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Research Article

Serum Micronutrients, Fasting Blood Sugar, Lipid Profile and their inter Relationship in Patients with Type II Diabetes

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Abstract: Diabetes is often associated with metabolic syndrome that is high blood pressure and abnormal lipid profile. Micronutrients mostly refer to vitamins and minerals. Micronutrients mainly exert their function as enzyme cofactors and transcription factors thus controlling the metabolic pathways. Metabolic syndrome is often characterized by various other clinical features like disturbance in glucose and insulin metabolism, obesity and abdominal fat distribution. Aim of the study was to determine the difference in serum Zinc, Copper, Magnesium, ceruloplasmin and ferritin levels in diabetic patients and to assess if there is a correlation between the micronutrients and metabolic parameters. The study was conducted in the Departments of Biochemistry and Medicine, Kasturba Medical College, Manipal. Serum Zinc, Copper and Magnesium were estimated using quantitative colorimetric assay kits. Fasting blood sugar was analyzed using cobas 912 and lipid profile and serum ferritin was estimated using cobas 6000 auto analyzers. Serum Ceruloplasmin were estimated by manual method. There is a statistically significant increase in serum Zinc level in the diabetic group ($p=0.003$) compared to controls. Fasting blood glucose varied among cases and controls significantly ($p<0.001$). However there was no statistically significant difference among the two groups in any of the other parameters. Also no statistically significant correlation between the minerals and metabolic parameters was obtained in either of the groups.
Keywords: Diabetes, Fasting Blood Glucose, Metabolic Syndrome, Micronutrients, Serum Copper, Serum Zinc and diabetes.

INTRODUCTION

Diabetes mellitus is one of the most common endocrinological disorders affecting the elderly population all over the world. The disease is a chronic condition where the cause is either lack of insulin secretion or impaired action of the hormone insulin which results in the characteristic of the disease, i.e. Hyperglycemia [1] Long term hyperglycemic condition is proven to cause major complications like damage to kidneys, nerves and other internal organs. The disease is also found to cause complete distortion of the body metabolism. The severity of metabolic distortion is dependent on the severity of hyperglycemia [2] Diabetes is often associated with metabolic syndrome that is high blood pressure and abnormal lipid profile. Metabolic syndrome is often characterized by various other clinical features like disturbance in glucose and insulin metabolism, obesity and abdominal fat distribution [3].

Micronutrients are required during all stages of development. Micronutrients mostly refer to vitamins and minerals. These are required in minute quantities and hence the term micronutrients. Micronutrients mainly exert their function as enzyme cofactors and transcription factors thus controlling the metabolic pathways. They control the basic cellular reactions like glycolysis, citric acid cycle and also amino acid and protein metabolism [4].

Magnesium is the second most abundant intracellular cation and plays a key role in important reactions as ATP hydrolysis, transphosphorylation, DNA and protein synthesis [5]. Studies have proven the association of Magnesium with various health complications like hypertension, insulin resistance, distorted lipid profile, diabetes and its complications. It's been studied that an inverse relationship exists between Magnesium levels and glycemic control in both types of diabetes. Low Magnesium in diet was also found to be associated with increase in insulin levels and extremely low Magnesium levels with insulin resistance [4].

Copper plays an important role in body metabolism as the regulator of various enzymes and transcription factors. It has been observed that increased oxidative stress in diabetes and the disturbances in

micronutrient levels have contributed to the complications in diabetes. Zinc is yet another important component of enzymes and transcription factors. Zinc has been found to be involved in the synthesis, storage and release of insulin. Various animal studies have shown that when dietary Zinc was deprived it led to the development of glucose intolerance. Zinc has also been found to enhance the action of insulin [6]. Both Copper and Zinc is involved in oxidant antioxidant mechanisms. Increased oxidative stress has been noted in diabetes and thus Zinc and Copper plays a role via Copper/ Zinc superoxide dismutase involved in protecting the cells from free radical damage [7].

Copper when present in free form is toxic. This causes oxidation reduction imbalance causing oxidative stress. Oxidative stress is one of the key factors associated with diabetes mellitus [8] Ceruloplasmin carries majority of plasma Copper and reduces its existence in the free form [9].

Calcium is yet another important micronutrient involved in insulin secretion and action. It has been postulated that serum calcium levels share a positive correlation with incidence of diabetes and metabolic syndrome. [10, 11, 12]. Ferritin is the storage form of iron. It has been studied that increase in serum ferritin has been found to be associated with development of glucose intolerance [13, 14].

Aim

To determine the association of micro minerals with metabolic parameters in diabetic patients.

Objective

To determine the difference in serum Zinc, Copper, Magnesium, ceruloplasmin and ferritin levels in diabetic patients and to assess if there is a correlation between the micronutrients and metabolic parameters.

METHODOLOGY

The study was conducted in the Departments of Biochemistry and Medicine, Kasturba Medical College, Manipal. A total of 48 patients of both sex in the age group of 40- 75, free from any major illness like cancer, HIV or any other infectious diseases were included in the study. 21 patients (n=21) with fasting blood sugar less than or equal to 125mg/dl and no history of diabetes were included as controls. 27 patients (n=27) with a history of diabetes and fasting blood sugar greater than 125 mg/dl were considered as cases. All the patients in diabetic group were either on oral hypoglycemic drugs or insulin. Patients in control group however were not on any medication.

Ethical clearance was obtained from institutional ethical committee and informed consent was obtained from patients included in the study. 4 ml of venous blood sample was drawn from patients after 8 hours of overnight fast. Plasma sample was used for blood sugar analysis. However, serum sample was used for the estimation of all other parameters. Serum Zinc, Copper and Magnesium were estimated using quantitative colorimetric assay kits. . Fasting blood sugar was analyzed using cobas 912 autoanalyser. Lipid profile and serum ferritin was estimated using cobas 6000 auto analyzers. Serum Ceruloplasmin was estimated by manual method.

Data entry and statistical analysis was done using SPSS 16 software. Mann Whitney test was done to analyze the difference in parameters between the groups. The results are expressed in median and interquartile range. P value < 0.01 is statistically significant. Spearman's correlation was used to find the correlation between the parameters. Comparison of correlation coefficients was analysed using students t test. Correlation is significant at the 0.05 level.

RESULT

There is a statistically significant increase in serum Zinc level in the diabetic group (p=0.003) compared to controls (table 1). Fasting blood glucose varied among cases and controls significantly (p<0.001) (table 2). However there was no statistically significant difference among the two groups in any of the other parameters. Also no statistically significant correlation between the minerals and metabolic parameters was obtained in either of the groups.

Table 1: comparison between diabetics and controls (median & interquartile range)

Parameter	Case (n=27)	Controls (n=21)	P value
Triglyceride (mg/dl)	149 (98, 192)	141 (106, 182)	0.992
HDL (mg/dl)	36 (28, 49)	41 (33, 46)	0.339
TC/HC	4.3 (2.92, 5.81)	4.54 (3.69, 5.29)	0.925
Magnesium (mg/dl)	2.28 (1.93, 2.46)	2.48 (2.14, 2.66)	0.119
Ferritin (ng/ml)	53.39 (39.6, 112.8)	54.76 (19.95, 88.6)	0.554
Zinc (µg/dl)	117.64 (109.5, 139.36)	107.69 (101.36, 118.1)	0.003*

***statistically significant p<0.01**

Table 2: Comparison between diabetics and controls (mean±SD)

Parameter	Case (n=27)	Controls (n=21)	P value
Fasting blood sugar (mg/dl)	195.77±79.68	110.71±8.71	<0.001
Cholesterol (mg/dl)	159.37±32.42	185.38±32.42	0.052
LDL (mg/dl)	89.77±30.36	114.14±48.39	0.041
Calcium (mg/dl)	12.69±4.9	11.04±3.8	0.207
Copper (µg/dl)	170.02±64.54	143.07±38.09	0.105
Ceruloplasmin (mg/dl)	45.9±17.86	37.26±15.27	0.09

Table 3: Comparison of correlation of fasting blood sugar, and lipid parameters with lipid profile and minerals between diabetics and controls

Test parameter	Comparison parameter	Diabetes (n=27) r value	Controls (n=21) r value	p value
Fasting blood sugar	Cholesterol	0.221	0.583	0.258
	Triglyceride	0.247	0.481	0.383
	HDL	-0.167	-0.196	0.923
	LDL	**0.188**	**-0.230**	0.173
	TC/HC	**0.404**	**-0.057**	0.316
	Calcium	**0.089**	**-0.026**	0.712
	Ceruloplasmin	0.182	0.085	0.388
	Copper	**-0.097**	**0.097**	0.533
	Magnesium	-0.139	-0.087	0.866
	Ferritin	**-0.180**	**0.003**	0.566
	Zinc	0.039	0.052	0.967
Cholesterol	Triglyceride	0.395	0.379	0.952
	HDL	0.201	0.383	0.522
	LDL	0.676	0.939	0.004*
	TC/HC	0.288	0.693	0.074
	Calcium	**0.225**	**-0.245**	0.124
	Ceruloplasmin	0.226	0.012	0.485
	Copper	**-0.221**	**0.063**	0.356
	Magnesium	**-0.219**	**0.255**	0.121
	Ferritin	**0.017**	**-0.261**	0.362
	Zinc	-0.367	-0.288	0.776
Triglyceride	HDL	-0.377	-0.252	0.656
	LDL	0.079	0.169	0.769
	TC/HC	0.513	0.478	0.882
	Calcium	0.169	0.233	0.831
	Ceruloplasmin	-0.056	-0.119	0.839
	Copper	**-0.063**	**0.212**	0.372
	Magnesium	**-0.356**	**0.231**	0.051
	Ferritin	0.162	0.156	0.984
	Zinc	**0.173**	**-0.123**	0.339
LDL	TC/HC	0.649	0.683	0.845
	Calcium	**0.301**	**-0.203**	0.098
	Ceruloplasmin	**0.245**	**-0.108**	0.25
	Copper	-0.184	-0.058	0.681
	Magnesium	**-0.141**	**0.204**	0.263
	Ferritin	**0.202**	**-0.196**	0.196
	Zinc	-0.320	-0.326	0.983
TC/HC	Calcium	0.220	0.032	0.539
	Ceruloplasmin	**0.210**	**-0.155**	0.236
	Copper	-0.176	-0.241	0.827
	Magnesium	**-0.325**	**0.219**	0.713
	Ferritin	0.240	0.205	0.906
	Zinc	**0.014**	**-0.141**	0.617

Table 4: Comparison of correlation of interelement relationship between diabetics and controls

Test parameter	Comparison parameter	Diabetes (n=27) r value	Controls (n=21) r value	p value
Calcium	Ceruloplasmin	-0.339	-0.538	0.426
	Copper	-0.054	-0.197	0.641
	Magnesium	-0.013	-0.325	0.298
	Ferritin	0.153	0.312	0.589
	Zinc	0.244	0.294	0.863
Ceruloplasmin	Copper	0.126	0.166	0.896
	Magnesium	0.042	0.181	0.651
	Ferritin	0.149	0.084	0.833
	Zinc	-0.472	-0.065	0.151
Copper	Magnesium	0.194	0.301	0.714
	Ferritin	-0.046	-0.254	0.493
	Zinc	**0.061**	**-0.276**	0.269
Magnesium	Ferritin	0.061	0.088	0.931
	Zinc	-0.246	-0.470	0.406
Ferritin	Zinc	**0.133**	**-0.216**	0.257

DISCUSSION

It was observed that in both the groups there was increase in serum cholesterol and triglyceride levels with fasting blood sugar (table 3). However there observed a reverse pattern in LDL cholesterol level. Among diabetics, with an increase in fasting blood glucose there observed an increase in LDL cholesterol whereas in controls the pattern was reversed. But the correlations were however not statistically significant.

Studies have proved that LDL cholesterol levels in people with diabetes are not higher than those in people without diabetes who are matched for age, sex, and body weight [15]. Even though statistically insignificant, it has been observed that with increase in fasting blood sugar there was an increase in TC/HC ratio in diabetic patients but in control group there was found to be a negative correlation between the two parameters (table3). Studies also suggest an increase in tc/hc ratio among diabetics [16].

Serum Copper and ferritin however shows an inverse relationship with blood glucose in diabetic patients however the correlation is positive in controls (table 3). Both the correlations are however statistically not significant. In both the groups however there was significantly increased total cholesterol with increased LDL (table 3). There exists a positive correlation between serum calcium and total cholesterol and negative correlation of total cholesterol with serum Copper and Magnesium in the diabetic group. However the reverse was observed in control group (table 3). A similar pattern was observed on correlation of triglyceride levels with Copper and Magnesium levels. However serum Zinc showed a negative correlation with triglyceride in controls (table 3). With LDL it was observed that serum calcium, ferritin and Ceruloplasmin had an inverse relationship in controls whereas in cases serum Magnesium was found to have an inverse relationship with LDL (table 3).

Considering the interelement relationship it was observed that with increase in serum Copper a decrease in serum Zinc was observed in case of diabetics unlike in controls (table 4). As associated with diabetes Zinc has been found to be involved in the synthesis, storage and release of insulin [6]. Copper Zinc antioxidant mechanism is important in combating the oxidative stress involved in diabetes [7]. Thus a Copper Zinc balance is to be maintained. This distortion could be one of the possible etiologies of diabetes.

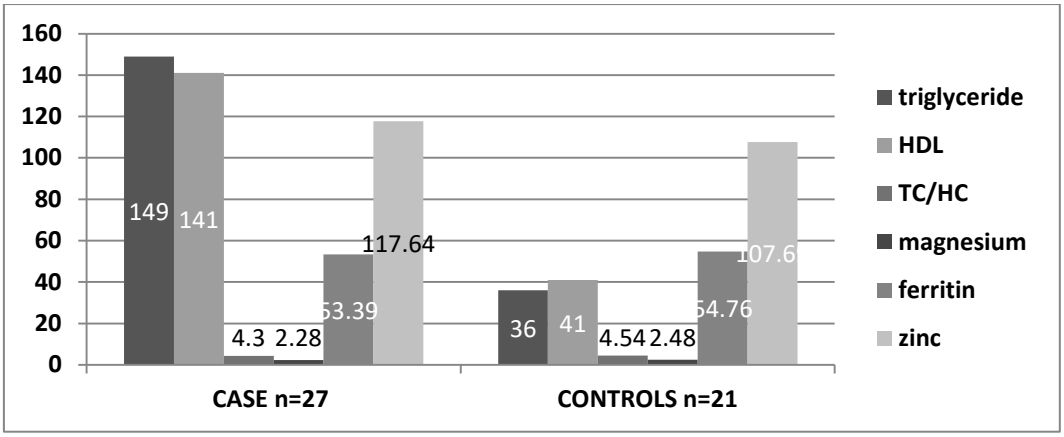

Fig-1: Diagrammatic representation of Table 1 comparison between diabetics and controls (median)

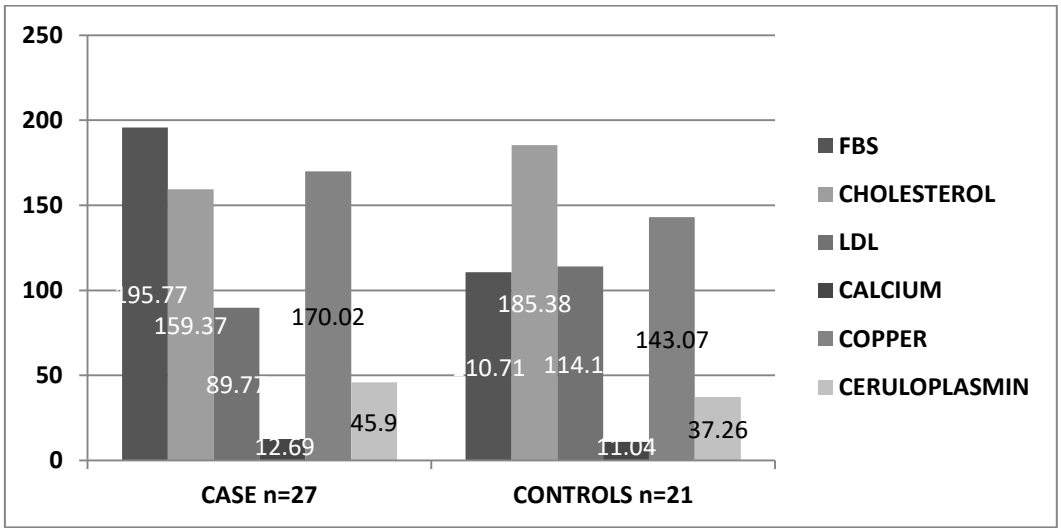

Fig-2: Diagrammatic representation of Table 2 Comparison between diabetics and controls (mean)

CONCLUSION

Serum micronutrients did not significantly vary with diabetes. However mineral to vary significantly among the groups was serum Zinc. Serum micro minerals may not have any association with lipid parameters. However the study did not consider the anti cholesterol drugs advised to the patients. Considering the drug history would have given a better insight into the association of minerals with lipid parameters in diabetic patients. The study also considered a smaller population. A larger study would have provided a better output. A larger study considering the drugs taken by diabetics can be preformed to analyze the variation in micronutrients with fasting lipid profile and fasting blood sugar.

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