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Original Research Article Trace elements (Copper and Zinc) in type 2 DM patients

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ARTICLE INFO	A B S T R A C T	
Article history: Received 29-11-2019 Accepted 12-12-2019 Available online 13-03-2020	Introduction: As Diabetes Mellitus is a metabolic disorder, where metabolism of various trace elements is being altered. Present study has been carried out to find out the association between Diabetes Mellitus and alteration in the level of trace elements. Aim: To analyse the level of trace elements (Copper and Zinc) in type 2 DM patients in comparison with healthy controls.	
Keywords: Trace element Copper Zinc Type 2 Diabetes Mellitus	Materials and Methods: The present cross sectional study was carried out in 100 patients, having minimum five-year duration of Type 2 Diabetes Mellitus. The study was carried out in Clinical Chemistry Laboratory, Department of Biochemistry, GMERS Medical College and Hospital, Vadnagar, Gujarat. FBS was estimated by GOD-POD method. Serum Copper and Serum Zinc levels were assessed colorimetrically. Results: In our study, serum copper level was found high in Type 2 DM patients and serum Zinc level is decreased in the patients of Type 2 DM. Conclusion: Alteration in levels of Copper and Zinc are found to be important predisposing factors for	
	patients of diabetes mellitus for developing complications. From the present study it may be concluded that alteration in levels of trace elements like Cu and Zn may have a role in the pathogenesis and progression of Diabetes Mellitus.	
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1. Introduction

Diabetes Mellitus is a metabolic disorder with macro and microvascular complications. This disease has been found to have effects on the levels of trace elements such as Copper and Zinc. Because of this metabolic abnormality there is damage to the cells. There is an established direct correlation between levels of trace elements with health and disease.

One of most important trace element of body is Copper. Cytochrome oxidase which is copper containing enzyme plays pivotal role in mitochondrial cellular respiratory chain. In conditions when copper is lacking, there is alteration in the structure of mitochondria. These changes are prevalently seen at liver cells, intestinal cells and pancreatic cells.¹

Zinc is an important trace element. There are many Zinc containing enzymes which are necessary for physiological functions of many organs. Zinc has an important role in biosynthesis and secretion of insulin.^{2,3}

In carbohydrate metabolism, Zinc has an important role.⁴ Various studies have shown that biological activity of insulin is being increased in vitro by Zinc. Further decreased level of Zinc may increase the insulin resistance in NIDDM.⁵

Derangement in the metabolism of copper can be a cause of chronic complications of diabetes mellitus.⁶ It has been postulated that high level of Copper is associated with increased oxidative stress. Oxidative stress is linked with impairment in glucose tolerance and insulin resistance.^{7–9} So estimation of Copper and Zinc is an important parameter for management of type 2 DM. The present study aimed to analyse the level of trace elements (Copper and Zinc) in type 2 DM patients in comparison with healthy controls.

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2. Materials and Methods

The present cross sectional study consists of 100 patients having minimum five years history of Type 2 Diabetes Mellitus, residing at North Gujarat. The study was carried out in Clinical Chemistry Laboratory, Department of Biochemistry, GMER S Medical College and Hospital, Vadnagar, Gujarat. Total duration of study was two months. Written consent was taken from all participants. Participants were asked not to change their usual diet and physical activities.

All cases and controls have more than 40 years of age. Every person included in study undergone detailed clinical and laboratory examination. Type 2 DM patients were diagnosed according to criteria of WHO.

Criteria for the diagnosis of Diabetes Mellitus¹⁰

Fasting Blood Sugar \geq 126 mg/dL. Fasting is defined as no caloric intake for at least 8h.*

2 hour Post Prandial Blood Sugar \geq 200 mg/ dL.

Patients were on oral hypoglycaemic drugs and 100 healthy non-diabetic controls.

Patients who were on Insulin and having nephropathy were not included.

Patients having chronic systemic dis ease, cancer, history of smoking and alcohol, pregnant ladies, lactating mothers, having acute infections and thyroid disorders were excluded from this study. Controls had no history of zinc supplementation.

2.1. Laboratory samples

Blood was collected in morning after 10-12 hours of overnight fast. For estimation of copper and zinc, 4ml of venous blood was collected in plain vacutainer. For estimation of glucose, 2 ml of venous blood was taken in fluoride vacutainer. Samples were processed within 2 hours of sample collection. Plasma glucose was analysed using GOD-POD (Glucose Oxidase-Peroxidase method) and Serum Zinc and Copper were analysed using colorimetric method.

Statistical analysis

For the statistical analysis, student 't' test was performed using SPSS software version 22. The probability less than 0.05 was considered significant.

3. Results

In the present study, 63 patients were males and 37 were females as illustrated in the table 1. FBS (154.46 ± 18.84), PPBS (171.52 ± 17.25) and copper (139.88 ± 9.12) levels were significantly increased in type 2 diabetes mellitus patients compared with controls. Serum zinc (54.93 ± 5.99) levels were significantly decreased in type 2 diabetes mellitus patients compared with controls as illustrated in table 2.

Table 1: Age of diabetes mellitus patients

Age of diabetes patient	Male	Female	
41-50	12	7	
51-60	34	23	
61-70	17	7	
Total	63	37	

Table 2: Comparative study of Trace elements in Control and Diabetes Mellitus Patients.

Parameter	Controls (Mean±SD) (n=100)	Diabetes Mellitus (Mean±SD) (n=100)
FBS(mg/dl)	87.52 ± 8.40	154.46 ± 18.84 *
PPBS(mg/dl)	107.62 ± 12.16	$171.52 \pm 17.25 *$
Copper ($\mu g / dl$)	95.48 ± 9.39	$139.88 \pm 9.12^*$
Zinc ($\mu g/dl$)	86.55 ± 10.82	$54.93\pm5.99*$

* p<0.0001

4. Discussion

Trace elements have been considered as essential for optimum health.¹¹ The clinical importance of trace elements is still controversial. Among the trace elements, copper and zinc are of particular importance.^{11,12}

In modern era, chronic disorders such as diabetes mellitus and hyper tension are major causes of death world wide.¹³ Sufficient evidences are present which shows alteration in metabolism of several trace elements in diabetes mellitus.^{14,15}

Zinc is a dietary metal required for the healthy functioning of the body. Zinc is one of the most important trace elements in the body and it is essential as a catalytic, structural and regulatory ion. It is involved in homeostasis, in immune responses, in oxidative stress, in apoptosis and in ageing.¹⁶ Zinc deficiency is linked to decreased immunity leading to increased infection susceptibility. But the role of Zn in the prevention, treatment and complications of DM is not clear.¹⁷

In our study Zn levels in diabetic patients was significantly lower (p<0.0001) compared to controls which matches with earlier studies.^{18–22}Copper (Cu) is an essential trace element that is required for physiological function of number of enzymes. Copper has important role in synthesis of hemoglobin and immune function. Increase in level of Copper, particularly the free fraction, may produce tissue injury apparently due to its pro-oxidant effects and the depletion of anti-oxidant reserves.²³ Major transported form of Copper is bind with ceruloplasmin (>95%); rest is bound to albumin, transcuprein and copperamino ac id complexes. Copper is harmful in its unbound form, c auses redox imbalance due to it's highly redox active nature, in which there is activation of stress sensitive intracel lular signalling pathways through Haber-Weiss

reaction.24

The rise in Copper ion levels in diabetes mellitus patients may be due to hyperglycaemia that may enhance glycation and release of copper ions and this increases the oxidative stress, so that, Advanced Glycation end products are produce which are involved in the pathogenesis of diabetic complications.²⁵ Copper like transition metal has greater affinity to attach with glycated proteins. In our study there is higher level of copper in patients of DM than the controls which correlates with other studies.^{26–31}

5. Conclusion

Alteration in levels of Copper and Zinc are found to be important predisposing factors for patients of diabetes mellitus for developing complications. From the present study it may be concluded that alteration in levels of trace elements like Cu and Zn may have a role in the pathogenesis and progression of Diabetes Mellitus. The decreased blood levels of Zn and increased blood levels of Cu as have been found in present study can be utilized for prognosis and management of diabetes mellitus. As there is vital role of trace elements like zinc and copper in diabetes mellitus, it is advised that sufficient provision of these trace elements in the diet of diabetic patients can be helpful in the long term management of diabetic patients. For better understanding effect of these trace elements in diabetes mellitus, further clinical studies are needed which should enroll larger number of patients and uses higher advanced methods.

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6. Conflict of interest

None.

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