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A Unique Element in a Unique Disease; Zinc in Diabetes Mellitus Type 2

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ABSTRACT

Background: Zinc is a ubiquitous element in humans having effects on various body systems. The versatile role of zinc is the basis of its involvement in Diabetes Mellitus type 2, a unique metabolic disorder. **Objective:** To find out the correlation between serum zinc levels and fasting blood sugar in Diabetics type 2 patients and to compare it with normal healthy population. **Study Design:** Cross sectional study. **Settings:** Department of Medicine, Madinah Teaching Hospital, Faisalabad Pakistan and Department of Biochemistry, University Medical & Dental College, Faisalabad Pakistan. **Duration:** 6 months study from February 2018 to July 2018. **Methods:** Fifty patients aged 40 years and above of either sex visiting the Madinah Teaching Hospital were enrolled. Thirty healthy controls were also included for comparison. Patients suffering from any other serious disease or from diabetes mellitus type1 were excluded from the study. History and baseline information was taken on a proforma. Fasting blood sugar and Serum Zinc were evaluated on both cases and controls. Data collected and analyzed by SPSS version 20. **Results:** There was a highly significant negative correlation between fasting blood sugar and serum zinc level in diabetic patients. **Conclusion:** Hypozincemia is related to hyperglycemia in diabetics type-2 patients. There was a substantial positive difference in zinc levels between diabetics and healthy groups.

Keywords: *Hyperglycemia, Hypozincemia, Diabetes Mellitus type-2.*

INTRODUCTION

Research encompassing decades has confirmed the connection between zinc and diabetes mellitus. The main hormone disturbed in DM is insulin. Zinc is unique in that it has been found to play a role at multiple places relating to insulin.[1]Enzyme catalysis: Zinc is a trace element playing a strong enzymatic role of either a coenzyme or an enzyme complex in the body. Zinc acts as a catalyst in various metabolic reactions[1,2,3]. Maintenance of protein structure**:** Stabilization of proteins and conservation of domains [1,2,3] Regulatory function: It involves almost 36 proteins including ZnT (zinc transporters), Zip (Zrt-/Irt-like proteins) and MTs (Metal binding proteins) [3]. Zinc plays vital for maintenance of immunity. [3,4,5]

Zinc deficiency has been found to be associated with numerous diseases related to gastrointestinal system, respiratory system, and malaria.[4,5] Zinc deficiency leads to skin lesions, loss of hair, increased frequency of stools, emotional disturbance, loss of weight, increased susceptibility to infections and diminished immunity. The immune related cells are highly coordinated by the zinc status of the body. [3,4]There is ample evidence to suggest that diarrhea in children is related to zinc and shows good response to zinc supplementation.[6,7] Zinc prevents formation of atheroma in the arteries thus protecting from ischemic heart disease.[6] Zinc has an antioxidant role and protects from the damage to inner lining of blood vessels and accompanying inflammation which is the key player of eventual vessel damage proved by a number of studies.[6]

Insulin synthesis: Insulin exists as a hexamer in a composition of 2 zinc and 6 insulin molecules. During formation, proinsulin forms by binding of dimers of insulin with zinc on His8. There is correlation between

onset of diabetes and zinc levels proved by many studies.[8]Insulin release from pancreas: Zinc transporter 8 transports zinc into pancreatic beta cells and mutations in this transporter underlie the development of diabetes .[8] Zinc is important in formation, storing and releasing of insulin.[8]The specific regulatory role of zinc is in preventing dephosphorylation of insulin receptor or IGF by tyrosine phosphatases, improving signal transduction of insulin.[2] Although zinc has a preventive role in diabetes mellitus, resembles insulin effects there is still scope for research whether the zinc relationship to diabetes is in its causation, prevention or outcome. Zinc is essential for maintaining normal height and normal sexual function [2,9]. The concentration of insulin like growth factor-1 is decreased in its deficiency. The subsequent effect is disruption of tyrosine kinase signal transduction which controls cell growth.[5]

Zinc has been crucially linked to a very important and unique disorder -- diabetes mellitus type 2.[9,10] There is multisystem involvement and complications involving a huge number of tissues in the human body. In this mega disease the major problem is that tissues do not respond to insulin which is the authority in lowering blood glucose. The loss of response to insulin leads to tissue damage at a cellular level by the elevated glucose.[10]Zinc is involved in the mechanism of action of insulin by increasing the phosphorylation of tyrosine as it inhibits the enzyme that dephosphorylates tyrosine kinase.[9,10] The high prevalence is like an epidemic that matches no other disease.[11]

Insulin is stored with zinc. The zinc transporter 8 is essentially found in the pancreatic insulin producing cells.[2,8,9]

METHODS

This was a **c**ross-sectional study performed on the local population visiting the Madinah Teaching Hospital, Faisalabad Pakistan. The duration of the study was six months from February 2018 to July 2018.

Eighty subjects in two groups. One was a case group consisting of 50 patients suffering from diabetes mellitus type 2 and the other was a control group of 30 healthy and normal people.

Persons having Type 2 diabetes mellitus with age 40 and above were included in the study. Patients suffering from any other disease affecting liver, lungs or kidney or having diabetes mellitus type 1 were excluded .[12,13]

The ethical review committee for The University of Faisalabad (TUF) granted approval for conduction of this study vide letter No. UMDC/ RERC/2018/11, Dated: Jan 19,2018. The aims were to find out the association between serum zinc levels and fasting blood sugar in Diabetics type 2 patients and to compare it with normal healthy population. Written consent from the patients was taken after informing them. History was taken from the patients and recorded on a proforma. Details regarding patient 's personal information, family history of the disease, drug history were specifically documented.

Proper history was taken on a proforma, and ruled out any zinc supplementation. The drugs taken for diabetes mellitus were also recorded. Patients were instructed to come without eating or drinking anything in the following morning. After taking informed consent, samples were collected for blood sugar in the fasting state and serum zinc.[11,12] Fasting blood sugar was estimated photometrically through Cobas C311 analyzer at the hospital laboratory of the Madinah Teaching Hospital. Serum Zinc estimation was performed through spectrophotometer in the Post graduate laboratory of The University of Faisalabad. [12,13]

FBS was evaluated on the principle of glucose oxidation to glucose 6-P by HK (hexokinase) and NADPH. The rate of coenzyme formation is directly proportional to level of glucose.[14] Normal level was in the range of sixty to hundred milligrams per deciliter. Serum zinc was estimated on photometric system by colorimetric test with 5-bromo-PAPS. The desired value of serum zinc for females was 70.6 -114 µg/dl in and 72.6-127 µg/dl for males.

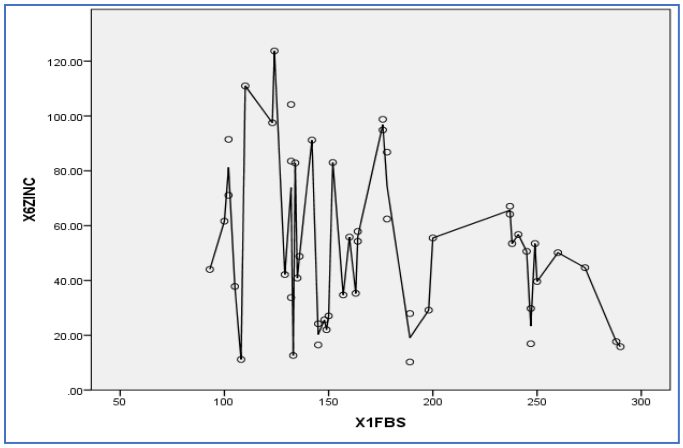
Proformas filled up by taking information from patients. Data collected and arranged. Statistical analysis of the data was done after calculation and rearrangement by SPSS version 20. Correlation of both cases and controls was found out. This was followed by comparison between controls and type 2 diabetics using ANOVA. Correlation of different parameters with blood sugar was calculated. Mean ± standard deviation, range and variance were calculated. Pearson's correlation coefficient was used for determining correlation. Results were considered significant if $p < 0.001$.

RESULTS

Correlation of FBS (fasting blood sugar) with serum zinc was estimated.

The graph shows that hyperglycemia is strongly associated with hypozincemia. There is negative association between serum zinc and fasting blood sugar. If blood sugar level is increased, the serum zinc level is decreased.

Figure 1: Relationship between Fasting blood sugar and Serum Zinc



X1FBS = Fasting blood sugar in mg/dl of diabetic patients.
X6ZINC = serum zinc in µg/dl of diabetic subjects.

The primary objective of this research was to find out the correlation between serum zinc and fasting blood sugar. There was statistically significant correlation between fasting blood glucose and Serum zinc in diabetic type 2 subjects.

Table 1: Correlation in diabetic subjects

Parameter	N value	r value	P value
Zinc	50	-0.284	0.046^{S}

HS: highly significant, S: Significant, NS: Non-Significant

Table 2: Correlation in control subjects

Parameter	N value	r value	P value
Zinc	30	-0.189	0.316^{NS}

HS: highly significant, S: Significant, NS: Non-Significant

Table 3: Analysis for biochemical parameters in type 2 diabetic group

	FBS (mg/dl)	Zn (µg/dl)
Mean ± SD	173.10 ± 55.17	53.02 ± 29.21
Range	93 - 290	10.23 - 123.72
Variance	3043.439	852.950

FBS= Fasting blood sugar, Zn = Zinc

Table 4: Analysis for biochemical parameters in healthy control group

	FBS (mg/dl)	Zn (µg/dl)
Mean ± SD	88.17 ± 10.54	90.04 ± 28.73
Range	57 - 104	24.55 - 128.37
Variance	111.178	825.340

Table 5: Comparison of in diabetes mellitus type 2 patients and control group subjects

Groups	FBS (mg /dl)	Zn (µg/dl)
DM vs Control	P<0.001	P<0.001

FBS=Fasting blood sugar, Zn = Serum Zinc

DISCUSSION

The graph shows that hyperglycemia is strongly associated with hypozincemia. There is negative association between serum zinc and fasting blood sugar. If blood sugar level is increased, the serum zinc level is decreased. Many studies show the same correlation between the mineral and glucose level.[14,15] In both studies there was significant low level of zinc in type 2 diabetics. Omidian *et.al* compared the levels of zinc, magnesium and chromium in diabetics and healthy population. [10,14] The results obtained depicted a remarkably lower level of zinc in disease patients in comparison to controls. They further evaluated zinc level according to socioeconomic status but found no remarkable difference. Hassan *et al* stated an improvement of lipid levels and fasting blood sugar in subjects after supplementation with zinc thus emphasizing on the important role of zinc.[16]

In a study on diabetic persons zinc and magnesium status was evaluated along with FBS, they reported a decrease in zinc level that was statistically remarkable as compared to controls.[12,15,16]

There is highly significant negative correlation between fasting blood sugar of controls and serum zinc level. The zinc level of controls is highly correlated. The low level of zinc found in healthy subjects may be due to dietary deficiency.

CONCLUSION

This study shows that serum zinc level is low in diabetic persons as depicted by the negative correlation among fasting blood sugar and serum zinc.

LIMITATIONS

The low socioeconomic conditions of the people are a hindrance for repeated blood tests especially mineral levels. Lack of awareness in general public of the importance of maintaining nutritional levels also contributes to the deterioration in disease of diabetics.

SUGGESTIONS / RECOMMENDATIONS

Diabetic patient is vulnerable to develop derangement of mineral levels including zinc. A proper health care system must be evolved which can involve repeated screening of all diabetics for serum lipids along with

serum zinc and magnesium in order to avoid complications.

There is still need for public awareness that magnesium and zinc are important factors that must be monitored to maintain a healthy status of the diabetic patient. Diabetes Mellitus may become a dilemma of the future and efforts at all levels contribute in improving the outcome of the diseased.

CONFLICT OF INTEREST / DISCLOSURE

There was no conflict of interest.

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