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Original Research Article

COPPER, ZINC LEVELS IN UNCONTROLLED TYPE 2 DIABETES MELLITUS WITH NORMAL SUBJECTS: A COMPARATIVE STUDY

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Abstract

Background: The burden of Diabetes is high and increasing across globe and particularly in India. Type 2 Diabetes , accounts for majority of the cases, can lead to multiorgan complications. Direct association of minerals , Trace elements and vitamins in the pathogenesis and natural cause of type 2 diabetes mellitus has been observed in many research studies. Aim: To estimate the levels of Copper, Zinc and HBA1c in uncontrolled Type 2 Diabetes mellitus patient.

Material and methods: A cross sectional analytical studies was conducted in DR B R AMC. Study group included 40 known case of uncontrolled Diabetes mellitus.

Results: In the present Study serum copper levels in uncontrolled Type 2 Diabetes Mellitus patients was 204.3 ± 49.0 and in controls it was132.4 ± 20.2. There was a statistically significant increase in the mean copper values in uncontrolled Type 2 Diabetes Mellitus patients (P< 0.0001). Serum Zinc levels in uncontrolled Type 2 Diabetes Mellitus patients was 174.7 ± 31.0 µg/dl and in the controls it was 207.4 ± 36.6 µg/dl. There was a statistically significant decrease inthe mean Zinc values (P<0.0001).

Conclusion: Trace elements play a vital role in maintaining the normal metabolism and homeostasis. It is very significant to note that any variation in the normal levels these trace elements has direct link in disturbing the normal metabolic activity very much noted in metabolic disease like Type 2 Diabetes Mellitus. The role of supplementing the trace elements appropriately may help in better outcome.

***Keywords*:** copper, zinc, HBA1c, uncontrolled type 2 diabetesmellitus.

Introduction

The burden of Diabetes is high and increasing across globe and particularly in India. Estimates in 2019 showed that 77 million had diabetes and expected to rise 134 million by 2045. Type 2 diabetes , accounts for majority of the cases, can lead to multi organ complications. These complications are a significant cause for increased premature morbidity and mortality among individuals with diabetes leading to reduced life expectancy and financial and other costs of

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diabetes leading to profound economic burden on the Indian health care system Direct association of minerals , trace elements and vitamins in the pathogenesis and natural cause of Type 2 diabetes mellitus has been observed in many research studies. Alteration in the metabolism of several trace elements including copper, zinc have been associated with impaired insulin release , insulin resistance and glucose intolerance.

Aims and objectives of the research were to estimate serum copper , zinc levels in uncontrolled type 2 diabetes mellitus patients and to compare with that of healthy individuals. This study helps to correlate the micro nutrient changes with respect to the uncontrolled Type 2 Diabetes Mellitus Patient in whom there is dynamic derangement happening leading to onset of complications which otherwise will be delayed or prevented in a well controlled Type 2 Diabetes Mellitus Patients and Normal Controls.

Materials and Methods

A cross sectional, analytical study was conducted in Jan 2021 to April 2021 in Dr B R Ambedkar Medical College, Bengaluru. After Ethical committee clearance and Consent of study population we started the study. The study included 40 uncontrolled type 2 Diabetes mellitus patients .The age of the Patient varies from 40 to 60 years. The cases were selected on the basis of simple random sampling method . Metabolic disease altering the levels of Zinc copper were excxluded . the results were compared with 40 randomly selected normal healthy individual after obtaining due consent. The controls were age and gender matched . The investigation included serum zinc, copper and HBA1c. The same were compared with controls.

The Investigations included serum copper, zinc and HBA1c. The same were compared with controls. Under all aseptic precautions, about 3ml of venous blood was collected in gel tubes was allowed to clot and it was centrifuged at 4000 rpm for 5 minutes. The serum separated was then used for the estimation of copper, zinc. 2 ml of whole blood was collected separately and was used for estimation of HBA1c Serum copper was estimated by colorimetric method using semi autoanalyser. At PH 4.7 Copper, which is bound to Caeruloplasmin, is released by a reducing agent. It then reacts with a specific color reagent, 3.5-Di- Br-PAESA-(3.5-Dibromo-2-Pyridylazo)-N-Ethyl-N-(3-Sulphopropyl) aniline, to form a stable, colored chelate. The intensity of the color is directly proportional to the amount of copper in the sample.

Serum Zinc was estimated by colorimetric method with deprotenization by EA-50 semiautoanalyser. Zinc present in the sample is chelated by 5-Br-PAPS [2-(5-bromo-2-Pyridylazo)-5-)N-propyl-N-sulfopropylamino)-phenol in the reagent. The formation of this complex is measured at a wavelength of 560nm. HBA1c is estimated by Latex enhanced Immunoturbidometry method. HBA1c is done as part of categorizing Type 2 Diabetes Mellitus Patients with uncontrolled Blood sugar levels.

Statistical analysis

Data obtained was analysed using statistics software SPSS version 23 . Significance of parameters was tested using Student T test . Results of Parameters are considered significant with P value < 0.005.

Results

The present study analyses the correlation between serum copper and zinc in Uncontrolled Type 2 Diabetes Mellitus. The results were compared with the

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controls. The study was conducted on 40 uncontrolled Type 2 Diabetes Mellitus patients and 40 healthy controls. The cases and controls were age and sex matched. The age group was between 40-60 years. The mean age in uncontrolled Type 2 Diabetes Mellitus patients was 50.9 ± 5.8 years in controls it was 51.3 ± 4.8 years.

Copper (Cu) : Table showing mean and SD, significant difference in the mean copper (Cu) between the study groups

Table 1:

Between groups	Mean + SD	'P' value	Inference
Uncontrolled Type 2 Diabetes Mellitus	204.3 ± 49.0	< 0.0001	Highly significant
Controls	132.4 ± 20.2		

As represented in the table the mean copper levels in uncontrolled Type 2 Diabetes Mellitus patients was 204.3 ± 49.0 µg/dl and in controls it was132.4 ± 20.2 µg/dl. There was a statistically significant increase in the mean copper values in uncontrolled Type 2 Diabetes Mellitus patients when compared to the control group (P< 0.0001).

Table 2:

Groups	Mean + SD	'P' value	Inference
Uncontrolled Type 2 Diabetes Mellitus	174.7 ± 31.0	<0.0001	Highly Significant
Controls	207.4 ± 36.6		

Zinc : Table showing the mean and SD, significant difference in the mean Zinc levels (µg/dl) in the study group.

As represented in the table, the mean Zinc levels in uncontrolled Type 2 Diabetes Mellitus patients was 174.7 ± 31.0 µg/dl and in the controls it was 207.4 ± 36.6 µg/dl. There was a statistically significant increase in the mean Zinc values in Uncontrolled Type 2 Diabetes Mellitus when compared to the control group (P<0.0001).

HBA1c

Table 3:

Groups	Mean + SD	'P' value	Inference
Uncontrolled Type 2 Diabetes Mellitus	9.4 ± 0.9	<0.0001	Highly Significant
Controls	5.3 ± 0.4		

Discussion

In this study Zinc levels in uncontrolled Diabetes were lower than the control group. Robert M et al noted marked hyperzincuria in diabetic subjects. The increase in urinary zinc excretion in the diabetic subjects may be a contributing factor to the hypozincemia[2] . In our study serum Zinc levels were found to be significantly reduced which can be due to low nutritional intake or increased excretion. Other studies in support of our findings are , Priyanka Mor et al, found significantly low level of Zinc in patients in comparisons to control[4] . Thowyba et al, found Zn levels in controlled diabetic patient and uncontrolled diabetic were

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lower than the healthy group[5]

Zinc is essential for the correct processing, storage, secretion, and action of insulin in beta (β)-cells. Insulin is stored inside secretory vesicles or granules, where two Zn++ ions coordinate six insulin monomers to form the hexameric-structure on which maturated insulin crystals are based.18 It is also known that like, most other chronic disorders, diabetes increases the excretion of minerals.19 Hyperglycemia in diabetes is usually associated with hyperzincuria and increased urinary loss of Zn++, which is responsible for decreases in total body Zn[1] Zinc has antioxidant properties; thus it can stabilize macromolecules against radical induced oxidation. Hyperglycemia and hyperinsulinemia increases the production of free radicals and there is evidence that lipid peroxidation is increased in type 2 diabetes mellitus patients[1] . Zinc supplementation resulted in a significant reduction of plasma total cholesterol, LDL-c and TAG, while increasing HDL-c levels in patients with type-2 diabetes[8].

In our study Copper levels in uncontrolled Diabetes were Higher than the control group. The increase in Cu ion levels in patients with diabetes mellitus may be attributed to hyperglycaemia that may stimulate glycation and release of copper ions and this accelerates the oxidative stress, so that, Advanced Glycation End products are formed38, that are involved in the pathogenesis of diabetic complications[1] Majority of plasma copper is transported bound to ceruloplasmin (>95%); rest is bound to albumin, transcuprein and copper-amino acid complexes. Ceruloplasmin is an acute phase reactant, has ferro-O2-ox-idoreductase (pro-oxidant) activity directed towards ferrous ion stimulated lipid peroxidation and formation of hydroxyl radical in Fenton reaction.36 Copper is toxic in its unbound form, causes redox imbalance due to it's highly redox active nature, which leads to activation of stress sensitive intracellular signaling pathways through Haber-Weiss reaction.

Robert M Walter et al observed that diabetic subjects are characterized by increased plasma copper compared with control subjects[2]. Our study is in agreement with study done by Priyanka Mor et al and T E Omer et al who have observed significant increase in serum copper levels in Type 2 Diabetes Mellitus compared to control subjects. Diabetes complications associated with the increased free radical production leading to oxidative damage, and many of the pathological effects of copper overload are consistent with an oxidative damage to membranes or various macromolecules. Cu is involved in oxidation-reduction reactions and has a dominant role in diverse proteins such as cytochrome oxidase at the terminal end of the mitochondria electron transport chain. This divalent cation is also involved in super oxide dismutase activity. Copper has the capacity to form covalent bounds and it takes part in many redox processes. Copper ions are involved in generation of reactive oxygen species through Fenton reaction, having a pro-oxidant action.[9]

Copper ion is well known for cytotoxic effect due to its redox chemistry. Excess of copper aggravate the hyperglycemia which causes glycation of various protein and also displaces copper from copper binding site of protein and thus further aggravates the hypercuperemia, which lead to more oxidative damage to various tissue and organs.[9]

Conclusion

Trace elements play a vital role in maintaining the normal metabolism and

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homeostasis. It is very significant to note that any variation in the normal levels these trace elements has direct link in disturbing the normal metabolic activity and over time leads to complication and this is very much noted in metabolic disease like Type 2 Diabetes Mellitus. In our study there is significant decrease in serum Zinc levels and correspondingly significant increase in serum copper levels which correlates with uncontrolled blood sugar levels indicating an association between trace elements role in maintaining normal metabolic Homeostasis. Disturbed normal metabolic homeostasis leads to various complications. The role of these trace elements in metabolic disease like Uncontrolled Type 2 Diabetes Mellitus is important to understand better treatment by appropriately correcting the micro nutrient deficiency which may help in better outcome , further interventional studies in this regard can establish the imporatance of these micronutrients and help in better Patient care.

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