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Original Article

Correlation Study Between Glycated Haemoglobin and Serum Zinc in People with Type 2 Diabetes

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Abstract

Type-2 Diabetes is the most common type form of diabetes, accounting for around 90% of all diabetes cases. Diabetes affects zinc homeostasis in many ways, mostly hyperglycemia, is responsible for the decrement of total body zinc level. The preponderance of evidence indicates that hyperglycemia increases the oxidative stress, may promote the generation of ROS by the activation of polyol and increased glucose auto oxidation. The role of zinc in carbohydrate metabolism has already been a subject of considerable interest. Approximately 0.5% of crystalline insulin is zinc. Zinc deficiency in some studies has been associated with reduced insulin secretion and increased tissue resistance to insulin action. This analytical type of cross sectional study was carried out in the outdoor and indoor patients of Upazila health complex, Bhuapur, Tangail, Bangladesh, between the periods from January,2019 to 30th June, 2019. A total of 140 subjects, age ranged from 35-65 years were included in this study. Among them 70 age matched type-2 diabetic patients were taken as study group (Group II) and 70 healthy subjects were taken as control group (Group I). Group I again subdivided into control group male (Group IA) and control Group female (Group IB). Group II also subdivided into study group male (Group IIA) and study group female (Group IIB). The results were calculated and analyzed by using SPSS software, laboratory analysis of HbA1c% by HPLC method, serum zinc by colorimetric method. In this study we found HbA1c, serum zinc is significant in study group in comparison with control HbA1c levels are significantly higher and scrum zinc levels significantly lower in the study group compared with controls group. In study group Mean(±SE) of serum zinc was decreased and the result was statistically highly significant ($p<0.001$) with 95% CI. Pearson's correlation coefficient test of Serum zinc with HbA1c in type II DM found that there were a weak negative correlation male ($r= -0.854$) & female ($r= - 0.838$) between serum Zinc with HbA1c. So, patients with an higher HbA1c% were associated with a lower serum zinc level in study group population.

Therefore, by this study we recommended that routine estimation of these parameters is important for prevention of complication related to type-2 diabetes for leading a healthy life .

Key words*: Type-2 diabetes, HbA1c, Serum zinc.*

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Introduction

Diabetes mellitus is one of the leading cause of death and disability worldwide. In 2021, approximately 537 million adults (20-79yrs) were living with diabetes and 1 of the 5 people who are above 65yrs old have diabetes with 6.7 million deaths/year (1 in every 5 seconds) worldwide.[1] Asia and the eastern Pacific region are particularly affected: in 2011, China was home to the largest number of adults with diabetes (i.e. 90.0 million, or 9% of the population), followed by India (61.3 million, or 8% of the population) and Bangladesh (8.4 million, or 10% of the population)[2].

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In Bangladesh, overall age-standardized prevalence of diabetes is 12.8% (Men 12.8%, women 12.7%), and the prevalence of prediabetes 14.0%, Prevalence of DM was 33.3% in 50-54 age group with 63% higher for individuals having hypertension.[3]

According to ADA (2019) diagnostic criteria of diabetes mellitus are fasting blood glucose e"7.0 mm0l/L and/or 2 hour after 75gm glucose e"11.1mmol/L and /or HbA1c e" 6.5%[4]. Type 2 diabetes encompasses individuals who have insulin resistance and usually relative (rather than absolute) insulin deficiency[5].

Nevertheless, an accurate index of a person's mean blood glucose level over a period of 6-8 weeks can be provided by measurement of specific blood. Hence, HbA1C% is one of the parameters which provides index of blood glucose control in cumulative sense. It is a reliable indicator of long-term hyperglycemia and the introduction of glycated hemoglobin as a monitor of long-term glucose control has helped in identifying those at risk of developing complications. A report published in 2009 by the he International Expert Committee on the role of HbA1c in the diagnosis of diabetes recommended that HbA1c can be used to diagnose diabetes and that the diagnosis can be made if the HbA1c level is 6.5% or more. Diagnosis should be confirmed in doubtful cases by repeat HbA1c test or OGTT unless clinical symptoms and plasma glucose levels e"11.1mmol/l(200mg/dl) are present in which case further testing is the most common variants. Level of HbA1c just below 6.5% may indicate the presence of intermediate hyperglycemia. The precise lower cut-off point for this has yet to be defined, although ADA has suggested 5.7-6.4% as the high risk range[6]

Naomi (2008) reported that in diabetes an increase in HbA1c by1% was associated with a 20% to 30% increase in mortality associated with cardiovascular events[7].

Zinc has a role in the regulation of insulin production as well as glucose utilization through muscles and fat cells, Zinc deficiency leads to elevated blood sugar and ability to synthesize and secrete insulin as well as to use glucose are impaired in zinc deficient state[8]. One of the causes or the development of diabetes associated complications can be attributed to the low levels of Zn as there are many antioxidant enzymes which contain zinc, decrease in these anti-oxidant enzymes results in decreased free radicals scavenging leading to tissue damage and peripheral organ damage.[9] It is identified that zinc plays an important role in synthesis, storage and secretion in response to carbohydrate intake and plays an important role in energy production. It also maintains the structural integrity of insulin. The decreased zinc concentration in blood, affects the ability of the islet cell of pancreas to produce and secrete insulin may lead to the development of insulin resistance responsible for incidence of type 2 diabetes. Oxidative stress plays an important role in the development of diabetic complications. Zinc not only has an antioxidative effect, but also constitutes a key constituent of many antioxidants. It inhibits the damage associated with lipid peroxidation and prevents the formation of free radicals.[10] Zinc-deficient diet resulted in decreased ability of the pancreas to secrete insulin in response to glucose load, suggesting that zinc deficiency also reduced the ability of the pancreas to respond appropriately.

Methods

The present study was a descriptive cross-sectional study. It was done in the outdoor and indoor patients of Upazila health complex, Bhuapur, Tangail, Bangladesh, between the periods from 1st January ,2019 to 30th June , 2019. A total 70 volunteers of T2DM aged 35-65 years & equal number of healthy subjects of same age group were included in this study. The participants were clearly informed about purpose of the study prior to take consent for this research. Data were collected by a face to face interview with the patients or attendants using a pre-designed format of data collection sheet. Blood was collected and analyzed for investigations. With all aseptic precautions 5 ml of venous blood were collected from the study subjects after overnight fasting by a disposable syringe from antecubital vein. In case of any delay, the serum samples will be stored in freeze at -15 to -25°C in Eppendorf's tubes after proper labeling.

Pearson correlation coefficient test was done to correlate the relationship between HbA1c and Serum Zinc. Data were analyzed by using SPSS software and Microsoft word and excel were used to generate graphs, tables etc.

Results

A total number of 140 subjects participated in this study. The results were expressed as HbA1c in %, serum zinc in ìgm/dl. Pearson correlation coefficient test is done to correlate the relationship between HbA1C% and Serum zinc. To evaluate their statistical significance we needed to calculate pearson's correlation coefficient. It is denoted by þr'. 'r' value range from -1 to +1. positivity indicates direct or positive relation. Negativity indicate indirect or negative relation. Larger the r value stronger the relation.

Table I. Comparative study of different biochemical parameter in different groups by unpaired student's þt' test

Biochemical parameter	Group IA n= 35 Mean (±SE)	Group IIA n=35 Mean(±SE)	Group IB n=35 Mean (±SE)	Group IIB n=35 Mean(±SE)
Fasting serum glucose (mmol/l)	4.88±0.13	8.51±0.19	5.01±0.11	8.13±0.16
HbA1c%	5.32±0.07	11.43±0.45	5.36±0.08	10.72±0.46
Serum zinc(ìgm/dl)	116.09±0.98	56.74±1.38	114.86±1.01	58.86±0.98

Table II . Statistical analysis of Serum HbA1C% between control group and study group by unpaired student's 't' test

	Mean deviation	t value	P value
IA vs IIA	-6.11429	-13.348	0.000
IB vs IIB	-5.36286	-11.592	0.000
IIA vs IIB	0.71143	1.109	0.272

Table III. Correlation of HbA1c with Serum Zinc in male & female type 2 diabetic patients

Serum Zinc		r value	P value
Male	HbA1c%	-0.854	0.000
Female	HbA1c%	-0.838	0.00

Pearson correlation is done to measure the level of significance. Level of significance p<0.01

Table III & Figure- 1 shown pearsons correlation coefficient test of Serum Zinc with HbA1c.There was weak negative correlation (-0.854) found between serum zinc with HbA1c. If HbA1c% increase then Serum Zinc may decrease in study group male (Group IIA).

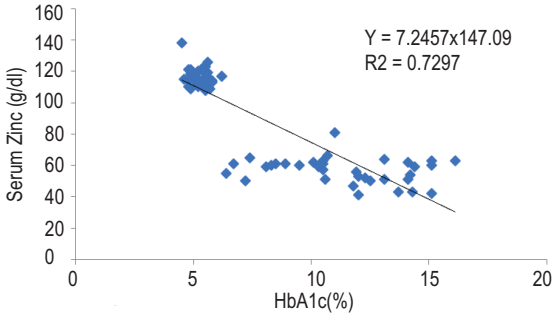

Figure 1: Negative correlation of Serum Zinc with HbA1c% in study group male (Group IIA)

Pearson correlation is done to measure the level of significance. Level of significance p<0.01.

Table IV & Figure -2 shown pearsons correlation coefficient test of serum zinc with HbA1c.There was weak negative correlation (r= -0.838) found between serum Zinc with HbA1c. If HbA1c% increase serum zinc may decrease in study group female (Group IIB).

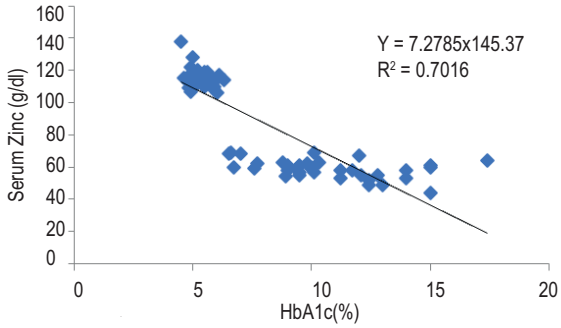

Figure 2: Negative correlation of Serum Zinc and HbA1c% in study group female (Group IIB)

Summary of the results

Biochemical parameters:

1. Serum HbA1c% of type2 diabetic patients (Group IIA&IIB) was significantly increased than nondiabetic healthy subjects (Group IA&IB).
2. Serum Zinc of type2 diabetic patients (Group IIA&IIB) was decreased than nondiabetic female healthy subjects (Group IA&IB).
3. There was weak negative correlation between Serum Zinc with HbA1c% in type2 diabetic patients (Group IIA& IIB).

Discussion

The present study was carried out to see the relation between HbA1c and Serum Zinc. Hypozincemia is frequently associated with diabetes mellitus. Similar study named" Serum zinc levels in diabetic patients and effect of zinc supplementation on glycemic control of type 2 diabetes" shows that Diabetic patients have significantly lower mean serum zinc levels compared with healthy controls. Zinc supplementation for type-2 diabetes has beneficial effects in elevating their serum insulin level, and in improving their glycemic control. These findings were in agreement with the result of study conducted by Naila Masood et al[11]. But this finding was in disagreement with the study by D.S. Pushparani et al.[12] That study observed that serum zinc was not decrease in diabetic patients. Comparison between study group male and female found that the mean value of serum zinc of study group male and study group female were 56.74±1.38 ìgm/dl & 58.86±0.98 ìgm/dl respectively. Mean value of serum zinc was decreased in both study group male and study group female and the result is statistically significant. Study conducted by J. Arnaud et al. showed that there was no significant difference c between male and female. This study was consistant with present study. Possible mechanisms may underline the association between serum

zinc and diabetes. In people with diabetes, zinc levels in the blood start to decline, it is because many zinc in the body excreted through polyuria. In diabetes, several of the complication related to increased intracellular oxidants and free radicals associated with decreases intracellular zinc and zinc dependent antioxidant enzymes. There was weak negative correlation found between HbA1c% with Serum Zinc in study group male (Group ^{22}A) and study group female (Group ^{22}B). In group ^{22}A, $r = -0.854$ & $p < 0.001$, In group ^{22}B, $r = -0.838$ & $p < 0.001$. In another study, Correlation of serum zinc and HbA1c was done, Serum zinc level shows negative correlation with HbA1c. The correlation coefficient was $r = -0.482$ and $p < 0.001$. This results were in agreement with the case control study done by Dhanoushyaa Seetharaman et al[14] and they reported that significant negative correlation between serum zinc with HbA1c in diabetic patients which was similar to the present study. Zinc supplementation causes significant reduction in FBG, PPBG and HbA1c in patients with type 2 diabetes.[15]There was significant decrease in serum concentrations of zinc in study group when compared to control. HbA1c was significantly high in study group when compared to control. The correlation of HbA1c and zinc was done using pearson's correlation coefficient and is inversely related $r = -0.4$[16], This study was consistent with the present study. Studies done by tripathy et al. reported negative correlations between serum zinc and HbA1c. Zinc levels in blood are decreased with the increase in HbA1c in in diabetics compared to healthier. Possible mechanism may underline the association between Fasting Serum glucose, HbA1c and Serum Zinc. Zinc plays a clear role in the synthesis, storage and secretion of insulin as well as conformational integrity of insulin in the hexameric form, the decreased zinc, which affects the ability of the islet cell to produce and secrete insulin, might them compound the problem particularly type 2 diabetes.[17] Zinc deficiency is associated with reduced insulin secretion and increased tissue resistance to insulin action. In the present study we found zinc levels were inversely correlated with HbA1c. The reason for decreased zinc levels in diabetes compared to controls may be due to gastrointestinal malabsorption or due to reduction in renal function associated with disease. So from above discussion it is found that in comparison with healthy individuals and type 2 diabetes mellitus patients had decreased serum zinc level. Concentration of serum zinc was inversely correlating with the glycated hemoglobin(HbA1c) of type 2 diabetic patients.

Conclusion

From this study, we may conclude that Serum zinc levels were decreased in type 2 diabetes mellitus patients and these levels were negatively correlated with HbA1c. So, regular assessment of these parameters might be helpful to prevent the complications. So, prevention of type 2 diabetes mellitus by taking necessary steps like regular physical exercise, intake of healthy diet with lifestyle modification and behavior therapy may help in prevention of type 2 diabetes mellitus. Therefore, every type-2 diabetic patient should undergo screening and regular monitoring of these parameters with appropriate steps to prevent cardiac, renal, ocular & metabolic complications.

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