

Original article

Trace elements status in type 2 diabetes

Hussain F¹, M Arif Maan², MA Sheikh³, H Nawaz⁴, A Jamil⁵

Abstract

Background: The metabolism of several trace elements has been reported to alter in diabetes mellitus and these elements might have specific roles in the pathogenesis and progress of this disease. **Objective:** The aim of the present study was to investigate serum levels of copper, zinc, chromium, magnesium and manganese in type 2 diabetic patients and their possible association with age, glycemic status and duration of diabetes. **Methodology:** The comparative study included 116 type 2 diabetic patients and 40 non-diabetic subjects. Fasting plasma glucose and HbA_{1c} were determined by the glucose oxidase method and affinity chromatography respectively. The element concentrations were measured by means of an atomic absorption spectrophotometer after microwave-induced acid digestion. **Results:** Mean (\pm SD) Mg and Zn levels were significantly reduced in blood samples of diabetic patients as compared to control subjects ($p < 0.0001 - < 0.05$). The alterations observed in serum levels of copper and manganese was not significant among diabetic and normal subjects. Glycemic status, duration of diabetes and age did not effect the trace elements concentrations. **Conclusion:** The results confirm that deficiency and efficiency of some essential trace metals may play a role in the development of diabetes mellitus.

Key words: Trace elements, glycemic status, type 2 diabetes.

Introduction

Burgeoning knowledge on the role of trace elements in biological systems is beginning to focus attention on their place in human metabolism. Direct association of trace elements with health and disease is already established. Diabetes mellitus is also linked to perturbations in mineral metabolism. It is not always clear whether diabetes

mellitus and hyperglycemia affect mineral metabolism or alterations in mineral homeostasis influence carbohydrate metabolism¹⁻⁵. Present study was undertaken to estimate the serum levels of Cu, Zn, Cr, Mg and Mn in type 2 diabetic patients and their association with age, glycemic status and duration of diabetes.

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1. **Fatma Hussain**, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Agriculture, Faisalabad-38040, Pakistan
 2. **Mohammad Arif Maan**, Punjab Medical College, Faisalabad-38040, Pakistan
 3. **Munir Ahmed Sheikh**, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Agriculture, Faisalabad-38040, Pakistan
 4. **Haq Nawaz**, Institute of Nutrition, Faculty of Animal Husbandary, University of Agriculture, Faisalabad-38040, Pakistan
 5. **Amer Jamil**, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Agriculture, Faisalabad-38040, Pakistan

Corresponds to:

Dr. Fatma Hussain PhD, Assistant Professor of Biochemistry, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Agriculture, Faisalabad, Pakistan.

Email: fatmauaf@yahoo.com

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Subjects and methods

The study included 116 type 2 diabetic patients and 40 nondiabetic subjects as controls. Written consent was obtained from all participants who were asked not to alter their usual diets and physical activities throughout the study. The participants were fully informed of the purpose, procedures and hazards of the study. The inclusion criteria for the case participants was as following: 1) be suffering from type 2 diabetes for >1 year, 2) age range 40-70 years, 3) no treatment with insulin or any other drugs known to influence the glucose metabolism at least four weeks prior to sampling, 4) no history of any recent acute illness or clinical evidence suggestive of kidney, liver, or endocrine diseases, 5) absence of chronic diabetic complications (proliferative retinopathy, albuminuria, symptomatic neuropathy, coronary, and other vascular diseases). Patients taking vitamin and/or mineral supplements, thyroid hormones, estrogen, progesterone, diuretics, or antihypertensive agents were excluded from the study. The institutional ethical board granted the approval of the research protocol.

Blood samples were drawn with metal-free, stainless steel needles into appropriately-coated tubes. Fasting plasma glucose and HbA_{1c} were determined by the glucose oxidase method (Biocon) and affinity chromatography (Biodiab Ion-exchange batch method) respectively. For estimation of Cu, Zn, Cr, Mg and Mn, 1 ml serum was used. Ashed serum was dissolved in diluted HCl and analyzed with atomic absorption spectrophotometer (Varian AA-1475) with airacetylene flame.

Results were expressed as mean \pm standard deviation (SD). Student's t-test was performed to compare variables among diabetic and non-diabetic subjects. Pearson's correlation coefficients (*r*) was used to identify trace elements association with age, glycemic status and diabetes duration. With 95% confidence interval (CI), statistical significance was defined as a $P < 0.05$. Statistical analysis was performed using SPSS for Windows (version 14.0).

Results

The diabetic patients had mean age 59.0 ± 8.83 years (range 42 -76 years). Age at onset of diabetes was 46.60 ± 5.38 years with duration of diabetes 12.2 ± 6.02 years. The mean age of nondiabetic controls was 58.6 ± 9.48 years (range 41 -74 years). In type 2 diabetic group, serum magnesium and zinc levels were found to be significantly low ($p < 0.0001$ - < 0.05) as compared to the non-diabetic group. Although copper was higher in case group compared to controls, difference did not reach to level of significance. Diabetic patients had lower manganese concentrations than that of their counterpart (Table 1). Chromium concentrations in all the study participants were below the in-built detectable limits of atomic absorption spectrophotometer.

Discussion

Interest in the biochemical and clinical consequence of trace element metabolism has been steadily increasing. Trace elements have important physiological effects when present at concentrations other than those associated with classical toxicity or with extreme deficiency. There is accumulating evidence that the metabolism of several trace elements is altered in diabetes mellitus^{1,6}.

The increased incidence of hypomagnesemia among patients with type 2 diabetes presumably is multifactorial. Altered insulin metabolism, poor glycemic control and osmotic diuresis may be contributory factors^{7,8}. We found decreased levels of Mg ($p < 0.0001$) in patients with diabetes when compared with controls. Literature survey indicates conflicting results reporting elevated or declined magnesium concentrations in diabetes mellitus^{1,5,9-11}. Zinc plays a clear role in the glucose metabolism^{12,13}. However the role of Zn in the clinical management of diabetes, its complications, or in its prevention is, at best, unclear¹⁴. Zinc levels in diabetic patients were significantly ($p < 0.05$) lower compared to nondiabetics as reported earlier^{1, 3,4,5,11,15}. However, comparable serum levels of zinc in the type 2 diabetic patients and normal subjects have been reported elsewhere¹⁶. The redox chemistry of Cu makes this both a powerful enzyme catalyst and a dangerous reactant that generates hydroxyl radical. Although virtually all cells from microbes to mammals must acquire Cu to drive important biochemical reactions, the potential toxicity of Cu demands an exquisite level of vectorial transport and homeostatic control¹⁷. Abnormal copper metabolism can lead to several chronic pathogenesis, such as diabetes or diabetic complications³. Serum Cu level in the diabetic group did not show statistical significant difference compared to the nondiabetic counterpart which is not consistent with findings of Kazi *et al.*¹⁵.

Manganese plays a role as a cofactor for the antioxidant enzyme, MnSOD, whose levels are reported to be lower in the

white blood cells of diabetics than in those of nondiabetic controls¹⁹. Although the routes of action of Mn has not been thoroughly demonstrated in terms of the pathology of type 2 diabetes, Mn is essential for glucose metabolism and deficiency may result in glucose intolerance similar to diabetes mellitus in some animal species. Studies examining the Mn status of diabetic humans have generated contradictory results²⁰. Diabetic patients showed lower level of Mn than that of normal nondiabetic subjects but the difference did not reach to the level of statistically significant difference. However, reduced or similar Mn levels in blood samples of diabetic patients as compared to control subjects are mentioned in previous studies^{1,15}. Chromium is required for normal carbohydrate metabolism and as a critical cofactor for insulin action^{2,21}. Reliable direct measurement of chromium status in human samples still not properly standardized. In the present study, repeated attempts to measure serum chromium were failed. In both the groups the element could not be detected. Trace elements under study were not influenced by glycemic control, age, and diabetes duration significantly.

The results confirm that deficiency and efficiency of some essential trace metals may play a role in the development of diabetes mellitus. In order to better understand the role of these trace elements in diabetes, further clinical studies are required enrolling larger number of patients and using more sophisticated techniques besides blood, urine and hair samples should also be obtained to allow clear conclusions.

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