Risk Factors and Biomarker Interleukin -12 of Breast Cancer Among Iraqi Women

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Abstract

Background: Breast cancer and a few other malignancies are significantly more likely to develop in people This study aimed to identify the risk factors of Breast Cancer among Iraqi women. Participants in the study comprised 50 girls with breast cancer, and 50 girls in good health. In this study the distributing of patients into age groups revealed that most patients 17cases (34%) were at the age group (50-39) years old, 13 cases (26%) were at the age group (40-49)years old, 12 (24%) cases were at the age group (≥60) years old, 8 cases (16%) were at the age group (30-39) years oldIn conclusion, Positive risk factor for breast cancer was old age≥60 years, widow or divorced women, menopause, age at menarche <12 years, . Family history, seconddegree relative,not associated with breast cancer. There are some discrepancies between our findings and other studies in the literature need further studies.

Keywords: Risk factors , interleukin-12 (IL-12) , breast cancer.

1 Introduction

Breast cancer .is an extremely heterogeneous. disease caused .by interactions of both inherited and environmental .risk factors which lead .to progressive accumulation .of genetic and epigenetic .changes in breast cancer .cells. Although epidemiological.evidence support the .existence of certain .risk factors (e.g., age, obesity, alcohol intake, estrogen exposure, and .mammographic .density) .

The family .history of breast cancer.remains the strongest risk factor for the disease. Familial forms occupy approximately 20% of all breast cancers and appear to have a distinctive pathogenesis dependent on particular susceptibility gene involved .(1)

In Iraq with a huge variation in life style modes, cultural,geographical, diets and habits, there are considerably limited information's sources of on cancer risk factors.

Actually, the factors for differences in breast cancer incidence in women are not fully understood, which are likely to be explained byreproductive and lifestyle factors such as literacy, diet, age at menarche and menopause, age at first delivery, abortion,family history of breast cancer. (2)

IL-12 is a heterodimeric cytokine produced mainly by macrophages/monocytes, with pleiotropic activities. It induces a range of cytokines and promotes the establishment of a Th1-type response reviewed in (3). IL-12 also induces regression and cure of a wide range of syngeneic transplantable tumors reviewedin (4).

Treatment with IL-12 promotes a cytotoxic anti-tumor immune response (5), and antiangiogenic effects have been described (6).

These actions of IL-12 can occur in a single model, as we have shown in a novel transplantable murine breast cancer, (7).

2 Method and Materials

In this experiment, 100 samples were protected, of which 50 were classified as routine samples and 50 as samples from patients who had breast cancer complaints (control group). The patients ranged in age from 26 to 70.The Margan Hospital for Research in Applied and Experimental Medicine at the National University of Science once hosted the authors' study. Human Interleukin 12 ELISA Kit was used to evaluate the presence of Human Interleukin12 (also known as IL-12), and this unit is an Enzyme-Linked Immunosorbent Assay (ELISA) (ELISA). Human IL12 neutralizer has been pre-applied on the plate. The IL12 from the example is introduced to the wells and binds to the antibodies. Then, in the example, biotinylated Human IL12 Antibody is introduced and bonds to IL12. Streptavidin-HRP is then added, which binds to the biotinylated IL12 immune response. During the washing stage after hatching, unbound Streptavidin-HRP is removed by rinsing. The substrate pattern is then implemented, shading is calculated based on the amount of Human IL12 present. (8)

3 Results and Discussion

Risk factor in Breast cancer

In this study the distributing of patients into age groups revealed that most patients 17cases (34%) were at the age group (50-39) years old, 13 cases (26%) were at the age group (40-49)years old, 12 (24%) cases were at the age group (≥ 60) years old, 8cases (16%) were at the age group (30-39) years old ,Table (1).

Breast cancer women enrolled in this study were divided according to menstruation into two

subgroups, pre-menopausal and post-menopausal, the results showed that 68% of patients in pre-menopausal age and 32% of women were in post-menopausal age, significant differences found atP≤0.001, this results agreed with (9),(10). Data in premenopausal women have been sparse, because of complexities in measuring estrogen levels during the menstrual cycle (11).

There was a statistically significant in the distribution of frequencies in Family history of breast cancer and controls (P<0.001, OR 18.39 ,95% CI (5.04 to 67.00). The higher incidence of breast cancer in in Family history is related to many factors which have collectively a cumulative effects including reproductive factors, genetic factors, hormonal factors, exposure to radiation and life style. (12)

Table (1) Distribution of the study sample according to Age, Marital status , Menopausal & Family History of Breast cancer.						
Variable	Cancer Patients N=50 %		Control N=50 %		OR(95%CI)	P-value
	N.	%	N.	%		
Age Group						
30-39 a	8	16%	52	50%	0.17 (0.05 to 0.58)	0.004*
40-49	13	26%	7	14%		
50-59	17	34%	8	16%	0.15 (0.04 to 0.47)	0.001*
Above 60	12	24%	10	20%	0.26 (0.08 to 0.84)	0.002*
Total	50	100 %	50	100 %		
Marital status						
Unmarried	1	2%	15	30%	0.04 (0.01 to 0.20)	0.003*
Married	49%	98%	35	70%		
Total	50	100	50	100%		
Menopause						
Postmenop ausal	16	32%	37	74%	0.16 (0.07 to 0.34)	0.001*
Premenopa usal	34	68%	13	(26%)		
Total	50	100%	50	100%		
Family History						
Positive	27	54%	3	(6%)	18.39 (5.04 to 67.005)	0.001*
Negative	23	46%	47	94%		
Total	50	100	50	100%		
P<0.001: OR =(95%Cl): a Reference						

Aging

Results presented in this work had shown that women (50 cases of
breast cancer) that most patients 17cases (34%) were at the age group (50-39) years old, 13 cases (26%) were at the age group (40-49) years old, 12 (24%) cases were at the age group (≥ 60) years old, 8cases (16%) were at the age group (30-39)years old, as

presented in Figure (1).
The results of present study came in agreement with (13), (14) who demonstrated that about 35–45% of Eastern breast cancer women aged less than 40 years. So that several observations which line with present study and were suggested that breast cancer in young women behave differently compared with breast cancer in middle-aged and elderly women.
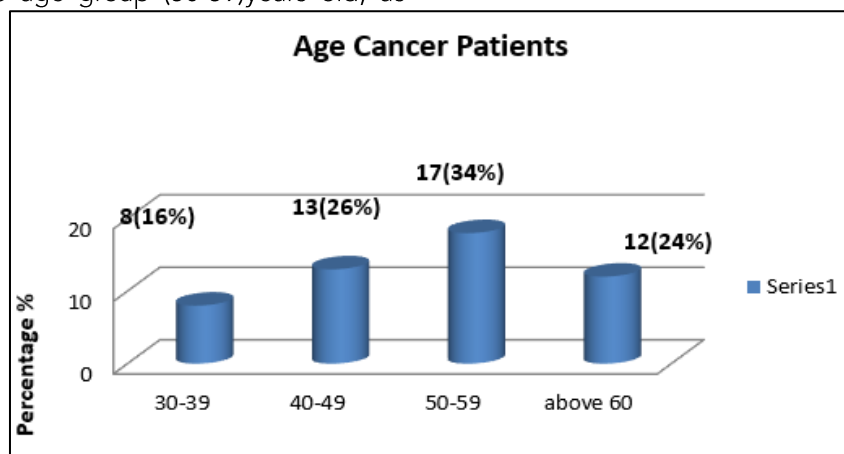

Figure.1:Distribution of the patients infected with breast cancer according to the age.

Marital status

Results indicated in table (1) ,Figure 4 shown that 49

(98%) patients were already married while the other patients 1 (2%) have unmarried, as presented in Figure 2.
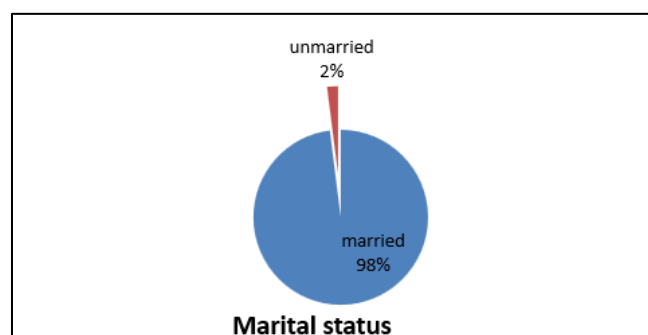
Figure 2: Distribution of Marital status among breast cancer cases

Marital status was not a risk for breast cancer in contracts to other studies which shows that unmarried women were at higher risk for breast cancer (15).

In most studies single and nulliparous married women were found to have a similar increased risk for breast cancer as compared with parous women of the same age (16). Thus, one may argue that marital status by itself is not a determining factor for increased or reduced breast cancer risk and rather the main protective effect is from early first full-term pregnancy.

In the present study no association with parity. Evidence suggests that there is an interaction between marital status and parity (17),(18) . supporting a dual effect of parity on breast cancer risk with pregnancy.

Menopause

Results indicated in table (1) shown that 16(32%) patients had have postmenopausal, while the other patients 34 (68%) have pretmenopausal. This may be due to effect of aging as the menopausal women are already old, or to the high postmenopausal blood estrogen levelswhich

is established as risk factors.(19),(20)
(21) in Iraq documented an increased serum estradiol and prolactin among the pre- and post-menopausal breast cancer women, and recommends emphasizing the necessity of co-operation between the Ministry of Health and the Ministry of Commerce and protecting them from dangerous behavior by providing them with sufficient support and guidance to stay away from the hormonic products and focusing on the extension programs in the protection of the community through educating them with the guidance

Late menopause increases the risk of breast cancer. Risk increases by almost 3% for each year older at menopause, so that a women who has the menopause at 55 years rather than 45 years, has approximately 30% higher risk. (22)

Case history

Family history of breast cancer indicates a strong association with risk of developing breast cancer. The present study showed that family history positive in 50 cases(54%) and (46%), had negative family history of breast cancer, as presented in Figure 3.
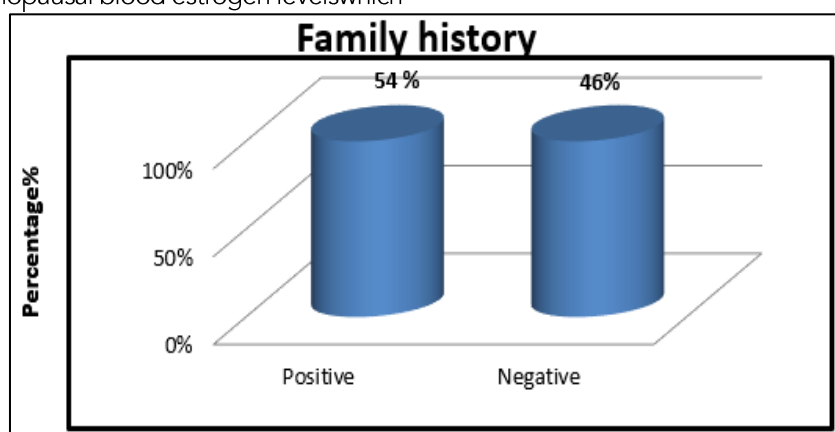

Figure 3: Distribution of Family history among breast cancer cases

Breast cancer, as a heterogeneous disease, is susceptible to genetic, hormonal and environmental risk factors that reflect a variety of characteristics which correlate with its prognosis. Women with a strong family history of breast cancer could inherit genetic alterations that modify their risk and clinical presentations. Accordingly, the second part of this study was designed to evaluate the clinico-pathological characteristics of patients with positive family history of breast cancer.

Family history of cancer is risk factors for breast cancer. This is in accordance with other research

findings indicating that a positive family history of breast cancer is a strong risk factor for breast cancer at young age (23 although this has a comparatively small effect on the absolute lifetime incidence of and mortality from breast cancer (24),(25).

Immunological factor in Breast cancer

The immunological parameters also have been increased in response to Breast cancer infection such as (IL-12). This results might be refer to that the immune system work as protective role and having prognostic indicator for disease, activity and past

infection (immunization). These result were showed   in Table (2).

Age and Immune Markers		Control Mean ± SD	Breast cancer Mean ± SD	P-Value
IL12(Pg/ml)	30-39 year	41.7906 ±5.2747	22.1938±5.1858	1.2
	40-49 year	38.4186±7.212978	33.007 ±5.7589	0.02*
	50-59 year	45.95349±7.365456	29.91473±7.649229	1.3
	Over 60	44.44961±4.299853	34.66408±5.77202	0.02*
T-test at P ≤ 0.005 (Mean ± SD): Mean± Standard Deviation .				

Table (2) : Age distribution in relation to IL12 levels in patients and control.

The current study results investigated whether immune system impairment manifested by reduced IL-12 levels ensue in BC patients. The present study demonstrated evidence indicating that IL-12 were decreased in BC patient's serum, suggested that tumor derived IL-12 were associated with tumor progression.These results were in agreement with Rao etal, in 2004 who demonstrated significant differences in levels of serum IL-2 in patients as compared with controls and revealed that the IL-2 level was not correlated with stages of BC disease. (26)

These findings are compatible with a study finding that indicated the reduced IL-12 production may contribute in the tumor formation and development (19).

Cytokines play varied roles in cancer pathogenesis, with increasing evidence suggesting their involvement in tumor initiation, growth and metastasis (27). IL-12 is a proinflammatory cytokine. The potent anti tumor activity of IL-12 has been demonstrated in many preclinical murine tumor models (28).

IL-12, which is produced primarily by monocytes/macrophages and B-cells, is an important cytokine in the activation of cell-mediated immunity. IL-12 has a potent antitumor activity, and is used in the immunotherapy of cancer. It appears that patients with elevated blood concentrations of IL-12 have a higher survival rate than patients with low concentrations (29).

4   Conclusion

The characteristics of patients with positive family history of breast cancer did not reveal distinct clinical markers for their identification .

Careful screening and regular follow up of the target population along with promoting public education onbreast health care seem to be essential approaches to identify high risk groups for breast cancer control in Iraq.

We also advised considering IL12 markers as a major factor to understand therapeutic response against the breast cancer.

in infected human populations to establish apopulation based therapeutic development as in personal medicine discovery by combining information about the immunological impact of IL12 Immunological markers s as reported earlier in breast cancer.

5   Acknowledgments

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