

## Original Article

# A Study of Serum Magnesium and Serum Zinc Concentration In Type 2 Diabetes Mellitus Patients with and without Diabetic Nephropathy

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**Background :** The deficiency of important trace elements like Magnesium and Zinc in terms of their serum concentrations in Type 2 Diabetes Mellitus patients, commonly claimed to be a cause of diabetic nephropathy. So the measurement of these two important trace elements in diabetic patients and their replenishment in deficient state could be a possible deterrent to the progression of diabetic nephropathy.

**Materials and Methods :** This study was undertaken at Silchar Medical College and Hospital, Silchar, from June 2018 to May 2019. A total of 100 patients were taken and divided into two study groups after satisfying the inclusion and exclusion criteria. Then the patients in each group were subjected test for estimation of zinc and magnesium concentration in serum.

**Results :** Decrease in Zinc level was seen in all Type 2 diabetic patients, but the decrease was more in the group with diabetic nephropathy ( $62.96 \pm 25.48 \mu\text{g/dl}$  versus  $106.06 \pm 27.94 \mu\text{g/dl}$ ). Also decrease in magnesium was more significant in the group of patients with diabetic nephropathy ( $1.75 \pm 0.38 \text{ mg/dl}$  versus  $2.07 \pm 0.18 \text{ mg/dl}$ ).

**Conclusion :** From this study it is evident that diabetic nephropathy is associated with lower serum zinc and magnesium level. There is a scope to study the impact of its replenishment to prevent diabetic nephropathy.

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**Key words :** Type 2 Diabetes Mellitus, Diabetic Nephropathy, Zinc, Magnesium.

**D**iabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of diabetes mellitus are caused by a complex interplay of genetics and environmental factors<sup>1</sup>. Chronic and progressive nature of the disorder, which is associated with obesity<sup>2</sup>, hypertension<sup>3</sup>, advancing age<sup>4</sup> and inadequate screening<sup>5</sup> leads to deposition of harmful substances in the vascular endothelium ultimately causing development of micro angiopathies or microvascular complications<sup>6</sup>. These complications include retinopathy, nephropathy and peripheral neuropathy, which produce early death and increased morbidity and health care costs<sup>7</sup>. Normally insulin action was reported to be potentiated by some trace elements as chromium (Cr), magnesium (Mg), vanadium (V), zinc (Zn), manganese (Mn), molybdenum (Mo) and selenium (Se). It has been suggested that hypomagnesaemia may induce altered cellular glucose transport, reduced pancreatic insulin secretion, defective post receptor insulin signaling, and/or altered insulin-insulin receptor interaction<sup>8</sup> and it is a possible

### Editor's Comment :

- Low serum magnesium and zinc concentration was found associated with diabetic nephropathy as compared to those without nephropathy.
- It gives us an insight, whether replacement of these micronutrients can prevent development of diabetic nephropathy.

metabolic factor involved in the pathogenesis of diabetic micro and macro vascular complications<sup>9,10</sup>. Again several complications of diabetes may be related to increased intracellular oxidants and free radicals associated to decreases in intracellular Zn and Zn-dependent antioxidant enzymes<sup>11</sup> and it has been observed to effectively ameliorate diabetes-related complications in various animal models<sup>12</sup>. Zn is also an effective inducer of gene and protein expressions of Metallothionein, a potent antioxidant<sup>13</sup>

### MATERIALS AND METHODS

This case control study was undertaken at Silchar Medical College and Hospital, Silchar, from June 2018 to May, 2019. Here 50 cases are diagnosed type 2 diabetes mellitus patients with diabetic nephropathy (DN) compared with 50 controls after age and sex matched from the same population, suffering from type 2 diabetes mellitus without diabetic nephropathy (NDN). Subjects suffering from hepatic disease, congestive heart failure and those taking mineral supplementation were excluded. Informed consent was obtained from participants and protocol was approved

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by Institutional ethical committee. Serum Zn and magnesium were estimated by colorimetric method. Also spot urine sample was collected to estimate urinary albumin and creatinine. Albumin creatinine ratio used to assess diabetic nephropathy. Statistical analysis used student 't' test and p value less than 0.05 were consider significant. The patients and control data were collected in excel sheet and calculated using Graph pad instat 3 software.

#### RESULT

In patients without diabetic nephropathy (control), the mean serum magnesium and mean serum zinc concentration were  $2.07 \pm 0.18$  mg/dl and  $106.06 \pm 27.94$   $\mu$ g/dl, and in those with diabetic nephropathy (case), the mean serum magnesium and mean serum zinc concentration were  $1.75 \pm 0.38$  mg/dl and  $62.96 \pm 25.48$   $\mu$ g/dl respectively and the difference were highly significant ( $p < 0.0001$ ). It is observed that patients without diabetic nephropathy had higher levels of mean serum magnesium and serum zinc in comparison with patients with diabetic nephropathy (Tables 1 & 2).

The range for the levels of mean serum magnesium in patients without and with diabetic nephropathy was (1.6-2.4) mg/dl and (1-2.3) mg/dl with confidence interval of (2.02-2.12) and (1.64-1.86) respectively. The median in control and case group was 2.0 mg/dl and 1.9 mg/dl, and the standard error of mean was 0.025 and 0.054.

The range for the levels of mean serum zinc in patients without and with diabetic nephropathy was (45-150)  $\mu$ g/dl and (21-117)  $\mu$ g/dl with confidence intervals of (98.11-114.01) and (55.71-70.20) respectively. The median in control and case group was 106.0  $\mu$ g/dl and 55  $\mu$ g/dl and the standard error of mean was 3.95 and 3.6 respectively (Table 3).

On comparing the two groups, the mean serum magnesium concentration in patients with diabetic nephropathy was observed to be lower by 0.32 than that in patients without diabetic nephropathy. This difference was highly significant ( $p < 0.001$ ). Similarly, the mean serum zinc concentration in patients with diabetic nephropathy was lower by 43.1 than that in patients without nephropathy. This difference was highly significant ( $p < 0.001$ ) (Table 4).

Table 1 — Serum Magnesium and Serum Zinc Concentrations in Patients with and without Diabetic Nephropathy

Group	Patients with NDN (Control)	Patients with DN (Case)	P-value
Mean Serum Magnesium Concentration (mg/dl)	$2.07 \pm 0.18$	$1.75 \pm 0.38$	<0.0001
Mean Serum Zinc Concentration ( $\mu$ g/dl)	$106.06 \pm 27.94$	$62.96 \pm 25.48$	<0.0001

The mean serum magnesium and serum zinc in patients without diabetic nephropathy were  $2.096 \pm 0.17$  mg/dl and  $107.51 \pm 29.58$   $\mu$ g/dl in patients aged 50 years or less, and  $2.034 \pm 0.19$  mg/dl and  $103.58 \pm 25.18$   $\mu$ g/dl in patients above 50 years respectively. The differences between means were not significant. The mean serum magnesium and serum zinc in patients who had diabetic nephropathy were  $1.65 \pm 0.48$  mg/dl and  $74.42 \pm 23.84$   $\mu$ g/dl in patients aged 50 years or less, and  $1.77 \pm 0.37$  mg/dl and  $61.09 \pm 25.51$   $\mu$ g/dl in patients above 50 years. The differences between means were not significant (Table 5).

The mean serum magnesium levels in female and male patients with and without diabetic nephropathy were  $1.8 \pm 0.40$  mg/dl,  $2.07 \pm 0.19$  mg/dl and  $1.71 \pm 0.36$  mg/dl,  $2.08 \pm 0.17$  mg/dl respectively. The differences were not significant.

The mean serum zinc levels in female and male patients with and without diabetic nephropathy were  $64.26 \pm 25.70$   $\mu$ g/dl,  $104.39 \pm 30.21$   $\mu$ g/dl and  $61.85 \pm 25.73$   $\mu$ g/dl,  $108.18 \pm 25.28$   $\mu$ g/dl. The differences were not significant.

#### DISCUSSION

In this study, it has been observed that in patients without diabetic nephropathy, the mean serum magnesium concentration was found to be  $2.07 \pm 0.18$  mg/dl, and in those with diabetic nephropathy, the mean serum magnesium concentration was found to be  $1.75 \pm 0.38$  mg/dl. The difference was found to be highly significant ( $p < 0.0001$ ).

Das N *et al*<sup>14</sup> in their study found that the mean serum magnesium level in normal ACR and in the high ACR subjects were  $2.416 \pm 0.14$  mg/dl and  $1.646 \pm$

Table 2 — Analysis of Serum Magnesium and Serum Zinc Levels of Sample Under Study

Group	Number of Patients	Median		Min		Max		95% Confidence Interval		Standard error of Mean	
		Mg	Zn	Mg	Zn	Mg	Zn	Mg	Zn	Mg	Zn
		(mg/dl)	( $\mu$ g/dl)	(mg/dl)	( $\mu$ g/dl)	(mg/dl)	( $\mu$ g/dl)	(mg/dl)	( $\mu$ g/dl)	(mg/dl)	( $\mu$ g/dl)
Patients with NDN (control)	50	2.0	106	1.6	45	2.4	150	2.02-2.12	98.11-114.01	0.025	3.95
Patients With DN (case)	50	1.9	55	1	21	2.3	117	1.64-1.86	55.71-70.20	0.054	3.6

Table 3 — Comparison of Serum Magnesium and Zinc Level between Patients without Diabetic Nephropathy and Patients with Diabetic Nephropathy

Mean Serum Magnesium and Serum Zinc in the Different Sub-groups of Patients	Mean Difference	P Value
Without Diabetic Nephropathy (Control) — Diabetic Nephropathy (Case)	2.07-1.75=0.32	p<0.001
Without Diabetic Nephropathy (Control) — Diabetic Nephropathy (Case)	106.06-62.96=43.1	p<0.001

Table 4 — Analysis of Serum Magnesium and Zinc with Regard to Age

Groups	Mean Serum Magnesium (Mg/dl) ±SD and Mean Serum Zinc (µg/dl) ± SD				P-value	
	Age 50 years or less		Age >50 years		Mg	Zn
	Mg	Zn	Mg	Zn		
Patients with NDN (Control)	2.096 ± 0.17	107.51±29.58	2.034 ± 0.19	103.58± 25.18	>0.24	>0.20
Patients with DN (Case)	1.65 ± 0.48	74.42± 23.84	1.77±0.37	61.09±25.51	>0.46	>0.64

Table 5 — Serum Magnesium and Serum Zinc Among Female and Male Diabetic Patients with and without Diabetic Nephropathy

Groups	Mean Serum Magnesium (Mg/dl) ± SD and Mean Serum Zinc (µg/dl) ± SD				P-value	
	Females		Males		Mg	Zn
	Mg	Zn	Mg	Zn		
Patients without DN (Control)	2.07±0.19	104.39±30.21	2.08±0.17	108.18±25.25	>0.85	>0.63
Patients with DN (Case)	1.8±0.40	64.26±25.70	1.71±0.36	61.85±25.73	>0.44	>0.74

0.030 mg/dl respectively and was statistically significant with p-value <0.05.

Kishan R H *et al*<sup>15</sup> found mean serum magnesium levels among Type 2 DM with renal dysfunction, Type 2 DM without renal dysfunction and healthy controls were 0.795±0.199mg/dl, 1.319±0.103mg/dl and 2.33±0.28mg/dl respectively but the type of renal dysfunction did not mention in the study.

The finding of the present series was in agreement with the findings of the workers stated above, and may suggest a correlation between magnesium deficiency and development of microvascular complications in diabetes but we did not find any association between serum magnesium with age and sex.

Also in the present study, the patients without nephropathy, the mean serum zinc concentration was found to be 106.06±27.94 µg/dl, and in those with nephropathy the mean serum zinc concentration was found to be 62.96±25.48 µg/dl. The difference was found to be highly significant (p<0.0001).

In a study done by Jyothirmayi B *et al*<sup>16</sup>, the serum

levels of zinc was low in uncontrolled diabetes patients with micro-vascular complications and found to be (50±12.5, 95 ±20.42) (p< 0.001) when compared to control.

Mosaad A Abou-seif and Abd-Allah Youssef<sup>17</sup> found plasma zinc to be significantly less in diabetic patients with microvascular complications as compared to healthy controls. In Punjab, Puri M *et al*<sup>18</sup>, found zinc levels to be more decreased in the group with microangiopathic complications than in the group with uncomplicated diabetes mellitus (81.16+24.34 versus

92.01+20.17; p<0.05) and also Al-Timimi DJ, *et al*<sup>19</sup> found that advancing diabetic nephropathy represented by decreasing GFR and increasing micro albuminuria is associated with lower serum zinc levels.

In this study, the finding was in agreement with the findings of the workers stated above, and may suggest a correlation between

Zinc deficiency and development of micro vascular complications in diabetes but we did not find any association between serum Zinc with age and sex.

#### CONCLUSION

The study showed that serum magnesium and serum zinc concentrations were lower in patients with diabetic nephropathy than in patients without diabetic nephropathy. So to elucidate the cause of this alternation, a large scale clinical trials are needed in order to determine whether the alterations in serum level of magnesium and zinc are cause or consequence of diabetes mellitus and correction magnesium and zinc deficiency could be effective to reduce the incidence of diabetic nephropathy and to further elucidate the association between serum magnesium and serum zinc with diabetic nephropathy.

#### Limitations :

- (1) Single center study.
- (2) Small sample size.
- (3) Short duration of study.

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**Conflict of Interest : None.**

**Ethical permission : Taken.**

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