

Prolactin Serum Levels and Breast Cancer: Relationships with Hematological Factors among Cases in Karbala Province, Iraq

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Abstract

Background: About one million of women are diagnosed with breast cancer globally and nearly half of whom will die from cancer. Breast cancer is the most common cancer and the leading of mortality among women. The present study aimed to find out the relationship breast cancer and levels of PRL and influence on some hematological parameters. **Materials and Methods:** A total of 71 specimens were collected from females with breast cancer. Blood specimens were collected, and a blood group, packed cell volume (PCV), hemoglobin (Hb), erythrocyte sedimentation rate (ESR), and prolactin (PRL) level was evaluated. **Results:** The results show that most breast cancer cases were 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⁺ and (26%) were A⁺ blood group, in compare to other blood groups. In addition, many women show a slight decrease in Hb and PCV level (<11.0 g/dl, <36% respectively), on the other hand, the mean value of ESR was increased nonsignificantly ($P > 0.05$). The PRL levels were increased (31.5 ng/ml) in compare to the range of normal value (14.5 ng/ml) in women at all age groups. **Conclusions:** The study concludes that there was a relationship between PRL level and breast cancer with a highly significant value.

Keywords: ABO, breast cancer, electrochemiluminescence immunoassay, prolactin

INTRODUCTION

Breast cancer is a malignant tumor which begins in the cells of the breast. The disease commonly in women, but also men can get it.^[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 once.^[2,3] (1) Ductal carcinoma *in situ* is the most common type of noninvasive breast cancer. In which, the cancer cells remain inside the ducts and not spread through into the surrounding breast tissue. (2) Lobular carcinoma *in situ* although it is not true cancer; however, it sometimes classified as a type of noninvasive breast cancer. It starts in the glands that produce milk and does not grow into the wall of the lobules. (3) Invasive (or infiltrating) ductal carcinoma which classifies 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. (4) Invasive (or infiltrating) lobular it is mostly similar to invasive ductal carcinoma.

Many women have no symptoms at the beginning of breast cancer but sometimes found after symptoms appear, thus it is

recommended to do the screening tests before any symptoms appear.^[4] Breast cancer can be diagnosis by two or more of these criteria (1) Signs and symptoms, a new lump or mass which is the most common sign. It mostly painless, hard mass that has irregular edges. (2) Imaging tests, use X-rays, magnetic fields, sound waves, or radioactive substances to make a pictures of the inside the breast.^[5,6] (A) Diagnostic mammograms is the most common testing that use to screening the breast tissue. A mammogram cannot prove that an abnormal area is cancer. To confirm this, a small tissue must be taken and investigating under a microscope.^[7,8] (B) 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] (C) Breast ultrasound, also known as sonography, uses sound waves to. Usually, used to specific area of concern found on the mammogram.^[10] (D)

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Ductogram, this test, sometimes uses to determine the cause of discharge of nipple.^[1,6] (E) 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 really present and what type it is.^[11] Prolactin (PRL) and breast cancer, the peptide hormone secreted from the anterior pituitary gland, has restricted to the lactation and infertility. The relationship between PRL and breast cancer has been suspected for years, but never conclusively proven. The PRL is similar to 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. PRL may cause infertility in several ways; PRL may stop a woman from ovulating. If this occurs, a woman's menstrual cycles will stop or may only disrupt ovulation once in a while. Women with high PRL levels may ovulate regularly but not produce enough of the hormone progesterone after ovulation. This is known as a luteal phase defect. Deficiency in the amount of progesterone produced after ovulation may result in a uterine lining that is less able to have an embryo implant.^[14] The present study was aimed to find out the relationship breast cancer and levels of PRL and influence on some hematological parameters.

MATERIALS AND METHODS

Study design and sampling

This was carried out at Al-Hussein hospital from period of January 2016 to March 2016 and included (71) women with breast cancer that diagnosed previously by physician. Before take the sample, the questionnaire was filled and it's including the age, family address, marriage, mastectomy, chemotherapy, or radiations.

Laboratory analysis

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

Data analysis

Statistical analyses were performed using SPSS statistics program version 18, (IBM, Armonk, NY, United states of America) and were the results with *P* values (<0.05) were considered statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the distribution of breast cancer cases among age groups; in which the majority of the overall 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 diagnostic at age 50 years and older, and the mortality rate about 89% occurs in that age groups.^[15]

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 think that the greater a 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]

Figure 1 illustrates four parameters, side of the breast affected, percent of women with mastectomy, percent of women with chemotherapy, and family history of cancer. There was almost an equal percentage between left and right breast cancer of all cases. 97% of cases were treated with chemotherapy; while, 3% were have not received chemotherapy at all. About one third of cases were having a family history of breast cancer (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 increased 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 three times higher for women with two relatives, and nearly four times higher for women with three or more relatives.^[17]

Figure 2 shows the frequency of blood groups among study cases in which O⁺ and A⁺ 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 have also an influence

Table 1: Classification of the study samples according to the age

Variable	Classes	Frequency (%)	<i>P</i>
Age groups (years)	20-30	2 (2.8)	<i>P</i> <0.01
	30-40	13 (18.3)	
	40-50	25 (35.2)	
	50-60	18 (25.4)	
	60-70	10 (14.1)	
	>70	3 (4.2)	
	Total	71 (100)	

Table 2: The comparable percentage between married and unmarried cases

Variable	Classes	Frequency (%)	<i>P</i>
Marriage	Yes	69 (97.1)	<0.01
	No	2 (2.9)	

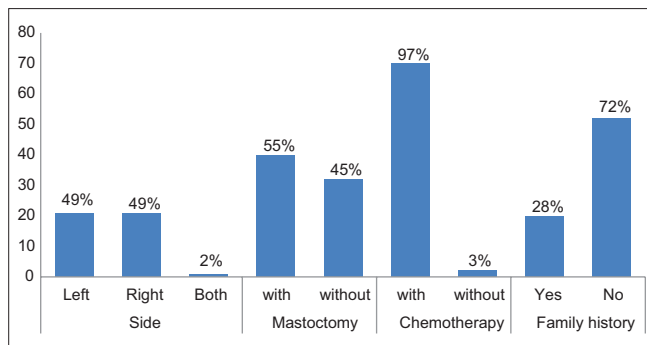


Figure 1: Illustrate four parameters, side of the breast affected, percent of women with mastectomy, percent of women with chemotherapy, and family history of cancer

on susceptibility and outcomes. Indeed, many researchers have been gone so far as to say that “blood groups were shown to possess a predictive value independent of other known prognostic factors” when discussing breast cancer. Other researchers have been suggested that a degree of the susceptibility to breast cancer, result from a gene perspective, might be a result of a breast cancer-susceptibility locus linked to the ABO locus located on band q34 of chromosome nine.^[18,19] Stamatakos *et al.*^[18] showed that a positive family history is more commonly found in Rh (+) patients irrelevantly of blood groups ABO. Rh (+) women with positive family history are more often presented in blood group A and less often in blood groups AB and B.^[17]

Table 3 shows the PCV, pH, and ESR mean value, all of these parameters show no abnormality among study cases. Kandemir *et al.*^[19] estimate the prevalence of anemia (Hb conc <12 g/dl) in women with breast cancer at early stage of breast cancer and its association with other known Prognostic factors and also, investigation show that patients survival and overall survival were shorter in patients with anemia. Low Hb levels in cancer patients may be due to increased level of pro-inflammatory cytokines, such as tumor necrosis factor-alpha, interleukin-6 (IL-6), and IL-1, that induce the retention of iron by liver, gastrointestinal tract and endothelial system, and exerting inhibitory action on erythrocytes,^[20] as well as William and Phillips (2000) were observed that there was an elevated level ESR in the patients with breast cancer.^[21]

Table 4 shows the percentage of cases with and without mastectomy in correlation with the left and right side of breast affected, in which there was a higher percentage (31%) of mastectomy with the right breast side compared to (17%) with left breast side, while the cases without mastectomy were 52% (33% in the left side and 19% at right side). The results show the differences were significant at $P < 0.05$.

Table 5 shows the percentage of women with high level of PRL hormone were 94.4% and only 5.6% with normal level. Ingram *et al.*^[12] show that the PRL levels were higher than the median value in control subjects which were found to be associated with a more than two-fold increase in the risk of breast cancer, and there was a downstream in the level of hormone at menopause,

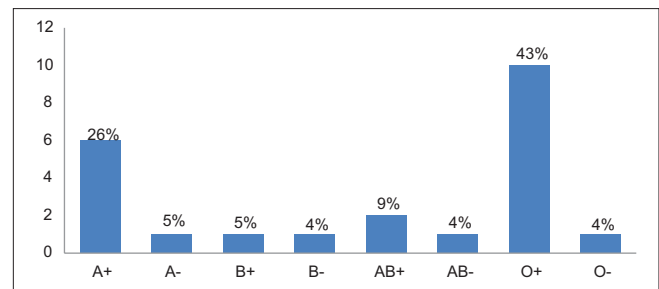


Figure 2: The frequency of blood groups among study cases

Table 3: The packed cell volume, pH, and erythrocyte sedimentation rate mean value

Test	n	Mean value	Normal range
PCV	71	35.9	36%-48%
Hb	71	10.68	11-16 g/dl
ESR	71	12	5-7 mm/h

PCV: Packed cell volume, Hb: Hemoglobin, ESR: Erythrocyte sedimentation rate

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

	Left (%)	Right (%)	P
With mastectomy	17	31	<0.05
Without mastectomy	33	19	
Total	50	50	

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

Prolactin level	Mean value (ng/ml)	Frequency, n (%)
High	31.5	67 (94.4)
Normal	12.02	4 (5.6)
Total		71 (100)

so those women with early menopause have a reduced period of exposure to high concentrations of PRL. In addition, there was a reduction in PRL level after the 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 be promote breast cancer through signaling pathway and increase the survival of breast cancer cells by stimulating the divisions of new cancer cells and decreasing cell death program (apoptosis) and promote cancer spread. PRL has also been implicated in causing resistance to cytotoxic drugs such as cisplatin and drugs like paclitaxel, which act on cellular microtubules.^[13,14] The increasing trends were driven by increases in hormone receptor-positive breast cancer, which increased among all racial/ethnic groups, whereas rates of hormone receptor-negative breast cancers decreased.^[20,21]

CONCLUSIONS

The study shows a high prevalence of breast cancer at age

group 40–50 years. Most cases were (O⁺ and A⁺) blood group. There was a relationship between PRL level and breast cancer with a significant value, PRL increased significantly ($P < 0.01$) in breast cancer patients as compare with normal value.

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Conflicts of interest

There are no conflicts of interest.

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