

Use of Serum Copper and Chromium as Biochemical Markers in the Diagnoses of Cancer in female subjects

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ABSTRACT

Aim: To find and compare Copper and Chromium serum levels in female cancer patients of different age groups in Peshawar city.

Study design: Comparative analytical study.

Place and duration: The study was conducted from 13/ 9/21 to 12/3/22 in Institute of Radiotherapy and Nuclear Medicine (IRNUM) Peshawar.

Methods: Patients include 116 female cancer patients divided into three classes age wise designated as A1, A2 and A3. Serum Cu and Cr were quantitatively analyzed by Atomic Absorption Spectrophotometer using acetylene flame (Model Perkin Elmer AAS 700). The collected data was analyzed using SPSS software version 22

Results: A1 includes patients below 18 years 28(24.13%), A2 consists of patients in the age range of 18–45 years 32(27.58%) and A3 includes patient above 45 years 56(48.28%). The mean age of A1, A2 and A3 was 11.69, 35.44 and 61.26 years respectively. The mean BMI of A1, A2 and A3 were 19.5, 27.21 and 31.02 respectively. Mean level of Cu in A1, A2 and A3 was 0.20, 0.44 and 0.19mg/L respectively. Mean level of Cr level was 2.78, 1.13 and 2.97 mg/L in A1, A2 and A3 respectively. A very significant correlation was observed between serum Cr and Cu and in A1 ($p = 0.02$) and A3 ($p = 0.04$) respectively.

Conclusion: We found that mean level of Cu was less than the normal level. Mean of Cr level was found to be greater than the normal serum level of Cr in all the groups.

Key words: Copper, Chromium, serum, cancer, Malignant

INTRODUCTION

Trace metals constitute only 0.02% of total body mass, but play important roles, such as cofactors for enzymes like copper (Cu) for uricase, Zinc (Zn) for Carbonic Anhydrase and iron for catalase¹. These are involved in a number of metabolic functions, mostly acting as a cofactor for enzymes and an integral part of vitamins¹. Their imbalanced level may cause various health related issues like cancer². Cancer is a serious health problem and is main cause of death on a global scale.

Cancer cells show metabolic variation necessitating the need for micronutrient like (Cu), selenium (Se), and Zinc (Zn) in malignant growth. There are evidences showing the significance of Trace Elements (TE) to be future demonstrative or prognostic markers³. Dietary sources of Zn include meat, meat products, grains, cereals, milk and dairy products.

Zinc is involved in the normal development of body and is a key component of cells⁴. Its anti-cancer activity and role in immunity is well established³. In vitro, lack of Zn affects the arrangement of Reactive Oxygen Species (ROS)⁴. Dietary Zn has a potential role in the prevention of cancer in human body. At normal concentrations, zinc retard the growth of cancer cells, its migration, maintain a balanced metabolism in the body, and cause cancer cells death. Mn is also an important trace element which is involved in a number of physiological functions like immune response, bone mineralization, metabolic regulation, production of cellular energy and protection against ROS, reproductive functions⁵.

Cu and Cr are also important trace metals involved in many vital functions in basic life processes in living organisms. Normal level of Cu and Cr in blood is 0.85 to 1.8mg/L and 0.18–0.92mg·L⁻¹ respectively.

High doses of Cu and Cr beyond recommended allowance may cause cytotoxicity. Toxicity of Cu and Cr may cause anemia, various types of allergies, hair fall, cancer, arthritis, diabetes, fatigue, depression, and hypertension⁶.

According to some reports Cu levels are elevated in malignant growth in serum/blood and tissue of the cancer patient due to the increased need of tumor for Cu to aid angiogenesis, growth, and metastasis⁷.

Mostly Cu level is determined in blood or in malignant tumor tissue of the patients⁸. Recent research shows no link between elevated Cu levels and high risk of malignant growth.

According to some clinical trials higher intake of Zn and Cu has shown to reduce the risk of lung cancer⁹. Lung cancer has been reported in some workers from Germany and USA involved in the chromate production¹⁰.

The aim of the present work was to find and compare Cu and Cr levels in female cancer patient of different age groups in Peshawar city.

METHODOLOGY

Patients: Patients include 116 female cancer patients visiting various tertiary care hospitals in Peshawar from various districts of Khyber Pakhtunkhwa for treatment purposes. Data was collected from all the patients on informed consent in accordance with standard global practice on a standardized questionnaire designed for the study. The patients were divided into three classes age wise designated as A1, A2 and A3. A1 includes patients below 18 years 28(24.13%). A2 consist patients in the age range of 18–45 years of age 32(27.58%) and A3 includes patient above 45 years 56(48.28%).

Collection of blood: Blood samples were collected from all the patients in clean labeled test tube and left for a few minutes to clot. Blood samples were centrifuge for ten minutes to collect serum. The serum were diluted to 15 ml with deionized water

Determination of serum Cu and Cr: Serum Cu and Cr were quantitatively analyzed by Atomic Absorption Spectrophotometer using acetylene flame (Model Perkin Elmer AAS 700) under standard conditions. Cu and Cr standard solutions were prepared by diluting their stock solutions to 2–6ppm. A 5% (v/v) solution of glycerol was used as a blank. Normal serum level of Cu and Cr were: 0.7–1.4 and 0.14–0.16mg/L respectively¹¹.

Data Analysis: The collected data was analyzed using SPSS software version 22. Values were expressed as Mean ± (SD) Standard Deviation. The collected data was analyzed statistically to find out the association between Cu and Cr and other various parameters of the patients. Two-tailed p values < 0.05 were considered statistically significant.

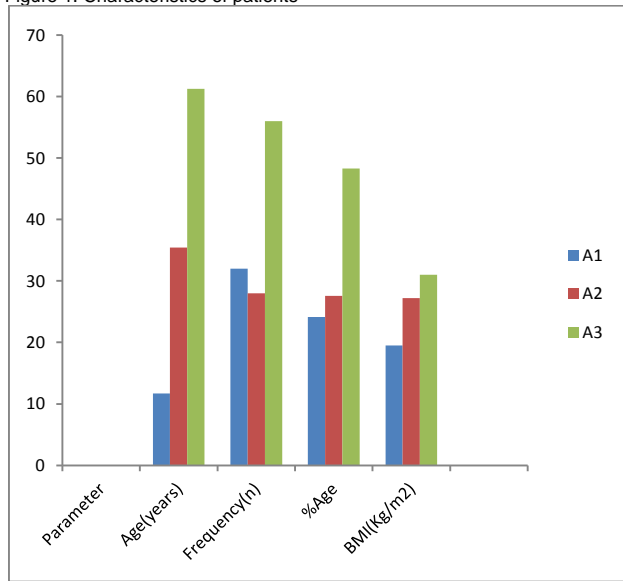
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RESULTS

Characteristics of the patients: Figure 1 shows the characteristics of patients in the patients. Patients include 116 female cancer patients which were divided into three class's age wise designated as A1, A2 and A3. A1 includes patients below 18 Years 28(24.13%). A2 consist patients in the age range of 18-45 years of age 32(27.58%) and A3 includes patient above 56(48.28%). The mean age of A1, A2 and A3 was 11.69, 35.44 and 61.26 years respectively. The mean BMI of A1, A2 and A3 were 19.5, 27.21 and 31.02 respectively.

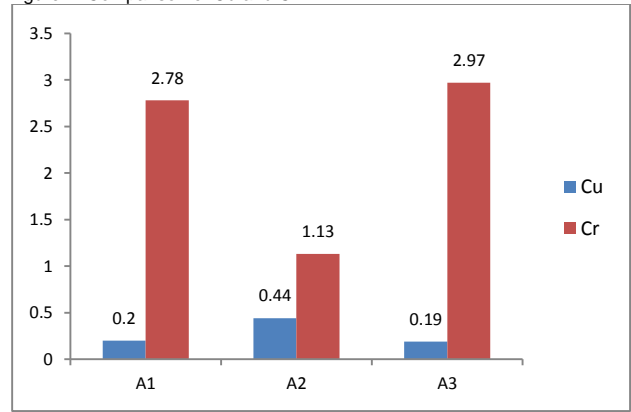
Figure 1. Characteristics of patients



Comparison of Cu and Cr level in serum of patients

Figure 2 shows level of Cu and Cr in serum of patients. Mean level of Cu in A1, A2 and A3 was 0.20, 0.44 and 0.19 mg/L respectively. Mean of Cr level was 2.78, 1.13 and 2.97 mg/L in A1, A2 and A3 respectively.

Figure 2: Comparison of Cu and Cr



Pearson's Bivariate Correlation Analysis of Study patients: Table1 shows Pearson's Bivariate Correlation analysis of the patients in various groups with the other parameters of the study subjects. A very significant correlation was observe between serum Cr and Cu A1 ($p = 0.02$) and A3 ($p = 0.04$), while no such correlation was observed in A2.

Multiple Linear Regression Analysis of Cr and Cu Serum of Study Patients: Multiple linear regressions analysis of Cr and Cu of the patient population is shown in table 2. Cu was found to be positively related with age of A1 (0.01), A2 (0.05), A3 (0.00) and BMI of G3 (0.01), and negative relation was observed with BMI of A1 (-0.00) and A2 (-0.06). Negative relation of Cr with age of A1 (-0.13), A2 (-0.00) & BMI of A1 (-0.15) and A2 (-0.02) and positive relation with age in A3 (0.07) and BMI of A3 (0.06).

Table 1: Pearson's bivariate correlation analysis of study patients

Parameter	A1(n=32)				A2(n=28)				A3(n=56)			
	Age	BMI	Cu	Cr	Age	BMI	Cu	Cr	Age	BMI	Cu	Cr
Age(Years)	1	0.01 (0.75)	0.18 (0.60)	-0.30 (0.34)	1	0.50 (0.06)	0.4 (0.13)	-0.05 (0.90)	1	0.09 (0.70)	0.05 (0.82)	0.2 (0.40)
BMI(Kgm ⁻²)	0.10 (0.75)	1	-0.13 (0.68)	-0.33 (0.27)	0.5 (0.06)	1	-0.06 (0.81)	-0.08 (0.77)	0.09 (0.70)	1	0.32 (0.14)	0.12 (0.59)
Cu(mg/L)	0.18 (0.55)	-0.13 (0.68)	1	-0.65 (0.02)	0.40 (0.13)	-0.07 (0.81)	1	-0.21 (0.44)	0.05 (0.82)	0.32 (0.14)	1	-0.43 (0.04)
Cr(mg/L)	-0.29 (0.34)	-0.32 (0.27)	-0.65 (0.02)	1	-0.05 (0.86)	-0.08 (0.77)	-0.21 (0.44)	1	0.18 (0.40)	0.12 (0.59)	-0.43 (0.04)	1

* Correlation is significant at 0.05 levels (2-tailed).

Table 2: Multiple Linear regression analysis of Cr and Cu serum of study patients

Parameter	Group	A1(n=32)		A2(n=28)		A3(n=56)	
		US		US		US	
		B	SE	B	SE	B	SE
Cu	(Constant)	0.21	0.20	0.24	1.21	-0.17	0.37
	Age (Years)	0.01	0.01	0.05	0.03	0.00	0.01
	BMI (Kgm ⁻²)	-0.00	0.01	-0.06	0.05	0.01	0.01
Cr	(Constant)	6.96	3.06	1.81	2.43	-3.40	6.64
	Age (Years)	-0.13	0.14	-0.00	0.05	0.07	0.10
	BMI (Kgm ⁻²)	-0.15	0.14	-0.02	0.10	0.06	0.13

US; Unstandardized Co-efficients

SE; Std. Error

DISCUSSION

Trace metals are the important components of living organisms and are required in small amounts for normal functions and health. The abnormality in their dietary intake and subsequent abnormality in the blood may cause various physiological disorders in the body. These disorders include diabetes, hyper tension, skin diseases, brain, cancer and other metabolic diseases.

Cu and Cr are also important trace metals involved in many vital functions in basic life processes in living organisms. Normal level of Cu and Cr in blood is 0.85 to 1.8mg/L and 0.18-0.92 mg·L⁻¹ respectively. In some studies it has been reported that Cu levels maybe elevated in serum/blood of cancer patients, exactly as they are in tumor tissue due to the tumor's need for Cu to grow and metastasis⁸.

While other researchers contradict a possible association of high Cu levels and risk of malignant growth in some patients. We

found that mean level of Cu in A1, A2 and A3 was 0.20, 0.44 and 0.19 mg/L respectively which was less than the normal level (Normal serum level of Cu: 0.7-1.4mg/L). A number of research paper reports higher concentration of Cu in cancer patients in higher quantity as compare to healthy subjects but we found no such results from our study¹¹.

Elevated levels of Cu and ceruloplasmin are found in some cancer patients. Determination of serum Cu and some antioxidants can be of significance in the diagnose of early stages of colon and prostate cancer¹². In a recent study from Korea involving 229 Breast Cancer(BC) patients and 200 controls showed high serum concentration of Cu in BC stage IV than in control (1.00 vs. 0.95mg/L, p=0.0002). A Second study did not found any difference between the two subjects (0.90 vs. 0.92mg/L, p=0.281). A study from India involving 100 BC patients and 140 healthy controls found higher levels of serum Cu in BC patients as compare to normal controls (1.17 vs. 0.89mg/L, p<0.0005)^{13,14}.

Hexavalent chromium is carcinogenic and cause oxidation reactions in blood causing hemolysis and, ultimately leads to liver and kidney failure¹⁵. We observed the mean Cr level to be 2.78, 1.13 and 2.97mg/L in A1, A2 and A3 respective greater than the normal serum level of Cr: 0.14–0.16mg/L. Our findings are supported by similar other studies¹⁴. EPA report shows that, if a person breathes air containing 8x10⁻⁸mg/m³ Cr in entire life, the risk of developing cancer in such person is very negligible (one-in-a-million)^{16,17}.

CONCLUSION

We found that mean level of Cu in A1, A2 and A3 was less than the normal level (Normal serum level of Cu: 0.7-1.4 mg/L). Mean of Cr level was greater than the normal serum level of Cr: 0.14–0.16mg/L.

Conflict of interest: Nil

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