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Research Article

CORRELATION OF SERUM MAGNESIUM, ZINC AND COPPER WITH INSULIN RESISTANCE (HOMA-IR) IN T2DM PATIENTS

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A B S T R A C T

Background: Diabetes is a long-standing disease characterized by hyperglycemia.Insulin resistance (IR) is the key pathophysiological defect that leads to the development of type 2 diabetes mellitus. The trace elements are association with insulin resistance.

Objectives: The purpose of the present study was to estimate serum zinc, magnesium, copper and insulin resistance (HOMA-IR) in type 2 diabetes mellitus patients and to see the correlation between them.

Material and methods: The present study was carried out in the Department of Biochemistry on 320 subjectsin the age group of 35-70 years, attended OP in Rama Medical College and Hospital. Among them 160 healthy subjects enrolled as control group remaining 160 T2DM patients were served as case group. Fasting venous blood sample was analyzed for fasting blood sugar (FBS), serum zinc, serum magnesium, serum copper and serum insulin. Insulin resistance was calculated by HOMA-IR method. Statistical analysis was done using student 't' test. Pearson's correlation between the study variables was performed to establish the relationship.

Results: The FBS, serum copper and Insulin resistance levels were significantly elevated in diabetics compared to healthy controls ($p<0.001$). There was significant decrease in the levels of serum zinc and magnesium levels in diabetics compared to the controls ($p<0.001$). A positive correlation found between serum copper with Insulin resistance, and a negative correlation found between serum zinc and magnesium with Insulin resistance in diabetic patients.

Conclusion: Diabetic patients showed anegative correlation between serum zinc and magnesium with insulin resistance and positive correlation found between serum copper with insulin resistance.

INTRODUCTION

Diabetes is a long-standing disease characterized by hyperglycemia that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces [1]. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs especially the nerves, eyes, kidney, heart and blood vessels[2]. *Many hypothesis have been proposed to explain the pathogenesis of type 2 diabetes mellitus that connects the disease to a state of subclinical chronic inflammation. Metabolically triggered inflammation has been proposed as a key step in the pathogenesis of type 2 DM*[3].

Insulin resistance is a condition where the insulin produced by the pancreatic cells does not exerts its action proportionately to its blood concentration [4].

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It generally develops and expands prior to disease and is followed by increased dysfunction in the type 2 diabetes. Insulin resistance often accompanies excess visceral adiposity, dyslipidemia, hypertension, impaired fibrinolysis, increased platelet aggregation, vascular inflammation, endothelial dysfunction and premature atherosclerosis[5]

The metabolism of several minerals has been reported to alter in diabetes mellitus and these elements might have specific role in the pathogenesis and progress of the disease. Among these the trace elements-magnesium, zinc and copper are having a great role in glucose homeostasis, insulin secretion, storage and action. 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 [6-7]. Reduced plasma levels of Mg have been documented in both T1DM and T2DM, especially in poorly controlled DM [8] Magnesium deficiency may have some

effects on the development of diabetic complications with other risk factors.

Zinc, another essential trace element, is required for normal glucose metabolism, strengthens the insulin-induced transportation of glucose into cells by its effect on the insulin signaling pathway is a component of many enzymes, and plays an important role in the maintenance of severaltissue functions. Zinc is useful in the synthesis, storage and secretion of insulin. Zinc may improve glycemia therefore a restored zinc status in patients with type 2 diabetes may counteract the deleterious effects of oxidative stress which helps to prevent complications associated with diabetes [9].

Copper is the third most abundant trace element in the body. Its role as a cofactor component of cytochrome oxidases, superoxide dismutase, tyrosinase, uricase, dopamine ß-hydroxylase, lysyl oxidase and ceruloplasmin make it a key micronutrient for oxidative pathways. The loss of this activity may contribute to the characteristic swelling and distortion of mitochondria which can be observed in copper deficiency, particularly in metabolically active tissues such as pancreatic acinar cells, enterocytes, and hepatocytes [10].

The aim of the present study was to compare the status of some minerals of patients with T2DM and to compare with nondiabetic healthy subjects and also to assess the association between these elements and Insulin resistance. (HOMA-IR)

MATERIAL AND METHODS

Study Participants*:* The present study comprises 160 patients in age group of 35-70 years suffering with type 2 Diabetes reporting to Rama medical college and Hospital. The criteria for the diagnosis of DM were according to the criteria of the American Diabetes Association (ADA) 2007 guidelines [11]. Age and sex matched 160 healthy subjects served as controls. The controls were free from any major aliment which could affect the parameters under study. . Informed written consent was obtained from all the subjects enrolled for the study. . Institutional ethical committee clearance was obtained for the study.

Exclusion criteria: individuals suffering with type 1 DM, Patients on diuretics, receiving magnesium supplements, taking drugs that affect blood glucose levels, cardiac, infectious and inflammatory disease were also excluded

Biochemical analysis-5ml of blood was collected from anti cubital vein with aseptic precaution in Fasting condition.2 ml blood was transferred to fluoride bulb for sugar estimation and 3ml of blood was collected in plain bulb for the estimation of copper, zinc, magnesium and Serum Insulin. It was allowed to clot and serum was separated by centrifugation at 3000 rpm for 10 minutes.

The following parameters were studied

1. ***Fasting blood glucose****:* GOD-POD, endpoint colorimetric method.
2. ***Serum Zinc****:* NITRO-PAPS method (kit supplied by Tulip diagnostics).
3. ***Serum Magnesium****:* XYLIDYL BLUE method (Kit by Tulip Diagnostics).
4. ***Serum Copper****:* Di-Br-PAESA method (Kit by Tulip Diagnostics)
5. All the parameters read using semi-autoanalyzer (ERBA CHEM 5).
6. ***Serum Insulin:*** Electrochemiluminescence immunoassay "ECLIA" by Roche Hitachi Cobas e 411 analyzers (kit by Roche Diagnostics)
7. ***Insulin Resistance:*** Homeostasis model assessment

Statistical Analysis

All the values were expressed as Mean ±SD .The statistical analysis was done using student 't' test for comparison between two groups and a p-value of <0.05 was considered statistically significant.

RESULTS

The present case-control study conducted on 320 subjects among them 160 people suffering with type 2 DM were chosen as case study group(group-II) and 160 age and sex-matched healthy subjects were served as control group (Group-I).

Table 1 Comparison of Biochemical parameters in Control and T2DM patients

Parameters	Control n=160 (mean ± SD)	Case group(T2DM) n=160 (mean ± SD)	Pvalue
AGE	47.56 ±8.49	50.37 ± 8.75	<0.001*
FBS	85.70 ±10.13	142.45 ±28.24	<0.001*
HbA1C	5.21 ± 0.04	6.84 ± 0.2	<0.001*

Values are mean (SD) or percentages, as appropriate, ∗p-value for difference between groups by t-test or chi-square, as appropriate

The descriptive biochemical characters of control and study group were shown in Table-1. Mean age of the study population was 47.56 ± 8.49 and for control group it was 50.37 ± 8.75. There was a significant difference seen in age of controls and diabetic patients (<0.001).

The Mean HbA1C value of case group was (6.84±0.2)was highly elevated in comparison to case group (5.21± 0.04) And highly significant difference was found between both the study groups (p<0.001).

Table 2 Comparison of Serum minerals and insulin resistance in control and T2DM patients

Parameters	Control n=160 (mean ± SD)	Case group(T2DM) n=160 (mean ± SD)	P value
Mg	2.12 ±0.40	1.69 ±0.42	<0.001*
Zn	96.90 ±12.24	83.70 ±14.13	<0.001*
Cu	107.26 ±12.87	120.04 ±18.31	<0.001*
Serum Insulin	5.64 ±0.89	10.09±0.74	<0.001*
Insulin Resistance	1.21±0.12	3.54±2.14	<0.001*

∗p-value for difference between groups by t-test or chi-square, as appropriate

Table 2 shows mean serum levels of zinc, magnesium, copper and insulin in control and diabetic patients. Diabetic subjects had significant lower levels (p<0.001) of serum magnesium and zinc than healthy subjects.

As shown in the table 2 mean serum copper and serum insulin levels were significantly elevated in diabetic patients compared to control group (p<0.001).

Table 3 Correlation of serum zinc, serum magnesium and serum copper levels with insulin resistance in diabetic subjects

Correlation between	Pearson's correlation coefficient (r)	p-value
Serum zinc and HOMA-IR	-0.07	0.21
Serum magnesium and HOMA-IR	-0.12	0.03*
Serum copper and HOMA-IR	0.15	0.007*

*p-value for difference between groups by t-test or chi-square, as appropriate

In type 2 diabetic subject'sserumzinc showed a negative correlation with Insulin resistance but the correlation is not statistically significant (r = -0.07, P=0.21). An inverse and statistical significant correlation was found between serum magnesium and insulin resistance (r = -0.12, P<0.05) in diabetic group. And highly significant correlation (r = 0.15; P<0.05) was found between serum copper and Insulin resistance.

DISCUSSION

Diabetes is chronic multifactorial disorder with worldwide prevalence**.** The metabolic alterations associated with diabetes are the prime culprits' causes for pathophysiological changes in multiple organs that impose a heavy burden of morbidity and mortality from macrovascular and microvascular complications [12].

Decline in the physiological functions with age may influencethe absorption, metabolism and excretion of micronutrients [13].

Zinc acts as cofactor in a variety of "antioxidant" enzymes, particularly superoxide dismutase, catalase and Peroxidase, alterations of zinc metabolism such that adequate zinc is unavailable for these enzymes might be expected to contribute to the tissue damage observed in diabetes [14]. In -vitro studies postulated the effect of Zinc on insulin synthesis, storage and release [15]. It has been reported that Zn deficiency is associated with reduced insulin secretion and increased tissue resistance to insulin action. In the present study we found zinc deficiency was more sever in diabetics and zinc levels were inversely correlated with insulin resistance (16-17). The reason for decreases zinc levels in diabetics compared to controls may be due to increased excretion and this may be due to gastrointestinal malabsorption or due to reduction in renal function associated with disease.[18].

Magnesium is important for the effectiveness of insulin.There is a strong relationship between magnesium and insulin action. A reduction of magnesium in the cells strengthens insulin resistance, **impaired glucose tolerance, and decreased insulin secretion.(19).** Our study Showed a significant negative correlation of serum magnesium with insulin resistance .Pham PC *et al* and Humphries *et al* (20-21) showed similar results in earlier studies. The reason for significant decreased magnesium in diabetic compared to controls may be due to higher urinary losses or impaired absorption of magnesium.

Copper a transitional element has affinity to bind with proteins that have been glycated. Generally, serum concentration of copper and ceruloplasmin is elevated in type 2 diabetes mellitus patients [21]. The increase in the Cu ion in patients with DM might be attributed to hyperglycemia that may stimulate glycation and release of copper ions and this accelerates the oxidative stress so that the formation of AGEs occurs [22]. In the present study we observedthe levels of serum copper was significantly increased in diabetics compared to controls, there is a strong positive correlation between copper and Insulin Resistance. Similar results were observed in previous studies.

CONCLUSION

In the present study, we found a significant and inverse correlation in the serum levels of magnesium with insulin resistance and serum zinc inversely associated with insulin resistance but the correlation was statistically insignificant in diabetics. The serum copper showed a highly significant positive correlation with insulin resistance diabetics. These alterations of micro minerals may be one of the factors for reducing the insulin sensitivity and may increase the risk of insulin resistance and secondary complications such as retinopathy, CAD, ketoacidosis.

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