RESEARCH ARTICLE

STUDY OF TRACE ELEMENTS (MG AND CU) AND DYSLIPIDEMIA IN TYPE 2 DIABETES MELLITUS (T2DM) PATIENTS PRESENTING IN A TERTIARY CARE HOSPITAL OF SOUTH EAST ASIA

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ABSTRACT

Introduction: Diabetes mellitus is a metabolic syndrome, which affect carbohydrates, lipid and protein metabolism. It is a heterogeneous disorder characterized by hyperglycemia due to impaired glucose utilization, resulting from defect in insulin secretion and insulin action. Alteration of some trace elements (mg and cu) has been reported in Diabetes Mellitus. These trace elements might have specific role in the pathogenesis and progress of the disease. Dyslipidaemia was seen in diabetic patients and was primarily responsible for risk of several complications in Type 2 Diabetes Mellitus (T2DM) patients.
Materials and Methods: The study was done in the Department of Biochemistry of two teaching medical college and hospitals of India, one in western India and one in North east India. The present study included total 100 subjects, divided into two group in which group 1 (healthy control) having 50 subjects and group 2 (Uncontrolled Diabetes mellitus) having 50 patients, groups were selected randomly without any bias of age, sex, socioeconomic status and duration of disease. Serum Mg estimated by calmagite method and serum Cu estimated by Calorimetric method of semi auto analyzer. Lipid profile was estimated by enzymatic method of semi auto analyzer.
Observation and Results: Mg level was found significantly decreased (p<0.001) in serum sample uncontrolled Diabetes mellitus patients compare to healthy subject. Cu level was found significantly increased (p<0.001) in serum of uncontrolled Diabetes mellitus patients compare to healthy subject. Lipid profile were found significantly increased level of total cholesterol (TC), very low density lipoprotein (VLDL), low density lipoprotein (LDL), triacylglycerol (TG) and HDL level was found significantly decreased
Discussion and Conclusion: According to our study showed decrease level of Mg and elevated Cu concentration in uncontrolled T2DM patients, and this alteration affect lipoprotein metabolism and caused several abnormalities and greater risk of secondary (cardiovascular and renal diseases) disorders.

INTRODUCTION

Diabetes mellitus is a metabolic disorder, in which impaired glucose metabolism and increase level of sugar in blood seen, known as a hyperglycemia. This hyperglycemia causes several complications like cardiac and renal disorders (Prabod *et al.*, 2011). Diabetes mellitus, a heterogeneous disease characterized by an absolute deficiency of insulin as well as insulin resistance.

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However, abnormal metabolism of trace element is observed in diabetic patients (Kamata *et al.*, 1996). Two important trace elements are (Mg and Cu) Involved in our study. These trace elements play important role in several metabolic pathways, and their abnormalities caused multiple effects on metabolism. Trace elements (Mg and Cu) are important for human growth and body biological function. Mg is a second most abundant intracellular cation and plays an important role in metabolism of glucose. Mg acts as a cofactor during the process of phosphorylation of glucose (McNair *et al.*, 1978). Serum Cu is essential trace element in metabolic system of body and can lead to several chronic complications such as diabetes and

diabetic complications (Zheng *et al*., 2008). Diabetic patients with T2DM are at greater risk of cardiovascular diseases. Abnormal lipoprotein levels seen in diabetic patients, low HDL, high Total cholesterol, increased triacylglycerol, increased LDL Cholesterol and elevated VLDL level are seen in T2DM patients. All these together contribute to several complications in T2DM patients (Miller *et al*., 1999).

MATERIAL AND METHOD

The study was done in the department of biochemistry of two teaching medical college and hospitals of India, one in western India and one in Northeast India. The present study included total 100 subjects, divided into two group in which group 1 (healthy control) having 50 subjects, group 2 (Uncontrolled Type 2 Diabetes mellitus) having 50 patients, they were selected randomly without any bias for age, sex, occupation, socioeconomic status and duration of disease. Study was approved by the Ethical committee of both the institutes. Informed consent was obtained from all patients. 5 ml of blood sample was withdrawn from the anticubital vein following fasting overnight. The blood sample was collected in plain, fluoride and EDTA vacutainers. The blood sample was centrifuged for 20 minute at 3000 rpm at room temperature. The serum was stored at 4^0C for biochemical investigations. Serum Mg was estimated by calmagite method and serum Cu estimated by Calorimetric method. Estimation of Total Cholesterol (TC) was done by enzymatic method as described by Allain *et al*. High density lipoprotein (HDL-C) was estimated by method of Burstein *et al*. Triacylglycerol (TAG) was estimated by an enzymatic method (Fossati and Prencipe, 1982) whereas Low density lipoprotein (LDL) and very low density lipoprotein were measured and calculated by Fried Wald's and Fredric son's formulae (1972).

$$LDL = TC - [HDL\text{-}C + VLDL]$$
$$VLDL = TG / 5$$

Statistical Analysis

Statistical analysis was done by using SPSS version 16. Results were expressed as mean ± SD and were analyzed by unpaired student's t-test. Value of $p<0.05$ was considered significant and $p< 0.001$ was considered highly significant.

RESULTS

Study group comprised 50 healthy subject and 50 T2DM patients.

Table 1. Demographic data and blood sugar level of control subjects and uncontrolled T2DM patients. (mean ± SD)

Parameters	Healthy (N=50)	Uncontrolled T2DM (N=50)	P Value
Age	49.7± 5.8	52.9±7.7[**]	<0.001
Sex	28:22	27:23	-
FBS mg/dl	83.3±6.1	170.2±16.1[**]	<0.001
PPBS mg/dl	120.6±12.4	250.5±16.2[**]	<0.001

T2DM: type 2 diabetes mellitus, FBS: fasting blood sugar,
PPBS: post prandial blood sugar p < 0.001: highly significant

Table 2. Trace element level of control subjects and uncontrolled T2DM patients (mean ± SD)

Parameters	Healthy (N=50)	Uncontrolled T2DM (N=50)	P value
Cu (µ/dl)	110.14±13.28	225.87±23.45[**]	<0.001
Mg (mg/dl)	1.84±0.45	0.77±0.69[**]	<0.001

T2DM: type 2 diabetes mellitus, p < 0.05: significant,
p < 0.01: highly significant

Table 3. Lipid profile of control subjects and uncontrolled T2DM patients. (mean± SD)

Parameters	Healthy (N=50)	Uncontrolled T2DM (N=50)	P value
Total cholesterol (mg/dl)	160.6±19.4	225.2±63.2[**]	<0.001
HDL-Cholesterol (mg/dl)	38.3±5.5	26.5±6.9[**]	<0.001
Triacylglycerol (mg/dl)	120.5±3.4	275.2±64.4[**]	<0.001
VLDL cholesterol (mg/dl)	21.8±7.4	48.4±25.7[**]	<0.001
LDL cholesterol (mg/dl)	144.5±25.6	156.6±37.8[**]	<0.001

T2DM: type 2 diabetes mellitus, HDL: high density lipoprotein,
LDL: low density lipoprotein, VLDL: very low density lipoprotein,
p < 0.01: highly significant

Table 1 Showed there is no significantly change seen in age and sex of uncontrolled T2DM patients compare to the control subjects. Fasting Blood Sugar and Post prandial Blood Sugar were found significantly higher ($p<0.001$) in uncontrolled T2DM patients compare to control subjects. Table 2 Showed Mg level was significantly ($p<0.001$) decreased (Figure 1) in uncontrolled T2DM patients compare to control subjects and Cu level was significantly ($p<0.001$) increased (Figure 2) in uncontrolled T2DM patients as compare to control subjects. Table 3 Showed significantly ($p<0.001$) increased level (Figure 3) of TC, LDL, VLDL, TAG compare to control subjects and HDL level was found significantly decreased ($p<0.001$) in T2DM patients compare to control subjects.

DISCUSSION

In our study we found decreased levels of Mg in uncontrolled T2DM patients. It is second most common intracellular cation. It is seen in hyperglycemic condition. Extra and intracellular Mg deficiency is characteristic of T2DM, Diabetic nephropathy and other complications associated with late stage of Diabetes Mellitus (Fox, 1999). Increased urinary loss of Mg causes osmotic diuresis (Muhammad *et al*., 2002; Garland *et al*., 1992). Elevated Cu levels are also found in diabetic subjects. Cu is an essential trace element, plays an important role in cytochrome oxidase present in the mitochondria. Deficiency of copper can cause swelling and distortion of mitochondrion in metabolically active tissues such as hepatocytes and pancreatic acinar cells (Agget, 1985). Abnormal Cu metabolism can lead to chronic complication in diabetic patients (Kazi *et al*., 2008). Cu level is not affected from glycemic control (Schlienger *et al*., 1988). According to other studies increased Cu level found in T2DM patients is due to increased level of ROS, which increases consumption of available antioxidants in the body. So these findings are due to various alterations of Cu in T2DM patients, due to antioxidant imbalance (Baloch *et al*., 2013). In our study we also found increased level of lipoproteins. Insulin resistance with T2DM is associated with plasma lipid and lipoprotein abnormalities, which includes reduced HDL Cholesterol and elevated LDL
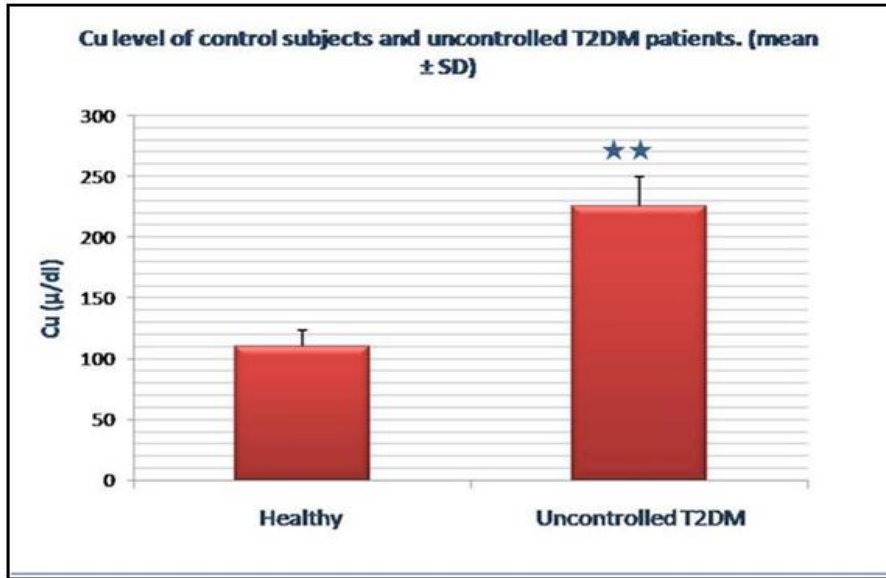
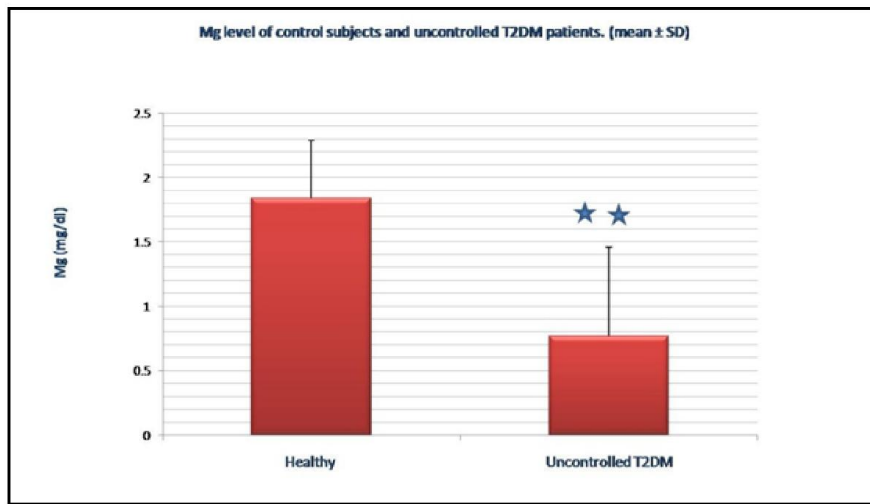**Figure 1. Showed Cu level of uncontrolled T2DM patients and control subjects**

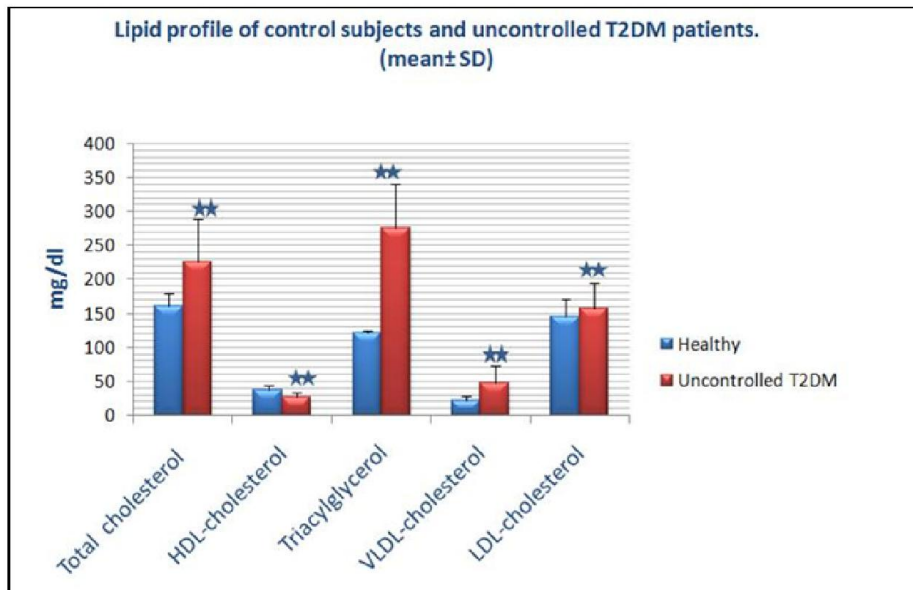**Figure 2. Showed Mg level of uncontrolled T2DM patients and control subjects**

Figure 3. Showed Lipid Profile of uncontrolled T2DM patients and control subjects

particles, and triglycerides (American Diabetes Association, 2003). Insulin resistance plays an important role in the development of diabetic Dyslipidemia which leads to increased efflux of free fatty acids from adipose tissue, impairs insulin dependent muscles uptake of free fatty acids and causes increased fatty acid release to the hepatic tissue (Boden *et al*., 1997; Kelley *et al*., 1994). HDL cholesterol levels is associated with low risk of dyslipidemia, more number of HDL particles contribute to normal lipid profile effect, in the form of, cellular cholesterol efflux and direct antioxidant and anti-inflammatory properties. Moreover, low level of HDL cholesterol is responsible for elevated triglyceride levels (Lamarche *et al*., 1996). Lipoprotein abnormalities increases with duration of T2DM (Shabana *et al*., 2013).

Conclusion

Our study showed deficiency of Mg and elevated Cu concentration in T2DM patients, and this alteration also effects lipoprotein metabolism causing several abnormalities. More work needs to be done whether Mg, Cu and other trace elements can be used therapeutically to the benefit of mankind.

Acknowledgements

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