

Estimation of some Trace Elements in the Sera of People with Myocardial Infarction Disease

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Abstract: Myocardial infarction is a heart problem with high risk of mortality worldwide. The epidemiological studies have shown an increase growth in the rates of cardiovascular problems globally, making this area of pathological investigations a trend to get better understanding and more clear information that help in controlling their diseases. Trace elements are dietary nutrients with very important roles in maintaining good quality of human health. Among the necessary trace elements, copper, zinc, and selenium are among the most crucial because of their roles in so many different processes throughout the body. Our goal was to determine the relationship between Cu, Zn, and Se in myocardial infarction patients, and to find their role in the disease. We have included 60 patients with myocardial disease and 30 healthy people in the study. The results have shown that Cu levels were significantly higher in myocardial infarction patients, and this would lead to raise the oxidative stress through the mediation of copper in Fenton reaction. Patients with myocardial infarction have considerably reduced levels of Zn and Se in their serum, which lowers their biological system's antioxidant ability. We suggest the use of antioxidants in diet and drugs to maintain the low risks of cardiovascular problems.

Keywords: cardiovascular disorders, zinc, selenium, copper.

1. Introduction

Both mortality and morbidity from myocardial infarction are among the highest worldwide [1]. More over 3 million people experience an acute ST-elevation myocardial infarction (STEMI) each year, and another 4 million experience a myocardial infarction that does not meet the criteria for ST-elevation (NSTEMI). Myocardial infarction was formerly exclusively seen in developed nations, but is becoming prevalent there as well. A large data base supports current practises for

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treating acute myocardial infarction [3-5], and registries have indicated a decline in mortality [2].

Approximately a third of deaths in developed countries occur due to coronary artery disease [8], with over 2.4 million deaths in the United States alone attributable to acute myocardial infarction [6]. Acute myocardial infarction can be either ST-elevation or non-ST-elevation [9]. Acute coronary syndrome includes unstable angina since it can lead to a heart attack (ACS). Because of their same pathophysiology, NSTEMI and unstable angina are both classified as non-ST-segment elevation acute coronary syndromes (NSTE-ACS). They have been categorised similarly for the sake of managerial decisions. Most cases of myocardial infarction may be traced back to either the rupture of a vulnerable atherosclerotic plaque or the breakdown of the endothelium lining the coronary arteries (type 1) [9,10].

Trace elements are a type of mineral found in food that are required in minute quantities for proper body functioning. Preventing nutritional deficiencies, immunological activities, regulating gene expression, providing antioxidant defence, and warding off chronic illness are all possible thanks to these structural components of enzymes or cofactors [11]. Human health is dependent on the ability to obtain trace elements from the environment, including meals, which cannot be produced in the human body. Essential trace elements are thus referred to as "micronutrients" [12]. Copper (Cu) is an essential element required at physiological levels in humans to maintain some of the most vital operations such as healthy bones, immunity [13], and it found bound to certain proteins and considered key part of the structural integrity and function of these proteins [14-16]. Because it's essential for the growth and development of bacteria, plants, and animals, zinc (Zn) is an essential metal for human health. Prostate and some areas of the eye have the highest zinc concentrations, but all tissues and secretions have some zinc. Muscle and bones contain 85% of the body's total zinc, while the skin and liver contain 11% and the rest of the body has the remaining 2%. Zn is considered to exhibits an antioxidant properties [18], as it is a cofactor of the first line antioxidant enzyme, superoxide dismutase (Cu/Zn-SOD) [19]. Selenium (Se) is another important metal for maintaining the good quality of health in humans [20]. Selenium is considered as an antioxidant [21], and it found as cofactor for the first line antioxidant enzyme family glutathione peroxidases (Se-GPx) [21, 22]. Nevertheless, the deficiency and overload of Se can cause serious health risks [23]. Our goal was to determine the relationship between Cu, Zn, and Se in myocardial infarction patients, and to find their role in the disease.

2. Materials and Methods

2.1. Patients

Consulting records from Al-Noman Teaching Hospital were used to compile patient information (Baghdad, Iraq). Participants in the study were briefed on the research's normative standards before giving their consent to participate. Between November 2021 and March 2022, sixty participants who had had a myocardial infarction were chosen to participate in the study, and they were compared to thirty healthy volunteers.

2.2. Methods

After 8 hours of fasting, both the participants with myocardial infarction and the healthy controls received a vein blood donation. Next, a medical centrifuge was used to separate the plasma from the blood (4000 rpm for 10 minutes), as well as the plasma was frozen at -20 °C until it could be evaluated by atomic absorption spectrophotometry for Cu, Zn, and Se (NovAA300, Germany).

2.3. Statistics

Statistical analysis was performed using IBM SPSS version 26.0; the Pearson correlation coefficient was employed to evaluate the degree of relationship between Cu, Zn, and Se; and the independent sample t-test was utilised to evaluate differences in mean values. Finally, we calculated the area under a curve (AUC) for each metric to evaluate protein carbonyl's diagnostic accuracy in detecting myocardial infarction.

3. Results

Table 1 lists some of the ways in which the volunteers helped out. Myocardial infarction patients (average age: 43.43±9.04) were older than the control group (average age: 42.5±38.77), although the difference was not statistically significant ($P>0.05$). Body mass index (BMI) was not substantially ($P>0.05$) different between those who had suffered a myocardial infarction and those who had not (24.86±2.23 kg/m² vs. 24.78±2.22 kg/m²).

Table 1: Volunteered traits of individuals.

Parameter	Myocardial infarction patients	Control people	P-value
N	60	30	-
Age (year)	42.53±8.77	43.43±9.04	0.651
BMI (kg.m ⁻²)	24.78±2.29	24.86±2.23	0.866
Cu (µg/dL)	118.50±12.04	154.57±11.18	0.0001
Zn (µg/dL)	102.60±11.88	79.32±10.92	0.0001
Se (µg/dL)	103.47±10.76	76.12±6.72	0.0001

The level of Cu was observed to be significantly ($P<0.05$) higher in the serum of myocardial infarction patients (154.57±11.18 µg/dL) compared to the serum of control people (118.50±12.04 µg/dL). On the contrary, the level of Zn was observed to be significantly ($P<0.05$) lower in the serum of myocardial infarction patients (79.32±10.92 µg/dL) compared to the serum of control people (102.60±11.88 µg/dL). Furthermore, the level of Se was observed to be significantly ($P<0.05$) lower in the

serum of myocardial infarction patients ($76.12 \pm 6.72 \mu\text{g/dL}$) compared to the serum of control people ($103.47 \pm 10.76 \mu\text{g/dL}$).

Trace elements were measured in the blood of those who had suffered a myocardial infarction, and as indicated in Table 2, there was no statistically significant correlation between any of the components.

Table 2: Correlation in myocardial infarction patients.

Parameter	Cu		Zn		Se	
	r	p-value	r	p-value	r	p-value
Cu ($\mu\text{g/dL}$)	-	-	-0.039	0.767	-0.042	0.752
Zn ($\mu\text{g/dL}$)	-0.039	0.767	-	-	0.149	0.255
Se ($\mu\text{g/dL}$)	-0.042	0.752	0.149	0.255	-	-
Age (year)	-0.179	0.171	0.072	0.586	0.019	0.886
BMI (kg.m^{-2})	0.172	0.190	0.063	0.634	-0.046	0.728

The area under the ROC curve for Cu demonstrates the potential of this biomarker for use in identifying myocardial infarction. As can be shown in Figure 1, Cu has a high sensitivity for identifying individuals with myocardial infarction compared to healthy controls (AUC = 0.986, $P < 0.0001$).

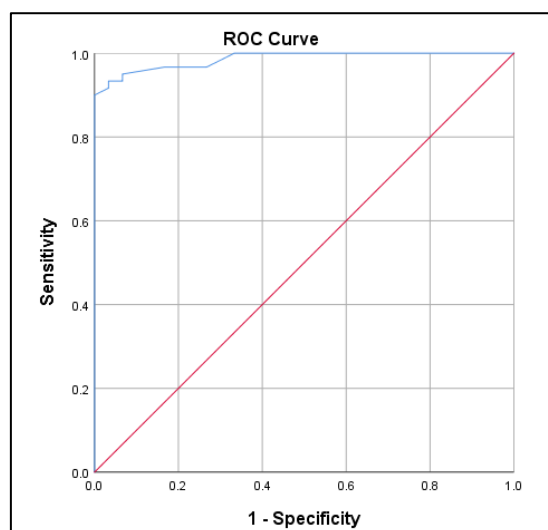


Figure 1: Cu's area under the receiver operating characteristic curve for identifying MI cases.

Zn's ROC curve demonstrates the biomarker's potential for application in detecting myocardial infarction. Zn has demonstrated remarkable sensitivity (AUC = 0.928,

$P < 0.0001$) in the differentiation of patients with myocardial infarction from healthy controls (Figure 2).

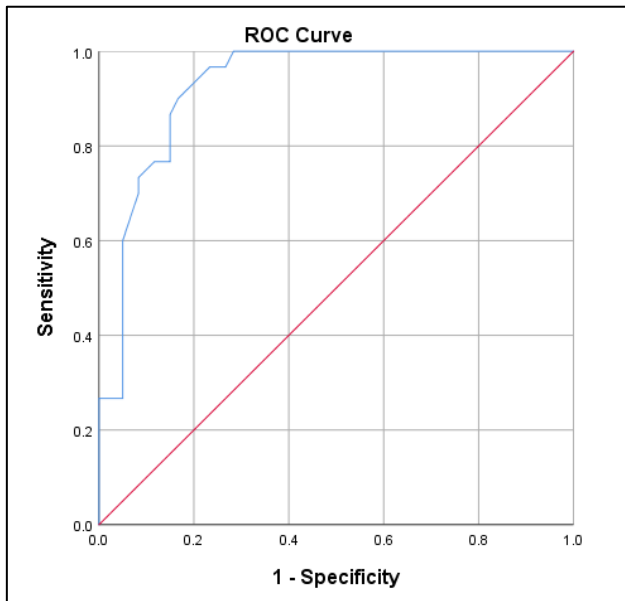


Figure 2: Zn's area under the receiver operating characteristic curve for identifying MI cases.

Myocardial infarction can be better diagnosed by Se, as seen by its high area under the receiver operating characteristic curve. As can be shown in Figure 3, her sensitivity in distinguishing between patients with myocardial infarction and healthy controls is quite high (AUC = 0.997, $P < 0.0001$).

4. Discussion

Copper, zinc and selenium trace elements were determined in myocardial infarction patients to predict their role in the pathophysiology of the disease. Cu was significantly increase in the serum of myocardial infarction, while Zn and Se were significantly reduced. Miura *et al.* have reported that people with acute myocardial infarction have shown significant high levels of Cu but low levels of Zn, Se and Fe in their circulation. Accordingly, the authors were indicated a disturbance in the homeostasis of trace elements in the disease [24]. Altekin *et al.* have reported significant high levels of Fe and Cu, but significant low levels of Se and Zn in patients with acute coronary syndrome. Researchers have found a link between trace element levels and the extent of cardiac damage, suggesting that these elements may play a role in the development of ischemic heart disease [25]. Saleh *et al.* have reported a significant elevated Cu levels, but non-significant change in the levels of Zn in patients with myocardial disorders. Nevertheless, the authors have suggest a link between myocardial disorders and trace elements [26]. Additionally, Quader *et al.* have reported that serum zinc levels were highly significantly reduced in the serum

of acute myocardial infarction patients, indicating an important role of Zn in the disorders of the heart [27].

Copper is linked to oxidative stress, through Fenton reaction. Cu can induce the conversion of the less toxic hydrogen peroxide to the highly toxic hydroxyl radical [28]. Therefore, the increase of copper level in myocardial infarction patients can cause very serious destructive effects that results essentially in increasing the health risks. Furthermore, both Zn and Se were reported to have antioxidant properties [29-31]. The reduction of these two important trace elements would leads to a decrease in the antioxidant capacity, and therefore, a reduced fighting system against oxidative stress.

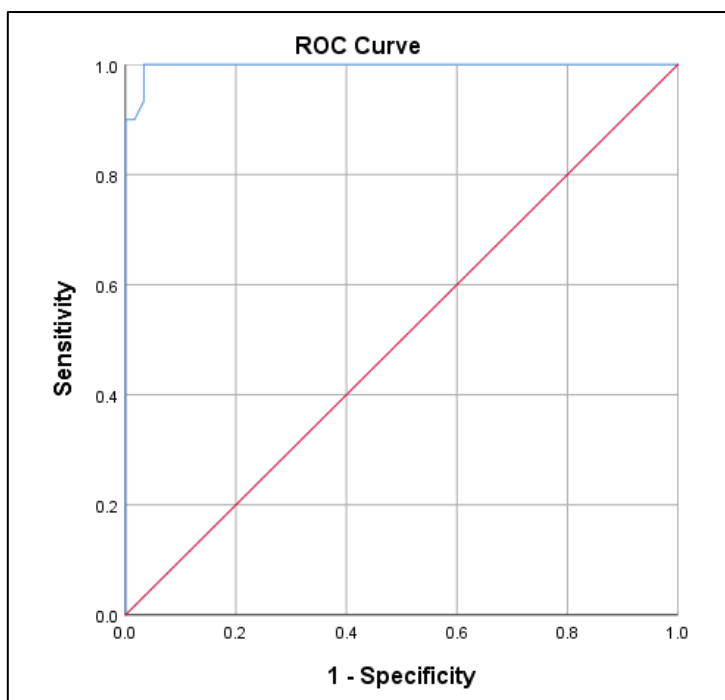


Figure 3: Se's area under the receiver operating characteristic curve for detecting myocardial infarction.

5. Conclusions

Myocardial infarction is a heart problem with high risk of mortality worldwide. The investigation of trace elements in this cardiovascular disease would help in the better understanding of pathophysiology of the disease and its association with dietary intake of micronutrients. The results have shown that Cu levels were significantly higher in myocardial infarction patients, and this would lead to raise the oxidative stress through the mediation of copper in Fenton reaction. Patients with myocardial infarction have considerably reduced levels of Zn and Se in their serum, which lowers their biological system's antioxidant ability. We suggest the use of antioxidants in diet and drugs to maintain the low risks of cardiovascular problems.

6. Highlights

This study investigated the relationship between trace elements copper, zinc, and selenium in myocardial infarction patients. The results showed that Cu levels were significantly higher in patients with myocardial infarction, which can lead to increased oxidative stress. Patients also had lower levels of Zn and Se, which reduces their antioxidant ability.

References

1. White, H.D. and D.P. Chew, Acute myocardial infarction. *The Lancet*, 2008. 372(9638): p. 570-584.
2. Bassand, J.-P., et al., Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology. *European heart journal*, 2007. 28(13): 598-1660.
3. Tan, Armand Delo Antone, Chito Caimoy Permejo, and Ma Consolacion Dolor Torres. "Modified Early Warning Score vs Cardiac Arrest Risk Triage Score for Prediction of Cardiopulmonary Arrest: A Case–Control Study." *Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine* 26, no. 7 (2022): 780.
4. Furman, M.I., et al., Twenty-two year (1975 to 1997) trends in the incidence, in-hospital and long-term case fatality rates from initial Q-wave and non-Q-wave myocardial infarction: a multi-hospital, community-wide perspective. *Journal of the American College of Cardiology*, 2001. 37(6): p. 1571-1580.
5. Mandelzweig, L., et al., The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. *European heart journal*, 2006. 27(19): p. 2285-2293.
6. Thyagarajan, Braghadheeswar, Casey Bryant, and Ashish K. Khanna. "An Incidental Finding of Coronary-cameral Fistulas in a Critically Ill Patient with a Metastatic Cardiac Tumor." *Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine* 25, no. 3 (2021): 340.
7. Nichols, M., et al., Cardiovascular disease in Europe 2014: epidemiological update. *European heart journal*, 2014. 35(42): p. 2950-2959.
8. Yeh, R.W., et al., Population trends in the incidence and outcomes of acute myocardial infarction. *New England Journal of Medicine*, 2010. 362: 2155-2165.
9. Thygesen, K., et al., ESC/ACCF/AHA/WHF Expert Consensus Document. *Circulation*, 2012. 126(16): p. 2020-2035.
10. Libby, P., Mechanisms of acute coronary syndromes and their implications for therapy. *N Engl J Med*, 2013. 368: p. 2004-2013.
11. Strachan, S., Trace elements. *Current Anaesthesia & Critical Care*, 2010. 21(1): p. 44-48.
12. Skalnaya, M.G. and A.V. Skalny, Essential trace elements in human health: a physician's view. House of Tomsk State University, Tomsk, 2018. 224.
13. Abbas, Z. S., Ismail, A. H., Al-Bairmani, H. K., Rheima, A. M., Sultan, A. R., & Mohammed, S. H. (2021). Inhibition Effect of Copper (II) Theophylline

- Nanocomplex on Phosphodiesterase (PDE) Enzyme Activity in Human Serum of Iraqi Patients with Asthma Disease. *Nano Biomed. Eng.*, 13(4), 364-371.
14. Klinman, J.P., Mechanisms whereby mononuclear copper proteins functionalize organic substrates. *Chemical reviews*, 1996. 96(7): p. 2541-2562.
 15. Palm-Espling, M.E., M.S. Niemiec, and P. Wittung-Stafshede, Role of metal in folding and stability of copper proteins in vitro. *Biochimica et Biophysica Acta (BBA)-Molecular Cell Research*, 2012. 1823(9): p. 1594-1603.
 16. Speisky, H., et al., Copper-binding proteins in human erythrocytes: Searching for potential biomarkers of copper over-exposure. *BioMetals*, 2003. 16(1): 113-123.
 17. Chasapis, C.T., et al., Zinc and human health: an update. *Archives of Toxicology*, 2012. 86(4): p. 521-534.
 18. Prasad, A.S., Zinc: an antioxidant and anti-inflammatory agent: role of zinc in degenerative disorders of aging. *Journal of Trace Elements in Medicine and Biology*, 2014. 28(4): p. 364-371.
 19. Lewandowski, Ł., M. Kepinska, and H. Milnerowicz, The copper-zinc superoxide dismutase activity in selected diseases. *European journal of clinical investigation*, 2019. 49(1): p. e13036.
 20. Brigelius-Flohé, R., Selenium in Human Health and Disease: An Overview, in *Selenium*, B. Michalke, Editor. 2018, Springer Publishing: Cham. p. 3-26.
 21. Zoidis, E., et al., Selenium-dependent antioxidant enzymes: Actions and properties of selenoproteins. *Antioxidants*, 2018. 7(5): p. 66.
 22. Taay, Y.M. and M.T. Mohammed, Evaluation of serum reactive oxygen species and glutathione peroxidase in iraqi obese/obese-hypertension females. *Plant Archives*, 2020. 20(2): p. 1165-1168.
 23. Vinceti, M., T. Filippini, and L.A. Wise, Environmental Selenium and Human Health: an Update. *Current Environmental Health Reports*, 2018. 5(4): 464-485.
 24. Miura, Y., et al., Simultaneous determinations of trace elements in sera of patients with acute myocardial infarction by PIXE. *International Journal of PIXE*, 1993. 3(04): p. 295-300.
 25. Altekin, E., et al., The relationship between trace elements and cardiac markers in acute coronary syndromes. *Journal of Trace Elements in Medicine and Biology*, 2005. 18(3): p. 235-242.
 26. Waleed, K.H., Y.M. Ali, and O.S. Basil, Status of Some Trace Elements in Idiopathic and Ischemic Cardiomyopathy and Coronary Artery Disease: Echocardiographic Correlation. *Journal of the Faculty of Medicine*, مجلة كلية الطب, 52. 2010(3): p. 331-335.
 27. Quader, M.R., S. Rahman, and S.K. Saha, A Study of Serum Zinc level in Patients with Acute Myocardial Infarction. *Faridpur Medical College Journal*, 2020. 15(2): p. 92-94.
 28. Sun, Y., et al., Revealing the active species of Cu-based catalysts for heterogeneous Fenton reaction. *Applied Catalysis B: Environmental*, 2019. 258: p. 117985.
 29. Heyland, D.K., et al., Antioxidant nutrients: a systematic review of trace elements and vitamins in the critically ill patient. *Intensive care medicine*, 2005. 31(3): p. 327-337.
 30. Tapiero, H., D. Townsend, and K. Tew, The antioxidant role of selenium and seleno-compounds. *Biomedicine & pharmacotherapy*, 2003. 57(3-4): p. 134-144.
 31. Powell, S.R., The antioxidant properties of zinc. *The Journal of nutrition*, 2000. 130(5): p. 1447S-1454S