



Association Between Altered Serum Mineral Levels and Micro Vascular Complications in Type 2 Diabetic Patients

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ABSTRACT

A relationship has been reported between trace elements and diabetes mellitus. The objective of the study was to evaluate serum minerals, HbA1C and their association with micro vascular complication in T2DM patients. To study the mineral status in diabetic complications – 180 subjects were divided in to three groups. 60 healthy controls with a age group Of 35-75 yrs (group-I), along with 60 uncomplicated type 2 diabetic patients(group-II) and 60 patients of type 2 diabetic with micro vascular complications were added in to groups (group-III) . Estimation of glycemic status, Serum magnesium, Zinc and Copper levels were done. Magnesium and zinc levels were found to be significantly decreased in the micro vascular complications which correlated negatively with glycolated haemoglobin. Copper level was found to be significantly increased in diabetic patient with and without micro vascular complications and seems to be associated with microvascular complication of diabetes mellitus as either causative factors or as a consequence of the disease. Screening of patients for these factors might help in the management of progression of the disease

KEYWORDS

Hypozaemia, Serum magnesium, microangiopathic complications,

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both [1]. People with diabetes are at high risk of microvascular complications including diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy, which have a major impact on quality of life and are associated with increased mortality [2-3].

A relationship between diabetes mellitus (DM) and minerals is frequently reported. Alterations in the metabolism of several trace elements, including copper, zinc, and magnesium have been associated with impaired insulin release, insulin resistance, and glucose intolerance in experimental animals and humans(4).

Magnesium (Mg) is an essential component in various enzymatic pathways involved in glucose homeostasis. The relationship between hypomagnesemia and insulin resistance, impaired glucose tolerance, as well as decreased insulin secretion has been suggested by recent studies [5-6]. Reduced plasma levels of Mg have been documented in both type 1 and type 2 Diabetes Mellitus, especially in poorly controlled DM [7]. Magnesium deficiency may have some effects on the development of diabetic complications with other risk factors. Patients with severe diabetic retinopathy have lower magnesium levels than do diabetic patients with minimal retinal changes, which suggest that hypomagnesaemia may be a risk factor in development of diabetic retinopathy [8].

Zinc, another essential trace element, is a component of many enzymes, and plays an important role in the maintenance of several tissue functions, including the synthesis, storage and release of insulin. Zinc has been found to enhance the effec-

tiveness of insulin in vitro, and it has been postulated that zinc deficiency may aggravate the insulin resistance in noninsulin dependent diabetes mellitus (NIDDM)[9]. Hyperglycemia causes the increased urinary losses of Zn and decreased Zn levels in the body. The decreased levels of Zn affect adversely the ability of the islet cell to produce and secrete insulin [10-11].

Copper is also a vital dietary nutrient, although only small amount of the metal are needed for well-being [12]. Transition metal like copper has affinity to bind with proteins that have been glyated. Generally, serum concentration of copper and Ceruloplasmin is elevated in type 2 diabetes mellitus patients . Ceruloplasmin and serum albumin are the main copper binding proteins in plasma and there is some evidence that chronic hyperglycemia can damage the Copper binding properties of both (13).

The aim of the present study was to evaluate and correlate the levels of serum minerals, in type 2 diabetes mellitus patients with microangiopathic complications in comparison to those without these complications and their relation with glycemic control.

MATERIAL AND METHOD

Study was conducted in the Department of Biochemistry in collaboration with Department of General Medicine in RAMA MEDICAL COLLEGE & HOPITAL, Kanpur , U P . A total 180 subjects in the age group of 35 – 70 years, were divided into 3 groups .Group-I consists of 60 healthy non diabetic subjects, Group-II 60 type2 diabetic patients without microvascular complications and Group-III consists of 60 type 2 diabetic patients with microvascular complications. Subjects suffering with type 1 diabetes, liver, renal disease, severe congestive heart failure and those taking trace elements were excluded from the study. The study was approved by the Ethical Com-

mittee of Institution. A written informed consent, in the vernacular language, was obtained from all the participants.

For each case and control group, Three ml fasting of venous blood sample was collected under aseptic precautions. An additional two ml venous blood was collected in EDTA vials for the estimation of glycated haemoglobin. Fasting blood glucose was estimated by GOD/POD method (14). Serum zinc, magnesium and copper were estimated by colorimetric kit method (15, 16 ,17). Diabetic retinopathy and neuropathy were diagnosed by fundoscopy and general physical examination of each patient.

Statistical method

Statistical analysis was done using SPSS software. Statistical significance for the study groups and controls were analyzed by using ANOVA and Pearson's correlation and $p < 0.05$ was considered as statistically significant.

RESU LTS

Table -1 serum minerals and glycated hemoglobin values with mean \pm S.D

Serum minerals	Control group (n=60)	T2DM patients without microvascular complications(n=60)	T2DM with microvascular complications(n=60)	p -value
FBS	83.9 \pm 6.74	132.4 \pm 22.88	189.16 \pm 44.72	<0.01
HbA1C	5.23 \pm 0.69	6.68 \pm 0.72	7.46 \pm 0.98	<0.01
Serum magnesium	2.37 \pm 0.4	1.51 \pm 0.46	1.12 \pm 0.36	<0.01
Serum zinc	91.42 \pm 13.49	77.7 \pm 10.08	57.40 \pm 15.39	<0.001
Serum copper	109.44 \pm 12.41	116.36 \pm 25.57	140.73 \pm 29.07	<0.01

The mean magnesium levels among cases with and without complications were 1.12 \pm 0.36 mg% and 1.51 \pm 0.46 mg% respectively as compared to 2.37 \pm 0.4 mg% among controls. There was a negative significant difference ($p < 0.01$) seen in serum magnesium levels among controls and cases.

The average concentration of zinc in groups I (control), group II (diabetic without complication), and group III (with complication) were measured as, 91.42 \pm 13; 77.7 \pm 10.08 and 57.40 \pm 15.39 μ g/dl respectively. The patients in group III and group II showed Hypozincaemia ($p < 0.001$) when compared to group I. But group III patients were having much lower values compared to group II

The mean serum Copper levels among cases with and without complications were 140.73 \pm 29.07 μ g/dl % and 116.36 \pm 25.57 μ g/dl % respectively as compared to 109.44 \pm 12.41 μ g/dl % among controls. There was a clear significance ($p < 0.01$) found between both the study groups and controls

The HbA1C (%) values in group I, group II and group III were measured as 5.23 \pm 0.69, 6.68 \pm 0.72 and 7.46 \pm 0.98 respectively. These were found to be significantly ($p < 0.01$) correlated with copper levels negatively correlated with values of magnesium and zinc in study groups.

DISCUSSION

Type 2 DM is a major global health problem that affects 200 million individual worldwide. The relationship of DM with minerals has been reported. The present study was undertaken to establish an association between the trace elements (zinc, magnesium and copper) and diabetes mellitus and its complications. In this study, serum magnesium concentration in both the study groups (type 2 diabetic with and without micro vascular complications) was found significantly ($p < 0.01$) lower than that of control group. Similar observations were reported by Schmits Chek H et al, Ashima et al 18,19 Tosiello L et al 20, Reason for hypo magnesemia is not clear but the possible reasons may be due to the magnesium depletion

caused by osmotic diuresis, and by indirect hormonal effects

Zinc acts as a cofactor for insulin, although its exact mechanism in carbohydrate metabolism is yet not clear. In this study, serum zinc levels in type 2 diabetic subjects were found significantly lower ($p < 0.01$) than that of control the findings are consistent with those of Walter et al 21, S Ferdousi 22, Nourmohammadi et al 23. According to Nourmohammadi et al, the possible reason for decreasing serum zinc concentration in diabetic patients is excessive urinary excretion of zinc especially in patients with diabetic nephropathy, gastrointestinal malabsorption or genetic factors or signs of infection during which zinc acts as a defense mechanism. There is a concurrent Hypozincaemia and a decrease in tissue zinc stores, abnormal zinc metabolism has been suggested to play a role in the pathogenesis of diabetes and / its complications. A negative correlation was observed between serum magnesium, zinc levels and glycated haemoglobin in study groups emphasizing its role in the progression of the disease

Copper plays a vital role in oxidative stress. Copper in its free form is a potent cytotoxic element because of its redox chemistry. A high level of copper enhances the toxic effect of metal dependent free radicals. Moreover the increase in copper levels in patients with type 2 DM might also be attributed to hyperglycaemia, which stimulates glycation and causes release of copper ions from copper binding sites of proteins. In the present study we obtained a significant increase in serum copper level in patients having type 2 DM as compared to controls. Zargar 24, Schlienger 25, Sarkar A et al 26, also found out a significant increase in serum level of copper in type 2 DM as compared to controls

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