

## Anthropometric and Hormonal Study of Breast Cancer Patients in Slemani City.

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### ABSTRACT

Cancer is a group of diseases characterized by uncontrolled cell division leading to growth of abnormal tissue.

The aims of the study were to evaluate the serum levels of Progesterone, Estradiol and Prolactin in women with breast cancer and to study the effect of anthropometric factors on breast cancer development. The subject enrolled in the study were divided into (58) breast cancer women and (30) healthy women as controls in Slemani city. The data obtained showed: highly significant elevation of Prolactin in breast cancer women compared with control ( $P < 0.005$ ), while no significant difference in Progesterone and Estradiol. The percentage of breast cancer is higher in urban areas than rural area, in the age  $\geq 45$  years, in the body weight  $\geq 70$  kg, in non smokers than smokers, and in those who did not have a family history of breast cancer.

**Key words:** breast cancer, PRL, PRG, E2, anthropometrics.

### الخلاصة

السرطان هو من الأمراض التي تتميز بانقسام الخلايا غير المنتظم يؤدي إلى نمو الأنسجة بصورة غير طبيعية. الهدف من هذه الدراسة هو تقييم مستوى هرمون البروجسترون والاستراديول والبرولاكتين لدى النساء المصابات بسرطان الثدي ودراسة تأثير بعض العوامل على سرطان الثدي. تم الدراسة على (58) امرأة مصابة بسرطان الثدي و(30) امرأة سليمة من مدينة السليمانية. وأظهرت البيانات التي تم الحصول عليها: ارتفاع كبير في هرمون البرولاكتين لدى النساء المصابات بسرطان الثدي ( $P > 0.005$ )، في حين لا يوجد فرق كبير في البروجسترون واستراديول. نسبة الإصابة بسرطان الثدي هي أعلى في المناطق الحضرية من المناطق الريفية، في عمر  $\leq 45$  سنة، بالاوزان  $\leq 70$  كلغم، في غير المدخنين من المدخنين، وفي أولئك الذين لم يكن لديهم إصابة عائلية بسرطان الثدي.

Cancer happens when cells do not die when they should. It believed that cancers arise from both genetic and environmental factors that lead to aberrant growth regulation of a stem cell population, or by the dedifferentiation of more mature cell types<sup>1</sup>.

Breast cancer is a malignant tumor that starts from breast cells. It may grow into (invade) surrounding tissues or spread (metastasize) to distant areas of the body. The disease occurs almost entirely in women, but men can get it, too<sup>2</sup>. Most breast cancers begin in the cells that line the ducts (ductal cancers), some begin in the cells that line the lobules (lobular cancers), while a small number start in other tissues<sup>3</sup>.

Breast cancer in women represents a significant health problem because of the numbers of individuals affected by this disease. Thirty percent of all cancers in women occur in the breast making it the most commonly diagnosed female cancer<sup>4</sup>.

Hormone is a substance released directly into the blood by specialized cells in response to a specific stimulus, carries messages to the cells for maintainance of chemical levels in the bloodstream that achieve homeostasis<sup>5</sup>. The most important hormones in breast cancers are:

1- Prolactin (PRL): a high molecular weight protein hormone secreted by the anterior lobe of pituitary gland, in

the mother's blood vessels. There is enough evidence now to support the belief that PRL hormone is directly responsible for promotion of milk secretion and that abnormally low level of this hormone is indicative of deficient lactation in mothers<sup>6</sup>. Its main target is the breast, where it stimulates lobulo-alveolar growth, differentiation and pro-survival<sup>7</sup>. Prolactin may influence mammary carcinogenesis<sup>8</sup>.

- 2- Progesterone (PRG): this steroid hormone is produced by the ovaries, placenta, and adrenal glands which it regulates menstruation, supports pregnancy, tempers the highly stimulatory effects of estrogen and helps an embryo develop by providing a source of corticosteroids<sup>9</sup>. A disorder at progesterone receptor (PR) is a condition that relates to the many female specific disorders which it plays a critical role in the development of breast cancer. Mutation within PR can be seen. Presently, prediction of protein nanostructure and function is a great challenge in the proteomics and structural genomics<sup>10</sup>.
- 3- Estradiol: Estradiol (E2 or 17 $\beta$ -estradiol, also oestradiol) is a steroid hormone which is considered as the predominant sex hormone present in females. It is also present in males, being produced as an active metabolic product of testosterone. It represents the major estrogen in humans. Estradiol has not only a critical impact on reproductive and sexual functioning, but also affects other organs including the bones<sup>11</sup>. Epidemiological and animal studies have indicated that E2 is involved in breast cancer; however, the mechanism is unclear. The development of breast cancer, mutation within prolactin receptor can be seen<sup>12</sup>.

Breast cancer risk in women was assessed relative to the risk factors including race<sup>13</sup>, increasing age<sup>14</sup>, family history<sup>15</sup>, genetic factors<sup>16</sup>, personal history of benign or cancerous breast disease<sup>17</sup>, hormonal history<sup>18</sup>, hormone replacement therapy (HRT)<sup>19</sup>, obesity and high fat diets<sup>20</sup> and alcohol<sup>21</sup>.

The aim of the present study is to extend our understanding of the breast cancer with the specific objectives like: study the relation between inhabitations and breast cancer in Kurdistan Region, study the relation between Breast cancer and anthropometric factors like: ages, smoking and family history of breast cancer and to determine the serum Estradiol, Progesterone and Prolactin for breast cancer patients after their diagnosis by consultant.

### Materials and Methods

This study was conducted over a period from July 2010 to February 2011 at the Breast clinic in the teaching hospital of Slemani city/ Iraq. The present study was carried out on 88 individuals, which were divided into two groups:

A- The control group (Normal group): Included (30) selected apparently healthy women. The range of their ages was (17-40) years old.

B- The case group (Breast cancer group): Included (58) breast cancer patients, they were diagnosed by family medicine and surgeries consultants. The range of their ages was (17-64) years old.

Informed consent was obtained verbally from all participants. All participants were carefully screened to exclude evidence of congestive heart failure, hepatic and renal diseases. The samples from healthy individuals and breast cancer patients were collected: PRG and E2 were taken at follicular phase, pregnancy excluded and PRL was taken during rest or early morning before mastectomy and before take

chemotherapy or/and radiotherapy for breast cancer patients.

Five milliliters of venous blood was withdrawn from the cubital vein of each individual using disposable syringes. The blood samples were allowed for 15 minutes at room temperature to clot and serum was separated by centrifugation at 3500 rpm for 10 minutes. Serum samples were either analyzed immediately or stored at -35 C° until they were analyzed<sup>22</sup>.

Enzyme-linked Immuno Fluorescent Assay for *in Vitro* used for determination of serum PRL, E2 and PRG<sup>23</sup>.

Data were analyzed statistically using SPSS 19.0 program; P-value was used for comparison. The data was considered not significant at  $P > 0.005$ .

## Results

The mean serum levels of PRG, E2 and PRL in control group are all within their reference ranges. On the other hand there was a clear difference between the breast cancer groups according to their age ranges, those of the age range between ( $\geq 45$ ) years represented the highest percentage (Table-1).

Of The (58) cases, the urban area samples were (36) and the rural area samples were (22) as shown in table (2).

The results indicated also highly significant elevation ( $P < 0.005$ ) in the mean serum levels of PRL in the case group compared with the control group, while there are no significant differences between control and case groups for the PRG and E2 hormones ( $P > 0.005$ ) (Table-3).

Table (1): The age distribution of case group.

Age Range/ years	Frequency	Percent	Mean $\pm$ Standard Deviation
15 - 24	4	6.9	44.81 $\pm$ 10.973
25 - 34	3	5.2	
35 - 44	21	36.2	
$\geq 45$	30	51.7	
Total	58	100.0	

Table (2): The geographical distribution of breast cancer samples.

Geographical distribution	Frequency	Percent
Rural	22	37.9
Urban	36	62.1
Total	58	100.0

Table (3): Levels of PRG, E2, and PRL in serum of breast cancer and controls.

Hormones level	Groups	Number	Mean $\pm$ Std. Deviation	P-Value
PRG ng/ml	Case	58	1.5585 $\pm$ 3.37149	0.064
	Control	30	0.4020 $\pm$ 0.1114	
E2 pg/ml	Case	58	82.7968 $\pm$ 82.33113	0.671
	Control	30	75.9533 $\pm$ 41.53950	
PRL ng/ml	Case	58	54.6812 $\pm$ 62.90860	0.003
	Control	30	19.5150 $\pm$ 7.96660	

Table (4): The weight of case group.

Weight Range/ Kg	Frequency	Percent	Mean±Standard Deviation
40 - 49	1	1.7	73.16±11.222
50 - 59	4	6.9	
60 - 69	16	27.6	
≥70	37	63.8	
Total	58	100.0	

Table (5): Family history of breast cancer distribution in case group.

Family history other cancer	Frequency	Percent
No	54	93.1
Yes	4	6.9
Total	58	100.0

Table (6): Smoking distribution in case group.

Smoking	Frequency	Percent
No	55	94.8
Yes	3	5.2
Total	58	100.0

The breast cancer group shows that, the breast cancer risk is increased (63.79%) with weight increase (≥70 kg) (Table-4).

The result showed that (93.1%) of case do not have a family history with breast cancer and (6.9%) have a family history of breast cancer (Table-5).

Finally the results showed that (94.8 %) non smoking and (5.2%) smoking (Table-6).

### Discussion

Breast cancer is the most commonly diagnosed malignancy in women, but is second to lung cancer in terms of cancer deaths for women. If a woman lives to be 90, she will have a 1 in 9 chance of developing breast cancer in her lifetime and a 1 in 27 chance of dying from it<sup>24</sup>.

Age is one of the risk factor of breast cancer, the data obtained in this study showed that breast cancer is high

(51.72%) in the age (≥45) years (Table-1). This finding is in agreement with other international studies in United State<sup>25</sup> and disagreement with other studies done in Iran and Kuwait because these countries have a different environment<sup>26, 27</sup>.

For the first time, the breast cancer occurrence in women was described in this study according to the geographical distribution in Kurdistan region. This study revealed that the percentage of breast cancer in urban areas was elevated (62.07%) (Table-2), when compared with the percentage of breast cancer in rural areas (37.93%). We can refer the reason to process of modernization and its accompanying processes: industrialization and urbanization<sup>28</sup>. These findings are in agreement with other population like: Egypt<sup>29</sup>, USA<sup>30</sup>, and India<sup>31</sup>.

Breast cancer is a common disease and the elevated PRL levels in breast cancer can be more widespread than usually believed. The most common hormone producing pituitary tumor in women is prolactinomas secreting PRL. At autopsy micro prolactinomas is a rather common finding, indicating that PRL producing pituitary tumors is an underestimated condition in an aged population. Therefore an association between prolactinomas/elevated PRL levels and breast cancer has been difficult to study<sup>32</sup>. In this study, the mean values of serum PRL were (19.5150±7.96660 ng/ml) and (54.6812±62.90860 ng/ml) in control and case groups respectively (Table 3), with the significant differences between them (P<0.005). This finding is in agreement with others studies<sup>33</sup> and<sup>34</sup>.

A large body of evidence from clinical trials and observational studies indicate that the use of estrogen-only therapy for less than five years has minimal if any impact on the risk of breast cancer. In contrast the use of combination estrogen-progestin hormone therapy for more than five years is associated with an elevated risk of breast cancer<sup>35</sup>. In this study, blood PRG levels were found not to be related to breast cancer risk. This finding is not agreement with other studies<sup>36</sup> and<sup>37</sup>; therefore more studies are needed in the future to clear this discrepancy.

The last hormone measured in this study was E2. The study showed no significant differences between control and case groups (P>0.005) (Table-3). This finding is agreement with other studies<sup>38</sup>. Serum PRG and E2 levels have been measured in 210 premenopausal women with operable breast cancer on samples taken within 3 days of tumors excision. There was no relation between E2 level and time since last menstrual period, nor any effect of E2 value on prognosis<sup>39</sup>. On another

hand breast cancer risk is increased by early menarche and late menopause, suggesting that the long duration of exposure of the breasts to the high levels of ovarian steroids in premenopausal women increases risk. Recent prospective studies have shown that postmenopausal women who develop breast cancer have significantly greater prediagnostic serum concentrations of E2 than postmenopausal women who remain healthy<sup>40</sup>.

The anthropometric breast cancer risk factors studied in this research were: The results obtained show that, high percentage (63.79%) in the weight ( $\geq 70$  kg) (Table-4), the breast cancer risk is increased with weight increase. This result is supported with other studies<sup>41,42</sup>, and<sup>43</sup>. In our 58 breast cancer cases, the result showed that (93.1%) of case do not have a family history with breast cancer and (6.9%) have a family history of breast cancer (Table-5). These findings are in disagreement with other international studied<sup>44</sup>, which might indicate to different factor or with additional risk, such as type and quality of food, lack of practicing exercise, banned mass killing and chemical weapons used in the region as well as lack of an active quality control center for imported goods into the region.

Breast cancer risks are higher among women with a family history of the disease that having a first-degree relative with breast cancer. While having more than first-degree relative who has or had breast cancer before the age of 40 or in both breasts increase a women risk even more<sup>45</sup>. The relationship between smoking and the risk of breast cancer has been unclear for several decades, and whether or not young women should be warned about smoking as a possible cause of breast cancer remains controversial<sup>46</sup>. The results were show that (94.83 %) non smoking and (5.17%) were smoking (Table-6). This result is

supported with other studies<sup>47</sup>. Smoking has effects that can both increase and decrease breast cancer risk. On one hand, tobacco smoke contains chemicals that can cause breast cancer in animals and could thus be associated with an increase in breast cancer risk. On the other hand, smoking has been shown to have many effects which suggest an opposition of the effects of estrogen and could decrease risk of breast cancer. The interplay between the effects of the cancer-causing chemicals and the apparent opposition of estrogen is critical to breast cancer risk. The nature of this interplay is poorly understood<sup>48</sup>.

### Conclusions

This study showed the higher incidence of breast cancer in the urban distributions, the age  $\geq 45$  years, in these with weight  $\geq 70$  kg, in non smoking, and in these who had no family history of breast cancer. Serum PRL level was significantly higher among the case group compared with control groups, while there were no significant difference in serum PRG and E2 levels.

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