Does Prolactin Have a Role in Breast Cancer? A study of Women in Mosul City

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ABSTRACT

Background: Breast cancer is the most common cancer in women, a second leading cause of cancer death; it affects about 12% of women worldwide.

Objectives: Our study was undertaken to find out the relationship between the levels of prolactin hormone in serum in a newly diagnosed woman with cancer breast and apparently healthy normal women who have no breast complain in Mosul city

Methodology: A case-control study was conducted on 52 women with newly diagnosed cancer breast (30 premenopausal women and 22 postmenopausal women) and 50 apparently healthy women as a control group (27 premenopausal women and 23 postmenopausal women). Blood specimens were collected and serum prolactin level measured.

Results: The results showed that the prevalence of cancer breast cases was more common in 40–50 years’ age group and less common among other age groups, the mean ± SD of serum prolactin level in premenopausal women with cancer breast and control groups were (15.02 ± 8.08), (13.76 ± 5.98) ng/dl respectively, and in postmenopausal women with cancer breast and control groups were (12.79 ± 6.90), (12.89 ± 4.04) ng/dl both statistically non-significant, about 20 % of cancer breast women had positive family history.

Conclusions: The study concludes that there was no relationship between prolactin level and cancer breast, one-third of breast women have a positive family history of cancer breast.

Keywords: cancer breast, prolactin hormone, premenopausal and postmenopausal women

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Introduction

Cancer (CA) of breast is the most common cancer in women and it is a second leading cause of cancer death in them, it affects about 12% of women globally. The signs of CA breast may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, a newly inverted nipple, or a red or scaly patch of skin. There are many risk factors for developing breast cancer, including being female, obesity, lack of physical exercise, drinking alcohol, hormone replacement therapy during menopause, ionizing radiation, early age at first menstruation, having children late or not at all, older age, prior history of breast cancer, and family history. Breast cancers can begin from different parts of the breast, most of them begin in the ducts that carry milk to the nipple (ductal cancers), some start in the glands that make breast milk (lobular cancers). Prolactin is a polypeptide hormone that is secreted by lactotroph cells in the anterior pituitary and is the main trophic factor for milk production by the breast.

Prolactin plays an important role in the proliferation and differentiation of normal breast epithelium. The hormone acts in an endocrine, autocrine and paracrine manner through the prolactin receptor and a large number of cytokine receptors. In 2007, Aisha Memon et al. found that prolactin hypersecretion is likely an etiological factor in some of the conditions of Aberration of Normal Development and Involution (ANDI), rest may be due to end-organ hypersensitivity to normal circulating prolactin or other hormones. Pharmacological manipulation of raised prolactin in patients can provide relief from symptoms.

The data about the role of prolactin level (PRL) in human CA breast appear to be controversial so, it has been difficult to establish definitive involvement of prolactin in human breast disease. PRL was first recognized as a hormone that plays an important role in CA breast initiation and development in rodents. It has been and still difficult to assign the function of this hormone in either the etiology or progression of the breast tumor. However, it is well established that prolactin is intimately involved in the development and differentiation of the normal gland in mammalian species. Prolactin’s role in rodent mammary cancer has been established for some time. The relationship between prolactin and breast cancer has been suspected for years, but never definitively proven. The prolactin is analogous to growth hormone and its actions by the growth-promoting JAK/STAT pathway suggest its tumor-promoting effects.

There have been some extensive investigations using large prospective cohorts to assess the risk of primary breast cancer in women with high levels of circulating PRL. In 2014, a study of postmenopausal women found a modest positive association between circulating prolactin levels and invasive CA breast risk among postmenopausal women (odds ratio (OR)Q4-Q1 = 1.29 (95% CI 1.05, 1.58), P trend = 0.09).

Materials and Methods

This is a case-control study; it had been approved by the College of Medicine, University of Mosul. Administration and ethical approval were obtained from the Nineveh Directorate of Health. It was carried out...
out at the early detection breast cancer Department of Al-Khansa’a Teaching Hospital in Mosul city during
the period from January 2019 to June 2019.
A case-control study was conducted on (52) newly diagnosed women with CA breast that diagnosed
previously by a physician, (30 premenopausal women and 22 postmenopausal) and 50 apparently healthy
women have no breast complain (27 premenopausal women and 23 postmenopausal women).
Before taking the sample, the questionnaire was filled and it's including age, family address, marriage,
menarche, history of lactation, family history of CA breast, medical history, menstrual cycle regularity,
drug, and any hormonal therapy.
Women with CA breast can be diagnosis by two or more of these criteria:

1. Signs and symptoms, a new lump or mass which is the most popular sign. It mostly painless, hard
mass that has irregular edges with restricted mobility.

2. Breast ultrasound and mammogram findings of breast CA.

3. Fine needle aspiration or core needle biopsy or excisional biopsy that confirms breast CA diagnosis.

Women who were \( \leq 44 \) years of age and reported having had at least nine menstrual periods in the last 12
months were classified as premenopausal. Women were classified as postmenopausal when they reported
no having any menses over the past 12 months aged 45 years or older.

Laboratory analysis

Serum prolactin test requires a sample that should be drawn in the morning at least two hours after patient
awakes as a sample drawn earlier may show sleep-induced peak level \(^{16}\). No restriction of food, fluid, and
physical activity is required but the patient should relax half an hour before the test \(^{17, 18}\).
Three ml. of venous blood was collected from each patient by venipuncture, centrifuged to obtain serum and
stored at freezing until analysis. Serum samples were tested for PRL by the “electrochemiluminescenceimmunoassay” by the Cobas immunoassay analyzers system.

Statistical analyses.
The study data are presented as numbers and percentage or mean and standard deviation. Statistical analyses
were performed using SPSS statistics program version 19, Chi-squared (\( \chi^2 \)) test was used to find the
statistical association P-value < 0.05 used as a significant statistical association. \(^{19}\)

Results

The Mean age \( \pm \) SD in women with CA breast was (47.73\( \pm \)10.69) years old which not significantly
different from age of control women (47.68\( \pm \)10.05) years as shown in (Table 1).

Table: (1) age groups in women with CA breast and control groups.

Table 2 showed that there was no significant difference in the number %of premenopausal and postmenopausal women.

Table (2): premenopausal and postmenopausal women % in both case and control groups.

<table>
<thead>
<tr>
<th>Menstrual cycle state</th>
<th>Cases</th>
<th>Controls</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>30(57.7)</td>
<td>27(54.0)</td>
<td>0.707</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>22(42.3)</td>
<td>23(46.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>52(100.0)</td>
<td>50(100.0)</td>
<td></td>
</tr>
<tr>
<td>P-Value**</td>
<td>0.267</td>
<td>0.572</td>
<td></td>
</tr>
</tbody>
</table>

* Chi-Square test was used.
** Z- test of one proportion was used.

Table (3) revealed that the mean PRL was lower in postmenopausal women in both case and control groups but the difference was statistically non-significant.

Table (3): Serum prolactin level in women with the premenopausal women and postmenopausal women in both case and control groups.

<table>
<thead>
<tr>
<th>Menstrual cycle state</th>
<th>Cases</th>
<th>Controls</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD prolactin ng/dl</td>
<td>Mean ± SD prolactin ng/dl</td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>15.02± 8.08</td>
<td>13.76 +5.98</td>
<td>0.510</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>12.79+6.90</td>
<td>12.89+4.04</td>
<td>0.951</td>
</tr>
</tbody>
</table>

* independent t-test.

Table 4 showed that in premenopausal women, only 20 %, 15 % in both case and control group respectively were hyperprolactinemia.

Table (4): No. % of premenopausal women with normal serum prolactin levels and hyperprolactinemia in case and control groups.
<table>
<thead>
<tr>
<th>Prolactin level (ng/dl)</th>
<th>Cases</th>
<th>Controls</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Normal (≤ 16 ng/dl)</td>
<td>24(80.0)</td>
<td>23(85.2)</td>
<td>0.734</td>
</tr>
<tr>
<td>High (&gt; 16 ng/dl)</td>
<td>6(20.0)</td>
<td>4(14.8.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30(100.0)</td>
<td>27(100.0)</td>
<td></td>
</tr>
<tr>
<td><strong>P-Value</strong></td>
<td>0.001</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher Exact test was used.

** Z- test of one proportion was used

In postmenopausal women, only 9 %, 17 % in both case and control group respectively were hyperprolactinemia as shown in (Table 5).

Table (5) No. % of postmenopausal women with normal serum prolactin and hyperprolactinemia in case and control group

<table>
<thead>
<tr>
<th>Prolactin level</th>
<th>Cases</th>
<th>Controls</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Normal (≤ 12 ng)</td>
<td>20(90.9)</td>
<td>19(82.6)</td>
<td>0.665</td>
</tr>
<tr>
<td>High (&gt; 12 ng)</td>
<td>2(9.1)</td>
<td>4(17.4)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>22(100.0)</td>
<td>23(100.0)</td>
<td></td>
</tr>
<tr>
<td><strong>P-Value</strong></td>
<td>0.000</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher Exact test was used.

** Z- test of one proportion was used.

There was a significant difference in a family history of CA breast between case and control group, but there was no significant difference in marriage % and history of lactation between the two groups (Table 6).

Table (6): Family history, marriage history of lactation in both case and control groups

<table>
<thead>
<tr>
<th>Characters</th>
<th>Cases</th>
<th>Controls</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>+ ve family history of Ca breast</td>
<td>10(19.2)</td>
<td>1(2.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>- ve family history of Ca breast</td>
<td>42(80.8)</td>
<td>49(98.0)</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>45(86.5)</td>
<td>39(78.0)</td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>7(13.5)</td>
<td>11(22.0)</td>
<td>0.258</td>
</tr>
<tr>
<td>+ ve history of lactation</td>
<td>40(76.9)</td>
<td>35(70.0)</td>
<td></td>
</tr>
<tr>
<td>- ve history of lactation</td>
<td>12(23.1)</td>
<td>15(30.0)</td>
<td>0.428</td>
</tr>
</tbody>
</table>

* Chi-Square test was used.

Figure(1) showed that most of the women affected with CA breast on the right side (55.8%), while the left side was (44.2%).
Discussion

This study is the first study on PRL in women with CA breast in our locality, it shows a high prevalence of breast cancer at age group 40–50 years were accounted 17 women (32.7%), while the smallest number was at age group 60–70 were accounted 9 women (17.3%), this findings show partial agreement with those from Ali JK, et al. (2018). (20)

We study 52 newly diagnosed women with CA breast after they diagnosed by physician, their mean age was (47.73) years, they were (30, 22) women in premenopausal and postmenopausal state respectively, those matched to control women, their mean age was (47.68), they were (27, 23) women in premenopausal and postmenopausal respectively.

The serum prolactin level in premenopausal women with CA breast was (15.02±8.08) ng/dl (normal range is 0.8–16ng/dl) which statistically non-significant from that of control group (13.76±5.98) ng/dl, high serum prolactin in premenopausal women were found in 6 women of cases and only 4 women of control. The serum prolactin level in postmenopausal women with CA breast and control group were (12.79±6.90, 12.89±4.0) ng/dl respectively (normal range is 0.5–12ng/dl) was statistically non-significant, high prolactin in postmenopausal women were found in two women of cases and four women of controlin agreement with the findings observed by other investigators (21) they found no strong associations were seen between prolactin and risk of breast cancer, the same finding also found by Wang, D. Y et al. (1999)(22) that no significant association between risk of breast cancer and prolactin in either pre- or postmenopausal women. So prolactin appears not to be an important determinant of breast cancer risk, and Bernstein L. et al.1990 (23) find no differences in the serum prolactin levels of cases and controls of their study.

Our study disagrees with other researchers (15, 20) that found statistically significant heterogeneity in the relation of prolactin levels with breast cancer risk between women who were either pre- or postmenopausal.
In 2015 Tikk K. et al research connects prolactin and invasive breast cancer to the outcome of in situ breast cancer and shows that higher circulating serum prolactin is linked with increased risk of in situ breast cancer. (24)

The function of prolactin in etiology and progression of human breast cancer is not obvious. The discovery of extra pituitary prolactin synthesis by breast tissue suggests that a re-examination of the role of prolactin in human breast cancer is in order, the fact that breast cancer cells themselves are a source of extra pituitary prolactin may give explanation because our patients are newly diagnosed the only 29% of women with Ca breast in our study were hyperprolactinemia may the cause is the time that women develop Ca breast and follow up of patient needed.

Women with CA breast has a positive family history of CA breast was about 20 % while only 2 % in control group has a positive family history of CA breast. About one-third of cases were having 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 means that there is a relationship between family history and CA breast.

There was no significant difference in marriage % and the history of lactation between case and control groups.

Conclusions
The study shows high prevalence of breast cancer at age (40-49) years and lowest was in (60-70) years, and there was no significant high serum prolactin level in women with newly diagnosed CA breast in pre and postmenopausal women. One-third of women with CA breast have a positive family history.

Acknowledgments
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References


