



Comparison Of Serum Copper And Zinc Levels In Cases With Breast Cancer With Healthy Controls In Jaipur District

Suresh Kumar Meena¹, Shrawan Kumar Meena²

¹Assistant Professor, Department of Biochemistry, JNUIMSRC, Jaipur National University, Jaipur, Rajasthan, India

²Professor, Department of Biochemistry, JNUIMSRC, Jaipur National University, Jaipur, Rajasthan, India

Correspondence Author: Suresh Kumar Meena, Assistant Professor, Department of Biochemistry, JNUIMSRC, Jaipur National University, Jaipur, Rajasthan, India

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Abstract

Background: Serum copper and zinc levels have been associated with all kind of cancers. The question of interaction between breast cancer and serum copper and zinc levels status in breast cancer patients of Jaipur district were not done earlier.

Aims: The aim of this study is to assess and compare maternal serum copper and zinc levels in breast cancer and healthy control subjects and the role of serum copper and zinc in the etiology of breast cancer.

Methods: This study was a cross section comparative study carried out on patients of breast cancer admitted in hospital. 50 patients of breast cancer were compared with equal number of healthy control subjects for serum copper and zinc levels.

Results: The mean serum Copper levels were significantly higher in breast cancer patients compared with control healthy subjects (94.1 ± 4.9 $\mu\text{g/dl}$ versus 62.8 ± 7.4 $\mu\text{g/dl}$). The mean serum Zinc levels were significantly lower in breast cancer patients compared with control healthy subjects (62.2 ± 8.0 $\mu\text{g/dl}$ versus 91.7 ± 7.2 $\mu\text{g/dl}$).

Conclusion: The present study gives us an idea that the variation in trace elements like copper and zinc might be one of the causes of breast cancer due to decrease immunity. The correction of serum trace elements concentration would have a beneficial effect on treatment, complication and progression of the diseases, which may be a subject of further study.

Keywords: breast cancer, trace elements, copper, zinc.

Introduction

Breast cancer is a highly heterogeneous disease globally. It is the most frequently diagnosed cancer in women worldwide affecting 1 in 8 women.^{1, 2} Although many studies have focused on breast cancer etiology, pathogenesis and treatment, various aspects of this disease remain unknown. However, it is believed that trace elements play important roles in biological processes relevant to breast cancer, especially those elements that are essential components of antioxidants.^{3, 4}

Trace elements are micronutrients that are part of our daily diets, they are required in minute quantity, but are very important in various biological processes,^{5,6} such as function of structural nutrients, normal healing,

metabolism of genetic materials for growth and differentiation, programmed cell death and necrosis, protection against oxidative injuries and anti-inflammatory and anti-carcinogenesis effect.⁷ On the other hand, some are also involved in undesirable events *in vivo*,⁵ such as participation in carcinogenesis and sustenance of cancerous cells in which lead, copper, chromium and zinc have been implicated. Some of the specific desirable anti-carcinogenetic activities of trace elements include the role of zinc in the application of brakes in the cell cycle and induction of apoptosis, as an activator of many enzymes involved in the synthesis of DNA and RNA, zinc has been the subject of investigations regarding its importance in biochemical processes and antioxidant **defense**. Some studies have shown that zinc can induce apoptosis in cancer cells and inhibit cell proliferation.⁸ High levels of zinc supplementation had a positive effect on reducing oxidative stress and improving immune responses in cancer patients.⁹ However, some studies have indicated that zinc serves as a co-factor for cancer cell fission and replication.¹⁰

Since indication of the possibility of the direct or indirect influence of trace element in the development and prevention of malignant diseases the contribution of the trace elements has been under scrutiny.¹¹ Trace elements have been implicated in the pathogenesis of breast cancer.^{12,13} In various body tissues, varying concentrations and relationships have been documented world-wide.^{13,14} Inverse relationship has also been found between the concentration of zinc in the blood and presence of cancer of the breast while a direct relationship has been found between serum copper and copper-zinc ratio (Cu/Zn) and cancer of the breast.^{12,15} Due to the inconsistencies in the documentations on trace elements and cancer of the breast, we decided to determine the serum concentration of trace element in serum of our

female patients afflicted with breast cancer in comparison with healthy controls at our center.

Material and Methods

Study Place and Design

This study **was** carried out in JNU Medical College and attached Hospital, Jaipur from the period of **December 2016 to Feb 2018**. It was observational cross-sectional study, which included 100 subjects. Out of 100 subjects, 50 subjects were patients of breast cancer and another 50 normal subjects were age and sex matched healthy volunteers as control group. The blood samples were taken at the surgery outpatient department and the collected serum was analyzed for zinc and copper **levels**. Serum trace element levels of patients and controls were estimated by atomic absorption spectrophotometry.

The eligibility criteria were: new patients with histological or fine needle aspiration biopsy confirmed cases of breast cancer and have not had any treatment for their disease, no intestinal parasite infection, no micronutrients supplementation (trace elements and vitamins and any herbal medicine) and without any known associated pathology. The patient should be fasted of at least 8 hours. The subjects who did not satisfy all these criteria were excluded from the study. Very sick patients and Patients having history of severe anemia were excluded. Patients who were pregnant or lactating, patients who have had any form of treatment for their disease and patients on hormone replacement therapy or oral contraceptives were also excluded. The subjects' consent **had been taken**.

Collection and Analysis of Samples

We followed the standard protocol of sample collection and analysis. The serum samples were assessed for serum copper and zinc **levels** by atomic absorption spectrophotometry.

Statistical Analysis

Results were expressed as Mean \pm SD. Data were analyzed with the help of Microsoft excel 2007, using student's t-test. A p-value < 0.05 was considered as statistically significant.

Results

The mean serum Copper levels were significantly higher in breast cancer patients compared with control healthy subjects (94.1 ± 4.9 $\mu\text{g/dl}$ versus 62.8 ± 7.4 $\mu\text{g/dl}$) (table-1). The mean serum Zinc levels were significantly lower in breast cancer patients compared with control healthy subjects (62.2 ± 8.0 $\mu\text{g/dl}$ versus 91.7 ± 7.2 $\mu\text{g/dl}$) (table-1). No statistically significant differences were found in age ($p=0.792$) and habituation between the two groups.

Discussions

The biologic and pathologic role of trace elements are numerous, complex and sometimes very inconsistent.¹⁶ Their role apparently depends on the concentration and the balance of the positively and negatively implicated elements among other factors.⁶ Because of the multiplicity of function and the varying role depending on balance and concentration, the role of trace elements in the management of patients is yet to be fully elucidated. Breast cancer is the most common malignant tumor in females and a leading cause of malignant death in females. Its etiology is multifactorial.^{13,17,18} Exposure to trace metals and tissue concentration of trace element is a modifiable risk factor. Hence, discovery of a credible and strong causal association between trace elements and cancer of the breast may create a new frontier for the attempt at prevention and for the overall management of an established disease. Emphasis has been directed at trace elements as one of the modifiable risk factors.^{17,19} Similar to other studies, our study shows that the serum concentration of copper and zinc differ between breast cancer bearing patients and healthy individuals.

Copper is a cofactor during redox reaction in cells. When in excess concentration, it binds to genetic material inducing oxidative damages. In support of previous studies,^{17,20} we found higher concentration of copper in blood of the breast carcinoma patients compared to healthy matched adults. This is in concordance with earlier documentation.¹⁷ Even though, the exact mechanism responsible for the alterations in blood concentration of trace elements in cancer patients is yet to be fully understood, the findings in this study further lends credence to the presence of an inverse relationship between the negatively implicated element, copper and the positively implicated elements, zinc in cancer bearing patients. Furthermore, in tune with previous documentations,^{15,21} the relationship is in favor of higher serum concentration of copper. Lin *et al.* have already suggested a diet deficient in copper for cancer bearing patients,²² while others have recommended a diet rich in selenium for prevention of malignancies.²³ As documented by earlier researchers, the serum concentration of zinc in this study was significantly lower in cancer bearing patients compared with healthy controls. This is in support of the finding of hypozincemia associated with the burden of breast cancer.^{17,20} The role of zinc as antioxidant defense is suspected to be the reason for its deficiency, whether this deficiency state precedes the disease or occurs in defense against the cancerous process is still undecided, it is however, suggested that a deficiency of zinc predisposes to chromosomal damage.²⁴ Aside from the use of zinc as antioxidant, other factors that could be responsible for the hypozincemia in cancer patients are the increased loss in urine, the increased uptake of zinc by cancer cells⁷ and the presence other normal homeostatic control mechanisms and pathologic processes not related to the presence of the malignancy.^{13,25}

A protecting effect of zinc against cancer has been reported by Szymanska et al.²⁶ It is probably due to the relation of this element with vitamin A when zinc activates the vitamin mobilization from the liver. This vitamin is involved in protection against free radicals and, therefore, in carcinogenic processes.

Moreover, zinc together with copper are the two most important metals that play important roles in a variety of biochemical reactions as cofactors of the superoxide dismutase enzyme^{27,28} which also prevents the initiation and progression of neoplastic events by protecting the cells against the substance (anion superoxide) that causes the free radical formation.^{29,30} Therefore, the low peripheral levels of zinc cannot be considered as carcinogenic promoters, but a decrease in the defense mechanisms of the organism during the development of the nutritional and metabolic disturbances, and inflammation processes related to cancer.³¹ Different studies related to breast cancer^{15,27} and prostate cancer showed significantly lower zinc levels in patients than in healthy controls. This result is similar to that observed in this study in patients with gynaecological cancer. Moreover, studies carried out by Kirpatrick et al. determined that the risk of suffering from melanoma decreases when the zinc intake from foodstuffs is related to an additional mineral supplementation of this element.³²

Conclusions

It is clear that the mean serum Copper levels were significantly higher in breast cancer patients compared with control healthy subjects and the level of Zinc were lower in breast cancer patients compared with control healthy subjects. The present study gives us an idea that the variation in trace elements like copper and zinc might be one of the causes of breast cancer due to decrease immunity. The Cu level increased due to increased oxidative stress while decreased Zn level is due to defense against increased oxidative stress and shift of Zn.

However, since the size of study group was very small, it needs to be studied further with groups.

Considering all that, the correction of serum trace elements concentration would have a beneficial effect on treatment, complication and progression of the diseases, which may be a subject of further study. Taking into account these results, a zinc supplementation trial in areas where inhabitants consume diets with a low content of this element could be necessary, as a preventive measure for protection against the development of carcinogenic processes, which may be a subject of further study.

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Table 1: Mean \pm SD of various trace elements of case & control group subjects

Parameters	Mean \pm SD		p-value	Significance
	Control	Case		
Cu	62.8 \pm 7.4	94.1 \pm 4.9	<0.01	HS
Zn	91.7 \pm 7.2	62.2 \pm 8.0	<0.01	HS

HS – Highly significant

Figure 1 : Mean \pm SD of various trace elements of case & control group subjects

