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Assessment of Plasma Copper and Zinc Levels among Sudanese Breast Cancer Patients in Taiba Cancer Center

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ABSTRACT

There is an indication of the possibility of the direct or indirect influence of trace element in the development of malignant diseases. This study aimed to assess the level of plasma Copper and Zinc among breast cancer women in Taiba Cancer Center Khartoum-Sudan. This is a descriptive cross sectional study conducted in Taiba Cancer Center in Khartoum State during the period from September 2016 to December 2016. Blood samples from 60 women (55 on chemotherapy and 5 on chemotherapy and surgery) were collected from select sample of patients after fulfillment of questionnaire under septic condition. Blood sample was drawn in heparinized container then centrifuged at 3000 RPM for 3 min to obtain plasma. Hemolyzed samples were excluded from study, and then 3.0 ml plasma samples were preserved at -20ºC prior to processing. Obtained plasma was tested for copper and zinc by using atomic absorption spectroscopy. The overall mean values of plasma levels of Zinc and Copper (mg/L) were significantly ($P < 0.05$) different between patients on chemotherapy and others on chemotherapy and surgery. Duration of cancer significantly affect the plasma levels of Zinc but not copper. Our study showed that plasma levels of Zinc and Copper were significantly affected by chemotherapy among women with breast cancer on chemotherapy; accordingly there is a need to consider the levels of trace elements when put the cancer patients on chemotherapy.

Key words: Zinc, Copper, Breast Cancer and Chemotherapy.

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INTRODUCTION

Breast cancer is a heterogeneous disease encompassing a wide variety of pathological entities and a wide range of clinical characteristics. This carcinoma originates from the terminal ductal lobular unit of breast tissue and has two different growth types: invasive or non-invasive. Most breast cancers are invasive at the time point of diagnosis (Simpson, 2005). Globally, breast cancer is the most frequent cancer among women. According to the International Agency for Research on Cancer, approximately 1.2 million new cases of invasive breast cancer and 410,000 breast cancer deaths occur every year worldwide (Ferlay et al., 2007). In United States, breast cancer accounts for nearly 34% of all cancers diagnosed among women (Desantis et al., 2011). Although, the incidence of breast cancer in Sub-Saharan African counties is low compared that in developed countries, the cancer picture in Sub-Saharan Africa and especially in Sudan is changing. Lately, breast cancer incidence and mortality has been rising (Parkin et al., 2014). Breast cancer in African women is characterized by younger age at onset, advanced stage at diagnosis, and consequently poor prognosis. For example in Nigeria, about two-thirds of women with breast cancer present with advanced stage disease (Adebamowo and Ajayi, 2014).

In Sudan a study by Elgaili et al. (2010) revealed that 74% of the women were <50 years old or premenopausal. Invasive ductal carcinoma was the most common pathology (82%) and women presenting with stage III or higher tumors that had already metastasized, while ductal carcinoma *in situ* was the least prevalent (0.5%) finding.

Another recent study by Elhaj et al. (2015) showed that breast cancer represents 20% of all cancer cases registered in the National Cancer Institute (NCI), University of Gezira, Sudan. It has become well established that many trace elements play an essential role in a number of biological processes through their action as activators or inhibitors of enzymatic reactions by competing with other elements and proteins for binding sites, by influencing the permeability of cell membranes, or through other mechanisms. It is therefore reasonable to assume that these trace minerals would exert action, directly or indirectly, on the carcinogenic process (Sunderman, 2011). New analytical techniques, such as neutron activation and energy dispersive X-ray fluorescence (EDXRF) make possible the simultaneous determination of ultra-trace quantities of elements in human tissues and body fluids. By using such techniques, it is possible to determine whether the simultaneous monitoring of the less abundant trace metals has diagnostic or prognostic significance (Tipton, 2014). Study in India by Singhal et al. (2015) showed that the level of Copper is significant higher in breast cancer patients where level of zinc is significantly lower among breast cancer patients as compared to controls. Ebrahem (2014) conducted a study at the Radiation and Isotopes Centre Khartoum (RICK) in Khartoum State to evaluate plasma copper levels in Breast Cancer Women; they found significant increase in the mean of plasma copper levels in patients when compared with control group. Also there was a significant decrease in the plasma copper levels in premenopausal women with breast cancer when compared with the mean of menopausal. The study showed insignificant increase in the mean of plasma copper levels in normal and overweight patient. Insignificant increase in the mean of plasma copper according to the durations of breast cancer less than or equal two year and more than two years. The result of current study indicated that there was significant decrease in the mean of plasma copper levels in women with breast cancer according to their number of children who have less than 3 children when compared with mean of patients who have more than 3 There for, this study aimed to assess the levels of plasma Copper and Zinc among Sudanese women with breast cancer.

MATERIALS AND METHODS

This is a descriptive cross sectional study conducted in Taiba Cancer Center in Khartoum State during the period from September 2016 to December 2016, the study population was diagnosed breast cancer women attending Taiba Cancer Center the during conduction of the study. Blood samples (55 on chemotherapy and 5 on chemotherapy and surgery) were collected from select sample of patients after fulfillment of questionnaire under septic condition. Estimation of Plasma Copper and Zinc Plasma samples were diluted 1:1 with deionized water. Instrumental and gas-flow settings and aspiration rate was established precisely, then signal was optimized and minimized background noise. After that the instrumental set the table of Standard atomic absorption conditions for Copper and Zinc were applied to the instrument according. Once the aspiration rate is optimized with 10-ml aliquots of water, the nebulizer flow adjusted in place was locked. Glycerol/water solution (5/95 by vol) will be aspirated into the luminescent flame and the baseline will be set to read 0.000±0.001 absorbance (A). Baseline reading was obtained before and after each sample and reset the baseline as required.

Ethical Consideration

This was approved from the Ethics Committee of Al-Neelain University, and all patients enrolled in this study was fully informed by the aim of the study and verbally with written consent was obtained from all participants.

Statistical Analysis

After reporting the data of serum level of cupper and the demographic and clinical information of the patients Statistical Packages for Social Sciences (SPSS) version 19.0 was used. Two independent samples t –test was applied to know the differences between the study groups. Confidence Interval of 95% was adopted, so the level of P value < 0.05 was regarded as significant.

RESULTS

The mean value of the plasma level of Zn (mg/L) in patient on chemotherapy was (0.157±0.08) significantly higher than in patients on chemotherapy and surgery (0.109±0.03) (P = 0.011, Figure 1). Significant differences in the plasma level of Zn (mg/L) according to duration of the disease (P = 0.031), where in patients with duration of disease less than 5 years the mean value of Zn (mg/L) was 0.162±0.095, higher than 0.123±0.040 in patients with duration 5 to 10 years (Table 1). No significant differences in the plasma level of Zn (mg/L) according to menopausal (P = 0.935), where in menopausal patients the mean value of Zn (mg/L) was 0.153±0.089, slightly higher than 0.151±0.084 in pre-menopausal patients (Table 2). No significant differences in the plasma level of Zn (mg/L) according to stage of cancer (P = 0.272), where the mean value of were 0.110±0.032, 0.110±0.032 and 0.153±0.084 mg/L in patients at stage II, III and IV, respectively (Table 3).

The mean value of the plasma level of Copper (mg/L) in patient on chemotherapy was (0.117±0.09) not significantly higher than in patients on chemotherapy and surgery (0.105±0.04) (P = 0.541, Figure 2). No significant

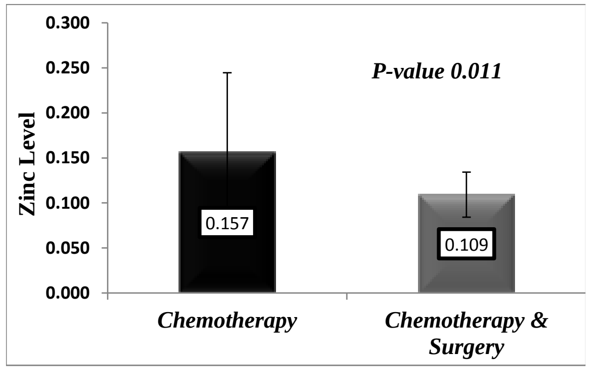

Figure 1. Mean concentration of zinc level (mg/L) among cancer patient *P-value* ≤ 0.05 consider as significant.

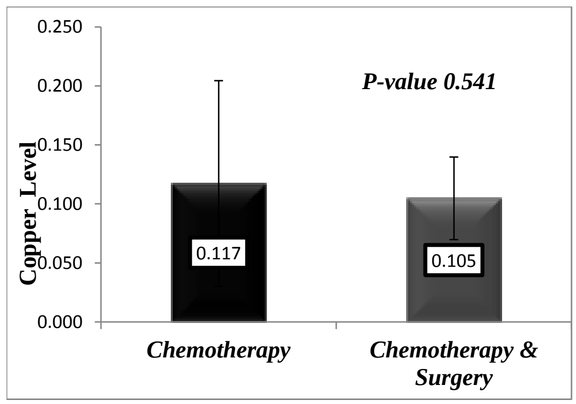

Figure 2. Mean concentration of copper level (mg/L) among cancer patient *P-value* ≤ 0.05 consider as significant.

Table 1. Mean concentration of zinc and copper levels across duration of disease.

Parameters	Group	Mean±SD	*P-value*
Zinc (mg/L)	< 5 Years	0.162±0.095	0.031
	5-10 Years	0.123±0.040	
Copper (mg/L)	< 5 Years	0.123±0.092	0.122
	5-10 Years	0.094±0.049	

P-value ≤ 0.05 consider as significant.

Table 2. Mean concentration of zinc and copper levels across menopausal state.

Parameters	Status	Mean±SD	*P-value*
Zinc (mg/L)	Menopausal	0.153±0.089	0.935
	Pre-menopausal	0.151±0.084	
Copper (mg/L)	Menopausal	0.107±0.061	0.352
	Pre-menopausal	0.132±0.114	

differences in the plasma level of Copper (mg/L) according to duration of the disease (P = 0.122), where in patients with duration of disease less than 5 years the mean value of Copper (mg/L) was 0.123±0.092, slightly higher than 0.094±0.049 in patients with duration 5 to 10 years (Table 1). No significant differences in the plasma level of Copper (mg/L) according to menopausal (P = 0.352), where in menopausal patients the mean value of Copper (mg/L) was 0.107±0.061, slightly lower than 0.132±0.114 in pre-menopausal patients (Table 2). No significant differences

Table 3. Mean concentration of zinc and copper levels across stage of cancer.

Parameters	Stage of cancer	Mean±SD	*P-value*
	II	0.110±0.032	
Zinc (mg/L)	III	0.110±0.032	0.272
	IV	0.153±0.084	
	II	0.118±0.099	
Copper (mg/L)	III	0.105±0.054	0.916
	IV	0.118±0.074	

in the plasma level of Copper (mg/L) according to stage of cancer (P = 0.916), where the mean value of were 0.118±0.099, 0.105±0.054 and 0.118±0.074 mg/L in patients at stage II, III and IV, respectively (Table 3).

DISCUSSION

In this study, 60 women with breast cancer (55 on chemotherapy and 5 on chemotherapy and surgery) were investigated to assess the level of plasma Copper and Zinc among breast cancer women in Taiba Cancer Center. Significant differences found in our study regarding plasma levels of Zinc between patients on chemotherapy and the others on chemotherapy and surgery. On the other hand, no significant differences found between the two groups regarding plasma levels of Copper. This agreed with previous studies by (Filomeni et al., 2007; Schrauzer, 2016) who found the same results. Other studies revealed dissimilar results such as (Kuo et al., 2012; Chan et al., 2013). This dissimilarity may be due to the sample size, ethnic differences, or nutrition status. Considering duration of breast cancer significant differences were found in plasma levels of Zinc but not in Copper. Which is same as found by Wintergerst et al. (2007). Regarding stage of cancer and menopausal stage in our study no significant differences were found in both plasma levels of Zinc and Copper which is different from previous studies for example (Filomeni et al., 2007; Silvera and Rohan, 2014). It has been reported that a decline in the cell mediated immunity predisposes to oncogenesis, and a close association has been found between immune responses and macro- or micronutrient status (Wintergerst et al., 2007). This implied that it may be possible to monitor the prognosis of cancers using the levels of trace metal; this is because cancer cells have abnormal regulated zinc, that means to locally regulate zinc levels promote survival of immune cells and promote tumor apoptosis.

CONCLUSION

Our study showed that plasma levels of Zinc and Copper were significantly affected by chemotherapy among women with breast cancer accordingly there is a need to consider the levels of these trace elements in breast cancer before and after chemotherapy.

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