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# STUDY OF WHITE BLOOD CELL COUNT AND SEX HORMONE LEVEL IN SAMPLE OF IRAQI WOMEN WITH UTERUS CANCER

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**ABSTRACT**
This study was aimed to investigate the effect of uterus cancer on WBCs count and level of some reproductive hormone. Sixty patients with uterus cancer, and 40 healthy control women (ages up to 45 year) were involved in this study during their attendance at the center of cancer in Medicine City Hospital of Baghdad from October 2016 to April 2017. The women were divided into two groups; Menopausal group (45-65) years which including (28 patient and 20 controls) and postmenopausal group (up to 65) years which including (32 patient and 20 controls). Blood samples were collected from each individual for assessment the WBCs count, level of sex hormones and Tumor marker CA125. The results showed a significant ($P< 0.05$) increase in white blood cells (WBCs) count, neutrophils and basophils in menopause and post-menopausal uterus cancer patients, and significant ($P< 0.05$) decrease in lymphocyte as compared with healthy controls. Monocyte in menopausal uterus cancer patients was significantly ($P< 0.05$) decrease as compared with healthy controls, While, in post-menopausal showed non-significant ($P< 0.05$) as compared with healthy controls. The result showed non-significant ($P< 0.05$) in eosinophil count in two patient groups when compared with healthy groups. The results of current study revealed that there was a significant ($P< 0.05$) increase in Estrogen ($E_2$) level and significant ($P< 0.05$) decrease in progesterone (PRG) in menopause and post-menopausal uterus cancer patients as compared with healthy controls. The level of Latinizing hormone (LH) and follicular stimulating hormone (FSH) showed significant ($P< 0.05$) increase in menopausal uterus cancer patients. While there was a significant ($P< 0.05$) decrease post-menopausal uterus cancer patients when compared with healthy controls. Cancer Antigen 125 (CA 125) result showed highly significant ($P<0.01$) increase in uterus cancer patients as compared with controls.

**KEY WORDS:** Uterus cancer, Sex hormone, WBCs count, CA 125.

## INTRODUCTION

Uterine cancer is the most common cancer occurring in a woman's reproductive system[1]. Uterine cancer begins when healthy cells in the uterus change and grow out of control, forming a mass called a tumor[2]. Uterus is a major female sexual reproductive organ that responsive to hormones in humans and most other mammals, especially steroids which have a big effect on endometrial cells[3]. Steroids regulate the normal functioning of female reproductive system[4]. Excess of the steroid hormone (estrogen) induces the hyper-plastic processes in tissue of uterus and promotes formation of benign or malignant tumors of uterine (mainly of myometrium and endometrium)[5]. Increased secretion of androgens induces enhanced estrogenic stimulation of the uterus because androgens are precursors of estrogens[6].

Menopause is the time in women's live when menstrual periods stop permanently, woman in menopause is no longer able to bear children, symptoms of menopause typically occur earlier, at an average age of up to 45 years[7]. The term "postmenopausal" describes women who have not experienced any menstrual flow for a minimum of 12 months, assuming that they have a uterus and are not pregnant or lactating in women without a uterus; menopause or pos-menopause can be indicated by a blood test showing a very high Follicular Stimulating Hormone (FSH) level[8]. Endometrial carcinoma has become the most common invasive malignant tumor of the female genital tract in the United State; endometrial cancer is clearly a tumor responsive to hormones by a critical role played by estrogens unopposed by progesterone hormone[9]. It is well known that diverse of hormones content in the blood of different age group women, accordingly, mechanisms responsible for development of tumor in uterine body in different age group women are not the same [10].

Tumor marker CA 125 (cancer antigen 125), known also as mucin 16 or MUC16, is a protein in humans which encoded by the MUC16 gene[11]. MUC16 is a member of the mucin family glycoproteins[12]. Cancer Antigen-125 has found application as a bio-marker or tumor marker that may be elevated in the blood of some patients with specific types of cancers ovarian cancer[13], endometrial cancer, fallopian tube cancer[14], lung cancer, breast cancer and gastrointestinal cancer[15]. Inflammation in cancer region will cause elevated white blood cells (WBCs), counts of total and types of WBCs predict a worse prognosis in patients with cancer or coronary artery disease and anemia predicts increased risk of death of cancer patients with heart failure[16]. In general, patients with an absolute granulocyte count of 6000/mm$^3$ or more were observed to have a shorter survival than the patients with less than 6000/mm$^3$, a similar phenomenon was observed independently in patients with advanced

carcinoma of the colon[17]. Peripheral blood lymphocyte counts were significantly lower in the short-survivors when compared with the long survivors[18]. Lymphocyte count may be a host factor that influences survival in breast cancer[17]. It is important to study full blood count in patients with cancer in order to determine their diagnostic and prognostic values, routine peripheral blood counts may be useful prognostic factor for evaluating the accuracy of risk stratification in cancer patients[19].

## MATERIALS & METHODS

**Subjects:** sixty women with uterus cancer and forty healthy women were involved in this study during their attendance at the center of cancer diseases in Medical City in Baghdad from October 2016 to April 2017. Uterus cancer was diagnosed by histopathology or periscope, X ray, sonar device. The healthy women have been clear ultrasound, haven't been any chronic disease, and normal uterus without any thickening when examined by sonar device. The women were divided into two groups as the following;

**Group one (G1):** group of menopausal women, including 28 patient with average age of (56.83 ±0.81 year), and 20 controls with average age of (56.05 ±1.08 year).

**Group two (G2):** group of post-menopause, including 32 patient with average age of (68.13 ±0.53 year), and 20 controls with average age of (68.55 ±0.28 year).

**Collection of Blood samples and assay procedures:**

About 8 ml were withdrawn from the participant's women via vein puncture using 10 ml disposable syringes. The blood sample was divided into two aliquots; 3 and 6 ml. The first aliquot blood (3ml) was kept in the tube containing ethylene diamine tetra acidic acid (EDTA) as anticoagulant with slow mix for WBCs count, (WBCs count and WBCs types were measured by using CELL-DYN Ruby hematology analyzer). The second aliquot (5ml) was dispersal in gel tube, left about 40 min in room temperature then centrifuged for 15 min at 3000 rpm to separate serum and stored in at -20 ° C until used for sex hormones (LH, FSH, PRG, $E_2$) assay by using ELISA (enzyme-linked immune-sorbent assay) and CA 125(The principle of tumor marker CA 125 is one _step sandwich assay).

**Statistical analysis:**

The Statistical Analysis System- SAS (2012) program was used to effect of difference factors in study parameters. T-Test was used to significant compare between means.

## RESULTS

The results of WBCs count were showed in (table 1).There was a significant ($p<0.05$) increase in WBCs count in menopause and postmenopausal women with uterus cancer (11.44 ±0.54 $10^3/\mu L$), (11.41 ±0.46 $10^3/\mu L$) as compared with the controls (5.81 ±0.14 $10^3/\mu L$), (6.48 ±0.20 $10^3/\mu L$) respectively. In menopause and postmenopausal women with uterus cancer, the result showed a significant ($p<0.05$) increase in count of neutrophil cells (8.899 ±0.52 $10^3/\mu L$), (8.85 ±0.42 $10^3/\mu L$) as compared with controls (2.849 ±0.11 $10^3/\mu L$), (3.196 ±0.15 $10^3/\mu L$) respectively. The results showed a significant ($p<0.05$) decrease in the count of lymphocyte in menopause and postmenopausal women with uterus cancer (1.562 ±0.09 $10^3/\mu L$), (1.657 ±0.12 $10^3/\mu L$) as compared with controls (2.157 ±0.07 $10^3/\mu L$), (2.590 ±0.07 $10^3/\mu L$) respectively. Monocyte count showed significant ($p<0.05$) increase in menopause women with uterus cancer (1.071 ±0.56 $10^3/\mu L$) as compared with healthy controls (0.475 ±0.02 $10^3/\mu L$), While there was non-significant ($p<0.05$) in monocyte count of post-menopausal uterus cancer patients (0.495 ±0.05 $10^3/\mu L$) when compared with healthy controls (0.437 ±0.03 $10^3/\mu L$). There was non-significant ($p<0.05$) in count of eosinophil cells in menopause and post-menopausal uterus cancer patients (0.323 ±0.10 $10^3/\mu L$), (0.251 ±0.09 $10^3/\mu L$) as compared with controls (0.321 ±0.01 $10^3/\mu L$), (0.258 ±0.02 $10^3/\mu L$) respectively.

**TABLE 1:** White Blood Cells count in uterus cancer patient and controls (Mean ±SE)

| Parameters | Menopause | | | Postmenopausal | | |
|---|---|---|---|---|---|---|
| | Patients N=28 | Control N=20 | T-Test | Patients N=32 | Control N=20 | T-Test |
| WBC $10^3/\mu L$ | 11.44 ± 0.54 | 5.81 ± 0.14 | 1.367 * | 11.41 ± 0.46 | 6.48 ± 0.20 | 1.188 * |
| Neutro $10^3/\mu L$ | 8.899 ± 0.52 | 2.849 ± 0.11 | 1.316 * | 8.85 ± 0.42 | 3.196 ± 0.15 | 1.071 * |
| Lymph $10^3/\mu L$ | 1.562 ± 0.09 | 2.157 ± 0.07 | 0.256 * | 1.667 ± 0.12 | 2.590 ± 0.07 | 0.322 * |
| Mono. $10^3/\mu L$ | 1.071 ± 0.56 | 0.475 ± 0.02 | 1.393 * | 0.495 ± 0.05 | 0.437 ± 0.03 | 0.136 NS |
| Eso. $10^3/\mu L$ | 0.323 ± 0.10 | 0.321 ± 0.01 | 0.254 NS | 0.251 ± 0.09 | 0.258 ± 0.02 | 0.243 NS |
| Bas. $10^3/\mu L$ | 0.386 ± 0.08 | 0.007 ± 0.002 | 0.217 * | 0.342 ± 0.07 | 0.004 ± 0.001 | 0.183 * |

* ($P<0.05$), NS: Non-Significant.

The results of reproductive hormones levels in uterus cancer patients and controls were showed in table (2), a significant ($p<0.05$) increase in Estrogen of menopause and post-menopause of uterus cancer patient (81.23 ±1.51 pg/ml), (59.46 ±0.80 pg/ml) as compared with controls (32.91 ±0.74 pg/ml), (19.19 ±0.60 pg/ml) respectively. A significant ($p<0.05$) decrease in PRG concentration of menopause and postmenopausal women of uterus cancer patient (0.074 ±0.002 ng/ml) (0.026 ±0.002 ng/ml) as compared with controls (0.840 ±0.02 ng/ml), (0.491 ±0.02 ng/ml) respectively A significant ($p<0.05$) increase in LH and FSH level in menopausal with uterus cancer (54.97 ±0.83 IU/L), (78.30 ±15.88 IU/L) as compared with controls (30.28±0.73 IU/L), (36.28 ±0.66 IU/L) respectively. While, there was significant ($p<0.05$) decrease in LH and FSH level in post-menopausal women with uterus cancer (34.76 ±0.71 IU/L), (45.14 ± 0.83 IU/L) as compared with controls (45.12 ±0.79 IU/L) (55.74 ±1.04 IU/L) respectively. Body mass index showed a significant ($p<0.05$) increase in both menopausal and post-menopausal women with uterus cancer as compared with their controls.

**TABLE 2:** reproductive hormones levels in uterus cancer patients and controls (Mean ±SE)

| Parameters | Menopause | | | Postmenopausal | | |
|---|---|---|---|---|---|---|
| | Patients N=28 | Control N=20 | T-Test | Patients N=32 | Control N=20 | T-Test |
| BMI ($m^2$/kg) | 29.97 ± 0.53 | 22.88 ± 0.28 | 1.376 * | 29.82 ± 0.48 | 23.43 ± 0.19 | 1.242 * |
| E2 (pg/mL) | 81.23 ± 1.51 | 32.91 ± 0.74 | 3.919 * | 59.46 ± 0.80 | 19.19 ± 0.60 | 2.221 * |
| PRG (ng/mL) | 0.074 ± 0.002 | 0.840 ± 0.02 | 0.036 * | 0.026 ± 0.002 | 0.491 ± 0.02 | 0.029 * |
| LH (IU/L) | 54.97 ± 0.83 | 30.28 ± 0.73 | 2.374 * | 34.76 ± 0.71 | 45.12 ± 0.79 | 2.177 * |
| FSH (IU/L) | 78.30 ± 15.88 | 36.28 ± 0.66 | 39.26 * | 45.14 ± 0.83 | 55.74 ± 1.04 | 2.684 * |

* (P<0.05), NS: Non-Significant.

The results in table (3) summarized the highly significant (P<0.01) increase of CA 125 in women with uterus cancer (286.40 ± 25.24 UI/mL) compared with healthy controls (13.68 ± 0.83 UI/mL).

**TABLE 3:** CA 125 in patients with uterus cancer and control (Mean ±SE)

| The Group | Mean ± SE of CA 125 (0-35) UI/Ml |
|---|---|
| Patients | 286.40 ± 25.24 |
| Control | 13.68 ± 0.83 |
| T-Test | 51.136 ** |
| P-value | 0.0001 |

** (P<0.01).

## DISCUSSION

Increasing of WBCs may happen as a result of inflammatory, immune respond against malignancy cells and anemia. This result agreed with several studies[20, 21] that conclude that cancer-related inflammation causes suppression of antitumor immunity by recruiting regulatory T cells and activating chemokines, which results in tumor growth and metastasis. Malignancy is one of causes that increase the neutrophils cells in blood. Neutrophil counts having the most significant association with endometrial cancer, correlated with all other complete blood component [22]. The results the in present study showed that there was a significant decrease in the count of lymphocyte in menopause and postmenopausal women with uterus cancer as compared with the healthy controls. Ray-Coquard *et al.,* [23] who conclude that Lymphopenia (lymphocyt cells decrease) happend in many type of cancers; the body fails to produce enough lymphocytes, because it is busy to producing neutrophil cells, or the body produces a sufficient number of lymphocytes, but is destroyed by cancer.

In the current study, monocyte count showed significant increase in menopause women with uterus cancer. Monocytes are a subset of circulating white blood cells that can further differentiate into a range of tissue macrophage [24]. There was non-significant in count of Esophil cells in menopause and post-menopausal uterus cancer patients. Because of these cells dependent with allergic and fungal infections[25]. In menopause and post-menopausal women, there was significant increase in count of Basophile cell in blood of women with uterus cancer. Basophils are implicated in multiple human diseases including autoimmune disorders, inflammatory disorders, cancer and allergies and asthma[26]. There was significant (p<0.05) increase in Estrogen of menopause and post-menopause of uterus cancer patient. Unopposed estrogen, hypothesis exposure is associated with an increased risk of endometrial cancer because estrogen has a mitogenic effect on endometrial tissue, by stimulating the endometrial glands and stromal cells to grow and proliferate[27]. Elevations of estradiol increase endometrial cell proliferation while inhibiting apoptosis in endometrial tissue[28]. Based on observations that exposure of the endometrium to estrogen without concomitant progesterone can stimulate endometrial cell proliferation that can increase the likelihood of genetic errors and malignant transformation, increased risks of endometrial cancer can result from either excessive estrogen or a deficiency in progesterone [9]. The result of this study agreed with several studies[6, 29] who revealed that amount of Estrogen was increased in menopause and post-menopause malignant growth cases compared to the control. In general, estrogen concentration in serum of post-menopausal women is generally lower than its concentration in serum of menopausal women[30]. Significant decreases in PRG concentrations of menopause and postmenopausal women of uterus cancer patient. Allen *et al.,* [31], who conclude that sharp increase of estradiol on the background of significant deficiency of progesterone may be responsible for the target organ-uterus tissues stimulation and formation of benign (fibromyoma, myoma) or malignant tumors after menopause age women. Progesterone is anti-mitogenic in endometrial epithelial cells, and as such, mitigates the tropic effects of estrogen[32]. The decrease in PRG level is due to the cessation of ovaries from PRG production after the menopause and not production from other parts of body, while Estrogen may be produced from another part [9, 11, 33]. In menopause hormone production by the ovaries is decrease (like Progesterone and Estrogen). So in generally level of estrogen and PRG in post-menopause is less than in menopause [34].

A significant increase in LH and FSH level in menopausal women with uterus cancer, While, there was significant (p<0.05) decrease in LH and FSH level in post-menopausal women with uterus cancer. Sharp gains of estradiol content in blood is in positive feed-back relation with hypothalamus-hypophysis system and as a result, increase of luteinizing hormones, and follicle-stimulating takes place in menopause age women[35]. Here, it must be

mentioned that the decreased level of FSH and LH in post-menopause patients with uterine malignant tumor may be caused by the functional status of the reproductive system, by the diversity of histological forms of the tumor and its differentiation degree [4]. Moreover, in little amounts progesterone increases the effect of estrogens and/or is responsible for intensification of gonadotropins secretion by the negative feed-back mechanism [36]. The results was showed the high significant ($P<0.01$) increase of CA 125 in women with uterus cancer. This result was agree with several study which preoperative serum CA125 as an important predictor for patients with endometrial cancer and it should be taken into consideration when surgical management is determined [37]. Cancer antigen 125 values increase with increase size of tumor in uterus [38, 39]. Because serum concentrations of CA-125 can be elevated in various malignancies, it is could by diagnostic but not specific for endometrial tumors [40].

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