Egyptian Journal of Chemistry
http://ejchem.journals.ekb.eg/

Evaluation of Some Trace Elements and Serum Electrolytes in Patients with Acute Myocardial Infarction

Muntadher Hussein Challoob[1] and Mustafa Taha Mohammed[1,2]
[1]*University of Mustansiriyah, College of Science, Chemistry Department*
[2] *Chemistry Department, College of Science, Mustansiriyah University. Iraq*

Abstract

Myocardial infarction (MI) is one of the most common causes of morbidity and mortality worldwide. MI is associated with an intelligible imbalance in some trace elements such as zinc (Zn), copper (Cu), manganese (Mn), iron (Fe), and selenium (Se), which are significant for immune and cardiovascular function. This study aimed to evaluate the clinical significance and correlation of serum trace elements and electrolytes in Iraqi patients as adjunctive parameters for a better prognosis of AMI. This study conducted 120 subjects who were divided evenly into patients and control groups for the period between September and December 2021. Serum trace elements were measured using atomic absorption spectroscopy while the Jokoh analyzer was used for serum electrolytes. There was no significant difference in BMI or age between patient and control groups (p>0.05) and these findings provide an excellent opportunity to conduct a case study comparing patients with acute myocardial infarction to healthy controls. The serum Zn, Se, Fe, and Na^+ of AMI patients were significantly lower when compared with that of the control group ($p < 0.001$) and significantly higher for Cu while, non-significant for Mn, K^+, and Cl^- (p>0.05).

Keywords: Myocardial Infarction; Reactive Oxygen Species; Ischemia; Necrosis.

Introduction

Myocardial infarction (MI) also known as heart attack is the irreversible death (ischemic apoptosis and necrosis) of cardiac cell muscles due to a lack of necessary oxygen supply to myocardial cell tissues, and is considered the most common type of cardiovascular disease due to occlusion of a coronary artery [1]. A heart attack occurs when blood flow decreases or stops in the coronary artery of the heart (tissue damage or infection of the myocardium caused by ischemia) [2]. The most widely recognized reason for myocardial dead tissue is the break of an atherosclerotic plaque on an artery that supplying heart muscle [3]. In 2015, there were 15.9 million myocardial infarctions worldwide, and it remains a major cause of morbidity and mortality [4]. In Iraq, statistical research on the number of myocardial infarction injuries and deaths is presently conducted, in the USA and UK, about 651,000 and 180000 patients get an MI every year, respectively [5]. The current MI prevalence rate is 1,653 per 100,010 people, with research predicting that this number will rise to 1,845 by 2030 [6]. MI is associated with intelligible imbalance in some trace elements such as zinc (Zn), cupper (Cu), manganese (Mn), iron (Fe), and selenium (Se), which are significant for the immune and cardiovascular function. These trace elements have an important role in regulatory, catalytic, and enzymes structure, transcription factors, and proteins [7]. Trace element imbalances have a variety of harmful outcomes to some extent, that excessive levels of trace elements can be toxic for the body health, on the other hand deficiency of trace elements can lead to many health problems such as anemia, delayed wound healing, anorexia [8]. The deficiency in some trace elements is associated with the activity of antioxidant enzymes that protect against reactive oxygen (ROS) and nitrogen species (RNS), which is believed to possibly underlie the

*Corresponding author e-mail: dr.mustafa@uomustansiriyah.edu.iq.; (Mustafa Taha Mohammed).
Receive Date: 27 May 2022, Revise Date: 13 August 2022, Accept Date: 29 August 2022.
DOI: 10.21608/EJCHEM.2022.141245.6172

onset of cancer, AMI, atherosclerosis, accelerated aging, developmental retardation in children, and immunological abnormalities [9]. After myocardial injury many cardiac biomarkers become detectable into venous circulation such as cardiac enzymes Troponin-I (TnI), Lactate Dehydrogenase (LDH), Creatine Kinase-MB (CK-MB), Aspartate Aminotransferase (AST), and many other inflammatory markers [10]. Electrolytes are important minerals that have an electric charge which are present in the blood, urine, and other body fluids [11]. Electrolyte equilibrium is important for maintaining cardiac cell function and ATP is essential particularly through the Na/K ATPase. Any intracellular changes, necrosis and apoptosis of affected cells that can cause electrolyte imbalance [12].

The main aim of the study is to explore the clinical significance of serum trace elements Zn, Cu, Mn, Fe, and Se levels as potential biomarkers, also plan to evaluate serum Na^+, K^+, and Cl^- in Iraqi patients with AMI to compare with normal healthy control subjects.

Subject and methods

The current study involved 120 subjects divided into two groups; group-C included 60 as healthy control and group-A 60 patients already diagnosed with MI based on the diagnosis of the mentioned hospitals through ECG, cardiac enzymes, patient history and symptoms. The study included only men aged between 43 and 66 years and the healthy subjects were collected from Mustansiriyah University, as well as AMI patients were collected from Baghdad teaching hospital-medical city, Baghdad, Iraq and Karbala cardiac center-Alhusaini hospital, Karbala, Iraq between September and December 2021. Only males under the age of 70 were included in this study, and those with any associated disease, particularly renal failure, as well as smokers, Non-ST-Segment Elevation Myocardial Infarction, and according to the BMI value, the patient with normal weight or overweight but not obese were excluded. The biochemical determination of parameters under investigation were carried out at the Biochemistry Research Laboratory of Mustansiriyah University, department of chemistry science.

Using disposable syringes, 5 ml of blood was drawn slowly through a vein puncture and then the blood translocated into gel tube carefully and slowly then left for 15 min at room temperature to clot. The gel tubes' samples were centrifuged for 10 minutes at 3000 rpm and four Eppendorf tubes used to store the obtained serum at -30 ºC until the time of analysis. Some information were taken from patients and control, which include height, weight and age.

Flam Atomic Absorption Spectrophotometer (FAAS) model AA646, Shimadzu Corporation, Kyoto, Japan used to determined Zn and Cu at wavelength 213.9 nm, 324.7 nm respectively and acetylene was the gas flow. Frozen serum were allowed to thaw then 0.5 ml diluted 10-fold with deionized water. The concentrations (0, 50, 100, 150, and 200) μg/dl of zinc, and copper were prepared from the dilution of the stock solution with deionized distilled water.

Graphite Furnace Atomic Absorption Spectrophotometry (GFAAS) model 210VGP, Buck Scientific, USA used for manganese and selenium 1000 ppm stock standard solution of Mn and Se diluted to (0.0, 0.5, 1, 1.5, 2, 2.5, 3) μg/dl and 20 μL injected into the graphite tube of the GFAAS at wavelengths 279.5 nm, 189.0 nm respectively and nitrogen was the gas flow. A standard curve used to find each element concentration in a sample.

Iron was determined by colorimetric method (Ferrozine) [13]. The complex's absorbance was measured at 560 nm by a (Spectrophotometry Model 210VGP, USA, and Buck Scientific). Jokoh electrolyte analyzer (EX-D/EX-DS, Tokyo, Japan) used for serum electrolytes. Statistical analysis was done using SPSS software version (17.1). Values were expressed as mean ± standard deviation (SD). The comparison of (mean ± SD) was performed using the Student’s t‑test where statistical significance was defined as $P \leq (0.001)$.

Results

The obtained results showed that the mean age of AMI patients and control were 55.45 and 53.91 with a non-significant p-value (p>0.05). BMI mean value were also non-significant p-value (p>0.05) between the patients and control, as shown in Table (1). These non-significant obtained results for age and BMI provide a unique opportunity to conduct a comparative study accurately.

The results indicated that the concentrations (mean±SD) of Zn, Cu, Mn, Fe and Se within the normal range as follows (57-144 μg/dl Zn; 95-175 μg/dl Cu; 0.06-0.22 μg/dl Mn; 24-105 μg/dl Fe and

90-120 μg/L Se. The serum concentrations of Zn, Fe and Se were significantly decreased ($p<0.001$) in patients group as compared with control group, while the concentration of Cu was significantly elevated in sera of the patients group ($p<0.001$), also non-significant changes for Mn concentration were observed between the two groups (Table 1).

Zn had a significantly positive correlation with Cl- (r = 0.265*, p= 0.041), while highly negative correlated between Mn and Cu (r = -0.375**, p < 0.01) and also negative to Se (r = 0.641*, p = 0.46). Moreover Na^+ electrolyte had highly positive correlation with and K+ (r = 0.407**, p <0.01) and a little less for Cl^- (r = 0.314*, p = 0.015 Table 2).

Table (1): Trace elements for AMI compared with control group.

	Group-C		Group-A		
Parameters	**Mean**	**SD**	**Mean**	**SD**	***P*-value**
Age (year)	53.91	5.70	55.45	6.93	0.183 **NS**
BMI (kg/m^2)	25.52	3.51	26.49	3.95	0.216 **NS**
Zn (μg/dL)	98.27	22.67	70.15	6.69	0.001* **S**
Cu (μg/dL)	128.71	16.32	152.65	9.84	0.001* **S**
Mn (μg/dL)	0.1257	0.0407	0.1255	0.0352	0.973 **NS**
Fe(μg/dL)	86.70	9.74	53.92	18.98	0.001* **S**
Se (μg/L)	74.00	5.94	45.80	13.71	0.001* **S**
Na^+ (mmol/L)	139.08	6.03	136.03	8.89	0.001* **S**
K^+ (mmol/L)	4.15	0.40	4.10	0.52	0.319 **NS**
Cl^- (mmol/L)	106.69	7.67	107.67	8.54	0.207 **NS**
TnI (ng/ml)	0.42	0.33	12.3	7.2	0.001* **S**
CK-MB (IU/L)	20.4	7.2	37.3	9.9	0.001* S
LDH (IU/L)	303.87	104.85	569.13	125.72	0.001* S
AST (IU/L)	28.02	6.91	51.84	7.85	0.001* S

***Significant at *P*<0.05, NS: Non-Significant.**

Table (2): Pearson correlation coefficients (*r*) between variables in the MI patients.

	Zn	**Cu**	**Mn**	**Fe**	**Se**	**Na^+**	**K^+**	**Cl^-**
Zn	1	-.094-	0.137	0.106	-.087-	0.104	0.053	.265*
Cu	-.094-	1	-.375-**	0.123	-.246-	0	-.001-	0.081
Mn	0.137	-.375-**	1	-.216-	-.641-*	0.119	0.018	-.145-
Fe	0.106	0.123	-.216-	1	0.304	-.239-	-.156-	0.095
Se	-.087-	-.246-	-.641-*	0.304	1	0.178	0.184	0.257
Na^+	0.104	0	0.119	-.239-	0.178	1	.407**	.314*
K^+	0.053	-.001-	0.018	-.156-	0.184	.407**	1	0.11
Cl^-	.265*	0.081	-.145-	0.095	0.257	.314*	0.11	1

***Correlation is significant at the 0.05 level (2-tailed).**
****Correlation is significant at the 0.01 level (2-tailed).**

The level of serum electrolyte Na^+ (mmol/L) in AMI cases reduced significantly when compared with healthy control group (136.03 ± 8.89, 139.08 ± 6.03, $p<0.001$) with no significant difference for K^+, Cl^- ($p>0.05$) between the two groups.

Discussion

Myocardial infarction is one of the leading causes of cardiovascular disease mortality in both men and women in developing and developed countries. AMI is the main cause of mortality as the high death rate is almost epidemic [2]. However, due of early detection and treatment, mortality has decreased over the previous three decades [14]. ECG changes, clinical symptoms and changes in cardiac enzymes, had used to diagnose AMI. The most extensively used approach for diagnosis is the electrocardiogram, but many times shows inclusive pattern. In such cases, serum biochemical indicators of myocardial damage become critical in confirming the diagnosis, so the use of these parameters is very important in the study [15]. Therefore, there was a need to develop new parameters to increase the accuracy of the diagnostic process. Intracellular zinc plays an important role in the prevention of cardiovascular diseases through redox pathways. Zinc replenishment has been demonstrated to restore cardiac function and prevent additional damage in such cases [16]. Several investigations have found that serum Cu levels in individuals with CAD are considerably higher than in healthy persons. Cu is an important component of some enzymes, such as superoxide dismutase, and has various functions including oxygen and electron transport, protection of the cell against ROS-induced injury, participating in anti-oxidative processes [17]. Also, the high Cu concentrations can lead to cell damage by increasing the formation of toxic free radicals [18].

Mn is a component of the antioxidant enzymes superoxide dismutase (SOD), and AMI is regarded as a stressor that affects the entire body. The chemical moiety of SOD contains some metal ions such as Cu, Zn, Mn, and Fe in the active site [19]. The study showed that there was no statistically significant difference between the patients and the control group, although a small percentage of the patients had low levels of Mn.

Iron deficiency is known to be associated with some cardiovascular diseases including heart failure, myocardial infarction and coronary artery disease [20, 21]. This hypothesis supports the results obtained during our study. Iron deficiency has been associated with increased myocardial oxidative stress (Nitrosative stress) by cytosolic superoxide ($O_2^{\bullet-}$) radical levels with reduced total myocardial antioxidant capacity [22]. In compared to healthy controls, Se levels were found to be decreased in patients with MI. Some studies indicate that selenium levels may decrease in both AMI and cardiac disorders. Oxidative stress is significant factors in AMI development, while GPx levels correlate with Se concentrations. It is not clear whether selenium deficiency contributes to the development of infarction or is a sign of its severity [23].

When comparing AMI cases to healthy controls, we found that serum sodium levels were significantly lower ($p<0.001$) in AMI cases. Hypoxia, ischemia, and infarction led in increased permeability of the sarcolemma to sodium, resulting in a reduction in serum sodium levels or may be due to use diuretics or analgesics. These results were consistent with findings from other studies for sodium and chloride, and inconsistent for potassium [24, 25]. As mentioned earlier, electrolyte equilibrium is important, any intracellular changes, necrosis and apoptosis cause electrolyte imbalance. For potassium, the obtained results show that the uptake of potassium by cells that have infarcted occurs naturally from extracellular to intracellular space [26]. It might be due to intravenous supplementary fluids used to restore or maintain normal fluid volume.

Conclusions

Serum trace elements (Zn, Cu, Fe, and Se) have an important role to identify patients at high risk. It can be used as a new biochemical marker for a better AMI prognosis. Serum sodium levels might be used as supplementary information for AMI patients' therapy and better prognosis.

Acknowledgments

The authors would like to thank Mustansiriyah University, College of Science, Chemistry Department, Baghdad, Iraq (www.uomustansiriyah.edu.iq) for their support in completing this work.

References

[1] Myocardial Infarction: Practice Essentials, Background, Definitions,(https://emedicine.medscape.com/article/155919-overview)

[2] Heusch, G., Myocardial ischaemia–reperfusion injury and cardioprotection in perspective. *Nature Reviews Cardiology*, 17(12), 773-789 (2020).

[3] Swirski, F. K., and Nahrendorf, M., Leukocyte behavior in atherosclerosis, myocardial infarction, and heart failure. *Science*, 339 (6116), 161-166 (2013).

[4] Vos, T., Abajobir, A. A., Abate, K. H., Abbafati, C., Abbas, K. M., Abd-Allah, F., and Criqui, M. H., Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, 390 (10100), 1211-1259 (2017).

[5] Hall, M., Dondo, T. B., Yan, A. T., Mamas, M. A., Timmis, A. D., Deanfield, J. E., and Gale, C. P., Multimorbidity and survival for patients with acute myocardial infarction in England and Wales: Latent class analysis of a nationwide population-based cohort. *PLoS medicine*, 15(3), e1002501 (2018).

[6] Khan, M. A., Hashim, M. J., Mustafa, H., Baniyas, M. Y., Al Suwaidi, S., AlKatheeri, R., Alblooshi, F., Almatrooshi, M., Alzaabi, M., Al Darmaki, R. S., & Lootah, S. Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study. Cureus, 12(7), e9349, (2020).

[7] Al-Taesh, H., Çelekli, A., Sucu, M., and Taysi, S., Trace elements in patients with aortic valve sclerosis. *Therapeutic Advances in Cardiovascular Disease*, 15, 1753944720985985 (2021).

[8] Zemrani, B., and Bines, J. E., Recent insights into trace element deficiencies: causes, recognition and correction. *Current Opinion in Gastroenterology*, 36 (2), 110-117 (2020).

[9] Bhattacharya, P. T., Misra, S. R., and Hussain, M., Nutritional aspects of essential trace elements in oral health and disease: an extensive review. *Scientifica*, (2016).

[10] Mert, H., Yılmaz, H., Irak, K., Yıldırım, S., and Mert, N., Investigation of the protective effect of kefir against isoproterenol induced myocardial infarction in rats. *Korean Journal for Food Science of Animal Resources*, 38 (2), 259 (2018).

[11] Rathore, V., Singh, N., and Mahat, R. K., Electrolyte Imbalance in Patients of Acute Myocardial Infarction: A Study from Central India. *Age (years)*, 58 (10.36), 61-96 (2018).

[12] Yin, Y., Han, W., and Cao, Y. Association between activities of SOD, MDA and Na+-K+-ATPase in peripheral blood of patients with acute myocardial infarction and the complication of varying degrees of arrhythmia. *Hellenic Journal of Cardiology*, 60 (6), 366-371 (2019).

[13] Stookey, L. L., Ferrozine---a new spectrophotometric reagent for iron. *Analytical chemistry*, 42 (7), 779-781 (1970).

[14] Sans, S., Kesteloot, H., Kromhout, D. O., and Force, T., The burden of cardiovascular diseases mortality in Europe: task force of the European society of cardiology on cardiovascular mortality and morbidity statistics in Europe. *European Heart Journal* (1997).

[15] Ericsson, C. G., Lindvall, B., Olsson, G., Rehnqvist, N., Strandberg, L. E., Svensson, G., and Erhardt, L., Trends in coronary care: a retrospective study of patients with myocardial infarction treated in coronary care units. *Acta medica Scandinavica*, 224 (6), 507-513 (1988).

[16] Perryman, M. B., Strauss, A. W., Buettner, T. L., and Roberts, R., Molecular heterogeneity of creatine kinase isoenzymes. *Biochimica et Biophysica Acta (BBA)-Protein Structure and Molecular Enzymology*, 747 (3), 284-290 (1983).

[17] Quader, M. R., Rahman, S., and Saha, S. K., A Study of Serum Zinc level in Patients with Acute Myocardial Infarction. *Faridpur Medical College Journal*, 15 (2), 92-94 (2020).

[18] Strecker, D., Mierzecki, A., and Radomska, K., Copper levels in patients with rheumatoid arthritis. *Annals of Agricultural and Environmental Medicine*, 20 (2), (2013).

[19] Phaniendra, A., Jestadi, D. B., and Periyasamy, L., Free radicals: properties, sources, targets, and their implication in various diseases. *Indian journal of clinical biochemistry*, 30 (1), 11-26 (2015).

[20] Roychowdhury, R., Khan, M. H., and Choudhury, S. Physiological and molecular responses for metalloid stress in rice a comprehensive overview. *Advances in rice research for abiotic stress tolerance*, 341-369 (2019).

[21] Sempos, C. T., Looker, A. C., Gillum, R. F., and Makuc, D. M., Body iron stores and the risk of coronary heart disease. *New England Journal of Medicine*, 330 (16), 1119-1124 (1994).

[22] Liao, Y., Cooper, R. S., and McGee, D. L. (1994). Iron status and coronary heart disease: negative findings from the NHANES I epidemiologic follow-up study. *American journal of epidemiology*, 139 (7), 704-712.

[23] Inserte, J., Barrabés, J. A., Aluja, D., Otaegui, I., Bañeras, J., Castellote, L., and Ferreira-González, I., Implications of iron deficiency in STEMI patients and in a murine model of myocardial infarction. *Basic to Translational Science*, 6 (7), 567-580 (2021).

[24] Frączek-Jucha, M., Kabat, M., Szlósarczyk, B., Czubek, U., Nessler, J., and Gackowski, A. Selenium deficiency and the dynamics of changes of thyroid profile in patients with acute myocardial infarction and chronic heart failure. *Kardiologia Polska (Polish Heart Journal)*, 77 (7-8), 674-682 (2019).

[25] Mudaraddi, R., Kulkarni, S. P., Trivedi, D. J., Patil, V. S., and Kamble, P. S., Association of serum electrolytes and urea levels with cardiac markers in acute myocardial infarction. *Group*, 29, 14-77 (2015).

[26] Mandole, M. B., Howale, D. S., Mamatha, M. T., Sharma, D., Gamit, D., and Pandit, D. P., Evaluation of renal function tests and serum electrolytes in patients with acute myocardial infarction. *Int J Biomed Res*, 7 (9), 676-679 (2016).