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Research Article

ASSESSMENT OF MAGNESIUM (MG) AND ZINC (ZN) IN CARCINOMA BREAST PATIENTS

NEERAJ SINGH SONGARA, AJAY KUMAR BHARGAVA, AKSHITA CHAUDHARY, ANUSHREE SHARMA*

Department of Biochemistry, Jhalawar Medical College, Jhalawar, Rajasthan, India. Email: songara.neeraj@gmail.com

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ABSTRACT

Objective: The objectives of the study were to determine and compare serum magnesium (Mg) and zinc (Zn) concentrations between breast carcinoma patients and healthy controls.

Methods: Determination and comparison of serum Mg and Zn was done between 50 breast carcinoma patients and 50 healthy controls. Determination and comparison of LFT in between 50 breast cancer patient during different course of chemotherapy. Trace element analysis was done using atomic absorption spectrophotometry. Statistical comparison was done, results were expressed as Mean±SD, $p<0.05$ was considered to be statistically significant.

Results: All groups were statistically matched in age, sex, and $p>0.05$. Serum Mg concentrations in cases and controls (0.9920±0.38 mg/dL) and (1.49±0.58 mg/dL) respectively, $p\leq0.0001$* serum Zn concentrations in cases and controls were (66.74±12.58 µg/dL) and (90.88±14.51 µg/dL), respectively, $p\leq0.0001$*.

Conclusion: Both serum (Zn) and (Mg) showed significant decreases in breast carcinoma patients as compare to healthy controls.

Keywords: Breast carcinoma, Trace elements, Atomic absorption spectrophotometry.

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INTRODUCTION

Carcinoma breast is commonest malignancy among females worldwide [1] and most common cause of death in middle-aged women in western countries [2]. Breast cancer is more common in developed countries but in developing countries its prevalence is increasing in alarming pace [3]. Total 205424 new cases of breast carcinoma were recorded in India in 2020 with incidence of 1 in 29 females [4]. The etiology of breast cancer have multi-factors which includes Genetic (mutation of tumor suppressor gene BARCA1/BARCA2) [5], Diet (low with phytoestrogen and high alcohol intake), Geographical (more in western world and less in Japan), Endocrine (late menarche, early menopause, no breastfeeding, and obesity) [2]. The carcinogenic chemicals contribute to the increasing number of breast cancer worldwide. Environment chemicals like metals may play a role in initiation, promotion and progression of breast cancer. Genotoxic effects of metals can be mediated either through metabolically activated electrophilic derivatives that interact with deoxyribonucleic acid (DNA) and other macromolecules, or through direct binding of DNA [6]. Many metals have been shown to directly modify and damage DNA by forming DNA adducts that induces chromosomal breaks [7]. The oxidative stress by the generation of reactive oxygen species (ROS) from metals plays important role in the many human pathologies such as carcinogenesis [8], radiation injury, and tumor promotion [9]. The ability of ROS to damage cellular components including DNA is well documented [10]. Estrogen is important hormone in development of breast cancer and its effects mediated through the two estrogen receptors (ER) α and β. The effect of some metals on estrogen regulated genes in human breast cancer line MCF-7 was examined [11] and some metals increases cell proliferation, decrease the concentration of ERα protein and mRNA by 40–60% and mimicked the effects of estrogen-regulated genes and progesterone receptors [12,13]. The tumor suppressor gene like p53 has been associated with breast cancer development [14]. The p53status have an important role in cellular response to metals in two breast cancer lines: MCF-7 and MDA-MB231 [15]. Since the beginning of the 1970s the minerals has received a lot of attention as per the variations of mineral concentration in serum have been related to increase risk for various types of cancer in humans [16].

METHODS

Study design

This study was an observational case–controls study as well as an experimental study. The subjects in our study were selected from outpatient department and inpatient department block of Department of Surgery S.R.G. Hospital, Jhalawar (Rajasthan). Biopsy reports were taken from Department of Pathology SRG Hospital Jhalawar. An estimation of serum trace elements was done by Atomic Absorption Spectrophotometer in the research laboratory of Department of Biochemistry, Jhalawar Medical College, Jhalawar (Rajasthan).

Inclusion criteria

Case

- Patients with history and clinical findings of breast cancer
- Radiological findings suggestive of breast carcinoma and not malignant to other site
- Patient's histopathology report shows breast carcinoma. Up to stages IV with no metastasis is included
- Females above 20 years of age.

Controls

- Healthy females above the age of 20 years.

Exclusion criteria

- History of taking anti-thyroid drugs
- Pregnancy
- Any other systemic disease (e.g., liver disease and connective tissue disorder)
- Chronic use of medicine (e.g., steroids and anti-cancer drugs)
- Breast cancer patients with carcinoma malignant to other site.

In the course of the study, the conditions of ethics and the regulation were followed and no experiments were carried out to impair the health of patients. The study was approved by Ethical Committee of Jhalawar Medical College, Jhalawar (Rajasthan), and patients involved in the study agreed to be included in the study by signing informed written consents.

Specimen collection

Blood samples were taken from healthy controls and from breast cancer patients. Around 5 ml of venous blood samples was taken under aseptic conditions in sterile tubes. Samples allowed to clot and centrifuged at 3000 rpm for 10 min and serum was separated. Thereafter, non-hemolyzed serum was used for trace element analysis.

RESULTS

In the present study, there were 100 female subjects in total, which were divided into two categories of groups. The case group comprising of 50 breast cancer patients, and the control group comprising 50 healthy subjects. Statistical analysis of data was done using SPSS software (version 20.0). Chi-square test, unpaired-t test, and paired-t test were used in data analysis. The data in the study were expressed as mean±SD, and $p<0.05$ was considered as statistically significant.

Comparison of age in cases and controls was statistically analyzed using unpaired-t test. The mean age in breast cancer patients was found to be (45.78±8.11 years). The mean age in healthy controls was found to be (42.56±10.91 years). Statistical analysis showed that p=0.097, that is, ($p>0.05$) therefore the age difference in both groups was statistically insignificant (Table 1 and Graph 1).

Comparison of serum magnesium (Mg) concentration in cases and controls was statistically analyzed using unpaired -t test. The mean serum Mg concentration in Breast Cancer patients was found to be (0.9920±0.38 mg/dL). The mean serum Mg concentration in healthy controls was found to be (1.49±0.58 mg/dL). Statistical analysis showed that $p<0.0001$* therefore the difference in serum Mg concentration in both groups was statistically significant.

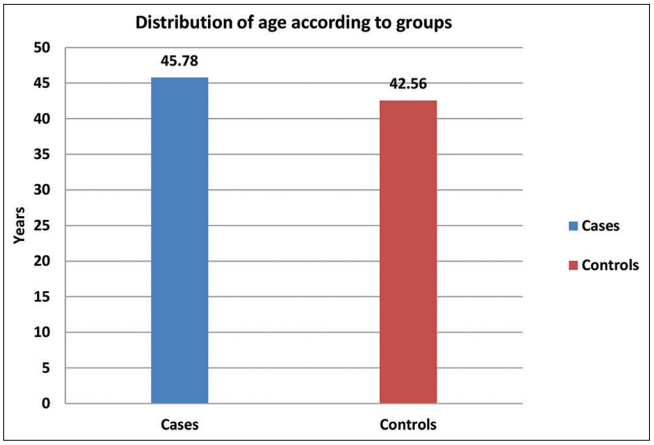
Comparison of serum zinc (Zn) concentration in cases and controls was statistically analyzed using unpaired-t test. The mean serum Zn concentration in breast cancer patients was found to be 66.74±12.58 µg/dL. The mean serum Zn concentration in healthy controls was found to be 90.88±14.51 µg/dL. Statistical analysis showed that $p<0.0001$* therefore the difference in serum Zn concentration in both groups was statistically significant.

DISCUSSION

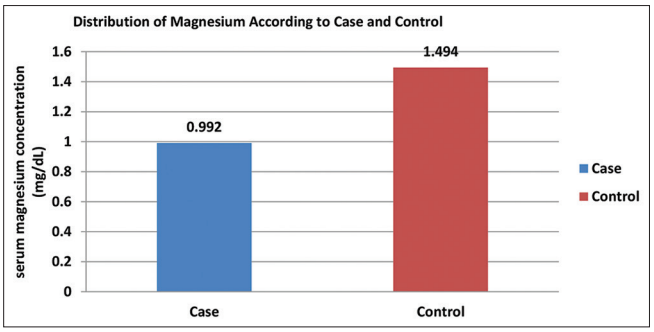
Comparison of serum Mg concentration between case and control is presented in Table 2 and Graph 2. The present observation showed that serum Mg concentration in breast cancer patients was found to be 0.9920±0.38 mg/dL. The mean serum Mg concentration in healthy controls was found to be 1.49±0.58 mg/dL. Statistical analysis showed that $p<0.0001$* therefore the difference in serum Mg concentration in both groups was statistically significant.

Thus, it was concluded that breast cancer patients have lower Mg concentration than healthy controls, and the difference was statistically significant. The mean value of serum Mg in breast cancer patients indicated that their concentration is low to the reference interval for serum Mg (1.7–2.4 mg/dL), and that breast cancer patients have hypomagnesemia, cause of which could be poor nutritional status or disturbances in Mg metabolism, however, investigation into this cause is beyond the scope of this study.

Results similar to our study were observed in study conducted by researchers Atoe *et al*., in 2014 in Nigeria. They demonstrated that serum Mg levels were lower in Breast Cancer patients as compared to healthy controls [17].



Graph 1: Comparison of age between Group – I and Group – II



Graph 2: Comparison of serum magnesium between Group – I and Group – II

Table 1: Comparison of age between Group – I and Group – II

Group	N	Mean	Std. deviation	t-value	p-value
Group–I cases	50	45.7800	8.11974	1.694	0.097
Group–II controls	50	42.5600	10.91556		

Table 2: Comparison of serum magnesium between Group – I and Group – II

Group	N	Mean (mg/dL)	SD	t-value	p-value
Group–I cases	50	0.9920	0.38377	5.084	<0.0001*
Group–II controls	50	1.4940	0.58324		

*Significant

However in 2015, researchers Pavitra *et al*. and associates conducted a study in Guntur, India and found that serum Mg was increased in breast cancer patients but not significantly as compared to healthy controls. Their results also demonstrated that breast cancer patients had serum Mg levels well above the upper limit of reference interval; however, those of healthy controls were within the limit [18].

In breast cancer, the concentrations of trace elements play very important role in different biological processes, 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-carcinogenic effects [18]. Mg is a cofactor of many enzymes, especially of the DNA polymerases. However, once tumors have formed, Mg supplementation causes accelerated growth. The Mg deficiency increases the susceptibility to cancer damage to cell membrane penetrability by oncogenic agents and interference with immuno-

competence, causing impaired surveillance against aberrant cells that can give rise to cancer [19]. It is known that carcinogenesis induces Mg distribution disturbance, which causes Mg mobilization through blood cells and Mg depletion in non-neoplastic tissue. Mg deficiency seems to be carcinogenic and in case of solid tumors a high level of supplemented Mg inhibits carcinogenesis [20].

Low serum Mg concentration in breast cancer patients observed in our study could be attributed to multiple causes. It could be due to low dietary intake, Mg is cofactor of many enzymes, especially of DNA polymerase. Mg is displaced by other metal cations so the frequency of misincorporation during DNA replication is increased. Temporary hypomagnesemia produced tissue anorexia, hormonal imbalance, and Vitamin D deficiency. Mechanism by which Mg deficiency increase the susceptibility to cancer:

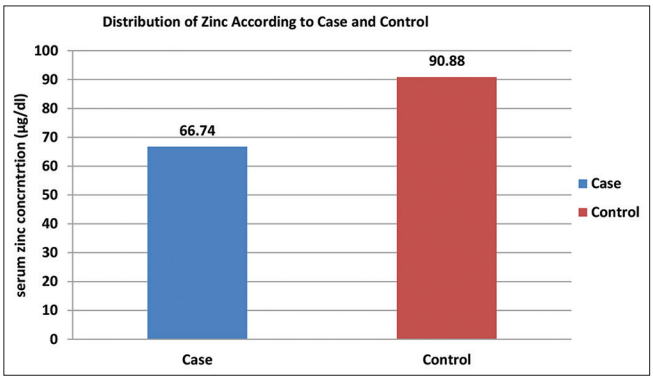
a. Damage to cell membrane with resultant easier cell penetrability by oncogenic agents
b. Interference with immuno-competence, causing impaired surveillance against aberrant cells that rise to cancer.

Impaired Mg excretion by kidneys. Kidneys primarily regulate Mg excretion [21]. Since 70% of Mg is excreted via kidneys, from proximal convoluted tubules and thick ascending limb of loop of Henle, it could be possible that due to glomerulosclerosis, tubulointerstitial fibrosis, and tubular atrophy that occur in chronic kidney disease, there might occur, impairment of Mg excreting capacity of kidneys.

Furthermore, administration of antibiotics and PPI drugs to patients is contributes to hypomagnesemia. Cardiovascular and kidney related complications can cause hypomagnesemia.

Comparison of serum Zn concentration in Group–I and Group–II is presented in Table 3 and Graph 3 was statistically analyzed using unpaired-t test. The present observation showed serum Zn concentration in breast cancer patients was found to be 66.74±12.58 µg/dL. The mean serum Zn concentration in healthy controls was found to be 90.88±14.51 µg/dL. Statistical analysis showed that p<0.0001* therefore the difference in serum Zn concentration in both groups was statistically significant.

Thus, it was concluded that breast cancer patients have lower serum Zn concentration than healthy controls and it was statistically significant.



Graph 3: Comparison of serum zinc between Group – I and Group – II

Table 3: Comparison of serum zinc between Group – I and Group – II

Group	N	Mean (µg/dL)	SD	t-value	p-value
Group–I cases	50	66.7400	12.58572	8.886	<0.0001*
Group–II controls	50	90.8800	14.51198		

*Significant

In 2017, researchers Tehseen Hassan and associates conducted study in Srinagar, India, and found that significant low levels of serum Zn in breast cancer patients [22].

In 2015, similar findings to our study are done by researchers ML Adeoti and associates in Nigeria. They found inverse relation of serum Zn with breast carcinoma [23].

Zn is the essential element that is incorporated into a number of Zn metalloproteins. Zn plays important roles in nucleic acid metabolism, cell replication, tissue repair, and growth [23]. It is found almost in every cell and plays a vital role in body's immune system affecting innate and acquired immunity [24]. It has both catalytic and structural roles in enzymes, while in Zn finger motifs; it provides platforms that organize protein sub-domains for the interaction with either DNA or other protein. Zn ions exist primarily in the form of complexes with proteins and nucleic acids and participate in all aspects of intermediary metabolism, transmission and regulation of the expression of genetic information, storage, synthesis and action of peptide hormones and structural maintenance of chromatin and biomembranes [25].

Decreased concentration of Zn is mainly related to nutritional intake, intestinal uptake, and altered distribution. Zn plays important role in stabilizing the structure of DNA, RNA, and ribosome, it is also necessary for functioning of several transcription factors, proteins that reorganize certain DNA sequences and control gene transcription and protects against free radical damage. So decline in Zn level is may be due to any of the above process get disturbed and may be acting as a causative agent for cancer. The exacerbation of Zn deficiency in breast cancer patients could, in part be explained due to increased oxidative stress [26], which demands more expenditure of Zn containing metalloenzymes such as superoxide dismutase. Aside from the use of Zn as a antioxidant, other factor could be responsible for hypozincemia in cancer patients are the increased loss of Zn in urine, the increased uptake of Zn by cancer cells [27].

CONCLUSION

Breast cancer begins when healthy breast cells change and grow out of control, usually forming a mass called a tumor. Breast cancer is one of the common cancers in females and highly combinatorial disease worldwide. Men can also develop breast cancer, but it is rare. The incidence of breast cancer in women widespread affecting 1 in 8 women. Total 205424 new cases of breast carcinoma were recorded in India in 2020 with incidence of 1 in 29 females. In Breast Carcinoma, the concentrations of trace elements are modified as a consequence of endogenous toxicities and of impaired renal function, partly due to dietary restriction and therapeutic measures. The relationship between the trace elements and cancer is some of them inducing the toxicity effect during the production of free radicals and acting as cofactors in oxidative destruction of the macromolecules and DNA. The exact role of the serum trace elements levels in carcinogenesis, breast cancer, oxidative stress, and different tumor markers is still shortage and pellicular.

From our assessment of the results of this study, we have concluded that trace element status in breast cancer patients, as well as in healthy population plays a significant role in maintaining the state of good health. Regular monitoring of trace elements status is an unavoidable step towards achieving a holistic approach to health. Moreover, regular assessment of trace element status in breast cancer patients becomes even more important in the light of trace element disturbances that were found to occur in these patients. Not only will it improve the prognosis of breast cancer patients, but will also help in understanding the cause of unregulated trace element exchange that was found to occur during the process of tumorigenesis.

CONFLICT OF INTEREST

None declared.

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ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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