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Study of Determination and Effect of The Level of Copper, Zinc, Selenium and Body Mass-Index in Hyperlipidemia Patients in Babylon Province

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Abstract

Background: Hyperlipidemia is common in public, the link between trace elements and Hyperlipidemia is not clearly studied. For humans, copper, zinc and selenium are essential trace elements in nutrients and required in very small quantities for various biological functions. During disease, trace elements used for diagnosis, it is essential to distinguish whether the balance is altered in free or bound elements.

Objective: For the assessment of copper, zinc, selenium and body mass index level and to examine the correlation between parameters and study the probable relation of them with diagnosis of hyperlipidemia in Babylon province.

Materials and Methods: Cu, Zn and Se were estimated in one hundred subjects; 50 patients with hyperlipidemia and 50 healthy subjects were participated in this study. Patients and control groups with an age ranged between (19-75) years. The level of Zn and Cu and Se were assessed in serum by Flameless Atomic absorption spectrophotometer method.

Results:

Serum levels of selenium and zinc displayed a significant decrease, while serum copper significantly elevated ($p < 0.001$) in hyperlipidemia patients. On the other hand, selenium and zinc correlated significantly with body mass index.

Conclusion:

Among hyperlipidemia patients in Babylon province, the variability in some trace elements indicate the significant relationship with hyperlipidemia.

Keywords: hyperlipidemia, zinc, copper, selenium, body mass index.

Introduction

Hyperlipidemia represent an elevation in one or more of the plasma lipids, comprising triglycerides, cholesterol, cholesterol esters and phospholipids and or plasma lipoproteins including very low density lipo-protein and low-density lipoprotein, plus reduction of high-density lipoprotein levels **[1]**.

Hyperlipidemia classified bases on the lipid type into (Hypercholesterolemia, Hypertriglyceridemia) or bases on causing factor into (primary: Familial: hyperlipidemia, secondary: Acquired hyperlipidemia) **[2]**.

In the arteries walls, the deposition of these lipids (especially cholesterol) causing in narrowing of these vessels and inadequate blood flow through these vessels and development of atherosclerosis. The presence of other dominant diseases (like hypertension, diabetes mellitus, and renal disorders) improved morbidity and mortality rates **[3]**.

Generally, the mortality by cardiovascular diseases in 1990 about 14.4 million subjects and this level elevated to 17.5 million in 2005, while in 2015 this number probably be 20 million. Thus, dyslipidemia represented the chief risk factor for cardiovascular diseases and mortality **[4]**.

Over 25 years ago, the unusual opinions on the sensitivity of plasma lipids to dietary fat and cholesterol was made. Hyperlipidaemias were limited to men, but the measurable relation advanced from these results has been freely generalized to women also. Still, the distribution of lipoprotein lipids and some enzymes that control lipoprotein metabolism, vagaries between men and women **[5]**.

Hyperlipidaemia associated with the development of atherosclerosis and ischemic heart disease (IHD). The treatment and prevention of hyperlipidaemia is promising to lower the prevalence of IHD-related mortality and morbidity significantly **[6]**.

The first-line drugs for the treatment of hyperlipidemia is Statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors), have an important role in the treatment of familial and severe hypercholesterolemia by decrease LDL-C and TG levels and increase HDL-C levels **[7]**.

Trace elements like copper (Cu), zinc (Zn) and selenium (Se) are crucial for humans nutrients and very little amounts are essential for several physiological functions, comprising immune function, antioxidant function, reproduction and growth. About 72 trace elements are need for humans, containing heavy metals with low concentration, such as Cu, Se, V, Cr, Mo, Mn and Co **[8]**.

Most metals at high concentrations are toxics, while other at low concentrations have harmful effects. The importance of nutritional and biochemical roles of trace elements is broadly documented, as metals are establish as component of numerous metalloenzymes and metalloproteins **[9]**.

Numerous studies demonstrated the link between body weight and hyperlipidemia disease. Beside several revisions established the link between body mass index (BMI) and hyperlipidemia is similar among men and women **[10]**.

Numerous enzymes, which may have a crucial role in preventing atherosclerosis, need copper, zinc, and selenium as part of their functional groups **[11]**.

Some of the current epidemic of IHD may be caused by copper deficiency. Copper Consumption has been on the decline, so, several people may be getting less amount of copper. Many of the complication of inflammatory heart disease (IHD) might be due to the involvement of copper in some biological processes, and copper deficiency can have severe consequences **[12]**.

Insufficient copper levels make lipoproteins (LDL, HDL, VLDL) more susceptible to oxidation. Lipoproteins (from copper-deficient animals) produce more thiobarbituric acid reactive compounds after exposed to oxidative courses involving iron, that mean copper may run a protective effect against oxidation induced by iron. Enzymes that protect against oxidative modification contain copper , like copper, zinc superoxide dismutase, and also may catalyse lipoproteins oxidation **[13]**.

For human health, selenium and zinc are essential micronutrient, might have a role in improvement of atherosclerosis. Zinc might involve in the atherogenic process by interaction with atherogenic cells, like endothelial cells (ECs), immune cells and vascular smooth muscle cells (VSMCs). Furthermore, zinc applies main positive or negative roles in various atherosclerosis complication, including blood pressure, lipid metabolism and glucose metabolism **[14]**.

Zinc deficiency even in small amount can causes change in pathological situations, specially age-related disease, such as atherosclerosis **[13]**.

The study conducted to estimate the association and changing of some trace elements among body mass index in hyperlipidemia patients.

Materials and methods

Study design

Case-control study is the design of this revision.

Patients and control

Daniel sample size formula equation were used for the designated of sample size. One hundred Iraqi subjects were participated in this revision, fifty of the members have hyperlipidemia (diagnosed based on elevated concentration of triglyceride,cholesterol and

LDL with decreased concentration of HDL), clinical history was taken from all patients, that comprise: age, body mass index, gender, family history, duration of treatment by statins and tobacco use.

Fifty subjects appear healthy were contributed as control group. The age of studied groups between 19 to 75 years. Pregnant women, concomitant acute or chronic inflammatory disorders and patients with malignancy, were excluded from the revision. SPSS version 20 was conducted for the statistical analysis. Mean ± SD were used for the expression of results, and P values considered significant when it is less than 0.05.

Chemicals and methods

1- The level of zinc copper and Selenium were assessed in serum by Flameless Atomic absorption spectrophotometer method by the technique of Graphite Furnace (GFAAS).

2- Triglyceride and total cholesterol levels were assessed by enzymatic colorimetric methods, but the enzymatic method after phosphotungsten/ magnesium precipitation was used for high-density lipoprotein cholesterol levels estimation.

3- Body Mass Index (BMI) was intended by weight (in kilograms) divided by the square of height (in meters) **[15]**.

BMI = Weight (kg) / Square Height (m^2).

Ethical approval

Before sample was taken, the study was approved with patients verbal and analytical approval. The study procedure and the subject information and agreement form were studied and approved by a local ethics committee.

Results

The studied individuals consist of 100 adults designated on two groups:

1- Adults have hyperlipidemia (n=50)

2- Adults as control group (n=50)

Age

The discrepancy in age (as mean±SD) showed significant different among control (33.8±9.42) and hyperlipidemia group (52.9±16.0), demonstrated in figure 1.

Gender

Spreading of hyperlipidemia group rendering to sexual characteristics that shown in figure. 2. The current review established that the prevalence of hyperlipidemia group in female (54%) is larger than males (46%).

Body mass index (BMI)

The mean [M] ± standard deviation [SD] of BMI for control and hyperlipidemia group were 23.2± 2.47 and 26.7± 2.0 respectively. The result of the study shown significant difference in BMI in patients and control group (p < 0.00), as shown in figure 3.

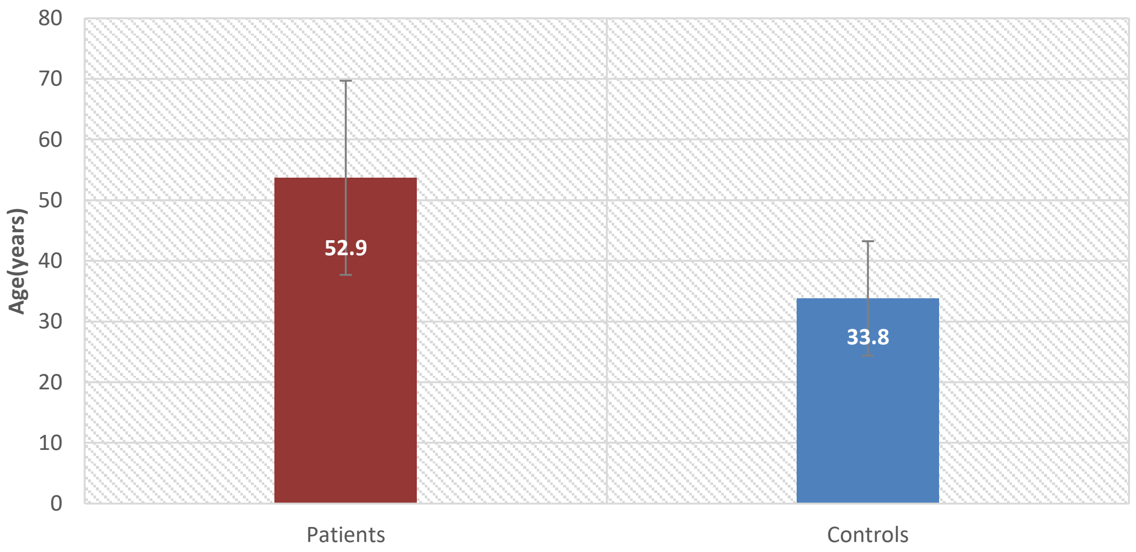
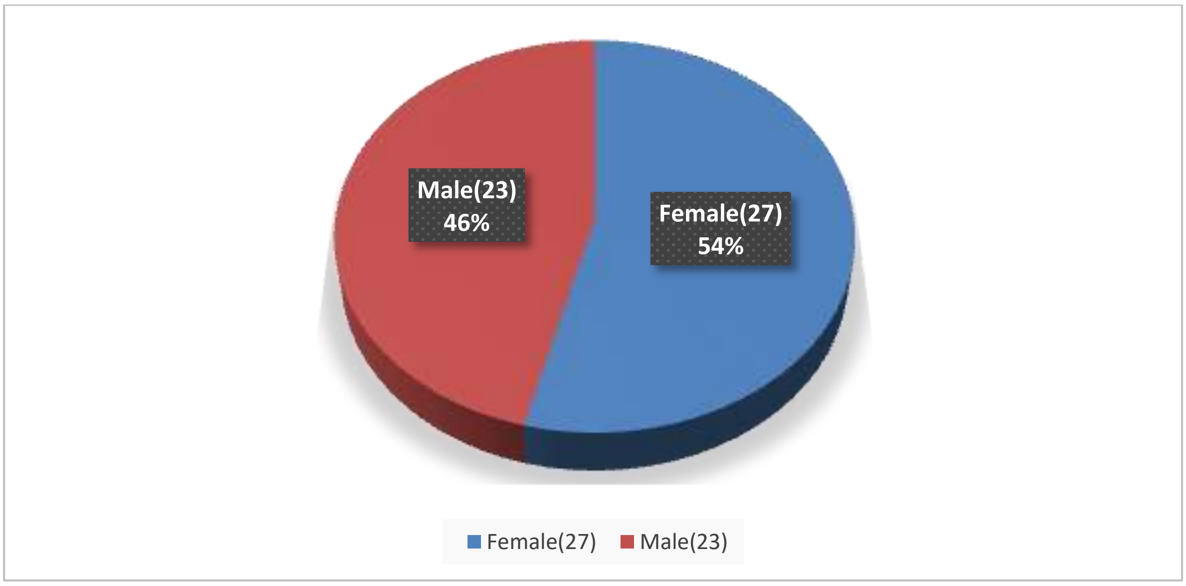


Figure (1): The mean differences of age according to study group (P 0.00)



Figure(2): The ratio of males to females in hyperlipidemia patients.

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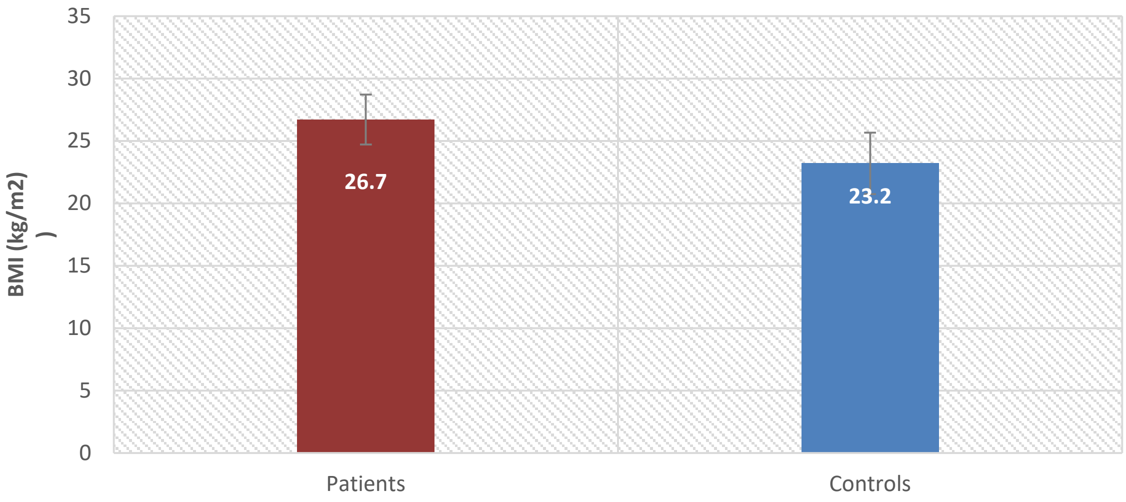

Figure (3): The mean differences of BMI according to study group

The biochemical parameters measured in hyperlipidemia patients and control group
Table (1) shows decrease concentration of selenium and zinc and increase concentration of copper in hyperlipidemia patients compared with the control with significant (p value < 0.05) mean differences between them.

Table (1): The mean differences of biochemical parameters rendering to study group

Parameter	Group	N	Mean ± SD	-Test	- Value
CHO(Mg/Dl)	Patient	50	252.2± 48.3	10.8	0
	Control	50	171.8± 20.0		0.001
TG(Mg/Dl)	Patient	50	338.9 ± 102.27	15.4	0
	Control	50	101.4 ± 36.13		0.002
HDL(Mg/Dl)	Patient	50	54.0 ± 12.0	- 2.2	0
	Control	50	59.1± 10.4		0.02
LDL(Mg/Dl)	Patient	50	123.1± 53.6	0.15	0
	Control	50	121.7± 28.69		0.87
VLDL(Mg/Dl)	Patient	50	67.7 ± 20.9	13.9	0
	Control	50	24.6 ± 6.38		0.00
Se (Ppb)	Patient	50	34.9±23.1	- -18.8	0
	Control	50	119.3±21.6		0.001
Cu (Ppb)	Patient	50	202.5 ± 14.46	38.1	0
	Control	50	101.1 ± 11.99		0.00
Zn (Ppb)	Patient	50	39.3 ± 6.2	- 36.2	0
	Control	50	95.4 ± 8.98		0.001

SD= standard deviation; p< 0.05: significant

Correlation between copper, zinc and selenium concentration with age and body mass index in hyperlipidemia patients.

A significant negative relationship was detected between copper with selenium and zinc (r = -0.714, p = 0.001 and r = -0.816, p = 0.001) concentration, respectively.

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Also, selenium was significantly correlated with body mass index and correlated negatively with zinc concentration in hyperlipidemia patients.
While, zinc have significant correlation with body mass index in patients group, (p<0.00) (Table 2).

Table (2): Correlation between parameters with age and BMI.

		AGE	BMI	CCu (ppb)	SSe (ppb	ZZn (ppb)
Cu (ppb)	**Rr**	**..020**	**--.266**	**11**	**--.714***	**--.816***
	pP-value	**..890**	**..061**		**..000**	**..000**
	nN	**550**	**550**	**550**	**550**	**550**
Se (ppb)	**Rr**	**..028**	**..314***	**--.714***	**11**	**..775***
	pP-value	**..849**	**..026**	**.000**		**..000**
	nN	**550**	**550**	**550**	**550**	**550**
Zn (ppb)	**Rr**	**..033**	**..309***	**--.816***	**..775***	**11**
	pP-value	**..821**	**..029**	**..000**	**.000**	
	nN	**550**	**550**	**550**	**550**	**550**

***. Correlation is significant at p< 0.05**

Receiver operating characteristic (ROC) analysis of the copper, zinc and selenium

A ROC curve (Table 3) was used to determine the threshold serum copper, zinc and selenium level for diagnosing hyperlipidemia in relation to the normal control.

Zinc and copper were showed an excellent sensitivity and specificity in discriminating hyperlipidemia from normal state with an AUC (area under the curve) of (94%, 91%) with sensitivity (92%, 90%) and specificity of (90%, 92%) at a cut off value (71.5 ppb, 147 ppb) respectively.

While, selenium was showed a good sensitivity and specificity in discriminating hyperlipidemia from normal state with an AUC (area under the curve) of (98%) with sensitivity (88%) and specificity of (92%) at a cut off value (≤ 70.0 ppb).

Table (3): ROC curve of copper, zinc and selenium

Parameter	CU	Se	Zn
Cut-off point	**≥ 147**	**≤ 70.0**	**≥ 71.5**
AUC	**0.91**	**0.98**	**0.94**
sensitivity	**90.0 %**	**88.0 %**	**92.0 %**
specificity	**92.0 %**	**92.0 %**	**90.0 %**
P value	**0.00**	**0.00**	**0.001**

Discussion

The most affected public illness round the word in both industrialized and unindustrialized countries is Hyperlipidemia **[2]**.

There are several factors that may have a role in the progression of hyperlipidemia, including: age or sex, family history, obesity, diabetes, change in lifestyle and some of drugs **[16]**.

This fact was in harmony with the measurements of this revision, the mean age of subjects who were established as hyperlipidemia patients and control were 52.9 and 33.8 years, respectively.

Furthermore, this review found a slight female predominance 54%, this outcome is in contrast with those of **[17]**, they found that women are more 'protected' than men against hyperlipidemia, but they have less effect on treatment.

In this study patients have a higher BMI than controls, and this is similar to Brown, C.D **[18]**, who suggested that hyperlipidemia is associated with a high BMI.

As showed in table-2, there were significant variances in the levels of lipid markers and hyperlipidemia prevalence between patients and control groups. The patients group displayed unusually elevation of total cholesterol, and very low density lipoprotein while low density lipoprotein non-significantly elevated.

There were numerous suggested causes for these alterations, i.e. elevation of lipid in aging people, with loss of hepatic LDL receptors according to age, obesity, higher waist circumference and inferior the level of sex hormone, among others **[19]**.

The association of triglycerides with central obesity is known, consequently hyperlipidemia patients in this study have higher body mass index, and this clarify why triglycerides level elevated significantly **[20]**.

High density lipoprotein decreased significantly in hyperlipidemia patients. This fact is consistent in previous studies: some assumed adverse correlation between age and HDL cholesterol levels, while another institute sex-differences in the alteration of HDL-levels with age **[21]**.

Trace elements might be used as a detecting markers through disease, it is essential to distinguish the balance is altered in free or bound elements.

Copper, zinc and selenium are vital constituents of the functional groups of numerous enzymes that may have a role in prevention of atherosclerosis. These comprise the antioxidant enzymes superoxide dismutase and glutathione peroxidase **[22]**, and endothelial nitric oxide synthase, the enzyme liable for the basal explanation of nitric oxide by the endothelium **[23]**. Several years ago, the ratio between serum copper and zinc projected a chief method for coronary risk determinant, concluded their effects on lipid metabolism **[24]**.

In Table-1, decrease Se and zinc with P-Value (0.00) in hyperlipidemia patient was sign, while Cu increase significantly with P-Value (0.00). Furthermore, Se and Zn correlated significantly with BMI. After taking statins, decrease in selenium, and zinc is very common in hyperlipidemia patients. Statins affect most trace elements in the body, preventing these elements absorption, and this is consistent with old and recent study.

Patients with hyperlipidemia have a decrease in zinc, and they should take supplements containing zinc, because zinc is vital element in fat metabolism **[12]**.

The natural role of trace metals, particularly serum Zn and Cu in diverse illness has been broadly examined in recent years **[25]**. Parallel observation was made by Lin CC, et al **[26]**.

This study is in consistent with Cunnane S C J **[27]**, while Koo and Willams **[28]**, originate non important association among the Cu and hyperlipidemia.

Engle T. *et al.***[29]**, recommended that insufficiencies of some trace elements, such as Zn, Cu and Se lead to changes in lipid metabolism and lipoprotein metabolism, this explain the negative correlation of trace elements with hyperlipidemia. Our findings consistent with the results of El-Hendy et al **[30]** ,presented that trace elements insufficiency increases serum cholesterol in a dose dependent.

The detection rate for hyperlipidemia was 94%, 91% and 98% using a threshold zinc value of 71.5 ppb, copper value 147 ppb and selenium value of 70.0 ppb, but these results must be taken cautiously because of the small sample. The effect of hyperlipidemia on the zinc, copper and selenium level in hyperlipidemia patients must also be considered.

This inconsistency with preceding outcomes might product from diverse ethnicities, the sample size and design of study.

Conclusion

Among hyperlipidemia patients in Babylon province, alteration in the level of copper, zinc, selenium with body mass index; may indicate the significant linked to hyperlipidemia diseases.

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