Relationship of Prolactin Serum Levels and Breast Cancer with Hematological Factors Among Cases in Karbala Province, Iraq

Jaafar Kh. Ali[1], Salim H. Hassan[1]*and Salam A. Oleiwi[3]

[1] *Community Health Department, Karbala Technical Institute, Al-Furat Al-Awsat University, Kufa, Iraq*

[2] *Community Health Department, Technical Institute of Kufa, Al-Furat Al-Awsat University, kufa, Iraq*

Corresponding e-mail: inkr.salm@atu.edu.iq

ABSTRACT

Background: *Globally, one million women are diagnosed with breast cancer and nearly half million die because of it. Breast cancer is one of the most common cancer which leads to mortality among women.* **Objectives:** *The main aim of this research is to find the relationship of prolactin level in women with breast cancer.* **Methods:** *The research was conducted in the Al-Hussein Medical City at Al-Hussein Center for the treatment of tumors and blood diseases. A total of 71 specimens were collected from females with breast cancer. Blood specimens were collected, and a blood group, PCV, Hb, ESR and prolactin level was evaluated.* **Results:** *The results show that most breast cancer cases were in age group 40-50 years, and less common among other age groups. The married women were 97% and the unmarried was 3% only. Most studied cases (43%) were O +ve and 26% were A +ve blood group, in comparison to other blood groups. Also, many women show a slightly decrease in hemoglobin and PCV level (<11.0 g/dl, <36% respectively), on the other hand the mean value of ESR was increased non-significantly (p>0.05). The prolactin levels were increased (31.5 ng/ml) significantly in compare to normal range (2-27 ng/ml) in women in all age groups.* **Conclusion:** *The study concludes that there was a relationship between prolactin level and breast cancer with a highly significant value.*

Keywords: Breast cancer, Prolactin, ABO, ECLIA

INTRODUCTION

Breast cancer is a malignant tumor which begins in the cells of the breast. Mostly women are affected by the disease, but men can also be affected [1]. There are many types of breast cancer, but some of them are rare. In some cases, a single breast tumor may have other types at the same time [2,3].

- Ductal carcinoma *in situ* is the most common type of non-invasive breast cancer, in which the cancer cells remain inside the ducts and don't spread into the surrounding of the breast tissue.

- Lobular carcinoma *in situ* although it is not a true cancer, but it is sometimes classified as a type of non-invasive breast cancer. It starts in the glands that produce milk and doesn't grow into the wall of the lobules.

- Invasive (or infiltrating) ductal carcinoma which is classified as the most common type of breast cancer. It begins in a milk duct of the breast, and then through the wall of the duct, grows into the fatty tissue of the breast, and then it can spread to other parts of the body through the lymphatic system and bloodstream.

- Invasive (or infiltrating) lobular (ILC) it is mostly like invasive ductal carcinoma.

Many women have no symptoms at the beginning of breast cancer but sometimes it is diagnosed after symptoms appear, thus it is recommended to do the screening tests before any symptoms appear [4]. Breast cancer can be diagnosed by two or more of these criteria.

Signs and Symptoms

A new lump or mass which is the most common sign. It is a hard mass that mostly painless and has irregular edges.

Imaging Tests

Use X-rays, magnetic fields, sound waves, or radioactive substances to take a picture of the interior of the breast [5,6].

- Diagnostic mammograms, is the most common testing that is used in screening of the breast tissue. A mammogram cannot prove that an abnormal area is cancer. To confirm this, a small tissue is taken and investigated under a microscope [7,8].

- Magnetic resonance imaging (MRI) uses radio waves and strong magnets instead of X-rays. MRI is used to measure the actual size of the cancer and to see any other cancers in the breast [9].

- Breast ultrasound, also known as sonography, uses sound waves. Usually, it is used to screen a specific area of concern found on the mammogram [10].

- Ductogram, this test sometimes is used to determine the cause of discharge of nipple [1,6].

- Biopsy, it is done by removing a small tissue from the suspicious area to be examined under a microscope. A biopsy is the only way to tell if cancer is present or not and its type [11].

Prolactin (PRL) and breast cancer, the peptide hormone secreted from the anterior pituitary gland restricts the lactation and infertility. The relationship between prolactin and breast cancer has been suspected for years, but never proved conclusively. The prolactin is like growth hormone and its actions by the growth-promoting JAK/STAT pathway suggest its tumor-promoting effects [12,13]. Hyperprolactinemia is the cause of fertility in both men and women [14]. The present study was aimed to find out the relationship breast cancer and levels of prolactin and influence on some hematological parameters.

PATIENTS AND METHODS

Study Design and Sampling

This randomized cross-sectional study was carried out at Al-Hussein hospital during the period of January 2016 to March 2016. Before taking the sample, the questionnaire was filled which included the age, family address, marriage, mastectomy, chemotherapy, or radiations of the patient.

Laboratory Analysis

Blood samples (5 ml) was collected from each patient by venipuncture, and the sample was divided into (3 ml) anticoagulant tube to estimate the packed cell volume (PCV), hemoglobin value (Hb), blood group (ABO) and erythrocyte sedimentation rate (ESR). While the remained (2 ml) was centrifuged to obtain serum and to store at freezing until analysis. Serum samples was tested for prolactin level by the electrochemiluminescence immunoassay "ECLIA" by cobas immunoassay analyzers system.

Data Analysis

Statistical analysis was performed using SPSS version 18, were the results with p-values (<0.05) was considered statistically significant.

Ethical Aspects

The informed consent was obtained from all patients included in the study and study protocols were followed according to the ethical guidelines in Iraq.

RESULTS AND DISCUSSION

Table 1 show the distribution of breast cancer cases among age groups, in which many of the samples were reported at the age ranged (40-50) years and were accounted 25 (35.2%). While the smallest number of individuals was reported at the age ranged (20-30) years and were accounted 2 (2.8%). Approximately 252,710 new cases of invasive breast cancer and 40,610 breast cancer deaths are expected to occur among US women in 2017, and approximately 80% of breast cancer in women is diagnosed at age ≥ 50 years, and the mortality rate about 89% occurs in that age groups. For all women, the average age for diagnosis is 62 years, but the mortality from breast cancer in white women is mostly at 70 years, and 62 years for black women [15].

Table 1 Classification of the study samples according to the age

Variable	Classes	Frequency	%	C.S.
Age Groups (Years)	20-30	2	2.8%	Chi-square test P=0.003 HS
	30-40	13	18.3%	
	40-50	25	35.2%	
	50-60	18	25.3%	
	60-70	10	14.0%	
	>70	3	4.0%	

Table 2 shows the comparable percentage between married and unmarried cases, in which the married cases contribute the higher percentage than unmarried (97.1% and 2.9% respectively). Married women are more exposed to hormonal change, a link between breast cancer and hormones are clear. Researchers reported that the greater is the woman's exposure to the hormone estrogen, the more susceptible she is to breast cancer. Estrogen tells cells to divide, the more the cells divide, the more likely they are to be abnormal in some way, possibly becoming cancerous [16].

Table 2 The comparable percentage between married and unmarried cases

Variable	Classes	Frequency	%	C.S.
Marriage	Yes	69	97.10%	Bin Test P=0.000 (HS)
	No	2	2.90%	

Figure 1 illustrate four parameters, side of the breast affected, percent of women with mastectomy, percent of women with chemotherapy, and family history of cancer. In which there was equal percentage between left and right side (49%), and (55%) of cases were with mastectomy in compare with (45%) without mastectomy, also (97%) of cases were with chemotherapy, and only (3%) of cases were without chemotherapy, 28% of cases was having family history i.e., there were another case of cancer within family or relatives, (such as parent, sisters, brothers, and sometime uncles, aunts, or their children). Women (as well as men) with a family history of breast cancer, especially in a first-degree relative (mother, sister, daughter, father, or brother), are at a higher risk of developing breast cancer, this risk is higher if more than one first-degree relative developed breast cancer. Compared to women without a family history, risk of breast cancer is 1.8 times higher for women with one first- degree female relative who has been diagnosed, nearly 3 times higher for women with two relatives, and nearly 4 times higher for women with three or more relatives [17].
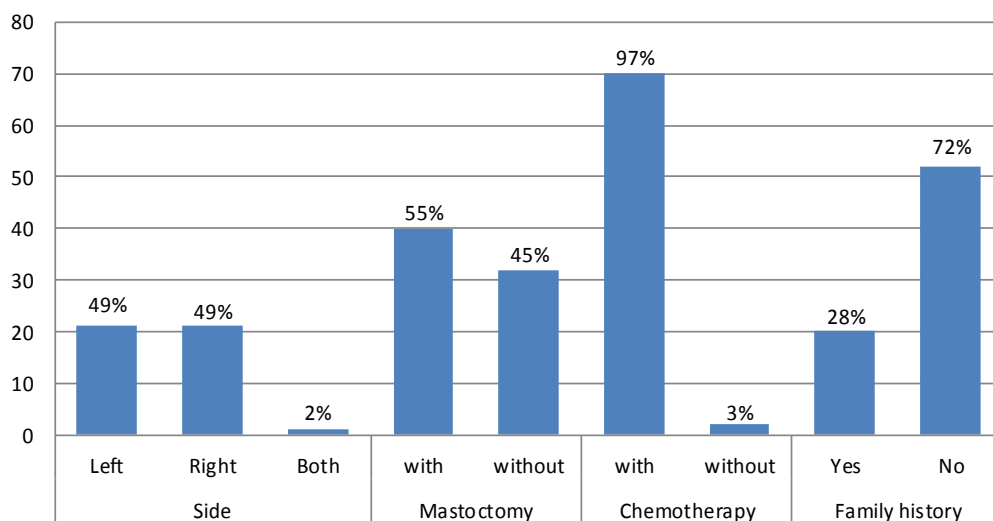

Figure 1 Illustrate four parameters, side of the beast affected, percent of women with mastectomy, percent of women with chemotherapy, and family history of cancer

Figure 2 shows the frequency of blood groups among study cases in which O +ve and A +ve contribute the large

percentage (43% and 26% respectively) in compare to other blood groups. While many risk factors are associated with the development of breast cancer, the blood groups also have an influence on susceptibility and outcomes. Indeed, many researchers have concluded that "blood groups were shown to possess a predictive value independent of other known prognostic factors" when discussing about breast cancer. Other researchers have suggested that a degree of the susceptibility to breast cancer, result from a gene perspective, might be due to a breast cancer-susceptibility locus linked to the ABO locus located on band q34 of chromosome nine [18,19]. Stamatakos, et al., showed that a positive family history is more commonly found in Rh +ve patients irrelevant to blood groups ABO [18]. Rh +ve women with positive family history is more often presented in blood group A and less often in blood groups AB and B [17].
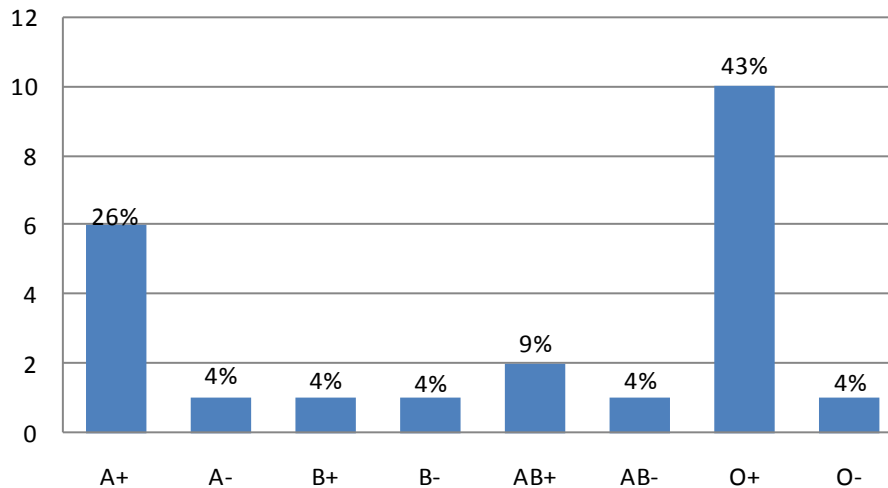

Figure 2 The frequency of blood groups among study cases

Table 3 shows the PCV, pH and ESR mean value, all these parameters show no abnormality among study cases. Kandemir, et al., in 2005 estimated that the prevalence of anemia (Hb <12 g/dl) in women with breast cancer at early stage. It was also investigated that survival of the patients was shorter in patients with anemia [19]. Low Hb levels in cancer patients may be due to increased level of pro-inflammatory cytokines such as tumor necrosis factor TNF-α, IL-6 and IL-1 that induce retention of iron by liver, gastrointestinal tract and endothelial system and exerting inhibitory action on erythrocytes [20]. William, et al., in 1983 observed that there was an elevated level of ESR in the patients with breast cancer [21].

Table 3 The PCV, pH and ESR mean value

Test	Mean value	Normal range
PCV	35.9	36-48%
Hb	10.68	11-6 g/dl
ESR	12	5-7 mm/hr

Table 4 shows the percent of cases with and without mastectomy in correlation with left and right side of breast affected. There was a higher percentage (31%) of mastectomy right breast side, as compared to (17%) the left breast side. While the cases without mastectomy were 52% (33% left side and 19% right side).

Table 4 The percentage of cases with and without mastectomy in correlation with left and right side of breast affected

Mastectomy status	Left	Right
With mastectomy	17%	31%
Without mastectomy	33%	19%

Table 5 shows the percentage of women with high level of prolactin hormone were 94.4% and only 5.6% with normal level. Ingram, et al., show that the prolactin levels were higher than the median value in control. Subjects were found to be associated with more than two-fold increase in the risk of breast cancer, and there was a downstream in the level of hormone at menopause, so those women with early menopause have a reduced period of exposure to high concentrations of prolactin [12]. Also, there was a reduction in prolactin level after first pregnancy [12]. The

mechanism by which high-normal circulating levels of PRL that leads to increased breast cancer risk is not exactly known but it may promote breast cancer via signaling pathway and increase the survival of breast cancer cells by stimulating divisions of new cancer cells and decreasing cell death program (apoptosis) and promote cancer spread. PRL has also implicated in causing resistance to cytotoxic drugs like cisplatin and drugs like paclitaxel, which act on cellular microtubules [13,14]. The increasing trends were driven by increase in hormone receptor-positive breast cancer, which is increased among all racial/ethnic groups, whereas rates of hormone receptor-negative breast cancers are decreased [20,21].

Table 5 The percentage of prolactin hormone level in breast cancer women

	Mean value ng/ml	Frequency	%
Prolactin level	31.5	67	94.40%
	12.02	4	5.60%

CONCLUSION

The study shows a high prevalence of breast cancer at age group 40-50 years. Most cases were (O +ve and A +ve) blood group. There was a relationship between prolactin level and breast cancer with a highly significant value, prolactin increased highly significantly ($p < 0.01$) in breast cancer patients as compare with normal value.

DECLARATIONS

Conflict of Interest

The authors have disclosed no conflict of interest, financial or otherwise.

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