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RESEARCH ARTICLE

Assessment of IL17BR Serum Concentration in Females with benign & Malignant Breast Tumors

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Abstract

Breast cancer is one of the most dangerous and most common malignancies among women in the world, which affects different age groups of women, IL-17 plays an important role in chronic inflammation and cancer, Serum IL-17BR concentration which useful in early diagnosis and staging of breast tumors. The aim of the study was to evaluate of IL-17BR serum concentrations in patients with benign and malignant breast tumors and study the relation between the above parameter and breast cancer development. The study population was composed of 120 samples 24 patients with recently diagnosed breast carcinoma, 6 patients with repetitive carcinoma, 40 patients with benign breast tumor (fibroadenoma) and 50 normal apparently health woman as a control.ELISA technique was applied for estimation of IL-17BR levels in patients as well as apparently healthy volunteers of women. The results revealed the mean age of malignant breast females was 52.8 ± 12.3 (Mean ± SD), while it was 26.9 ± 8.3 years for women with benign tumor with highly significant difference (P<0.001), IL-17BR level was determined and found that was a highly significant difference in its level among benign breast females subjects (72.48 Ng/ µL) and healthy control (50.87 Ng/ µL) P< 0.001), no significant difference in the mean of sIL-17BR level among the different patients' groups (49.83, 64.33 Ng/ µL) for recurrent and primary breast cancer respectively. Estimation of IL-17BR level showed significant elevation of the concentration among the sera of recurrent breast cancer in comparison with other groups which perhaps regarded as a prognostic marker.

Keywords: *IL-17BR, Fibro adenoma, Breast cancer, Carcinoma, ELISA.*

Introduction

Breast cancer was the most common kind of malignancy in women with the exception of non-melanoma skin cancers. It is the second leading cause of death by cancer in women, following lung cancer [1] .The breast cancer remains the most prevalent cancer among women in Iraq. According to the latest Iraqi Cancer Registry, breast cancer account for approximately one-third of the registered female cancers in Iraq indicated that the breast cancer is the leading cancer site among females [2].

During the last years, interleukin-17 (IL-17) has become noted as a key mediator at the interface between adaptive and innate immunity. Interleukine-17 performs a critical role in host defense and remains relevant in inflammatory and autoimmune diseases [3, 4]. Perhaps credible surprisingly, notwithstanding the work of IL-17 in autoimmunity relatively; scarce is known about its role in malignancy, and data received so far are somewhat conflicting. Some reports show that IL-17 supports tumor growth, probably by stimulating angiogenesis of human cervical cancer and murine fibrosarcoma cells when transfected with IL-17 [5].In contrast, other studies proposed that IL-17 raises T-cell mediated tumor rejection,therefore, IL-17, similar another cytokines seems to be a pleiotropic cytokine with likely protumor or antitumor effects on tumor growth, which frequently depends on the immunogenicity of tumor models [5, 6].

The results of past study indicate that in patients with early-stage breast cancer, the expression of sIL-17BR is significantly raised.

The aforementioned finding may indicate a vigorous proinflammatory reaction arranged by the host immune system against a tumor. In early stages of the disease, the preliminaries of anticancer immunotherapy may hold the expected emergence of immunosuppression induced by Treg cells [1, 6].

In spite of studies have revealed associations between serum IL-17 and breast cancer that is often indistinct how these associations change in the clinical application of the diagnosis, serum IL-17 showed the moderate ability for detecting breast tumor. Nevertheless, they are apparently more indicative of secondary effects such as that inflammation than particular for malignancy [7].

Material and Methods

The study population was composed of 120 samples 24 patients with recently undergoing diagnostic biopsy for breast carcinoma, 6 patients with repetitive carcinoma, 40 patients with benign breast tumor (fibroadenoma) and 50 normal apparently health woman as control at Middle Euphrates Cancer Center in Najaf province from September 2017 to February 2018.

The women who provided blood for this study was either diagnostic biopsy to diagnose the primary breast lesion (benign or cancer) or continued routine breast examination and did not refer to breast abnormalities (normal). All cases were barely registered after obtaining written give permission for study. All blood samples were separated to prepare the serum which stored about (-80ºC) until assayed.Blood serum was assayed using the Enzyme-Linked ImmunoSorbent (ELISA)the OmniKine™ Human IL-17BR ELISA Kitcontains the components necessary for a quantitative determination of natural or recombinant hIL-17BR concentrations within any experimental sample including cell lysates, serum, and plasma.

This particular immunoassay utilizes the quantitative technique of a Sandwich Enzyme-Linked Immunosorbent Assay (ELISA) where the target protein (antigen) was bounded in a sandwich arrangement by the primary capture antibodies coated to each well bottom and the secondary detection antibodies added subsequently by the investigator,the applied technique was performed according as recommended in leaflet with kit [8].

Statistical Analysis

The statistical analysis was performed using a Student *t* test provided in SPSS software.

Results

Patients distribution in groups according to clinical diagnosis and the study included 120 females distributed into 70 breast tumors patients (58.3%) and 50 apparently healthy women (41.6%) as a control group. Patients group was subdivided in to three subgroups, those subgroups were 24 females with primary breast cancer patients (20 %) and 6 females with frequently breast cancer patients (5 %), and 30 Fibroadenoma subjects (25%). The following (Table1) illustrates the data distribution study.

Table 1: Distribution of the studied groups

Study group		Frequency	Percent.
Primary breast Cancer	Primary breast Ca	24	20 %
	Recurrent cancer	6	5%
	Total	30	25%
Fibroadenoma (Benign tumor)		40	33.3
Healthy controls		50	41.6
Total		120	100.0

That was evident from (Table 2) revealed that all the benign tumor female patients were older than malignant females that covered the majority of above menopause age (52.06±0.33) cases with highly significance P value (< 0.001) while the table showed the disease duration among the studies groups no significant P value (0.42)

Table 2: Demographic description of the studied groups

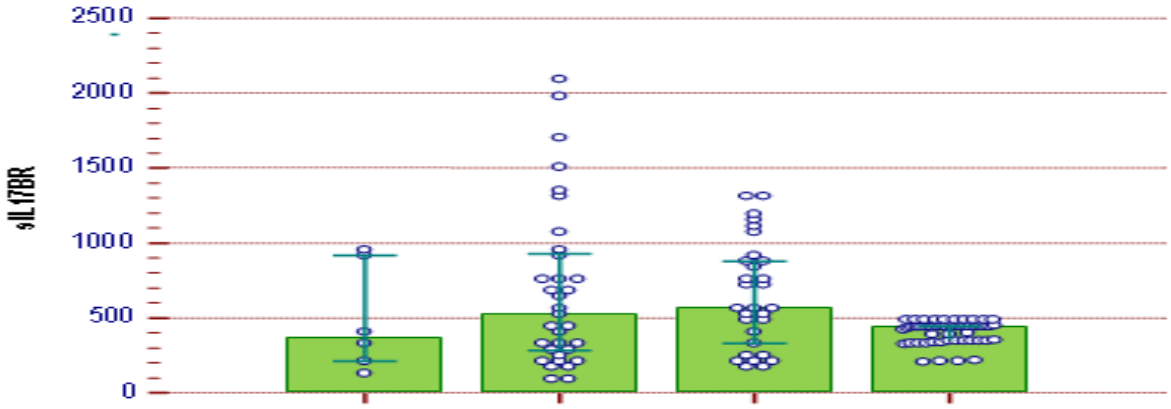
descriptive parameter	Malignant Breast Cancer	Benign Breast Tumor	Healthy Control Group	Pvalue
Age (Mean ±SD)	**52.8 ± 12.3**	**26.9 ± 8.3**	**43.1 ± 12.9**	**< 0.001**
Age of disease **onset (years) (Mean ±SE)**	**52.06 ±0.33**	**25.95± 0.38**	**0.0± 0.0**	**<0.001**
disease **duration (years) (Mean ±SE)**	**0.74 ±0.17**	**0.95 ± 0.11**	**0.0**	**0.42[NS]**

The (Table 3) explained the mean level values of sIL-17BR concentration. This is evidence that there was a significant difference among the different values of IL-17BR (P=0.037). In spite of, there was significant difference between patients groups of recurrent brease cancer versus health control group and Fibroadenoma cases versus.The healthy control group (P= 0.001).while was no significant difference between patients control groups that as shown in (Fig. 1)the mean rank values of -sIL-17BR concentration.

Table 3: Concentration of IL-17 BR level (Ng/ µL) among the sera subjects

sIL-17BR Level (Ng/ µL)	Recurrent breast Ca	Primary breast Ca	Fibroadenoma (Benign tumor)	Healthy controls	P (Kruskal-Wallis)
Median	368.2	525.1	564.4	441.5	
Recurrent breast Cancers vs. Primary breast Ca					0.52*
Recurrent breast Cancers vs. Fibroadenoma (Benign tumor)					0.33 *
Recurrent breast Cancers vs. Healthy controls					0.001**
Primary breast Cancers vs. Fibroadenoma (Benign tumor)					0.69 *
Primary breast Cancers vs. Healthy controls					0.15 *
Fibroadenoma (Benign tumor) vs. Healthy controls					0.001**

* non signifecnt
** signifecant



Recurrent BC primary BC benign tumorhealthy control
Fig. 1: Mean rank and distribution of sIL-17BR values among the different studied group

Determination the optimum significant value of sIL-17BR for discrimination between benign & healthy individuals In order to distinguish between healthy individuals and recurrent breast cancer, the selection depends on the positive cut-off value with highest specificity and sensitivity.That was reveald listed in (Table 4).

Table 4: Optimum cut-off value of IL-17BR with the highest percentage of sensitivity, specificity and accuracy for each in distinguish between benign breast tumors & healthy individuals

Positive if ≥ cut-off value	Sensitivity	Specificity	Accuracy	PPV at pretest probability =		NPV at pretest probability =
				50%	90%	10%
sIL17BR (Ng/ µL)						
152.25 (Highest specificity) and (Optimum cut-off)	16.7	93.9	82.1	73.3	96.1	91.0
1015.8 (Highest sensitivity)	100.0	21.2	33.3	55.9	92.0	100.0

NPV: Negative predictive value PPV: Positive Predictive Value

Discussion

The level of IL-17BR were measured in the sera of subjects with breast cancer. The detected data guided to the high level of IL17BR in patients' sera of primary BC and Fibroadenoma in comparison with healthy control group. furthermore, its level among recurrent BC was lower than its corresponding level among healthy control.

The current result was supported by the facts mentioned by Zhang et al., who detected increased expression of IL-17 and IL-23 mRNA in tumor tissues from patients with gastric cancer. These authors suggested that Th17 cell differentiation may increase in gastric cancer [9]. Furthermore, The research results provided by Zhu et al. referred to that IL-17 expression in breast cancer tissue is mostly restricted to its role in promoting tumor progression and invasion ,that almost agreed with that of the current results [10]. Certain events are true considering Wang et al. described that IL-17 might promote tumor cell growth, an effect mediated through IL-17-induced IL-6 release via activation of the signal transducer and activator of transcription 3 factor (STAT 3), both in tumor cells and nonmalignant stromal cells [11]. The present finding of increased expressions of IL-17 in primary Breast cancer from a group of patients that included many women in the early stages of breast cancer can be interpreted as a reflection of a protective proinflammatory response. The purpose of this response is to support the systemic recruitment of the host‘s immune cells at the site of early initiation of a malignant transformation in breast tissue.

In conclusion, the outcomes of the present study show that in patients with early-stage breast cancer, the expression of sIL-17BR was significantly increased. This finding may reflect a vigorous proinflammatory reaction orchestrated by the host immune system against cancer. In early stages of the disease, the initiation of anticancer immunotherapy may delay the expected emergence of immunosuppression induced by Treg cells.

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