

# Study to Correlate Trace Minerals Status with Glycaemic Control in Type 2 Diabetes Mellitus

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## ABSTRACT

**Introduction:** Diabetes mellitus (DM) is lingering disease embodied by persistent hyperglycemia and derangement in homeostasis of metabolism of protein, fat, and carbohydrate. Disturbance in trace mineral metabolism was uniformly encountered in clinical studies of trace mineral status in DM patients. Hence the present study was conducted with the aim of analyzing trace mineral status like Zn, copper (Cu), Mg, Mn, Cr in DM.

**Material and methods:** This was a cross sectional study conducted on 55 participants, who were clinically examined and oral glucose tolerance test and glycosylated hemoglobin (HbA1c) was done. They were divided into three groups, controls, newly diagnosed diabetics, known case of diabetics. Trace elements like copper, zinc, magnesium, manganese and chromium were noted in these participants and analyzed.

**Results:** Out of 55 study participants, 34 were diabetic and 21 were control groups. Mean duration of DM in known cases was 8.7 years. On comparing mean serum values of trace elements in cases and controls of old and newly diagnosed cases of DM, it was found that there was statistically significant difference in Cu, Mg and Cr levels in known cases of DM ( $p < 0.05$ ).

**Conclusion:** The findings of present study are in line with that of other such studies in case of Cu, Mg and Cr levels and their correlation with DM.

**Keywords:** Diabetes Mellitus, Trace Elements, Zinc, Copper, Magnesium, HbA1c.

## INTRODUCTION

Diabetes mellitus (DM) is lingering disease embodied by persistent hyperglycemia and derangement in homeostasis of metabolism of protein, fat, and carbohydrate. Numerous causes have been established for DM and basic pathogenesis of DM is typified by lack of insulin secretion, action or both. The after effects of DM can be short term or long term, which includes disturbance of function of organ systems and end organ damage in severe cases. Deaths in DM occur due to irreversible cell injury resulting in permanent organ damage. Cardiovascular and renal systems are particularly prone to diabetic complications.<sup>1</sup>

Disturbance in trace mineral metabolism was uniformly encountered in clinical studies of trace mineral status in DM patients.<sup>2,3,4</sup> It has been cited in literature that oxidative stress and trace mineral metabolism disturbance promote the elaboration of plethora of complications of DM.<sup>5</sup> Also, action of insulin has been found to be enhanced by variety of trace elements, some of which are magnesium (Mg), zinc (Zn), selenium (Se), manganese (Mn), chromium (Cr).<sup>6</sup> Postulated mechanism for these actions are insulin

receptor activation, reduction in oxidative stress by acting as antioxidants, facilitating glucose metabolism by acting as cofactor for the enzyme of the same, increased insulin sensitivity.<sup>7,8</sup>

Hyperglycemia is the core pathogenic factor in DM.<sup>9</sup> Role of Zn in enzymatic activation in metabolism of carbohydrates is known, and this happens by virtue of its metallo-enzymatic complex formation. Various clinical and pre-clinical studies have demonstrated Zn metabolism disturbance in DM.<sup>10</sup> It is well known that Zn is required in normal physiology of insulin like vital factor for insulin synthesis, secretion of insulin in the form of Zn crystals and storage, maintenance of veracity of insulin structure.<sup>11</sup> It has been postulated that immune dysregulation related to Zn homeostasis disturbance may contribute to diabetic complications development.<sup>12,13</sup> Similarly, Mg concentration derangements have been implicated in DM. This may be due to role of Mg in glucose metabolism, specifically phosphorylation reactions. Also, it has been incriminated in plethora of diabetic disturbance like lipid and carbohydrate metabolism disturbance, insulin resistance.<sup>14</sup> It is matter of debate, as to whether disturbance in trace mineral homeostasis leads to diabetic complications or vice versa is true. There is no doubt that prevention of metabolic derangements reflect in postponement of diabetic complications, most notably atherosclerosis.<sup>15</sup>

Hence we conducted the present study in the pursuit of analyzing trace mineral status like Zn, copper (Cu), Mg, Mn, Cr in DM.

## MATERIAL AND METHODS

The present study was a cross-sectional one, done at Medicine inpatient department, D Y Patil Medical College, Navi Mumbai. 55 patients were enrolled in the present study. Patients were selected and excluded on the basis of following criteria:

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**Inclusion criteria**

**Cases:** All subjects aged more than 30 years, both sex who were diagnosed as type2 diabetes by a random plasma glucose level of 200 mg/dL or higher, together with classic features of DM, such as polyuria, polydipsia, polyphagia, and weight loss, or a fasting blood glucose level of >126 mg/dL or glycated hemoglobin (HbA1C) levels of 6.5% or higher.

**Controls:** Controls were chosen from inpatient department of internal medicine after matching for age and sex.

**Exclusion criteria:** Patient on diuretics, magnesium containing laxatives, patients diagnosed with renal failure,

malignancy, type 1 Diabetes, alcoholics, those taking vitamin and mineral supplements, patients with history of any recent acute illness or clinical evidence suggestive of kidney, liver, or endocrine diseases, digestive disorders, or patients with any weight change in the previous 6 months were excluded from the study.

All the selected participants were initially evaluated with detailed clinical history taking and clinical and laboratory examination. Thereafter, participants were divided into 3 groups:

- Non-diabetic: control
- Diabetic: newly diagnosed cases
- Diabetic: known cases.

Ethical permission was taken from Institutional Ethics Committee, prior to start of the study.

**STATISTICAL ANALYSIS**

The data was analyzed by applying Chi square test. P value <0.05 was considered as statistically significant.

**RESULTS**

Out of 55 study participants, 34 were diabetic and 21 were control groups. Of the 34 diabetics, 18 were male and 16 females, while control group comprised of 11 males and 10 females. Among diabetics 14 were newly detected who did not receive treatment and 20 were known diabetics on treatment. Among these 19 were hypertensive, 12 patients had prior history of cardiovascular disease and 11 patients had metabolic syndrome. Mean duration of DM in known cases was 8.7 years (table-1).

On comparing mean serum values of trace elements in cases

Sr. No.	Items		n
1	Age	31-40	13
		41-50	15
		51-60	15
		>60 yrs	12
2	Sex:		
		Case	
	Control	Male	18
		Female	16
3	DM	New Diagnosis	20
		Known case	14
4	Comorbidity	Hypertension	19
		Other CVD	12
		Metabolic syndrome	11

**Table-1:** Showing the demographic details of study participants.

Element	Mean		P value	Mean		P value
	Control	Case		New case	Known case	
Copper	0.69	0.79	0.04	0.73	0.85	0.47
Zinc	0.46	0.53	0.23	0.54	0.56	0.63
Manganese	3.78	3.58	0.59	3.44	3.49	0.85
Magnesium	2.27	1.9	0.002	2.16	1.8	0.04
Chromium	0.64	0.59	0.01	0.55	0.6	0.17

**Table-2:** Mean serum values of trace elements in cases and control.

Element	Control			Newly detected case			Known case		
	Male	Female	P value	Male	Female	P value	Male	Female	P value
Copper	0.54	0.88	0.05	0.71	1.01	0.29	0.78	0.89	0.19
Zinc	0.41	0.52	0.26	0.62	0.52	0.01	0.54	0.4	0.01
Manganese	3.55	4.17	0.07	3.49	3.72	0.59	3.64	4.04	0.33
Magnesium	2.35	2.14	0.22	1.86	1.76	0.69	2.1	2.04	0.75
Chromium	0.65	0.62	0.31	0.58	0.62	0.81	0.57	0.56	0.45

**Table-3:** Showing mean serum trace element levels in males and females.

Element/HbA1c	6 to 8			8 to 10			10 to 12		
	New	Known	P value	New	Known	P value	New	Known	P value
Copper	0.66	0.87	0.21	0.58	0.87	0.8	0.85	1.14	0.63
Zinc	0.55	0.46	0.3	0.59	0.46	0.27	0.49	0.73	0.02
Manganese	3.54	3.8	0.43	3.89	3.8	0.1	3.35	4.38	0.19
Magnesium	2.1	2	0.31	2.13	2	0.24	1.9	1.8	0.18
Chromium	0.63	0.62	0.69	0.5	0.62	0.4	0.56	0.49	0.44

**Table-4:** Showing correlation of mean serum levels of trace elements and HbA1c levels.

and controls of old and newly diagnosed cases of DM, it was found that there was statistically significant difference in Cu, Mg and Cr levels in known cases of DM ( $p < 0.05$ ), while only Mg was the only trace element where difference between cases and controls in newly diagnosed cases was statistically significant. In all the above cases, these trace elements were less in cases as compared to controls. In rest of the trace elements, no statistically significant difference was found (table 2).

On comparing mean serum levels of trace elements between males and female controls, newly diagnosed and known cases of DM, it was found that there was significant difference between male and female control group in Cu and Mn. In newly diagnosed and known cases of DM only Zn was significantly different, with less concentration in females as compared to males. In other trace elements, there was no statistically significant difference (table 3).

On analyzing glycosylated hemoglobin (HbA1c) and mean serum trace element levels in newly diagnosed and known cases, it was found that there was no statistically significant difference in trace elements between the 2 in HbA1c range 6-8. Similar results were obtained in HbA1c ranges 8-10 and  $>10$ , except that difference for Zn was statistically significant in HbA1c  $>10$  ( $p 0.02$ ) with less Zn in newly diagnosed cases as compared to new cases (table 4).

## DISCUSSION

Plethora of clinical studies have found that disturbance in trace elements homeostasis is associated with DM and diabetic complications. The present study noted significantly low levels of Cu, Mg, and Cr in diabetic patients as compared to control. These findings are partly corroborated and partly different from that of other such studies, which found decrease in zinc levels as well.<sup>16,17,18</sup> The reduction in trace elements levels were more in known cases of DM as compared to newly diagnosed cases. This might be attributed to duration of DM. However, one study found no significant effect of duration of DM on trace element levels.<sup>19</sup> Poor dietary intake in the present study seems to be the plausible reason for such finding.

In HbA1c and trace element analysis, only low serum Zn levels and raised HbA1c had a significant association. Lower levels of Zn in diabetic patients is very well cited in literature.<sup>20</sup> The possible mechanism for lower Zn levels might be increased clearance of Zn through urine at such high HbA1c levels where complications of DM are more likely.<sup>21</sup> The antioxidant and anti-inflammatory role of Zn is documented as is corroborated in newly published study citing reduction in inflammatory markers, post Zn supplementation in geriatric patients.<sup>22,23</sup>

Mg was also found to be reduced in the present study in cases as compared to controls. Usual causes of low Mg levels are inadequate dietary intake, hyperglycaemia induced reverse transport of Mg between plasma and red blood cells, reduced reabsorption in nephrons induced by insulin resistance, etc.<sup>24</sup> Also, it has been found that Mg supplementation improves insulin sensitivity.<sup>25</sup> Thus, optimal Mg levels seem to lower

the risk of diabetic complications by imparting better glycaemic control.

There is paucity of concrete clinical data regarding association of reduced serum Cu levels and DM or its complications. In the present study, it was reduced in known cases of DM as compared to newly diagnosed cases and control groups. Various in vitro and clinical studies have demonstrated antioxidant action of Cu by acting as cofactor for cytochrome oxidase and superoxide dismutase, which act as free radical scavengers.<sup>26</sup> This might play beneficial role in retarding the development of diabetic complications.

The present study had certain limitations. The sample size of the present study was small, so the generalization of results cannot be recommended. Secondly, lipid levels and micro albuminuria in relation to trace elements concentration was not studied, since dyslipidaemia and nephropathy are frequent accompaniments of DM. Lastly, due to study design exact dietary intake could not be noted.

## CONCLUSION

The findings of present study are in line with that of other such studies in case of Cu, Mg and Cr levels and their correlation with DM. However, Zn was significantly reduced only in severe diabetics i.e. HbA1c  $>10$ , which is contradictory to other study findings, which report reduced Zn levels even in moderately severe DM. Similar studies should be conducted in multiple centres with larger sample size to allow generalization of results to a broader population.

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