Evaluation of the Potential Role of Serum Selenium in Diabetic Patients

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Abstract

Background: The altered status of some essential trace elements observed in diabetes could have deleterious influences on the health of the diabetics.

Objectives: To estimate and study the potential role of serum Selenium in type 1, type 2 diabetics and healthy subjects; and its relation with lipid profile and glycemic index.

Methods: A case control designed study was carried out at the National Diabetes Center (NDC) / Al-Mustansiria University; on a total of 94 participants formed of 32 type 1 diabetics, 32 type 2 diabetics and 30 healthy control participants. Data collected about age, sex and BMI; also, blood samples examined for FPG, HbA1C, serum total cholesterol, HDL cholesterol, non-HDL cholesterol, serum triglyceride and sera were examined for Selenium by using atomic absorption technique.

Results: Type 1 and type 2 diabetic groups show respectively 75% and 65% decrement in S. Selenium, <70 µg/L. The mean of S. Selenium, age, BMI, waist/hip ratio, FPG, HbA1c, total cholesterol, triglyceride, HDL, Non-HDL and atherogenic index (total cholesterol/HDL cholesterol) for the type 1 and type 2 diabetics shows statistically significant differences from control group. Type 1 diabetics versus type 2 diabetics shows statistically insignificant differences between mean of the S.Selenium, total cholesterol, HDL cholesterol and atherogenic index (t-test, P > 0.05) while the mean of FPG, HbA1c and triglyceride show highly statistical significant differences (t-test, < 0.001).Simple linear correlation and regression analysis of FPG, HbA1c, total cholesterol, triglyceride, HDL, Non-HDL and atherogenic index of the studied groups shows weak to moderate correlation with their serum Selenium levels.

Conclusions: The inverse relationship between Selenium status and glucose tolerance suggest the potential role of Selenium in diabetics. Serum Selenium levels show high statistically significant differences from healthy subjects; while the differences between type1 and type 2 diabetic groups' shows no statistically significant differences. Inverse correlations and regression were noticed between S.Selenium levels of all studied groups with their FPG, HbA1c, total cholesterol, triglyceride, HDL, Non-HDL and atherogenic index. Low S.Selenium and HDL-cholesterol plus an increase in total cholesterol, non-HDL and atherogenic index enhance risk of cardiovascular diseases progression among the diabetics.

Key Words: Serum Selenium, diabetes mellitus

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Introduction

Diabetes mellitus is a growing important health problem which triggers major mass pathologies and micro-vascular complications.[1,2] Diabetes mellitus, cardiovascular disease (CVD) and dyslipidemia continue to be the main health scourge of most developed countries and are becoming dominant in many populous areas of the developing countries [2]. In the United States, between 2000 and 2001, the prevalence of diabetes rose from 7.3% to 7.9%[3].Type 1 diabetes mellitus is the first common endocrine and metabolic disease during childhood; also, it is considered as the third common chronic disease in childhood[4]. At present time, the most prevalent form of DM is type 2 (approximately 90 % of diabetic patients)[5] which has reached epidemic proportions[3] Diabetes, in general, is considered as the fourth most common cause of death in USA.[6] Moreover, The overall prevalence of diabetes approaches 8 % of adult population of the USA and most of Europe.[7]

The altered status of some essential trace elements and altered antioxidant minerals ratio observed in type 1 diabetic patients could have deleterious influences on the health of diabetics [8] .Diabetes is characterized by hyperglycemia which is considered as primary cause of diabetic vascular complications and is associated with oxidative stress, impaired trace element and lipid metabolism [9] .Trace element concentrations were believed not to be dependent on the degree of glucose control as determined by correlation analysis between HBA1c versus mineral levels in the blood [10].

Serum Copper, Zinc and Selenium concentrations are influenced by physiological conditions such as age, diet and gender. Their serum concentrations are also associated with coronary risk factors, including body mass index, levels of physical activity, serum HDL-C [11].

The inverse relationships between Selenium status and glucose tolerance are consistent with earlier observations that suggest a link between Selenium and glucose metabolism. Observer noticed the changes in serum glucose were not accompanied by changes in insulin suggests that Selenium may affect glucose metabolism downstream from insulin, or through independent energy regulatory pathways [12].

Serum level of Selenium was different in patients with either (type 1) insulin-dependent or (type 2)

non insulin-dependent diabetes mellitus when compared with the healthy control group[13] .The decreased levels of Selenium in serum and erythrocytes of diabetic patients suggest the possible role of glutathione peroxidase activity.[13]
Epidemiological studies have implicated perturbations in Selenium, Copper, and Zinc metabolism in the etiology of cardiovascular disease [14] .So, metabolic changes in trace metals status appear to be associated with risk of atherosclerosis [14].Furthermore; low Selenium status draws much attention because of the possible involvement in the etiology of cardiovascular disease. [11]
The objective of this study is to estimate and study the potential role of serum Selenium in type 1, type 2 diabetic and healthy subjects; and its relation with lipid profile and glycemic index.

Methods

A case control study was carried out at the National Diabetes Center (NDC) / Al-Mustansiria University; on a total of 94 participants formed of 32 type 1 diabetics, 32 type 2 diabetics and 30 healthy control subjects, after obtaining their agreements according to the medical research and ethical regulations, thus an oral consent was taken from all enrolled people.
Data were collected from all participants regarding their age, sex, BMI, duration of diabetes and other comorbid conditions. Fasting blood samples were taken for laboratory investigations which included; Fasting Plasma Glucose (FPG), glycosylated hemoglobin (HbA1c), serum total cholesterol, HDL cholesterol, non-HDL cholesterol, serum triglyceride and the atomic absorption technique were used to measure serum Selenium (S.Se) levels.
Statistical analysis and recording of obtained data were carried out by using Microsoft Excel - Windows XP professional program. Differences are considered to be of significance according to the t-test at level of $P \leq 0.05$ and 0.001.

Results

The studied groups were subdivided according to their serum Selenium level into two subgroups, Selenium deficient <70 µg/L subgroup and normal Selenium level subgroup ≥70 µg/ml, type 1 and type 2 diabetic groups shows 75% and 65% respectively were found to be Selenium deficient, below 70 µg/L, while the healthy control group subjects were found to be more than 70 µg/L (**Table-1).**
Comparing the mean of S.Selenium, age, BMI, waist/hip ratio, FPG, and HbA1c of type 1 and type 2 diabetics versus healthy control group **(Table-1)** were examined statistically and shows statistical significant differences from control group. While the mean of FPG, HbA1c, total cholesterol, triglyceride, HDL, Non-HDL and atherogenic index (total cholesterol/HDL cholesterol) of type 1 and type 2 diabetics versus healthy control group **(Table-2)** were examined statistically and shows statistically significant differences from control group.
Comparison of type 1 diabetics versus type 2 diabetics **(Table-3);** shows high statistically significant differences for the mean of FPG, HbA1c and triglyceride levels ($P < 0.001$); and shows no statistically significant differences between the diabetic groups for the mean of S.Selenium, total cholesterol, HDL cholesterol and atherogenic index ($P > 0.05$).
Simple linear correlation and regression analysis of FPG, HbA1c, total cholesterol, triglyceride, HDL, Non-HDL and atherogenic index of the studied groups were calculated **(Table-4)** and shows weak to moderate correlation with their serum Selenium levels.

Discussion

Significantly more information about trace elements status could be obtained by investigating its concentrations in blood cells instead of only evaluating its concentrations in plasma. Ignoring this important biochemical role, trace elements concentrations determined in whole blood or plasma very often lead to conclusions contrary to the actual intracellular concentration [15]**.** However, the current study using the atomic absorption technique to measure actual serum levels of Selenium among study population because of its availability and to make clear its real status in the sera of diabetics and healthy subjects.
Low levels of Selenium in sera and erythrocytes of diabetic patients suggest the possible role of glutathione peroxidase activity [13] **.**This relation proved by Hawkes *et al.* Who found that Women with lower plasma glutathione peroxidase activities during pregnancy also tended to have higher fasting glucose levels? These inverse relationships between Selenium status and glucose tolerance are consistent with earlier observations that suggest a link between Selenium and glucose metabolism [12].
A serum Selenium concentration of 70µg/L is considered to be sufficient for glutathione peroxidase (GSHPx) activity, a Selenium-dependent enzyme reflecting the body Selenium

status, [16] therefore all the studied groups were subdivided into two subgroups **(Table-1)** according to their serum Selenium concentrations below or above 70µg/L. Type 1 and type 2 diabetic groups shows that 75% and 65% of them respectively had S.Selenium below 70µg/L; while all the healthy control group participants were above 70µg/L. Also, mean of S.Selenium, FPG and HbA1c of the diabetic groups when compared with control group show high statistically significant differences (t-test, $p < 0.001$). Moreover, statistical comparison between type1 and type 2 diabetics **(Table-2)** shows insignificant statistical difference between mean of S.Selenium (t-test, $p > 0.05$) and high statistically significant differences for the mean of FPG and HbA1c (t-test, $p < 0.001$); these observations noticed by Lee *et al*. and make clear that changes in serum glucose were not accompanied by changes in insulin, so they suggests that Selenium may affect glucose metabolism downstream from insulin, or may be through an independent energy regulatory pathways such as thyroid hormone pathway [12] .

Selenium is an essential trace element in nutrition for the prevention of disease in humans. Epidemiological studies indicate an association between low nutritional Selenium status and increased risks of cardiomyopathy, cardiovascular disease, and carcinogenesis in various sites of the body[17,18] .Inverse correlations between mean S.Selenium of all groups and their own FPG, HbA1c, total cholesterol, triglyceride, HDL, Non-HDL and atherogenic index were noticed **(Table-4)**. These inverse correlations might be explained by Selenium is a powerful antioxidant regulating the activity of the glutathione peroxidase enzymes, which catalyse the detoxification of hydrogen peroxide and organic hydroperoxides; [19] or by the role of selenoproteins which discovered in mammalian cells and may account for the essentiality of Selenium in the body's antioxidant defense system, thyroid hormone function, immune system function, particularly the cellular immunity, formation of sperm and functioning of the prostate gland [18] .Remarkable decrease of mean S.Selenium and HDL-cholesterol while an increase of total cholesterol, non-HDL and atherogenic index were noticed in diabetic groups when compared with healthy control group **(Table-2),** differences proved to be of high statistical significance (t-test, $p < 0.001$); this model of lipid profile enhance risk of cardiovascular diseases. There has been a renewal of interest in the protective role of Selenium in vascular disorders, inspired by experimental evidence that this trace element could modulate leukotriene and prostaglandin synthesis in both endothelial cells and platelets [20] .In people living in low-Selenium areas, a relationship has been established between a decrease in plasma Selenium and an increase in the risk of coronary disease, atherosclerosis, platelet hyperaggregability and synthesis of proaggregant and proinflammatory compounds like thromboxane A2 and leukotrienes. In these Selenium deficient subjects, Selenium administration increases platelet glutathione peroxidase activity and inhibits platelet hyperaggregation and leukotriene synthesis. [20] These results support the hypothesis established by Vitoux *et al* who found In France, more than 10% of the population were Selenium-deficient and long-term supplementation with low doses of Selenium could have a beneficial effect on the prevention of both thrombosis and coronary heart disease in these subjects.[20] So that Selenium supplementation has a positive effect on platelet aggregation in Selenium-deficient subjects. [20] The nutritionally recommended dose of elemental Selenium is estimated at 50 to 200 mg per day. [17] Endpoints for assessing Selenium overexposure are much less satisfactory, but toxicological standards for Selenium have nevertheless been established.[18] However, there is increased discussion of a pharmacological dose of Selenium, significantly higher than the nutritional dose of the microelement, to treat deficiency conditions. One way of increasing tissue levels of Selenium is to combine its ingestible form with a nutrient bioavailability enhancing compound [18].

Conclusions

The inverse relationship between Selenium status and glucose tolerance suggest the potential role of glutathione peroxidase activity. A 75% and 65% of type 1 and type 2 diabetic groups, respectively, were Selenium deficient; while there are no Selenium deficient healthy control subjects were noticed.

Serum Selenium levels of diabetic patients' were found to be of high statistically significant differences from healthy control group. While comparison of serum Selenium levels between type1 and type 2 diabetic groups' show no statistically significant difference.

Inverse correlations and regression were noticed between S.Selenium levels of all studied groups with their FPG, HbA1c, total cholesterol, triglyceride, HDL, Non-HDL and atherogenic index.Low S.Selenium and HDL-cholesterol plus an increase in total cholesterol, non-HDL and atherogenic index were noticed among diabetics

when compared with healthy control group, such pattern of lipid profile in combination with low Selenium enhance risk of cardiovascular diseases progression among diabetics.

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(Table-1)

The Mean of S.Se, Age, BMI, Waist/Hip Ratio, FPG and Hba1c of Type 1, Type 2 Diabetics and Healthy Control Groups who's below or above 70 µg/L Serum Selenium Level.

	Type 1 Diabetes mellitus		Type 2 diabetes		Control	
	S.Se <70 µg/L (n=24) (75%)	S.Se ≥70µg/L (n=8) (25%)	S.Se <70µg/L (n=21) (65%)	S.Se ≥70 µg/L (n=11) (35%)	S.Se <70 µg/L (n=0) (0%)	S.Se ≥70 µg/L (n=30)(100%)
S.Se(m±SD)	60.08±6.50 *	74.74±4.61 *	63.11±5.97 *	74.55±5.00 *	-----	92.55±11.88
Age (years)	25.45±5.97 †	28.37±9.28	50.66±14.7 *	52.4±13.3 *	------	28.8±9.49
BMI (kg/m^2)	21.68±4.42	21.67±4.72	27.11±5.02 *	27.97±5.40 *	------	21.81±4.11
Waist/hip ratio	0.848±0.076	0904±0.056 *	0.964±0.247	0.905±0.043	------	0.897±0.235
FPG (mmol/L)	13.007±5.203 *	8.37±1.854 *	8.377±1.904 *	8.572±2.298 *	------	4.915±0.711
HbA1c (%)	8.6±1.83 *	6.96±1.02 *	7.16±1.62 *	6.92±1.58 *	------	4.1±0.82

† t-test (P < 0.05), * t-test (P < 0.001)

(Table-2)
The Mean of S.Selenium, Fpg, Hba1c, Total Cholesterol, Triglyceride, Hdl, Non-Hdl and Atherogenic Index of Type 1, Type 2 Diabetics and Healthy Control Groups

	Type 1 diabetes	Type 2 diabetes	Control
S.Selenium (µg/L)	63.75±8.82 *	67.04±7.84 *	92.55±11.88
FPG (mmol/L)	11.84±5.00 *	8.44±2.01 *	4.91±0.71
HbA1c (%)	8.19±1.80 *	7.07±1.59 *	4.10±0.82
Total cholesterol (mmol/L)	5.15±0.89 †	5.27±1.12 †	4.79±0.76
Triglyceride (mmol/L)	2.49±0.52	1.70±0.87 *	2.39±0.22
HDL (mmol/L)	1.43±0.47 †	1.29±0.212 *	1.59±0.40
Non-HDL (mmol/L)	3.71±1.33 †	3.97±1.13 *	3.20±1.17
Atherogenic index	4.35±3.00 †	4.18±1.26 *	3.28±1.16

† T-test (P < 0.05), * t-test (P < 0.001)

(Table-3)
Comparison between Mean of S.Selenium, FPG, Hba1c, Total Cholesterol, Triglyceride, HDL, Non-HDL and Atherogenic Index of Type 1, Type 2 Diabetics.

	Type 1 diabetes	Type 2 diabetes	t-test (p value)
S.Selenium (µg/L)	63.75±8.82	67.04±7.84	> 0.05
FPG (mmol/L)	11.84±5.00	8.44±2.01	< 0.001
HbA1c (%)	8.19±1.80	7.07±1.59	< 0.001
Total cholesterol (mmol/L)	5.15±0.89	5.27±1.12	> 0.05
Triglyceride (mmol/L)	2.49±0.52	1.70±0.87	< 0.001
HDL (mmol/L)	1.43±0.47	1.29±0.212	> 0.05
Non-HDL (mmol/L)	3.71±1.33	3.97±1.13	> 0.05
Atherogenic index	4.35±3.00	4.18±1.26	> 0.05

(Table-4)
Simple Linear Correlation and Regression Analysis of Fpg, Hba1c, Total Cholesterol, Triglyceride, Hdl, Non-Hdl and Atherogenic Index Among Type 1, Type 2 Diabetics And Healthy Control Groups With Their S.Selenium Level.

Coefficient of correlation (r)	Type 1 diabetes	Type 2 diabetes	Control
FPG	-0.3597 *	0.1149	0.1213
HbA1c	-0.4001 †	-0.1609	-0.4071 †
Total cholesterol	-0.1957	-0.1100	-0.3643 *
Triglyceride	-0.1300	-0.0164	-0.4908 †
HDL	0.2542 *	-0.0019	-0.5413 †
Non-HDL	-0.2213	-0.1080	-0.4507 †
Atherogenic index	-0.2082 *	-0.0497	0.2124 *

† weak correlation, * moderate correlation

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