Original Research Article

A study of serum zinc and copper in obese and non- obese type 2 diabetic patients

S Ramya[1], K Ponsuganthi[2*]

[1]Assistant Professor, [2]Associate Professor, Department of Biochemistry, Annapoorna Medical College and Hospital, Salem, INDIA.
Email: drramyasathish@gmail.com

Abstract

Background: The association of diabetes and obesity with trace elements is complex; alterations in their metabolism can be induced by the diseases and their complications. To study the role of the trace elements in obese and Non-Obese type 2 diabetic patients, serum trace elements levels (Zinc and Copper) were measured in Obese and Non-Obese groups. Further, correlation between serum trace elements levels and body mass index (BMI), waist-hip ratio, Fasting glucose and Lipid profile were also determined in these groups. **Methods:** Hundred patients of type 2 diabetes mellitus attending Medicine OPD were recruited into the study. According to the Indian Council of Medical Research recommendations for Indians, patients with BMI≤24.9 kg/m2 are categorized as Group I Non-Obese and those with BMI ≥ 25 kg/m2 as Group II Obese. Anthropometric measurements were taken and Biochemical parameters Fasting Glucose, Lipid profile and levels of serum Zn and Cu were determined. Statistical analysis was performed using SPSS Software and p value less than 0.05 was considered significant. **Results:** The Diabetic Obese individuals had lower serum zinc concentrations and higher serum copper concentrations compared to non-obese individuals. **Interpretation and conclusions:** Findings from our study showed significant association between Zinc and Copper levels with obesity. Also, obese women with diabetes may be at a greater risk of developing imbalances and deficiencies of trace elements.

Key Word: serum zinc and copper, type 2 diabetic

[*]**Address for Correspondence:**
Dr K Ponsuganthi, Associate Professor, Department of Biochemistry, Annapoorna Medical College and Hospital, Salem, INDIA.
Email: drkponsuganthi@gmail.com

Received Date: 02/07/2020 Revised Date: 30/08/2020 Accepted Date: 18/09/2020
DOI: https://doi.org/10.26611/10021611

Access this article online

Quick Response Code:

Website: www.medpulse.in

Accessed Date: 03 October 2020

INTRODUCTION

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[1]. 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[2]. 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[3]. 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[4]. Most of the interest in the role of nutrients in diabetes is cantered on macronutrients, such as carbohydrate and fat, but micronutrients, such as iron, copper and zinc, are also closely associated with diabetes [5, 6]. Trace elements are accepted as essential for optimum human health, because of their diverse metabolic characteristics and functions.

How to cite this article: S Ramya, K Ponsuganthi. A study of serum zinc and copper in obese and non- obese type 2 diabetic patients. *MedPulse International Journal of Biochemistry.* October 2020; 16(1): 01-05. https://www.medpulse.in/Biochemistry/

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. Impaired metabolism of trace elements like copper (Cu) and zinc (Zn) has been reported to result in higher sensitivity to oxidative damage and development of diabetes and diabetic complications[7]. Both of these metals are involved in glucose homeostasis and their status is modulated in DM [8, 9]. Trace elements and minerals influence the pathogenesis of obesity and diabetes by peroxidation and inflammation[10]. Oxidative stress results from imbalance between free radical and anti-oxidants enzymes such as super-oxide dismutase. Copper and zinc are the major components of antioxidant enzyme SOD (super oxide dismutase) and protects from free radicals.

MATERIALS AND METHODS

The present study was carried out at Annapoorna Medical College and Hospital, Salem in the department of Biochemistry. Hundred 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. Clearance from the Institutional Ethical Committee was obtained prior to the advent of 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[11]. 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 was measured at the widest part of the gluteal region.The Asia-Pacific guidelines for defining the Waist circumference (WC) cut-offs were used[12]. 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 Glycerolphosphate 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't' 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 AND OBSERVATION

Forty nine Non-Obese diabetic patients and fifty two Obese diabetic patients were compared for BMI, Waist-Hip ratio, Fasting glucose level, trace elements "copper and zinc' and lipid profile. The age of each group was between 30 to 60 years. In - Table 1.The mean and SD of BMI and Waist-Hip ratio in Non-Obese group was (23.88 ± 0. .84) and (0.89 ± 0.14) which was lower than that of the Obese group (27.41 ± 2.73) and (0.94 ± 0.06). BMI and waist-hip ratio were significantly higher ($P < 0.05$) in obese group than those of the Non-Obese group. In -Table: 2.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.

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	23.88 ± 0. .84	27.41 ± 2.73	< 0.05
Waist- Hip Ratio	0.89 ± 0.14	0.94 ± 0.06	< 0.05

All values were expressed as mean ±SD, *mean difference is significance at p < 0.05

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	150.67 ± 56.11	154.10 ± 67.98	0.78
Total Cholesterol	227.81 ± 50.51	237.80 ± 66.16	0.99
Triglycerides	212.95 ± 76.38	221.22 ± 85.23	0.61
HDL	44.52 ± 7.34	41.15 ± 8.33	< 0.05
LDL	112.62 ± 49.36	170.13 ± 53.24	< 0.05
Zinc	69.83 ± 15.47	50.24 ± 15.11	< 0.05
Copper	110.14 ± 20.55	143.90 ± 24.99	< 0.05

All values were expressed as mean ±SD, *mean difference is significance at p < 0.05

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

Parameters	Non-Obese group			Obese group		
	Pearson correlation	P value	Significance (2-tailed)	Pearson correlation	P value	Significance (2-tailed)
BMI	0.003	0.986	>0.05 NS	0.171	0.195	>0.05 NS
Waist Hip ratio	0.155	0.326	>0.05 NS	0.058	0.660	>0.05 NS
Fasting Glucose	0.087	0.582	>0.05 NS	0.107	0.421	>0.05 NS
Total Cholesterol	-0.378	0.014	<0.05*	-0.298	0.022	<0.05*
Triglycerides	-0.194	0.218	>0.05 NS	-0.284	0.029	<0.05*
HDL	-0.171	0.278	>0.05 NS	-0.046	0.727	>0.05 NS
LDL	0.436	0.004	<0.05*	0.085	0.520	>0.05 NS
Copper	-0.176	0.265	>0.05 NS	0.018	0.893	>0.05 NS

**Correlation is highly significant at P<0.001 level; * Correlation is significant at P<0.05 level

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

Parameters	Non-Obese group			Obese group		
	Pearson correlation	P value	Significance (2-tailed)	Pearson correlation	P value	Significance (2-tailed)
BMI	0.152	0.338	>0.05 NS	0.494	0.000	<0.001**
Waist Hip ratio	-0.281	0.071	>0.05 NS	0.093	0.485	>0.05 NS
Fasting Glucose	-0.135	0.394	>0.05 NS	0.094	0.481	>0.05 NS
Total Cholesterol	0.048	0.761	>0.05 NS	-0.200	0.128	>0.05 NS
Triglycerides	-0.245	0.119	>0.05 NS	-0.172	0.192	>0.05 NS
HDL	0.426	0.005	<0.05*	0.078	0.55	>0.05 NS
LDL	-0.470	0.002	<0.05*	-0.021	0.878	>0.05 NS
Zinc	-0.176	0.26	>0.05 NS	0.018	0.893	>0.05 NS

**Correlation is highly significant at P<0.001 level; * Correlation is significant at P<0.05 level

DISCUSSION

Diabetes mellitus, one of the commonest diseases of the mankind is linked with alteration in mineral metabolism. Obesity is a medical condition that has an adverse effect on health, leading to increased health problems. [WHO, 2000]. Trace elements are essential for optimum human health, due to their diverse metabolic characteristics and functions. A few literatures indicate the influence of the obese condition on the tissue status and metabolism of essential trace metals. Zinc is essential for assembling insulin into structurally stable and functional hexamic structure. Zinc is also related to the synthesis, storage and secretion of insulin. In hypozincaemia the storage, synthesis and function of insulin can be affected. 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[13]. Zinc affects antigenic properties of insulin which leads to hyperglycemia. Costarelli L *et al.*[14] 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[15] 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[16]. Decreased serum Zinc concentration in obese patients plays a role in insulin resistance. In trace element metabolism the best known interaction is the reported antagonism between zinc and copper [17.] The present study demonstrated that serum Cu levels in the diabetic obese group were significantly higher than diabetic Non-Obese group. Earlier studies on obese subjects found that serum Cu levels were significantly higher in obese group than controls subjects[18]. 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[19]. 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[20]. 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[21] Metin Ozata, 2002 [22] 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. In one of the prospective study[23] the authors noted an elevation of serum copper in obese subjects ($p < 0.001$), also they noticed that the levels of serum copper rises with the BMI. However Gjorup *et al.*. reported no significant differences of serum zinc concentrations between obese and non-obese subjects, and Marreiro *et al.*[24] found that serum zinc concentrations in obese children were significantly higher than the control group. Zinc and copper are known to have an inter-relationship that can be either synergetic and/or antagonistic (Dessoki, Raafat, Blaurock-Busch, and Rabah, 2012). Copper toxicity can be exasperated when zinc concentrations are lower in the body (Dessoki, Raafat, Blaurock-Busch, and Rabah, 2012[25]. Therefore, studying the relations of Cu-Zn as a factor (or other combined elements known from the literature) in relation to obesity could be investigated. A systematic review and meta-analysis showed satisfactory effects of Zn supplementation on diabetes and other metabolic markers[26]. 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

The bioavailability of trace elements may be disturbed in obese patients, and the exact prevalence of this alteration is still unknown. Song H, Kim K evaluated that Disturbance of trace elements are associated with metabolic syndrome[27] 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.

REFERENCES

1. Scheen AJ. Pathophysiology of type 2 diabetes. Acta Clin Belg. 2003; 58(6):335–341.
2. Ershow AG. Environmental influences on development of type 2 diabetes and obesity: challenges in personalizing prevention and management. J Diabetes Sci Technol. 2009;3(4):727–734
3. A1-Saleh E,Nandakumaran M,A1-Harmi J,Sadan T,A1-Enezi H Maternal-fetal status of copper,iron,molybdenum,selenium and zinc in obese pregnant women in late gestation.Biol Trace Elem Res.2006;113:113-23.
4. Hossain P; Kawar B; and Nahas MEI, Obesity and Diabetes in the Developing World—A Growing Challenge. The New England Journal of Medicine 2007;356(3):213–5.
5. Simcox, J.A.; McClain, D.A. Iron and diabetes risk. Cell Metab. **2013**, 17, 329–341. [CrossRef] [PubMed]
6. Maret, W. Zinc in Pancreatic Islet Biology, Insulin Sensitivity, and Diabetes. Prev. Nutr. Food Sci. **2017**, 22, 1–8.[CrossRef] [PubMed]
7. Soinio M, Marniemi J, Laakso M, Pyorala K, Lehto S, Ronnemaa T. Serum zinc level and coronary heart disease events in patients with type 2 diabetes. Diabetes Care. 2007;30(3):523–8. doi: 10.2337/dc06-1682. [PubMed] [CrossRef] [Google Scholar]
8. Viktorinova A, Toserova E, Krizko M, Durackova Z. Altered metabolism of copper, zinc, and magnesium is associated with increased levels of glycated hemoglobin in patients with diabetes mellitus. Metabolism. 2009;58(10):1477-82.doi:10.1016/j.metabol.2009.04.035. [PubMed] [CrossRef] [Google Scholar]
9. Xu J, Zhou Q, Liu G, Tan Y, Cai L. Analysis of serum and urinal copper and zinc in Chinese northeast population with the prediabetes or diabetes with and without complications. Oxid Med Cell Longev. 2013;2013:635214. doi: 10.1155/2013/635214. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Bougle D,Bouhallab S,Bureau F,Zunquin G.Effects of trace elements and calcium on diabetes and obesity and their complications.dairy science and technology.2009;89213-8.
11. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, *et al.*. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India. 2009 Feb;57:163-70.
12. Expert Panel on Detection, Evalution, and Treatment of High Blood Cholesterol in Adults. JAMA 2001;285:2486-97. [PubMed]
13. Quilliot D., Dousset B., Guerci B., Dubois F., Drouin P., Ziegler O.,2001-Evidence that diabetes mellitus favors impaired metabolism of zinc, copper, and selenium in chronic pancreatitis. Pancreas Apr; 22(3): 299-306.
14. Costarelli L, Muti E, Malavolta M, Cipriano C, Giacconi R, Tesei S, *et al.*. Distinctive modulation of inflammatory and metabolic parameters in relation to zinc nutritional status in adult overweight/obese subjects. J Nutr Biochem 2010; 21 : 432-7.
15. Dildar Konukoglu, Mehtap Sultan Turhan, Meltem Ercan and Ozden Seri. Relationship between plasma leptin and zinc levels and the effect of insulin and oxidative stress on leptin levels in obese diabetic patients. The journal of Nutritional Biochemistry 2004;15(12):756-760
16. Farasani G, Targhi F, Pishgahroudsari M, Mokhber S, Pazouki A. High prevalence of zinc deficiency in Iranian morbid obese patients undergoing bariatric surgery. J Minim Invasive surg Sci. 2015; 4(3): e33347. doi: 10.17795/minsurgery-33347
17. Dambal SS, Indumati V, Kumari S. Relationship of obesity with micronutrient status. IJABPT 2011; 2 : 280-4.
18. Lima SC, Arrais RF, Sales CH, Almeida MG, de Sena KC, Oliveira VT, *et al.*. Assessment of copper and lipid profile in obese children and adolescents. Biol Trace Elem Res 2006; 114 : 19-29.
19. Mosaad A., Abou-Seif., Abd-Allah Youssef.,2004-Evaluation of Some Biochemical Changes in diabetic patients. Clinica Chimica Acta, 346: 161-170.
20. Kazi T, Afridi I, Kazi N, *et al.*. Copper, chromium, manganese, iron, nickel, and zinc levels in biological samples of diabetes mellitus patients. Biol Trace Elem Res. 2008; 122(1): 1-18. doi: 10.1007/s12011-007-8062-y
21. Olusi S, Al-Awadhi A, Abiaka C, Abraham M, George S. Serum copper levels and not zinc are positively associated with serum leptin concentrations in the healthy adult population. Biological Trace Element Research. 2003; 91(2):137-144. doi: 10.1385/BTER:91:2:137
22. Metin Ozata, Mehmet Mergen, Cagatay Oktenli, Ahmet Aydin, S. Yavuz Sanisoglu, Erol Bolu, M. Ilker Yilmaz, Ahmet Sayal, Askin Isimer and I. Caglayan Ozdemir Increased oxidative stress and hypozincemia in male obesity. Clinical Biochemistry Volume 35,Issue 8, November 2002, Pages 627-631
23. Omar S , Abdennebi M, Ben Mami F, Ghanem A, Azzabi S, Hedhili A, Zouari B, Achour A, Guemira F. Serum copper levels in obesity: a study of 32 cases. Tunis Med. 2001 Jun-Jul; 79(6-7):370-3. PMID: 11771433 [PubMed - indexed for MEDLINE)
24. Marreiro DN, Fisberg M, Cozzolino SM. Zinc nutritional status in obese children and adolescents. Biol Trace Elem Res 2002; 86: 107–22
25. Dessoki H., Raafat O., Blaurock-Busch B. B., and Rabah T. P. (2012) 27, S. (2012). Toxic metals and essential minerals and severity of symptoms among children with autism. European Psychiatry, 27(1), 1.
26. Jayawardena R, *et al.*. Effects of zinc supplementation on diabetes mellitus: asystematic review and meta-analysis. Diabetol Metab Syndr. 2012;4(1):13.
27. Song H, Kim K. Associations of serum minerals with body mass index in adult women. European Journal of Clinical Nutrition.2007; 61: 682-685. doi: 10.1038/sj.ejcn.1602568

Source of Support: None Declared
Conflict of Interest: None Declared