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Research Article

SERUM IMMUNOGLOBULIN AND COMPLEMENT LEVELS IN PATIENTS WITH BREAST CANCER IN IRAQ

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ABSTRACT

Objective: The objective of this study was to estimate the serum immunoglobulins (IgA, IgM, and IgG) levels, and complements (C3 and C4) level in Iraqi women with breast cancer pre-treatment and post-treatment.

Methods: A total number of 100 patients aged 25–47 years were enrolled in this study, including 35 breast cancer treatment patients, 30 treatment patients, and 10 and 25 healthy women benefactor. All samples were collected from August 2016 to February 2017 from Oncology Hospital/Medical city in Baghdad exception of the control group were collected from outside the hospital. Serum levels of IgG, IgA, IgM, C3, and C4 were measured by radial immunodiffusion technique.

Results: Serum mean values of IgA, IgG, and C3were significantly higher ($p<0.01$) in patients pre-treatment than in post-treatment. The level of the serum for patients pre-treatment was significantly higher than post-treatment.

Conclusion: The present study showed the increase of serum IgA, IgG, and C3 levels can be considered as biomarker for breast cancer diagnosis pre-treatment and post-treatment.

Keywords: Breast cancer, Iraqi women, Complements, Immunoglobulins.

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INTRODUCTION

Breast cancer is the most widespread cancer among women worldwide [1,2]. The latest Iraqi Cancer Registry [3] revealed that it is still the most common malignancy among the general population since 1986 and the leading cause of death from female cancers in Iraq; accounting for 34% of the registered cancers among women and 23% of cancer-related mortality. The peak frequency is often observed among middle-aged women where the disease is frequently diagnosed at relatively advanced stages [4], with a likely prevalence of aggressive forms [5]. Studies conducted in the past decade have confirmed the role of immunological response in the breast cancer disease process [6,7] and the possible use of immunological parameters in the prognosis of breast cancer [8]. High serum immunoglobulin levels were found to be associated with tumor load in breast cancer patients. The obvious alteration in serum such as IgA and IgG levels in breast cancer patients reflects a disturbance in cell-mediated immunity and humoral immunity [9]. The effective role of the complement is found to be raised in breast cancer patients and increased with the progression of the disease [10]. The complement system is an integral part of the immune system. It involves more than 30 soluble and cell-bound proteins that circulate in the plasma in an inactive form [11]. These proteins can be activated by three independent pathways, namely - classical, alternative, and lectin pathway leading to generation of products that have important biologic activities including tumor cell destruction [12]. The complement components eliminate cancer cells through the binding of complement-fixing antibodies to tumor cell membrane, promote attachment of complement component that makes pores in the membrane, and resulting in cell distraction due to loss of osmotic and biochemical integrity [13]. The complement components enhance the tumor cells killing by a process involving opsonization and subsequent phagocytosis by macrophages [14].

Aim of the study

This study aims to estimate the levels of immunoglobulins (IgG, IgM, and IgA) and levels of complement component (C3 and C4) in Iraqi women with breast cancer and compared with the control group.

METHODS

This study was conducted from August 2016 to February 2017 on a total number of 100 subjects including 35 breast cancer patients (they are still not receiving adjuvant treatment), 30 treated patients, 10 worker group (working in the room, they do blending and preparer of chemotherapy for patients in the hospital), and 25 healthy women benefactor. All samples were collected from Oncology Hospital/Medical City in Baghdad exception of the control group were collected from outside the hospital. Collected blood samples 4 mL were taken from each women patients and control group, placed into Gel tubes, left around 15 min at room temperature, and it is centrifuged at 2000×*g* for 10 min to get the serum, to be used while in the measurement of each of immunoglobulin and complement.

Determination of serum immunoglobulin and complement component

Radial immunodiffusion test

Serum IgG, IgM, IgA, C3, and C4 proteins were determined for 100 patients were measured by single radial immunodiffusion method, in which equal volumes of reference sera and test samples are added to wells in an agarose gel, containing monospecific antisera.

The samples diffuse radically through this gel and the substance being assayed from a precipitin rings with the monospecific antisera. Ring diameters are measured and a reference curve is constructed on graph

Table 1: Comparison of serum immunoglobulins levels in patients with breast cancer and the control group

Parameter	Mean±SE of immunoglobulin		
	IgA (mg/dl)	IgM (mg/dl)	IgG (mg/dl)
Pre-treatment group	390.37±13.19^{B}	292.86±14.35^{AB}	1416.66±49.73^{A}
Post-treatment group	282.73±18.04^{C}	258.30±15.65^{B}	1084.00±85.28^{B}
Worker group	467.60±13.05^{A}	317.40±22.53^{A}	1211.40±133.68^{AB}
Control group	173.16±15.46^{D}	108.92±10.10^{C}	1009.64±64.65^{B}
LSD value	51.850**	48.404**	235.51**
p value	0.0001	0.0001	0.0002

*p<0.05, **p<0.01. Means having with the different letters in same column differed significantly, NS: Non-significant, SE: Standard error, LSD: Least significant difference, p value: Probability value of significance

Table 2: Comparison of serum complements levels in patients with breast cancer and the control group

Parameter	Mean±SE of complement	
	C3 (mg/dl)	C4 (mg/dl)
Pre-treatment group	163.26±5.98^{A}	43.71±2.10^{A}
Post-treatment group	127.30±5.33^{B}	47.97±4.21^{A}
Worker group	139.00±4.93^{B}	47.20±1.54^{A}
Control group	108.20±4.19^{C}	29.28±1.73^{B}
LSD value	18.224**	9.796**
p value	0.0001	0.0001

*p<0.05, **p<0.01. Means having with the different letters in same column differed significantly, NS: Non-significant, SE: Standard error, LSD: Least significant difference, p value: Probability value of significance

paper. Unknown concentrations are determined from the reference standard curve [14].

RESULTS AND DISCUSSION

Serum immunoglobulins (IgG, IgA, and IgM)

Table 1 summarized that there were a significant p value changes in the levels of IgA, IgM, and IgG in breast cancer of patients sera in comparison with healthy controls**.**

The results revealed that patients with breast cancer have a higher values in concentration of IgA, IgM, and IgG which reached (390.37 ± 13.19, 292.86 ± 14.35, and 1416.66 ± 49.73 mg/dl, respectively) with highly significant differences (p<0.01) compared to that of healthy control (173.16 ± 15.46, 108.92 ± 10.10, and 1009.64 ± 64.65 mg/dl, respectively).

The results of this study are confirmed with most other studies [15], according to which the IgA levels in breast cancer patients are higher than in controls and that the levels of IgA increase with the advancement in disease stages or post-treatment. Explanation [16] the breast cancer cell line proved to secrete their own IgA, this may reflect the increase in level IgA the activity of the malignant cells through host immune modulation or secretion of IgA by their own cells. Anyhow, this gives serum IgA a novel role in breast cancer patient prognosis.

Furthermore, the present study found no significant difference in the IgM level between the pre-treatment group and the post-treatment group; this may be the result of no interest because generally the serum IgM level is still within the normal level [19].

The present study found a significant difference in the IgG level between the pre-treatment group and the post-treatment group. The present study is in accordance with that of Ali *et al*. [19] and Alsabti [17] which revealed the increase in the IgG level in pre-treatment when compared after three cycles of chemotherapy. It has been shown that IgG expressed by cancers of epithelial origin [18] such as breast cancer and contributed to the growth and development of epithelial tumor cells, this supported the findings of IgG contribution in cancer initiation in the precancerous stage in epithelial cells [20].

Serum complements C3 and C4

The C3 values pre-treatment (163.26±5.98 mg/dl) were high significantly than the C3 values, post-treatment (127.30±5.33 mg/dl), p<0.01, as shown in Table 2. The serum C4 levels for the patients with breast cancer pre-treatment (43.71±2.10 mg/dl). It was similar to values post-treatment (47.97±4.21 mg/dl).

The presence of C3 and C4 in cancer samples, associated with C5b-9 deposits, indicates that the complement component has been activated through the classical pathway [21]. Their results are corresponding with results Vijayakumar *et al.* [11] No significant changes were found in the C4 levels between the pre-treatment and post-treatment groups are shown in Table 2, while, the serum C4 levels for pre-treatment or post-treatment showed significant difference with the control group.

Results were in agreement with the findings of Ferda *et al*. [22] which confirm the hypothesis that malignant tumors contribute to elevation of complement components levels. Post-treatment the levels of serum C3 and C4 decreased, which is in accordance with the study of Vijayakumar *et al*. [11] and Ail *et al.* [19]. Thus, the reduction of serum complement level after chemotherapy may be in part due to increase in malignant cells susceptibility and so patients who exhibit a persistent high complement level may indicate treatment-resistant tumors.

CONCLUSION

Serum IgA, IgM, IgG, and C3 can use as important biomarker in the diagnosis of breast cancer, also used as predictors for breast cancer recurrence.

AUTHOR'S CONTRIBUTION

Rana H. and Mohammed Q. achieved and analysis of immunological study. Evaluation of clinical approach was done by Fareed A. All authors contributed ideas and thought to the writing of this paper.

CONFLICTS OF INTEREST

The authors declared that they have no conflicts of interest.

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