Original Article

The Impact of Body Mass Index and Some Trace Elements in Iraqi Women with Breast Cancer

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Summary:

Background: Breast cancer is a highly heterogeneous disease globally. Trace elements such as copper and zinc have a role in many biochemical reactions as micro source, their metabolism is profoundly altered in neoplastic diseases especially breast cancer which is ranked as the first of female cancers

Objective: The aim of the present study is to study the impact of body mass index and some trace elements in Iraqi women with breast cancer.

Patients and methods: The group of the study consisted of 25 breast cancer patients; their age range was (25–65) years recruited from the Al-Kadhimia Teaching Hospital and 25 apparently healthy women age matched, over a period of 6 months from January 2015 until June 2015. After the diagnosis was made using a histopathological examination for the malignant tumor, blood was obtained from all patients and control, centrifuged and serum samples without blood hemolysis were separated and stored at – 20 until assayed.

Results: There was a significant increase in body mass index in breast cancer women as compared to control group. Copper and zinc levels were significantly different between the patients and controls group with higher level of copper, zinc. Also copper/zinc ratio in patients was higher than in the control group.

Conclusions: The excess copper and zinc in breast cancer women in comparison to healthy control highlights the role of these trace elements in the initiation or promotion of breast cancer. It is recommended to use trace elements and the copper/zinc ratio as biomarkers for breast cancer disease and its progression.

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Introduction:

Breast cancer is a highly heterogeneous disease worldwide. It is the most frequently diagnosed cancer in women worldwide affecting 1 in 8 women (1).

Tumor genesis in mammary glands can be induced biochemically by irregular expression level of circulating hormones or from a mechanical change in the tension of mammary stroma. Mammary epithelial cells would grow out of control and eventually result in cancer. The role of estrogen appears to be pivotal (2). Estrogen is important in the development of breast cancer, and its biological effects are mediated primarily throughout the two estrogen receptors (ER), α and β. The ability of metals to activate ERα was measured in the human breast cancer cell line (3).

Numerous studies have demonstrated obesity to be associated with a poorer prognosis overall and disease-free survival among breast cancer patients (4, 5). Obesity has not only been linked with comorbid health conditions such as diabetes and hypertension, but also with various cancers, including breast cancer (6). Obesity has not only been shown to be an independent risk factor for the development of postmenopausal breast cancer, but also a poor prognostic factor in patients already diagnosed with breast cancer (7).

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Traces elements copper) Cu (and zinc) Zn (have a role in many biochemical reactions as micro source .Copper has many physiological functions .It affects the activity of many enzymes (Cu/Zn-superoxide dismutase) (Cu/Zn-SOD) (ceruloplasmin ,cytochrome oxidase ,tyrosinase ,dopamine hydroxylase and lysine oxidase),both as a cofactor and as an allosteric component .These enzymes are necessary for cellular respiration ,defence against free radicals ,melanin synthesis, and formation of connective tissue and for iron metabolism. Additionally ,copper dependent transcription factors play an important role in gene expression (8).

Copper metabolism is extremely altered in neoplastic diseases. It has been found that raised serum copper concentration correlates with tumor occurrence and burden, malignant progression, and recurrence in a variety of human cancers (9). Zinc, on the other hand, is present in more than 200 enzymes and transcription factors as a functional component. Therefore, zinc affects major metabolic processes, as well as instruction of the cell cycle and cell division. The first symptom of Zn deficiency is an inhibition of cell growth and proliferation. In addition, Zn is necessary for the optimum performance of the immune system (10).

The aim of the present study was to study the impact of body mass index (BMI) and some trace elements in Iraqi women with breast cancer.

Materials and Methods:

The group of the study consisted of 25 breast cancer patients; their age range was (25–65) years recruited from the Al-Kadhimia Teaching Hospital and 25 apparently healthy women age matched, over a period of 6 months from January 2015 until the June 2015 after the diagnosis using a histopathological examination for the malignant tumor, the blood was obtained from all the patients and control, centrifuged and serum samples without hemolysis were separated and stored at – 20 until assayed.

Anthropometric Measurements: Body mass index was calculated from the height and weight of the participants using the formula: BMI (kg/m^2) = Weight (kg) / Height^2 (m^2) (11). Waist and hip were measured for every patients and control according to world health organization (WHO) protocol (12). Blood pressures were recorded according to the guidelines adopted by WHO (13)

Determination of Serum Trace Elements: Serum Cu& Zn were determined by atomic absorption spectrophotometry (Model AA–6200, Shimadzu) using air-acetylene atomic absorption spectrophotometer (AAS). The sample for analysis is dispersed in a beam of energy from a hallow-cathode lamp and atoms of Cu and Zn in the ground state absorb the incident energy of certain wave length. The absorption causes a decrease in emerging energy and with suitable instrumentation, the decrease could be measured and the metal ions concentration was assayed (14).

Statistical Analysis:

The statistical analysis was done using SPSS software (statistical Package for the Social Sciences), version 19.0 and Microsoft Excel 2010 for data processing. The results were expressed as means ± SD values. The means values for Cu, Zn, and the Cu/Zn ratio were compared using t-test between the patients and control group. The P value of <0.05 was considered to be significant.

Results:

Table 1 shows the demographic and anthropometric measurement of breast cancer patients with healthy controls. The means of BMI, waist-hip-ratio (WHR), and diastolic blood pressure (DBP) were significantly different from the controls.

Table 2 shows the means levels of trace elements in patients and controls. Copper and zinc levels were significantly different between the patients and controls group. Being higher in patients (p=0.001) .Also Cu/Zn ratio was higher in patients compared with control, although the different was not significant.

Table 1: Demographic and anthropometric measurement of patients and controls (means±SD)

Characteristics	Patients	Control	P-Value
Number	25	25	-
Age (Years)	52.95±5.73	48.50±5.18	0.36 NS
BMI (Kg/m^2)	30.37±2.50	25.39±0.50	0.001
WHR	0.88±0.05	0.72±0.04	0.001
SBP (mmHg)	12.86±2.36	12.11±2.17	0.42 NS
DBP (mmHg)	98.5±1.50	76.02±0.80	0.0001
Family history of breast cancer	89%	-	-

NS: not significant

Table 2: Biochemical characteristics between the patients and the control group (means±SD)

Characteristics	Patients	Control	P-Value
Cu (µg/dl)	165.0 ± 0.36	78.0±0.24	0.001
Zn (µg/dl)	180.0± 0.21	112.0±0.16	0.001
Cu/Zn ratio	0.92±0.52	0.69±0.29	0.42 NS

NS: not significant

Discussion:

The present study focused on the relationship between the BMI and breast cancer in women. Meta-analysis of studies of obesity in relation to postmenopausal breast cancer overwhelmingly supports elevated relative risk in comparison with normal BMI (15). The biological mechanisms underlying the association between BMI and breast cancer are thought to primarily involve sex hormone pathways (16). Estrogen levels are positively connected with breast cancer among postmenopausal women; relationships between endogenous estrogens and breast cancer development emerge to be more complex along with premenopausal women (17). Some authors suggest that the observed association between hypertensions and breast cancer is confounded by obesity, which is a risk factor for both breast cancer and hypertensions (18). In addition, there was a significant variation in the Cu and Zn among patient with breast cancer as compared with the control group. The elevation in serum Cu concentration may be due to the destruction and necrosis of involved tissues, leading to the liberation of Cu into circulation (19). Farquharson et al. (20) mapped the distribution of elements in breast cancer in comparison with normal tissues and the levels of Cu and Zn were found to be

increased significantly in neoplastic cells. This indicates a strong association between the location of cancer cells and areas of high content of these metals. In the present work, a statistically significant elevation of Cu and Zn concentrations was detected in breast cancer women in comparison to healthy control group. They were also significantly increased with the development of malignancy and occurrence of metastasis. The present results are virtually similar to other findings reported by Magalhaes et al. (21) irrespective of the samples examined in diverse types of cancers. The increased levels of Cu and Zn in plasma and their suggested role in tumor development could be interrelated to their action as enzymatic co-factors involved in carcinogenesis. In addition, Cu and Zn belong to the group of oxidant metals causing disruption of the oxidative balance. Furthermore, the demand for increased blood supply for a growing tumor provides a source for the accumulation of many elements (22). Yiicel in (1994) claimed that Cu/Zn ratio is higher in malignant breast tissue and could be a better indicator of grade of cancer (23). Metals and metal compounds interfere with breast cancer in multiple ways. On one side, they are an important risk factor for the development of breast cancer, while on the other hand their cytotoxicity might have also beneficial effects inducing apoptosis and cytotoxicity in breast cancer cells. There is need to understand, under which circumstances specifically cancer cells could be targeted by metals and their compounds (24).

Conclusions:

The alteration of the elemental content (excess Cu and Zn) in breast cancer women in comparison to healthy control highlights the role for these trace elements in the initiation or promotion of breast cancer. It is recommended to use trace elements and the Cu/Zn ratio as biomarkers for breast cancer disease and its progression.

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