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Low level of serum zinc may be associated with early onset diabetes mellitus

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Abstract

Background:

Zinc is an important element of our body that is thought to be involved in the etiopathogenesis of diabetes mellitus (DM). A low level of serum zinc has been observed in people with DM. Very limited data are available regarding zinc levels among young patients with newly diagnosed DM.

Aims:

To determine the serum zinc level and its association with glycemic status in newly diagnosed young patients with DM.

Materials and Methods:

In this observational case-control study, 40 newly diagnosed young patients with DM were recruited from the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU) to see the serum zinc level and glycemic status. An equal number of matched controls with normal glucose tolerance (NGT) was also enrolled from the nursing student of the same university. Serum zinc level was measured by using Atomic Absorption Spectrophotometry. Plasma glucose was measured by the glucose oxidase method while HbA1c was measured using the national glycosylated hemoglobin standardization program (NGSP) certified Bio-Rad D-10TM Hemoglobin A1c Program 220-0101, USA.

Results:

Serum zinc level was significantly lower in persons with newly diagnosed DM than NGT (DM vs. NGT; 0.87±0.10 vs. 0.93±0.12 mg/L, mean±SD; p=0.02). A significant inverse correlation was observed between serum zinc level & HbA1c (r=-0.370, p=0.019) among newly diagnosed DM patients. The study subjects (both DM and NGT) were divided into two BMI groups by using cut off at 23 kg/m2 and serum zinc level was found significantly lower in the low BMI group (BMI <23 vs. < 23 kg/m2: 0.86±0.13 vs. 0.92±0.10, mean±SD; p=0.029).

Conclusion:

Serum zinc level was found lower in newly diagnosed young patients with DM than NGT and showed a significant negative relationship with glycemic status

Keywords: Serum zinc level, diabetes mellitus, glycemic status, young adults, Bangladesh.

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Introduction

The number of people with diabetes is exponentially increasing worldwide and has become an important global public health problem. The incidence of type 2 diabetes mellitus (DM) is increasing in the South Asian population among children and adolescents.[1] This may be due to eating habits, increasing obesity, and physical inactivity.[2] Many hypotheses have been proposed to explain the pathogenesis of diabetes mellitus. Insulin resistance and pancreatic beta-cell function impairment play a cardinal role in the pathogenesis of diabetes. Impaired insulin secretion is generally progressive, and its progression involves glucose toxicity and lipotoxicity. The progression of the impairment of pancreatic cell function greatly affects the long-term control of blood glucose.

Zinc is the second most common trace metal in the body which has an important role in the functioning of hundreds of enzymes, in insulin metabolism and acts as an efficient antioxidant.[3] Recently there has been a growing interest in the role of zinc signalling in diabetes based on the fact that reduced levels of serum zinc have been observed in patients with diabetes[4-7] and zinc supplementation in several animal models of diabetes and human patients showed improved glycaemic control.[8-11]

The pancreas is the site of insulin synthesis, storage, and secretion, and zinc is involved in each of these processes. Zinc is co-secreted with insulin, has an autocrine effect on the beta-cell, a paracrine effect on glucagon secretion from alpha-cells, and possibly an endocrine effect on the liver by inhibiting hepatic insulin clearance. Several studies also found that secretory granules contain one-third of islet zinc.[12] Moreover, zinc is thought to be a positive regulator of adenosine triphosphate (ATP) sensitive potassium (K-ATP) channels, localized on islet cells as well as secretory granule membranes, which are essential for insulin secretion in response to glucose.[13] Thereby, decreased serum zinc level is associated with beta-cell dysfunction and disrupting glycemic control.[14] Moreover, zinc deficiency also decreases insulin sensitivity by decreasing the binding ability of insulin to its receptors.[15]

Diabetes in the young is regarded as evolving epidemic. Despite the young age of onset and short duration of diabetes, this group tends to develop diabetes-related complications such as nephropathy and cardiovascular disease early in the disease process.[16] Thus, they require urgent attention.The role of zinc in the pathogenesis of diabetes in young needs careful consideration. Very limited data is available regarding zinc level and its association with glycemic status among young patients with newly diagnosed DM in Bangladesh. So, we designed our study to determine the serum zinc level in young patients with newly diagnosed DM and to find out its correlation with glycemic status. This might give an insight into understanding the role of zinc in the development, as well as the progression of DM in the young population and guide the diabetologists or clinicians to manage the issue efficiently.

Materials and Methods

This observational cross-sectional study was done at the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from July 2017 to February 2019. Ethical approval was obtained from the Institutional Review Board and informed written consent was obtained from participants or guardians as indicated.

Although a sample size of 94 was calculated, as a pilot project forty newly detected patients with DM, age range 13 to 29 years, irrespective of diabetes type were recruited from the Department of Endocrinology, BSMMU. Forty age and sex-matched controls with normal glucose tolerance (NGT) were also enrolled from the healthy nursing students of the same university. Although a higher sample size was calculated for the study, we could not recruit more participants due to resource constrain. A screening oral glucose tolerance test (OGTT) was done for the participants who were not previously diagnosed with DM. Screening and diagnosis of subjects were done by American Diabetes Association (ADA) 2017 DM diagnostic criteria. [17] They were enrolled by using purposive non-probability sampling.

Patients who were receiving zinc supplementation or taking a drug that can modify zinc metabolism (e.g. penicillamine, thiazide, ethambutol, sodium valproate, iron), patients with gestational diabetes mellitus (GDM), patients suffering from chronic diseases (e.g. malabsorption syndrome, chronic liver disease, chronic kidney disease, malignancy), alcoholics, drug-induced diabetes or diabetes secondary to endocrine disorders, acute systemic illness were excluded from the study.

Following a complete explanation of the procedure and purpose of the study, data was collected using a data collection sheet. Subjects were enrolled based on OGTT results until the desired number of cases and controls were recruited. Fasting plasma glucose(FPG) & 2-hrs after 75 g glucose (2hPG)

was measured by the glucose oxidase method while hemoglobin A1c (HbA1c) was measured using the national glycosylated hemoglobin standardization program (NGSP) certified Bio-Rad D-10TM Hemoglobin A1c Program 220-0101, USA. Serum zinc level was measured by using Atomic Absorption Spectrophotometry.All data were processed by using IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. Data were expressed as frequencies or percentages for qualitative values and mean (±SD) for quantitative values with normal distribution.

When quantitative values with skewed distribution were found, they were presented as the median and interquartile range (25th -75th percentile). Different subgroups made based on clinical and metabolic or biochemical parameters were compared by Chi-square test and unpaired Student's t-test as applicable. Comparison of zinc and HbA1c between subgroups was done by Student's unpaired t-test or by one-way analysis of variance (ANOVA). The correlation of serum zinc level with HbA1c and glucose level were analysed by Pearson's correlation test. P values ≤ 0.05 were considered statistically significant.

Table 1: Characteristics of the study subjects

Variables	DM	NGT	P
N	40	40	
Age (years, mean±SD)	24.13±3.96	25.88±4.17	0.058
Gender			
Male	17 (42.5)	21 (52.5)	0.370
Female	23 (57.5)	19 (47.5)	
BMI (kg/m2 , mean±SD)	25.02±5.07	24.12±4.31	0.393
WC (cm, mean±SD)	86.77±12.38	81.40±8.65	0.027
WHR (mean±SD)	0.88±0.06	0.86±0.06	0.174
Acanthosis nigricans	16 (40)	6 (15)	0.012

Within parentheses are percentages over column total; Significance values stand for comparison between DM and NGT groups by Student's t-test and $\chi 2$-test, as applicable. DM: diabetes mellitus, NGT: normal glucose tolerance, BMI: body mass index, WC: waist circumference, WHR: waist-hip ratio.

Results

The present study recruited 80 young subjects (age: 25±4.13 years, BMI: 24.57±4.7 kg/m^2; mean±SD) in an attempt to determine the serum zinc level. Among them, 40 subjects with newly diagnosed DM (age: 24.13±3.96 years, BMI: 25.02±5.07 kg/m^2; mean±SD) were included as case and an equal number of matched subjects with NGT (age: 25.88±4.17 years, BMI: 24.12±4.32 kg/m^2; mean±SD) were included as a control. Subjects in the DM group had significantly higher waist circumference (DM vs. NGT: 86.77±12.38 vs. 81.40±8.65 cm, mean±SD; p=0.027) and frequency of acanthosis (DM vs. NGT: 40% vs. 15%, p=0.012) than that of the NGT group. However, the BMI (DM vs. NGT: 25.02±5.07 vs. 24.12±4.31 kg/m^2, mean±SD; p=0.393) and waist-hip ratio (DM vs. NGT: 0.88±0.06 vs. 0.86±0.06, mean±SD; p=0.174) were not statistically different between the groups (Table-1).

The mean serum zinc level of the study subjects was 0.90 ± 0.114 mg/L (mean ±SD). The frequency distribution of serum zinc among study subjects has been shown in Figure 1. Serum zinc concentration was significantly lower in DM group (DM vs. NGT; 0.87±0.10 vs. 0.93±0.12 mg/L, mean±SD; p=0.02) than NGT (Table-2).

All the study subjects were divided into two groups according to gender and body mass index (BMI). The level of serum zinc was not different between the male and female (male vs. female: 0.88±0.12 vs. 0.91±0.10 mg/L, mean±SD; p=0.430), but serum zinc level was significantly lower in low BMI group (BMI <23 vs. 23 kg/m^2: 0.86±0.13 vs. 0.92±0.10, mean±SD; p= 0.029) (Table-3).

Level of serum zinc positively corelated with BMI (r=0.316, p=0.047), WC (r=0.468, p=0.002) and WHR (r=0.428, p=0.006) in the DM group; but none of them corelated with zinc level in the NGT group

(BMI: r=0.121, p=0.456; WC: r=0.009, p=0.991; WHR: r=-0.103, p=0.528). Serum zinc level corelated inversely with HbA1c (r=-0.370, p=0.019) in DM group but not in NGT group (r=0.123, p=0.450) (Table-4).

Table 2: Comparison of serum zinc level between DM and NGT groups

Groups	Serum zinc (mg/L) [Mean±SD]
DM (n=40)	0.87±0.10
NGT (n=40)	0.93±0.12
P	0.020

Comparison between groups was done by Independent Student's t-test
DM: diabetes mellitus, NGT: normal glucose tolerance

Table 3: Comparison of serum zinc level according to gender and BMI among all participants (n=80)

Groups	Serum zinc (mg/L) [Mean±SD]
Gender	
Male (n=38)	0.88±0.12
Female (n=42)	0.91±0.10
p	0.430
BMI groups	
BMI < 23 kg/m2 (n=30)	0.86±0.13
BMI ≥23 kg/m2 (n=50)	0.92±0.10
p	0.029

Comparison between groups was done by Independent Student's t-test
BMI: body mass index

Table 4: Correlations of serum zinc level (mg/L) with BMI (kg/m2), WC and WHR

Determinants of 'r'	DM (n=40)		NGT (n=40)	
	r	p	r	p
Serum zinc vs. BMI	**0.316**	**0.047**	**0.121**	**0.456**
Serum zinc vs. WC	**0.468**	**0.002**	**0.009**	**0.991**
Serum zinc vs. WHR	**0.428**	**0.006**	**-0.103**	**0.528**
Serum zinc vs. HbA1c	**-0.370**	**0.019**	**0.123**	**0.450**

by Pearson's correlation coefficient test ,DM: diabetes mellitus, NGT: normal glucose tolerance, BMI: body mass index, WC: waist circumference, WHR: waist-hip ratio, HbA1c: Hemoglobin A1c

Discussion

This study clearly observed that young subjects with newly diagnosed DM had significantly lower serum zinc levels in comparison to subjects with NGT. This is in agreement with some previous studies that observed a reduced level of serum zinc was observed in newly diagnosed diabetic patients. [18. 19] Similarly, Islam et al. reported that respondents with prediabetes as well as diabetes had lower serum zinc levels than normal participants in a cross-sectional study among 280 Bangladeshi adults aged ≥ 30 years, similar to the observations of Zuberi et al. in Pakistan. [14,19] We observed the same findings in younger people with newly diagnosed DM. The present study also revealed a significant negative relationship of serum zinc level with HbA1c in newly diagnosed DM patients. Similar findings were also observed by Viktorinova et al. and Tripathy et al. [20,21]

Although it is still not clear which came first, the effects of DM and hyperglycemia on zinc metabolism or the effects of alterations in zinc homeostasis on carbohydrate metabolism, there are pieces of evidence that hyperglycemia interferes with the active transport of zinc back into the renal tubular cells leading to more urinary excretion of zinc and thereby causing zinc deficiency which in turn disrupting glycemic control.[22]

A clear and strong relationship between zinc homeostasis and pancreatic function has been established by numerous investigations over the past decade. Meta-analysis of studies evaluating the effects of oral zinc supplementation in diabetes patients had shown that zinc supplementation improved glycemic control with probable improvement in anti-oxidant status.[23]

By antioxidant properties, zinc can protect against progressive beta-cell injury in type 2 diabetes by inhibiting oxidative stress, apoptosis, and inflammation.[24]Gunsekara et al. also observed a significant reduction in fasting blood glucose, postprandial blood glucose, and glycated hemoglobin (HbA1c) after zinc supplementation. [25]

There are various established risk factors associated with the development of DM in young including features or conditions associated with insulin resistance such as increased BMI, WC, acanthosis nigricans, etc.[26] The present study compared different risk factors like BMI, WC, WHR, and acanthosis nigricans between DM and NGT groups. This study-found significantly higher WC among the DM group than NGT. Acanthosis nigricans was also significantly higher in DM than that in the NGT group. These findings were also reflected in some previous studies.[27,28] The mean BMI of the study

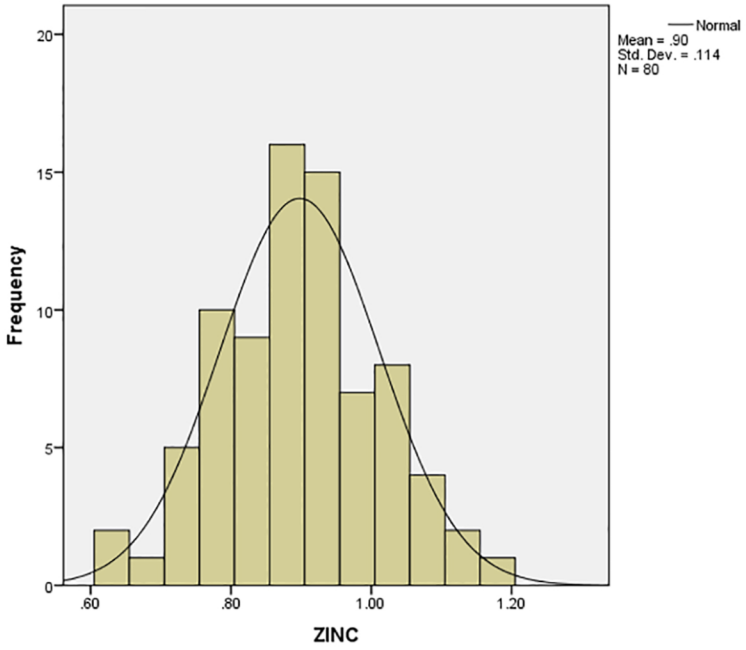

Figure 1: Distribution of serum zinc (mg/L) among study subjects (n=80)
Mean ±SD : 0.90 ± 0.114

population was in the range of 'overweight', although no statistically significant difference in BMI was observed between the groups.

In the present study, the serum zinc level was not statistically different between males and females. Similar findings were also observed by Islam et al. and Zargar et al.[14,29] But contrary to our findings, Nsonwu et al. and Rajib et al. observed that zinc level is significantly lower in females than males.[30,31] Though it is thought that females are more prone to nutritional deficiency due to lack of education and negligence this study does not reflect the rural community scenario as done in a tertiary care hospital.About 62% of our study subjects were overweight and serum zinc level was statistically higher in the overweight group.There was a significant positive relationship of serum zinc level with BMI, waist circumference and waist-hip ratio in the DM group though not significant in the NGT group or when all subjects were considered together. S imilar findings were also observed by Hafez et al.[32] Some studies also observed that zinc supplementation resulted in a significant increase in mean serum zinc level and BMI.[33] It indicates that low BMI people are more prone to zinc deficiency and demands zinc supplementation.

Conclusion

A significantly lower serum zinc level was observed in newly diagnosed young patients with DM compared with NGT and there was a significant negative relationship of serum zinc level with HbA1c. These study findings might guide us to look forward to the role of zinc supplementation in managing DM, especially in young patients.

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