Evaluation of Some Heavy Metals Levels in Serum of Women with Breast Cancer (Premenopausal and Postmenopausal) in Baghdad City/Iraq

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Abstract

In this study, the level of heavy metals was examined in the serum of 100 cases for two groups which were 60 cases of breast cancer and 40 not infected cases. All samples have been Frozen and allowed later to thaw at room temperature. Inorganic elements (Zn, Cu, Pb) were determined by Flame Atomic Absorption Spectrophotometry (FAAS). Data have been analyzed and compared using SPSS-18 and student's T-Test. The results showed the mean serum zinc concentration of the infected group was (71.7 ± 5.1 and 70.4 ± 5.4 µg/dl) which was highly significantly (P≤0.001) lower than the results of the non-infected group (89.7 ± 10.2 and 97.5 ± 13.2 µg/dl) for Premenopausal and Postmenopausal respectively of each group. Furthermore, the mean serum copper concentration of the infected group was (157.2 ± 13.9 and 157.4 ±11.9 µg/dl) which was highly significantly (P≤0.001) higher than the results of the non-infected group (122.2 ± 15.5 and 112.2 ± 15.8 µg/dl) for Premenopausal and Postmenopausal respectively of each group. Moreover, the mean blood lead level was (20.7 ± 2.5 µg/dl and 19.9 ± 1.7 µg/dl) of breast cancer group was significantly higher (P≤0.001) when compared to the other group with (15.1 ± 2.0 µg/dl and 14.6 ± 2.3 µg/dl) Premenopausal and Postmenopausal respectively of each group. The results of this study indicate that levels of trace metals were little in the breast cancer women in Baghdad city.

Keywords: Breast Cancer, Heavy Metals, Risk Factors, Premenopausal and Postmenopausal.

تقويم مستويات المعادن الثقيلة في مصول النساء المصابات بسرطان الثدي (قبل وبعد انقطاع الطمث) في مدينة بغداد-العراق

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الخلاصـــة

في هذه الدراسة تم فحص تركيز المعادن الثقيلة لمئة حالة قسمت على مجموعتين والتي كانت 60 حالة مصابة بسرطان الثدي و40 حالة سليمة. كل الاختبارات أجريت على امصال دم مجمد جمعت مسبقا منهن وسمح لها بالذوبان في درجة حرارة الغرفة. قيمت العناصر غير العضوية الخارصين والنحاس والرصاص بواسطة جهاز مطياف الامتصاص الذري اللهبي (FAAS). حللت البيانات وقورنت باستخدام برنامج SPSS-18 وT-Test. أظهرت النتائج ان متوسط تركيز الخارصين لمجموعة المصابات بسرطان الثدي كان (71.7 ± 5.1 و70.4 ± 5.4 ميكروغرام / ديسيلتر) حيث انه أقل بكثير من تركيزه في امصال الاصحاء والتي كانت (89.7 ± 10.2 و97.5 ± 13.2 ميكروغرام / ديسيلتر) قبل وبعد انقطاع الطمث على التوالي وكانت هذه النتائج عالية المعنوية (P ≤0.01). أما متوسط تركيز النحاس في امصال المصابات كان (157.2 ± 13.9 و157.4 ± 11.9 ميكروغرام / ديسيلتر) وهو أعلى بكثير من تركيزه في النساء الأصحاء على التوالي (122.2 ± 15.5 و112.2 ± 15.8 ميكروغرام / ديسيلتر) قبل وانقطاع الطمث على التوالي وكانت هذه النتائج عالية المعنوية (P ≤0.01). ومن جانب اخر، سجل عنصر الرصاص في نماذج المصابين متوسط تركيز (20.7 ± 2.5 ميكروغرام / ديسيلتر و19.9 ± 1.7 ميكروغرام / ديسيلتر) وهو اعلى بكثير من تركيزه في امصال النساء الاصحاء (15.1 ± 2.0 ميكروغرام /ديسيلتر و14.6±2.3 ميكروغرام / ديسيلتر) قبل وبعد انقطاع الطمث على التوالي وكذلك كانت هذه النتائج عالية المعنوية (P ≤0.01). تشير هذه النتائج الى وجود نسب ضئيلة من هذه المعادن في دم النساء المصابات بسرطان الثدي في مدينة بغداد.

الكلمات المفتاحية: سرطان الثدي، المعادن الثقيلة، قبل وبعد انقطاع الطمث والعناصر النزرة.

Introduction

A breast cancer was considered as the almost type of solid tumor diagnosed in females. It accounts for 16% of all kinds of cancer deaths globally (Total Mortality Rate of Cancer is 7,600,000, the Total Mortality Rate of Breast Cancer is 460,000), this according to the World Health Organization. According to the latest Iraqi cancer registry that found the breast cancer is the commonest type of women malignancy in Iraq and accounting for about one-third of the recorded women cancers. There are several well-known risk factors for breast cancer involve female gender, age, earlier breast cancer, benign breast disease, hereditary (Genetic) factors, for example, family history of breast cancer or other cancer types, females who have inherited mutations in the BRCA1 or BRCA2 genes have raised breast cancer risks. Moreover (Kaaks, *et al*., 2013), early age at menarche, late age at menopause, late age at first full-term pregnancy, using of exogenous hormones or oral contraceptives, obesity, lack of exercise, diet, smoking, consumption of alcohol, low physical activity, and exposure to high dose of ionizing radiation during early life, considered as risk factors for breast cancer in relation to breast cancer risk, overall and by hormone receptor status-results from the EPIC. Nevertheless, all these risk factors have been shown to have different (Associations) to breast cancer among various ethnic populations around the world trace elements or the metallic elements are natural constituents of earth's crust. They can be classified into two categories; those that are essential for survival that compose a nutritional requirement and those that are non-essential which have toxic effects on human health (Wang, *et al*., 2009). The essential elements are absorbed via food along with proteins and compound carbohydrates and are required to preserve normal functions of numerous enzymes and transcriptional factors. Several trace elements are shown to play a preventive role against growth of malignant through involving in protection against oxidative stress which can generate free radicals in the body cells that contribute to development of cancer (Ismail, *et al*., 2017). The general population is exposed to non-essential heavy toxic metals at various concentration through consumption of contaminated food and water or by contact with contaminated soil, air, alcoholic drinks, and tobacco smoking. The toxic heavy metal can affect the health of human through an oxidative cell stress, neurological or renal injury, DNA damage or altered glucose (Mattison, 2010). this study indicated, to Evaluate of some trace metals levels for breast Cancer women in Baghdad City.

Materials and Methods

This prospective study was conducted at two main medical facilities in Baghdad City: The Main Training Center for Early Detection of breast cancer, A total of 100 subjects were enrolled in this study and divided into two groups. The first group included 60 patients' women aged between 30-60 years, this group divided into subgroups 31 Premenopausal breast cancer women and 29 Postmenopausal breast cancer women. The second group included 40 (20 Pre and 20 Postmenopausal) healthy women that have normal breast tissue and without any previous history of any systemic diseases. Heavy metals estimated for all cases by using the Frozen serum, which was allowed to thaw at room temperature, assessment of inorganic elements (Zn, Cu, and Pb) was performed by Flam Atomic Absorption Spectrophotometry (FAAS). Data were analyzed using SPSS-18. Data of two groups was compared by the student's T-Test.

Results and Discussion

As shown in Table (1), the mean serum zinc concentration in (Premenopausal and Postmenopausal) study groups were (71.7 ± 5.1 and 70.4 ± 5.4 µg/dl) respectively which was highly significantly lower than that of the healthy control (89.7 ± 10.2 and 97.5 ± 13.2 µg/dl) respectively, results were highly significant (P≤ 0.01). It also showed highly significant increasing of mean when Premenopausal compared to Postmenopausal of the study group (P≤ 0.01), while the comparison of mean between healthy control group showed that the Premenopausal was higher than that of Postmenopausal group (P≤0.01). These results were compatible with a study in India by (Singhal, *et al*., 2015). which showed that the level of zinc is significantly lower among breast cancer patients as compared to controls. In the pre and postmenopausal breast cancer women, a highly significant decreased in serum zinc as compared with controls was observed by Mohammed which agreement with the present study (Abdul-Mounther, 2016). Zinc is an essential trace element and deficiency of its level is associated with several diseases including breast cancer. There is some evidence for an inverse association between breast cancer and zinc. The reason for decreased serum zinc levels in breast cancer women possibly due to the interference of zinc with intestinal absorption of copper. Therefore, any absorbed copper could replace zinc due to copper which has a high affinity to metallothionein protein. The function of zinc as an antioxidant defense is thought to be the cause of its deficiency, whether this deficiency state leads to the disease or happens in defense against the cancerous process which is still unclear. However, it is suggested that a deficiency of Zn predisposes to chromosomal damage. Moreover, other factors could be responsible for the hypozincemia in breast cancer patients such as, increased its loss via the urine and increased uptake of Zn by cancer cells to be utilized for proliferation (John, *et al*., 2010).

Distribution of Serum Zinc (µg/dl) in the Study Population According to Duration of Disease

Table (2) represents the distribution of serum zinc concentration in study group (New and Old) cases compared to healthy control group. The results in the mentioned table showed that the mean serum zinc concentration in the new and old cases of study group (70.9 ± 5.4 and 67.7 ± 6.3 µg/dl) respectively, was significantly lower than that of control group (93.6 ± 12.3 µg/dl) (p< 0.01), while mean serum zinc concentration in new cases (70.9 ± 5.4 µg/dl) was significantly higher than that of old cases (67.7 ± 6.3 µg/dl) (P≤ 0.05).

Table (1) Comparison of (Mean± SD.) of Serum Zinc Concentration (µg/dl) Among (Premenopausal and Postmenopausal) Study and Control Groups.

Sig.	P-Value	T-Test	Post-M (Mean ± SD)	Pre-M (Mean ± SD)	Groups
P≤0.01(HS)	0.000	7.742	97.5 ± 13.2	89.7 ± 10.2	Control (n=40)
P≤0.01(HS)	0.000	6.902	70.4 ± 5.4	71.7 ± 5.1	Study (n=60)
			8.585	6.745	T-Test
			0.000	0.000	P-Value
			P≤0.01(HS)	P≤0.01(HS)	Sig.

Table (2) Comparison of (Mean± SD) of Serum Zinc Concentration (µg/dl) Among Study (New and Old) Cases and Controls.

Compared with New Cases		Compared with Control		Zinc (µg/dl) Mean ± SD	Groups
P-Value	T-Test	P-Value	T-Test		
				93.6 ± 12.3	Control (n= 40)
		P<0.01(HS)	10.624	70.9 ± 5.4	New Cases (n=40)
P<0.05 (S)	2.055	P<0.01(HS)	8.795	67.7 ± 6.3	Old Cases (n=20)

Table (3) Comparison of (Mean± SD.) of Serum Copper Concentration (µg/dl) Among (Premenopausal and Postmenopausal) Study and Control Groups.

Sig.	P-Value	T-Test	Post-M (Mean ± SD)	Pre-M (Mean ± SD)	Groups
P≤0.01(HS)	0.000	10.46	112.2 ± 15.8	122.2 ± 15.5	Control (n=40)
P≤0.01(HS)	0.000	7.891	157.4 ± 11.9	157.2 ± 13.9	Study (n=60)
			11.112	6.745	T-Test
			0.000	0.000	P-Value
			P≤0.01(HS)	P≤0.01(HS)	Sig.

These results were compatible with the results of (Ali, *et al*., 2017), who showed that serum level of zinc was significantly affected by chemotherapy among women with breast cancer and found significant differences in the serum level of zinc according to the duration of the disease, where the mean value of zinc in newly diagnosed patients was higher than that in old patients that exposure to chemotherapy. Zinc deficiency has been related to destruction and oxidative alterations in DNA that may raise an individual's risk of cancer. Furthermore, Zn metabolism may be altered in cancer patients, leading to changes in its distribution that would support carcinogenesis. However, a recent study has shown that zinc acts as a co-factor for the division of cancer cell and replication. The possible reason which explains the decrease of serum zinc level after chemotherapy in old breast cancer women may be to rejection of certain kinds of the food that supplement essential trace elements including zinc throughout chemotherapy. This may happen be due to the side effects of treatment, for example, nausea and vomiting (Kottschade, *et al*., 2016). Conversely to these findings, who indicated that the zinc concentrations in breast cancer patients were found to be significantly higher than in the control group.

Distribution of Serum Copper (µg/dl) in the Study Population According to Menstrual Status

Data demonstrated in Table (3) showed that the mean serum copper concentration was (157.2 ± 13.9 and 157.4 ±11.9 µg/dl) for (premenopausal &postmenopausal) study group respectively, which was significantly higher than that of healthy control women respectively (122.2 ± 15.5 and 112.2 ± 15.8 µg/dl) (P≤ 0.01).

These results were compatible with (Pavithra, *et al*., 2015) who found a statistically significant elevation in serum copper of patients with breast cancer when compared to controls. Also, these results agreed with that found by Mohammed who reported a significantly increased in serum levels of copper in postmenopausal breast cancer group when compared to controls group (Abdul-Mounther, 2016). Copper is considered as an essential trace element that is necessary for the many biological functions. Elevation of serum copper level acts as compounding factors in breast carcinogenesis due to the generation of the ROS trough activation of several organic peroxides. These free radicals induce mutations through damaging DNA (Pavithra, *et al*., 2015). Moreover, the molecular processes of angiogenesis need copper as essential co-factor. Furthermore, the low zinc status could raise levels of serum copper. Low zinc levels may reduce synthesis of metallothionein which is an intestinal protein that binds copper with high affinity and inhibits its absorption. These findings disagreed with (Abdel-Salam, *et al*., 2011) who reported that there was no significant difference in the mean of serum copper among controls and breast cancer patients.

Distribution of Serum Copper (µg/dl) in the Study Population According to Duration of Disease

The results in Table (4) reveals that the mean serum copper concentration in the (New and Old) study groups (157.3 ± 12.7 µg/dl), (157.9 ± 8.1 µg/dl) respectively, was a highly significant elevation compared to healthy controls (117.2 ± 16.2) (P< 0.01),while the mean serum copper concentration of old cases (157.9 ± 8.1 µg/dl) was a non-significantly higher than that of new cases(157.3 ± 12.7 µg/dl) (p>0.05). These results agreed with the study carried out by (Ali, *et al*., 2017) who showed that no significant differences in the serum level of copper according to the duration of the disease. Another study also agreed with the current study carried by (Abdel-Salam, *et al*., 2011), who showed that the level of copper before and after radiotherapy in breast cancer patients was statistically significantly increased when compared with a healthy control group. The elevation of copper level in the cancer tissue may be due to its function as a main angiogenic factor in tumors, consequently, should reduce the angiogenesis by applying drugs that decrease the levels of copper to increase survival of breast cancer patients. Furthermore, the serum copper level was significantly influenced by chemotherapy among females with breast cancer.

Table (4) Comparison of (Mean± SD) of Serum Copper Concentration (µg/dl) Among Study (New and Old) Cases and Controls.

Compared with New Cases		Compared with Control		Copper (µg/dl) Mean ± SD	Groups
P-Value	T-Test	P-Value	T-Test		
				117.2 ± 16.2	Control (n=40)
		P<0.01(HS)	12.258	157.3 ± 12.7	New Cases (n=40)
P > 0.05 (NS)	0.175	P<0.01(HS)	10.494	157.9 ± 8.1	Old Cases (n=20)

Table (5) Comparison of (Mean± SD.) of Blood Lead Concentration (µg/dl) among (Premenopausal and Postmenopausal) Study and Control Groups.

Sig.	P-Value	T-Test	Post-M (Mean ± SD)	Pre-M (Mean ± SD)	Groups
P<0.01(HS)	0.000	7.494	14.6 ± 2.3	15.1 ± 2.0	Control (n=40)
P<0.01(HS)	0.000	6.710	19.9 ± 1.7	20.7 ± 2.5	Study (n=60)
			7.452	8.639	T-Test
			0.000	0.000	P-Value
			P<0.01(HS)	P<0.01(HS)	Sig.

Distribution of Blood Lead (µg/dl) in the Study Population According to Menstrual Status

Results obtained from Table (5) showed that the mean blood lead level in the (Premenopausal and Postmenopausal) study group (20.7 ± 2.5 µg/dl), (19.9 ± 1.7 µg/dl) respectively was significantly higher when compared to the healthy control group (15.1 ± 2.0 µg/dl),(14.6 ± 2.3 µg/dl) respectively (P< 0.01).Also the mean of blood lead level in Premenopausal (study and control) groups (20.7 ± 2.5 µg/dl) , (15.1 ± 2.0 µg/dl) was significantly higher when compared to the mean of the Postmenopausal (study and control) groups (19.9 ± 1.7 µg/dl), (14.6 ± 2.3 µg/dl) (P< 0.01). These results were consistent with (Olusegun and Schrauzer, 2010) who reported that blood lead levels were significantly higher in breast cancer women as compared with the healthy control group. Lead is a harmful metal to the several organs of the human body which interfere with the DNA binding properties of zinc-finger regions of transcription factors, and this interference could possibly cause various consequences. Also, it may inhibit repair of DNA and has genotoxic effects. The possible reason that explains the elevation of blood lead levels in the breast cancer patients may be due to lowering the levels of zinc in those patients. The gastrointestinal absorption of lead and sensitivity to its effects are influenced by the sufficiency of essential elements. So, the deficiency of zinc resulting in competes of the lead with zinc in the intestine on the same metallothionein-like transport protein and using the lead instead of zinc by the body (Duruibe, 2007).

Distribution of Blood Lead (µg/dl) in the Study Population According to Duration of Disease

Results summarized in Table (6) shows that the mean value of blood lead level was highly significant increase in the study (New and Old) groups (20.3 ± 2.2 µg/dl, 21.9 ± 2.0 µg/dl) respectively compared with the mean value of the control group (14.8 ± 2.1 µg/dl) (P<0.01), while the mean blood lead level in new cases of study group (20.3 ± 2.2 µg/dl) was significantly decreased in comparison with that in the old cases of same group (21.9 ± 2.0 µg/dl) (P< 0.01). According to menstrual status, the mean levels of all the selected trace elements (Zn, Cu, and Pb) showed a highly significant difference in the blood and serum of pre and postmenopausal breast cancer women compared to healthy control women.

Table (6) Comparison of (Mean± SD) of Blood Lead Concentration (µg/dl) among Study (New and Old) Cases and Controls.

Compared with New Cases		Compared with Control		Lead (µg/dl) Mean ± SD	Groups
P-Value	T-Test	P-Value	T-Test		
				14.8 ± 2.1	Control (n = 40)
		P<0.01(HS)	11.147	20.3 ± 2.2	New Cases (n=40)
P < 0.01 (NS)	2.654	P<0.01(HS)	12.079	21.9 ± 2.0	Old Cases (n=20)

These results concluded that the alteration in trace elements metabolism may be related to the development and even progress of breast cancer among women. According to duration of disease, the mean levels of the selected trace elements (Zn, Cu, and Pb) except the zinc showed a highly significant elevation in blood and serum of old breast cancer women, while serum zinc level was highly significant decreased as compared with those of new breast cancer and healthy control women. This expects that various breast cancer therapy may alter the metabolism of several trace elements which can lead to the progression of the disease.

Conclusions

The study emphasizing the necessity of cooperation between the Ministry of Health and the Ministry of Commerce foe protecting the woman from dangerous behavior by providing them with sufficient support and guidance to stay away from the hypnotic products and focusing on the extension programs in the protection of the community through educating them with the guidance programs.

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