Study the Role of Interleukin-6 and Interleukin-17 in Iraqi Women with Breast Cancer

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Abstract
The incidence of breast cancer is now higher than that of any other kind of female malignancy, leading it the most prevalent form of the disease in both emerging countries and established nations. Reason for doing it investigation would be to measure the the extent to which pro-inflammatory cytokines (IL-6 and IL-17) in patients with early-stage inflammatory disease. breast cancer patients from Iraq. A total of 90 Iraqi females (50 patients and 40 controls) participated in the research, and their blood was used to measure the ratios of both IL-6 and IL-17, with concentrations and correlations being determined using the Pearson correlation test. The cytokines, IL-6 and IL-17 were determined to be significantly better than normal in the current investigation. (P>0.05) when it comes to breast cancer in women, also were significantly correlated (P>0.05). our study concludes that both, IL6 and IL17 are correlated during early stage of breast cancer.
Keywords: Breast cancer, Interleukin-6, Interleukin-17.

1. Introduction

Most types of cancer in women, specifically 'breast cancer', are the most common cause of cancer-related deaths among women worldwide. most prevalent female malignancy in both developing and industrialized nations [1].
Breast cancer, is highly molecularly heterogeneous disease, resulting from a group of distinctive genetic changes, in the epithelial cells of the breast, which in turn leads to different pathological manifestations in cases with cancer.[2].
According to 2020 statistics, the number of breast cancer cases reached about 2.26 million new cases. the most common cancer in the world is now female breast cancer [3]. It is estimated that nearly 685,000 women will lose their lives to breast cancer in 2020, making it the primary woman's most common cancer-related cause of death [4].
The statistics of the "Global Cancer Observatory" showed that breast cancer is the most common tumor among Iraqi women, with an estimated rate of about 37.9% of all cases of gynecological malignancies [5]. Among 2016, it was responsible for 897 female deaths, making it the mortality rate among cancer patients in Iraqi citizens overall (12.1%), behind only bronchogenic cancer (23.6%) [6].
Cancer of the breast detected early can enhance the likelihood that the patient will survive since the disease is easier to treat when it is tiny and has not spread [7].
A healthy immune system has a dual role in cancer, as it can act to prevent or control and can promote tumor growth through the process of "cancer immunoediting" [8]. As inflammatory cytokines are known to affect tumor formation, they have been the subject of substantial research. Potential prognostic indicators in many forms of human cancer. Being a pro-inflammatory cytokine, IL-6 is a multidirectional cytokine engaged in numerous different physiological and pathological processes in the body. Macrophages, B cells, T cells, endothelium cells, and osteoblasts all produce IL-6 [9].
Th17 cells generate IL-17 (interleukin-17), an anti-inflammatory cytokine that paradoxically promotes tumor growth. Its activation causes cytotoxicity in cancer cells, which may slow tumor development and is essential for inducing angiogenesis [10].
The concentration of (IL6) is elevated in patients with breast cancer, as indicated by a previous study [11]. The results of another study showed, a high concentration of (IL17) in women with breast cancer [12]. While a study indicated different results, indicating a decrease in the concentration of (IL6 and IL-17) in patients with breast cancer [13].
Present study goaled to Assessment of increases in pro-inflammatory cytokine levels, including interleukin (IL- 6, IL -17) in breast cancer patients, and a control group of healthy women.

2. Material and Methods

2.1 Study population and design

The study included 90 women ranging in age from 31 to 83 years old in the current study. 50 of them were breast cancer patients visiting the Iraqi-German Center for Functional Diagnosis and Oncology in Baghdad, after confirming their diagnosis by oncologists and before starting chemotherapy, radiotherapy or immunotherapy and before performing a mastectomy, and the remaining 40 were apparently healthy women.
Cases that underwent a mastectomy, and cases that underwent chemotherapy, radiotherapy,

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immunotherapy and other types of cancer treatment were excluded, and cases of refusal of consent.
Each of the patients participating, in the current study gave, written informed consent to participate. The research was conducted after obtaining approval the"Central Scientific Research Ethics Committee, at Tikrit University".

2.2 Sampling

Five milliliters of blood were collected from the patients included in the study. It was placed in gel tubes, left to coagulate for 20 minutes, and then placed in a centrifuge and centrifuged for 15 minutes, at 3000 rpm to collect serum. The serum was placed in Eppendorf-tubes, and stored in a deep freezer at a temperature (-20 °C), and the samples were brought to room temperature again before performing these tests.

2.3 Evaluation of serum concentrations of both IL-6, and IL-17

Commercial kits (SunLung/China), were used to evaluate the concentrations of both IL -6 and IL -17, using "ELISA" (Enzyme-Linked Immunosorbent Assay) technique.

2.4 Statistical analysis

Summaries of results were presented as MeanStandard Deviation, and the Duncan test in SPSS V.23 was used to compare groups at the P0.05 level..

3. Result

Results from this study show that IL-6 and IL-17, two pro-inflammatory cytokines, are significantly (P>0.05) higher in breast cancer patients' serum compared to that of healthy people (see Figures 1 and 2, and Table 1).

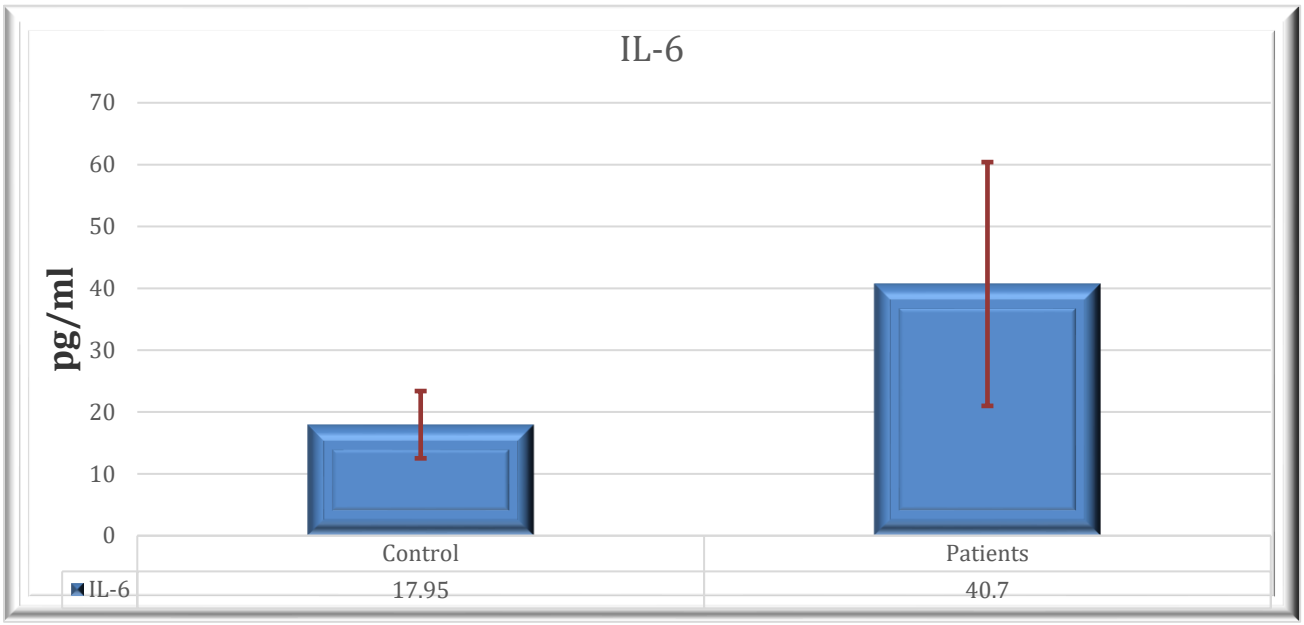

Figure (1): Assessment Serum IL-6 (pg/ml) in studied groups.

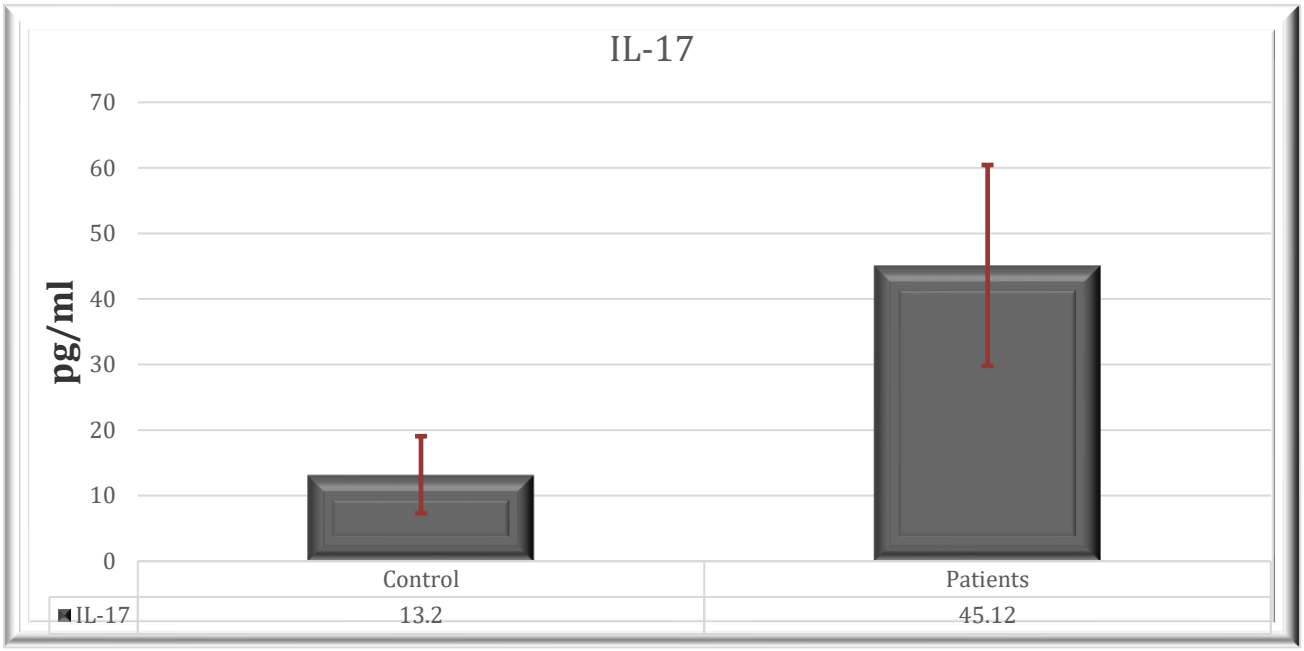

Figure (2): Assessment Serum IL-17 (pg/ml) in studied groups.

Table (1): The concentration levels of IL-6 and IL-17 in the serum of breast cancer patients compared to the control group.		
Group	IL-6 (pg/ml)	IL-17 (pg/ml)
	Mean±SD	
Healthy women	17.95±5.44	13.2±5.87
Women with breast cancer	40.74±19.71	45.12±15.32
P-value	0.000	0.000
P≤0.05		

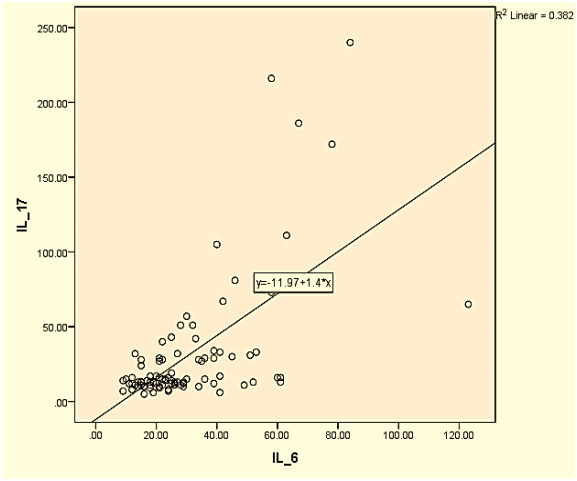

Figure (3): Pearson correlation between IL-17 and IL-6.

4. Discussion

IL-6 and IL-17, two pro-inflammatory cytokines, were measured in blood samples of women with 'breast cancer'. The immune system's ability to communicate between cells is facilitated by cytokines, which are secreted proteins with high inducibility. Interleukins, tumor necrosis factors, and interferons are just a few examples of the many protein families that make up this category. Some cytokines regulate the inflammatory tumor microenvironment. Some cytokines such as Il-6,Il-17and IL-1 stimulate the division of cancer cells, which leads to their proliferation and invasion[14]; NF-kB-mediated intracellular signaling, cytokine receptor activation, and tumor development are also facilitated by these cytokines [15].

IL-6 was one of many immunological indicators shown to be considerably elevated in women with breast cancer، compared to healthy women. Similarly, Thwani [16] found that The levels of IL-6 in the group of sick women were significantly higher (P > 0.01) compared to the group of healthy women.

The results that appeared in the current research, are consistent with the search results of Chaloob [17], who found that IL6 levels in the women with 'breast cancer were considerably higher than, in those without the disease. A correlation between IL-6 levels and the presence of estrogen and progesterone receptors in breast cancer patients was also discovered in the latter study, lending credence to the former.

It has been shown that elevated levels of interleukin-6 correspond with the progression and severity of several inflammation and cancer, especially breast cancer that has spread to other parts of the body [18]. Some malignant cells may survive, as can benign stromal cells like fibroblasts and endothelial cells. Because of its role as a growth factor, IL-6 promotes the survival and progression of malignant tumor cells, by raising their levels of angiogenesis proteins and antiapoptotic proteins. The Interleukin-6(IL-)6 it is a cytokine that has a critical role in the pathogenesis of cancer disease as a mediator of the inflammatory response.

Consistent with the findings of a prior study conducted in Iraq by Ayed [19] with There were 75 people diagnosed with breast cancer and 15 people who served as healthy comparisons. He 75observed a clear correlation between the elevated IL-6 levels in his patients' blood and the progression of their disorders by comparing their levels to those in healthy females.

Ahmed et al. [20] found that IL-6 and IL-8 levels in patients' blood were greater than in healthy Egyptians. Moreover, Sullivan [21] in his research shows that IL-6 IL-6 levels in breast cancer patient, are relevant from a therapeutic standpoint. Increases in serum IL-6 have also been seen in women with breast cancer, as shown by Fontvielle et al. [22].

In one of the previous researches, it was suggested that there is a putative relationship between cytokines and steroid hormones such as "ER" [23]. In view of this, the amplification of estradiol-converting enzyme and aromatase activity, gives more evidence of the function of IL- 6 in estrogen synthesis in breast cancer. The researchers found that the Il-6 receptor was also expressed, by ER-positive breast cancer cells[24].

This research confirms the findings of many others by showing a statistically significant increase in IL-17 levels relative to healthy volunteers [25,26,27]. The disparity between studies finding reduced IL-17 and related cytokine blood levels in breast cancer patients, like the one conducted by Baharlou et al. [13], and others that do not may be attributable to differences in methodology.

Subsets of CD4+ T cells, called "Th17" cells have been found to produce and release IL-17, as well as other cytokines such as TNF- α, IL-22 and GM-CSF.[28]. Blood levels of IL-17 were found to be much higher than expected, which may be due to the significant rise in lymphocyte counts seen in the present study.

One or more of these variables is at work if the three types of lymphocytes studied in this research – lymphocytes (B and T lymphocytes) and ,natural killer (NK) cells - are increased. NK cells activity against cancer cells, may be related to the high level of IL-17 in patients.[29], some cells, including NK cells,

release IL-17 into the tumor microenvironment [30,31]. Recent studies by Garcia-Chagollan et al. [32], have shown that NK receptors increase in number during breast cancer.

IL-17 stimulates the production of chemokines such as (CXCL-2 and CXCL-8) and also stimulates the production of intestinal stimuli such as (GM-CSF), which stimulates some inflammatory cytokines such as (IL-6 and IL-1). It indicates that the elevated level of IL_17 may be the cause of the elevated level of IL_6 in patients in this study. Inflammatory tissue receives a boost in granulocytes and granulopoiesis from GM-CSF, which also causes inflammation [33]. Moreover, as shown in Figure 3 below, there is a positive-association between ,IL-6 and IL-17 that is statistically significant at the P0.05 level in the current research.

5. Conclusion

Results from the current research show, that both "IL-6 and IL-17" are increased and high correlated during breast cancer.

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