

Determination the relationship between cadmium and Zinc levels with myocardial infarction

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ABSTRACT

Myocardial infarction (MI) is responsible for any condition that causes a sudden decrease in blood flow to the heart. Certain trace elements play a role in the development of MI. This work aimed to assess the association between serum cadmium and zinc levels and cardiac markers in myocardial infarction. The present study, included 100 patients with MI and matches them 100 healthy controls, age range 39-80 years for both. Serum concentrations of Cd and zinc levels were determined by flameless atomic absorption spectrophotometry using an atomic absorption spectrophotometer, zinc was measured at wavelength 213.9 nm using a slit width of 0.5 nm and lamp current 5 mA, while Cd was measured at wavelength 228.8 nm using a slit width of 0.7 nm and lamp current 8 mA. The cardiac biomarker (TNHS) was measured using immunoassay kits. Serum lipids were measured using standard commercial kits. It was observed that the average concentration of Cd and Zn ($1.00494 \pm .261670$) vs. ($.60573 \pm .149274$), ($p < 0.001$) were significantly higher in MI group patients in compared with control objects. Conversely, the concentration of Zn ($.55412 \pm .053294$) vs. ($.69462 \pm .101595$), ($p < 0.001$) were significantly lower in MI group patients in compared with control objects. The same result was also obtained after adjustment for cardiovascular risk factors including diabetes mellitus (DM-HBA1C and DM-FBS) and TNHS ($p < 0.001$). The mean concentration of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and S-LDL were strong significantly higher in MI patients ($p < 0.001$), except S-T.G in spite of appear its mean higher in comparison to control subjects, However, there was no statistically significant difference. The present results appeared that serum level of essential trace element (Zn) and trace element of Cd are associated with the presence of MI. These results add to an increasing body of evidence that, the Cd is important for cardiovascular health.



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1. INTRODUCTION

The cardiovascular or circulatory system consists of the heart and blood vessels (arteries, arterioles, capillaries, venules and veins). When it functions normally, effective circulation of blood maintains perfusion

of the tissues, so that substrates for cellular metabolism are provided and excretory products removed. Among other vital functions, it also allows hormones to be transported from their organs of origin to their target tissues, defends against infection through facilitation of the movement of white cells and cytokines, and promotes homeostasis through the delivery of platelets and clotting factors to traumatized tissue [10], [25].

However, ischemic heart disease is the leading cause of death globally. Despite recent advances in interventional and medical therapies, survivors of myocardial infarction are at high risk of recurrent cardiovascular events. In recent years, coronary microvascular function has attracted more attention as the main target for risk stratification and as a possible target for pharmacological intervention as a part of the multifaceted treatment of ischemic heart disease. Coronary flow reserve (CFR) is one of the central indices that reflex the status of coronary circulatory function [11].

However, the significance of elevated serum cholesterol levels, arterial hypertension, oxidants, and cigarette smoking as risk factors for the development of coronary heart disease (CHD) has been well documented in numerous studies [2]. On the other hand, there are studies that have proven, in addition to the possible role of trace elements with myocardial infarction, their relationship with polycystic ovaries in women [3]. An epidemiologic study by who was indicated that variables other than traditional risk factors may contribute to the risk of CHD among American men." Furthermore, there are regional differences in the death rate caused by CHD that are not fully understood. In the search for other causes of CHD, attention is being focused on metal and trace element imbalance. Deficiencies in several essential minerals due to poor dietary intake or failure to control the homeostatic mechanism have been postulated as causes of coronary artery disease and sudden death. Furthermore, it has been assumed Excessive intake of various elements such as copper, cadmium, and zinc May contribute to regional differences in cardiovascular mortality. However, only a few studies relate metals and trace elements as determined in human blood samples to CHD. These investigations have introduced conflicting results due to the diagnosis of CHD has been established only by clinical data but not by angiographic findings [5]. To evaluate the significance of a relationship between metals and CHD, one must determine if there is a truly independent association between metals and CHD. Subsequently, the goal of the present study was to assess the concentrations of Cd and Zn in the blood sample of myocardial infarction patients of both genders and correlated with control subjects of matched age group (39–80 years).

2. Material and methods

2.1 Apparatus

Apparatus Vidas Biomrieux, france, Atomic absorption spectrophotometer, Shimadzu, 7000f, Uv visible spectrophotometer, Cecil, france. Oil path, F3 hake Germany, Afinion HBA1c, Biolabo of glucose and lipid profile Maizy, france.

2.2 Subjects and samples

Collection The study included 200 (100 patients and 100 healthy) suffering from symptoms of unstable angina or myocardial infarction. Their ages between 39 _ 80 years, for both groups. In the current study, we aimed to the level of cadmium and Zinc in blood samples of myocardial infarction (MI) patients of age ranged (39-80 years) Heart attack (n=100), hospitalized in cardiac ward of Basra hospitals (in the emergency and cardiac care unit at al-sadder teaching hospital, al-fayhaa teaching hospital and al-qurna general hospital)/ Iraq. Sample of 4ml pink blood were withdrawn using a vacuum tube containing an anticoagulant EDTA K3.

As well as 4 ml of a vacuum gel and clot activator tube and separated by centrifuge where isolated serum and the analyses required for the study and keep the samples at -20 C⁰. Where the Ethics Committee of the Basra

Health Department approved the Iraq Study Protocol Committee. In this study patient diagnosed with acute myocardial infarction (MI) by measuring cardiac marker high sensitive troponin (hsTn) in addition to clinical feature collected from enrolled patients. Form and determination some essential elements in MI patients.

2.3 Biochemical studies

2.3.1 Determination of Zn levels

The serum levels of Zn was determined at the Chemical Analysis by flameless atomic absorption spectrophotometry using an atomic absorption spectrophotometer (Shimadzu, GFA-7000f, Japan). Zn was measured at wavelength 213.9 nm using a slit width of 0.5 nm and lamp current 5 mA. The levels of Zn was gained by extrapolation of the criterion curve followed by multiplication with the dilution Factor.

2.3.2 Determination of Cd levels

The serum levels of Cd was determined at the Chemical Analysis by flameless atomic absorption spectrophotometry using an atomic absorption spectrophotometer (Shimadzu, GFA-7000f, Japan). Cd was measured at wavelength 228.8 nm using a slit width of 0.7 nm and lamp current 8 mA. The levels of Cd was gained by extrapolation of the criterion curve followed by multiplication with the dilution Factor.

2.3.3 Assay of high sensitive troponin I (TNHS)

The serum was divided into aliquots to be used for the determination of cardiac biomarker (TNHS) was measured with immunoassay kits (Vidas Biomrieux France) according to the manufacturer's instructions Journal of Cardiovascular Disease Research ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021 537

2.3.4 Determination of Lipid profile

Total cholesterol (TC), triglycerides (TG), low-density lipoprotein-cholesterol (LDL-C) and high-density lipoproteins-cholesterol (HDL-C). Were measured using standard commercial kits By Biolabo, Maizy, france

2.3.5 Determination of Glucose and HBA1C

Determination of glycated hemoglobin (HBA1C) in human whole blood by afinion HBA1C Eurption.

2.4 Statistical analysis

The Statistical Package for Social Sciences was used to investigation any significant relationships between the targeted variables. Chi-Square test was used to investigate any significant statistical association between qualitative variables, Student t-test for parametric quantitative variables, Mann Whitney test for non-parametric qualitative ones, Spearman's test to investigate correlations between non-parametric quantitative data, and Pearson test to investigate correlations between parametric quantitative ones. For the purpose of testing relationships, a level of probability value of less than 0.05 was considered significant.

3. Results

The present study was based on hospitalized myocardial infarction patients. The blood samples were analyzed for the concentrations of Zn and Cd in blood samples. However, table (1) shows Zn and Cd concentrations assessment in this study in related to DM as risk factor to myocardial infarction as well as the lipid profile and cardiac biomarker (Cardiac- TNHS).

However, the blood samples were analyzed for the concentrations of Cd and Zn. The data of the current study showed that myocardial infarction was clearly associated pronounced imbalance with primary analysis in compared to healthy subjects.

The concentration of elements in the studied samples varies greatly between individuals; hence, a hugely large number of samples from the population must be analyzed if the results are statistically evaluated for meaningful correlation. The concentrations of S. Cd level ($1.00494 \pm .261670$) in MI patients was significantly increased ($P < 0.001$) than control subjects ($.60573 \pm .149274$). While, our results were appeared that the concentration of S. Zn level ($.55412 \pm .053294$) in MI patients was significantly increased ($P < 0.001$).

there were significant pronounced associations between Cd and Zn levels and other MI risk factors (HbA1c, fasting blood sugar (FBS), Cardiac- TNHS, total cholesterol (Chol), S. HDL and S. LDL ($P < .001$, $P < .001$, $P < .001$, $P < .001$ and $P < .001$) respectively in all subjects (MI patient and normal control) except TG was appeared non-significant ($P > 0.05$) (Table 1).

Table 1; Cadmium, Zinc and TNHS levels of some risk factors of MI patients and healthy control. Values were expressed as (mean \pm SD).

Sample	Control (n=100)	Patients (n=100)	P-Value (P<0.05)
DM-HBA1C %	5.984 ± 1.3043	8.683 ± 2.7303	0.000
DM-FBS (mg/dl)	116.72 ± 43.951	191.49 ± 79.334	0.000
Cardiac- TNHS ng/mL	5.506 ± 4.7220	262.444 ± 240.1104	0.000
ESSENTIAL METAL- Zn (μ g/L)	$.69462 \pm .101595$	$.55412 \pm .053294$	0.000
Trace element Cd (ng/L)	$.60573 \pm .149274$	$1.00494 \pm .261670$	0.000
Total cholesterol (mg/dl)	$.59973 \pm .139003$	$1.00714 \pm .248821$	0.000
S.triglycerides (mg/dL)	177.52 ± 33.781	184.12 ± 51.889	NS
S. HDL cholesterol (mg/dL)	31.86 ± 7.466	26.12 ± 8.126	0.000
S. LDL cholesterol (mg/dL)	113.53 ± 22.840	172.41 ± 34.317	0.000

NS: Nonsignificance ($P > 0.05$)

4. Discussion

Globally, cardiovascular disease (CVD) is the leading cause of mortality, taking an estimated 17.9 million lives annually. Myocardial infarction and stroke account for 80% of these deaths [7]. Over decades, through epidemiologic, basic, and clinical studies, physician-scientists have recognized that increasing age, male sex, heredity, tobacco smoke, high blood cholesterol, high blood pressure, physical inactivity, obesity, diabetes mellitus, stress, excessive alcohol use, and diet/nutrition promote the development of atherosclerotic heart disease [24].

In this current study, concentrations of essential and trace elements (Zn, Cd) of the metals was estimated. To recapitulate, the results indicated that concentrations of the analyzed heavy metals were significantly higher in the blood of (Cd) and lower in serum of (Zn) in group of individuals who had MI. However, our study was appeared that the patients have significantly lower value of Zn ($P < 0.000$) in blood sample in comparison to healthy individuals.

Serum zinc levels were found low concentration in the blood after acute tissue injury irrespective of its origin, including myocardial infarction, which produces some of the most striking falls. Levels of zinc fall by 30% within one- or two days following AMI. At the same time, the extent of falls also correlated with the complications of AMI. Therefore, it may serve as an indicator in assessing the prognosis following AMI [19].

Imbalances in Zn homeostasis contribute significantly to the development of CVDs, such as coronary heart disease (CHD), myocardial infarction (MI), PCOs, and sudden cardiac death [13], [3].

In a meta-analysis with 2886 subjects from 41 case-control studies, the authors revealed that the subjects with MI had lower zinc levels in serum and hair than healthy controls, as well as in type 2 diabetic patients with or without nephropathy [15], [1] and that agrees with the results of our study.

Some other studies as [9], [18] also agree with us in that significant decrease in serum zinc level of AMI patient when compared with the corresponding control and it was clear that zinc level of the AMI groups was significantly lower than that of control groups.

Furtherless, Cadmium is a widespread toxic metal with potential cardiovascular effects, but no studies have evaluated cadmium and incident cardiovascular disease. Our data was appear that Statistical analysis as in table (1) the total Cd concentration in blood of patients group (1.00494 ± 0.261670) ng/ml that is higher than concentration in control group (0.69462 ± 0.101595) ng/ml with high statically significant ($p < 0.001$). This findings from our meta-analysis indicate statistically significantly higher risk with higher cadmium level for all clinical cardiovascular endpoints. Overall, this is supportive evidence that cadmium is a cardiovascular risk factor, where agreement with other studies conducted in different areas of world [17], [22], [16], [12]. However, In addition to clinical cardiovascular outcomes, chronic exposure to cadmium has also been associated with CVD risk factors and with subclinical endpoints. Increasing evidence supports that cadmium may play a role in the development of a number of traditional CVD risk factors, including hypertension [14], [8], [23] and chronic kidney disease [8], [23], [21], [20] which could mediate in part the cardiovascular effects of cadmium. The association with diabetes is inconsistent across studies [21], [6]. As well as [21], [6] were found the association with diabetes is inconsistent across studies who observed in (195) young women from Austria, cumulative cadmium exposure was associated with increased prevalence of elevated intima media thickness. However, lipid profile (Cholesterol, HDL and LDL) except T.G were Non-significantly elevated in the patients with diabetes. Lipoprotein abnormalities are usually present in type 2 diabetes, which includes hypertriglyceridemia, increased LDL and plasma HDL- cholesterol and also LDL's are converted to smaller, and more atherogenic, lipoproteins. These abnormalities are related to the increased metabolism of apolipoprotein B (apoB). Experimental evidence propose that regulation of apoB production, increment lipolysis in adipocytes due to poor insulin activity results in increased fatty acid release from adipose cells. Insulin has also been shown to directly increase the degradation of apoB which ameliorates dyslipidemia [4]. Therefore, insulin deficiency or hepatic insulin resistance may increase the secretion of apoB, and upregulate VLDL and LDL and increase cardiovascular risk. Anyhow, apart from the lipid profile, the metabolism of the biomarkers which are affected by Cd and Zn metabolism may be predictors of cardiovascular risk. However, the results showed that the levels of (DM-HBA1C and DM- FBS) of patients significantly increased

compared with control ($P < 0.000$) for both diabetes criteria included in this study in compared with control.

On the other hand, regarding Level of Cardiac-TNHS and Cd and Zn levels in the current study showed the inverse relationship and direct with Cd, where the Cardiac-TNHS higher significantly in patient, i.e., statistically significant decrease ($P < 0.001$) in comparison to control.

In conclusion, the role of trace elements including Cd and Zn in humans has not yet been fully characterized and has remained unclear. Nevertheless, several abnormalities of potential clinical, Relevance have been identified. In summary, in order to prevent some complications in patients, it may be significant to monitor the trace elements levels (Cd and Zn). Trace elements supplementation may be indicated in some diseases with no controversy concerning the importance of decreased or increased serum and/or tissue levels and documented positive effects of Zn supplementation on the quality of life (e.g. hyperlipidemia).

5. Conclusion

The current results was appeared that serum level of (Zn) was lower in patients while blood Cd level was increased with the present of MI in comparison to control subjects. These results add to an increasing body of evidence that, the Cd is important for cardiovascular health.

6. References

- [1] Adnan Jassim Mohammed Al-Fartosy, Nadhum Abdulnabi Awad Sadoun Abbas Alsalm. Osteoprotegerin and some trace elements in type 2 diabetic patients with or without nephropathy: effect of insulin resistance. *International medical journal* 2020; 4(25): 1771-1784
- [2] Adnan Jassim Mohammed Al-Fartosy, Nadhum Abdulnabi Awad, Rsha Abdulradha Mahmood .A comparative study of leptin, oxidant/antioxidant status and some trace elements in women of healthy control anf unexplained infertility in Basrah-Iraq. *The Indonesian biomedical journal* 2019; 11(3): 327-37
- [3] Amel H Mohmmmed, Nadhum A Awad Adnan J M AL-Fartosy. Study of trace elements selenium, copper, zinc and manganese level in polycystic ovary syndrome (PCOS). *International journal for research in applied sciences and biotechnology* 2019; 6(6): 16-22
- [4] Avramoglu RK, Qiu W, Adeli K. Mechanisms of metabolic dyslipidemia in insulin resistant states: deregulation of hepatic and intestinal lipoprotein secretion. *Front Biosci.* 2003; 8:464–76.
- [5] Ali Abdul Razzaq Abdul Wahid Al-Atbee. Determination of some Essential Trace Elements, Malondialdehyde and Total Antioxidant Status for Ischemic Heart Disease Patients in Basrah Province. 2013; Thesis in doctorate philosophy.
- [6] Barregard L, Bergstrom G, Fagerberg B. Cadmium exposure in relation to insulin production, insulin sensitivity and type 2 diabetes: a cross-sectional and prospective study in women. *Environmental research.* 2013;121:104–109.
- [7] Brunier A, Muchnick A. WHO reveals leading causes of death and disability worldwide: 2000-2019. December 9, 2020. <https://www.who.int/health-topics/cardiovascular-diseases#tab=tab>. Accessed January 24, 2021.
- [8] Caciari T, Sancini A, Fioravanti M, et al. Cadmium and hypertension in exposed workers: A meta-

analysis. International journal of occupational medicine and environmental health. 2013

- [9] Dasti MA, Hashmi SFA, Baloch GH, Shas SZA. Acute myocardial infarction serum zinc level in patients. Professional Med J.2013; 20(4):556-61.
- [10] Ali Abdul Razzaq Abdul Wahid, Nadhum Abdul Nabi Awad. Determination of selenium, magnesium and malondialdehyde (MDA) for ischemic heart disease patients. Iraqi national journal of chemistry, 2014, vol.54; 131-140.
- [11] F. Thomas, W. Patrick and A. Camm, "Cardiovascular Disease", 2nd edition, Wiley-Blackwell, US, (2007).
- [12] Fagerberg B, Bergstrom G, Boren J, Barregard L. Cadmium exposure, intercellular adhesion molecule-1 and peripheral artery disease: a cohort and an experimental study. BMJ Open. 2013;3(3)
- [13] Huang L, Teng T, Bian B, Yao W, Yu X, Wang Z, et al. Zinc levels in left ventricular hypertrophy. Biol Trace Elem Res. (2017) 176:48–55
- [14] Lee MS, Park SK, Hu H, Lee S. Cadmium exposure and cardiovascular disease in the 2005 Korea National Health and Nutrition Examination Survey. Environmental research. 2011;111(1):171–176.
- [15] Liu B, Cai ZQ, Zhou YM. Deficient zinc levels and myocardial infarction: association between deficient zinc levels and myocardial infarction: a meta-analysis. Biol Trace Elem Res 2015
- [16] Navas-Acien A, Tellez-Plaza M, Guallar E, et al. Blood cadmium and lead and chronic kidney disease in US adults: a joint analysis. American journal of epidemiology. 2009;170(9):1156–1164.
- [17] Nawrot TS, Van Hecke E, Thijs L, et al. Cadmium-related mortality and long-term secular trends in the cadmium body burden of an environmentally exposed population. Environmental health perspectives. 2008; 116(12):1620–1628.
- [18] Nazir S, Ullah E, Hussain S, Bukhari SA. Study of Serum zinc levels among patients of coronary artery disease conducted in a Tertiary Care Hospital. Biomedica 29. 2013
- [19] Shekokar P, Kaundiny S. Effect of acute myocardial infarction on serum zinc level. Indian Journal of Basic & Applied Medical Research. 2013; 3(1):80-87.
- [20] Swaddiwudhipong W, Limpatanachote P, Mahasakpan P, Krintratun S, Punta B, Funkhiew T. Progress in cadmium-related health effects in persons with high environmental exposure in northwestern Thailand: a five-year follow-up. Environmental research. 2012;112:194–198.
- [21] Swaddiwudhipong W, Mahasakpan P, Limpatanachote P, Krintratun S. Correlations of urinary cadmium with hypertension and diabetes in persons living in cadmium-contaminated villages in northwestern Thailand: A population study. Environmental research. 2010;110(6):612–616.
- [22] Tellez-Plaza M, Guallar E, Howard BV, et al. Cadmium Exposure and Incident Cardiovascular Disease. Epidemiology. 2013; 24(3):421–429.

[23] Tellez-Plaza M, Navas-Acien A, Crainiceanu CM, Guallar E. Cadmium exposure and hypertension in the 1999–2004 National Health and Nutrition Examination Survey (NHANES) Environmental health perspectives. 2008;116(1):51–56.

[24] U.S. EPA. Integrated Science Assessment (ISA) for Lead (Final Report, Jul 2013). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-
<https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=255721>. Accessed January 24, 2021.

[25] William J. Marshall, Ruth M. Ayling, Andrew P. Day and Marta Lapsley “CLINICAL