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## Original Research Article

## Study of serum copper and zinc levels in type-II diabetes mellitus patients

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## ABSTRACT

Diabetes mellitus is one of the world's most prevalent diseases. The International Diabetes Federation estimates a worldwide prevalence of 387 million (8.3%) and the global burden of Type-II diabetes is expected to increase 592 million by 2035. It is found that the trace elements like copper and zinc, which act as cofactors for the essential enzymes, which are involved in many metabolic pathways, are found to be altered in the diabetics when compared to non-diabetics.

This is an observational, prospective and case-control study which is conducted to assess the levels of Cu and Zn in relation to hyperglycaemia and HbA1c in the patients with uncomplicated T2DM. Newly diagnosed uncomplicated Type-II Diabetes Mellitus patients are selected as study group. The observations were arranged in suitable tables for analysis under the relevant headings. The findings were averaged as (mean  $\pm$  standard deviation) for each parameter subgroups separately. Each variable, including Serum levels of Cu ( $\mu\text{g/dL}$ ), Zn ( $\mu\text{g/dL}$ ), FBS (mg/dL) and HbA1C (%) were analysed by Paired Sample t-test. A number of studies with varied findings have been found stating deranged Copper and Zinc in diabetics. The levels of Cu can be measured as an early therapeutic measure of DM. It is well-known that higher levels of Cu may result in generation of free radicals through Fenton reaction, which in turn results in increased oxidative stress. Zn being important trace element for functioning of oxidoreductases, hydrolases, ligases and lyases.

T2DM is related to altered levels of trace elements like Zn, Cu. Zn can be better analysed from 24 hours collected urine sample. Early detection of the trace elements Cu, Zn is very useful in early detection of onset of T2DM along with factors like FBS, HBSAg. The study can be further made more appropriate by considering more trace elements in more number of subjects for a prolonged period of study. Once the T2DM is detected early or the stage of pre-diabetes is confirmed the subject can be prevented or delayed from the chance of occurrence of Diabetic. Early detection of the trace elements Cu, Zn is very useful in early detection of onset of T2DM along with factors like FBS, HBSAg.

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## 1. Introduction

Diabetes mellitus is one of the world's most prevalent diseases. The whole world should be cautious and more attentive to the prevalence of the Diabetes mellitus and more particularly to the physiological and pathological changes

that occur because of the increased blood sugar levels in the body. These physiological and pathological changes results in derangement of the functioning of the bodily activities which not only results in diseases, but also impairs in the healing process of the body. These effects of the prevalent diabetes mellitus makes the world more cautious about the diabetes. The International Diabetes Federation estimates a worldwide prevalence of 387 million (8.3%) and the

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global burden of Type-II diabetes is expected to increase 592 million by 2035.<sup>1,2</sup> The chronic hyperglycaemia of diabetes is associated with long term damage, dysfunction and failure of different organs, and these changes in turn lead to development of well-defined clinical entities, the so called complications, which may affect especially the eyes, kidneys, heart, blood vessels, the skin and the nervous system.<sup>3</sup> The prevalence of diabetes mellitus is increasing in India also in people of all socio-economic status.

In the previous studies, it is found that the trace elements like copper and zinc, which act as cofactors for the essential enzymes, which are involved in many metabolic pathways, are found to be altered in the diabetics when compared to non-diabetics. Zinc (Zn) is one of the most important trace elements in the body. It is required for over 300 different cellular processes, including enzyme activity, protein synthesis and intracellular signalling.<sup>4</sup> It is involved in homeostasis, in immune responses, in oxidative stress, in apoptosis and in ageing.<sup>5</sup> Copper (Cu) is an essential trace element, capable of fluctuating between the oxidized Cu<sup>2+</sup> and the reduced Cu<sup>+</sup> state, being co-factor for many enzymes. This divalent cation is involved in SOD 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. Moreover, the deficiencies and the excess of Cu are associated with specific clinical manifestations.<sup>6</sup>

## 2. Materials and Methods

This present study was conducted at Dr.Patnam Mahender Reddy Institute of Medical Sciences, Chevella, Telangana after obtaining clearance from the Institutional Ethical Committee. This is an observational, prospective and case-control study which is conducted to assess the levels of Cu and Zn in relation to hyperglycaemia and HbA1c in the patients with uncomplicated T2DM. Newly diagnosed uncomplicated Type-II Diabetes Mellitus patients are selected as study group. Age and Sex matched healthy volunteers were recruited as control group. Inclusion criteria for the present study of subjects as group 1 patients having FPG $\geq$ 126mg/dL and HbA1c $\geq$ 6.5%. Exclusion criteria for all the groups was the persons known as smokers, alcoholics and subjects suffering with cancers, hypertension, renal and hepatic diseases, and any other acute/chronic illness; pregnant and post-menopausal females.

After obtaining informed written consent from both the groups, fasting venous blood was collected. A total of 6mL of blood is obtained from the subjects. 2mL of this blood was put in EDTA (Ethylene Diamine Tetra Acetic Acid) vacutainer for HbA1c estimation. Another 2mL of blood is put in fluoride vacutainer for blood glucose estimation and rest of the 2mL was transferred to plain vacutainer for estimation of Cu and Zn. Blood sample in EDTA

vacutainers and Fluoride vacutainers was mixed properly. The blood sample in plain vacutainer was allowed to clot at 37°C for 20min. Then, the plain vacutainers were centrifuged for 15 minutes at 3,000 rpm to obtain aliquots of serum which are stored at -20°C for analysis of Cu and Zn levels. The fasting blood glucose level is estimated by fully automatic analyser (Transasia XL-640) using glucose oxidase-peroxidase method.<sup>7</sup> HbA1c was analysed using ion exchange resin method. Cu and Zn were analysed using semi-autoanalyser (Erba Chem 5) using calorimeter method.<sup>8,9</sup>

The observations were arranged in suitable tables for analysis under the relevant headings. The findings were averaged as (mean  $\pm$  standard deviation) for each parameter subgroups separately. Each variable, including Serum levels of Cu ( $\mu$ g/dL), Zn ( $\mu$ g/dL), FBS (mg/dL) and HbA1C (%) were analysed by Paired Sample t-test. Statistical analysis was done using IBM SPSS Statistics 20 package. P value  $<0.05$  was considered as statistically significant and p-value  $<0.005$  was considered as statistically highly significant.

## 3. Results

In our present study, we have observed that the levels of Cu, FBS and HBSAg were significantly changed in diabetic subjects when compared to non-diabetic control group. It is further found that the levels of Zn in diabetic and non-diabetics has not known shown any significant change. The mean Cu levels in diabetics is 99.98 and 99 in non-diabetics. Similarly the levels of Zn, FBS, HBSAg were found to be 66.30, 85.84; 140.78, 87.14; 6.60, 5.78 respectively in diabetic subject and non-diabetic control groups.

## 4. Discussion

Hyperglycemia condition in diabetes have an considerable impact on the metabolism of Zinc and Copper. A number of studies with varied findings have been found stating deranged Copper and Zinc in diabetics. Bozkurt et al and Ferdousi et al. in their independent studies have noted a significant increase in the Cu levels in new cases of T2DM.<sup>10,11</sup> In the research work by Zargar et al, they found an increase in the serum copper levels in T2DM.<sup>12</sup> But in our present study, we could not find any significant correlation between the increased serum levels of Cu in diabetics. Babalola et al also had noted a similar findings in their study.<sup>13</sup>

Altered levels of Zn in diabetics has been shown in number of studies done in the past. In the present study we have found significant decrease in the levels of Zn in subjects of diabetes mellitus. Our findings are similar to the findings of Ferdousi et al.<sup>11</sup> Walter et al. also have recorded hyperzincuria in a 24 hour collected urine sample in the diabetic subjects with significant decreased levels of Zn and normal Mg levels.<sup>14</sup>

**Table 1:** Paired samples statistics between diabetic subjects and non-diabetic control group

		Mean	N	Std. Deviation	Std. Error Mean
Cu ( $\mu\text{g/dL}$ )	Subjects	99.98	50	6.629	.937
	Control	99.00	50	5.959	.843
Zn ( $\mu\text{g/dL}$ )	Subjects	66.30	50	8.162	1.154
	Control	85.84	50	8.115	1.148
FBS(mg/dL)	Subjects	140.78	50	22.675	3.207
	Control	87.14	50	6.174	.873
HbA1C (%)	Subjects	6.60	50	.495	.070
	Control	5.78	50	.648	.092

**Table 2:** Paired samples correlations between diabetic subjects and non-diabetic control group

	N	Correlation	Sig.
Cu ( $\mu\text{g/dL}$ )	50	.491	.000
Zn ( $\mu\text{g/dL}$ )	50	.159	.269
FBS(mg/dL)	50	.303	.032
HbA1C (%)	50	.420	.002

**Table 3:** Paired samples test between diabetic subjects and non-diabetic control group

	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Cu ( $\mu\text{g/dL}$ )	.980	6.378	.902	-.832	2.792	1.087	49	.283
Zn ( $\mu\text{g/dL}$ )	-19.540	10.553	1.492	-22.539	-16.541	-	49	.000
FBS(mg/dL)	53.640	21.618	3.057	47.496	59.784	13.093	49	.000
HbA1C (%)	.820	.629	.089	.641	.999	17.545	49	.000

The levels of Cu can be measured as an early therapeutic measure of DM. It is well-known that higher levels of Cu may result in generation of free radicals through Fenton reaction, which in turn results in increased oxidative stress. Zn being important trace element for functioning of oxidoreductases, hydrolases, ligases and lyases.

## 5. Conclusion

T2DM is related to altered levels of trace elements like Zn, Cu. Zn can be better analysed from 24 hours collected urine sample. Early detection of the trace elements Cu, Zn is very useful in early detection of onset of T2DM along with factors like FBS, HBSAg. The study can be further made more appropriate by considering more trace elements in more number of subjects for a prolonged period of study. Once the T2DM is detected early or the stage of pre-diabetes is confirmed the subject can be prevented or delayed from the chance of occurrence of Diabetic.

## 6. Source of Funding

None.

## 7. Conflict of Interest

The authors declare no conflict of interest.

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