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Original Research Article

A Hospital-Based Assessment of the Role of the Serum Trace Elements Levels (Zinc and Copper) In Obese and Non-Obese Type 2 Diabetic Patients: An Observational Study

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Abstract

Aim: The aim of the present study was to assess the role of the serum trace elements levels (Zinc and Copper) in obese and non-obese groups.

Methods: The present study was carried out in the Department of Biochemistry and 200 patients of type 2 diabetes mellitus attending Medicine OPD were recruited into the study. Informed about the details of the study and the written consent was obtained from all the participants of the study.

Results: The mean and SD of BMI and Waist-Hip ratio in non-obese group was (24.86 ± 0.88) and (0.88 ± 0.12) which was lower than that of the Obese group (26.43 ± 2.68) and (0.92 ± 0.08). BMI and waist-hip ratio were significantly higher ($P < 0.05$) in obese group than those of the non-obese group. The mean and SD of Fasting Glucose, Total Cholesterol, Triglycerides, LDL and Copper levels in Obese group was higher than non-obese group, whereas mean and SD of HDL-cholesterol and Zinc levels is lower in Obese group when compared to those of the non-obese group). In addition, LDL and Copper levels in Obese group were significantly higher ($P<0.05$) whereas HDL-Cholesterol and Zinc levels were significantly lower than those of the non-obese group. Correlation analysis in the diabetic Obese and Non-Obese group was done between trace elements, BMI, Waist-Hip ratio, Fasting Glucose and lipid profile. Statistically significant positive correlation was observed between Zinc and LDL, Copper and HDL levels whereas significant negative correlation was observed between Zinc and Cholesterol, Copper and LDL levels in non-obese group. The levels of Zinc have significant negative correlation with Cholesterol and Triglyceride levels whereas significant positive correlation was observed between copper levels and BMI in Obese group.

Conclusion: Deficiency of Serum Zinc is inversely related to body weight and Body Mass Index (BMI) and directly related to high copper levels. Dietary supplementation with Controlled weight reduction should be considered with extreme care and also the therapeutic replacement of zinc with chelating excess copper may prove beneficial in delaying the further progress of diabetic complications.

Keywords: serum zinc and copper, type 2 diabetic, obese, non-obese

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Introduction

Obesity is a worldwide disease affecting population of all age groups and socio-economic levels, in both developed and developing countries. It is known to be a contributory risk factor for several disease states, including diabetes mellitus. [1,2] Trace elements are essential nutrients with regulatory, immunologic, and antioxidant functions resulting from their action as essential components or cofactors of enzymes throughout metabolism. [3] Trace elements and minerals influence the pathogenesis of obesity and diabetes and their complications, mainly through their involvement in peroxidation and inflammation. [4]

In obese people the metabolic disturbances are decompensated. Although, overweight is a preclinical condition, obesity is the clinically manifested metabolic disorder, including mineral imbalances. [5] Women seemed to be more at risk for toxic metal exposure than men and at the same time more vulnerable to micronutrient deficiency. [6] Trace elements are accepted as essential for optimum human health, because of their diverse metabolic characteristics and functions. They serve a variety of catalytic, structural and regulatory functions, in which they interact with

macromolecules such as enzymes, pro-hormones, pre-secretory granules and biological membranes.

Copper is one of the essential trace elements, and has a particular role in cytochrome oxidase function at the terminal end of the mitochondrial electron transport chain. 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. [7] In subjects with insulin dependent diabetes mellitus (IDDM), zinc concentrations have been demonstrated to be lower in leucocytes and erythrocytes than in serum, while no such alteration has been found with copper. [8] No definite relationship has been described between copper concentrations and the clinical status of patients with diabetes mellitus. [9] Zinc, another essential trace element, is a component of many enzymes, and plays an important role in the maintenance of several tissue functions, [10] including the synthesis, storage and release of insulin. [11] Zinc has been found to enhance the effectiveness of insulin in vitro, and it has been postulated that zinc deficiency may aggravate the insulin resistance in noninsulin dependent diabetes mellitus (NIDDM). [12]

The aim of the present study was to assess the role of the serum trace elements levels (Zinc and Copper) in obese and Non-obese groups.

Materials and Methods

The present study was carried out in the Department of Biochemistry, PMCH, Patna, Bihar, India for one year and 200 patients of type 2 diabetes mellitus attending Medicine OPD were recruited into the study. Informed about the details of the study and the written consent was obtained from all the participants of the study. Confidentiality of the study participants was maintained throughout the study. A criteria for the selection of the patients included in this study was that all the type 2 Diabetic Patients (both male and female) attending the out patients department of Medicine were taken. Patients suffering from severe chronic diabetic complications (proliferative retinopathy, nephropathy, neuropathy), malignant diseases, chronic liver disease, infectious disease, hypertension, cardiovascular disease, thyroid disorder, infectious disease, pregnancy, alcohol and smoking habit and taking a supplement vitamin, mineral, antioxidant and fish oil tablet were excluded from the study. All patients and controls were subjected to a detailed history and physical examination and investigations. Anthropometric, clinical and biochemical measurements, Information on age, sex, body weight, height, waist and hip circumference, and BMI were obtained. All anthropometric measurements were made with participants wearing light clothing and no shoes. BMI was measured in all participants and calculated as weight (in kilograms) divided by height (in meters) squared. The Indian Council of Medical Research recommendations for Indians-obese if BMI was ≥25 kg/m2 and overweight when BMI was 23-24.9 kg/m2-were used.[13] Based on this the participants were categorized into two groups namely Group-I with BMI ≤ 24.9 as non obese and Group-II with BMI ≥ 25 as obese. The participant's waists were measured with a soft tape midway between the lowest rib and the iliac crest. The hip circumferences were measured at the widest part of the gluteal region. The Asia- Pacific guidelines for defining the Waist circumference (WC) cut-offs were used.[14] The fasting blood sample will be collected in a sterile disposable syringe under aseptic condition and then blood will be transferred to a dry clean test tube and allowed to clot. After the retraction of the clot, the sample will be centrifuged and serum will be separated. Glucose estimation was done by Glucose Oxidase- Peroxidase method, Total Cholesterol by Cholesterol oxidase- peroxidase method, Triglycerides by Glycerol phosphate oxidase/ peroxidase method, HDL Cholesterol by direct enzymatic end point method, LDL and VLDL cholesterol will be calculated according to Friedwald's formula. Zinc and Copper also analyzed. All estimations were done on fully automated analyser – Transasia EM200. The analytes estimated are subjected to standard quality control (QC) guidelines. The clinical Biochemistry lab is a participant of External Quality Assurance Scheme (EQAS) from CMC Vellore and Internal Quality assessment done with both first party and third party controls daily.

Statistical Analysis

All observations were tabulated and analysed. Results are expressed as Mean and Standard Deviation (S.D).Statistical analysis was done by students'' test and correlation between variables were studied by Pearson's correlation coefficient test. A two-tailed p-value was used for calculating statistical significance. The p values less than 0.05 were considered significant. The statistical analysis was done by using SPSS software (version – 25) for data analysis.

Results

Table 1: The mean and SD of BMI and Waist-Hip ratio in Non-Obese and Obese group

Parameters	Non-obese group Mean ± SD	Obese group Mean ± SD	P Value
BMI	24.86 ± 0.88	26.43 ± 2.68	< 0.05
Waist-Hip ratio	0.88 ± 0.12	0.92 ± 0.08	< 0.05

The mean and SD of BMI and Waist-Hip ratio in non-obese group was (24.86 ± 0.88) and (0.88 ± 0.12) which was lower than that of the Obese group (26.43 ± 2.68) and (0.92 ± 0.08). BMI and waist-hip ratio were significantly higher (P < 0.05) in obese group than those of the non-obese group.

Table 2: The mean and SD of Biochemical parameters and Trace elements Zinc and Copper in Non-Obese and Obese group

Parameters	Non-obese group Mean ± SD	Obese group Mean ± SD	P Value
Fasting Glucose	152.68 ± 54.16	155.12 ± 66.94	0.72
Total Cholesterol	228.82 ± 50.54	236.84 ± 65.15	0.95
Triglycerides	213.97 ± 75.35	222.23 ± 84.26	0.68
HDL	43.57 ± 7.43	40.16 ± 8.32	< 0.05
LDL	114.66 ± 48.32	172.18 ± 52.28	< 0.05
Zinc	68.82 ± 16.44	50.25 ± 14.12	< 0.05
Copper	112.18 ± 20.54	144.86 ± 23.97	< 0.05

The mean and SD of Fasting Glucose, Total Cholesterol, Triglycerides ,LDL and Copper levels in Obese group was higher than Non-Obese group, whereas mean and SD of HDL-cholesterol and Zinc levels is lower in Obese group when compared to those of the Non-Obese group.). In addition LDL and Copper levels in Obese group were significantly higher (P<0.05) whereas HDL-Cholesterol and Zinc levels were significantly lower than those of the Non-Obese group.

Table 3: Correlation between Zinc levels and glucose, lipid profile and Copper in Non- Obese and Obese group

	Non-obese group		Obese group	
Parameters	**Pearson correlation**	**P value**	**Pearson correlation**	**P value**
BMI	0.004	0.988	0.173	0.196
Waist Hip ratio	0.158	0.322	0.055	0.662
Fasting Glucose	0.088	0.580	0.108	0.422
Total Cholesterol	-0.375	0.017	-0.294	0.025
Triglycerides	-0.198	0.222	-0.288	0.028
HDL	-0.175	0.280	-0.048	0.723
LDL	0.438	0.005	0.086	0.525
Copper	-0.178	0.268	0.017	0.890

Correlation analysis in the diabetic Obese and Non-Obese group was done between trace elements, BMI, Waist-Hip ratio, Fasting Glucose and lipid profile. Statistically significant positive correlation was observed between Zinc and LDL, Copper and HDL levels whereas significant negative correlation was observed between Zinc and Cholesterol, Copper and LDL levels in non-obese group.

Table 4: Correlation between Copper levels and glucose, lipid profile and Copper in Non- Obese and Obese group

	Non-obese group		Obese group	
Parameters	**Pearson correlation**	**P value**	**Pearson correlation**	**P value**
BMI	0.154	0.336	0.496	0.000
Waist Hip ratio	-0.282	0.075	0.094	0.486
Fasting Glucose	-0.136	0.396	0.096	0.482
Total Cholesterol	0.046	0.762	-0.202	0.129
Triglycerides	-0.248	0.120	-0.174	0.194
HDL	0.428	0.007	0.076	0.56
LDL	-0.474	0.003	-0.022	0.879
Zinc	-0.178	0.28	0.019	0.895

The levels of Zinc have significant negative correlation with Cholesterol and Triglyceride levels whereas significant positive correlation was observed between copper levels and BMI in Obese group.

Discussion

Diabetes Mellitus is a metabolic disorder characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. Type 2 diabetes is characterized by insulin resistance with relative insulin deficiency and it accounts for 90% of all diabetic cases. [15] The pathophysiology of the development of type 2 diabetes mellitus is complex and multifactorial. The increased prevalence of obesity, physical inactivity, poor diet, and urbanization leads to increase in number of patients diagnosed with type 2 diabetes. [16] Obesity is a global health issue affecting population of all age groups and socio- economic levels, in both developed and developing countries. Several non-communicable diseases such as diabetes, metabolic syndrome, ischaemic heart diseases and certain cancers are strongly associated with obesity. It is a contributory risk factor for diabetes mellitus. [17] The increase in the prevalence of type 2 diabetes is closely linked to the upsurge in obesity. About 90% of type 2 diabetes is attributable to excess weight. Furthermore, approximately 197 million people worldwide have impaired glucose tolerance, most commonly because of obesity and the associated metabolic syndrome. This number is expected to increase to 420 million by 2025. [18]

The mean and SD of BMI and Waist-Hip ratio in non-obese group was (24.86 ± 0.88) and (0.88 ± 0.12) which was lower than that of the Obese group (26.43 ± 2.68) and (0.92 ± 0.08). BMI and waist-hip ratio were significantly higher ($P < 0.05$) in obese group than those of the non-obese group. The mean and SD of Fasting Glucose, Total Cholesterol, Triglycerides, LDL and Copper levels in Obese group was higher than non-obese group, whereas mean and SD of HDL-cholesterol and Zinc levels is lower in Obese group when compared to those of the non-obese group. Escobar et al. in 1995 reported that low level of zinc in diabetes mellitus is due to loss of zinc via urine or may be due to loss of zinc from cells as glucose is translocated into muscle. Hence it can be stated low level of zinc can affect the function of pancreas and plays an important role in pathogenesis of DM. A number of studies have reported correlation between diabetes and trace elements such as zinc, copper. Scott and Fischer (1938) first recognized the relationship between zinc and insulin. [19] Zinc affects antigenic properties of insulin which leads to hyperglycemia. Costarelli L et al [20] reported that the level of zinc is known to be altered in conditions such as obesity and type 2 diabetes. Dildar K, et al 2004 [21] evaluated the relationship of zinc in obese and non-obese type 2 diabetic patients and its relationship with oxidative stress and insulin. They found that Obese diabetic subjects had significantly lower plasma zinc levels than non-obese diabetic subjects ($P<0.01$). Zinc deficiency has been reported in obese subjects. However, the exact mechanism is unclear. It may be due to Zinc accumulation in the adipose tissue, as result of increased production of adipokines, increased Leptin production. They induce chronic inflammation and expression of metallothionein and Zinc-Copper transporter in hepatocytes. These proteins result in accumulation of these metals in hepatocytes and adipose tissue and decreased serum concentration. [22]

In addition, LDL and Copper levels in Obese group were significantly higher ($P<0.05$) whereas HDL-Cholesterol and Zinc levels were significantly lower than those of the non-obese group. Correlation analysis in the diabetic Obese and Non-Obese group was done between trace elements, BMI, Waist-Hip ratio, Fasting Glucose and lipid profile. Statistically significant positive correlation was observed between Zinc and LDL, Copper and HDL levels whereas significant negative correlation was observed between Zinc and Cholesterol, Copper and LDL levels in non-obese group. The levels of Zinc have significant negative correlation with Cholesterol and Triglyceride levels whereas significant positive correlation was observed between copper levels and BMI in Obese group. Increase in the copper ion levels in patients with diabetes mellitus (DM) may be attributed to hyperglycemia that may stimulate glycation and release of copper ion and this accelerate the oxidative stress. [23] Serum Copper levels were reported to be significantly higher in obese patients compared to normal body weight controls. Some authors reported a negative correlation between serum Copper and High-density lipoprotein (HDL)-cholesterol. [24] The mechanism for its elevation in obese patients is unclear but it is thought to be due to pro-inflammatory cytokines released from adipose tissue as IL-1 enhance intra-cellular Zinc accumulation with intra-cellular Copper efflux, and when released to blood it binds to Ceruloplasmin. High serum copper and low serum zinc were associated with increased cardiovascular mortality. [25] Metin Ozata, 2002 [26] concluded in their study that obesity is associated with defective antioxidant status and hypozincemia, which may have implications in the development of obesity related health problems. We found that lower serum zinc concentrations and higher serum copper concentrations in obese compared with non-obese subjects. The presence of different correlations between the studied groups implies different roles might copper and zinc play in diabetes.

Conclusion

Deficiency of Serum Zinc is inversely related to body weight and Body Mass Index (BMI) and directly related to high copper levels. The Medical practitioners must be aware of nutritional deficiencies in overweight and obese patients and all these observations suggest that serum zinc and copper estimation should be a part of the screening panel in the risk detection and progression of diabetic complications. Dietary supplementation with Controlled weight reduction should be considered with extreme care and also the therapeutic replacement of zinc with chelating excess copper may prove beneficial in delaying the further progress of diabetic complications.

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