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# Homocystein and Trace Elements Levels in Patient with Ischemic Heart Disease and some Associated Diseases

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## Abstract

This paper includes the determination homocysteine level and trace elements magnesium (Mg), zinc (Zn) and iron (Fe) in ppm (part per million); lead (Pb), cadmium (Cd), selenium (Se), chromium (Cr) and germanium (Ge) in ppb (part per billion) in random serum of patients with pure ischemia, ischemia with hypertension and ischemia with diabetes. Homocysteine level was significantly increased ( $P < 0.01$ ) in pure ischemic patients, ischemia with hypertension and ischemia with diabetes in comparison with control group. A comparison had also been done between male & female groups in patients and control groups and no significant changes ( $P > 0.05$ ) were observed. The result of this study showed that concentration of the trace elements (Pb & Cd) were significantly increased ( $P < 0.01$ ) in patients groups in comparison with control group and the concentration of (Mg, Zn, Se, Cr and Ge) were significantly decreased ( $P < 0.01$ ) among patients groups in comparison with control group.

**Keywords:** Homocysteine, High performance liquid chromatography, Trace elements, Atomic absorption spectrography. Ischemic heart disease.

## 1. Introduction

Homocysteine (Hcy) is an intermediate of methionine metabolism [1]. Elevated blood homocysteine concentration was an independent risk factor for cardiovascular disease [1, 2]. High-normal serum homocysteine concentrations are associated with an increased prevalence of carotid artery wall thickening [3]. The significance of the contribution of homocysteine to the variation of carotid intima-media thickness suggests a role for homocysteine as an independent risk factor for early carotid artery atherosclerosis in the asymptomatic subjects. Different studies indicated that the elevated level of total homocysteine (tHcy) had increased the risk of cardiovascular diseases and stroke [4]. Homocysteine is elevated in the case of inborn errors of methionine metabolism and excessive amount of homocysteine and its derivatives are found in blood and tissues of cardiovascular patients [5]. Moderate hyperhomocysteinemia up to ( $30 \mu\text{mol/l}$ ) is a major independent risk factor of a number of diseases characteristic of old ages, primarily occlusive vascular disease [6]. Non metallic elements (hydrogen, oxygen, carbon and nitrogen) make 99% of all the elements in human body, while major elements, which are calcium, magnesium, phosphorus, sulfur and chlorine, make 0.9% of the total. However, essential trace elements provide approximately less than 0.1% of human body [7]. Trace metals are metals in extremely small quantities,

almost at the molecular level, that reside in or are present in animal and plant cells and tissue. Trace metals are a group of metals that include both heavy and transitional elements present in micrograms quantities in the blood. There are divided into two groups, essential for health and have no known biological function.

In human body, there are some metals which naturally exist and are essential to human health. These essential metals at trace levels play vital role when present in human body and may cause some diseases when present beyond specific concentrations [8, 9].

## 2. Designing

### MATERIALS AND METHODES

**Patients:** The study was conducted during the period from August, 2008 to May , 2009 in Merjan hospital in Hilla city , Babylon province, Iraq. A total 57 patients were included from urban and rural area(35 males and 22 females) (Table 3-1). Twenty three patients had pure ischemic heart disease (17 males and 6 females), 18 had ischemic heart disease with hypertension (10 males and 6 females),18 had ischemia heart disease with diabetes (8 males and 10 females ). The age of the patients varying between 40-85 years old (mean± SD 57.82±10.25).

**Control Group:** The control group consisted of 40 healthy person who were chosen as healthy, non smokers , didn't have any history of chronic disease and didn't take any treatment for chronic diseases

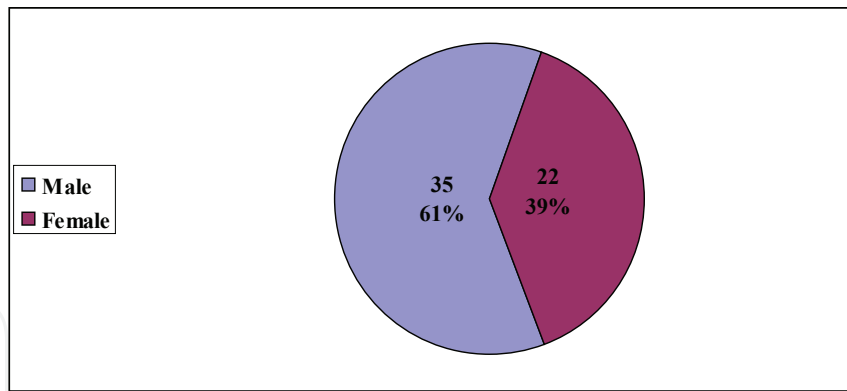
## 3. Results

The patients and control were divided according to ages into two groups group 1 in which the age range between 40-60 year and age group two in which the age is > 60 year as shows in table 1.

	Patients	Age	
		40- 60 year	60 year<
Ischemic patients	Pure ischemia	11	12
	Ischemia with hypertension	14	12
	Ischemia with diabetes	8	10
	Control	124	16

**Table 1.** Patients and control number according to age group

The sex distribution of total ischemic patients, was clearly obvious . The highest percentage in male was 61% while female was 39% ( figure 1).



**Figure 1.** Sex distribution of total ischemic patients.

Table 2 show the sex distribution for all patients in this study. Number of female patients in ischemia with diabetes was more than male patients while in ischemia and ischemia with hypertension male patients were more than female.

	Groups	Number			
		Male	%	Female	%
Patients	Pure ischemic patients	17	31	6	14
	Ischemic patients with hypertension	10	18	6	14
	Ischemic patients with diabetes	8	15	10	24
	Control	20	36	20	48
	Total	55		42	

**Table 2.** Sex distribution in the study groups

Comparison between ischemic male or female and similar sex healthy controls results indicate an increase in level of homocysteine among patients groups. This elevation in homocysteine concentration value was highly significant ( $P < 0.01$ ). When similar comparisons were done between ischemia with hypertension and ischemia with diabetes and control group a similar behavior were observed ( $P < 0.01$ ). Table 3 shows the mean values of serum level of homocysteine in male and female compared with the mean values in control group. No significant changes was observed when comparison was done between two age groups as shown in table 4.

Groups	Male Mean $\pm$ SD	Female Mean $\pm$ SD
Control	9.58 $\pm$ 0.93	9.11 $\pm$ 0.65
Ischemic patients	24.11** $\pm$ 5.45	25.4** $\pm$ 2.5
Ischemia with hypertension	20.84** $\pm$ 3.38	23.9** $\pm$ 4.85
Ischemia with diabetic	22.16** $\pm$ 3.59	21.26** $\pm$ 1.44 $\pm$

\*\*  $P < 0.01$

**Table 3.** The mean serum level of homocysteine in male and female patients groups and control group

Age group	Pure ischemia	Ischemia with hypertension	Ischemia with diabetes
40-60	23.29±5.3	19.83 ± 1.81	24 ± 4.62
> 60	25.32 ±4.93	22.88 ±4.87	21.02 ±1.23

**Table 4.** Comparison of levels of homocysteine ( $\mu\text{mol/l}$ ) between two age groups ( age group 1 (40-60) and age group 2 (>60))

There is a highly significant increase in homocysteine level in ischemic patients compared with control values ( $P < 0.01$ ). Also there is significant increase in homocysteine level in patients with ischemia with hypertension & ischemia with diabetes compared with control patients as shown in table 5.

Groups	Mean $\mu\text{g/ml} \pm \text{SD}$
Control	9.35±0.82
Ischemic patients	24.31 **±5.09
Ischemia with hypertension	22.46**±4.61
Ischemia with diabetic	21.84**±2.96

\*\*  $P < 0.01$

**Table 5.** The mean serum level of homocysteine ( $\mu\text{mol/l}$ ) in different patients groups and control groups

There is no significant changes in serum homocysteine level between pure ischemic patients, ischemia with hypertension and ischemia with diabetes ( $P > 0.05$ ).

Measurements of trace elements in serum of two age groups (40-60) and > 60 years shows no significant changes in their levels ( $p > 0.05$ ). Table 6 shows comparison of trace metal concentration in control group between two age groups

Trace elements	Concentration ( mean $\pm$ SD )		
	Age groups of 40- 60 year	Age groups of >60 years	
$\mu\text{g/ml}$	Mg	19.6±1.47	19.59±1.84
	Zn	1.04 ±0.37	1.03±0.13
	Fe	1.06±0.18	1.05±0.13
	Pb	0.09±0.15	0.12±0.19
ng /ml	Cd	0.00	0.00
	Se	102.65±18.03	103.75±10.05
	Cr	55.22±6.79	55.98±6.17
	Ge	42.43±4.41	41.54±4.18

**Table 6.** Comparison of trace metal concentration in control group between two age groups

Measurements of trace elements in two age groups (40-60) and > 60 years in all patients groups shows no significant changes in their levels ( $p > 0.05$ ) as shown in table 7.

Age groups	Pure ischemia			Ischemia with hypertension			Ischemia with diabetes		
	Mg	Zn	Fe	Mg	Zn	Fe	Mg	Zn	Fe
40-60	14.43 ±2.33	0.73 ±0.17	1.5 ±1.77	14.25 ±1.08	0.73 ±0.11	1.01 ±0.13	17.9 ±3.73	0.95 ±0.23	0.94 ±0.19
>60	14.32 ±3.03	0.6 ±0.12	1.15 ±0.76	14.5 ±1.36	0.68 ±0.2	1.41 ±1.23	13.14 ±1.95	0.68 ±0.24	0.96 ±0.19
All ages	14.38 ±2.46	0.66 ±0.16	1.33 ±1.36	14.43 ±1.27	0.96 ±0.18	1.3 ±1.06	15.26 ±3.66	0.8 ±0.26	0.95 ±0.18

**Table 7.** Comparison of levels of (Mg , Zn and Fe ) between two age groups { age group 1 (40-60 year) and age group 2 (>60 year)}.

**Trace elements level:**

There is a significant decrease in the level of magnesium, zinc ,selenium , chromium & germanium in all patients groups in comparism with control group ( $P < 0.01$ ) & significant increase level of both lead & cadmium in all patients group than that of control group ( $P < 0.01$ ) while there is no significant changes in the level of iron ( $p < 0.5$ ) as shown in table 8.

	Trace elements	Control	Pure ischemia	Ischemia with hypertension	Ischemia with diabetes
g/mlµ	Mg	19.59±1.58	14.38±2.64**	14.44±1.27**	15.25±3.66**
	Zn	1.16±0.22	0.66±0.15**	0.68±0.18**	0.8±0.26**
	Fe	1.06±0.18	1.33±1.36	1.30±1.06	0.95±0.19
ng/ ml	Pd	0.11±0.17	6.39**±2.89	5.63**±1.73	3.58**±1.06
	Cd	0.00±0.00	5.07**±2.69	4.78**±1.83	4.89**±1.75
	Se	103.64±11.95	53.37**±14.85	61.53**±11.17	61.81**±7.19
	Cr	55.21±6.93	32.42**±6.95	32.05**±11.77	31.02**±3.21
	Ge	42.37± 4.76	18.51**±6.14	16.9**±5.19	14.61**± 6

**Table 8.** Trace elements level in control & patients groups. \*\* ( $P < 0.01$ )

**4. Discssion**

The relationship between increased homocysteine and heart disease is well established in the medical community. Unlike the other three predictors of heart disease which are cholesterol, triglycerides and C Reactive Protein, homocysteine levels are influenced by what the person does not eat rather than what he does eat. This is due to the fact that homocysteine is a sulphhydryl-containing amino acid derived from demethylation of methionine. Nutritional deficiencies in the

vitamin cofactors (folate, vitamin B12, and vitamin B6) required for homocysteine metabolism may promote hyperhomocysteinaemia [10]. This means that increased homocysteine levels are associated with increased risk of cardiovascular disease and then tHcy measurement will become another useful marker of vascular risk, multivitamin therapy will be another therapeutic option for people at risk of atherothrombotic vascular disease, and fortification of food with folic acid will rise high on the political and public health agenda. Homocysteine level in all patients with heart disease in this study ( pure ischemia, ischemia with hypertension and ischemia with diabetes ) were found to be elevated significantly ( $P < 0.01$ ) compared with control groups. Only about two-thirds of all episodes of symptomatic atherothrombotic vascular disease in developed countries can be attributed to established genetic and environmental vascular risk factors [11]. An additional causal vascular risk factor may be raised plasma levels of homocysteine (hyperhomocysteinaemia).

Mild hyperhomocysteinaemia occurs in approximately 6% of the general population [12,13 ]. Patients with mild hyperhomocysteinaemia are typically asymptomatic until the third or fourth decade of life when premature coronary artery disease develops, as well as recurrent arterial and venous thrombosis. The elevation of serum level of homocysteine (hyperhomocysteinemia) in this study could be considered as a risk factor for cardiovascular disease. Research has shown that increased homocysteine level is associated with both the hyperinsulinemia seen with insulin resistance and increased urinary albumin excretion. It is also associated with low serum levels of vitamin B12 [14]. However, supplementation with vitamin B12 has resulted in reduction of homocysteine levels, but as failed to show subsequent reductions in incidence of cardiovascular disease [15]. Trace elements are micro-nutrients, present in blood and tissues. They are essential for enzymatic activities and metabolic processes and even for vital functions [16, 17] . Some trace metals have antiviral activity, while others may alter the genome of the viruses enhancing their virulence [18]. Several trace elements are of great importance in a number of biological processes, mostly through the following terms:

- 1- Their action as activators or inhibitors of enzymatic reactions,
- 2- Competing with other elements and proteins for binding sites,
- 3- Influencing the permeability of cell membranes.

It is therefore reasonable to assume that these minerals would also exert an action, either directly, or indirectly, on the cardiac cell, on the blood vessel walls, on the blood-pressure-regulating centers, or on other systems related to cardiovascular function. A study showed that the mean values of serum magnesium were lower in patients with acute myocardial infarction than in non cardiac patients. The authors suggested that a lowering or elevation of serum trace elements could be useful in the diagnosis of recent infarction and could possibly have other implications [19]. Table 6 shows that serum magnesium level was decreased in all patients in comparison with control & this is in agreement with most studies [20]. The disturbances of magnesium metabolism may have profound effect on the contractile state of vascular smooth muscle and as a result on blood pressure. Accordingly, magnesium is particularly important for assessment of hypertension. [20] Reported that magnesium deficiency has a role in the pathogenesis of hypertension.



The results of this study show that there was a reduction in iron serum level of ischemia with diabetes patient and an elevation in patients with ischemia and ischemia with hypertension compared with control group. However, these changes were not significant ( $P>0.05$ ). This was explained due to the fact that ischemic heart diseases, diabetes and hypertension as diseases occurs with variant risk factors mostly not affect the levels of iron if these diseases occur from risk factors other than those in the previous points. The results reveal a significant increase  $p<0.01$  in serum lead of ischemic heart disease, hypertension and diabetes patients where when compared with the corresponding control values. Till (1997), believed that there was no known biological requirement for germanium (Ge) which was regarded as not an essential element [21, 22]? However, recent study observed that different symptoms in the deficiency of germanium such as cardiovascular disease, atherosclerosis, higher risk for several cancers, osteoporosis, and arthritis weakened immune system, decreased oxygen [23].

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