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Research Article

EVALUATION OF SERUM COPPER, MAGNESIUM AND GLYCATED HAEMOGLOBIN IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

INTRODUCTION: Type 2 diabetes mellitus (DM) is an endocrinological disease associated with hyperglycemia characterized by both insulin resistance and defective insulin secretion. It is associated with the alteration of trace elements like copper and magnesium, which may be a contributing factor in the progression of DM and its complications.AIMS AND OBJECTIVES: The aim of the present study was to estimate serum copper, magnesium and glycated haemoglobin in patients with type 2 DM and compare it with controls (non diabetic healthy subjects). The association of glycated haemoglobin with serum copper and magnesium was also evaluated.MATERIALS AND METHODS: This study was conducted in 200 subjects, out of which 100 were type 2 diabetes mellitus patients (cases) and 100 were non diabetic healthy subjects (controls). Serum magnesium, glycated haemoglobin were measured by using the auto analyzer Beckman Coulter DXC 600. Serum copper was measured by modified spectrophotometric micromethod using Guanidine hydrochloride and Bathocuprine disulphonate disodium salt (BCDS).RESULTS AND OBSERVATIONS: We found a significantly increased level of copper and glycated haemoglobin and decreased level of magnesium in cases as compared to controls. Our study also revealed a significant positive correlation between serum copper and glycated haemoglobin and a negative correlation between serum magnesium and glycated haemoglobin.CONCLUSION:Patients with type 2 DM had altered metabolism of copper and magnesium and this may be related to the increased level of glycated haemoglobin. Impaired metabolism of these trace elements may have a contributory role in the progression of DM and its complications.

Keywords: Copper, Hypomagnesemia, Glycated haemoglobin, type 2 diabetes mellitus, Oxidative Stress

INTRODUCTION

Type 2 DM is an endocrinological disease associated with hyperglycaemia characterised by both insulin resistance and defective insulin secretion[1]. A relationship between DM and minerals is frequently reported. Alteration in the metabolism of trace elements like copper, magnesium is associated with DM [2]. Trace elements are accepted as essential for optimum health, because of their diverse metabolic characteristic and functions [3]. Trace elements participate in production of reactive oxygen species (ROS), which contribute to oxidative stress. Oxidative stress contributes to the pathogenesis of many diseases including DM. Previous studies have shown that copper causes oxidative stress [1, 2, 4, 5]. Copper acts as a pro oxidant and may participate in metal catalysed formation of free radicals [2]. The increased production of free radicals is likely to be associated with development of type 2 DM.

Magnesium is an essential element involved in glucose homeostasis. It is a cofactor for various enzymes in carbohydrate metabolism. It is also involved at multiple levels in insulin secretion, binding and activity. Reduced level of magnesium has been documented in type 2 DM [2, 3, 4, 5]. Hypomagnesemia may have negative impact on glucose homeostasis and insulin sensitivity in type 2 DM patients [6]. Hypomagnesemia may also have some effect in the development of diabetic complications with other risk factors [7]. Keeping in mind the above facts, the aim of the present study was to evaluate the serum levels of copper, magnesium and glycated haemoglobin in patients with type 2 DM and compare it with controls and also to assess the association of these minerals with glycated haemoglobin.

MATERIAL AND METHODS

The study was approved by the Ethics Committee; a written informed consent was obtained from all participants for participation in this study. A total of 100 patients (aged 30-70 years) with type-2 DM recruited from Institute's Medicine and Endocrinology departments. The diagnosis of type-2 DM was confirmed by biochemical investigations as per WHO criteria. Patients were excluded when diagnosed with type 1 DM, acute complications such as severe infection, major operations, trauma, GI disorders, severe cardiovascular/respiratory diseases, pregnant and breast feeding women. Patients taking supplements such as antioxidants, vitamins, minerals were also excluded. Age and sex matched 100 controls were recruited after clinical and biochemical evaluation. The baseline demographic data and family history were obtained. 3 mL of venous blood sample was collected for estimation of blood glucose, HbA1c, magnesium and copper. Serum magnesium was measured by a timed end point calmagite method [8] and serum copper was measured by modified spectrophotometric micro-method using guanidine hydrochloride and bathocuprine disulphonate disodium salt [9]. Hb and A1c concentration were measured using IFCC reference method [10]. All the above mentioned parameters were measured using the autoanalyzer Beckman Coulter DXC 600.

STATISTICAL ANALYSIS

Statistical analysis of data was performed using the SPSS (Version 15.0). For the comparison of values between the groups, students't' test was used, represented by 'p' value. Statistical significance was considered at a 'p' value of < 0.05. For the correlation, Pearson's correlation coefficient was used.

RESULTS

A total of 200 subjects were included in our study, 100 Type 2 DM patients (70 males and 30 females) and 100 gender matched non-diabetic apparently healthy control subjects. The age group of cases and controls were between 30-70 years with a mean age of 54.36±11.25 for cases and 51.81±10.25 for controls (Table 1). A significant rise ($p < 0.001$) in the serum levels of HbA1c and copper were observed in diabetic patients, in comparison with controls. Serum magnesium was significantly decreased ($p<0.001$) in diabetics than controls (Table 1) (Fig 1: A-C). Table 1 also shows routine biochemical parameters such as fasting and post prandial blood sugars done in all subjects. They were significantly higher in cases than in controls.

Pearson's correlation coefficient was used to find out the association between HbA1c with copper and magnesium. A significant negative

correlation between serum HbA1c and magnesium was observed (r = -0.381, p=0.011).

A significant positive correlation was observed between HbA1c and serum copper (r= 0.422, p=0.002). (Table 2)

TABLE 1: COMPARISON OF PARAMETERS IN TWO GROUPS (CASE AND CONTROLS) STUDIED

PARAMETERS	CASES (n=100)	CONTROLS (n=100)	P VALUE
Gender (M/F)	70/30	70/30	-
Age(mean± SD)	54.36±11.25	51.81±10.25	0.131
Duration of diabetes (years)	11.02±8.9	-	-
Fasting Blood Glucose (FBS) (mg/dL)	218.62±97.86	81.96±12.04	<0.001**
Post Prandial Blood Glucose (PPBS) (mg/dL)	285.04±121.7	113.56±22.39	<0.001**
HbA1c %	9.95±3.12	4.83±0.70	<0.001**
Serum magnesium mg/dL	1.58±0.28	1.91±0.22	<0.001**
serum copper mg/dL	155.32±17.99	104.62±25.99	<0.001**

**** Highly significant**

TABLE 2: PEARSON'S CORRELATION COEFFICIENTS OF SERUM MAGNESIUM AND SERUM COPPER WITH HBA1C

PEARSON CO RELATION	CASES	
	r VALUE	p VALUE
Serum magnesium v/s HbA1c	-0.381	0.011
Serum copper v/s HbA1c	0.422	0.002

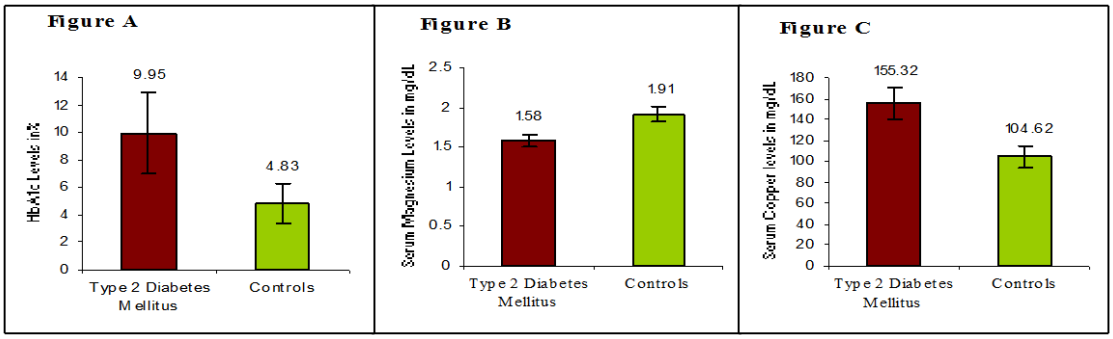

FIGURE 1:(A-C): MEAN±SD OF HBA1C, SERUM MAGNESIUM AND SERUM COPPER IN PATIENTS WITH TYPE 2 DM CONTROLS

DISCUSSION

Type 2 DM is a major global health problem that affects 200 million individual worldwide [7]. It is characterised by insulin resistance in peripheral tissues and an insulin secretory defect of beta cells of the pancreas [11]. The relationship of DM with minerals has been reported [1, 2, 3, 5]. Among these minerals copper and magnesium are of particular interest.

In the present study we obtained a significant increase in serum copper level in patients having type 2 DM as compared to controls. Zargar HA et al showed that copper levels were significantly elevated in NIDDM patients than in non diabetic subjects [4]. In a study done by Schlienger et al, elevated levels of copper were found in patients with IDDM and NIDDM [12]. Sarkar A et al, also found out a significant increase in serum level of copper in type 2 DM as compared to controls[1].

It is well known that copper plays a vital role in oxidative stress [1, 2]. Copper in its free form is a potent cytotoxic element because of its redox chemistry. It readily participates in Fenton and Heiber Weiss reactions to generate reactive oxygen species [13, 14]. 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. The release of copper ions into blood further accelerates the oxidative stress [15].

The other finding of this study was a significant decrease in serum magnesium level in type 2 DM as compared to controls. Similar such decrease in serum magnesium level in diabetics patients as compared to controls has been reported by some authors [2,3,4,16].

Magnesium is a cofactor for several enzymes involved in carbohydrate metabolism [17]. Magnesium is important for the effectiveness of insulin. It is involved at multiple levels in insulin secretion, binding and its activity. A reduction of magnesium in the cells strengthens insulin resistance [18, 19]. Magnesium deficiency decreases insulin sensitivity via alteration of the insulin receptor associated tyrosine kinase in type 2 DM patients [17]. Hypomagnesemia can increase the platelet reactivity, increase vascular and adrenal responses to angiotensin II enhanced thromboxane A2 release and lead to organ damage from free radicals [20, 21].

Magnesium itself has been reported to possess antioxidant properties by scavenging oxygen radicals probably by affecting the rate of spontaneous dismutation of superoxide anions. Increased free radical formation and reduction in antioxidant potential contributes to the development of oxidative stress in type 2 DM [4]. The cause of hypomagnesemia may be attributed to osmotic renal loss from glycosuria, and also decrease in net tubular reabsorption of magnesium [22]. The present study showed a significant (p<0.001) rise in HbA1c level in cases as compared to controls, which is similar to the findings of other studies [2, 5, 22]. The study also showed that HbA1c levels significantly correlated positively with serum copper (r=0.422, p=0.002) and inversely with serum magnesium (r=-0.348,p=0.013) in diabetic patients, which is in agreement with the study done by Viktorinova et al [2].

The patients with DM who had altered metabolism of copper and magnesium was probably related to increase in HbA1c. The

impaired metabolism of these elements may contribute to the progression of DM and its complications.

CONCLUSION

In conclusion the present findings demonstrate the imbalance in levels of serum copper and serum magnesium among the patients of type 2 DM in comparison to controls. These changes may play an important role in the pathogenesis of type 2 DM by the involvement of these elements in the oxidative stress. Moreover increased levels of copper and decreased level of magnesium are associated with increased values of HbA1c. This suggests that the impaired metabolism of these minerals may have a contributory role in the progression of DM and later development of complications.

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DECLARATION OF CONFLICTING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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