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The Role of Serum Follicle Stimulating Hormone in Prognosis of Chemotherapy Effect on Ovarian Reserve in Iraqi Breast Cancer Women

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Abstract: *Breast cancer is the most common cancer in reproductive-aged women. Most young women diagnosed with breast cancer will undergo chemotherapy. While chemotherapy improves cancer outcomes, it also induces ovarian damage by direct toxicity to the finite pool of ovarian follicles. FSH is secreted by the anterior pituitary and its main work of regulating the growth of the follicles. A low basal FSH level would thus indicate a good ovarian reserve and vice versa.This cohort prospective study was carried out at the Biochemistry Department, College of Medicine, University of Baghdad and at Oncology Clinic,Oncology Teaching Hospital. It included 30 women (25-45 years) who were newly diagnosed to have had breast cancer and underwent chemotherapy (CT) treatment.The mean (±SEM) value of serum FSH levels was significantly increased in after CT treatment (79.83±4.81 IU/L) compared with that before treatment (5.8±0.5 IU/L, p<0.0005).The measurement of serum FSH may be a useful biochemical marker for defining the damage of the ovaries after CT.*

Key words*: FSH, Breast cancer, Chemotherapy, Ovarian reserve.*

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I. Introduction

Breast cancer (BC) "is the most frequent cancer in women worldwide, Forming 23% of all cancer cases in women. Now it's become the most common cancer both in developed and developing countries"[1]. Jemal*et al*.found that BC was occurred in 25% before menopause and 15% in the reproductive age[2].

Follicle Stimulating Hormone (FSH) is a 35.5kDa glycoprotein heterodimer, consisting of two polypeptide units, alpha (α) and beta (β). Its structure is similar to those of luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and human chorionic gonadotropin (hCG). LH, FSH, TSH, and hCG are identical in their alpha subunit of the glycoproteins and consist of about 96 amino acids, while the beta subunits are different[3].

FSH is secreted by the anterior pituitary and its main work of regulating the growth of the follicles. Its level will be altered during the menstrual cycle and is changed by feedback mechanisms on the pituitary and the hypothalamus by estrogen together with regulatory peptides (inhibin A and B, activin and follistatin) from the ovaries. Decrease levels of estrogen and inhibins will lead to elevation in FSH secretion, while high levels of estrogen and inhibin do the opposite[4].Broer*et al*.study showed that the WHO classified the ovarian dysfunction depending on the base of serum FSH and estradiol levels[5].

Fowler *et al*.mentioned that the FSHmain function is to save the small antral follicles (size between 2-5 mm) from apoptosis "(programmed death of the somatic cells of the follicle and oocyte)" and to start the initial recruitment and the growth of immature ovarian follicles. As a result, from day 1-3 of the menstrual flow, the FSH will be at a peak level. When the levels of serum estradiol and progesterone from the ovaries will be declined in the luteal phase, there will cause an increase in FSH levels as a feedback to the hypothalamus-pituitary axis. Consequently, these growing follicles are able to secrete enough amount of AMH and inhibin B that lead to decrease the FSH levels[6].

Basal FSH that bemeasured on menstrual cycle (day 3±1). It serves as an indirect measure of follicle cohort size through the feedback mechanisms on the pituitary and the hypothalamus. A low basal FSH level would thus indicate a good ovarian reserve and vice versa[7,8]. Chemotherapy (CT) is one type of cancer treatment that works by stopping or slowing the growth of cancer cells, which grow and divide quickly. The most of patients with cancer treated with chemotherapy at some time during the course of their illness, purpose for either at cure, prolongation of life, or palliation, depending on tumor type, stage, and the relative fitness of the patient[9].

But, the main side effect for young women is the suppression of ovarian function. That could lead to infertility and increase the risks of premature menopause[10].

II. Subjects and Methods

This study was carried out at the Biochemistry Department, College of Medicine, University of Baghdad and at the Oncology Clinic at Oncology Teaching Hospital during the period from September 2016 to February 2017. It included 30women who were newly diagnosed by oncology group to have had breast cancer, their age range (25-45). They have had a regular menstrual cycle. The study design included; group I (GI): thirty women newly diagnosed with breast cancer before starting chemotherapy and group II (GII): the same thirty women of GI who finished 4 cycles of Anthracycline and Cyclophosphamide chemotherapy. Exclusion criteria included pregnant woman, chronic diseases (DM, hypertensive), alcoholic, Smoker, menopausal and women with any infertility causes.Five milliliters of venous blood were taken from each individual at time 8:00-11:00 a.m. Blood samples were collected in serum-separating tubes which allowed to clot at room temperature for thirty minutes, then the samples were centrifuged at (2000 x g) for 10 minutes, the obtained serum was frozen at– 20 ^{o}C till the time of FSH measurement by using the enzyme linked immunosorbent assay (ELISA) technique.

III. Results

Table 1 shows the clinical characteristics of the study group. The mean (±SEM) values of age and BMI of women of the present study were (38.83±4.74 year) and (29.92± 4.88 kg/m^2), respectively. Table 2 shows the mean value of serum FSH in relation to chemotherapy treatment effect. The mean (±SEM) value of serum FSH levels was significantly increased in post chemotherapy group GII(46.9±4.29 IU/L, p<0.0005)in comparison to that of the same women but before chemotherapy treatment GI (5.8±0.5 IU/L).

TABLE- 1-Mean (±SEM) values of age and BMI of women with breast cancer

Characteristic	GI (n=30)
Age (Year)	**38.83±4.74**
BMI (kg/m^2)	**29.92± 4.88**

TABLE-2-The mean (±SEM) values ofserum FSH concentrations in GI, GII

Parameters	GI (n=30)	GII (n=30)
FSH IU/L	5.8±0.5*	46.9±4.29**

*****t-test reveal a significant increase in GII compared to GI**.**

IV. Discussion

The results of the present study revealed significant changes of serum FSH due to chemotherapy treatment with level became in postmenopausal levels post the CT. this finding is an agreement with that of Ben-Aharon*et al.*who showed significant increased of serum FSH immediately after finishing their chemotherapy and became in postmenopausal values, women of age < 35 year present with high recovery rate after 6, 12 months after treatment[11].Yoshimura and Furuyashowed that serum FSH levels increased to postmenopausal values as early as 6 weeks (after two cycles of CT using only adjuvant docetaxel/cyclophosphamide) and at 9 weeks. Furthermore, at 12 weeks (after receiving the fourth cycle), FSH levels will be still constant values[12].D'Avila*et al.*found that levels of FSH became in the postmenopausal levels after finishing the treatment and return to normal after 6 months after completion of the CT[13].

In conclusion, serum FSH levels increased to the postmenopausal values that means damaged occurred to the ovaries leading to an ovarian failure. The measurement of the serum FSH is a sensitive biochemical marker for assessment of ovarian reserve post CT treatment.

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