higher than that of the control group ($P \leq 0.01$), Illustrated in figure below.

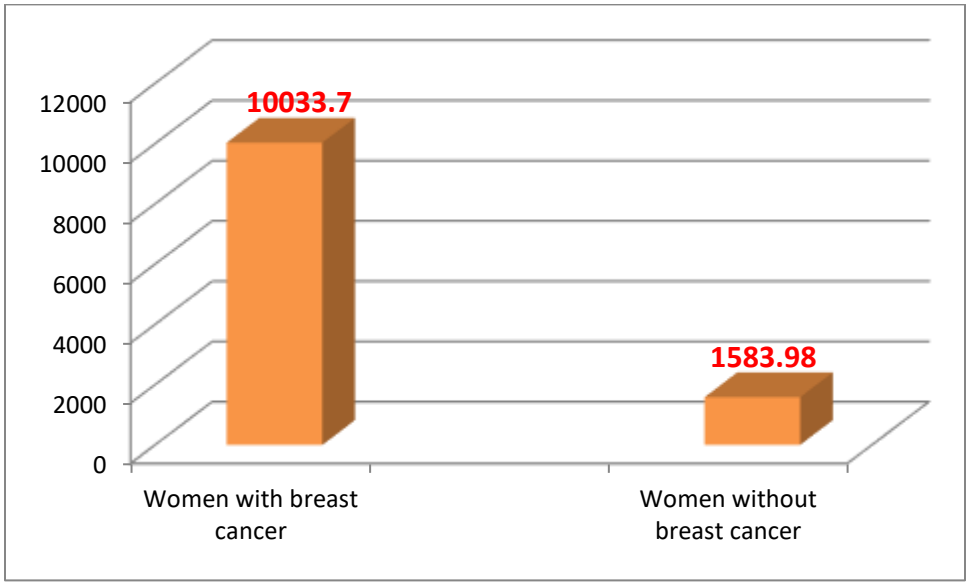

Fig. 3 Toll-like receptors 3

Discussion

IL-23 is a cytokine that activates and modulates type 17 (Th17) helper T cells, essential for the immunological response to infections and diseases. This cytokine is essential in some inflammatory and immunological conditions, but its influence on cancer, especially breast cancer, is neither significant nor direct (12). In breast cancer, IL-23 may have little to no effect on the tumor microenvironment at the

microscopic level, according to previous studies, IL-23 is not thought to have any direct impact on the growth or spread of breast cancer cells On the other hand, it only works on certain cancers, such colon cancer (13). Studies suggest that the tumor microenvironment may influence IL-23 levels in different cancers. In breast cancer, environmental factors such as hypoxia and nutritional deprivation may modify cytokine production, leading to reduced IL-23 activation compared to other inflammatory cytokines (14).

Various cancers display tumor-promoting effects of IL-27; gastric cancer shows elevated blood levels associated with lymph node involvement, whereas patients with invasive cutaneous melanoma and breast cancer exhibit high expression levels (15). Patients with lung cancer demonstrated a significant increase in serum IL-27 levels compared to the controls (16). conducted a study revealing a significant increase in blood IL-27 levels in breast cancer patients compared to the control group, with an association between these levels and the clinical stage of breast cancer. Patients exhibiting ER and PR positive demonstrated elevated levels of IL-27, which decreased subsequent to a radical mastectomy The cytotoxicity of dendritic cells towards viable human tumor cells is reduced by apoptotic tumor cells via the production of IL-27, potentially leading to elevated levels of IL-27 (17). Several research investigate the influence of IL-27 on carcinogenesis. IL-27 has been linked to tumor proliferation (18).

In breast cancer, TLR3 has complex and different functions. it is an essential part of the innate immune system. Regarding breast cancer, TLR3 mostly serves as a tumor suppressor. Human breast cancer cells undergo death when TLR3 is stimulated by its agonist, dsRNA (19). Studies indicate that the TLR3 receptor acts as an antitumor agent in breast cancer (20). Later studies showed Furthermore, the activation of TLR3 receptors plays a very significant role in reducing the proliferation of cancer cells in breast cancer and improves mortality, therefore preventing tumor growth and metastases in animal models (21) .

ascribed these effects to cytotoxic T cells help boost the immune response against cancerous tumors and angiogenesis suppression, hence inducing death. Breast cancer depends critically on the expression of TLR3 in dendritic cells Increased TLR3-activated conventional dendritic cells generate IFN-l, which corresponds with better clinical results in breast cancer. Consequently, researchers are investigating TLR3 ligands, including poly I:C, as potential therapies for breast cancer (22).

TLR3 activation in can induce inflammation, angiogenesis, and immune suppression, so promoting tumorigenesis and metastases (23). Understanding the pathways controlling TLR3 activation events can aid in comprehending TLR3 intricate roles in altering the tumor microenvironment and promoting BC growth Higher risk of corresponds with increasing TLR3 expression in tumor cells (24).

breast cancer cells show higher TLR3 expression than normal cells Thus, multiple elements affect functions Targeted breast cancer treatment has great potential from using TLR3's immunostimulatory qualities while reducing its pro-tumorigenic effects. TLR3's generated exosomes show therapeutic potential since they can cause immunogenic cell death especially in breast cancer cells (25).

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