Turkish Online Journal of Qualitative Inquiry (TOJQI)
Volume 12, Issue 7, Month 2021: 480-487

Hormonal Evaluation of Obesity As a Risk Factor For Breast Tumors

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Abstract

The purpose of this study was to estimate some of the indicators as a risk factors of breast tumors. The study included the measurements of the Body Mass Index (BMI), Cortisol, Leptin and Vitamin D in blood serum of: 165 samples: (85) of them satisfactory sample of patients with breast cancer, (30) with benign breast diseases and (50) healthy women were used as a control. Samples were collected from the Oncology and Nuclear Medicine Specialized Hospital in Mosul. The results were as showed a highly significant increase ($P \geq 0.01$) in serum levels of cortisol and leptin in patients with breast cancer with controls groups, while there were no significant differences in the levels between patients with benign breast disease and control groups. The patients with breast cancer were found significant lower ($P \geq 0.01$) in the levels of serum Vitamin D in patients with breast cancer and no differences in patients with benign breast diseases compared with controls groups. The results also showed a significant increase in the (BMI) for the first age group of benign breast tumors and a significant increase ($P \geq 0.01$) for all groups of malignant tumor compared with control groups . The results showed increased with the progression of tumor stage progresses from first to third stage while decrease in the fourth stage. The highest level of cortisol was observed in the first stage of tumor and decreased in the second stage, more decreased was noticed in third stage, while in forth stage was increased. The results showed that levels of leptin increased with progression of tumor stages. Also the results indicates decrease in the level of Vitamin D as the tumor stages progress.

Keywords: Breast cancer, Benign Breast diseases, BMI, Vitamin D , Leptin, Cortisol.

1. Introduction

Breast cancer represent one of the most generic malignant tumors in the world and main cause of death among women (Siegel et al. 2019; Ferlay et al, 2019), because of both women's lifestyle changes and early detection programs(Arnold et al, 2015). Inactivity and obesity are the most important risk factors for breast cancer (Harvie et al, 2015), breast cancer is a malignant tumor originate from epithelial cells of glandular milk ducts or lobules of the breast, it assorted into four distinct differences according to (TNM staging system) which attend Tumor, Node, Metastasis, it uses a combination of tumor size (T). Lymph node involvement (N) and presence or absence of metastasis (M) which result four stages(Gabriel et al, 2017). Benign breast diseases is made up of a heterogeneous group of lesions that have varies symptoms, it may be asymptomatic or have a clinical appearance, such as palpable

nodularity, thickening, mass, pain, inflammation or nipple discharge (Ramesh and Bookya, 2017).

Obesity is recognized a risk factor for the development of breast cancer, the efficacy of cancer treatments is significantly lower in obese breast cancer survivor (Lee et al, 2017) .

Cortisol, a steroid hormone, is synthesized from cholesterol, it is synthesized in the zona fasciculate layer of the adrenal cortex. Cortisol has a variety of effects on different functions throughout the body, cortisol levels are associated with greater disease severity in women with breast cancer, neuroendocrine regulation of cortisol may contribute to cancer progression and health outcome through multiple mechanisms(Philips, et al. 2018).

Leptin is a peptide hormone contains 167 amino acid it called a pleiotropic hormone, there are opinions about the relationship of leptin to the cancer(Samad, 2019).

Animal studies show that Vitamin D may affect cancer cell growth, apoptosis and tumor angiogenesis at cellular level (Huss et al. 2019). Vitamin D refers to a group of fat-soluble secosteroid that are produced in two forms: D2 and D3, the D3 form is produced from 7-dihydroxycholesterol under the skin that is exposed to U V-B light (Atoum and Alzooughool, 2017).

2. Materials and Methods

In this study, 165 blood samples were collected: (85) samples of females with breast cancer, (30) with benign breast diseases and (50) as control, from Oncology and Nuclear Medicine Specialized Hospital in Mosul, divided into four age groups as follows:

20-30 , 31-40 , 41-50 and 50≥

Blood samples were collected in a volume of 5ml and serum was obtained according to (Tietz,1994 and Pushpa, et al.,2011).

Statistical analysis was performed by using t-value test(Salim and Adnan, 2017).

2.1. Calculation of Body Mass Index (BMI)

The (BMI) of each participant is calculated as weight (Kg) divided by the square of height (meters), and classified in accordance with the international classification system of the World Health Organization (Who,2019).

2.2. Biochemical Tests

The blood serum was used to estimate the levels of some biochemical parameters:

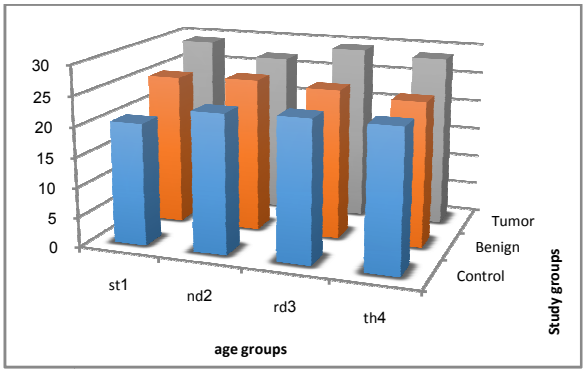
1. Cortisol and Vitamin D :

Cortisol hormone and Vitamin D concentrations in serum were estimated by using AFIAS Kit provided by boditechMed Incorporated Korea (Bartles et al.,2003, Holick, 2006)

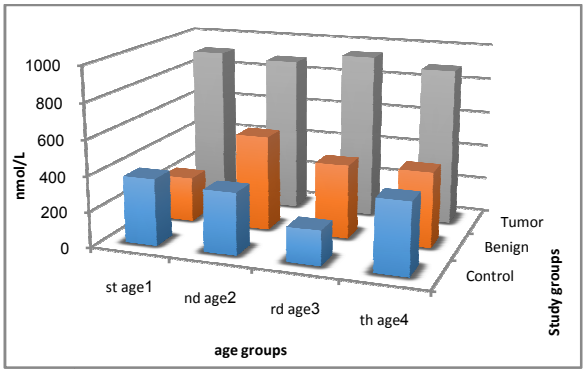
2. Leptin hormone:

Leptin concentration is serum was estimated by using ELISA Kit provided by DBC USA(Dagogo, et al., 1996).

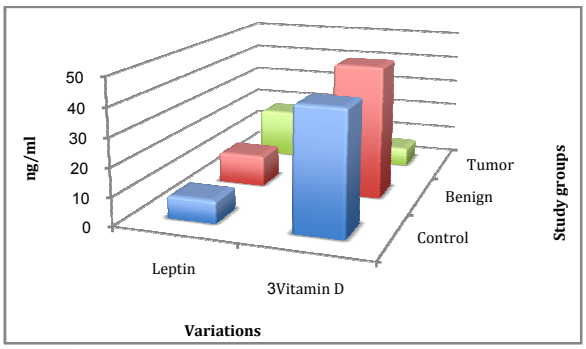
3. Results and Discussion



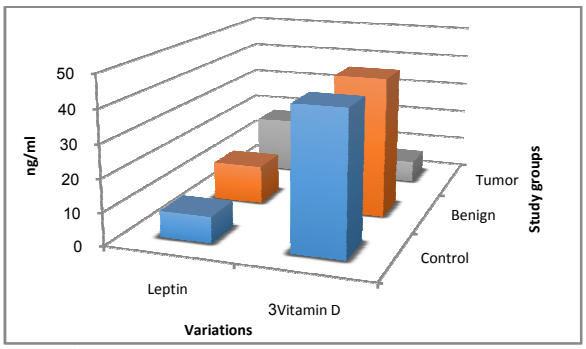
Figure(1): BMI value in four age groups.



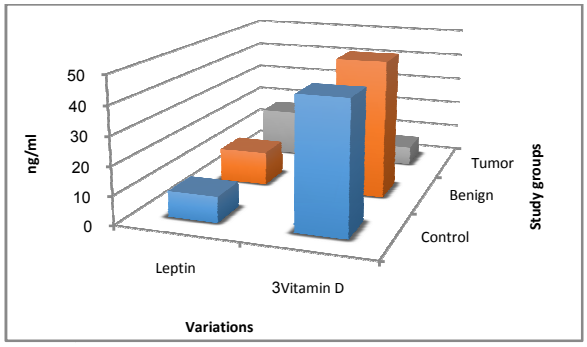
Figure(2): Cortisol concentration in all age groups.



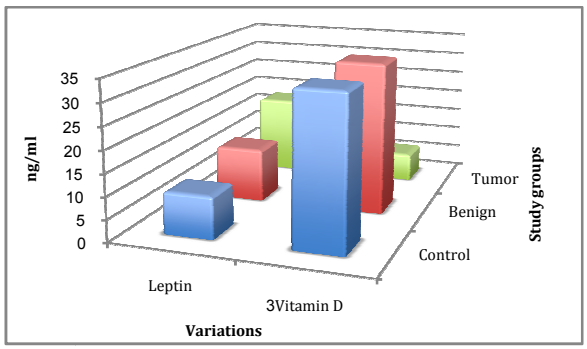
Figure(3): Leptin and VitaminD3concentrations in first age group.



Figure(4): Leptin and VitaminD3 concentrations in second age group.



Figure(5): Leptin and VitaminD3 concentrations in third age group.



Figure(6): Leptin and VitaminD3 concentrations in fourth age group.

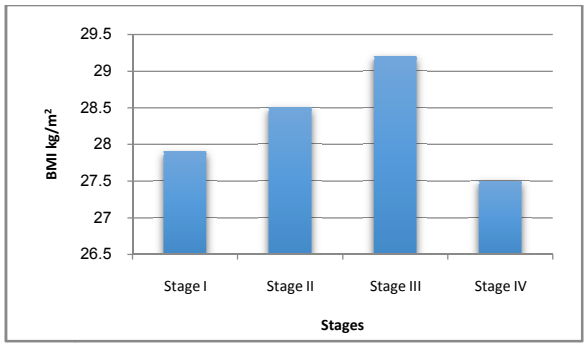
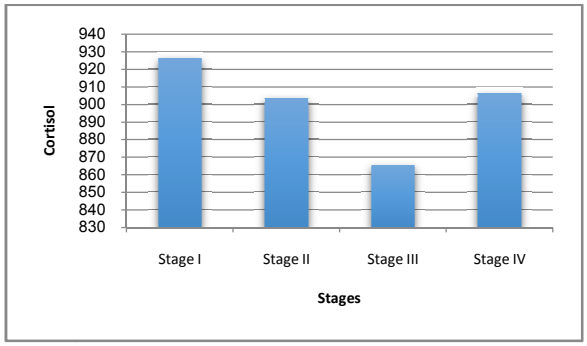
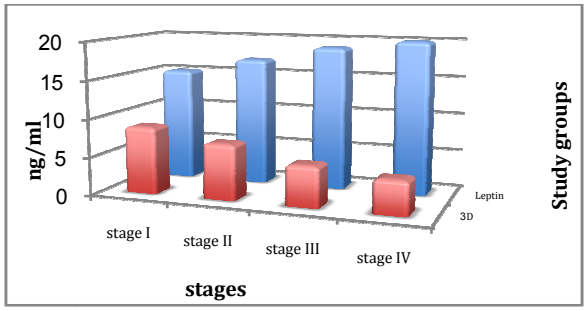


Figure (7): BIM value at each stages.



Figure(8): Cortisol concentration in four stages of cancer.



Figure(9): Leptin and VitaminD3 concentrations at each stages.

4. Discussion

Figure (1) shows a significant increase at (P≥0.01) in Body Mass Index in women with benign breast tumors in the first age group, while no significant change was observed in the rest of the age groups compared to the control, this is consistent with a study of (Protani, et al. 2010), whereas a significant increase in (BMI) was observed for breast malignant tumors for all age groups compared with control (Morales et al.,2018).

The obesity effect was larger in pre-menopausal than post-menopausal women, while (Stacey and Gobal,2014) proved that BMI it is a risk factor for breast cancer, as (Mehreen, et al.,2019), explained that BMI seems to be a substantial risk factor for the development of a fibroadenoma, particularly in young adolescent females, this is associated with histopathologic patterns of active fibroadinomas reflecting estrogenic stimulation.

In breast cancer, the positive association between BMI and B.C. risk in postmenopausal women was speculated to result from the higher level of estrogen derived from the aromatization of androstenedione with in the larger fat reserves of women of higher BMI while in premenopausal the relation came from a protective effect of increased weight which is a predictor of longer anovulatory cycles and a lower level of progesterone and estrogen (Lui et al.,2018).

The results showed as in figure (2) a significant increase in the concentrations of cortisol in the second and third categories of benign tumors, this is due to the fact that cortisol is required for lobuloalveolar development during pregnancy, but it is also known to downregulate expression of the BRCA1 gene and to induce the activity of aromatase(Timothy et al.,2019), and in all categories of malignant tumor at (P≥0.01), several clinical studies have demonstrated that cortisol concentrations correlate positively with cancer severity and mortality rate, cortisol was linked to fatigue among breast cancer patients, abnormalities could be result of Hypothalamic-Pituitary Adrenal (HPA) feed back system malfunction, hypersensitivity towards stress, inability to inactivate cortisol or even sleep irregularities (Victor, et al.,2020; Motahareh, et al.,2020).

The figure (3,4,5,6) also showed an increase in the concentrations of leptin in benign and malignant tumor patients (P≥ 0.01), these results are consistent with what mentioned by(Luis et al. 2017), leptin consistently stimulates the proliferation of benign and malignant epithelial breast cell and could be directly related to breast carcinogenesis by underlying the effects of obesity on cancer development (Goodwin, et al.,2020; Gelsomino, 2020).

The results showed as in figures (3,4,5,6) that there was no change in the concentration of Vitamin D when suffering from benign breast diseases and a significant decrease in the incidence of malignant breast diseases ($P \geq 0.01$), these results are consistent with what was reported by (shao,et al. 2012, Huss, et al. 2019)

Decreased serum Vitamin D concentrations results in enriched cellular growth, neoangiogenesis, and cancer development(Atoum and Alzoughool,2017). Also associations with estrogen receptor-negative disease and obesity that association of deficiency with more advanced and aggressive disease (Ioannis,2021).

When comparing the body mass index values of the four tumor stages as in the figure (7), it was found that the value increased with the progression of the tumor stage progresses, from the first stage to the third, but decreases in the fourth stage, this is due to an increase synthesis of peripheral estrogen in adipose tissue and reduce sex hormone binding globulin and enhanced aromatase activity may induce and stimulate the growth of abnormal mammary cells (Bulun, et al., 2012; Li, et al., 2018). The reason for the decrease in the value of BMI is attributed to metabolic dysregulation and worse prognosis (Silvia, et al., 2020).

Figure (8) showed the highest concentrations of cortisol was observed in the first stage of the tumor and decreased in the second stage, more decrease was observed in third stage while increase in the fourth stage, this disturbance in cortisol concentrations is due to psychophysiological process and stress response which promote cancer progression as a result of dysregulation of sympathetic nervous system and hypothalamic pituitary-adrenal axis (Mohammad pour, et al., 2019; Rohit, et al., 2020).

The increase concentrations of leptinindicates the progression of the tumor stages as in the figure(9), this may be due to the adipocytes in the tumor microenvironment that play a crucial role in disease progression by providing fatty acids, pro-inflammatory cytokines and proteases, cancer cells utilize adipocyte-released fatty acids for energy production through β-oxidation, in the breast tumor microenvironment, adipocytes have been reported to produce a number of biologically active compound such as leptin(Xiong, et al.,2015; Amitabha& Margot, 2017).

Figure (9) indicates a decrease in the concentrations of Vitamin D as the tumor stage progress, this due to the fact that vitamin D plays an important role in the modulation of cancer invasion and metastasis, it has the ability to inhibit the invasive potential of human breast cancer, this associated with diminished activity of the metalloproteinase and down regulation of the plasminogen-activator, this is indicative of the dual effect of vitamin D in the invasive process: on hand , it decreases the activity and expression of metalloproteinase and serine proteases, at the same time induces their inhibitors (Huss, et al., 2019).

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