SERUM CALCIUM LEVEL IN PATIENTS WITH TYPE II DIABETES MELLITUS

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ABSTRACT

Background: Evidence for a disturbance of mineral metabolism in diabetes has accumulated since the eighties of the last decade. Calcium ion shown to play an important role in the biosynthesis, storage, release and activity of insulin, in addition, to glucose tolerance in human beings.

Objective: To examine if serum calcium level (SCaL) is influenced in patients with type II diabetes mellitus (type 2 DM).

Methods: The study comprised one hundred twenty subjects of both sexes. Sixty patients of newly diagnosed type 2 DM with a mean±SD age of 47.6±11.6 years and 60 healthy controls with a mean age±SD of 35.2±14.3 years. Main outcome measures (SCaL) and serum glucose level (SGL) in fasting blood samples.

Results: Serum calcium level and SGL were significantly higher in newly diagnosed type 2 DM as compared to healthy non-diabetic controls. Furthermore, there was no correlation between SCaL and hyperglycemia in diabetic patients.

Conclusion: Hypercalcemia may be a result of other factors in diabetes mellitus rather than hyperglycemia.

Key words: Type 2 diabetes mellitus, calcium, glucose, hypercalcemia, hyperglycemia.

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Introduction

Approximately 97% of people who have diabetes mellitus have type II diabetes mellitus (DM)[1]. Evidence for a disturbance of mineral metabolism in diabetes has accumulated since the eighties of the last decade[2]. Extracellular calcium provides calcium for maintenance of intracellular calcium ion, bone mineralization, renal function, hormone secretion, and a second messenger affecting enzyme activity[3].

Calcium ion shown to play an important role in the biosynthesis, storage, release and activity of insulin. In addition to, glucose tolerance in human beings[3-7]. Pancreatic ß-cells of the islets of Langerhans are rich in Ca^{+2}[4]. The role of Ca as a mediator of insulin action was originally proposed by Clausen et al[8] and Kissebah et al in the mid seventies[9]. Although some investigators failed to observed a relationship between Ca and insulin action[10-11] diverse aspects of insulin action have been demonstrated to be dependent upon extracellular and cytoplasmic Ca^{+2}[12-15].

Several studies among diabetics of both types I and II have demonstrated abnormalities in Ca^{+2} metabolism[16-18]. Also, type II DM results in altered cellular Ca^{+2} regulation and transport[19]. Homeostasis of Ca^{+2} is disturbed in animal models with diabetes mellitus; nevertheless the effects of DM on Ca^{+2} metabolism in human are controversial. Although some authors have found no significant alterations, apart from excessive urinary loss of Ca^{+2}[20], increased Ca^{+2} absorption has been reported following oral Ca^{+2} loading in type I diabetics[21] and slightly higher levels of serum calcium have been found in type II DM patients than in normal subjects[2, 5, 22].

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The aim of the present study was to examine serum calcium level in newly diagnosed type II diabetics attending Al-Waffa Diabetic Clinic in Mosul .

Patients & Methods

Sixty patients with newly diagnosed type II DM of both sexes with a mean±SD age of 47.6±11.6 years who were attending Al-Wafa Diabetic Clinic in Mosul during the period from September 2002-Febraury 2003, and sixty non-diabetic healthy controls with a mean±SD age of 35.2±14.3 years, were included in this study. No participants were taking any mineral supplements or medication, during the period of the study.

The median and range of the SCaL and SGL in controls and type II diabetics presented in the table 1. The proportion of patients who had hypercalcemia was 81.7%.

Table 1: Median and range for the SCaL and SGL in healthy controls and type 2 diabetics

Parameters (mmol / L)	Controls n = 60		Type II diabetics n = 60	
	median	range	median	range
SCaL	2.22	1.64 - 2.71	3.08	2.21– 4.01
SGL	4.96	3.47 – 6.87	11.84	3.37 – 21.85

Venous blood samples were taken between 8 and 10 a.m. after overnight fast and collected into an acid-rinsed metal-free covered glass test tube and allowed to clot for 1-2 hours at room temperature. After centrifugation, the serum removed. Glucose measurement performed immediately, while serum for estimation of calcium level was stored at -20 ºC in other metal free plastic test tubes for further analysis.

Serum glucose concentration was measured by spectrophotometric enzymatic end point method[23]. Serum calcium level analyzed by dye colorimeteric method, which uses O-cresolphthalein complexone (CPC). In alkaline solution, CPC forms a red chromophore with Ca^{+2} [24]. The kit purchased for estimation of SCaL and SGL was from Biocon Co. (Germany).

Z-test and Pearson's correlation coefficient (r) used for the analysis of the data. The accepted level of significance was at $P < 0.05$.

Results

Serum calcium and serum glucose levels were significantly higher in type II diabetics ($P< 0.001$) compared with those in healthy controls (Table 2 and Figure 1).

Table 2: Mean±SD for SCaL in type II diabetics compared to the healthy non-diabetic controls (data presented as mean±SD)

Variables (mmol/L)	Control (n = 60)	Type II diabetics (n = 60)
SCaL	2.17±0.27	3.11±0.45**
SGL	5.17±0.85	12.62±4.33**

** Significantly different from the respective control value, p<0.001

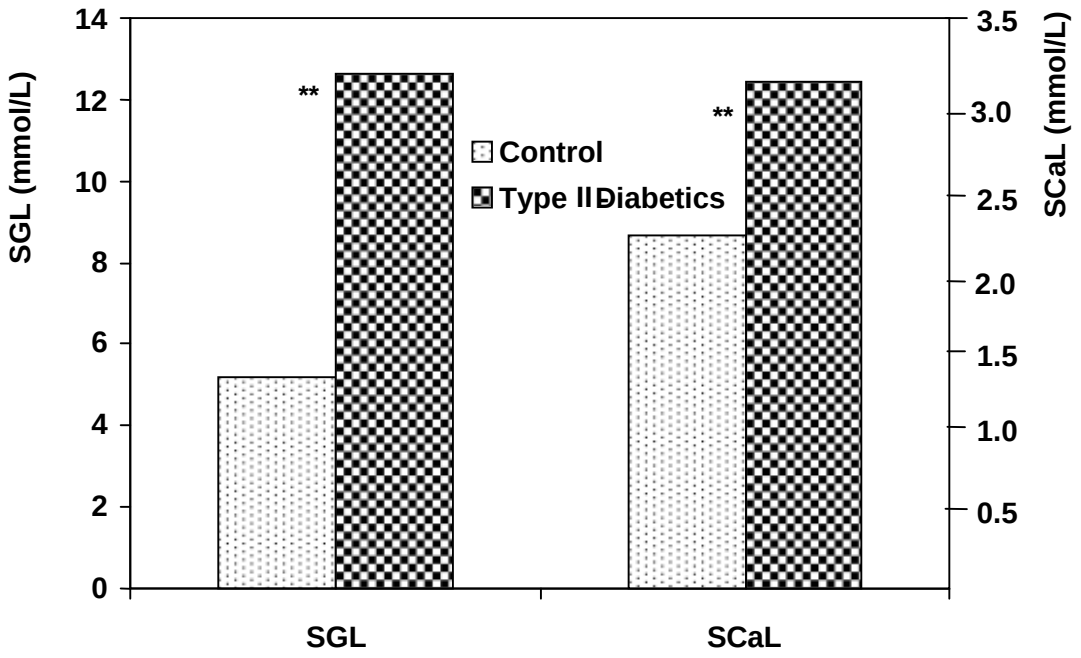

Figure 1: Comparison between mean values of SCaL and SGL in control subjects and type 2 diabetics.

There was no significant correlation between SGL and SCAL (r = - 0.03, p > 0.05) in type 2 diabetics, or in healthy controls (r = - 0.091, p > 0.05).

Discussion

The exact manner by which defective glucose homeostasis interferes with mineral metabolism remains unsettled[2]. A series of reports suggest the existence of altered Ca metabolism in diabetes mellitus[16-18, 25].

Hypercalcemia has been reported by several another to be present in type II diabetics[2,5,22,26] which is in agreement with the observation in the present study, but in contrast with the report of others[27-31].

Hypercalcemia occurs because of an increased flux of Ca^{+2} into the extracellular fluid compartment from the skeleton, intestine, or kidney[23].

The assumed hypercalcemia in this study may be due to dehydration; this is expected in the newly diagnosed diabetics with severe hyperglycemia[32].

Bone mineral loss is another abnormality that recognized as a feature of the diabetic patients. This suggests that hypercalcemia may be as a result of calcium loss from bone[33].

Hypercalcemia in diabetic patients is speculated to be partly attributed to the low level of serum albumin[5,26]. Normally about 47% of Ca^{+2} in the plasma combined with plasma proteins[34].

The tendency of hypercalcemia observed in diabetic patients could be also due to the decreasing renal tubular reabsorption[2,5], and increasing intestinal absorption of calcium[24]. Such inhibition of tubular reabsorption could be caused by hyperglycemia per se[35-36] or by some other direct action of abnormal glucose homeostasis on the renal tubules. The definitive mechanism is still unknown.

Many interactions occur between Ca^{+2} and insulin metabolism. Calcium ion shown to be associated with the conversion of pro-insulin into insulin or

glucose tolerance in human beings and numerous laboratory animals[3-5,7]. This suggests that hypercalcemia may be a result of insulin resistance[3, 6].

The other probable causes of hypercalcemia may include primary hyperparathyroidism which is a common disorder resulting from increased secretion of parathyroid hormone from parathyroid adenomas, carcinomas or hyperplasia.

Parathyroid hyperplasia may be associated with other inherited endocrine disorders (multiple endocrine neoplasia 1 and IIa). Multiple endocrine neoplasia; type I (MENI) which also called wermer's syndrome, this disorder includes tumor or hyperplasia of parathyroid, pituitary, and non- β cells of pancreas.

Hypercalcemia secondary to malignancy is relatively common and occurs in 10 to 20 of patients with cancer. The degree of hypercalcemia is worse with malignant disease (often greater than 3.5mmol/L) than with hyperparathyroidism (serum calcium less than 3.5 mmol /L[37,38].

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