STUDY OF SERUM METALS AND LIPIDS PROFILE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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SUMMARY: The changes of serum lipids and metals' levels in acute myocardial infarction (AMI) patients were studied in comparison to normal subjects. The same parameters were also determined in presence of other diseases in conjunction to AMI such as diabetes and/or hypertension. Results showed that all patients' magnesium, copper, triglycerides and low density lipoprotein cholesterol (LDL-Ch) levels were significantly higher than the corresponding values of controls. Serum high density lipoprotein cholesterol (HDL-Ch) levels were lower than values of controls but the decrease was significant in patients with AMI and AMI with diabetes. Also, serum iron significantly decreased in patients with AMI, diabetes and hypertension. In all patients serum zinc and total cholesterol (T-Ch) showed an appreciable increase compared to the control. Our findings emphasize the importance of lipids and metals measurements in AMI patients.

Key Words: Iron, Zinc, Copper, Magnesium.

INTRODUCTION

Many prospective studies have implicated metal ions and lipids in the genesis of AMI (1). The association of lipids and lipoproteins with AMI has been reported by some authors (2). Increased risk of cardiovascular disease is associated with raised serum cholesterol levels (3). There has been considerable interest in the role of HDL-Ch as a protective factor against AMI (4). On the other hand, attention is being focused on metals as risk factors for AMI (5). There is an association between low dietary magnesium (6), high dietary iron (7) and increased induction of the disease. Moreover, the values of serum copper, magnesium and zinc were changed in AMI patients than controls (8).

Although AMI has been the object of most epidemiological studies, more informations on its possible

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causes are needed to predict its future occurrence, that is among an apparently healthy population we can distinguish those individuals with a high risk from those with a low risk of subsequently developing AMI. Furthermore, additional knowledge is required about various lipid parameters and metals' levels in AMI patients as they can be useful as markers for the disease.

The aim of the present study is to investigate the changes in serum levels of triglycerides, total cholesterol, HDL-Ch, LDL-Ch and of some metals as magnesium, iron, zinc and copper in AMI patients. Moreover, we aimed at investigating the effects of some risk factors such as diabetes and hypertension in AMI patients on these variables.

MATERIALS AND METHODS

The present study included 88 individuals, categorized into two groups. The first group contains 58 patients consecutively admitted to the intensive care unit, Kobri El-Kobba Military Hospital. Patients were admitted with prolonged chest pain and were diagnosed as recent AMI on clinical examination, electrocardiographic and laboratory basis. They were classified into four subgroups according to the presence of other diseases: In the first one (n=32) patients had AMI. The second subgroup was composed of patients with AMI and diabetes (n=8), and the third contained patients with AMI and hypertension (n=8) and the last one was of patients with diabetes and hypertension (n=10). Patients' age ranged between 25 - 83 years (mean ± S.E. = 51 ± 1.4).

The second group included 30 normal subjects considered as apparently healthy by clinical examination and with no history of any disease. Their age ranged between 30-60 years (mean ± S.E = 44.1 ± 1.84).

Patients' blood samples were collected on the seventh day of chest pain. Patients were fasted from 8 p.m. to 8 a.m. Specimens were collected at a standardized time to minimize any effect of diurnal variation. Sterile, disposable plastic syringes were used. Blood samples were transferred immediately and carefully to clean trace element free polypropylene tubes, left to clot and the serum was separated by centrifugation. Serum was divided into several polypropylene tubes, stoppered, labelled and stored at -20°C until analyzed. Blood samples were collected from controls under the same limitations.

Serum copper and zinc levels were determined by flame atomic absorption technique (9,10). Measurement of serum magnesium value was performed colorimetrically without deproteinization using calmagite (11). Iron level was estimated by forming a colored complex with ferrozine (12). Serum triglycerides and total cholesterol were estimated enzymatically (13,14). Serum HDL-Ch was determined in the clear supernatant after precipitating other lipoprotein fractions (15). Finally, LDL-Ch was determined enzymatically (16).

Statistical analysis was performed using Student's t-test. The degree of association between lipids and metals was measured by the Spearman's correlation coefficient.

Table 1: Serum magnesium, iron, zinc and copper levels in both control and acute myocardial infarction patient groups.

	Control group n = 30	Patient group n = 58
Metals	Mean ± S.E	Mean ± S.E
Magnesium (mg/dl)	2.01 ± 0.052	2.23**** ± 0.041
Iron (ug/dl)	105 ± 4.83	97.3 ± 3.39
Zinc (ug/dl)	68.4 ± 1.91	72.6 ± 1.97
Copper (ug/dl)	96.7 ± 3.13	127***** ± 4.97

Values significantly different from control group:
**** $p \leq 0.005$
*****$p \leq 0.001$

RESULTS

Table 1 reveals a significant increase in serum magnesium and copper of AMI patients where $p<0.005$ and <0.001 respectively when compared with the corresponding control values. Iron level is slightly decreased with respect to that of the control while serum zinc does not show a significant change compared with the control series.

Table 2 illustrates serum mean values of magnesium, iron, zinc and copper for different patients subgroups; AMI group (A), AMI with diabetes (B), with hypertension (C), and with diabetes and hypertension (D). It was clear that magnesium levels of all AMI patients subgroups except group (B) were significantly higher than that of control value irrespective of the accompanied disease where $p \leq 0.05$, ≤ 0.005 and ≤ 0.005 in subgroups A, C and D respectively. Also, the copper values of the patients in the above mentioned

Table 2: Comparison between serum magnesium, iron, zinc and copper levels in different groups with acute myocardial infarction and healthy control group.

Group	Serum mean value ± S.E			
	Magnesium (mg/dl)	Iron (ug/dl)	Zinc (ug/dl)	Copper (ug/dl)
Healthy subjects n=30	2.01 ± 0.052	105 ± 4.83	68.4 ± 1.91	96.7 ± 3.13
Patients with AMI (A) n=32	2.19* ± 0.065	95.5 ± 4.76	71.1 ± 2.24	116** ± 7.07
Patients with AMI and diabetes (B) n=8	2.23 ± 0.109	101 ± 11.2	77.3 ± 5.41	123* ± 12.6
Patients with AMI and hypertension (C) n=8	2.29**** ± 0.067	104 ± 5.98	74.7 ± 8.30	138***** ± 9.92
Patients with AMI and diabetes and hypertension (D) n=10	2.30**** ± 0.08	88.8** ± 4.43	72.3 ± 4.83	157***** ± 6.77

Values significantly differ from healthy subject:
*p ≤ 0.05, **p ≤ 0.025, ****p ≤ 0.005 and *****p ≤ 0.001

subgroups were significantly higher and compared to the subgroups the p values were ≤0.025, ≤0.05, ≤0.01 and ≤0.001 respectively. On the other hand, zinc and iron levels in patients were not significantly changed except in diabetic and hypertensive subgroup in which iron level was significantly decreased than control level (p≤0.025).

Serum lipids profile in both normal and in acute myocardial infarction patients groups is illustrated in Table 3. Serum levels of triglycerides and LDL-Ch were significantly higher at p≤0.001 and ≤0.005 respectively than controls. Serum level of HDL-Ch in patients decreased significantly (p≤0.001) when compared to control value. Serum T-Ch level in patients was slightly higher than the corresponding value of control.

Table 4 demonstrates that serum triglycerides and LDL-Ch levels for different subgroups of patients A, B, C, and D increased significantly than those of control where statistical values for triglycerides were <0.01, <0.001, <0.001 and <0.001 respectively, also for LDL-Ch they were <0.025, <0.001, <0.05 and <0.01 respectively. Total cholesterol showed pronounced increase in all patients subgroups if compared with the control group. On the other hand, HDL-Ch levels in all subgroups showed appreciable decrease, which was only significant in subgroups A and B, where p <0.001 and <0.005 respectively when compared with that of control.

In patients' group, there were significant positive correlations between LDL-Ch and magnesium, zinc and copper r=0.344, p≤0.01; r=0.306, p≤0.05 and r=0.391, p≤0.01 respectively. Iron exhibited no correlation with LDL-Ch. No significant relationships were seen between HDL-Ch and metals (Figure 1).

DISCUSSION

In recent years, coronary heart diseases have been shown to be a major cause of death (17). The

Table 3: Serum lipid profile in both control and acute myocardial infarction patient groups.

Lipid Profile	Control group n=30	Patient group n=58
	Mean ± S.E	Mean ± S.E
Triglycerides (mg/dl)	111 ± 7.12	167***** ± 8.65
Total cholesterol (mg/dl)	197 ± 6.51	206 ± 6.84
High density lipoprotein cholesterol (mg/dl)	45.3 ± 1.95	35.8***** ± 1.6
Low density lipoprotein cholesterol (mg/dl)	93.1 ± 4.69	118**** ± 5.68

Values significantly differ from control group:
****$p \leq 0.005$ and *****$p \leq 0.001$

prevalence of these diseases in developed countries has reached immense proportions which represent a major problem. Atherosclerosis has been reported as the most common cause of coronary heart diseases (18). Therefore, there are direct correlations between the incidence of AMI and plasma lipid abnormalities (19). Moreover, metals are important constituents of various metalloenzymes which are responsible for the maintenance of myocardial integrity. Imbalanced serum concentrations of metals have been assumed to share in the causes of AMI (5).

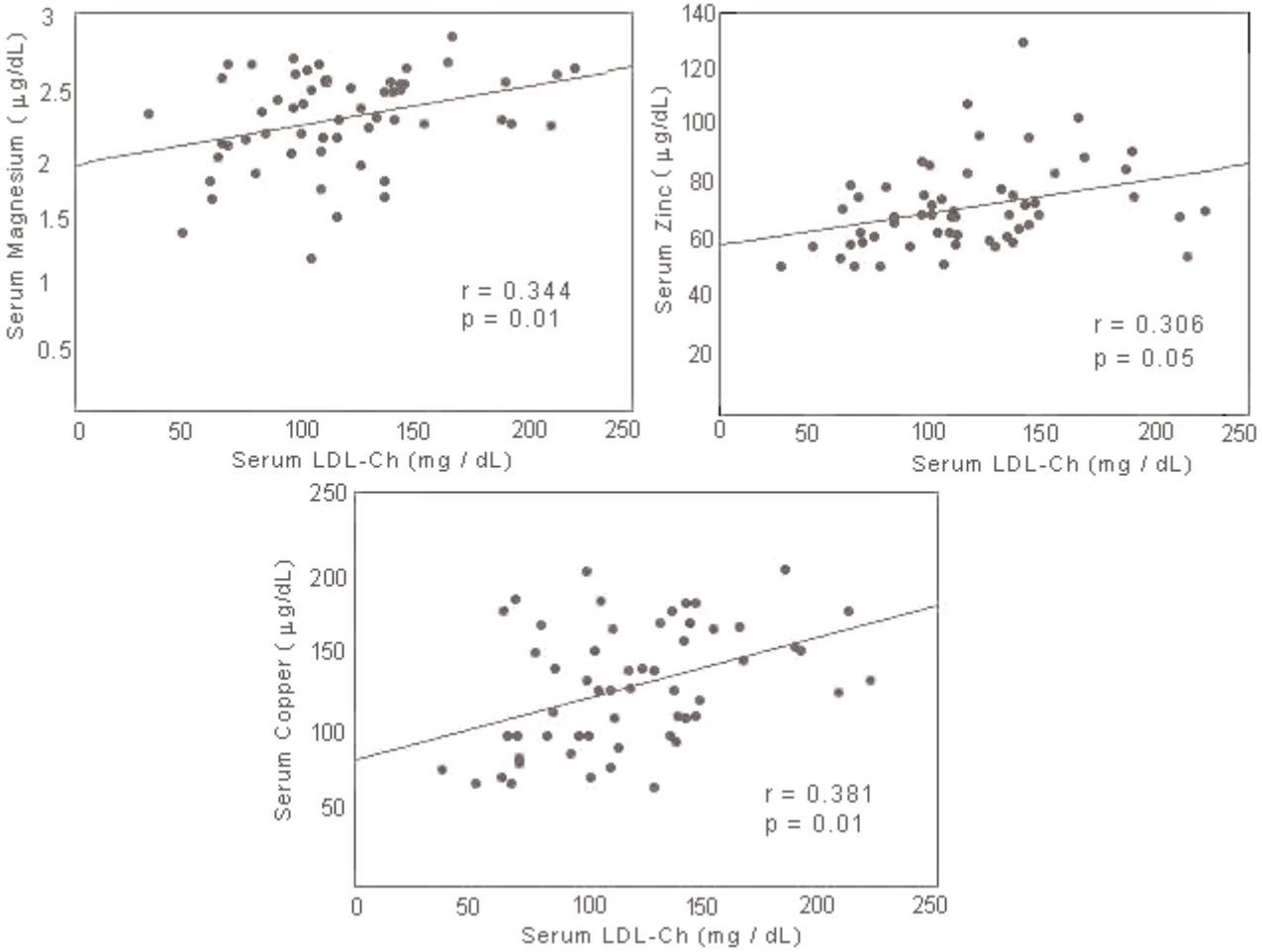
In the present study, serum magnesium level of AMI patients was significantly higher than that of healthy controls. The elevated serum magnesium may be due to the release of magnesium not only by the infarcted left ventricle but also by the non necrotic left ventricle and the right ventricle. The released magnesium entered the circulation (20). It is clear that all patients subgroups had significantly higher serum magnesium levels than controls but not group B.

AMI patients showed a slight decrease in serum iron levels as compared with control values. Also in the present study, various patients subgroups showed the similar reduction in iron levels but this decrease was significant in the last subgroup D. This decrease may be explained by infarction inducing a shift of serum iron into the reticuloendothelial system which may initiate ferritin synthesis (21). In addition, stress accompanying infarction increases the steroid activity which causes impairment of ferrokinetics (22). Reduced dietary iron intake may participate in the decrease of serum iron level but in the presence of infarction serum iron level continues to fall even during increasing dietary intake of iron (23).

Serum zinc levels of AMI patients or in various subgroups were not significantly different than that of control group. It was reported that a drop in serum zinc level occurred within the first three post-infarction days. This change rose back to near normal level by the tenth day (24). Our finding is in accordance with this result since our blood samples were withdrawn on the seventh day after onset of infarction.

Our results showed increased copper levels both in AMI patients and in all subgroups. Increased patients serum copper levels are a part of a specific defense mechanism to provide more copper at the site of infarction to reduce its size and the extent of damage (25). Also, the increase of ceruloplasmin, which is a copper containing enzyme and acute phase reactant,

Figure 1: Regression lines between serum LDL-Ch and magnesium, zinc and copper.



may account for the significant increase in serum copper levels (8).

It was demonstrated that there was an increase in the serum triglycerides during AMI (26), our finding was in agreement with this result. In general increased triglyceride levels may have a genetic basis (27). Nutritional habits may increase serum triglycerides as high consumption of saturated fats (28) and/or sucrose (29). Moreover, inherited or acquired abnormalities of lipoproteins especially very low density lipoprotein cause alterations in triglyceride levels (30). Furthermore, high concentration of apoprotein B in survivors of AMI may lead to accumulation of chylomicron remnants, very low density lipoprotein and intermediate density lipoprotein (31).

In the present research, serum triglyceride levels showed significant increase in all patients subgroups A, B, C and D when compared with that of control.

AMI has been reported to present in normocholesterolemic subjects (19) or hypercholesterolemic ones (3). This means that serum cholesterol level does not discriminate well between individuals with and without AMI. The reason of this may be attributed to changing the dietary habits of patients for better direction with regard to the quantity and quality of dietary fat intake (19). On the other hand, increased cholesterol level in some AMI patients may be attributed partly to alterations in the genetic characters (27). Also, high intakes of total fat have increased serum cholesterol (32). Since most of cholesterol in the plasma is carried by

Table 4: Comparison between serum triglycerides, total cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol levels in different groups of myocardial infarction patients and healthy control group.

Group	Mean ± S.E			
	Triglycerides (mg/dl)	Total cholesterol (mg/dl)	High density lipoprotein cholesterol (mg/dl)	Low density lipoprotein cholesterol (mg/dl)
Healthy subjects n=30	111 ± 7.11	197 ± 6.51	45.3 ± 1.95	93.1 ± 4.69
Patients with AMI (A) n=32	158*** ± 14.5	197 ± 10.2	32.9***** ± 2.18	114** ± 7.76
Patients with AMI and diabetes (B) n=8	177***** ± 11.5	208 ± 7.09	36.8**** ± 1.39	120***** ± 5.47
Patients with AMI and hypertension (C) n=8	172***** ± 11.6	210 ± 15	40.2 ± 6.11	125* ± 15.2
Patients with AMI and diabetes and hypertension (D) n=10	185***** ± 13.9	233 ± 17.2	41.1 ± 4.03	135*** ± 14.7

Values significantly differ from control group:
*$p \leq 0.05$, **$p \leq 0.025$, ***$p \leq 0.01$, ****$p \leq 0.005$ and *****$p \leq 0.001$.

LDL, an increase in LDL level directly may lead to an increase in total cholesterol level (33). The increase in apoprotein B serum level may have produced LDL-Ch increase which in turn raises T-Ch concentration (34). Different AMI subgroups showed non significant increase in their T-Ch levels.

Decreased levels of HDL-Ch in AMI patients were reported (19) which is a characteristic finding in this disease. The mechanisms responsible for this change may reside in the decreased synthesis and secretion of HDL-Ch from the liver or intestine and/or accelerated elimination from the blood stream by extravasation. Increased permeability of the capillary membranes during the acute inflammation after AMI lead to an extravasation of HDL-Ch (35). Suppressed synthesis of HDL-Ch due to lowered lecithin cholesterol acyl transferase activity and increased transfer of HDL-cholesteryl ester to apoprotein B containing lipoproteins as the cholesteryl ester exchange rate was increased (36). On the other hand, decreased levels of apoprotein A affect directly the HDL-Ch level (37).

Similar results were obtained from AMI subgroups, where HDL-Ch levels were decreased in all subgroups but the decrease was significant only in subgroups A and B.

Concerning the increase of LDL-Ch level, this finding is in concurrence with that reported by Sandkamp *et. al.* (38). LDL-Ch is probably the most atherogenic of all lipoproteins when the plasma concentration of LDL-Ch is elevated; accumulation of cholesterol and therefore formation of atherosclerotic lesion take place of the wall of the vessels. Elevated plasma LDL-Ch may be due to either a decrease in its clearance or overproduction of this lipoprotein (39). LDL-Ch is cleared from

the circulation partly by cellular uptake via specific LDL receptors located on the cell surface. Coronary heart disease modifies these receptors by blocking some of them (40). As a result serum LDL-Ch uptake is reduced. A high production rate of LDL consequently might be due to either overproduction of VLDL (precursor of LDL) or to a decrease in fractional removal of VLDL remnants. The latter may result from the decrease in LDL receptors activity. Moreover, apoprotein B plays an important role in elevating LDL-Ch levels since increased concentration of it may merely increase the concentration of LDL-Ch (41).

Also, patients with associated diseases had significant increase in LDL-Ch levels as compared with control. These data reveal that diabetes and/or hypertension were not the causes of the observed changes in lipid parameters in our patients. This finding is in accord with the documented results presented over a decade (37).

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