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Case Report

Estimation of Serum Copper and Zinc Levels Among Tuberculosis Patients in Khartoum State

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2. Keywords

Copper; Impaired immunity; Trace element; Tuberculosis; Zinc

1. Abstract

1.1. Background: Trace elements play an important role in tuberculosis infection because their deficiencies can be associated with impaired immunity. The aim to assessment the serum copper and zinc levels among the tuberculosis patients in Khartoum state

1.2. Material: This is cross sectional study was conducted in Aboanja hospital in Khartoum state during the period from November 2016_January 2017.Citrated samples were collected from 100 study group, 50 tuberculosis patients, and 50 apparently healthy Individuals, Serum level of Zinc and Copper was measured by atomic absorption spectrometry.

1.3. Result: The result is the mean level of Zinc in tuberculosis patients were significant decreased when compared with control group (P. value= <0.001) and also the mean level of Copper in tuberculosis patients significant increase when compared with group (P. value = <0.001).

1.4. Conclusion: This study showed significant decrease in level of Zinc and increase in level of Copper once compared with control group among tuberculosis patients.

3. Introduction

Tuberculosis (TB) is among the top ten causes of global mortality [1, 2]. It is estimated that approximately one-third of the world's population is infected with tuberculosis bacillus, and each year eight million people develop tuberculosis disease which annually kills 1.8 million worldwide [3, 4]. Approximately 80% of TB cases are found in 23 countries; the highest incidence rates are found in Africa and South-East Asia [3, 4]. In 2014, there were an estimated 9.6 million new TB cases: 5.4 million among men, 3.2 million among women and 1.0 million among children. The TB situation has worsened over the past two decades in Africa owing to the HIV/AIDS epidemic and in Eastern Europe in association with multidrug resistance, following deterioration of the health infrastructure [4, 5]. TB is caused by Mycobacterium tuberculosis, a microorganism whose principal reservoir is humans. M. tuberculosis is spread by patients with pulmonary tuberculosis, especially those with positive sputum smears [6, 7]. Of those becoming infected, 10-12% will develop tuberculosis disease after a period ranging from weeks to decades [8-10]. The risk of disease declines steeply with time after infection. Disease may also occur after re-infection [9, 11]. In Sudan, an estimated annual risk of TB is 1.8%, which gives an incidence of 90/100,000 smear positive cases, and puts Sudan among the high prevalence countries for TB in the Eastern Mediterranean region [23]. Also, the Khartoum state (population of 5 752.425 in the year 2005) has the annual risk of 1.8 % of TB. In 2005, the programmed was able to detect 2981 new smear positive cases (82% from the target) and achieve the cure rate of 43% from the detected cases [23]. The case fatality rate was 3.2%, which relatively increased compared with previous two years (2003: 2.6%; 2004: 2.3%).

[24] Copper (Cu) is a trace element essential for the development of almost all aspects of mammalian physiology, thus defects in Cu homeostasis almost certainly impact immune responses to microbial infections. Dietary Cu-deficiency in farm animals is linked to a higher incidence of bacterial infections [34]. To counteract the host-supplied Cu, increasing evidence suggests that Mycobacterium tuberculosis have evolved Cu resistance mechanisms to facilitate their pathogenesis. [33] Cu is antimicrobial, it is also essential. Cu can undergo reversible oxidation states between reduced Cu+ and oxidized Cu2+ and has a high redox potential, making it a critical cofactor of enzymes used for electron transfer reactions in the presence of oxygen. In Mycobacterium tuberculosis, the most prominent Cu binding enzymes include cytochrome c oxidase and the Cu/Cu superoxide dismutase11, which contributes to resistance to oxidative stress. [31] Thus, like for most life forms, Cu is essential for Mycobacterium tuberculosis viability. [31] Of course,

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too much Cu is toxic to Mycobacterium tuberculosis. [7, 13,14] Zinc is a potent mediator of host resistance to infection because it can influence the innate and adaptive immune response in many ways [34, 35]. It can increase the release of INF-y and other cytokines by PBMC although at high concentrations [36], and induce the proliferation of CD8+ T-cells in combination with an exposure to IL-2. In such studies, the addition of zinc can also affect the proliferation of different cell types in response to various mitogenic stimuli although an excessive supplementation by zinc could also have a deleterious effect on immune functions [34, 35]. Copper and zinc are important elements for the human body, copper and zinc are imbalanced in TB patients. This fact (imbalanced of copper and zinc) could be recommended as method for follow up of treatment in TB, the regular estimation of copper and zinc lowering the complications of disease. Low zinc causes hair loss, diarrhea, delayed sexual-maturation, impotence, hypogonadism in males, and eye and skin-lesions. Weight loss and impaired appetite, delayed healing of wounds, taste abnormalities, and altered cognition can also occur. [34] And copper increasing cause hematemesis, hypotension, melena, coma, jaundice and gastrointestinal distress [33].

4. Materials and Method

Study designed as cross-sectional study, conducted in Khartoum state.

The sample was being collected from adult Sudanese between age (12-65) years old. Sample size One hundred participants divided into two category 50 participants in the case group and 50 participants in the control group. Blood sample collection

Local antiseptic used for cleaned the skin (70% ethanol) 5ml of venous blood was collected in plain and heparin containers from each individual including in the study. The serum was collected by centrifuged the blood (2000 R / min for 5 min) at centrifuge and be store at 20-degree centigrade deep freeze until the collection of the samples. All reagents and the samples brought to 37c, the reagents stability at 37c for 6 hours. Biochemical measurements of serum Zinc and Copper was measured by atomic absorption method. Serum zinc was estimated by dilution of sample with deionized water. The analysis was performed against standers prepared in glycerol to approximate the viscosity characteristics of the diluted samples. Zinc standers are prepared by diluting the stock standard solution, for zinc A5% (v/v) glycerol solution should be used as blank solution when determined zinc. Serum copper was estimated by dilution of sample with deionized water. the analysis was performed against standers prepared in glycerol to approximate the viscosity characteristics of the diluted samples. Copper standers are prepared by diluting the stock standard solutions, for zinc A5% (v/v) glycerol solution should be used as blank solution when determined copper. The precision and accuracy of all method used in this was checked each time a batch was analyzed including commercially prepared control sera.

4.1. Inclusion Criteria

This study was being conducted in patients aged from 12-65 whom had chest pain, coughing up blood and productive prolonged cough for more than 3 weeks.

4.2. Exclusion Criteria

Pregnancy, Women on oral contraceptives, Chronic liver disease, Chronic renal failure, Myocardial infarction, Metastatic carcinoma, Nephritic syndrome, and Malabsorption Syndrome.

4.3. Ethical Considers

Permission of this was obtained from the authorities. The individual induced on this study was notify well about the objectives and the need of this study and must accept to donate the blood sample before the start of collection process.

4.4. Data Analysis

T-Test statistical analysis by one-way ANOVA Test. Statistical Package for Social Science (SPSS version 17). Significant at a level of $P \leq 0.05$

5. Results

100 participants consented to be enrolled for the study within the study period from March 2017 to June 2017. Of them 50 as patients and 50 were controls.

Most of the study participants were within 20-40 years shows it in (Table 1). There was significant difference in zinc and copper compared between case and control group ($p > 0.05$), as seen in (Table2 and 3) show that the Cu/Zn ratio significantly increased in the case group compare by control group.

Figure (1): That show weak negative correlation between copper and ZN and duration (month) in case group (R -0.09 P value 0.564), Figure (2): That found negative correlation between the copper and duration in case group (R -0.265p. value 0,099). Figure (3): Show weak negative Correlation between copper and zinc in case group (R --0.002 P value0.990).

Table 1: The Percentage Distribution according age among Study Group

		Frequency	Percent
Age groups	20-40	26	65.0%
	41-60	12	30.0%
	More than 60	2	5.0%
	Total	40	100.0%

Table 2: The Comparison Between the Means of Zn and Cu in Case and Control Group. (n =50)

Tests	Case	Control	P value
Zn	.164±.05 (.06-.300)	.526±.12 (.216-.684)	<0.001
Cu	.808±.21 (.466-1.346)	.170±.06 (.062-.3)	<0.001

Table 3: Cu/Zn Ratio in Case and Control Group.

Ratio Statistics for Cu / Zn					
Study group	Mean	Std. Deviation	Price Related Differential	Coefficient of Dispersion	Coefficient of Variation
					Median Centered
Case	5.6	2.6	1.1	0.413	54.40%
`control	0.351	0.168	1.082	0.42	55.60%

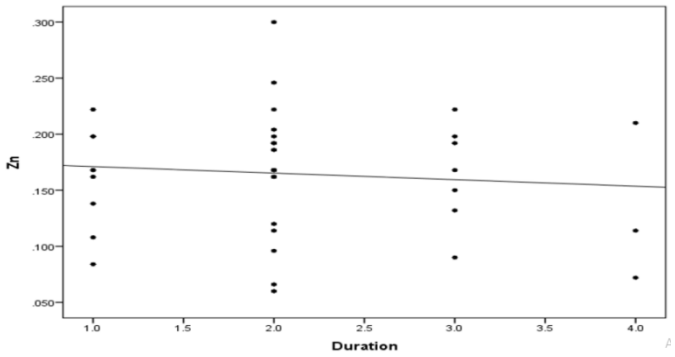

Figure 1: Correlation Between Duration per Months and Serum Zn in Case Group
R-0.094 - P value 0.564

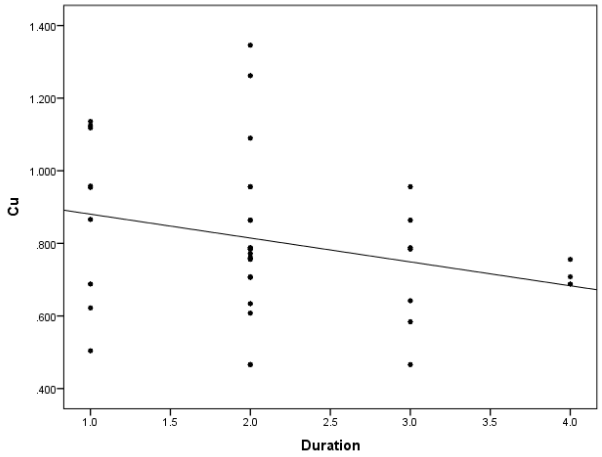

Figure 2: Correlation Between Duration per Months and Serum Cu in Case Group.
R -0.265 - P value 0.099

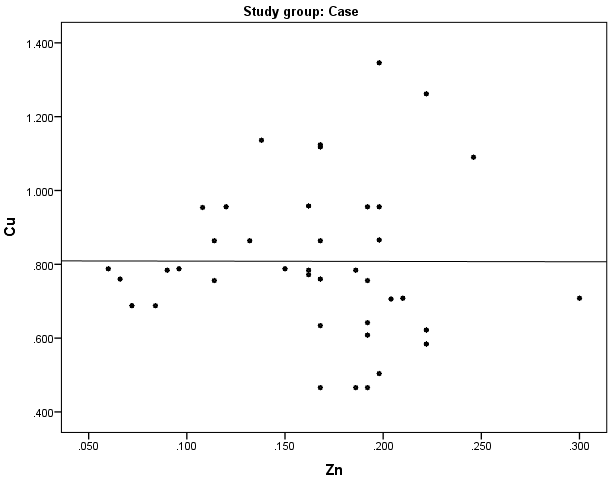

Figure 3: Correlation between Serum Zn and Cu in Case Group
R -0.002
P value 0.990

6. Discussion

Tuberculosis is wide spread disease in Sudan it affects a considerable number of the population. The trace elements Copper and zinc are important elements for the human body, copper and zinc are imbalanced in TB patients. This fact (imbalanced of copper and zinc) could be recommended as method for follow up of treatment in TB, the regular estimation of copper and zinc lowering the complications of disease.

In this study data analysis serum levels of copper and zinc among tuberculosis patients in present study, the patients have higher copper more than control, while Zn decreased inpatients; the results of this study confirmed the findings of the study conducted in India. [36, 37] Researchers mainly believe that decreasing the levels of serum Zn in patients is because of the redistribution of Zinc in their liver. Increasing in serum Cu level and mentioned that the reason of increase serum Cu is associated with an increase in the synthesis of the Copper binding protein, ceruloplasmin [38] the level of serum Copper also increases in other infectious disease such as Pneumonia, Cancer [39] and Leishmaniasis [40] in a survey conducted in Korea, patients with pulmonary TB had significantly higher serum copper and cobalt than healthy controls, while zinc were significantly lower. [41] According to the results of the present study, the serum levels of zinc were significantly lower in TB patients compared to healthy controls. Similar study was carried out by Taneja et al. They reported that the mean serum zinc concentration in pulmonary TB patients was significantly lower in contrast to the control group. [42] Ciftci et al. conducted a study on the serum concentrations of zinc in TB infected patients in Turkey. Similarly, they observed a low zinc concentration in serum of patients. [43] Low serum zinc in TB patients could be due to the redistribution of zinc from plasma to other tissues, reduction of hepatic production of zinc-carrier protein α−2 macro globulin (α−2 M), and increasing the production of metallothionin, a protein that transports zinc to the liver [44, 45].

There is a logical explanation for the association of high copper concentration in TB patient. Decrease in zinc levels, which occurs in TB patient, prevents entrance of the copper to the tissues, and this leads to elevation of serum level of copper [48].

On the other hand, increase in serum level of some metals such as copper or cadmium results in lower absorption of serum iron that is in compliance with our study [46, 47].

Elevated serum Cu/Zn ratio has been reported in patients with tuberculosis. The serum copper/zinc declined in patients' blood after anti-tuberculosis treatment. [48] Similarly, we indicated that the ratio of copper/zinc was higher in serum of TB patients compared to that in healthy individuals.

7. Conclusions

This study concluded that the serum level of zinc is lowering in tu-

berculosis patients, and the serum copper is increasing in patients when compare with control. The disease causes imbalance levels of copper and zinc, the regular measurement of copper and zinc lowering the complications of tuberculosis disease.

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