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**Endocrinology**

# Serum Zinc Level and Glycemic Status in Newly Diagnosed Type 2 Diabetes Mellitus Patients in a Tertiary Care Hospital of Bangladesh

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**Abstract** **Original Research Article**

***Background:*** Reduced level of serum zinc has been observed in patients with type 2 diabetes mellitus (T2DM). ***Objectives*:** Estimation of serum zinc level and HbA1c in newly detected T2DM. ***Materials and methods:*** This cross-sectional study encompassed 100 newly detected non-pregnant T2DM subjects diagnosed on basis of ADA 2015 criteria (n=100; age: 44.74±11.34 years, mean±SD; Sex: 56/44, M/F) from the department of Endocrinology, BSMMU consecutively. Study period was March, 2015 to April, 2016. Blood sample was collected for measurement of zinc and HbA1c. Height, weight, waist circumference, hypertension, dyslipidaemia, ischemic heart disease (IHD), cerebrovascular disease (CVD), retinopathy, neuropathy, nephropathy, serum creatinine were recorded as confounding variables. HbA1c was measured using the NGSP certified Bio-Rad D-10$^{TM}$ Hemoglobin $A_1C$ Program while Zinc by using Atomic Absorption Spectrometric Analysis. ***Result:*** There was no statistically significant difference for zinc level in gender groups (M vs. F: 0.91±0.02 vs. 0.88±0.02 mg/L, p= 0.580; M±SEM), age groups (age <25 years: 0.89±0.82, 25 – 34 years: 0.90±0.03, 35 – 44 years: 0.90±0.32, 45 – 54 years: 0.91±0.03, and ≥55 years: 85±0.03 mg/L, M±SEM; F= 0.379, p= 0.823), body mass index (BMI) groups (BMI <25 vs. ≥25 kg/m$^2$: 0.92±0.02vs. 87±0.02, p= 0.107), socioeconomic groups (low vs. middle vs. high socioeconomic status: 0.90±0.02 vs. 0.91±0.02 vs. 0.86±0.03 mg/L, M±SEM; F= 0.548, p= 0.580) as well as with and without family history of diabetes (0.90±0.01 vs. 0.89±0.02 mg/L, M±SEM; p= 0.705). Also zinc level was statistically similar among glycemic status groups (HbA1c < 6.5% vs. 6.5-9% vs. > 9%: 0.89±0.40 vs. 0.87±0.02 vs. 0.91±0.02 mg/L, F= 0.568, p= 0.569). Comparisons between groups with or without risk factors like: smoking (0.93±0.10 vs. 0.89±0.10 mg/L, p=0.724), hypertension (0.87±0.02 vs. 0.91±0.02 mg/L, p= 0.237), dyslipidemia (0.87±0.02 vs. 0.90±0.02 mg/L, p=0.393) and also co morbidities like: ischemic heart disease (0.87±0.02 vs. 0.90±0.01 mg/L, p=0.643), cerebrovascular disease (0.87±0.06 vs. 0.89±0.01 mg/L, p=0.791), diabetic retinopathy (0.80±0.07 vs. 0.90±0.01 mg/L, p=0.329), diabetic nephropathy (0.86±0.08 vs. 0.89±0.01 mg/L, p=0.741) and diabetic neuropathy (0.94±0.06 vs. 0.89±0.01 mg/L, p=0.336) showed no statistically significant difference of zinc level. None of the variables like age (r= -0.015, p=0.884), BMI (r= -0.03, p=0.979), fasting (r=0.161, p=0.108) and 02 hours glucose (r=0.028, p=0.728), HbA1c (r=0.124, p=0.221), serum creatinine (r=0.006, p=0.949) and SGPT (r= -0.030, p=0.770) showed any significant relationship with level of zinc. ***Conclusions*:** It is concluded that newly diagnosed T2DM has serum zinc level within normal limit and there was found no statistically significant relationship between HbA1c and zinc.

**Keywords:** Serum zinc, type 2 diabetes mellitus, hemoglobin, serum creatinine.



## INTRODUCTION

Diabetes mellitus (DM) is a major noncommunicable disease, ranking as a leading cause of death and disability worldwide [1]. It is a metabolic disorder of multiple etiologies, characterized by chronic hyperglycemia together with disturbance of carbohydrate, fat and protein metabolism resulting from defects of insulin secretion, insulin action or both [2].

The number of people with diabetes is exceptionally increasing worldwide due to population growth, aging, urbanization, unhealthy eating habits, increasing prevalence of obesity and physical inactivity [3].

Worldwide ninety to ninety five percent patients with diabetes are suffering from Type 2 diabetes mellitus. Among them 80% of people lives in low and middle income countries [4]. In the South Asian region, Bangladesh has the second largest number of adults with diabetes (5.1 million adults, 6.3%) [4].

As diabetic patients have such many devastating outcome, extensive research work have been undertaken throughout the world to understand the details of the disease though many aspects of the disease are yet to be explored.

The metabolism of several minerals has been reported to alter in diabetes mellitus and these elements might have specific role in the pathogenesis and progression of the disease – notably zinc [5]. It is seen that zinc plays a clear role in the synthesis, storage and secretion of insulin as well as conformational integrity of insulin and reduced levels of serum zinc have been observed in patients with type 2 diabetes [6, 7]. Type 2 diabetes is characterized by defects in both insulin secretion and insulin sensitivity, the decrease level of zinc normally affects the ability of pancreas to produce and secrete insulin but also develop insulin resistance, particularly in type 2 diabetes [8].

Diabetes affects zinc homeostasis in many ways, but hyperglycemia is the most important primary lesion, responsible for the decreases in total body zinc in diabetes mellitus [9]. Hyperglycemia causes high amount of zinc loss in the urine and such loss cannot be compensated by increasing intestinal absorption or decreasing excretion [10]. And it is seen that zinc supplementation 30mg/day for 3-6 months is known to be helpful in improving glycemic status [11].

So, measurement of serum zinc level in newly diagnosed type 2 diabetes mellitus may help in exploring concurrent serum zinc deficiency, a condition which can be treated very easily. Despite evidence suggestive of widespread zinc deficiency in Bangladeshi population, attempts to assess serum zinc concentration in vulnerable group have been very few. Thus, we have undertaken this study to evaluate the serum zinc concentration and glycemic status in newly diagnosed type 2 diabetes patients in a tertiary care hospital of Bangladesh.

# OBJECTIVE

**General objective**

- To determine the distribution of serum zinc concentration and glycemic status in newly detected type 2 diabetic patients

**Specific objectives**

- To estimate serum zinc level in newly detected diabetes patients
- To measure HbA1c in newly detected diabetes patients
- Correlation of HbA1c and Serum zinc level

# METHODOLOGY

| **Type of study** | **Cross-sectional study** |
|---|---|
| Place of study | Outpatient department of Endocrinology, BSMMU |
| Study period | March, 2015 to April, 2016 |
| Study population | Adults (≥18 years) with newly detected type 2 diabetes mellitus attending the outpatient department of Endocrinology, BSMMU |
| Sampling technique | Purposive |
| Sample Size | Estimated sample size was 76, but for this study we enrolled 100 cases |

**Selection criteria**

**Inclusion criteria:**

- Newly diagnosed type 2 diabetes mellitus patients.
- Adults (Age ≥18 years).

**Exclusion criteria:**

- Patient receiving zinc supplementation or taking drug that can modify zinc metabolism e.g. penicillamine, thiazide, ethambutol, sodium valproate, iron.
- Pregnant and lactating women.
- Persons suffering from chronic diseases e.g. malabsorption syndrome, chronic liver disease, chronic kidney disease, malignancy, alcoholics.

**Procedures of data collection**

Subjects were recruited on the basis of ADA 2015 criteria for diagnosis of DM from Endocrine outpatient department of Bangabandhu Sheikh Mujib Medical University (BSMMU) after complete explanation of the steps and purpose of the study and taking written consent from patient. Data was collected in questionnaire after completion of history, physical examination. Then 5 ml blood was taken from each subject in two separate test tubes maintaining all aseptic precaution. Serum was separated and stored at Biochemistry department under – $20^0$ C for zinc assay while HbA1c assay was done on the same day.

**Statistical analysis**

Data was analyzed using computer-based SPSS program (version 22.0). All data were expressed as frequencies and mean (±SD or ± SE). Comparison of zinc and HbA1c between subgroups was be done by Student's unpaired t-test or by one way- ANOVA. Pearson's correlation test was used to see correlation among different variables. P values ≤ 0.05 were considered as significant.

# RESULTS

**Table - I: Demographic characteristics of the participants**

| Parameter | Values |
|---|---|
| Age (Years, mean + SD) | 44.74±11.34 |
| Gender | |
| Male | 56 |
| Female | 44 |
| Occupation | |
| Service holder | 26 |
| House wife | 40 |
| Business | 11 |
| Others | 23 |
| Socioeconomic status | |
| Low | 43 |
| Middle | 34 |
| High | 23 |
| Family history of diabetes | 55 |
| History of smoking | 25 |

The present study measured serum zinc level in 100 newly diagnosed type 2 diabetic patients (Age: 44.74±11.34 years, mean + SD; Sex: 56/44, M/F) recruited consecutively from the outpatient department of Endocrinology of BSMMU. Among them 40% were housewife, 26% service holder, 11% businessman and rest 23% were others by profession. Socioeconomically 43% were in low income group, 34% average income and 23% from high income group. Among the subjects 55% had family history of diabetes while 25% had history of smoking (Table–I).

**Table-II: Zinc level (mg/L) in newly detected type-2 diabetes: Gender difference**

| Gender | Zinc Level (mean + SEM) | t , p |
|---|---|---|
| Male | 0.91±0.02 | t=0.556 |
| Female | 0.88±0.02 | p=0.580 |
| Total | **0.89±0.01** | |

By Student's t-test

As shown in table – II, level of zinc was not significantly different between the male and female (M vs. F: 0.91±0.02 vs. 0.88±0.02 mg/L, p= 0.580; M±SEM).

**Table-III: Zinc level (mg/L) in newly diagnosed type-2 diabetes: Age groups**

| Age group | Zinc Level (mean + SEM) | 95% CI | F, p |
|---|---|---|---|
| <25 | 0.89±0.82 | 0.53-1.25 | |
| 25 – 34 | 0.90±0.03 | 0.82-0.98 | |
| 35 – 44 | 0.90±0.32 | 0.83-0.97 | F=0.379 |
| – 54 | 0.91±0.03 | 0.84-0.97 | P=0.823 |
| > 55 | 0.85±0.03 | 0.79-0.92 | |
| Total | **0.89±0.01** | | |

By one-way ANOVA; there was no difference between any two groups

Like the gender group, among the age group, there was no statistically significant difference of zinc level (which was for age <25 years: 0.89±0.82, 25 – 34 years: 0.90±0.03, 35 – 44 years: 0.90±0.32, 45 – 54 years: 0.91±0.03, and ≥55 years: 85±0.03 mg/L, M±SEM; F= 0.379, p= 0.823; Table–III).

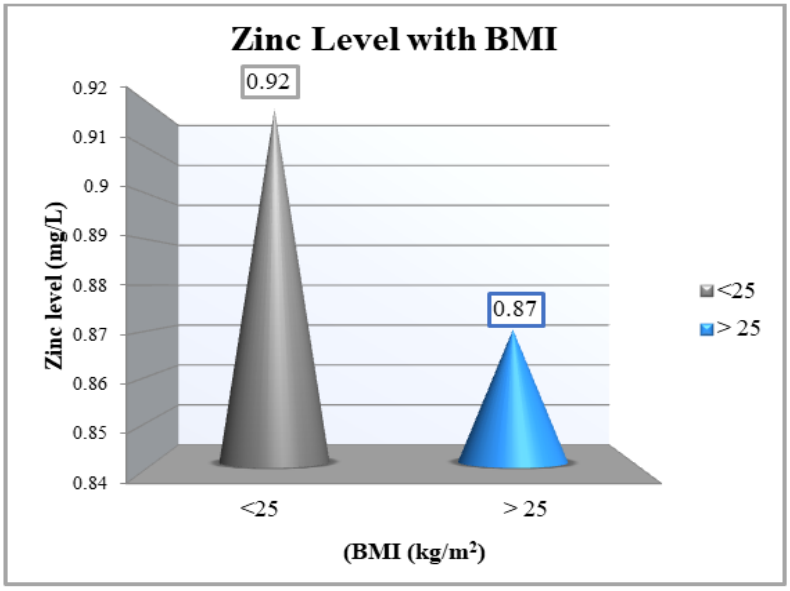


**Figure-1: Zinc level (mg/L) in newly detected type 2 diabetes: BMI group**
By Student's t-test; t=1.628, p= 0.107

In Figure 1 BMI was divided into two group by use of cut off at 25 kg/m$^2$, it was found that there was no statistically significant difference of zinc level (BMI <25 vs. ≥25 kg/m$^2$: 0.92±0.02vs. 87±0.02, p= 0.107; Figure-1).

**Table-IV: Zinc level (mg/L) in newly detected type –2 diabetes: Socioeconomic status**

| Socio. Status | Zinc Level (mean + SEM) | 95% CI | F, p |
|---|---|---|---|
| Low (n=43) | 0.90±0.02 | 0.85-0.95 | F=0.548 |
| Middle (n=34) | 0.91±0.02 | 0.85-0.97 | p=0.580 |
| High (n=23) | 0.86±0.03 | 0.79-0.93 | |
| Total | **0.89±0.01** | | |

By one-way ANOVA

Table–IV shows zinc level among the socioeconomic groups. There was found no statistically significant difference of zinc level among the groups (low vs. middle vs. high socioeconomic status: 0.90±0.02 vs. 0.91±0.02 vs. 0.86±0.03 mg/L, M±SEM; F= 0.548, p= 0.580).

**Table - V: Zinc level (mg/L) and family history of diabetes**

| Family History of DM | Zinc Level (mean + SEM) | t , p |
|---|---|---|
| Positive (n=55) | 0.90±0.01 | t=0.380 |
| Negative (n=45) | 0.89±0.02 | p=0.705 |
| Total | **0.89±0.01** | |

By Student's t-test

Table – V depicts the zinc level in newly diagnosed diabetic subjects with and without family history of diabetes. There was no statistically significant difference for zinc level between two groups (0.90±0.01 vs. 0.89±0.02 mg/L, M±SEM; p= 0.705).

Level of zinc in light of glycemic status is shown in Figure – 2. Glycemic status as stratified by HbA1c < 6.5%, 6.5-9% and > 9% showed no statistically significant difference for zinc level (HbA1c < 6.5% vs. 6.5-9% vs. > 9%: 0.89±0.40 vs. 0.87±0.02 vs. 0.91±0.02 mg/L, F= 0.568, p= 0.569).

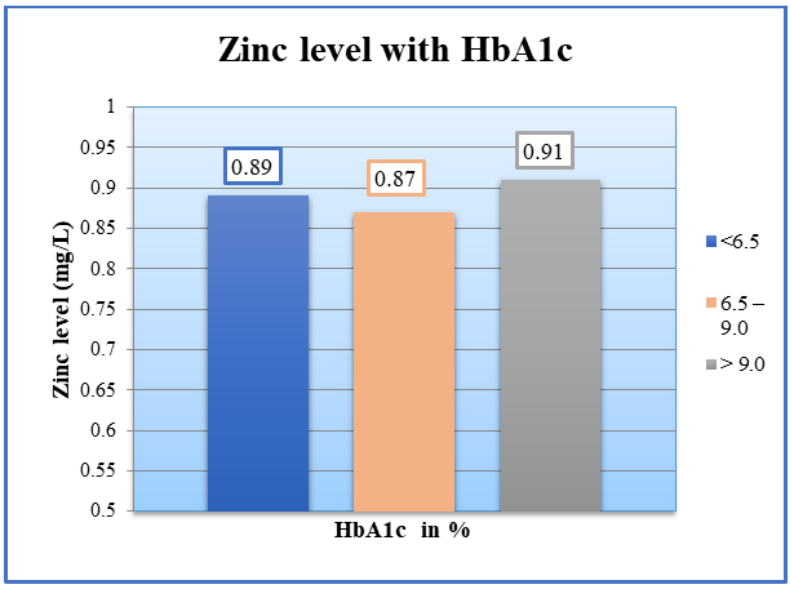


**Figure-2: Zinc level and HbA1c in newly detected diabetes**
By one-way ANOVA; F= 0.568, P= 0.569

**Table VI: Zinc level: relation with risk and co-morbidities**

| Risk factors | Zinc Level (mean + SEM) | | p |
|---|---|---|---|
| | Positive | Negative | |
| Smoking | 0.93±0.10 | 0.89±0.10 | 0.724 |
| Hypertension | 0.87±0.02 | 0.91±0.02 | 0.237 |
| Dyslipidemia | 0.87±0.02 | 0.90±0.02 | 0.393 |
| IHD | 0.87±0.02 | 0.90±0.01 | 0.643 |
| CVD | 0.87±0.06 | 0.89±0.01 | 0.791 |
| Diabetic retinopathy | 0.80±0.07 | 0.90±0.01 | 0.329 |
| Diabetic nephropathy | 0.86±0.08 | 0.89±0.01 | 0.741 |
| Diabetic Neuropathy | 0.94±0.06 | 0.89±0.01 | 0.336 |

By Student's t-test; IHD= Ischemic heart disease, CVD= Cardiovascular disease

Table – VI display the comparisons of zinc level between groups with and without various risk factors and co morbidities. None of the comparisons between positive and negative groups of risk factors as: smoking (0.93±0.10 vs. 0.89±0.10 mg/L, p=0.724), hypertension (0.87±0.02 vs. 0.91±0.02 mg/L, p= 0.237), dyslipidemia (0.87±0.02 vs. 0.90±0.02 mg/L, p=0.393) and also co morbidities like: IHD (0.87±0.02 vs. 0.90±0.01 mg/L, p=0.643), CVD (0.87±0.06 vs. 0.89±0.01 mg/L, p=0.791), diabetic retinopathy (0.80±0.07 vs. 0.90±0.01 mg/L, p=0.329), diabetic nephropathy (0.86±0.08 vs. 0.89±0.01 mg/L, p=0.741) and diabetic neuropathy (0.94±0.06 vs. 0.89±0.01 mg/L, p=0.336) showed any statistically significant difference.

## DISCUSSION

Diabetes is a complex and multifactorial disease. Published data revealed that type 2 diabetic patients have suboptimal zinc status in blood due to its increased urinary depletion [12]. Present study was intended to observe serum zinc level encompassing 100 newly diagnosed patients with type-2 DM at a tertiary level hospital. Virtually all the subjects were found to have zinc level within normal limit. No statistically significant difference for zinc level either among age groups, glycemic status groups and different socioeconomic classes or between gender or BMI groups was found.

The trace elements play a vital role in different metabolic processes in the body. Among them zinc has many antioxidant properties and has been suggested that chronic zinc deprivation may result in increased sensitivity to oxidative stress [5]. Most of the studies demonstrated relatively low zinc level in patients with diabetes though inference about it still remains controversial [13]. In context to this, we did not find the level of zinc in the newly diagnosed type 2 diabetic subjects.

Regarding age group, the level of zinc was observed to be lower in the older age groups in comparison to younger age group (though not statistically significant) [14]. These findings may be attributable to the increased urinary loss of zinc associated with ageing. El- Yazigi *et al*., (1993)

explained some reduction of zinc level due to reduction in renal function, diabetic nephropathy and gastrointestinal malabsorption [15]. However, these factors would not come into consideration to our studied subjects. Therefore, it seems that duration of diabetes has little to do, if at all, with the low level of zinc observed by some investigators [16, 17].

Neither gender difference nor any difference for socioeconomic status was observed for the level of zinc in the study. It is to be mentioned that Islam *et al*., (2013) did not find any difference for sex and socioeconomic status [18]. But contrary to our findings, they observed that the level of zinc was lower in diabetic and prediabetic subjects than that for nondiabetic as well as the level in the prediabetic and diabetic was also lower than the reference normal value. In this regard, it needs be mentioned also that all their patients were newly diagnosed type 2 diabetic subjects like ours. Like the findings in the present study, Akhuemokhan *et al*., (2010) also found no gender difference for zinc level in diabetic subjects; on the other hand, Nsonwu *et al*., (2006) observed contradictory findings [19, 14].

Regarding family history, we found 55% of our patient had family history of diabetes. But important to observe that there was no statistically significant difference for zinc level between groups with and without family history of diabetes [20].

According to our study 50% of the study subjects had HbA1c > 9.0% though the zinc level was highest in this group (0.91±0.02 mg/L). This finding was contradictory to the findings as observed by others [21]. They found significantly lower zinc concentration in diabetic subjects than the healthy controls though they could not be clarified which came first: the effects of hyperglycemia on zinc metabolism or the effects of altered zinc homeostasis on carbohydrate metabolism. On the contrary, Hassan *et al*., (2013) observed relatively higher zinc level in patients with higher HbA1c like that found in our patients. However, present study did not observe any correlation between zinc and HbA1c level [22].

On evaluation of relationship between risk factors and zinc level, we found – no significant differences in serum zinc level among the persons who are positive for risk factors in comparison to negative for risk factors. Regarding comorbidities we observed no significant relationship with serum zinc. These findings were in conformity with Agarwal *et al*., (2013) but contradictory to Walter *et al*., (1991), they showed lower zinc level in patients of type 2 diabetes mellitus with complications than those without these complications [23, 24].

In conclusion, newly diagnosed diabetic subjects were found to have zinc level within normal limit. There was no statistically significant difference for zinc level in age groups, glycemic status groups; different socioeconomic classes and between gender or BMI groups. Subjects having risk factors like smoking, HTN, dyslipidaemia and complications of DM at diagnosis as IHD, CVD, retinopathy, nephropathy and neuropathy showed normal level of zinc.

## CONCLUSION

Newly diagnosed T2DM has zinc level within normal limit. Level of zinc was found to be statistically similar in age groups, glycemic status groups, socioeconomic classes and gender or BMI groups.

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