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Original Article

The impact of age on antimullerian hormone serum level in women attending chemotherapy Unit for primary breast cancer

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ABSTRACT

Objective: The aim of the study is to evaluate serum level of Anti-Mullerian Hormone in patients with primary breast cancer proposed to have chemotherapy and to study the effect age on Anti-Mullerian Hormone and menstrual cycle pattern after chemotherapy.
Background: In reproductive-aged breast cancer survivors, there is a need for "real-time" biomarkers of post-chemotherapy ovarian function.
Method: This prospective cohort study had been conducted upon one hundred twenty women, sixty women as a patient group (n = 60), who are newly diagnosed with primary breast cancer and Sixty women as a control group (n = 60). Their ages between (21 and 41) years. Patients were subgrouped according to age as ≤35 and >35 years.
Results: There were significant differences between patients and control groups regarding BMI,regularity of menstrual cycle ($P < 0.05$). There were significant differences between antimullerian hormone before and after the first dose of chemotherapy, in all age groups ($p < 0.05$). There was a significant difference in antimullerian hormone before and after administration of second dose of chemotherapy in those who are less or equal to 35 years. But no such difference in antimullerian hormone after the second dose of chemotherapy in those who were above 35 years.
Conclusion: Serum AMH is a convenient and sensitive indicator of follicular depletion and recovery in young women during and after chemotherapy, this needs to be confirmed by larger size group.

1. Introduction

Breast cancer is the most common type of malignancy recorded in the cancer registries of almost all countries within the Eastern Mediterranean Region. In Iraq, the continuous rise in the incidence rate is associated with an obvious trend to affect premenopausal women [1]. It accounts for approximately one-third of the registered female cancers [2,3].

The incidence rate of all female breast cancer in Iraq increased from 26.6 per 100,000 in 2000 to 31.5 per 100,000 in 2009 and is still affecting younger age group [4].

Some women with breast cancer will have chemotherapy. Chemotherapy treats a woman's whole body, not just her breast. Many different sites are possibly affected from taking chemotherapy drugs, but not all women get the same ones [5].

Ovarian function can be challenging to assess, especially in the postchemotherapy setting. Potential markers of ovarian reserve include biochemical markers and imaging assessments [6,7].Serum concentrations of anti-Müllerian hormone (AMH) and inhibin B both decrease with declining ovarian function, whereas follicle-stimulating hormone (FSH) increases [8].Serum AMH concentration has been shown to be the best biochemical marker for assessment of a decline in reproductive capacity in healthy women [8].

2. Aim of study

1. To evaluate serum level of AMH in patients with primary breast cancer proposed to have chemotherapy.
2. To study the effect age on AMH and menstrual cycle pattern of these patients after chemotherapy.

3. Subjects and methods

This study was designed as a prospective cohort study. Sixty patients attending Oncology Center of Marjan Medical City in

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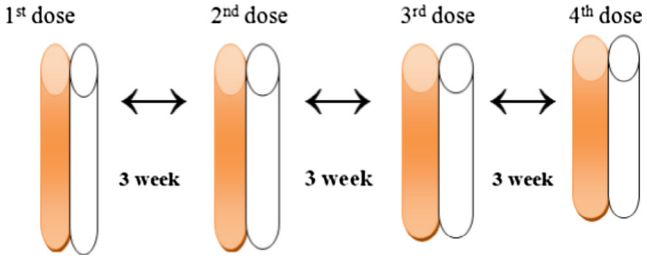
Babylon /Iraq were recruited; from November of 2015 to June 2016. These patients were newly diagnosed as primary breast cancer and were referred by surgeons for chemotherapy after mastectomy. The have been proved by the medical ethical committee of college of medicine /university of Babylon. Informed written consent has been signed by all participants.

These women underwent full medical and gynecological examination; their mean age ± SD was (33.15 ± 7.86), ranging from (21 to 41) years. A standard questionnaire (Fig. 1) was used for collecting demographic data which include Age, education, occupational state, exposure to environmental toxins, family history of breast carcinoma, any hormonal therapy, menstrual cycle history (menarche, regularity, duration, bleeding days). The control group was volunteers N = 60, their mean age and SD (32.85 ± 5.09) ranges from (20 to 40) years. The same questionnaire was applied for them. Anthropometric indices as weight and height were estimated to calculate BMI. Blood test for serum level AMH was performed for all females.

3.1. Standard regimen used for chemotherapy administration



(Evaluation of the female)
Case No. :
(Female) Name:
Age:
Education:
Live in: urban rural
Menstrual cycle History:
Menarche:
Regularity Regular Irregular
Infertility History: if any: primary secondary
Type of tumour :
Famliy History:
Surgical History:
Examination (Female):
Weight Height Body mass index
(Female): Basal follicle stimulating hormone, Prolactin hormone , Anti-mullarian hormone and Estradiol hormone.

Fig. 1. Standard questionnaire for collecting demographic data.

Adriamycin(doxorubicin hydrochloride solution vial 10 mg \ 5 ml of 0.09% normal saline, (Pfizer, australia), 60 mg/m^2) for 4 cycle every 3 weeks.

Endoxan (Baxter Germany) (600 mg/m2) 4 cycle every 3 weeks (Endoxan 200 mg vial(213.8 mg cyclophosphamide monohydrate)

The fallow up of patient were done only for 4 cycle, it was not dose intense. Because of limitation of study period.

3.2. Hormonal analysis

Blood samples from the patient and control group were collected for Anti mullerian Hormone (AMH) analysis. Samples collection were done in three occasions:

1. Before chemotherapy administration. (AMH0)
2. After first menses following the 1st dose of chemotherapy. (AMH1)
3. After the 4th dose of chemotherapy. (AMH2)

Blood samples were collected between 08:30–11:00 a.m. by venipuncture for each female participant into 10 milliliter (ml) gel tubes; these samples were left to stand at least 15 min at room temperature. Centrifugation at 3000 revolution per minute (rpm) for 10 min to separate the serum. The serum aliquots were obtained stored at −20 °C for the month. The assay for AMH was examined by sensitive Enzyme Linked Immuno Sorbant Assay (ELISA) method. The kit and method of analysis of AMH hormone Beckman coulter Inc.(USA) and The reference range values of the AMH hormones (1−4) ng/ml.

3.3. Exclusion criteria

1. Patient had taken chemotherapy before.
2. Patient age less than 18 years or more than 45 years.
3. Patient that take Zoladex. (Gonadotropin releasing hormone agonist).
4. Menopause state.
5. Patient taking the oral contraceptive pill.
6. Patient of ovarian surgery.
7. Patient who have diabetes.
8. Patient who have endocrine disorder.

3.4. Statistical analysis

Statistical analysis of the data was performed with (Statistical Package for Social Science; SPSS, Inc., Chicago, IL) SPSS version 20 for Windows. Continuous variables were expressed as mean ± standard deviation and range, categorical variables as percentages. Between- group differences were tested with Compare means –independent samples *t*-test for continuous parameters and nonparametric tests – Chi –square for categorical parameters (education, environmental and work hazard and MC history).

A p value of <0.05 was considered significant for all analyses.

4. Results

4.1. Comparison of demographic data of control and patient group.

Table 3.1 shows the comparison between patient and control groups regarding age, BMI, residence, educational level, regularity of menstrual cycle and menarche.

There were significant differences between patients and control groups regarding BMI, residence, educational level, regularity of

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