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Analysis of Serum Trace Elements (Copper, Iron and Zinc) Level in Women with Breast Cancer

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Original Research Article

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Abstract: Breast cancer is one of the mainly common cancers in females and highly assorted disease worldwide. ICMR said in 2016 the total number of new cancer cases is likely to be about 14.5 lakh in India. Trace elements are present in small levels, but they act a vital part in plentiful biochemical enzymatic reactions and have been evaluated as a potential key constituent in various human diseases involving cancer. Natural trace elements such as: zinc, copper have some dictatorial functions that may affect immune reactions and free radical generation. The cancerous tissue directly indicates changes of trace elements that are evoked by the disease. Blood or blood constituents such as serum are considered to be the best indicators of the present exposure of an individual to many metals due to its easy sampling. In our study I was include 100 cases and 100 healthy control in which, Serum iron, copper, tumour marker CA15-3 level, Cu/Zn and Cu/Cp ratio were significantly high in breast cancer patient ($p<0.001$) and. Serum Zinc level is significantly decreased in breast cancer patient ($p<0.001$).
Keywords: Breast cancer, Trace Element, Iron, Copper & Zinc.

INTRODUCTION

Breast cancer is one of the mainly common cancers in females and highly assorted disease worldwide. It is the most commonly diagnosed cancer in women widespread affecting 1 in 8 women [1,2]. The complete risk of breast cancer increases with age and is higher in postmenopausal women. The Indian Council of Medical Research (ICMR) said in 2016 the total number of new cancer cases is likely to be about 14.5 lakh in India. Cancer of breast among estimated 1.5 lakh (over 10 per cent of all cancers) new cases throughout 2016 [3].

Tumorigenesis in mammary glands can be induced bio-chemically with atypical expression level of circulating hormones or since a mechanical change in the apprehension of mammary stroma. Under either of the two state of affairs, mammary epithelial cells would grow out of control and ultimately result in cancer. The function of oestrogen appears to be pivotal [4,5]. Oestrogen is imperative in the development of breast cancer, and its biological property are mediated chiefly through the two oestrogen receptors (ER), α and β. The capacity of metals to activate ERα was calculated in the human breast cancer cell line, MCF-7. Similar to estradiol, treatment of cells with the divalent metals copper, cobalt, nickel, lead, mercury, tin, and chromium, or with the metal anion vanadate encouraged cell proliferation. The metals also decreased the concentration of ERα protein and mRNA by 40–60% and induced turn of phrase of the oestrogen-regulated genes and progesterone receptor. The replacement of zinc with either nickel or copper inhibits the binding of the DNA binding domain to an oestrogen response element, while replacement of zinc with either cadmium or cobalt has no effect on binding [6].

Trace elements are present in small levels, but they act a vital part in plentiful biochemical enzymatic reactions and have been evaluated as a potential key constituent in various human diseases involving cancer. Some trace elements do take part in a preventive role not in favour of spiteful growth by linking in safety against oxidative stress which can generate free radicals in the cells to aid contributes to cancer development [7].

Natural trace elements such as: zinc, copper, lead in addition to iron are originate in the environment, and human introduction derives from dissimilar sources concerning air, drinking water and food. It is identified that trace elements have chief effects as a part of

different enzymes on a massive number of biological processes. They have some dictatorial functions that may affect immune reactions and free radical generation. The cancerous tissue directly indicates changes of trace elements that are evoked by the disease. Blood or blood constituents such as serum are considered to be the best indicators of the present exposure of an individual to many metals due to its easy sampling [8].

Iron plays an imperative role in many metabolic processes, is included in the delivery of oxygen to cells and redox processes. Deficiency or excess of iron can lead to multiple organ failures and in extreme cases to death. The most modern studies explain that the iron can significantly sway the risk of cancer development and progression. Scientists reported alliance between high levels of iron in the serum and the risk of colon, liver, stomach and breast cancers. The low iron level was detected in patients with bladder and lung cancers. There are also studies in which authors showed lower iron level in patients with colorectal cancer along with breast or they did not discover any link between iron levels and the risk of breast cancer [9].

Cu can be apprehensive in the activation of several organic peroxide and making them more carcinogenic [10]. Zn plays an anti-carcinogenic function by stabilizing the structure of DNA, RNA and ribosome [11] also Zn is necessary to the functions of numerous transcriptional factors, proteins that recognize definite DNA sequences and organize gene transcription [12]. Zn protects against free radical damage and may influence immune response [13, 14]. The intend of the present study was to determine the factual status of serum Fe, Zn, Cu ,Cu/Zn and Cu/Cp ratio in BC patients against the serum of healthy control.

Objectives

1) To estimate the distinction of serum copper level with healthy women and those with breast carcinoma. 2) To calculate the distinction of serum iron level with healthy women and those with breast carcinoma. 3) To evaluate the disparity of serum zinc with healthy women and those with breast carcinoma. 4)To consider the correlation flanked by tumour marker CA15-3 and these metabolic parameters. 5)To evaluate the variant of serum copper/zinc ratio and copper ceruloplasmin ratio with healthy women and those with breast carcinoma.

MATERIAL AND METHOD

This study was conducted in section of medical biochemistry, MGM medical college its associated MY hospital, from 2014 to 2016, On approval from ethical committee, 100 histopathologically proven breast cancer cases were analysed in our study and they were compare 100 healthy age matched females controls . Seven ml of venous blood was withdrawn from each entity using not reusable syringes in blue vial. The samples were instantly centrifuged for 10 min at 3000 rpm, the serum obtained was standing apart and kept at -20c• till scrutiny. Biochemical parameters were done by fully automatic biochemistry analyser.

Exclusion criteria

For Cases group, subjects having benign breast tumour or with group anywhere else in the body; those who have ever received treatment for breast cancer in any appearance like surgery, hormones, radiotherapy or chemotherapy; patients with history of liver or kidney impairment, acute inflammatory and infectious diseases, anaemia (Hb less than 10g%), diabetes and those on medications like iron supplements, OC pills, steroids or thyroxin, etc. were expelled from the study, as any of these factors may affect serum ferritin . For manage group, subjects with BMI >30 Kg/m2 , fasting plasma glucose >100 mg/dl, blood pressure >130/85 mm Hg and central obesity were debarred from the study.. Also, controls satisfying the International Diabetes grouping (IDF 2006) investigative criteria8 for Metabolic Syndrome were excluded from study.

Statistical analysis

Data were computed and analysed using Statistical Package for Social Science (IBM SPSS version 20.0) computer software. Student t-test, Pearson correlation analysis and One-way ANOVA were used. P. value at 0.05 was considered statistically significant.

RESULT

In our study I was include 100 cases and 100 healthy control in which, serum iron in healthy control is 100.04 ±20.7 µg/dl and in breast cancer patient (BC) is 124.87±39.12 µg/dl. Serum iron,copper, tumour marker CA15-3 level, Cu/Zn and Cu/Cp ratio were significantly high in breast cancer patient ($p<0.001$) and. Serum Zinc level is significantly decreased in breast cancer patient ($p<0.001$).(Table 1)

Pearson correlation analysis between CA15-3 and variables of interest breast cancer cases in showed that serum CA15-3 was significantly ($P > 0.001$) positively associated with serum iron ($r=0.85$), ferritin ($r=0.26$), TIBC ($r=0.55$). No significant correlation found with UIBC(Table 2).

All three different stages of breast cancer cases showed a higher concentration of copper($P < 0.001$), iron ($P < 0.01$), CA 15-3 ($P < 0.001$), Cu/Zn ratio ($P < 0.01$), and lowered concentration of serum zinc ($P < 0.01$)if compared to healthy control. The mean serum ceruloplasmin level were higher inadvanced stage (III+

IV) ($P < 0.001$) if compare with stage I & II. The mean serum iron level were higher inadvanced stage (III+ IV) ($P < 0.001$) if compare with stage I.

Table-1: Comparison of Serum trace elements and tumour marker in healthy control and breast cancer patients

PARAMETERS	FEMALE CONTROL (100)	BREAST CANCER(100)	t VALUE	P VALUE
	MEAN±SD	MEAN ±SD		
S IRON	100.04 ±20.7	124.87±39.12	5.60	< 0.001
S. COPPER	102.18± 15.08	156.15 ±28.45	16.76	< 0.001
S. ZINC	88.51±18	59.55 ±16.12	11.98	< 0.001
S.CERULOPLASMIN	45.12± 17.19	57.59 ±18.20	4.97	< 0.001
CA15-3	23.45±6.83	49.26±10.45	20.6	< 0.001
Cu/Zn RATIO	1.37±1.99	2.88±1.17	6.52	< 0.001
Cu/Cp RATIO	2.61±1.0	2.95±0.94	2.46	< 0.05

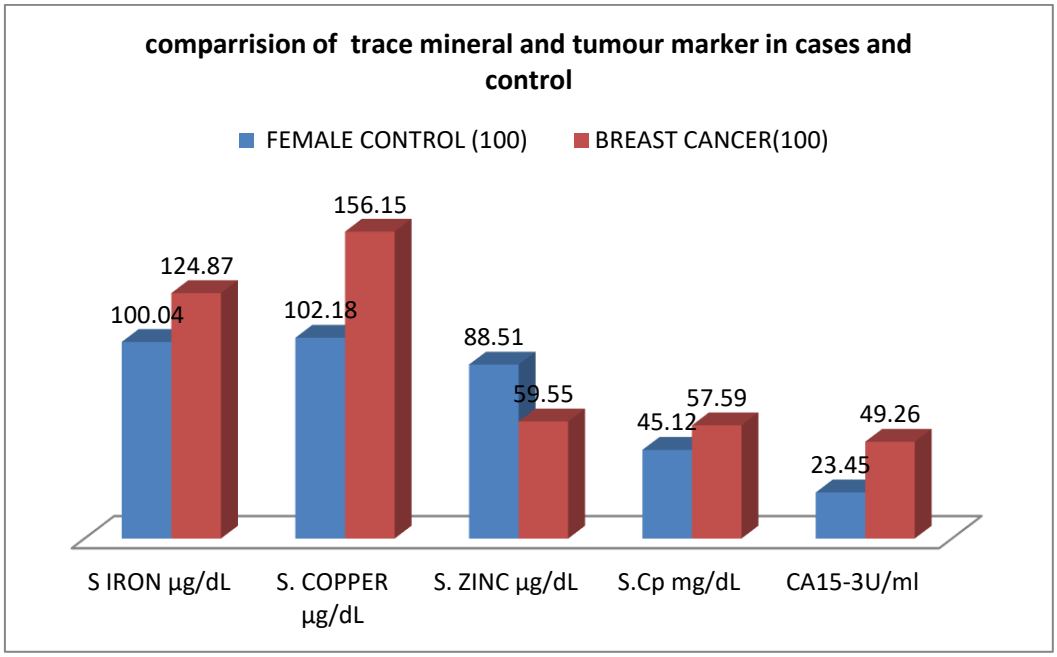

Fig-1: Comparrision of trace mineral and tumour marker in cases and control

Table-2. Correlation of tumour marker with biochemical parameters in breast cancer cases

BIOCHEMICAL PARAMETERS	r- VALUE	p- VALUE
SERUM IRON	0.85	<0.001
SERUM COPPER	0.64	<0.001
SERUM ZINC	-0.53	<0.001
SERUM CERULOPLASMIN	0.50	<0.001

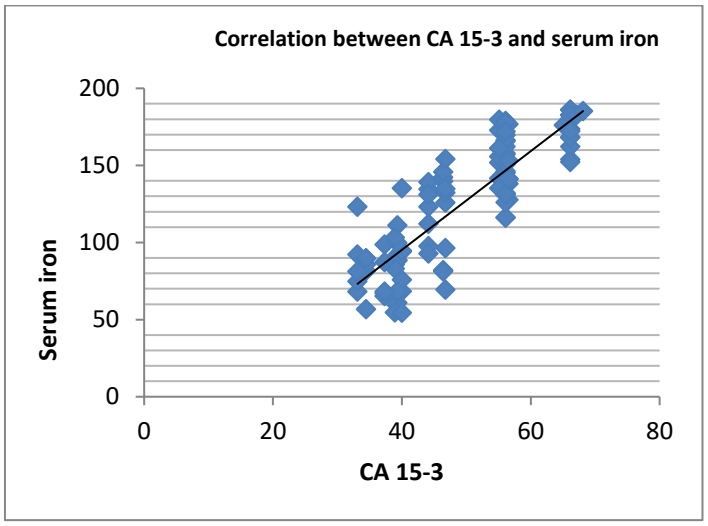

Fig-2: Correlation between CA 15-3 and serum iron

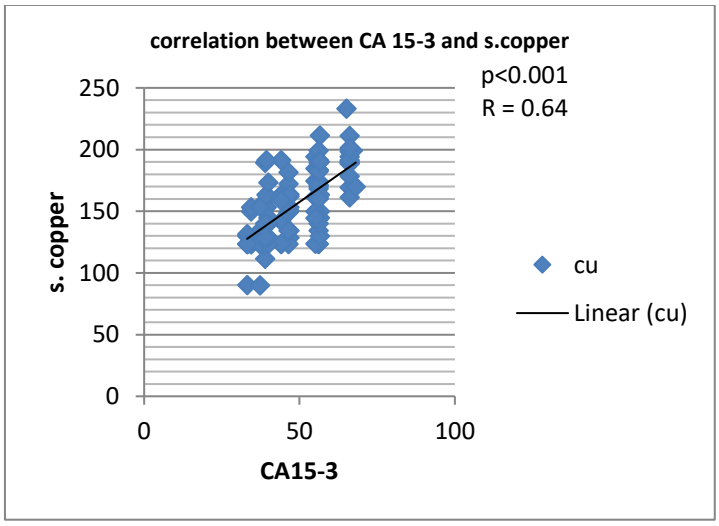

Fig-3: Correlation between CA 15-3 and s.copper

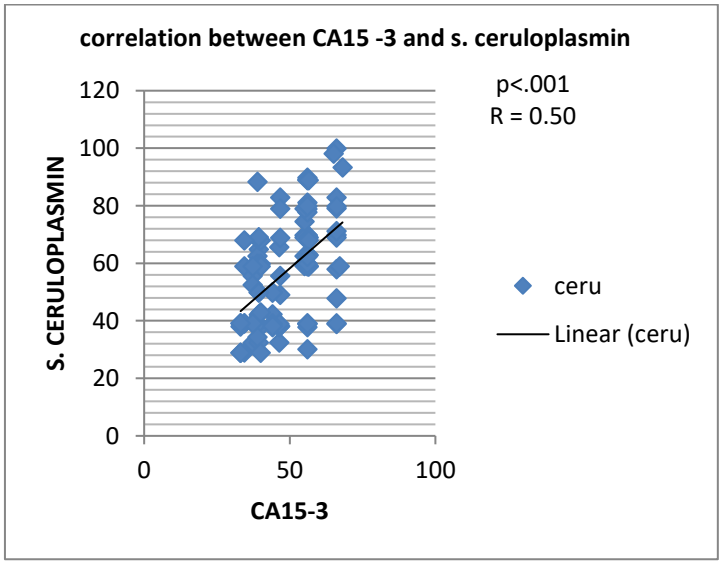

Fig-4: Correlation between CA15 -3 and s. ceruloplasmin

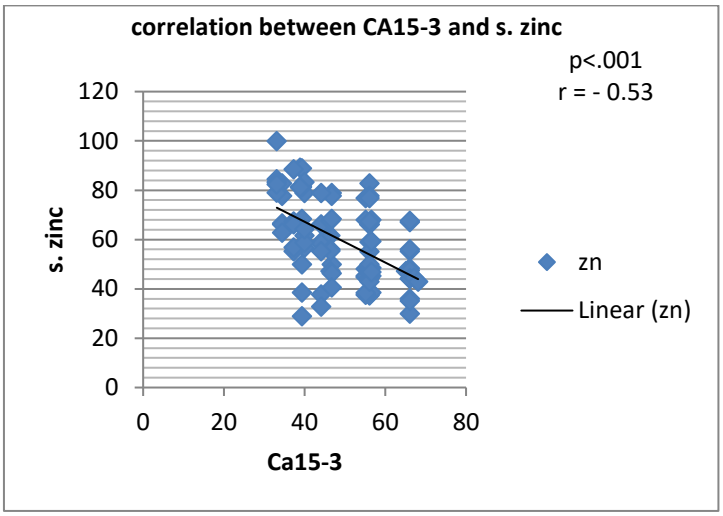

Fig-5: Correlation between CA15-3 and s. zinc

DISCUSSION

Overall, we were found significant increased levels of serum trace elements copper and iron in patients of breast cancer as compared to healthy controls ($p<0.001$)and significant decreased level of serum zinc were found in breast cancer patients. Tehseen Hassan *et al*. reported a concentration of Cu was increased significantly ($p<0.05$), significant ($p<0.05$) decline in the concentration of Zn and Level of difference of Fe remain insignificant ($p>0.05$) in serum of BC patients on comparison with the healthy individuals [15].

Rufaida Mustafa Ahmed Mustafa *et al*. in their study on 120 females, 50 cases with breast cancer and 70 as non-breast cancer controls were found statistically significant increase in the mean of serum iron in women with breast cancer as compare to healthy control groups [16]. The finding of Pavithra *et al*. in their study is similar to this study in serum iron level; they found significantly high level so serum ferritin 54female patients with breast cancer when compared to 54 female controls [17]. In the study conducted by Dhankhar *et al*. it was found that the serum iron level were significantly elevated in sixty breast cancer patients as compared to thirty healthy controls [18].

This study also supports the previous studies were it was shown that Cu can be concerned in the activation of several organic peroxides [19, 20] and can produce the hydroxyl radicals which cause mutation in DNA which may be one of the causes of cancer development.

As documented by earlier researchers that the Zn concentration in cancer patients was decreased as compared to healthy individuals which was in accordance with the results of our study were serum concentration of zinc was significantly lower in serum samples of breast cancer patients as compared to serum samples of healthy controls [21-23]. Zn plays an important role in stabilizing the structure of DNA, RNA and ribosome, it is also necessary for functioning of several transcription factors, proteins that recognize certain DNA sequences and control gene transcription and protects against free radical damage [24-26]. So may be due to decline in the concentration of Zn in breast cancer patients any of the above process get disturbed and may be acting as a causative agent for cancer.

In our study we were found significant increase level of ceruloplasmin in breast cancer patients as compare to healthy control ($p<0.001$) and the CA 15-3 levels and ceruloplasmin levels were significantly positively correlated($r=0.50$). In a study by Schapira & Schapira [27], the ceruloplas- min levels were found to be elevated in 89% of 103 patientswith breast carcinoma and then fell by 35% as soon as patients responded to treatment. These results are in accordance with those obtained by O ozyilkan *et al*. [28] in their study. They have shown that patients with carcinoma of the breast, compared to patients in remission, BBD, and normal healthy volun- teers, had higher levels of ceruloplasmin, which correlated with the spread of disease and the CA 15-3 levels and ceruloplasmin levels were positively correlated. Schapira & Schapira(27)also showed that the cerulplasmin levels of patients with breast carcinoma increased 16-34 weeks before their metastases became clinically overt.

In present study we found significant negative correlation of zinc ($r=-0.53$)and positive correlation of iron ($r=0.85$),copper ($r=0.64$) and Ceruloplasmin($r=0.50$) with tumour marker CA15-3 in breast cancer individuals.

Miłosława Zowczak *et al*. reported in their study a significant increase in the mean of total serum Cu levels and the serum Cu/Zn ratio in all patient groups with cancer compared to a control group [29]. Similar result were reported by Cigdem Yenisey *et al*. [30]. The possible role of ceruloplasmin in oncogenesis is not clear, but, it has been suggested that it may be involved in angiogenesis and neovascularization at the site of tumor growth. Breast cancer cell lines have been found to contain ceruloplasmin mRNA whilst normal breast cells do not express this gene. One may thus speculate that patients with breast carcinoma have increased levels of ceruloplasmin in blood due to an extrahepatic production, proportional to breast cancer cell proliferation [31].

CONCLUSION

Our study strongly supports that the serum copper, iron, and ceruloplasmin level were often increased and serum zinc is decreasedin breast cancer patients and suggests that all these trace elements can be used as a tumour marker for follow-up of breast cancer patients. In a future study, serial determination of trace elements(copper ,iron zinc and Ceruloplasmin) and CA 15-3 in patients with malignant lesions of the breast would be useful for evaluat ing the role of trace elements as a prognostic predictor.

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