Evaluation of Changes in Levels of Serum Selenium in Diabetic Pateints and in Diabetic Pateints with Cardiovascular Disease

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Abstract

Selenium, an essential micronutrient, may affect several cardiometabolic risk factors, such as glucose homeostasis and lipid concentrations. The aim of this study is to examin the relation between serum selenium concentrations with serum lipids in diabetic patients and in diabetic patients with cardiovascular diseases (CVD).A case control study conducted in the National Diabetes Center, College of Medicine at Al-Mustansiryia University. Fasting glucose, total cholesterol, high density lipoprotein–cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), and very low density lipoprotein-cholesterol (VLDL-C), HbA1c and Serum selenium were determine. Diabetes mellitus (n=256) divided into tow groups, group I (n=156) diabetic patients and group II (n=100) diabetic patients complicated with CVD. Normal healthy subjects were taken as control (n= 100).In the present study a significant decrease in selenium levels was found in patients groups compared to control also there is decrease in selenium levels of diabetic patients with CVD (group II) compared with diabetic patients (group I). These findings indicate that the decrease in serum selenium was associated with elevated serum concentrations of fasting blood glucose, total cholesterol, LDL-C, VLDL-C, triacylglycerols and duration of diabetes. In general despite their classification according to sex or diabetes type highly negative correlations ($p<0.0001$) were found with linear regression equations between fasting serum selenium concentration and HbA1c in patients group II. In conclusion the significant reductions in the level of selenium in diabetic patients may be response on the developing t he diabetic to anther disease like CVD.

Keywords: Selenium, lipid profile, antioxidant, diabetes, cardiovascular diseases.

Introduction

Selenium is an essential trace element. Its importance is underlined by the fact that it is the only trace element to be specified in the genetic code - as selenocysteine. Selenium is a key component of several functional selenoproteins [e.g., glutathione peroxidases (GPx), thioredoxin reductases, iodothyronine deiodinases and selenoprotein P] that protect tissues and membranes from oxidative stress and control the cell redox status [1,2]. Evidence from in *vivo* and in *vitro* studies suggests that selenium could enhance insulin sensitivity by mediating insulin-like actions [3,4]. Oxidative stress reduces insulin secretion and increases insulin resistance in some experimental models and may thus play a causal role in the pathogenesis of diabetes [5-9]. Selenium, an essential trace element, is involved in the complex system of defense against oxidative stress through selenium-dependent glutathione peroxidases and other selenoproteins [10,11]. Because of its antioxidant properties, selenium might thus prevent the development of diabetes [12,13]. These metabolic changes associated with compromised selenium status may lead to damage of the vascular endothelium and increased platelet adhesion which increase the risk of atherosclerotic heart disease [14]. Studies in rats show a beneficial effect of selenium supplementation on lipid abnormalities in plasma, aorta, and adipose tissue [15]. Observation studies of assiation between selenium and lipids are inconsistent, finding positive association of serum selenium with total cholesterol [16,17,18], with LDL cholesterol [12,18], or with HDL cholesterol or ratio of HDL cholesterol to total cholesterol (HDL cholesterol: total cholesterol) [18-20]. Those studies were conducted mostly in populations with relatively low serum concentrations of selenium, and their generalizability to a selenium-replete population is uncertain [10-14].

In addition, selenate, an inorganic form of selenium, mimics insulin activity in experimental models [21, 22]. Results from human studies on selenium and diabetes are

conflicting. Two studies found lower serum selenium concentrations in diabetic patients than in control subjects [23,24] while in the Health Professionals Follow-up Study, by contrast, higher serum selenium concentration was associated with a higher prevalence of diabetes [26,27], higher fasting plasma glucose and glycosylated hemoglobin levels [27] in the National Health and Nutrition Examination Survey [26,27]. Randomized trials again showed discordant findings: in the SUVIMAX trial, despite positive correlations between plasma selenium and plasma glucose both at baseline and at the end of the follow-up, no effect of supplementation with a mixture of antioxidants, including 100 μg/day selenium, on plasma glucose levels after 7.5 years of follow-up, was found [28]. A recently-published analysis of Nutritional Prevention of Cancer Trial data showed that supplementation with 200 μg/d selenium as high-selenium yeast for 7.7 years increased the risk of self-reported type 2 diabetes [29]. Since the risk of CVD is higher in individuals with diabetes than in those without diabetes, this study was conducted to evaluate the association between selenium levels in CVD patient among patient with diabetes.

Material and Methods

The present study was conducted in the National Diabetes Center, College of Medicine at Al-Mustansiryia University from 1 August 2008 to 25th of May 2010, 256 patients with DM were divided into 2groups: group I (diabetic patients), n = 156 {male=39 (25%) and female=117 (75%)} and group II (diabetic patients complicated with CVD), n=100 {male=60 (60%) and female=40 (40%)}. Their results were compared with 100 healthy subjects as a control their age and sex were matched {male=32 and female=68}. ***Serum glucose*** was measured at biochemistry Laboratory at College of Science/chemistry Department at Al-Nahrain university from a fasting sample of participants 8-12 hr by enzymatic colorimetric method (GOD-PAP). ***Serum lipids***, cholesterol, triglycerides, HDL-C, LDL-C, and VLDL-C, were measured at the Biochemistry Laboratory at National Diabetes Center by enzymatic colorimetric method (Linear). ***HbA1c*** was measured by column chromatography method (Varna-Biurat /HPLC). To measure ***serum selenium***, whole blood was collected in containers previously screened for selenium contamination. After clotting and centrifugation, serum was collected, frozen at -20 C, and shipped to the laboratory for measured with the use of atomic absorption spectrometry (shimadzu, modale 680-AA in Ibn Seena Company).

Information about age, sex, smoking, Duration of diabetes, diabetes type, family history, usage of drugs, drugs duration, body mass index, hypertension, history of cardiovascular disease …etc for both patients and control groups.

All data were analyzed by SPSS version 17. Descriptive statistics in terms of mean and Standard Deviation calculated for the two groups and healthy control. Pearson's correlation as well as linear regression equation was calculated to estimate the slope (B) in order to know the amount of change in dependent variables with per unit change in serum selenium concentration. A P-value of <0.05 was considered as significant.

Results and Discussion

The basic characteristics of the subjects were shown in (Table 1) .Two hundred fifty six diabetic patients divided into two group, mean age of group I was 54.83±3.81 years [mean ± SD] and group II, participants with coronary heart disease CVD, mean age was 49.36±6.93 .One hundred healthy subjects, aged 48.36±5.71 years with no diabetes mellitus or any other hormonal disturbances, hypertension, family history, usage of any medication used as a control.

Table (1) shows the level of blood glucose, HbA1c, and serum lipids was significantly increased in diabetics with and without CVD than non-diabetic subjects. On the other hand, the levels of serum selenium were significantly decreased in two group patients when compared to healthy control subjects. Serum selenium concentration in group I was 0.1344±0.0012ppm and in group II was 0.1262±0.1166 ppm, compare to the control, 0.1700±0.0107 ppm.

In group I as a general without sex and type classifications, positive correlation was found between fasting serum selenium concentration and, cholesterol, TG, LDL-C and duration of diabetes where $p < 0.05$,on the

other hand there is negative correlation with fasting glucose where $p<0.05$, (Table (2)). In group II also as a general without sex andtype classifications, a highly negative correlation was found between fasting serum selenium concentration and fasting HbA1c (p values <0.0001), while with total cholesterol and duration of diabetes found with positive correlation where $p <0.05$, with fasting glucose there is negative correlation where $p<0.05$ (Table (3)).

Among patients group II, highly negative correlations was found between serum selenium concentration and HbA1c with linear regression equations as shows in Fig.(1).

In this study was determined a significant decrease in selenium levels of diabetic patients with or without CVD compared to controls (Table (1)). Results from studies predicting heart disease using serum levels of selenium [22–25] have bee inconsistent. Serum selenium levels of diabetic patients were reported to be increased [30-32] decreased [33, 34] or unchanged [35] compared to controls. Swapnil Rajpathak *et al* [20] have found that levels of selenium are lower among diabetic men with or without CVD than among healthy controls, In this study, by contrast between two groups of diabetic patient there is significant decrease in selenium level in group II(diabetic patients with CVD) than in group I(diabetic patients).

Selenium is an important component of the antioxidant enzyme, glutathione peroxidase (GSH-Px) that protects cells from the adverse effects of free radicals and lipid peroxides. A deficiency of selenium lowers the tissue activity of GSH-Px which in turn may have unfavorable effects on lipoprotein and arachidonic acid metabolism [25, 26]. These metabolic changes associated with compromised selenium status may lead to damage of the vascular endothelium and increased platelet adhesion which increase the risk of atherosclerotic heart disease [27].

Table (1)
Descriptive analysis including mean and stander deviation of Mean for DM patients, CVD patients and Healthy control.

DM Patients	*General*	*Male*	*Female*	*Type I*	*Type II*
	(n=156)	*(n-39)*	*(n=117)*	*(n=93)*	*(n=63)*
Age(years)	54.83±3.81	55.92±3.95	54.46±3.75	54.88±4.00	54.75±3.6
Fasting glucose(mg/dl)	152.26±13.89	155.38±12.99	151.26±14.21	151.50±12.53	154.25±16.02
Fasting cholesterol(mg/dl)	270.87±25.21	267.69±25.00	271.92±25.51	272.44±22.47	268.35±29.51
Triglyceride	288.85±28.83	293.85±16.60	278.18±31.89	289.37±28.73	288.00±29.71
(mg/ml)	38.33±4.30	37.46±3.86	38.62±4.45	38.56±4.38	37.95±4.26
Fasting HDL(mg/dl)	183.08±6.03	182.77±7.35	183.18±5.62	183.41±6.12	182.95±6.00
Fasting LDL(mg/dl)	54.65±11.59	57.54±8.29	53.69±12.44	55.66±12.79	53.05±9.44
Fasting	0.1344±0.0012	0.1329±0.0015	0.1362±0.0019	0.1351±0.017	0.1336±0.017
VLDL(mg/dl)	8.271±0.430	8.292±0.386	8.264±0.448	8.253±0.438	8.300±0.427
Selenium(ppm)	36.34±6.13	35.86±5.56	36.77±6.36	36.63±6.71	36.40±5.22
HbA1c					
BMI(Kg/m^2)					
CVD Patients	***(n=100)***	***(n=60)***	***(n=40)***	***(n=25)***	***(n=25)***
Age(years)	49.36±6.93	47.73±8.10	51.80±13.65	50.12±6.91	48.60±7.01
Fasting glucose(mg/dl)	163.06±14.25	166.90±14.91	157.30±11.24	162.63±14.99	163.76±13.75
Fasting cholesterol(mg/dl)	238.14±41.91	247.33 ±36.57	224.35±46.43	38.28±50.74	238.00±31.82
Triglyceride	243.08±105.28	193.63±93.62	317.25±74.54	254.24±99.83	231.92±111.38
(mg/ml)	37.76±9.82	41.93±9.97	31.50±5.31	38.24±9.13	37.28±10.63
Fasting HDL(mg/dl)	123.14±8.94	121.37±8.09	125.80±9.68	123.80±10.60	122.48±7.06
Fasting LDL(mg/dl)	29.80±3.48	28.80±3.75	31.30±2.81	29.44±3.58	30.16±3.41
Fasting	0.1262±0.1166	0.1295±0.0165	0.1240±0.0167	0.1292±0.0196	0.1235±0.0128
VLDL(mg/dl)	7.664±0.604	7.465±0.527	7.797±0.669	7.592±0.661	7.736±0.545
Selenium(ppm)	30.6106±0.611	30.2217±4.51	31.194±2.91	30.369±3.19	30.85±4.627
HbA1c					
BMI(Kg/m^2)					
Healthy control	***(n=100)***	***(n=32)***	***(n=68)***		
Age(years)	48.36±5.71	47.21±5.52	50.81±5.48	----	----
Fasting glucose(mg/dl)	85.06±3.65	85.82±3.34	83.44±3.85	----	----
Fasting cholesterol(mg/dl)	154.24±3.31	154.42±3.37	154.1±3.37	----	----
Triglyceride	64.46±5.56	66.06±5.80	61.06±2.98	----	----
(mg/ml)	52.58±5.49	52.03±5.94	53.75±4.31	----	----
Fasting HDL(mg/dl)	84.30±2.45	84.21±2.27	84.50±2.88	-----	----
Fasting LDL(mg/dl)	16.68±4.15	16.65±3.72	16.75±5.09	----	----
Fasting	0.1700±0.0107	0.1697±.0103	0.1707±0.0119	----	----
VLDL(mg/dl)	6.488±0.378	6.532±0.375	6.394±0.380	----	----
Selenium(ppm)	25.6716±2.384	25.1518±1.895	25.7438±2.958	----	----
HbA1c					
BMI(Kg/m^2)					

Diabetes has been shown to be associated with numerous thrombotic, atherosclerotic, and Cardiovascular diseases. Cholesterol has been singled out as the cause of atherosclerosis. However, other lipids, such as triglycerides and phospholipids, also show similar correlations [30]. In the present study, the levels of serum lipids were found to be elevated in diabetic patients. The abnormally high concentration of serum lipids in diabetes is mainly a result of the increase in mobilization of free fatty acids from peripheral depots, because insulin inhibits the hormone-sensitive lipase. On the other hand, glucagons, catecholamines, and other hormones enhance lipolysis the levels of VLDL-C, LDL-C, and HDL-C increase or decrease with the level of total serum cholesterol, and it is their ratio that determines the path physiology of lipoprotein metabolism [30, 3].

Kuen-Cheh Yang [32] repoted that serum selenium concentrations were positively associated with serum concentrations of total cholesterol, LDL cholesterol, triglycerides, and glucose this is agreed with this study except glucose, in the two groups serum selenium level was negative associated with glucose level (Table (2) and (3)).

Positive relationships between serum selenium and total cholesterol concentrations are discussed in several studies of various serum selenium concentrations [2, 19, 32, 36-41, 43]. However, most participants have been young and middle-aged adults. This study showed that serum total cholesterol concentration was positively associated with serum selenium concentration in group I (Table (2)); and in group II (Table (3)).

Many studies failed to show a significant association between serum selenium and triglycerides concentrations [36, 38, and 42] and few has shown a positive association [31, 32]. This study demonstrated that serum selenium concentrations were positively associated with serum triglycerides in group I (Table (1)).

Table (2)
Correlation between fasting selenium, fastingblood sugar, cholestrol, TG,HDL,LDL,VLDL, Duration of daibetes and BMI among DM patients group.

Fasting Selenium(ppm)		
	r	***P value***
HbA1c	.312	0.102
FBS	–.694*	0.040
Cholesterol(mg/dl)	.840*	0.020
TG(mg/dl)	.348*	0.012
HDL(mg/dl)	.441	0.078
LDL(mg/dl)	.276*	0.040
VLDL(mg/dl)	–.043	0.671
Duration of diabetes (year)	.865*	0.017
BMI(kg/sqm)	.557	0.059

*** Significant correlation when p<0.05;**
**** Highly significant correlation when p <0.01 and r= correlation.**

The present study supported that in group I serum LDL cholesterol concentrations were positively associated with serum selenium levels (Table (2)) while in group II no significant relation (Table (3)). In the other hand, there is no significant relation between HDL cholesterol concentrations and serum selenium in group I and II (Table (2) and (3)). Five studies showed a positive association between serum selenium and LDL-C [7-9, 14, 44] but others revealed no significant relationship [11, 16-18]. The variable sample sizes, age groups, and lack of adjustments for possible confounders may account for the inconsistencies in those studies. The association of serum selenium with HDL cholesterol, five studies report a positive association [8,9,11,15,16], one has a negative association [7], and three do not show any significant association [10,12,19].

HbA1c was found to increase in patients with diabetes to approximately 16% and the amount of increase is directly proportional to the fasting blood glucose level. During diabetes the excess glucose present in blood reacts with hemoglobin [27, 28]. In the present study was noticed a marked increase in HbA1c level in diabetic patients with or without CVD, which could be due to excessive glycosylation of hemoglobin. In addition in this study there

is highly negative correlation between serum selenium concentration and HbA1c in group II (Fig.(1)) this result agreed with Manal Kamal *et a*l [45] in 2009 have found that highly negative correlation between serum selenium concentration and HbA1c while in 2009 Muhittin A Serdarrepoted *et al* [46] showed that there is no correlation between HbA1c and selenium.

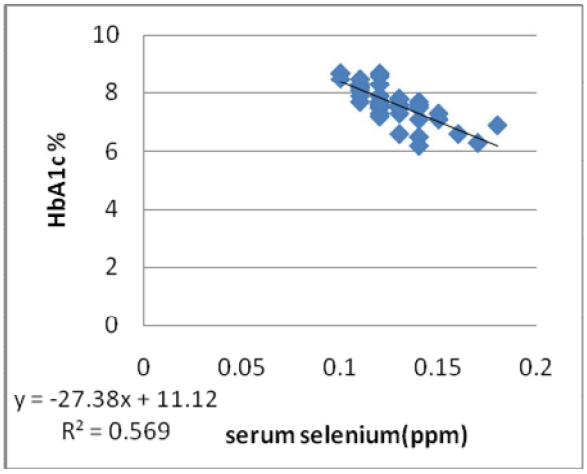

Fig. (1) Negative correlation with linear regression equation between fasting serum selenium and HbA1c in group II. (R^2= 0.569, r=0.755, p<0.0001).

Table (3)
Correlation between fasting selenium, fasting blood sugar, cholestrol, TG, HDL, LDL, VLDL, Duration, and BMI of diabetes with CVD among DM patients group.

Fasting Selenium (ppm)		
	r	***P value***
HbA1c	**.755*** **	**0.0001**
FBS	**-.018***	**0.018**
Cholesterol(mg/dl)	**.945***	**0.010**
TG(mg/dl)	**.094**	**0.239**
HDL(mg/dl)	**.102**	**0.234**
LDL(mg/dl)	**.139**	**0.212**
VLDL(mg/dl)	**.589**	**0.078**
Duration of diabetes (year)	**.828***	**0.032**
BMI(kg/sqm)	**.161**	**0.201**

*** Significant correlation when p <0.05;**
**** Highly significant correlation when p <0.01 and r= correlation.**

In conclusion, the levels of serum selenium are lower among diabetic patients with or without CVD than among healthy controls. Serum selenium concentration was associated with serum concentrations of total cholesterol, LDL-C, triglycerides, and glucose in diabetic patients in addition serum selenium concentration was associated with HbA1c in diabetic patients with CVD. The role of selenium on lipid and glucose metabolism in humans deserves further research in the future.

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الخلاصة

السلنيم من العناصر المهمه في عمليات الاكسدة في الجسم و من العوامل المؤدية الى أمراض اخرى عند مرضى السكري ومن اهمها امراض القلب لذالك اجريت هذه الدراسة في المركز الوطني لمرض داء السكري في كلية الطب– الجامعة المستنصرية وقد تم قياس مستوى عنصر السلنيم في مصل الدم لمرضى السكري (156) ومجموعة اخرى من مرضى السكري مصابون بامراض قلبية (100) ومقارنتهم بمجموعه ثالثة من الاصحاء (100) مع مراعت تقارب العمر والجنس بين المجموعتين من مرضى السكري ومجموعة الاصحاء. وبلاضافة الى عنصر السلنيم قد تم قياس كل من السكر الصائم والدهون ونسبة الهيموكلوبين.

وقد اضهرت النتائج نقصان في مستوى عنصر السلنيم في المجموعتين من مرضى السكري مقارنتا بالاصحاء. وقد لوحضى ان مستوى عنصر السلنيم اقل في مرضى السكري المصابون بامراض قلبية (المجموعة الثانية) مقارنتا بمرضى السكري (الجموعة الاولى).

وبغض النظر عن تقسيم المرضى المصابين بداء السكري (حسب الجنس ونوع الداء، وجدت علاقة خطية سالبة الارتباط عالية الاهمية بين مستوى عنصر السلنيم ونسبة هيموكلوبين الصائم (HbA1c) عند المرضى المصابين بداء السكري وامراض قلبية (المجموعة الثانية). بلاضافة الى ذلك لقد وجدة علاقة مهم بين مستوى عنصر السلنيم و كل من السكر الصائم و الكولسترول وTG والدهون قليلة الكثافة LDL في المجموعة الاولى. اما بالنسبة للمجموعة الثانية فقد وجد علاقة مهمة بين مستوى عنصر السلنيم و كل من السكر الصائم و الكولسترول. الاستنتاج من هذه الدراسة ان النقصان الملحوض في مستى عنصر السلنيم في مرضى السكري هو من اسباب تطور المرض واصابت المرضى بامراض اخرى من اهمها امراض القلب.