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Original Research

Role of the Trace Elements and Cardiac Markers in Assessment of Acute Coronary Syndromes

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ABSTRACT:
Aim: Role of the Trace Elements and Cardiac Markers in Assessment of Acute Coronary Syndromes. **Methods:** 150 adult patients were included in this study. 120 patients were suffering from ischemic heart disease (68 males and 52 females) with ages ranged from 44 to 66 years. 30 healthy individuals (20 males and 10 females) with ages ranged from 45 to 65 years, who served as a control group. The control group had no clinical evidence of coronary artery disease (CAD) or family history of CAD. All study participants were subjected to full history taking including Age, sex, socioeconomic status and occupations, smoking, history of Diabetes Mellitus, hypertension, coronary artery disease, ischemic heart disease and previous myocardial infarction. **Results:** The CK-MB levels were significantly increased in group II and group III ($p< 0.001$, $=0.014$), respectively as compared to control group. Also, group II was significantly higher than group I ($p< 0.001$). The AST levels were significantly increased in group III ($p< 0.001$) as compared to control group. Also, group III was significantly higher than group I, group II and group IV ($p< 0.001$). The Tn levels were significantly increased in group I, group II and group III (p=0.015, 0.007 and 0.001), respectively. There were significantly differences on comparing Tn levels among patients; group II and III were significantly higher than group I (p=0.007, 0.001 respectively), group I, group II and III (p=0.013, 0.004, < 0.001 respectively). No significant difference was found between group II and group III (p=0.884). No significant differences were found between patient groups and control group. Group II showed significantly lower iron level than group I (p=0.023). Also, group III showed significantly lower iron level than group I and group IV (p=0.013, 0.039 respectively). Serum zinc was significantly lower in group II than group I and group IV (p= 0.031, 0.003). No other significant correlation was observed. No significant correlation was obtained for the serum copper levels among the studied groups. The correlation between Fe, Zn and Cu versus Tn, CK and CK-MB in all studied groups were demonstrated in Table 6. There were significant positive correlation only between Fe versus Tn and CK-MB in group II (r=0.512, p=0.015), (r=0.506, p=0.016) respectively. There were significant negative correlation between Zn versus CK-MB in group I (r=-0.487, p=0.021). Otherwise no significant correlation were obtained between Zn versus Tn and CK in all studied groups and versus CK-MB in group II, group III, group IV and group V.There is no significant correlation were obtained between Cu versus Tn, CK, CK-MB in all studied groups. This cut-off values showed the highest accuracy to predict Fe usage (sensitivity of 77.47% and specificity of 72.69%), Cu usage (sensitivity of 84% and specificity of 87%) and Zn usage (sensitivity of 81% and specificity of 81%). **Conclusion:** We concluded that the Fe and Zn values were lower in ACS patients. Cu values did not show difference.

Keywords: Cardiovascular diseases, cardiac markers, acute coronary syndromes

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INTRODUCTION

Cardiovascular diseases are increasing day by day due to over utilization of fats or due to genetic reasons. It isa leading cause of morbidity and mortality from infancy to old age. Though conventional risk prediction algorithms are made available on presence of major cardiovascular risk factors identified in diseased population, authentic and accurate biomarkers of CVDs are lacking. It not only delayed clinical diagnosis but also increased risk manifold and resulted in accidental death of patients. Therefore, an early identification and treatment of risk factors are much needed to accelerate disease prevention and morbidity improvement.[1] Numerous risk scores have been developed to predict cardiovascular risk. These scores are based on observations of the relative degree of importance of individual major risk factors. Till the date numerous physiological biomarkers based on serum lipid, glucose and hormone biomarkers serum lipid, glucose and hormone profile have been identified that are associated with increased cardiovascular risks. Some of them are simple traditional biomarkers based on lipid profile and risk factors. More often, levels of plasma, serum, and blood are proved to be best cardiovascular risk biomarkers .[2] These markers display cellular lipid interactions and physiological functions of serum lipid bearing proteins and assist in clinical decision making and authenticated risk type.[3] There are so many established cardiovascular risk markers based on confirmed clinical outcomes related to biomolecules, its structure, and functions. There are new mini- and microlevel clinical factors associated with an elevated prospective risk of developing coronary heart diseases. However, various physical factors if known can work as biophysical markers, but all these are not enough to evaluate the disease and status of emerging risks in patients, hence, other biomarkers to be included in risk analysis. Many of these biomarkers, alone or in combination, can be incorporated into risk prediction models to determine whether their addition increases the model's predictive ability. Moreover, various cardiovascular risk prediction models have been updated by incorporating traditional risk factors and molecular, immunological genetic, imaging, and biophysical factors for more authentic and reliable estimation of cardiovascular risk. Trace elements are being increasingly recognized as essential mediators for the development and progression of cardiovascular diseases (CVD). Zinc (Zn) and copper (Cu) levels in the body interact with and balance each other. Zinc (Zn) interacts with cardiovascular cells and its deficiency leads to cellular damage and atherosclerosis and cause an increase in endothelial cell apoptosis.[4,5]

MATERIAL AND METHODS

150 adult patients were included in this study. 120 patients were suffering from ischemic heart disease (68 males and 52 females) with ages ranged from 44 to 66 years. 30 healthy individuals (20 males and 10 females) with ages ranged from 45 to 65 years, who served as a control group. The control group had no clinical evidence of coronary artery disease (CAD) or family history of CAD.

Patients were classified according to their clinical data and investigation into 4 groups each comprise 30 patients. Group I, with ages range from 39 to 64 years had unstable angina. Group II, their ages range from 40 to 62 years with acute myocardial infarction (AMI early 6 h). Group III, their ages range from 52 to 66 years with acute myocardial infarction (AMI late 6 h). Group IV, their ages range from 42 to 65 years with reperfusion therapy.

All selected patients had diagnosed as acute coronary syndrome. Subjects with the following diseases had been excluded: Valvular heart diseases, Congenital cardiac lesions, Cardiomyopathy, Renal diseases, Hepatic diseases, CNS manifestations, Heart failure, Pregnant females, Patient on estrogen therapy and Female on oral contraceptive pills.

All study participants were subjected to full history taking including Age, sex, socioeconomic status and occupations, smoking, history of Diabetes Mellitus, hypertension, coronary artery disease, ischemic heart disease and previous myocardial infarction.

Clinical & Laboratory examination of the patients

The general, chest and cardiac clinical examination were performed for all participant. Standard 12-lead Electrocardiography (ECG) was taken at speed of 25 mm/sec and a sensitivity of 1 mv/cm using Hellige simplicriptor EK 31. Electrocardiography (ECG) was used for analyze the signs of ischemia and/ or infarction. Observation of any arrhythmia, conduction defect or signs of chamber enlargement were also observed. Echocardiography was used for measuring left ventricle ejection fraction (LVEF%). 8 ml of peripheral venous blood were withdrawn for every subject by venipuncture under complete aseptic conditions and aliqueted into 2 tubes. One ml was delivered to tube containing EDTA for CBC. Seven ml were placed in plain polypropylene tube and allowed to clot; then centri- fuged at 3000 rpm for 10 min and serum was separated for assessment of Serum glucose level: (Human; Wiesbaden, Germany), Liver function tests (LFTs) (Human; Wiesbaden, Germany), Renal function tests (RFTs) (Human; Wiesbaden, Germany), Serum total cholesterol using enzymatic colorimetric method (Diasys; Holzheim, Germany), Serum total triglyceride using enzymatic colorimetric method (Diasys; Holzheim, Germany), Serum total high density lipoprotein (HDL) using enzymatic

colorimetric method (Diasys; Holzheim, Germany) and Serum total low density lipoprotein (LDL).
Cholesterol was calculated from total serum cholesterol (TC), the HDL cholesterol and the triglyceride concentration (TG) according to the equation of Friedewald *et al*. provided that TG does not exceed 400 mg/dl and LDL= serum cholesterol-(1/5 Triglyceride + HDL).[6]

Cardiac markers measurement
Serum level of lactate dehydrogenase (LDH), Serum level of creatine kinase (CK), Serum level of creatine kinase-isoenzyme (CK-MB) and Serum level of troponin (Tn) were measured using kinetic enzymatic method. Assessment of serum trace elements via colorimetric principle: Serum samples were preserved in 1.5 ml eppendorf tubes at – 80ºC for subsequent estimation of Serum level of zinc (Zn), copper (Cu) and iron (Fe) by colorimetric method. The assessment of serum Zn and Cu were measured via colorimetric principle using a commercial kits (Centronic GmbH, Wartenberg, Germany) according to the manufacturer's instruction. The assessment of serum iron via colorimetric principle was measured using commercial kit (Biotechnology, S.A.E., Cairo, Egypt) according to the manufacturer's instruction.

STATISTICAL ANALYSIS
The program used was SPSS version 21.0. Quantitative data were analyzed using mean and standard deviation, while frequency and percentage were used with qualitative data. Student t test and F test were used to compare means of different groups, while chi square test was used to compare frequencies.

RESULTS
There is no significant differences between group I, group II, group III, group IV regarding age, sex, weight, height and BMI (Table 1). The blood glucose (BG) and lipogram (total cholesterol TC and triglyceride TG levels) of studied groups demonstrated that Group II, III and IV showed higher BG and TG. Group III and IV showed higher TC (p=0.21, 0.031). There was significant difference between different groups regarding diabetes (P < 0.001), but no significant difference regarding total cholesterol and triglyceride (P =0.802, 0.274), respectively (Table 2).
The serum cardiac enzymes levels showed significant variation in the studied groups Table 3. The CK levels were significantly increased in group II and group III (p< 0.001). Group I show significant decrease than control (p< 0.001). The CK-MB levels were significantly increased in group II and group III (p< 0.001, =0.014), respectively as compared to control group. Also, group II was significantly higher than group I (p< 0.001).The AST levels were significantly increased in group III (p< 0.001) as compared to control group. Also, group III was significantly higher than group I, group II and group IV (p< 0.001).The Tn levels were significantly increased in group I, group II and group III (p=0.015, 0.007 and 0.001), respectively. There were significantly differences on comparing Tn levels among patients; group II and III were significantly higher than group I (p=0.007, 0.001 respectively), group I, group II and III (p=0.013, 0.004, < 0.001 respectively). No significant difference was found between group II and group III (p=0.884)

Table 1: Demographic data of the studied groups

Parameter		Group I n=30	P-value*	Group II n=30	P-value*	Group III n=30	P-value*	Group IV n=30	P-value*	Control Group n=30	P-value*
Age / year		53.20 ± 6.33	0.878	52.87± 6.17	0.879	54.55 ± 6.33	0.488	50.98 ± 7.50	0.574	52.73 ± 4.97	0.796
Sex; n (%)	Male	12 (40%)	0.298	25 (83.33%)	0.263	20 (66.67%)	0.693	18(60%)	0.875	20(66.67%)	0.289
	Female	18(60%)		5(16.67%)		10 (33.33%)		12(40%)		10(33.33%)	
Weight /kg		90.2 ± 10.95	0.174	93.30 ± 8.15	0.663	94.10 ± 11.59	0.515	96.96 ± 7.98	0.876	96.00 ± 6.31	0.164
Height / cm		172.05 ± 11.16	0.318	178.95 ± 6.72	0.369	178.45 ± 6.57	0.773	177.90 ± 7.78	0.546	177.73 ± 10.62	0.218
BMI**		30.73 ± 4.51	0.388	31.86 ± 12.05	0.399	29.92 ± 3.01	0.885	29.15 ± 3.24	0.807	29.21 ± 3.74	0.388

P-value significance between investigated group and healthy control
**BMI, body mass index

Table 2: Prevalence of some risk factors in the studied groups

Parameter		Group I n=30	Group II n=30	Group III n=30	Group IV n=30	Control n=30	X2	P-Value
Diabetes Mellitus	Diabetic n (%)	1 (3.33 %)	24(80%)	30 (100%)	26 (86.67%)	6 (20%)	54.12	< 0.001*
	Non Diabetic n (%)	29 (96.67%)	6(20%)	0 (0.00%)	4 (13.33%)	24(80%)		
Obesity BMI >30	Obese n (%)	18 (60%)	12(40%)	10 (33.33%)	13 (43.33%)	7 (46.67%)	1.824	0.650

	Non Obese n (%)	12 (40%)	18(60%)	20(66.67%)	17 (56.67%)	8 (53.33%)		
Hyper cholesterol	n (%)	13(43.33%)	10 (33.33%)	12 (40%)	17(56.67%)	0 (0.00%)	0.676	0.802
Hyper triglyceride	n (%)	18 (60%)	25 (83.33%)	20(66.67%)	24 (80%)	15 (50%)	4.835	0.274

*highly significant

Table 3: Comparison of serum cardiac markers levels in the studied groups

		CK (U/L) (Mean ± S.D.)	CK-MB (U/L) (Mean ± S.D.)	AST (U/L) (Mean ± S.D.)	Troponin (U/L) (Mean ± S.D.)
Group I (n=30)		91.05 ± 41.25	4.27 ± 1.78	30.98 ± 11.78	0.029 ± 0.021
Group II (n=30)		732.87 ± 601.11	8.54 ± 4.26	32.20 ± 11.25	0.302 ± 0.409
Group III (n=30)		1136.45 ± 801.21	28.57 ± 82.98	171.95 ± 130.28	0.377 ± 0.302
Group IV (n=30)		196.35 ± 55.94	5.27 ± 9.25	34.87 ± 10.56	0.015 ± 0.006
Control Group (n=30)		188.13 ± 48.03	2.89 ± 1.23	30.13 ± 14.07	0.016± 0.008
G-I vs Control	t-value	4.54	0.93	0.04	2.96
	p-value	< 0.001*	0.226	0.94	0.015*
G-II vs Control	t-value	3.46	4.73	0.96	3.39
	p-value	0.001*	< 0.001*	0.31	0.007*
G -III vs Control	t-value	4.42	3.38	4.25	4.11
	p-value	< 0.001*	0.014*	< 0.001*	0.001*
G -IV vs Control	t-value	0.42	0.81	0.65	0.000
	p-value	0.67	0.31	0.34	1.00
G -I vs G -II	t-value	4.83	4.43	0.95	3.12
	p-value	< 0.001*	< 0.001*	0.335	0.007*
G -I vs G -III	t-value	5.77	1.28	4.89	4.05
	p-value	< 0.001*	2.17	< 0.001*	0.001*
G -I vs G -IV	t-value	8.17	0.47	0.98	2.84
	p-value	< 0.001*	0.62	0.34	0.013*
G -II vs G -III	t-value	1.91	1.09	4.48	0.12
	p-value	0.07	0.28	< 0.001*	0.884
G -II vs G -IV	t-value	4.12	1.64	0.06	3.36
	p-value	0.001*	0.12	0.93	0.004*
G -III vs G -IV	t-value	5.05	1.21	4.62	4.23
	p-value	< 0.001*	0.24	< 0.001*	< 0.001*

The serum Fe, Zn and Cu levels among the studied groups were demonstrated in Table 5. No significant differences were found between patient groups and control group. Group II showed significantly lower iron level than group I (p=0.023). Also, group III showed significantly lower iron level than group I and group IV (p=0.013, 0.039 respectively). Serum zinc was significantly lower in group II than group I and group IV (p= 0.031, 0.003). No other significant correlation was observed. No significant correlation was obtained for the serum copper levels among the studied groups (Table 5). The correlation between cardiac enzymes and Fe demonstrated significant positive correlation between Fe versus Tn, CK and CK-MB. In subjects with positive Tn, the mean value ± S.D of Fe was 151.16 ± 78.28 compared to 188.17 ± 112.18 in subjects with negative Tn. The difference was found to be statistically significant (p< 0.001). In subjects with high CK, the mean value ± S.D of Fe was 145.12 ± 87.13 compared to 191.50 ± 114.81 in subjects with low CK. The difference was found to be statistically significant (p< 0.001). In subjects with high CK-MB, the mean value ± S.D of Fe was 151.96 ± 82.27 compared to 193.24 ± 117.36 in subjects with low CK-MB. The difference was found to be statistically significant (p< 0.001). Regarding to the correlation between cardiac enzymes and Zn, there were significant positive correlation between Zn versus Tn, CK and CK-MB. In subjects with +ve Tn, the mean value ± S.D of Zn was 102.87 ± 29.12 compared to 117.10 ± 36.09 in subjects with-ve Tn. The difference was found to be statistically significant (p< 0.001). In subjects with high CK, the mean value ± S.D of Zn was 101.00 ± 31.07compared to 115.16 ± 35.88 in subjects with low CK. The difference was found to be statistically significant (p< 0.001). In subjects with high CK-MB, the mean value ± S.D of Zn was 107.06
± 29.11 compared to 109.87 ± 40.98 in subjects with low CK-MB. The difference was found to be statistically significant (p< 0.001). While the correlation between cardiac enzymes and Cu showed significant positive correlation between Cu versus Tn, CK and CK-MB. In subjects with +ve Tn, the mean value ± S.D of Cu was 125.77 ± 109.87 compared to 131.11 ± 85.73 in subjects with -ve Tn. The difference was found to be statistically significant (p< 0.001). In subjects with high CK, the mean value ± S.D of Cu was 145.57 ± 119.11 compared to 126.68 ± 80.62 in subjects with low CK. The difference was found to be statistically significant (p< 0.001). In subjects with high CK-MB, the mean value ± S.D of Cu was 139.98 ± 112.13 compared to 125.02 ± 81.16in subjects with low CK-MB. The difference was found to be statistically significant (p< 0.001).

The correlation between Fe, Zn and Cu versus Tn, CK and CK-MB in all studied groups were demonstrated in Table 6. There were significant positive correlation only between Fe versus Tn and CK-MB in group II (r=0.512, p=0.015), (r=0.506, p=0.016) respectively. There were significant negative correlation between Zn versus CK-MB in group I (r=-0.487, p=0.021). Otherwise no significant correlation were obtained between Zn versus Tn and CK in all studied groups and versus CK-MB in group II, group III, group IV and group V. There is no significant correlation were obtained between Cu versus Tn, CK, CK-MB in all studied groups. This cut-off values showed the highest accuracy to predict Fe usage (sensitivity of 77.47% and specificity of 72.69%), Cu usage (sensitivity of 84% and specificity of 87%) and Zn usage (sensitivity of 81% and specificity of 81%).

Table 4: Comparison of serum iron, Zinc and Cupper levels among the studied groups

Mean (µg/ml)			**Serum Fe**			**Serum Zn**			**Serum Cu**	
		± S.D.	**Range**	**Mean (µg/ml)**	**± S.D.**	**Range**	**Mean (µg/ml)**	**± S.D.**	**Range**	
Group I (n=30)		195.11	± 76.53	105 - 399	117.98	± 31.04	77 - 177	116.23	± 90.19	11.48 - 317
Group II (n=30)		132.47	± 95.32	11 - 321	95.45	± 35.20	18 - 151	117.00	± 41.83	45 - 197
Group III (n=30)		128.88	± 75.56	10 - 300	101.75	± 37.25	23 - 151	115.401	± 35.71	48 - 176
Group IV (n=30)		174.77	± 73.75	9.87- 296	127.45	± 41.85	27 - 177	120.60	± 65.68	68 - 317
Control Group (n=30)		194.53	± 120.58	83 - 439	110.88	± 3380	74 - 211	114.99	± 31.38	60 - 201
G-I vs Control	t-value		0.64			0.15			0.19	
	p-value		0.96			0.57			0.98	
G-II vs Control	t-value		2.11			1.65			1.51	
	p-value		0.08			0.21			0.33	
G -III vs Control	t-value		1.31			0.47			0.18	
	p-value		0.06			0.37			0.38	
G -IV vs Control	t-value		0.61			0.92			0.67	
	p-value		0.56			0.22			0.81	
G -I vs G -II	t-value		2.41			2.39			1.05	
	p-value		0.023*			0.031*			0.31	
G -I vs G -III	t-value		2.67			1.65			1.04	
	p-value		0.013*			0.18			0.32	
G -I vs G -IV	t-value		0.97			0.53			0.15	
	p-value		0.34			0.33			0.87	
G -II vs G -III	t-value		0.09			0.30			0.11	
	p-value		0.92			0.76			0.90	
G -II vs G -IV	t-value		1.64			3.54			0.84	
	p-value		0.117			0.003*			0.42	
G -III vs G -IV	t-value		2.17			1.87			0.68	
	p-value		0.039*			0.07			0.51	

Table 5: Correlation between Fe, Zn and Cu versus Tn, CK and CK-MB in the studied groups.

			Serum Fe			**Serum Zn**			**Serum Cu**	
Groups	*Corr.	Tn	CK	CK-MB	Tn	CK	CK-MB	Tn	CK	CK-MB
Group I (n=30)	r-value	0.21	-0.42	-0.38	0.011	-0.31	-0.487*	-0.04	-0.03	0.05
	p-value	0.32	0.07	0.08	0.97	0.16	0.021	0.83	0.85	0.82
Group II (n=30)	r-value	0.512*	0.43	0.506*	0.29	0.40	0.29	-0.07	-0.03	0.02
	p-value	0.015	0.05	0.016	0.21	0.06	0.21	0.77	0.88	0.91
Group III (n=30)	r-value	-1.88	0.17	-0.37	-0.08	-0.21	0.27	0.14	-0.24	0.32
	p-value	0.41	0.49	0.11	0.70	0.39	0.23	0.57	0.20	0.10
Group IV (n=30)	r-value	-0.05	0.08	-0.08	0.19	0.29	0.28	-0.24	-0.22	-0.13
	p-value	0.8	0.72	0.72	0.41	0.20	0.24	0.38	0.35	0.65
Control Group (n=30)	r-value	0.08	0.28	0.46	-0.24	-0.34	-0.13	-0.16	-0.46	-0.48
	p-value	0.76	0.30	0.08	0.37	0.21	0.62	0.57	0.08	0.07

DISCUSSION

This study was aimed to access the relation between some trace elements (Fe, Zn and copper) and acute coronary syndrome (ACS). There is no difference regarding age, sex, weight, height and BMI was found between patients and healthy control.

In the current study, The blood glucose (BG) and lipogram (total cholesterol TC and triglyceride TG levels) of studied groups demonstrated that Group II, III and IV showed higher BG and TG. Group III and IV showed higher TC (p=0.21, 0.031).

In the present study, There was significant difference between different groups regarding diabetes (P < 0.001), but no significant difference regarding total cholesterol and triglyceride (P =0.802, 0.274), respectively.

These results harmonize with the INTERHEART Study that the risk of MI increases 2.48 folds in presence of diabetes mellitus.[7] This study showed statistically significant differences between patients with UA and AMI (p< 0.001) as compared to control group in CK enzyme, statistically significant relation between patients with UA and others with AMI, also we found statistically significant relation between patients with UA and AMI and those who received reperfusion therapy

However, no significant relations were observed among patients with AMI (early or late 6 h).

Concerning CK-MB, there was statistically significant difference in patients with AMI (p< 0.001) as compared to control group and in patients with AMI within 6 h and those with UA.

In a previous study, the increase in serum levels of Cu and Fe and the decrease in serum levels of Zn and Se in patients with higher levels of Tn and CK-MB reveal that trace element levels are related to the degree of myocardial damage.[8] Moreover, zinc levels were significantly inversely correlated with CK, CKMB and cTnT levels and the prevalence of AMI decreased with increasing zinc level.[9]

As regard to AST, levels were significantly different in patients with AMI within six hrs (p< 0.001) as compared to control group, patients with UA and others with AMI (late six hrs), patients with AMI and patients with AMI (late six hrs) and those who received reperfusion therapy. No other significant correlation was observed.

The Tn levels were significantly increased in group I, group II and group III (p=0.015, 0.007 and 0.001), respectively as compared to control group, also there was significant correlation between patients with UA and AMI and in patients with UA and AMI and those who received reperfusion therapy.

There were statistically significant differences between patients with UA and AMI patients and statistically significant differences between patients with AMI and those who received reperfusion therapy.

The current finding is consistent with the results of Regnström *et al*. 1994 showed that serum iron was significantly lower in patients than in controls and suggested that low stored iron levels are a risk factor for premature coronary atherosclerosis and MI.[10] Study conducted by Kervienen *et al*. 2004 was proved that their is association between serum iron and CHD as the subjects with low iron, high-sensitivity C-reactive protein (hs-CRP) and a high total leukocyte count were at an increased risk.[11]

The presence of anaemia was associated with a 1.4 times increased risk of a cardiovascular event.[12] Contrary to previous findings, Morrison *et al*. 1994 were observed a significantly higher risk of acute myocardial infarction in the highest category of serum iron (i.e., more than 175 μg/dl, versus less than 120 μg/dl) with rate ratios of 2.18 (95 % confidence interval (CI) 1.01– 4.74) for men and 5.53 (95 % CI 1.69–18.12) for women. The risk was further increased in people with elevated levels of LDL cholesterol. No association was found with dietary iron or the use of iron supplements.[13] In a cross-sectional study, the total iron binding capacity (TIBC) was significantly increased in the high-frequency blood donors when compared with the low-frequency blood donors (mean ± standard error of the mean (SEM) = 363 ± 10 μg/dL versus 325 ± 7 μg/dL; p = 0.003.[14] However, other studies were found no association between body iron stores and risk of CHD. For example, Daphne et al. 2006, Sun et al. 2008 and Sempase *et al.* 2010 reported lack of association between serum ferritin and CHD in both men and women.[15-17] There was no significant difference in serum zinc level between patients and control. Patients with AMI showed significant decrease in serum zinc level than patients with UA and those who received reperfusion therapy.

These results were in agreement with the study of Giannoglou *et al*. 2010 and Cebi *et al*. 2011 showed that serum Zn was not significantly associated with CHD risk and severity (P = 0.320).[18,19] In contrast, a study of Islamoglu *et al*. 2011 found that serum Zn was significantly lower in patients than in healthy control (P < 0.010).[20] Moreover, in the study of Bayir *et al*. 2013, serum Zn concentration was significantly less in the CHD group compared to the control group (P < 0.010).30 Also, Lui *et al*. 2015 meta-analysis study indicated that subjects with MI had lower Zn levels than healthy controls (SMD=−1.848, 95 % CI=(−2.365, −1.331).[21] However, other study suggested that the occurrence of lower serum Zn in MI patients may be an acute phase response rather than a cause of cardiovascular disease.[21]

Serum copper level did not show any significant change among the studied groups in this study which in agreement with study of Oster *et al*. 1993 that found no association between concentrations of Zn and Cu in serum and the corresponding concentrations in heart tissue.[22]

In contrary, Klevay (1992) had proposed that Cu deficiency rather than excess is a risk factor for CAD and it had effects on various risk factors including cholesterol level, blood pressure, glucose tolerance and electrocardiographic abnormalities.[23] In addition, Shokrzadeh *et al*. 2009 revealed that the mean Cu level of the ischemic cardiomyopathy (ISCMP) group (1.54 ± 0.52 mg/L) was significantly higher than the Cu levels of the healthy volunteers (1.31 ± 0.24 mg/L; $p = 0.048$).[24]

CONCLUSION

We concluded that the Fe and Zn values were lower in ACS patients. Cu values did not show difference.

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