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Original Research Article

Study of Serum Trace Element Copper in Breast and Prostate Carcinoma Patients

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ABSTRACT

Background: Cancer of the breast is the most common cancer and is leading cause of death from cancer in women. Prostate cancer is the second most common cause of cancer and fifth leading cause of cancer death among men worldwide. Several studies have been conducted to identify trace element association with different cancers. Copper plays physiological role in body. Its excess in body often leads to pathological condition.

Methods: This study was conducted to see the serum level of copper in breast cancer and prostate cancer patients. Biopsy confirmed 50 breast cancer women and 50 prostate cancer men were included and compared with 50 women and 50 men as control respectively. Both control study group patients were of same socio-economic status. Serum copper level was estimated using atomic absorption spectrometer technique.

Results: We observed significant high serum level of copper in carcinoma patients, as compared with healthy control subjects.

This shows an association of serum copper with cancer of breast and prostate.

Key words: Breast Cancer, Prostate Cancer, Serum Copper, Biopsy, Atomic Absorption Spectrometer.

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INTRODUCTION

Cancer has become one of the leading causes of death in India. Incidences are increasing due to industrialization and urbanization and also with facilities for detection. It is estimated that there are nearly 2 to 2.5 million cancer cases at any given point of time in India.[1] Breast cancer is the most common form of cancer among women in recent years, its prevalence is increasing in alarming pace.[2] Breast cancer found to be more common in developing countries constitute 40% of all cases.[3] In India, breast cancer is the most common form of malignancy among women in urban area. In rural area, it is the second most common form of cancer accounting for 25 to 32%.[4]

Globally prostate cancer is the second most common type of cancer and the fifth leading cause of cancer-related death in men.[5] In 2012 it occurred in 1.1 million men and caused 307,000 deaths.[5] It was the most common cancer in males in 84 countries[6], occurring more commonly in the developed world. Rates have been increasing in the developing world.[7]

Factors that increase the risk of prostate cancer include: older age, a family history of the disease, and race. About 99% of cases occur in those over the age of 50. Other factors that may be involved include a diet high in processed meat, red meat,

or milk products or low in certain vegetables. Prostate cancer is diagnosed by biopsy. Medical imaging may then be done to determine if the cancer has spread to other parts of the body.[8]

Copper is an essential micronutrient for all organisms. It is required as a catalytic cofactor or as a structural component for proteins, with roles in critical biological functions such as enzyme activity, oxygen transport and cell signaling.[9] The functional role of copper in COX-mediated ATP production illustrates the importance of copper in sustaining life.[10] While the redox activity of copper is essential for enzymatic reactions, this property also renders it potentially toxic. Copper can catalyze the production of free radicals and this can be damaging to lipids, proteins, DNA and other biomolecules.[11,12]

All organisms have evolved sophisticated mechanisms to strictly regulate both copper levels and the delivery of copper to copper-requiring proteins.

The involvement of copper in cancer has been studied for several decades and there have been numerous reports on copper levels being aberrant in cancerous tissues of tumor-bearing mice andin cancer patients.[13-17] The role of trace elements including copper, in the context of cancer, underlining their potential roles as

carcinogens and as diagnostic/prognostic markers.[18] More recently, Gupte and Mumper (2009) provided an updated review on copper dysregulation in cancer.[19] High serum copper concentrations are associated with a variety of cancers including lymphoma, reticulum cell sarcoma, bronchogenic and laryngeal squamous cell carcinomas, cervical, breast, stomach and lung cancers.[18,19]

Strikingly, elevated serum copper correlated with the stage of the disease and its progression in colorectal and breast cancers.[16,20] Elevated copper in malignant tissues has also been established in a range of cancer types, including breast, ovarian, cervical, lung, stomach and leukemia.[19] Surprisingly, leukemic and breast cancer cells can have up to four-fold and three-fold more copper, respectively.[14,21] Recently demonstrated that only a small subset of patients with prostate cancer harbor elevated intratumoral copper despite previous reports of a more general occurrence.[19,22] While there are clear demonstrations of elevated copper in several cancer types (e.g. leukemia, breast and colorectal cancers), larger scale studies are needed to validate many other reports on other cancer types.[19]

Copper concentrations have also been reported to increase in nails and/or hair of patients with acute lymphoblastic leukemia,[23] prostate,[24] breast[25] or cervical cancers.[26]

Serum copper levels are thought to be of diagnostic significance in breast cancer, Trace elements have been implicated in the pathogenesis of breast cancer.[27,28] A direct relationship has been found between serum copper and copper-zinc ratio (C/Z) and cancer of the breast.[27,29] Copper is a cofactor during redox reaction in cells. When in excess concentration however it binds to genetic material inducing oxidative damages.

MATERIALS AND METHODS

50 female patients of breast carcinoma (mean age 45.2 ±6.11 year) and 50 male patients of prostate carcinoma (mean age 54.6±6.8 years) were studied. The control group consisted of 50 healthy female (mean age 44.5±6.3 year) and 50 healthy male (mean age 53.10±6.42 years). Both study and control group were matched by socio-economic status, age, sex, race, dietary habits, smoking and drinking status. Patients were randomly selected irrespective to their caste and creed amongst the persons attending the medicine and oncology OPD and indoor.

Detailed history was taken and patients were examined clinically in detail and biochemical evaluation done to exclude any illness likely to effect serum copper level such as Wilson disease, chronic inflammatory disease etc. such patients were excluded from the present study. Tumor marker were analysed in all subjects. Biopsy was done for conformation.

Blood samples were obtained by vein puncture and collected in clean dry centrifuge tube. Standered precautions for trace element determination were taken, hemolysed sample were discarded. The blood was centrifuged at 3000rpm for 10 minutes and serum was stored until the day of the test, serum cooper was determined by direct measurement method using atomic absorption spectroscopy. Analytical reagent grade chemicals, standards were used. Water used for washing laboratory apparatus and for preparing solutions and standards was purified by deionization of redistilled water.

Table 1: Comparison of mean serum copper concentration (µg%) in Breast Cancer Patients with Control Subjects.

S.No	Value	Breast cancer patients	Control subjects
1.	Mean	179.0	113.9
2.	Range	150.4-215.0	86.0-130.0
3.	S.D.	19.6	11.7
4.	SE	6.21	2.13
5.	T	9.9	-
6.	p-value	<0.001	-

Table 2: Comparison of mean serum copper concentration (µg%) in prostate Cancer Patients with Control Subjects.

S.No	Value	Prostate cancer patients	Control subjects
1.	Mean	171.1	112.6
2.	Range	146-195.0	100.0-128.0
3.	S.D.	16.5	8.0
4.	SE	5.8	2.85
5.	T	9.22	-
6.	p-value	<0.001	-

Fig 1: Comparison of mean serum copper concentration (µg%) in Breast Cancer Patients with Control Subjects.

Fig 2: Comparison of mean serum copper concentration (µg%) in Prostate Cancer Patients with Control Subjects.
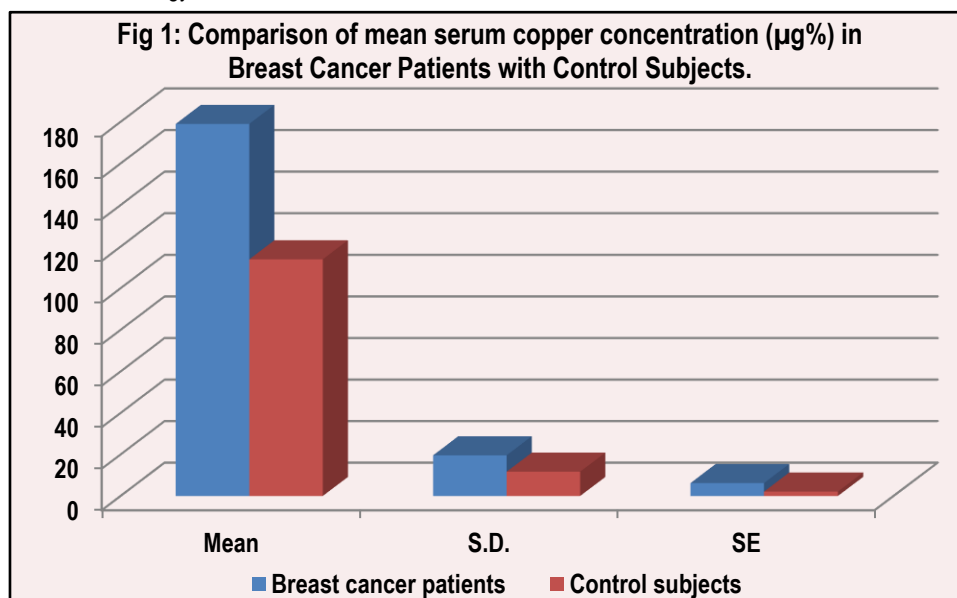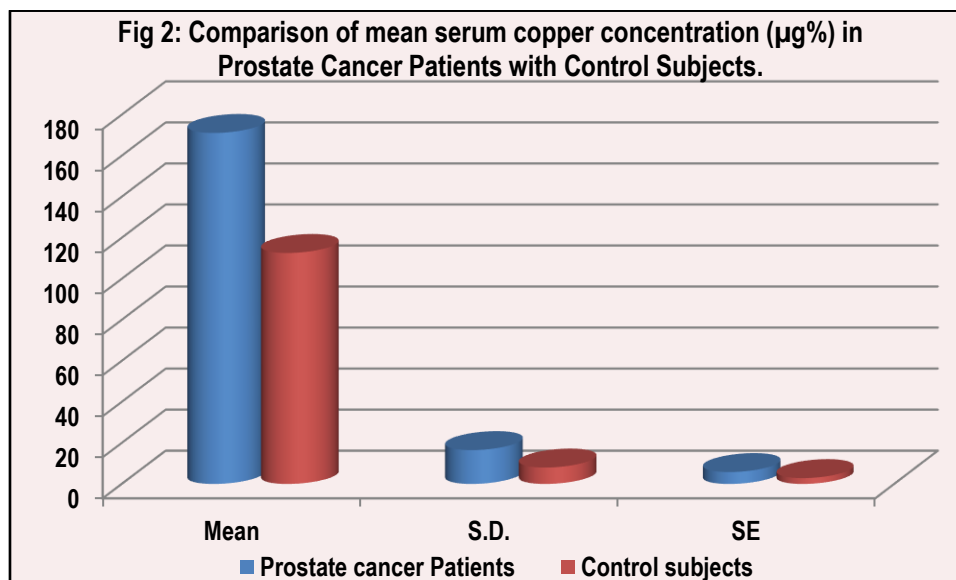
RESULTS

The results as presented in the table 1 and figure 1 show that the serum copper level was higher and statistically significant (p<0.001) in women suffering from breast carcinoma as compared to control subjects. Table 2 and figure 2 show that the serum copper level was significantly higher (p<0.001) in prostatic cancer subjects as compared to that of control subjects.

DISCUSSION AND CONCLUSION

Trace element and metal are known to play a vital role in metabolism. The mean serum copper value was found to be increased in breast cancer patient and prostate cancer patients as compared to their respective control group. Copper acts as catalytic and structural cofactor in biology, it plays role in metabolic changes in cancer cells, essential for angiogenesis in tumor and metastasis of tumor cells.[30]

In support of previous studies, we found higher concentration of copper in blood of the breast carcinoma patients[31,32] and prostate cancer patient[33-35] compared to healthy matched adults. The association of serum copper and high incidence of cancer has been found in many studies.

Our data does not allow us to conclude whether high copper level occurred as a result of copper. However the results of present study indicate the role of copper as compounding factor in the development of breast and prostate cancer. The individuals with abnormal serum level can be subjected to further investigation to identify precancerous changes or early malignant changes. Further studies are required to establish the role of estimation of serum metal ions in this regard.

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