



## Role of Trace Element Zinc In Development Of Diabetic Nephropathy Attending A Tertiary Care Hospital In Southern Rajasthan Region Of India

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### Abstract

**Background:** In diabetic patients, chronic hyperglycemia due to glycosylation and peroxidation leads to increased oxidative stress and thereby proteins and lipids structure are changed. Lipid peroxidation produces toxic malondialdehyde (MDA). Zinc particle as a strong antioxidant and may decrease lipid peroxidation and recover antioxidant status in patients with diabetes. Study aims to find out the level of zinc and its causal relationship in diabetic patients with diabetic nephropathy.

**Methods:** A complete data of all clinically diagnosed cases of type 2 DM with and without nephropathy who attended the biochemistry, and nephrology department during year 2021. A standardized pre-structured questionnaire with consent was filled by direct interview of admitted patients including the demographic and laboratory data.

**Results:** In case and control groups group maximum subjects belong to age group 46-60 years, male preponderance, more from rural background, non-tribal area and Hindu religion. In case group 37.5% subjects were smokers, 45% subjects were alcoholics and 60.0% were vegetarians. While in control group 26.25% subjects were smokers, 42.5% subjects were alcoholics and 48.75% were vegetarians. The mean $\pm$ SD of case group came to be 58.14  $\pm$  5.7 in diabetic nephropathy & 67.16  $\pm$  6.3 in control group. The p value of this difference was <0.0001 which is statistically significant.

**Conclusions:** In our study we found out that there is direct association of trace element Zinc with diabetic and diabetic nephropathy. Altered blood level of zinc may have a role in the development of diabetic complication.

**Keywords:** Diabetic nephropathy, Zinc, trace elements, Diabetes melitus

### Introduction

Diabetic nephropathy a progressive kidney disease due to longstanding Diabetes Melitus is the leading cause of ESRD in the western world<sup>1</sup>. However not all patients with diabetes mediated hyperglycemia will increase this disorder<sup>2,3,4</sup>.

Diabetic nephropathy progresses from stage 1 to 5 characterized with progressive kidney damage, decreasing GFR, deteriorating kidney functions and

microalbuminuria which finally leading to end stage renal disease (ESRD). The mechanism by which hyperglycemia lead to (ESRD), through incompletely defined, involve the effects of soluble factors (growth factors, angiotensin 2, endothelin, AGES) hemodynamic alterations in the renal microcirculation (glomerular hyper filtration or hyper perfusion, increase glomerular capillary pressure), and structural changes in the glomerulus (increased

extra cellular matrix, basement membrane thickening mesangial expansion, fibrosis).

Diabetic nephropathy is among the leading causes of chronic renal disease worldwide. It is responsible for long-term complications in the individuals suffering from diabetes mellitus that leads to morbidity and mortality. An interaction of metabolic and hemodynamic factors has been considered as traditional aspect in the development of kidney lesions in patients with type 2 diabetes mellitus (DM).

Zinc plays a functional role in nervous and immune systems, the major role is hormones action, development, taste and smells function and wound healing as well as proteins and nucleic acids synthesis<sup>5-7</sup>, sexual development, release of vitamin A from the liver and cell wall formation<sup>8</sup>. Zn is an important micronutrient, which has a major role in synthesis storage, secretion and role of insulin and its metabolism is transformed in diabetes<sup>9,10</sup>. Zn deficiency is associated with insulin resistance<sup>11,12</sup>. In diabetic patients, chronic hyperglycemia due to glycosylation and peroxidation leads to increased oxidative stress and thereby proteins and lipids structure are changed<sup>13</sup>. Lipid peroxidation produces toxic aldehydes; malondialdehyde (MDA) is one of the most poisonous particles<sup>14</sup>. Zn particle as a strong antioxidant<sup>15,16</sup> and may decrease lipid peroxidation and recover antioxidant status in patients with diabetes<sup>17,18</sup>.

This study aims to find out the level of zinc and its causal relationship in diabetic patients with diabetic complication.

## Methods

**Study Design** - Cross-sectional, Descriptive, Duration Based, Hospital based Study

**Place of study** – This study was conducted in biochemistry and nephrology department at Pacific Medical College & Hospital, Udaipur (Rajasthan).

**Study Population & Inclusion Criteria** – Clinically diagnosed cases of type 2 DM with nephropathy and without complication who attended the biochemistry, and nephrology department during year 2021 which included Southern region of Rajasthan (Udaipur, Chittorgarh, Bhilwara, Rajsamand, Dungarpur, Banswara, Pratapgarh districts)

**Study Duration** – All criteria defined patients attended from October 2021 to March 2022.

**Sample Size** – Purposive sampling done. The total sample of 160 patients including cases and control was taken with equal division of 80 controls and 80 cases complication.

Group 1 - Clinically diagnosed cases of DM type 2 without complication

Group 2 - Clinically diagnose cases of DM type 2 with nephropathy complication

**Data Collection-** A standardized pre-structured questionnaire with consent was filled by direct interview of admitted patients including the demographic and laboratory data of patients like age, sex, residence, smoking, alcohol, diet and laboratory test values.

**Ethical issues** – Ethical clearance from ethical committee has been obtained prior to beginning of study.

## Exclusion criteria -

1. Cardiac disease patients are excluded.
2. Cancer patients are excluded.
3. Systemic disease patients are excluded.
4. Other disease (retinopathy, neuropathy are excluded).
5. Hypertensive patients are excluded.

## Collection and Analysis of Blood Samples -

Informed consent has obtained from all subjects for participating in the study. Blood sample was collected by vein puncture under aseptic precaution. Serum was separated from the sample and analyzed for following biochemical parameters.

**Principle** - Zinc reacts with 25-bromo PAPS form a red chelate complex in ph=9.8. The increase of absorbance measure at 546/600 nm is proportional to the concentration of total zinc in the sample.

Normal serum value 46-150 µg/dl

Procedure — wavelength filter 546nm,

Method — End Point

Temperature = R.T.

Light Path = 1 cm

Measurement — Against Reagent Blank

Reaction — End Point

Addition sequence	Blank	Calibrator	Sample
Reagent	1000 µl	1000 µl	1000 µl
Calibrator	-	50 µl	-
Sample	-	-	50 µl

MIX incubated for 10min at 37°C read the absorbance of standard and sample against the reagent blank.

Calculations - Zinc in µg/ dl = (Abs. T/Abs.C) x conc. calibrator (µg/dl)

**Statistical analysis** – Done by using excel sheet and statistical software SPSS.

### Results

Table 1 show that in our study, in case group maximum subjects (53.75%) belongs to age group 46-60 years, male preponderance (67.5%), more from rural background (56.25%), non-tribal area (68.75%) and Hindu religion (93.75%). While in control group majority subjects (62.5%) belongs to age group 46-60

years, male preponderance (62.75%), more from rural background (67.5%), non-tribal area (90.0%) and Hindu religion (83.75%). (Table 1)

Table 2 shows that in our study, in case group 37.5% subjects were smokers, 45% subjects were alcoholics and 60.0% were vegetarians. While in control group 26.25% subjects were smokers, 42.5% subjects were alcoholics and 48.75% were vegetarians. (Table 2)

Figure 1 shows the comparison of zinc level between study group and control group. The mean±SD of case group came to be 58.14 ± 5.7 in diabetic nephropathy & 67.16 ± 6.3 in control group. The p value of this difference was <0.0001 which is statistically significant. (Figure 1)

**Table No. 1 Demographic distribution of cases and control**

S. No.	Variables	Cases (n= 80)		Control (n= 80)	
		n	%	n	%
<b>Age group</b>					
1.	0-15	0	0	0	0
2.	16-30	3	3.75	0	0
3.	31-45	5	6.25	11	13.75
4.	46-60	43	53.75	50	62.5
5.	>60	29	36.25	19	23.75
<b>Sex</b>					

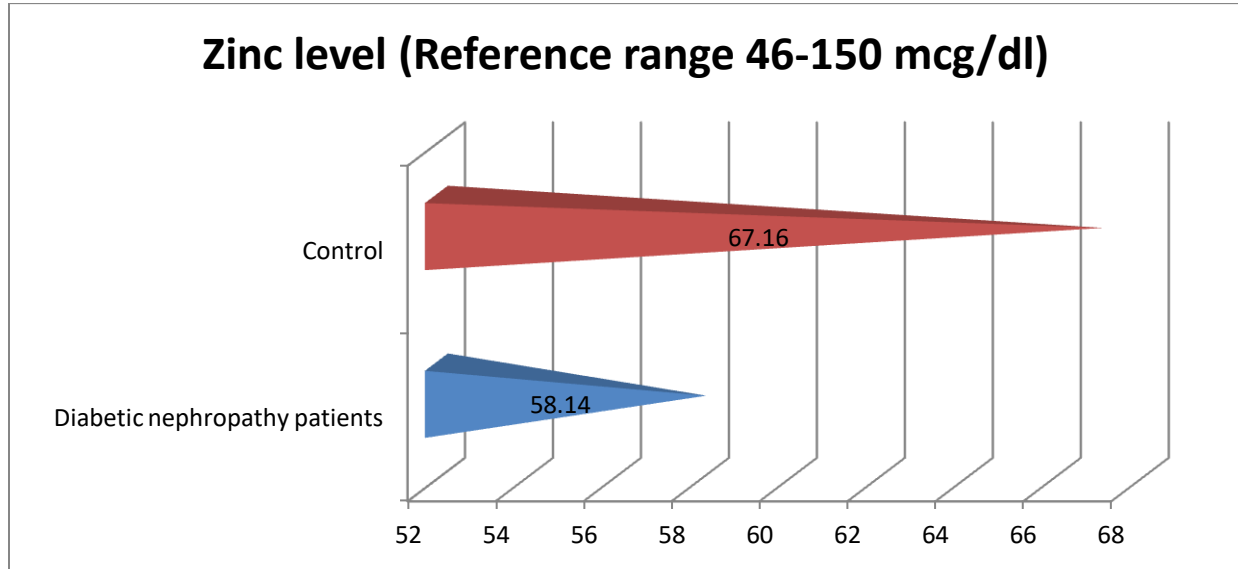
1.	<b>Male</b>	54	67.5	50	62.5
2.	<b>Female</b>	26	32.5	30	37.5
<b>Area</b>					
1.	<b>Rural</b>	45	56.25	54	67.5
2.	<b>Urban</b>	35	43.75	26	32.5
<b>Tribal Status</b>					
1.	<b>Tribal</b>	25	31.25	8	10.0
2.	<b>Non-Tribal</b>	55	68.75	72	90.0
<b>Religion</b>					
1.	<b>Hindu</b>	75	93.75	67	83.75
2.	<b>Others</b>	5	6.25	13	16.25

**Table No. 2 Distribution of cases and control according to smoking, alcohol and dietary history**

S. No.	Variables	Cases (n= 80)		Control (n= 80)	
		n	%	n	%
<b>Smoking History</b>					
1.	<b>Smoker</b>	30	37.5	21	26.25
2.	<b>Non smoker</b>	50	62.5	59	73.75
<b>Alcohol History</b>					
1.	<b>Alcohol</b>	36	45.0	34	42.5
2.	<b>Non-Alcohol</b>	44	55.0	46	57.5
<b>Dietary History</b>					

1.	<b>Vegetarian</b>	48	60.0	39	48.75
2.	<b>Non-vegetarian</b>	32	40.0	41	51.25

Figure 1. Comparison between the patients with diabetic nephropathy and control group for zinc.



**Discussion**

In our study - mean SD of zinc was  $58.14 \pm 5.7$  in diabetic nephropathy which was lower than mean $\pm$ SD of control  $67.16 \pm 6.3$  and the difference was statistically significant ( $p < 0.0001$ ). (Figure 1)

In our study, serum zinc levels in diabetic patients were significantly lower in comparison to control group.

Zn deficiency often occurs in patients with diabetes. Therefore, the effect of Zn deficiency or Zn supplementation on diabetes-induced cardiac and renal pathogenesis has been explored. Furthermore Zn deficiency was found to significantly enhance the renal damage induced by diabetes. Several clinical observations also support the preventive effect of Zn in the increase of diabetic cardiomyopathy and nephropathy. Therefore, Zn plays an important role in the protection of the heart and kidney against diabetes-induced oxidative damage, inflammation, and fibrosis. These studies suggested that diabetic patients should be monitored and treated for Zn deficiency to avoid the acceleration of diabetes-induced cardiac and renal injury<sup>19</sup>.

Nasli-Esfahani et al the level of elements in hair, nail, urine and serum were evaluated in type 2 diabetic patients; their results indicated a meaningful decrease in serum level of Zn in patients compared to healthy individuals<sup>20</sup>.

The cause of zinc deficiency in people with diabetes is hyperzincuria as an effect of hyperglycosuria. The complication of diabetes may be mediated at least in part, through oxidative stress, and zinc play an influential role in cellular antioxidative defence. If there is insufficient zn available in the tissue, oxidative stress may damage the cell irreversibly, prefiguring or exacerbating some of the classic complication of diabetes (chausmer 1998)<sup>21</sup>.

**Summary & Conclusion**

The findings of our study can be summarized as most of the patients and control were non vegetarian, Hindu and male patients were more than female patients, most of the patients of the study non smoker, alcoholic patients are rises then control.

In our study we found out that there is direct association of trace element Zinc with diabetic and diabetic nephropathy. Altered blood level of zinc

may have a role in the development of diabetic complication. The decreased blood levels of Zinc have been found in present study can be utilized for the screening, diagnosis and management of diabetes mellitus and its complication.

Our study throw some light on the facts which can have role in disease development though study have its own limitations but results shows statistically significant association with low level of zinc.

### Limitations

The data was taken only from hospitalized patients. This study was conducted on a small population group with limited resources and financial restrictions.

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