To Study the Levels of Serum Chromium, Copper, Magnesium and Zinc in patients with Diabetes Mellitus Type 2

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ABSTRACT

Objective: To study the correlation of trace elements deficiency with diabetes Mellitus.
Study design: This is a prospective, cross sectional and comparative study.
Settings: The study was conducted at diabetes management center of Jinnah hospital.
Material and Methods: A total of 100 subjects were selected, 50 were diagnosed patients of diabetes type 2 and 50 were normal healthy individuals. . The study was conducted at diabetes management center of Jinnah hospital and normal healthy individuals were selected from relatives of the patients. It was a continuous study and the required samples were collected form the diabetic patients and normal healthy individuals over a period of two months, from January to February2011. Plasma glucose level was estimated by using glucose oxidase method. The modified colorimetric procedure of Fluckiger and Winterhalter was employed for estimating HbA1c levels. Serum trace elements were estimated by atomic absorption spectrophotometer.
Results: The mean fasting blood glucose level in Diabetics was significantly greater (151.38±37.970) mg/dl than in Non Diabetics healthy controls (88.320±9.707mg/dl). Mean HbA1-c level in case of Diabetics was significantly greater (7.470±1.183gm%) than Non Diabetic healthy controls (5.664±0.0747mg%). No statistically significant difference (P value is >0.05) in the mean Cu^{++} level was observed between Diabetics (88.4±40 µ g/dl) and in normal healthy controls (101±39 µ g/dl) . Serum Zn was significantly lesser (P value <0.05) in Diabetics (510±89 µ g/dl) than in Non Diabetics(603±91µ g/dl). Similarly serum chromium level was significantly lesser in Diabetics (1.99±0.8 µ g/dl) than in normal healthy controls(2.61±0.054 µ g/dl). Mean serum level of Mg^{++} was significantly lesser (P value is <0.05) in Diabetics (17.76± 0.66 µ g/dl) than in normal healthy controls (22.13±1.65 µ g/dl).
Conclusion: In the present study serum chromium, zinc and magnesium were found to be significantly lower in patients with diabetes type 2 as compared to normal healthy individuals. Serum copper was also low but it was not statistically significant
Key words : Diabetes, glcosylated hemoglobin, trace elements

INTRODUCTION

Diabetes mellitus is a chronic disorder of carbohydrates , lipids and protein metabolism. There is defective or deficient insulin secretary response, that results in impaired carbohydrates metabolism. This is characteristic feature of diabetes mellitus resulting in hyperglycemia. Approximately 100 million people suffer from diabetes mellitus , making this one of the most common non communicable disease[1]. In Pakistan, 6.9 million people are affected by diabetes. The International Diabetes Federation estimated that this number will grow to 11.5 million by 2025 unless measures are taken to control the disease. Type 2 diabetes mellitus was once considered a rare disease but recently an explosive increase in its incidence has been observed. Insulin resistance and hyperinsulinemia are characteristics of both type 2diabetes and impaired glucose tolerance[2]. Interest in the role of trace elements in medical research has been growing in recent decades. Many trace elements seem to be essential for humans and various metabolic processes are dependent on normal trace elements concentrations. Their deficiency has been implicated

in various diseases including Diabetes, Anaemia, Depression, Ageing, low sexual potency and Heart disease[3]. Morradian and Morrely (1987) in their review article on the serum micronutrient status in diabetes stated that the relationship between nutrition and diabetes was suspected as early as 1674, and that over the last twenty years, numerous studies have found alterations in micronutrient status of patients with diabetes mellitus[4]. Diabetes mellitus, is a heterogeneous disease characterized by an absolute or relative deficiency of insulin as well as insulin resistance. Numerous authors have evaluated mineral levels and status in diabetic subjects yet, often inconsistent and contradictory results (frequently to the point of non-validity) have been presented[5,6,7]. This difference may be due to the number of subjects, sex and laboratory processing. Some trace elements act as antioxidants and prevent membrane peroxidation. Others act directly on glucose metabolism. Ceruloplasmin, the major plasma copper-transporting protein, possesses a potent antioxidant property. Manganese is a cofactor for a number of enzymatic systems including Arginase which has been found to be elevated in diabetic animals such as rats and mice[8]. Magnesium has an important role as a cofactor in the phosphorylation of glucose and in many other enzymatic reactions. Chromium, as a component of the Glucose Tolerance Factor (GTF) is essential for normal carbohydrate and lipid metabolism in mammals[9]. It acts by activating insulin receptor kinase activity up to seven fold[10], thus increasing insulin autoamplification and efficiency[11,12].

Magnesium, on the other hand, serves as a cofactor for some enzymes of the glycolytic pathway and enhances the ability of insulin to activate tyrosine kinase[13]. Zinc (Zn) is an essential micronutrient which has an important role in the functioning of hundreds of enzymes in insulin metabolism and acts as an efficient antioxidant[14,15,16]. Concerning metabolic diseases (insulin resistance, metabolic syndrome, diabetes), Zn is important because, it plays a major role in the stabilization of insulin hexamers, pancreatic storage of the hormone and is an efficient antioxidant[17,18], while oxidative stress is considered to be a main component in initiation and progression of insulin resistance and diabetes[19] .

In this study we evaluated the serum levels of Zn, Cu, Cr and Mg in patients of diabetes mellitus type 2 and compared with normal healthy individuals with same ratio of age, sex and BMI to ascertain if diabetics were deficient of these trace elements.

MATERIAL AND METHODS

This is a prospective, cross sectional and comparative study which has been conducted on patients with diabetes mellitus type 2 and compared with normal healthy individuals. A total of 100 subjects were selected, 50 were diagnosed patients of diabetes type 2 and 50 were normal healthy individuals. The study was conducted at diabetes management center of Jinnah hospital and normal healthy individuals were selected from relatives of the patients. It was a continuous study and the required samples were collected form the diabetic patients and normal healthy individuals over a period of two month, from January to February2011.

The subjects were selected after taking written consent, detailed history and examination. Patients suffering from endocrinal disorders, hepatic disease, renal diseases, alcoholism or other drug abuse and in case of female patient, having pregnancy and using oral contraceptive pills were excluded. Both patients and normal healthy individuals were requested to come with 10-12 hours of fasting for fasting blood glucose level, and two hours after breakfast (2HABF). Samples were collected for blood glucose level, glcosylated hemoglobin, serum Cr, Cu ,Mg and Zn after breakfast. 1.5 ml of blood was taken aseptically in 5cc disposable syringe for estimation of fasting blood glucose level. 7 ml of second blood sample was drawn in 10 cc disposable syringe two hours after breakfast for the determination of blood glucose level (2HABF), HbA 1-c and serum levels of trace elements. Out of 7, three ml was placed in EDTA tube for HbA 1-c estimation, 4 ml of blood was placed in a second test tube and allowed to clot for determination of glucose and trace elements. Clotted blood in the test tube was centrifuged ay 2000 rpm for three minutes and serum was separated and stored at -20^0C until shifted to laboratory for biochemical analysis.

Plasma glucose level was estimated by using glucose oxidase method. The modified colorimetric procedure of Fluckiger and Winterhalter was employed for estimating HbA1c levels. Serum trace elements were estimated by atomic absorption spectrophotometer.

RESULTS

Among two groups , in diabetic all were married, 40% were male and 60%were female. Out of 40% males, 64% were smoker and 30% were non smoker. In case of Non Diabetics, 10%were single and 90% were married, 50% were males and 50% were female. Out of 50% males, 76%wre non smoker and 24% were smoker. Out of Diabetics , 24% were using Biguanides, 7o% sulphonyluria and 6% insulin along with oral hypoglycemic agents.

The age, height, weight and BMI of the two groups is shown in table (1). The mean age of Diabetics was 43.26±2.912 years and for non Diabetics healthy controls was 43.36±3.306. The P value was >0.05 showing no significance.

The mean height of was lesser(155.820± 11.272 cm) in Diabetics than in non diabetics (159±10.102 cm), and P value > 0.05 which is not significance. The mean weight for diabetic group was 71.120±13.452 Kg and for non diabetic healthy control it was 72.10±13.452Kg and P value was >0.05. Body mass index (BMI) was significantly greater (P <0.05) in Diabetics(29±4.702) than in non diabetic healthy control (27.671±0.257). The mean fasting blood glucose level in was significantly greater(P value < 0.05) (151.38±37.970 mg/dl) in Diabetics than in non Diabetics healthy controls (88.320±9.707mg/dl) (Table 2)

The mean HbA1-c level was significantly greater (P value <0.05) in Diabetics (7.470±1.183gm%) than in Non Diabetic healthy controls (5.664±0.0747mg%) (Table 2) .

No statistically significant difference (P value is >0.05) in the mean Cu^{++} level was observed between Diabetics (88.4±40 µ g/dl) and in normal healthy controls (101±39 µ g/dl) (Table 3).

Serum Zn was significantly lesser(P value <0.05) in Diabetics (510±89 µ g/dl) than in Non Diabetics(603±91µ g/dl) (Table 3) .

Similarly serum chromium level was significantly lesser (P value <0.05) in Diabetics (1.99±0.8 µ g/dl) than in normal healthy controls(2.61±0.054 µ g/dl) (Table 3).

Mean serum level of Mg^{++} was significantly lesser(P value is < 0.05) in Diabetics (17.76± 0.66 µ g/dl) than in normal healthy controls (22.13 ±1.65 µ g/dl) (Table 3).

Table 1: Descriptive of age, height weight and BMI of diabetics and non diabetics P value less than 0.05 is significant

Variable	Diabetics (n=50)		Non diabetics (n=50)		P value
	Mean	SD	Mean	SD	
Age –years	43.26	2.912	43.36	3.306	0.245
Height –cm	155.820	11.272	159.73	10.102	0.677
Weight – kg	71.12	8.665	72.10	13.452	0.001
BMI	29.59	4.702	27.671	6.241	0.257

Table 2: Descriptive of fasting blood glucose level and Hb A1-c in diabetics and non diabetics P value less 0.05 is significant

Variables	Diabetics (n=50)		Non diabetics (n=50)		P value
	Mean	SD	Mean	SD	
Fasting blood glucose level mg/dl	151.38	37.970	88.320	9.97-	<0.05
Hb A 1-c	7.470	1.183	5.664	0.747	<0.05

Table 3 : descriptive of serum Cu, Zn, Cr and Mg levels in diabetics and non diabetics healthy controls (P value less than 0.05 is significant)

Trace element	Normal healthy controls	Patients with diabetes type 2	P Value
Copper	101 ±39	88.4±40	0.1
Zinc	603±91	510.4±89	0.001
Chromium	2.61±0.054	1.99±0.8	0.001
Magnesium	22.13±1.65	17.76±0.66	0.005

DISCUSSION

In reviewing clinical studies published on this topic over the last few years, it becomes apparent that several minerals are of great importance and have potential impact on the typical diabetic individuals. The minerals found to be subjects of concern in the diabetics most commonly are, Magnesium, Zinc, chromium and copper. Alteration in the status of trace elements has been reported in a number of disease states, trauma and infections. Diseases of liver and kidney have been known to affect tissue distribution and excretion of trace elements[20]. Excessive accumulation or depletion of trace elements may have significant clinical implication including increase risk of Cancer, Cardiovascular disease, Immune deficiency anemia, Renal function impairment and Bone diseases[21]. The actual status of these elements in Diabetes and other ailments is still uncertain. A number of signs and symptoms of Diabetes are shared in common with different trace elements deficiencies. These include Impaired glucose tolerance, fasting hyperglycemia, Glucoseuria, Hypoglycemia, elevated circulating insulin, Nephropathy and Peripheral neuropathy[21].

The present cross sectional study was conducted between two groups, diabetics and non diabetics healthy controls. Fasting blood glucose level and glycosylated hemoglobin were significantly higher in diabetics as compared to non diabetics healthy controls . According to Anetor et al 2002 it has been established that Diabetics have higher levels of fasting plasma glucose and glcosylated hemoglobin[22].

The serum chromium level in Diabetic group was significantly lower as compared to Non Diabetic normal healthy controls which confirmed the finding of Nouramonamadi et al 2000, who also reported lower level of serum chromium in Diabetics[23].

Significantly low serum chromium level was also reported by Ding et al 1998 in elderly diabetics[24]. Reduced chromium level was also reported in patients with Diabetes type 2 by Davis et al 1997[25].

In this study the serum zinc level of the patients with Diabetes Mellitus type 2 is lesser as compared to normal healthy individuals. This has been proposed that the decreased serum zinc level is due to its complex formation with insulin and hence the lack of free insulin enhances the appearance of the symptoms of Diabetes that occurred in these patients[26].

In our study Mg levels were found significantly lower as compared to healthy controls. This decrease in serum Mg levels has also been described in an earlier study[27]. Though serum Mg may not accurately reflect the level of total body Mg stores, persistent glycosuria with osmotic diuresis leads to Mg wasting and contributes to high frequency of hypomagnesemia in poorly controlled diabetics[28]. Concentration of serum copper in patients is decreased but that is not significant. This may be due to excretion of copper in urine or there may be slow transfer of loosely bound copper of ceruloplasmin to the tissues[28]. In a study by Schlienger et al elevated levels of serum copper were found in patients with IDDM and NIDDM. Our study shows that glycaemic control affects copper levels but this result is different from results of study conducted by Schlienger[29].

CONCLUSION

We conclude that levels of serum chromium, Zn and Magnesium were lower in patients with Diabetes type 2 as compared to normal healthy controls, while level of serum Copper was low but not significant.
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. Blood, hair and urine samples should also be obtained to clear picture.

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