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Original Research Article

Evaluation and Correlation of Serum Zinc with Oxidative Stress and Insulin Resistance

Mr. P. Krushna Kishore[1], Dr. Ipsita Chodhary[2], Dr. Pallavi Anand[2], Dr. U.N Singh[3]

[1]Research Scholar, [2]Associate Professor, [3]Professor & HOD,
Dept of Biochemistry, Rama Medical College, Kanpur, UP

Corresponding Author: Mr. P. Krushna Kishore

ABSTRACT

Background: Zinc is an important mineral in regulating glucose homeostasis and oxidative stress Zn dyshomeostasis is often associated with pathogenesis of T2DM and its complications.
Objective: to Evaluate the serum zinc levels and to find the possible correlation between serum zinc and oxidative stress, Insulin resistance in healthy and T2DM patients.
Materials and methods: The present study was carried out in the Department of Biochemistry on 360 subjects patient in the age group of 35-70 years, attended OP in Rama Medical College & Hospital. Among them 180 healthy subjects enrolled as control group remaining 180 T2DM patients were served as case group. Serum zinc and Serum Insulin were measured .Insulin resistance was calculated from HOMA-IR method.MDA levels were measured in order to asses oxidative stress.
Results: The concentration of serum Zn levels were significantly ($p<0.0001$) lower in cases (82.70 ±14.13) as compared to the controls (93.90 ±12.24). There was negative correlation found between serum Zn levels and Insulin resistance, MDA levels in cases of type 2 DM.
Conclusions: There is an association exits between serum Zn and Oxidative stress and there is an inverse correlation found between Serum Zn and Insulin resistance in T2DM patients.

Keywords: Serum Zinc, HOMA-IR, Oxidative stress, T2DM

INTRODUCTION

Type 2 diabetes mellitus is a metabolic disease characterized hyperglycemia and the presence of glucose intolerance. [1] The two metabolic defects that characterize type2 Diabetes are reduced insulin secretion from pancreatic beta cell dysfunction and decreased insulin action (insulin resistance at a cellular level. [2] Chronic hyperglycemia of diabetes mellitus favors the manifestation of oxidative stress by increasing the production of reactive oxygen species and/or by reducing the antioxidant defense system activity. [3] The reactive oxygen species (ROS), attack the membrane lipids resulting into lipid peroxidation. This forms a number of potentially toxic lipid aldehydes like Malondialdehyde (MDA) and 4-hydroxy-trans-2-nonenal. MDA level is commonly known as a marker of oxidative stress. [4]

Zinc (Zn) is the second most abundant trace element in the human body. Zinc plays a relevant role in human health being an essential cofactor for more than 300 enzymes, such as superoxide dismutase. [5] Zinc plays a key role in Insulin synthesis, storage and transport. Zinc is considered as an integral component of Cu-Zn SOD which acts as anti oxidant and protects from free radicals. This mineral also facilitates

reduction and neutralization of free radicals. [6-8]

Insulin resistance is a condition in which insulin in the body does not exert sufficient action proportional to its blood concentration. The impairment of insulin action in major target organs such as liver and muscles is a common pathophysiological feature of T2DM. Insulin resistance develops and expands prior to disease onset. [9] Insulin resistance is related to genetic factors and environmental factors (hyperglycemia, free fatty acids, inflammatory mechanism, etc. Known genetic factors, include not only insulin receptor and insulin receptor substrate (IRS)-1 gene polymorphisms that directly affect insulin signals but also polymorphisms of thrifty genes such as the β3 adrenergic receptor gene and the uncoupling protein (UCP) gene, associated with visceral obesity and promote insulin resistance. Glucolipotoxicity and inflammatory mediators are also important as the mechanisms for impaired insulin secretion and insulin signaling impairment. [10]

So the present study was aimed to evaluate and correlate the serum Zinc levels with insulin resistance and MDA (an index of lipid peroxidation) both in T2DM and non diabetic patients.

MATERIALS AND METHODS

Present study was conducted on 360 subjects aged between 35-70 years attended OP in Rama Medical college & Hospital Kanpur, U.P. These 360 subjects were divided into following groups.

Group-A contains 180 healthy individuals (without T2DM) serving as control group

Group-B includes 180 subjects suffering with T2DM (not more than 5 years).

All the subjects were informed and consent letter was taken. Study was approved by Institutional ethical committee.

Exclusion criteria: T2DM patients taking Insulin, Lactating and pregnant women were excluded. Individuals suffering with T1DM, myocardial infarction, renal problems and patients on Zinc supplementation were also exempted.

Biochemical analysis: Using aseptic precautions 5 ml of venous blood was collected from antecubital vein in Fasting condition. Samples were centrifuged after 30 minutes; serum was isolated and used for the measurement of following parameters.

1 **Fasting Blood Glucose:** was measured by GOD-POD METHOD. (End point colorimetric method).
2 **Serum Zinc:** was measured by NITRO-PAPS method(kit supplied by Tulip diagnostics by using ERBA CHEM 5 semi auto analyzer
3 **Serum Insulin:** was measured by sandwich ELISA method
4 **Insulin resistance :** was calculated by HOMA-IR method
5 **MDA(malondialdehyde):** was measured by Thiobarbituric acid reagent (TBA) Method
6 **HbA1C:** was estimated by ion-exchange high-performance liquid chromatography method by using ERBA EM 360.

STATISTICAL ANALYSES:

All the values were expressed as Mean±SD. The statistical analysis was done using student 't' test and Pearson's correlations for comparison between two groups and a p-value of <0.05 was considered statistically significant.

RESULTS

The present study conducted on 360 subjects among them 180 people suffering with type 2 DM were chosen as control (group-I) and 180 age and sex matched healthy subjects were served as case group (group-II). Serum MDA was measured in order to assess the oxidative stress. Insulin resistance was calculated by HOA-IR method. All the results were expressed in Mean ± standard deviation.

Table-1 showing biochemical parameters with Mean value and S.D

Parameters	Control Group	Case Group	P value
FBS	83.70 ±14.13	154.45 ±25.24	<0.001*
Serum Zinc	93.90 ±12.24	82.70 ±14.13	<0.001*
Serum Insulin	14.83±2.64	22.31±4.63	<0.001*
Insulin Resistance (HOMA-IR)	3.26±0.67	7.97±2.36	<0.001*
MDA(malondialdehyde)	1.29±0.40	1.86±0.65	<0.001*
HbA1C	5.21 ± 0.04%	6.84 ± 0.2%	<0.001*

Data is presented as mean ± std. dev. for variables.* Highly significance.

Biochemical parameters are displayed in table-1: The mean FBS and HbA1C values of case group was 154.45 ± 25.24 mg/dl, 5.21 ± 0.04%and that of controls was 83.70 ± 14.13 mg/dl. 6.84 ± 0.2% respectively and was significantly higher (p-value less than 0.001); in control group.

The mean serum Zinc level (ng/mL) in controls was 93.90 ±12.24 while in cases it was 82.70 ±14.13. From table-1 it is clear that serum zinc levels were significantly lowered in Diabetic population compared to control group. Correlation was found between the two groups ($p < 0.001$).

Table-1 also displaying Mean serum Insulin level and insulin Resistance of control group 14.83±2.64, 3.26±0.67 and for the study the group it was 22.31±4.63; 7.97±2.36 respectively. Highly significant difference was found ($p < 0.0001$) between the two groups.

Mean serum MDA levels of case group (1.86±0.65) were significantly higher than control group (1.29±0.40).significant difference was found between two groups.

Table: 2 correlation of serum Zinc with oxidative stress, insulin Resistance and HbA1C in T2DM Patients

	Case Group(T2DM)	P value
ZINC with MDA	-0.59	<0.001*
Zn with Insulin Resistance	-0.64	<0.001*
Zn with HbA1C	-0.57	<0.001*

*statistically highly significant

Correlation of Serum Zinc with MDA and Insulin resistance: In Diabetic patients the levels of serum zinc showed a negative correlation with MDA and Insulin resistance. ($r = -0.59$ and $r= -0.64$) Which was statistically highly significant ($p<0.001$) Table- 2.

Serum Zinc levels and HbA1c: There was significant negative correlation found between serum zinc levels and HbA1c, $r = -0.57$, $p < 0.0001$ and was highly significant. (Table 2)

DISCUSSION

Many people with T2DM remain unaware of their poor health for a long time since symptoms may take years to appear, during which time the body is being damaged by excess blood glucose. [11] Chronic hyperglycemia statue noticed in diabetes mellitus favors the manifestation of oxidative stress.

Numerous in-vitro and in-vivo studies have shown that Zinc plays an important role in β-cell function, insulin action, glucose homeostasis and the pathogenesis of diabetes and its complications. [12-14] Zinc reduces glucose absorption and synthesis, whilst promoting glucose metabolism and storage. This is primarily via the enhanced activity of key enzymes involved in these metabolic processes, such as α-glucosidase, PFK, PK and glycogen synthase. Its action on insulin possibly mediated via Zinc-α2-glycoporteins increases cellular GLUT4 levels in skeletal muscles and adipose tissue facilitating glucose absorption. [15] In our present study we found Insulin resistance was more severe in diabetic group and inversely correlated with serum Zinc levels.

In Our present study we observed that serum zinc values were inversely correlated with HbA1C and FBS. Earlier studies have proved that Zinc supplementation reduces Fasting Blood Glucose, 2 h Post Prandial Blood Glucose and HbA1c in patients with diabetes, as well as reducing total cholesterol, LDL cholesterol and triglycerides in both patients with and without diabetes. [16-17]

Zn has antioxidant properties and protects tissue from oxidative stress by two

main mechanisms: (i) protection of protein sulfhydryl groups from free radical attack and (ii) reduction of free radical formation through the antagonism of redox-active transition metals, such as iron and copper (Cu). [18] Present study demonstrated hypozincemia is significantly correlated with oxidative stress (MDA). In a earlier Study by Liu et al noticed that zinc supplementation decreased malondialdehyde concentration and stimulated the transcription of metallothionein genes in peripheral nerves of diabetic mice.

CONCLUSION

Serum Zinc is inversely associated with Oxidative stress and Insulin resistance. Zinc supplementation may helps in prolonging the diabetic complications.

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