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# Serum Zinc and Copper Levels among Patients with Prostatic Cancer Attending National Cancer Institute, Gezira University, Sudan

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## Abstract

**Backgrounds:** Prostate cancer is the most common cancer among Sudanese men and is equally distributed among its different tribes. Zinc (Zn) and copper (cu) are one of the most important microelements and ubiquitously present in the human body, and it is critical for maintaining prostate health and inhibiting prostate cancer development.
**Objective:** To assess serum zinc and copper levels among Sudanese prostatic cancer patients.
**Materials and Methods:** Case control study carried out in National Cancer Institute from August 2020 to December 2020. The study included 60 Sudanese subjects, 30 of them were patients with prostate cancer and 30 were as controls. The age of patients ranged between58-88. (43%) of patients were >70 Years and (57%) were <70 Years serum zinc and copper were measured by using atomic absorption spectrophotometer. Data was analysed using SPSS version (22).
**Results**: Highly significant decrease in zinc level in case group (0.08±0.06) when compared with control group (0.7±0.2) with p. value (p=0.000) and highly significant increase in copper level in case group (1.6±0.3) when compared with control group (0.9±0.2) with p.value (p=0.000). There were no significant differences on Zn and copper levels according to age, BMI and duration with p. value (0.10, 0.70, 0.30), (0.28, 0.06, 0.52) respectively. Regarding gleason stages patients with advanced stage > score 7 (43%) (0.06±0.05) showed more decrease in zinc than patients with non-advanced stage ≤ score 7 (57%) (0.09±0.06) without significant differences (P=0.3) andshowed more increase in copper than patients with non-advanced stage ≤ score 7 (57%) (1.47±0.50) without significant differences (P=0.37).There was weak negative correlation between age, grade, stage and PSA with serum zinc with a coefficient r (-0.3, -0.03, -0.003, -0.2) respectively. While there was weak positive correlation between BMI and duration with serum zinc with a coefficient r (0.07, 0.07) respectively.There was moderate negative correlation between age, and duration with serum copper with a coefficient r (-0.20, -0.14).While serum copper had moderate positive correlation with BMI, Stage, grade and PSA levels with a coefficient r (0.34, 0.28, 0.27, 0.27) respectively.
**Conclusion:** Serum zinc level in cases was lower than in controls; whileserum copper level in cases was higher than in controls. The study recommended regular monitoring of serum zinc and copper in prostatic cancer patients.
**Keywords:** Prostate cancer, Zinc, Copper, Risk factors, Grade, Stage, Sudanese.
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## Introduction

It is recognized now that prostate cancer is one of the most serious medical problems facing men with a number of additional factors leading to increased risk of the condition, such as age, race and family history (1), Western industrialized countries face a significant challenge with prostate cancer; as it is the most common type of cancer among men, and with an aging male population, the number of cases being diagnosed

is increasing (2). It is estimated that 1.3 million new male cases of (PCa) occur annually, and it is also the fifth most prevalent male cancer in Saudi Arabia (3). However, its mortality rate and future incidence are predicted to be stronger in the Middle East (4). Among men in Sudan, prostate cancer is the most common cancer and affects all tribes equally. About 85.4% of these men present with stage III and IV at the mean age of 72.2 ± 9.25 years (5). Despite being a sporadic disease in Sudan among men under 50 years of age, prostate cancer rate increases exponentially later in life (6). Age, education level, and a family history of prostate cancer are the most common risk factors. Among the common risk factors associated with prostate cancer in Sudan are age, education level, and a positive family history. Other factors include smoking and alcohol consumption, body mass index (BMI), and occupation (7,8). Several studies have reported that PCa is greatly affected by lifestyle and diet, including the intake of zinc (Zn) and other trace elements (TE) (9). TE serve vital physiological functions, such as maintaining and regulating cell function, regulating gene expression, and modulating metabolic reactions and membrane function (10). Excessive accumulation or an imbalance of the TE may disrupt cellular functions and result in cellular degeneration or death, in fact, one of the main functions of the prostate gland is to produce prostatic fluid with high levels of zinc and other chemical elements (11). The presence of trace elements is known to play a significant role in a wide variety of biological functions through activating or inhibiting enzyme cascades, which can lead to metabolic disorders and cellular growth impairment, including cancer (12). An essential element deficiency is most commonly suggested to cause cancer as it may lead to oxidative stress and failure of antioxidant defense, among them, Copper, Zinc, Selenium, Iron, and Manganese play a critical role in intra- and extracellular antioxidant defense (13). There are several studies showing that Cu is an important component of many enzymes that significantly affect many biological processes, including the growth of cancer cells by creating free radicals (14). Monitoring and periodic measurement of serum zinc levels is important in prostatic cancer patients to prevent zinc deficiency (15). Zinc is essential to keeping the prostate healthy and inhibiting prostate cancer, and its level in serum is easier to calculate than that in the prostate tissue (16). This research was done to evaluate the serum zinc and copper levels among patients with prostatic cancer attending national cancer institute, Wad medani city, Gezira state, Sudan.

**Materials and Methods**

This is a case control hospital based study was done in National Cancer Institute, Gezira State, Sudan from August to December 2020. Total of 60 individual were include by randomized sampling technique, 30 patients with prostate cancer and 30 control healthy subjects. Any known diagnosed patients with prostate cancer who agree to participate in the study was included in this study, whereas any patients with other disease that may disrupt zinc and copper normal distribution as

diabetes and gastrointestinal diseases or patients under treatment that contains zinc and copper was excluded. Data was collected by using a questionnaire which includes all necessary information like (age, grade, stage, duration, serum PSA, wright, length and calculated BMI). Three ml of venous blood were collected into plain tube to measured serum zinc (normal value 0.5-1.2 mg/L) and copper (normal value 0.7-1.4) mg/L) levels by using Atomic absorption spectrophotometer (ASC-7000-Shimadzu) instrument in Mohamed Obaid Mubarak Laboratory, Gezira University. Written consent from each patient had been taken, and overall study was approved by the ethical committee at Gezira University, faculty of Medical Laboratory Sciences and Ministry of Health, Gezira State, Sudan. Data was analyzed using statistical package for social science (SPSS) computer program Version (22) when used t-test presented as (mean and SD) and correlation test (R value). A *P*-value of less than 0.05 was considered statistically significant.

**Results**

A total of 30 patients and 30 normal men were included in this study, the distribution of demographic data showed that 13 (43%) of patients age >70 years and 17 (57%) of patients age <70 years. According to the BMI distribution 8(27%) of patients was overweight and 22 (73%)of patients was normal weight. According to grade 8(27%) of patient were in grade I, 3 (10%) in grade II, 6 (20%) in grade III, 9 (30%) in grade and 4 (13%) in grade V. The copper level in case group was highly significant increase (1.6±0.3) when compared with control group (0.9±0.2) with p. value (p=0.000), while zinc level in case group was highly significant decrease (0.08±0.06) when compared with control group (0.7±0.2) with p. value (p=0.000). There were no significant differences on Zn and cupper levels according to age, BMI and duration with p. value (0.10, 0.70, 0.30),(0.28, 0.06, 0.52)respectively. Regarding gleason stages patients with advanced stage > score 7 (43%) (0.06±0.05) showed more decrease in zinc than patients with non-advanced stage ≤ score 7 (57%) (0.09±0.06) without significant differences (P=0.3) andshowed more increase in copper than patients with non-advanced stage ≤ score 7 (57%) (1.47±0.50) without significant differences (P=0.37).There was weak negative correlation between age, grade, stage and PSA with serum zinc with a coefficient r (-0.3, -0.03, -0.003, -0.2) respectively. While there was weak positive correlation between BMI and duration with serum zinc with a coefficient r (0.07, 0.07) respectively.There was moderate negative correlation between age, and duration with serum copper with a coefficient r (-0.20, -0.14) respectively. There was moderate positive correlation between BMI, Stage, grade, PSA and serum copper with a coefficient r (0.34, 0.28, 0.27, 0.27) respectively.

**Table 1:** Socio-demographic and clinical characteristics of study population

| | Parameters | Frequency | Percent |
|---|---|---|---|
| **Age Group** | < 70 Years | 17 | 56.7 |
| | >70 Years | 13 | 43.3 |
| | Total | 30 | 100 |
| **BMI Category** | Normal weight | 22 | 73.3 |
| | Over weight | 8 | 26.7 |
| | Total | 30 | 100 |
| **Grade** | 1 | 8 | 26.7 |
| | 2 | 3 | 10 |
| | 3 | 6 | 20 |
| | 4 | 9 | 30 |
| | 5 | 4 | 13.3 |
| | Total | 30 | 100 |
| **Stage** | 6 | 8 | 26.7 |
| | 7 | 9 | 30 |
| | 8 | 9 | 30 |
| | 9 | 2 | 6.7 |
| | 10 | 2 | 6.7 |
| | Total | 30 | 100 |
| **Status** | Non advance | 17 | 56.7 |
| | Advance | 13 | 43.3 |
| | Total | 30 | 100 |
| **Serum Cu Level** | Normal | 13 | 43.3 |
| | Abnormal | 17 | 56.7 |
| | Total | 30 | 100 |
| **Serum Zn Level** | Normal | 0 | 0 |
| | Abnormal | 30 | 100 |
| | Total | 30 | 100 |

**Table 2:** Compared serum Cu and Zn between case and control group

| | Cases Control | N | Mean | SD | P. Value |
|---|---|---|---|---|---|
| **Copper** | Cases | 30 | 1.53 | 0.45 | 0.000 |
| | Control | 30 | 0.90 | 0.18 | |
| **Zinc** | Cases | 30 | 0.08 | 0.06 | 0.000 |
| | Control | 30 | 0.72 | 0.22 | |

**Table 3:** Correlation between serum zinc and copper levels with age, PSA level, BMI and gleason stage of prostatic cancer

| | | Age | BMI | Stage | PSA | Cu | Zinc |
|---|---|---|---|---|---|---|---|
| **Age** | Pearson Correlation | 1 | -0.05 | 0.209 | 0.051 | -0.202 | -0.302 |
| | Sig. (2-tailed) | | 0.803 | 0.269 | 0.787 | 0.284 | 0.105 |
| | N | 30 | 30 | 30 | 30 | 30 | 30 |
| **BMI** | Pearson Correlation | -0.047 | 1 | 0.221 | 0.235 | 0.346 | 0.076 |
| | Sig. (2-tailed) | 0.803 | | 0.241 | 0.211 | 0.061 | 0.688 |
| | N | 30 | 30 | 30 | 30 | 30 | 30 |
| **Stage** | Pearson Correlation | 0.209 | 0.221 | 1 | 0.239 | 0.284 | -0.033 |
| | Sig. (2-tailed) | 0.269 | 0.241 | | 0.203 | 0.128 | 0.863 |
| | N | 30 | 30 | 30 | 30 | 30 | 30 |
| **PSA** | Pearson Correlation | 0.051 | 0.235 | 0.239 | 1 | 0.273 | -0.248 |
| | Sig. (2-tailed) | 0.787 | 0.211 | 0.203 | | 0.145 | 0.187 |
| | N | 30 | 30 | 30 | 30 | 30 | 30 |
| **Cu** | Pearson Correlation | -0.202 | 0.346 | 0.284 | 0.273 | 1 | -0.096 |
| | Sig. (2-tailed) | 0.284 | 0.061 | 0.128 | 0.145 | | 0.616 |
| | N | 30 | 30 | 30 | 30 | 30 | 30 |
| **Zinc** | Pearson Correlation | -0.302 | 0.076 | -0.033 | -0.248 | -0.096 | 1 |
| | Sig. (2-tailed) | 0.105 | 0.688 | 0.863 | 0.187 | 0.616 | |
| | N | 30 | 30 | 30 | 30 | 30 | 30 |

## Discussion

Prostate cancer (PCa) is the second prevalent male cancer worldwide, with approximately 1.3 million annual new cases. Additionally, many dietary constituents may play significant roles in initiation and progression of the tumor such as trace element (17). Trace elements play an important role in the structure of proteins, enzymes and complex carbohydrates to participate in biochemical reactions. Copper (Cu) and Zinc(Zn)are essential trace element they involved in many biochemical processes as energy metabolism, iron homeostasis and antioxidant protection. Despite copper being an essential element for humans, high Cu concentrations may lead to cancer via toxic free radicals and producing DNA damage thus increasing serum Cu levels in several malignancies. Moreover, Cu levels could potentially cause progression of prostate cancer by improving blood supply to the tumor, which explains elevated Cu levels in involved tissues (18).While, Zinc level is significantly higher in prostate gland when compared to all tissues in the human body. Different studies indicated that Zn

content increased in benign prostatic hyperplasia when compared to normal prostate tissue and that there was a decrease in prostate cancer, thus zinc levels are an important factor in the malignant prostate cells progression, which agrees with our study showing that serum zinc concentrations were significantly lower in prostate cancer patients than control subjects (19). Our study was case-control study conducted at National cancer Institute, Wad Medani, Gezira State, from October to December 2020, to assess the serum copper level and zinc level in prostatic cancer patients. A total of 30 patients and 30 normal men were included in this study, the distribution of demographic data showed that43% of patient's age >70 years and 57% of patient's age <70 years. According to the BMI distribution 27% of patients were overweight and 73% of patients were normal weight. According to grade 27% of patient were in grade I, 10% in grade II, 20% in grade III , 30% in grade and13% in grade V, and according to serum Cu levels among study subjects high level was 57%and 43% was normal level. In this study comparison means of serum copper level between case and control showed highly significant increase in copper level in case group when compared with control group, this finding agree with other studies (12, 14, 20) ,there were mild increase in copper level in patients <70 than patients >70 without significant differences and there were moderate negative correlation. Comparison means of serum zinc levels between cases and controls showed highly significant decrease in zinc level in case group when compared with control group and this agreed with study done by Li, D. *et al..*, While disagreed with study done with Białkowska, K. *et al..*; which this disagreement may be due to genetic alterations among proteins related to zinc metabolism (16, 21). There was mild decrease in zinc in patients >70 years than those <70 years without significant differences, this agreed with Li, D. *et al.* Regarding to BMI there were mild increased in copper level in overweight group when compared with normal weight group without significant differences. Furthermore there were moderate positive correlation, and there was mild decrease in zinc level in normal weight group without significant differences. This agreed with research authored by Mahmoud, A.M.*et al*. (22).Regarding Gleason stages>7 was accepted as high (advanced) stage was (73%) and ≤7 as low grade tumors (non-advanced) was (27%), there were increase in copper level in high (advanced) stage when compared with low (non-advanced) stage without significant differences and there were moderate positive correlation, and showed more decrease in zinc than patients with non-advanced stage≤ score 7 without significant differences, this agreed with (23) .27% was grade Ⅰ,10% was grade Ⅱ,20% was grade Ⅲ,30% was grade Ⅳand 13% was grade Ⅴ ,there were increase in copper level in advanced when compared with low advanced. Regarding to duration of disease there were increase in serum copper level in less than one year's group when compared with group of more than one year without significant differences and there were moderate negative correlation, and

mild decrease in serum zinc level than patients >1 year without significant differences. This study find moderate positive correlation between serum copper and serum PSA without significant differences, this finding disagree with study done by Saleh who find negative correlation (4).This may be due to sample size, environmental and Nutritional factors. There was weak negative correlation between age, grade, stage and PSA with serum zinc. While there was weak positive correlation between BMI and duration with serum zinc with, this agreed with study done by Mahmoud, A.M.*et al*. (22).

**Conclusion**

In conclusion, our study showed that there is an association between prostate cancer and trace elements. There is a significant Increased of serum copper among patients with prostate cancer and Serum zinc level significantly decreased compared to controls. In this study age, grade, stage and PSA showed negative correlations when correlated with copper and zinc levels, while BMI and duration showed weak positive correlation.

**Limitations**

Sample size lacked due to research time zone, as it was conducted during the pandemic peak and covid 19 spread due to high cost of reagents.

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