Original Research Article

Attentive evaluation of Trace elements in Patients with breast Cancer-A Cross Sectional Study of Nawabshah, Sindh, Pakistan

ABSTRACT

Background: Breast cancer has recently become one of the most obsessing and life threatening issues in the world. Globally, females suffered mostly by breast cancer. Breast cancer is multifactorial etiological disorder. Trace elements are acts as cofactors and biological catalyst. They play a very essential role in the metabolic pathways.

Methods: A cross sectional study with two hundred (200) subjects and divided into two groups. 50 females were normal healthy as a control while 150 females were patient with breast cancer. Blood was collected from all participant after taking history, clinical data, mammographic and histopathological findings. Consent and predesign performa were filled by all participants of study. The trace elements (Na, K, Zn, Fe, Ca) were determined through atomic absorption spectrophotometer (ASS) and other biochemical analysis such as Total Protein, serum albumin and Total cholesterol were analyzed on Micro Lab.300. Data was entered on SPSS 22.0 version, and applied student t-test for continuous variables. Results were analyzed as Mean and standard deviation.

Results: The results of serum Na^{+}, K^{+}, Ca^{++}, Zn^{++}, Cu^{++} and Fe in breast cancer patient were observed and found significantly fluctuated in breast cancer patients as compared to normal healthy subjects. Serum Total Protein significantly increased whereas serum Albumin decreased in patient with breast cancer.

Conclusions: in Present study we found significantly abnormal concentration of Na^{+}, K^{+}, Ca^{++}, Zn^{++}, Cu^{++} and Fe in breast cancer these elements may contribute in early diagnosis of breast cancer. Increased body weight and total cholesterol are also risk factors of Ca breast.

Keywords: Breast cancer, Trace elements, Atomic Absorption Spectrometry.

INTRODUCTION

Breast cancer is most common and second leading cause of mortality in female worldwide.[1, 2] In Pakistan the prevalence of breast cancer in females is about 14.5% [3,4]. The Environmental, genetics, carcinogens radiation, viruses and chemicals are primary causative agents for the

development of benign or malignant tumors.[5] Trace elements acts a cofactor in metabolic pathways in the human body.[6] Abnormal levels of trace elements lead to develop the breast cancer and responsible for the generation of reactive oxygen species (ROS). ROS disturb the metabolic activity of cells by production of free radicals.[7] International Agency for Research on cancer (IARC) has listed carcinogenic possessing properties, such as Fe, cu, Mg, Mn. Be, Ni, PB Sr.[8] The Potassium (K^+) ion play a very important role in the co-transport across the cell and also responsible for the normal nerve transmits. Fluctuation in the concentration of K^+ either decreased or increased can cause adverse effect in human body, such as delayed reflex response, muscle weakness and paralytic disorders.[9] Sodium ion (Na^+) is involved in action potential and regulation many cascades inside the cell. In breast cancer the Na^+ involve in progression of abnormal cells.[10] Zinc (Zn) is act as cofactor of many enzymes and responsible for the growth, development and wound healing.[11] Zn significantly higher in malignant cancers than in those of benign whereas, copper (CU^{++}) levels decreased in malignant breast tumor. The level of serum copper may be considered as a biomarker for treatment response.[12] All living cells having great concentration of K+ inside the cell, excluding Ca^{++} and Na^+. The free Ca^{++} responsible for many messenger functions inside and between the cells.[13, 14] Obesity and cholesterol be noticeable for their potential causal association with breast cancer.[15] Postmenopausal phase of women life, the estrogen receptors declined which may a risk factor of increased cholesterol in breast cancer.[16],[17]Total protein and albumin increased in inflammation, stress and tissue narcosis. Many researchers observed higher concentration of albumin and total protein in diverse types of malignancies including breast and ovarian cancer.[18, 19] The aim of present study was to find out serum levels of Na^{++}, K^{++}, Ca^{++}, Zn^{++}, Fe, and Cu^{++}. The BMI, serum albumin, Total Protein and serum cholesterol also analyzed in breast cancer patient as compared to normal healthy females.

Objectives of this study are to analyzed and compare the level of essential trace elements, Na^{++}, K^{++}, Ca^{++}, Zn^{++}, Fe, and Cu^{++} in breast cancer patients with normal healthy adult women.

METHODOLOGY

A Cross sectional comparative study was conducted in the department of Biochemistry Peoples University of Medical and Health Science(PUMHSW), SBA with the collaboration of Nuclear Medicine & Oncology Institute Nawabshah (NORIN) during the period of six months from July 2020 to December 2020. Simple random technique was used to recruited the subjects. Sample size was calculated according to the biostatistics Rao software with 14.5% prevalence of breast cancer in females of Pakistan by using the proportion of 95% confidential interval and 5% of margin of error, the sample size stands to be n=189. Total 200 participants will be included in present study and divide in two groups. Group A: Comprises of 50 women normal healthy women as control group, whereas Group B: Comprises of 150 Breast cancer women with different stages as case group. Females with breast cancer with age of 20-70 were included in present study whereas, patients with other cancer, endocrinal disorder, cardiac disease, or any comorbidity were excluded from the study. The diagnosis was based on clinical, mammography and histopathological characteristics. After taking clinical data, taking history and fill the pre-designed proforma, collecting the blood sample from the study participants. The verbal and written consent was taken from all study subjects by explaining them about study purpose.

The blood drawn from each participant by venepuncture under aseptic measures, Blood collected into gel test tubes, centrifuge at 3500 rpm for 10 min, fractionated and transferred to eppendorf cups then stored at −20°C till required for analysis for the biochemical tests. The Trace elements were analysed by using Standard solutions of serum levels of Na^{+}, K^{+}, Ca^{++},

Zn^{++}, Cu^{++} and Fe in breast cancer patient prepared by dilution of certified standard solutions (1,000 ppm) Fluka Kamica (Bush, Switzerland), used ultrapure water obtained from ELGA lab water system (Bucks, UK), concentrated nitric acid 65% and hydrogen peroxide 30% were purchased from Merck (Darmstadt, Germany). The samples were digested by chemical and analysed on flame atomic absorption spectrometer (Perkin-Elmer model A. Analyst 700 Norwalk, CT, USA). Data was entered in Microsoft Excel and SPSS (Statistical package for Social Sciences) Version 22.0. The student t-test was applied for continuous variables.

RESULTS

The biochemical parameters were analyzed, BMI and Total cholesterol and Total Protein level significantly increased in breast cancers patients, whereas albumin level was declined as compared to control subjects shown in Table-1 respectively. Some trace elements such as Na^{+}, K^{+}, Ca^{++}, Zn^{++}, Cu^{++} and Fe in breast cancer were analyzed. Serum K^{+}, Ca^{++}, $Cu^{++}$and Fe^{++}level in breast cancer patient increased significantly in cases group as compared to control whereas Na^{+} and Zn both were found as low in cases subjects compared with control group, shown in table-2 respectively.

Table 1. Anthropometric characteristics and Biochemical analysis of study Participants

Variables	Control (n=50)	Cases (n=150)	P-Value
Age (Years)	24.98±16.92	26.81±19.5	<0.058
Body Mass Index Kg/m^2	22.5±2.69	36.6±3.98	<0.001
Total Protein (g/dL)	6.5±2.8	10.58±4.69	<0.001
Serum Albumin (g/dL)	4.5±2.13	2.10±3.1	<0.001
Total Cholesterol (mg/dl)	145.3±26.2	255.2±24.5	<0.001

Table 2. Compassion of Trace elements in Breast Cancer and Normal healthy females.

Elements	Control (n=50)	Cases (n=150)	p-value

Sodium (mEq/L)	136.5±4.65	126.3±5.32	<0.001
Potassium (mEq/L)	4.5±2.56	6.36±2.4	<0.05
Calcium (mg/dl)	7.45±1.95	11.75±1.25	<0.001
Zinc (mg/dl)	79.47±16.4	52.26±32.58	<0.001
Copper (µg/dl)	109.6±29.7	202.1±80.32	<0.001
Iron (mcg/dL)	66.84±28.41	185.7±46.7	<0.001

DISCUSSION

Trace elements play a key role on cellular level and performed many biological functions.[20] Iron is a vital trace element and acts as catalyst for many metabolic pathways. Fe is releases from cancer cells due to oxidative stress in the breast malignancies due abnormal concentration in the body results in production reactive oxygen species (ROS).[21] Barrera G [22]reported in his study the oxidative stress produce free radicals by lipid peroxidation leads to cell damage. The leakage of many elements are cause of abnormal concentration in breast cancers. Present study having similar finding. Pizzino G [23] and coworkers reported that copper similarly generates ROS from peroxides and produce free radicals results in DNA damage. Therefore, abnormal level of free Fe and Cu^{++} causes act as carcinogenic factors in ca breast. Zinc act as an antioxidant and play major role in many transcription factors. It is also recognizing the specific protein in DNA sequences which is responsible for gene regulation results in transcription.

Wu X [24] metanalysis revelaed that zinc and brast cancer having no any assoiation but we found declined concentration of zinc.

Zinc, copper and iron contribute in process of carcinogensis but calcium has no such role but having association in systematic changes in breast cancer. The parathyroid hormone is responsible for the hemostasis of calcium in the body so, metastasis of tumor in bone enhance

the phosphatase levels. Xiao Q revealed that increase intake of calicum may be risk factor of breast cancer. In psent study we reveled that incresed concentartion of calicium inon

Garcia-Estevez L et al., revealed that obesity and high cholesterol level are the risk factor of Breast cancer, our finding was consistence with their results. As these metal ions play an important role in carcinogenesis through various mechanisms, the estimation of their serum levels in high risk individuals may help in early detection of breast cancer.

CONCLUSION

The present study observed the fluctuation sodium, potassium, calcium, copper, iron and Zinc may be play a role in the pathogenesis of breast cancer. The analysis of serum levels of these trace elements has a potential role in early detection of breast cancer. Obesity and increased cholesterol level also risk factor of breast cancer.

Recommendation

Further studies will be done to confirm the present study and other environmental factors, genetic analysis will be performed to find out more causes of this life threating disease.

Competing interests

Authors have declared that no competing interests exist.

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