



Serum Levels of Zinc, Selenium and Homocystine among Iraqi Patients with Type-2 Diabetes Mellitus

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Abstract

Background and Objectives: The disease of Diabetes Mellitus is a main medical, economic and social big problem, because the high pervasion and increment incidence of this depilating disease with subsequent cascading of several disabling complications and it needs for special medical care. High prevalence of this disease occur in Middle East. Its prevalence in Iraq increased from 5% in 1978 to 19.7% in 2012. The current study initially focuses on the investigation of serum micronutrients [zinc (Zn), selenium (Se)] and homocystin (Hcy) levels as well as their relatedness with type 2 Diabetes Mellitus in Iraqi patients. **Subjects and Methods:** This study was designed as a case - control investigation and conducted at diabetic center in Baquba General Hospital in Diayla, Iraq. This study involves 50 patients with type 2 DM and 25 apparently healthy, age and sex matched subjects for that represent as control group. The patients were classified into two sub-groups including, type 2 DM with nephropathy (33 patients) and type 2 DM without nephropathy (17 patients). Fasting blood sugar, creatinine as well as some selected serum levels including two important micronutrients (Se, Zn) with addition and all of them were measured in each group. **Results:** The prevalence of DM Type2 was at age of 60 to ≥ 70 years. Diabetes was more prevalent in males than in females (58 % , 42 % consecutively). The mean level of blood glucose and creatinine were typically higher in both diabetic groups as compared to the control group ($p = .000$). Selenium level was lower in diabetic patients with a significant difference when it compared with healthy control. Study groups according to zinc level (p -value= 0.149) did not indicate a significant difference. In this study homocysteine levels was higher in DM patients with nephropathy than diabetes without nephropathy (17.09 ± 1.942 vs 16.72 ± 2.323) with statistically significant differences comparing with the control group (6.74 ± 0.946) No significant correlation was found among Zn , Se and Hcy with plasma glucose and creatinine. **Conclusion:** The findings of the current research show obvious decreased in the serum Se among Type2 DM patients with and without nephropathy comparing with control. Additionally, serum homocystine levels were elevated regarding to the occurrence of diabetic nephropathy so it could be an indicator for observed DM and progression of DM nephropathy.

Keywords: *Type 2 Diabetes, Zinc, Selenium, Homocysteine.*

Introduction

Type 2 DM represent primary global and public health trouble that affects over two hundred million persons [1, 2]. The Federation of International Diabetes) clears latterly that 382 million patients affected with this debilitating disease [3]. The prevalence of this disease is higher than the prevalence of all infectious diseases combined, and due to this, the "World Health Organization" (WHO) and the "United Nations" have determined DM as the most serious challenge according to International Community in the twenty-first century [4].

Diabetes relationship with trace a mineral is complex and not clear. Which affect which? Hyperglycaemia effects on minerals metabolism, or mineral homeostasis affects carbohydrate metabolism. In the present study, we have selected two trace important elements, i.e. selenium and zinc that have important roles in regulating processes of the glucose homeostasis, insulin metabolism. In addition, it serves as a co-factor in anti-oxidation of the enzymes [5, 6, 7]. Zinc (Zn) is one of important antioxidant and has an efficient role in the function of many enzymes and in insulin metabolism [8, 9].

Zinc has importance in (metabolic diseases like diabetes, insulin resistance and metabolic syndrome) because it has an important role in the stability of (hexamers) and storage of insulin in the pancreas [10]. Selenium (Se) is one of the important micronutrients that maintain biological functions through the containing proteins actions of the selenium which known as selenoproteins [11]. It mediating a number of insulin actions in both vivo and vitro, involving glucose uptake stimulation and regulation of metabolic processes like glycolysis, gluconeogenesis and also fatty acid synthesis [12].

Homocysteine (Hcy) is a sulfur amino- acid, 70 to 80% of total homocysteine circulating in plasma is bound to proteins like albumin while the remaining circulating as free sulphides [13]. Plasma Hcy normal value ranges from 5-15 μ mol/L. Elevated Hcy greater than 15 μ mol/L called Hyperhomocysteinemia [14]. Many studies [15, 16] linked Hyperhomocysteinemia with renal failure, endothelial dysfunction, and cardiovascular disease.

In addition, other studies revealed a positive linking between homocysteine and pathophysiology of diabetes mellitus [16, 17]. This association in diabetic patients may contribute to the evolving of chronic vascular complications. Despite of many researches on Hcy in DM patients, the association between these two is not totally clear [18].

Methods

Fifty patients (29) males and (21) females of patients with type 2 diabetes (1.5:1) and the age range of 48-76 years with mean age of 63.76 \pm 12 years, all these patients were attending the diabetic center in Baquba General Hospital in Diayla, Iraq were selected randomly for a period from March till June 2016. Type 2 DM was diagnosed by consultant physician using clinical history of the disease, physical examination and fasting plasma glucose (FPG) \geq 7.0 mmol/L [19]. The diabetic patients were further classified into two groups – diabetics with nephropathy (N=33), and diabetics without nephropathy (N=17). The oral informed consent was obtained from each patient to make him/her

to participate in the current study. Patients with Type 1 diabetes mellitus, liver diseases or other general diseases were excluded from the study. Twenty five (25) healthy volunteers consisting of twelve (15) males and eight (10) females (1.5: 1) age range of 45-70years with mean age of 57 \pm 11.7 years who were randomly selected and included as controls. Blood samples of subject were collected in the morning after overnight fasting in plain tubes then centrifuged immediately for 10 minutes at 3500 rpm.

Fasting blood glucose using glucose oxidase method [20], Serum creatinine based on the Jaffe reaction [21]. The serum was kept in (-20) for measuring Zn, Se and Hcy by Axis-Homocysteine Enzyme Immunoassay (EIA) kit from Axis-Shield Diagnostic, UK. SPSS versions (19) were used to enter and analyze data. The results were expressed as mean \pm SD, student t-test, ANOVA test used to assess differences between means for independent samples and significance was assessed by 'p' value, labeled as significant if the value was < 0.05.

Results

The demographic characteristics of the randomly selected study population are shown in Table 1. It shows that of the 50 patients screened, (34%) Of subjects included in the study belong to the age group from 60 to \geq 70 years and (32%) belong to the age group < 60 years.

Among the participants, 58 % were men and 42 % were women. In the present study, the mean level of blood glucose, creatinine and homocysteine were significantly higher in the diabetic groups (both with and without nephropathy) as compared to the healthy group (p= .000).

The mean level of selenium was significantly lower in both diabetic with and without nephropathy patients (46.24 \pm 3.409 vs 46.233 \pm .614) when compared with healthy control (p<0.001). According to zinc level, there was no significant difference among study groups (p-value= 0.149) (Table 2). No significant correlation was found among zinc, selenium and homocysteine with plasma glucose and creatinine (Table 3).

Table 1: Demographic characteristics of the study population

Characteristics		Diabetic patients N=50		p-value
		No.	%	
Age	< 60 years	16	32	0.520
	60-69 years	17	34	
	≥ 70 years	17	34	
	Total	50	100	
Gender	Men	29	58	0.161
	Women	21	42	
	Total	50	100	

Table 2: Levels of selected serum markers in type 2 DM patients with and without Nephropathy, and in healthy controls

Serum markers	DM with nephropathy N= 33	DM without nephropathy N= 17	Healthy control N= 25	p-value
	M±SD	M±SD	M±SD	
Glucose (mmol/L)	12.66±5.077	10.76±5.055	5.487±0.878	0.000
Creatinine (mmol/L)	159.29±153.61	70.32±10.91	40.81±8.387	0.000
Zinc (ppm)	0.6879±.08234	0.6588±0.09526	0.7052±0.04053	0.149
Selenium (µg/L)	46.24±3.409	46.233±.614	88.0400±16.30	0.000
Homocysteine (µmol/L)	17.09±1.942	16.72±2.323	6.74±0.946	0.000

Table 3: Correlation of Zinc, Selenium and homocystin with Glucose and Creatinine in type 2 Diabetic patients

Minerals/ Homocysteine	Parameters	Glucose	Creatinine
Zinc	r	-.091	-.046
	p	.534	.754
Selenium	r	-.001	-.089
	p	.995	.545
Homocysteine	r	.012	-.106
	p	.936	.470

Discussion

Individuals with Type 2 DM in middle age and elderly) represent about (85% of all DM cases in developed countries [22]. According to surveys from 2006 to 2007, Iraq is one of the countries in the Middle East with a medium prevalence of diabetes and it estimates with 9.3 % [23].

The study aimed to evaluate some serum minerals including (Zn and Se) and also homocystin levels in type 2 diabetes mellitus patients with diabetic nephropathy in comparison to those normal individuals and there relation with hyperglycemia and creatinine status. The results of present study showed that prevalence of diabetes was in the sixth through over seventh decades. Certain studies in Saudi Arabia found increased DM prevalence in patients aged 45–60 years [24, 25].

The study results represent that diabetes was high prevalent in men than women (table 1) in similar to findings in Saudi Arabia and Lebanon [24, 26]. In contrast, it was lower in men in Iran [27]. Data illustrated in (table 2) cleared a significant difference in glucose level among study groups comparing with control due to DM plugging. There was also significant

increment in creatinine level between groups of DM with and without nephropathy (159.29±153.61, 70.32±10.91 respectively) with significant difference in comparison with control group (p=0.000). Diabetes mellitus included several complex processes for progression, in which micronutrients are involved in different ways, some act as a part of antioxidant enzymes (e.g. Se, Cu and Zn) other work as co-factors in lipid and glucose metabolism (e.g., Cu, Mn, Zn) [28].

Hyperglycemia cause damage for all cell types through over production of reactive oxygen species (ROS) [29] and Se is important in redox status homeostasis, so it may have a role in diabetes and its complications. The study outcomes showed that serum selenium level was low in DM patients with and without nephropathy (46.24±3.409, 46.233±.614 respectively) with significant difference when compared with control (88.0400±16.30, p=0.000).

This finding was in agreement with study of SotIropoulos et al [30]. Study, that represented Se concentration did not differ between the diabetic subjects with and without complications. Other study by Kumar [31] showed that Se levels in patients with diabetic complications had 2-fold lower

level compared to the control subjects. (Decreased serum zinc levels may due to hyperglycaemia that in turn promotes increased elimination of that trace element in patient's urine). This study represented no significant difference among study groups according to zinc level (p-value= 0.149).

This results adverse to that observed in south Indian population and in Iran which suggested low Zn level in diabetics [32, 33]. In this study homocysteine levels are higher in DM patients with nephropathy (17.09±1.942) than diabetes without nephropathy (16.72±2.323) with statistically significant differences comparing with the control group (6.74±0.946).

These results were in agreement with the findings of Rafah S. (2016) that found elevated plasma Hcy concentrations in type 2 diabetic patients . Lakshman et. al. (2012) found that higher Hcy levels are found in diabetics who have developed micro-/macro-vascular complications. Elevated Hcy level might either result from disturbed Hcy clearance from kidneys [36, 37] or could be

due to insulin resistance [38]. Homocysteine level might be an indicator for observed DM and progression of DM nephropathy. Serum Se,Zn and Hcy obtained in this study did not correlate with glucose and creatinine levels in diabetes(table 3), that opposite to earlier study by Wang et.al [39] which suggested that positive association between serum selenium levels and T2DM .Other study showed a strong association between Hcy and diabetic nephropathy [40]. In contrast, the significant negative linking between the levels of zinc and DM was reported in Sahar et.al .Study [41].

Conclusion and Recommendations

Alterations in levels of some serum parameters including micronutrients (Zn and Se) and homocystine occur at development of diabetes and could be associated with medical complications. The further research should focus on the potential and exact relationship between these altered micronutrients in diabetic patients and reveal their key role of their correction on the development and progression of the disease.

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