RESEARCH ARTICLE

CO-RELATION OF TRACE ELEMENTS (MAGNESIUM & COPPER) AND LIPID PROFILE IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS PATIENTS – A CASE CONTROL STUDY

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ARTICLE INFO	ABSTRACT
	Introduction: Type-2 Diabetes mellitus is the most rapidly growing chronic disease in the world. - cell dysfunction is required to develop T2DM. Many with T2DM have relative insulin deficiency and early in the disease, absolute insulin levels increase with resistance to the action of insulin. Alteration of some trace elements (Mg & Cu) has been reported in Diabetes mellitus. Lipid profile abnormalities were seen in diabetic patients. They were responsible for risk of several complications. **Aim**: Study of trace elements (Magnesium & Copper) and Lipid profile in newly diagnosed type 2 diabetes mellitus patients and control subjects. **Materials and Methods:** The study was done in the Department of Biochemistry and Central Research Lab in United Institute of Medical Sciences Prayagraj, UP. The present study included total 78 subjects, divided into two groups in which group 1 (healthy control) having 39 subjects and group 2 (Diabetes mellitus) having 39 patients. Serum Mg was estimated by Calmagite method and serum Cu was estimated by DI-BR-PAESA method of semi-autoanalyzer. Lipid profile was estimated by enzymatic method of semi-autoanalyzer. **Observations and results:** Magnesium level was found significantly ($p<0.001$) decreased in diabetic patients as compare to control subjects and copper level was found significantly ($p<0.001$) increased in diabetic patients as compare to control subjects. Levels of cholesterol and LDL was found significantly ($p<0.001$) increased, and levels of TG was found significantly ($p=0.0125$) increased, and level of VLDL was also found significantly ($p=0.001$) increased, whereas level of HDL was found significantly ($p<0.001$) decreased in diabetic patients as compare to control subjects. **Discussion and conclusion:** Study was showed decreased level of Mg and increased level of Cu concentration in diabetic patients, and this alteration also affect lipoprotein metabolism and caused several abnormalities.

INTRODUCTION

Type 2 diabetes is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. (Fauci *et al*., 2012). Trace elements are essential substances for optimum human health, because of their diverse metabolic characteristics and functions (Dev *et al*., 2016). Magnesium plays a vital role in glucose homeostasis. It is a cofactor in phosphorylation of glucose and helps in carbohydrate metabolism (Fari, *et al*. 2013).

It serves as a cofactor for all enzymatic reactions that require ATP for kinases, activates neuromuscular excitability and cell permeability, regulates ion channels and mitochondrial functions, and an important factor in both cellular and humoral immune reactions (Phuong-Chi *et al*. 2007). Moreover, magnesium ion plays a critical role in lipid metabolism due to its essential cofactor in various enzymatic pathways such as in cholesterol metabolism where HMG-CoA reductase requires Mg^{++} for its metabolic regulation (Deepti *et al*. 2014). Also, magnesium plays a critical role in the regulation of lipoprotein lipase and lecithin cholesterol acyltransferase activities (LCAT) (Takaya, *et al*. 2004).

It is an important factor for insulin secretion and insulin action (Barbagallo *et al.* 2015). Hypomagnesemia impaired tyrosine kinase activity at insulin receptors and further it aggravates insulin resistance which leads to micro and macro vascular complications observed in diabetes, such as cardiovascular disease, retinopathy, and neuropathy (Rasic-Milutinovic *et al.*, 2004). Serum copper is an essential trace element in the metabolic system of the body and can lead to several chronic complications such as diabetes and diabetic complications (Zheng, Y, *et al.*, 2008). Copper is present in the body is important for metalloenzymes such as ceruloplasmin and superoxide dismutase (SOD). These enzymes play major roles in oxidation-reduction reactions and antioxidant defense mechanisms (Olaniyan *et al* 2012)**.** The increased productions of free radicals are likely to be associated with the development of type 2 DM. The free form of copper is toxic for our body because it causes oxidation-reduction imbalance by causing oxidative stress, which is one of the key factors associated with DM (Sarkar *et al.*, 2010). Ceruloplasmin carries the majority of plasma copper and reduces its existence in the free form (http://en.wikipedia.org/wiki/Ceruloplasmin).

Dyslipidemia is the major risk factor for CVD in diabetic patients. Type 2 DM is associated with plasma lipid and lipoprotein abnormalities, including reduced High-Density Lipoprotein HDL cholesterol, a predominance of small sense Low-Density Lipoprotein LDL particles, and elevated Triglycerides TGS (American Diabetes Association: 2009). An important characteristic of hyperlipidemia associated with magnesium deficiency is an accumulation of triglyceride-rich lipoproteins and a decrease in the concentration of HDL (Kenji Ueshima.2005). Type 2 DM is associated with a cluster of interrelated plasma lipid and lipoprotein (LP) abnormalities that are all recognized as predictors for coronary heart disease (Taskinen, 2002). Insulin resistance has a central role in the development of diabetic dyslipidemia and the main cause of the three cardinal features of diabetic dyslipidemia is the increased free fatty acid release from insulin-resistant fat cells. The increased flux of free fatty acids into the liver in the presence of adequate glycogen stores promotes triglyceride production, which in turn stimulates the secretion of apolipoprotein B (ApoB) and VLDL cholesterol. The impaired ability of insulin to inhibit FFA release leads to enhanced hepatic VLDL cholesterol production, which correlates the degree of hepatic fat accumulation (Arshag D Mooradian.2009).

Aim: Aim of this study to evalvate the level of trace element (Mg and Cu) and lipid profile level in Type II diabetes patients and compared with normal individuals.

Objectives

⌡ To estimate the level of trace elements (Magnesium & Copper) in cases and control subjects.
⌡ To evaluate the Lipid profile in cases and control subjects.
⌡ To find out the correlation of trace elements (Magnesium & Copper) and Lipid profile in cases and control subjects, if any.

MATERIAL AND METHODS

In this study we selected the total equal number of normal individuals and patients.

This study was conducted in the central lab of United Institute of Medical Sciences, Praygraj. In which we take total 78 samples. The distribution of samples is equal 39 normal and 39 patients.

Collection of data- The case was selected as per the Performa enclosed. A detailed clinical history including age, sex, occupation, duration of illness was collected from the patients.

Selection of cases: Minimum of established 39 cases of newly diagnosed type 2 diabetes mellitus patients were selected from those attending IIMS&R OPD with following inclusion and exclusion criteria.

Inclusion criteria

⌡ Age group 35-60 years
⌡ Newly diagnosed type 2 diabetes mellitus patients without any complications.
⌡ Subject who has signed the consent form.

Exclusion criteria

⌡ History of cardiac disease.
⌡ History of renal disease.
⌡ Type 1 diabetes mellitus.
⌡ Pregnant women
⌡ Smokers.
⌡ History of alcoholism.

Selection of control- In this study we selected healthy subjects with age group 35-60 years.

Collection of sample- Under aseptic condition total 4 ml venous blood was collected from the subjects in plain vial after an overnight or 12 hours of fasting. It was immediately centrifuged at 3000 rpm for 5 min and serum was separated.

⌡ For estimation of total cholesterol.
⌡ For estimation of serum triglycerides.
⌡ For estimation of serum HDL.
⌡ For estimation of serum magnesium.
⌡ For estimation of serum copper.

Serum Magnesium was estimated by Calmagite Method, serum Copper was estimated by DI-BR-PAESA method. Estimation of total Cholesterol (TC), Triglycerides (TG) and High Density Lipoprotein (HDL) was done by enzymatic method, whereas Low Density Lipoprotein (LDL) and Very low density lipoprotein (VLDL) were measured and calculated by Friedwarld's equation.

Serum LDL = Total cholesterol – triglycerides / 5 – HDL cholesterol
Serum VLDL =Ttriglycerides / 5

Statistical analysis: Statistical analysis was applied to all data using SPSS software (version 20.0). Mean ± SD of all quantitative clinical parameters was calculated in type 2 diabetes mellitus patients and control subjects. Studen 't' test was used to calculate significance (p value) in between the groups. Value of $p<0.05$ was considered statistically significant.

RESULTS

Magnesium level is significantly (p<0.001) decreased in diabetic patients as compare to control subjects and copper level is significantly (p<0.001) increased in diabetic patients as compare to control subjects. Levels of cholesterol and LDL is significantly (p<0.001) increased, and levels of TG is significantly (p=0.0125) increased, and level of VLDL is also significantly (p=0.001) increased, whereas level of HDL is significantly (p<0.001) decreased in diabetic patients as compare to control subjects.

Table 1. Trace element level of control subjects and T2DM patients. (mean ± SD)

Parameters	Controls	Cases	p value
Cu(μ /d)	128.529±8.079	209.529±45.885	p<0.001
Mg (mg/dl)	1.928±0.267	0.618±0.258	p<0.001

Table 2. Lipid profile of control subjects and T2DM patients (mean ± SD)

Parameters (mg/dl)	Controls	Cases	p value
Total cholesterol	145.412±16.640	244.200±49.758	p<0.001
Triglycerides	90.412±22.864	203.197±174.250	p=0.0125
HDL-cholesterol	44.941±3.363	33.206±4.090	p<0.001
VLDL- cholesterol	18.094±4.580	41.357±34.670	p=0.001
LDL- cholesterol	82.435±16.046	165.755±24.943	p<0.001

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

DISCUSSION

In the present study on newly diagnosed patients of type 2 diabetes mellitus, we found decreased levels of Mg. Similar such decrease in serum Mg level in diabetic patients as compared to non-diabetic has been reported by some authors (Monanty *et al.*, 2013). In our study the serum values of Mg and lipid profile showed significant difference when compared with control subjects and T2DM. Extra and intracellular Mg deficiency is characteristic of T2DM (Fox, 1999). Increased urinary loss of Mg causes osmotic dieuresis (Muhammad *et al.*, 2002). In a study conducted by Lal *et al.*, 2003, a significant fall in serum total cholesterol and triglycerides & a rise in HDL-c levels was observed after initiation of Mg supplementation. They concluded that Mg supplementation resulted in a beneficial effect on the lipid profile of these patients.

Our study suggests that diabetic patients should take Mg rich foods like whole grains, legumes, fruits and vegetables everyday which will help to provide recommended intake of Mg and maintain normal storage levels of this mineral. We observed significantly increased TC, TG, LDL levels and decreased HDL levels in patients as compared to control. Our study correlates with previous studies (Kamble P.M. *et al.*, 2015). The reason for increasing TC, TG, LDL are increasing in the incidence of the obesity, sedentary life lack of physical activity, the diet and risk factors like hypertension. The observed increase in TC, LDL-C, TG and CAD risk ratio accompanied with reduce HDL-C in diabetes shows lipid abnormalities and is synonymous with increased risk of atherosclerosis (Frohlich *et al.*, 1989. Grundy *et al.*, 1997). This abnormal lipid profile in diabetics might have resulted from insulin deficiency which plays major roles in intermediary metabolism (Dun *et al.*, 1982. Jama, 1993).

In type 2 diabetic, patients abnormalities in lipoproteins are presumed to be responsible for the increased risk of macrovascular disease because each lipid and lipoprotein fraction is affected by insulin resistance and hyperglycemia (Winicour *et al.*, 1992). In the present study, we found a significant elevation in serum copper content in T2DM patients as compared to control subjects. Copper is toxic in its unbound form, causes redox imbalance due to its highly redox active nature, which leads to activation of stress sensitive intracellular signaling pathway (Cunningham J, *et al.*, 1995. Mateo, 1978). 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).

CONCLUSION

The serum Mg, Cu and Lipid profile of various T2DM patients was studied and compared with control subjects. The mean values of entire Mg & Cu and lipid fractions TG, TC, VLDL-C & LDL-C, were significantly higher in diabetic patients than control subjects. In conclusion present findings demonstrate the deficiency of Mg and elevated Cu concentration in T2DM patients, and this alterations also effects lipoprotein metabolism causing several abnormalities. Hypomagnesaemia has role in perturbation of lipid metabolism in diabetes. Regular monitoring of serum Mg and Lipid profile along with Mg supplementation in T2DM may prevent its progression in diabetic complications.

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