Serum Zinc Level in Children Suffering from Type 1 Diabetes Mellitus and Its Relationship with Glycemic Control: An Experience from A Tertiary Level Specialized Diabetic Hospital in Bangladesh

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Abstract

A cross-sectional study was conducted in the Department of Biochemistry and Molecular Biology of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh, between July 2016 and June 2017, to evaluate serum zinc level and its relationship with glycemic control in type 1 diabetic children. A total of 160 participants (all aged between 1 and 18 years) were selected from the outpatient department (OPD) of BIRDEM General Hospital-2, Dhaka – 80 type 1 diabetic children as cases and 80 apparently healthy children as controls. We measured anthropometric parameters all study subjects. Serum zinc level was assessed using colorimetric method. Fasting plasma glucose level was estimated using enzymatic glucose-oxidase method. Glycemic control was evaluated through estimation of HbA1c using a high-performance liquid chromatographic method. The mean serum zinc levels were significantly lower in patient with type 1 DM compared to control (72.5±16.5 vs. 82.4±13.3 µg/dl; P<0.001). Lower levels of zinc were found in subjects with poor glycemic control compared to good glycemic control (62.8±14.6 vs. 78.8±14.6 µg/dl; P<0.001). Moreover, serum zinc levels were significantly lower in patients who have duration of diabetes mellitus for 5 years or more (P<0.05). To summarize, serum zinc level is lower in type 1 diabetic children in comparison to its healthy counterpart and this lower zinc level is strongly associated with poor glycemic control which may potentially contribute to the early development of diabetic complications in children.

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Introduction

Diabetes Mellitus (DM) is a major non communicable disease which is a leading cause of disability and death worldwide. Type 1 diabetes mellitus is a disorder that arises following the autoimmune destruction of insulin-producing pancreatic beta cells.[1,2] It is a usually develops during childhood or adolescence. Globally, the number of children (0-14 years) with type 1 diabetes is 542,000 and the number of newly diagnosed cases each year is 86,000, while the incidence in Bangladesh is 4.2 new cases /100,000 children of same age group per year.[3,4]

Zinc plays a key role in the synthesis, storage, and secretion of insulin.[5-7] Hyperglycemia causes the increased urinary losses of zinc and decreased zinc levels in the body. The decreased levels of zinc affect adversely the ability of the islet cell to produce and secrete insulin.[5,6]

Zinc deficiency has been reported as a contributing factor to the diabetes related complications such as retinopathy, nephropathy and neuropathy.[5,7] Research showed that hyperglycemia increases the production of free radicals and decrease the efficiency of antioxidant defense systems.[5,8]

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Imbalance in the levels of zinc may influence the equilibrium in the antioxidant defense system and enhance the toxic effect of metal-dependent free radicals. These associations may initiate and potentiate the pathogenic processes leading to diabetic complications.[6-8] Researchers found that diabetes is strongly associated with zinc deficiency along with poor glycemic control in adult population.[9-11] Moreover, some other studies confirmed that supplementation with zinc is helpful for the glycemic control and prevention of oxidative damage in diabetic patients.[12,13] Children with type 1 diabetes mellitus (T1DM) are especially interesting patient group, because any findings concerning the mechanisms of diabetes and the development of diabetic complications in these children can be used to improve their future quality of life.[14] Hence, we proposed the present study to evaluate the serum zinc level in children with Type 1 diabetes mellitus and its relationship with their glycemic control.

Methods

This cross-sectional study was conducted between July 2016 and June 2017 in the Department of Biochemistry and Molecular Biology of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh, which is the largest tertiary level specialized diabetic hospital in the country. A total of 160 participants (all aged between 1 and 18 years) were selected from the outpatient department (OPD) of *"Changing Diabetes in Children (CDIC)"* Programme Clinic at BIRDEM General Hospital-2, Dhaka. The participants were divided into two groups – 80 type 1 diabetic children as cases and 80 apparently healthy children as controls. All diabetic children were being treated with insulin. After selection of the subject, the aims and objectives of the study along with procedure, risks and benefits of this study was explained to the guardian of the patient. When parents agreed for participation, written informed consents were obtained from them and structured questionnaire was filled up for each patient. Participants below 1 year and above 18 years, with any chronic illness and any medication that may influence serum zinc level were excluded from the study. Detail personal, medical and family history of the participants were recorded. After measuring weight (in kg) and height (in meter), body mass index (BMI) was calculated as weight divided by height squared. Systolic and diastolic blood pressure were also recorded. Then under all aseptic precautions, 5 ml blood sample was collected from study subjects after an overnight fasting. 4 ml was delivered in a plain test tube for estimation of fasting plasma glucose and serum zinc, while remaining 1ml blood was delivered into EDTA tube for estimation of HbA1c. Fasting plasma glucose level was assessed by means of enzymatic glucose-oxidase method in Semi-Automatic Analyzer BTS-350 (made by Biosystems S.A., Spain). Then, serum zinc was assessed by colorimetric method in STAT FAX 3300 Semi Automated Clinical Chemistry Analyzer (made by Awareness Technology, Inc., USA). Glycemic control was evaluated through estimation of HbA1c using a high-performance liquid chromatographic (HPLC) method in Clover A1c (HbA1c Measuring System) (made by Infopia Co., Ltd., Korea).

To define 'glycemic control', we used standard international criteria that are based on HbA1c levels – as subjects were divided into two groups: (i) those with good glycemic control (normoglycemic group), defined as HbA1c levels

<9 %; and (ii) those with poor glycemic control, defined as HbA1c levels ≥9%.[15] Reference value of normal serum zinc concentration was taken 64–124µg/dl.[16] Participants who had zinc level <64µg/dl were considered as zinc deficient patients. All data were collected, tabulated and statistically analyzed using Statistical Package for Social Science (SPSS) version 20.0 (Chicago, USA). Quantitative data was expressed as mean (±SD) and unpaired Student's 't' test was done to see the level of significance, while qualitative data were expressed as frequency and percentage, and Chi-square (χ2) test was done to obtain the level of significance. The P-value <0.05 was considered statistically significant. The study was approved by the Institutional Review Board (IRB) of BIRDEM Academy, Dhaka, Bangladesh.

Results

Among 160 participants, male participants were 40 (50%) and 39 (48.8%), while female participants were 40 (50%) and 41(51.2%) in case and control groups respectively. Anthropometric and clinical characteristics of the study population are shown in the Table-I. The mean age of the cases and controls were 14.9±2.9 and 14.8±2.9 years respectively; the difference is not statistically significant. The mean age of onset during diagnosis and duration of diabetes were 10.5±3.6 and 4.5±2.7 years respectively in diabetic patients. There is no significant difference in weight, height, BMI, systolic and diastolic blood pressure between cases and controls (Table-I). The mean serum zinc levels were significantly lower in children with Type 1 DM (cases) compared to controls (72.5±16.5µg/dl vs. 82.4±13.3µg/dl; P<0.001) (Table-II). 24 (30%) of the total participants in case group and 3 (3.8%) of control group had zinc deficiency (Fig. 1). Among eighty Type 1 diabetic children, 48 (60%) had good glycemic control and 32 (40%) had poor glycemic control. Mean serum zinc level was 62.8±14.6µg/dl in patients with poor glycemic control, while 78.8±14.6µg/dl was found in patients with good glycemic control. The difference was statistically significant (P<0.001) (Table-III). Moreover, serum zinc levels were significantly lower in patients who have duration of diabetes mellitus for 5 years or more (P<0.05) (Table-IV).

Table I: Clinical characteristics of the study population (n=160)

Variables	Case (n=80) Mean±SD	Control (n=80) Mean±SD	P value
Age of the respondent	14.9±2.9	14.8±2.9	>0.05^{NS}
Age of onset of diabetes (in year)	10.5±3.6	-	-
Duration of diabetes (in year)	4.5±2.7	-	-
Weight (in kg)	50.5±16.7	48.7±13.5	>0.05^{NS}
Height (in cm)	150.8±13.7	151.7±12.2	
BMI (kg/sq.m)	21.5±4.7	20.9±3.9	
Systolic Blood Pressure (mm of Hg)	101.0±11.6	102.1±10.9	
Diastolic Blood Pressure (mm of Hg)	68.2±8.1	67.1±7.9	
Fasting Plasma Glucose (mmol/L)	9.2±4.2	-	
HbA1c (%)	9.2±2.2	-	

Data was expressed as mean±SD; P value reached from Student's unpaired 't' test, NS=not significant.

Table-II: Comparison of serum zinc level in study population (n=160)

Variable	Case (n=80)	Control (n=80)	P value
Serum Zinc Level	72.5±16.5 µg/dl	82.4±13.3 µg/dl	<0.001^S

Data was expressed as mean±SD; P value reached from Student's unpaired 't' test, S=significant.

Table-III: Relationship of serum zinc with glycemic status in Type 1 diabetic children (n=80)

Variables	Good glycemic control (n=48) (HbA_{1c} <9)	Poor glycemic control (n=32) (HbA_{1c} ≥9%)	P value
Serum Zinc Level	78.8±14.6 µg/dl	62.8±14.6 µg/dl	<0.001^S

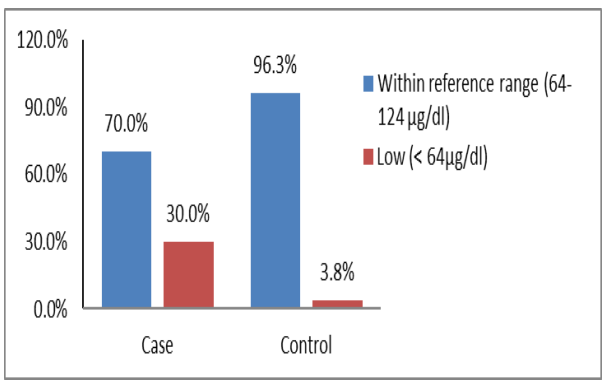
Data was expressed as mean±SD; P value reached from Student's unpaired 't' test, S=significant.

Table-IV: Relationship between duration of Diabetes Mellitus (DM) and serum zinc level (n=80)

Serum Zinc Level	Relation with duration of DM		P value
	<5 years	≥ 5 years	
Low (<64µg/dl)	10 (41.7%)	14 (58.3%)	<0.05^S
Within range (64–124 µg/dl)	41 (73.2%)	15 (26.8%)	

Figures in the parentheses indicate percentage; P value reached from Chi-square test, S=significant.

Fig. 1: Percentage of zinc deficiency in cases (n=80) and controls (n=80)



Discussion

In the present study, we measured serum zinc levels, as well as other clinical and biochemical parameters, in children with Type 1 diabetes mellitus. Considering a cut off level of serum zinc <64 µg/dl, we found in 30% diabetic patients had zinc deficiency, which was significantly higher compared to its control counterpart (3.8%). Similar observations were reported by Salmonowicz & colleagues, Özenç *et al*., Ahmed & Helal.[17-19]

Zinc deficiency in diabetes could result from the hyperglycemia or the impaired intestinal zinc absorption, but in the absence of compensatory mechanisms, excessive zinc loss in urine may be the main cause of inducing a deficient or marginal zinc status.[6,8,15] However, Uğurlu *et al*., Estakhri *et al.,* and Viktorínová *et.al.* did not find any significant alteration of serum zinc level in children with Type 1 DM. Moreover, in contrast, Zargar *et al.* found an elevated level of zinc in Type 1 diabetic patients.[20-23]

Our study revealed that serum zinc was significantly low in Type 1 diabetic children with poor glycemic control. This finding is consistent with the results of other studies done by Salmonowicz & colleagues, Özenç *et al*., Ahmed & Helal, Lin *et al*., and Mohammadian *et al*..[17-19,24,25] On the contrary, Estakhri *et al.,* and Fatemah & colleagues found no significant relationship between serum zinc level and glycemic status.[21,26] We assume that the differences in observations could be attributed to the difference in study populations and degree of diabetic control among them, also to the different methods adopted to evaluate serum zinc and HbA1c. In our study, we found serum zinc level was low with patient having a duration of DM for 5 years or more. Similar observations were

reported by Al-Maroof & Al-Sharbatti, and Kim & Ahn.[12,27] However, Al-Timimi & Mahmoud showed that there was no association between duration of diabetes mellitus and patients' serum zinc status. [28]

Conclusion

To summarize, serum zinc level was significantly lower in Type 1 diabetic children compared to healthy controls. We also found that lower zinc level is associated with poor glycemic control in those patients. Hence, to ensure proper glycemic control, a supplementation of zinc and close monitoring may be employed. This might also be beneficial for preventing further diabetic complications in those Type 1 diabetic children. Further studies with larger samples and multi-centre settings as well as inclusion of a zinc supplement are recommended.

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