Study of Zinc and Glycated Hb Levels in Diabetic Complications.

B. Jyothirmayi*, M. Vasantha

Department of Biochemistry, SRM Medical College Hospital & Research Centre, Kattankulathur.

ABSTRACT

Aim & Objective: Zinc has a significant role in various physiological metabolisms as it is an important cofactor for numerous enzymes. Alterations in serum concentrations of zinc in type 2 DM has been reported by several studies. We tried to evaluate the association of zinc and HbA1C in diabetic complications. Diabetes and its complications usually lead to increased production of free radicals which disturbs the internal milieu. Antioxidant enzymes like SOD are decreased due to low zinc concentrations resulting in tissue damage and various complications. Materials and Methods: In present study 50 type 2 DM persons diagnosed clinically with microvascular complications like neuropathy and retinopathy are included as study group and 50 diabetic people without any complications as control group. Fasting blood samples were collected to analyse Zinc and HbA1C. HbA1C was estimated by HPLC method in D10 analyser. Zinc was analysed by colorimetric kit method. Results: There was significant decrease in serum concentrations of Zinc in study group when compared to control (50±12.5, 95±20.42) (p≤0.001) HbA1C was significantly high in study group when compared to control (9.5.7±2.5.) (6.5±1.5) (p≤0.001). The correlation of HbA1C and zinc was done using Pearsons correlation coefficient and is inversely related \( r = -0.4 \).

Conclusion: In DM, HbA1C influences the profile of trace elements especially zinc and can be explained as one of the cause for delayed wound healing especially in patients with complications. Good glycemic control and zinc supplementation can prevent the complications.

INTRODUCTION

Type 2 diabetes mellitus is a major health problem affecting nearly about 170 million people all over the world, and triggering most of the micro vascular complications\(^1\). The major metabolic disturbance affects the functional and structural integrity of cells leading to complications which affect the nervous system, eye, cardiovascular system and kidneys\(^2\).

Persistent hyperglycemia causes spontaneous non enzymatic glycosylation of proteins leading to thickening of basement membrane, particularly of small blood vessels (microangiopathy), leading to diabetic complications like retinopathy, nephropathy and neuropathy. Zinc has a role in the regulation of insulin production as well as glucose utilization through muscles and fat cell, 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 \(^3\). 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\(^4\).

The action of insulin in reducing blood glucose was reported to be enhanced by micro-minerals like zinc, chromium and selenium\(^5\). They activate insulin receptors and acts as cofactors for several enzymes of metabolisms, particularly glucose metabolism and restricted function of these enzymes disturbs the internal milieu of the cell. Zinc is required for the synthesis, storage and secretion of insulin. It also maintains the structural stability of insulin. Decreased zinc levels affects insulin and leads to decreased insulin production\(^6\). Altered zinc status is also harmful as suggested by Niewohner et al.,\(^7\) who reported improvement in T- lymphocytes response to phytohemagglutinin with zinc supplementation in type II diabetic subjects. Hyperzincuria in diabetics was also observed by some of researchers in their study. It has been suggested that pertubations in mineral metabolism are more pronounced when metabolic control is poor or if vascular complications are present. Changes in peroxidative status may also be anticipated when trace element status is altered. An increased level of lipid peroxides and peroxidative damage was also considered as one of the contributory factors in development of diabetic complications\(^8\).\(^9\).

The aim of our present study was to evaluate the relationship of zinc and HbA1C in diabetic complications.

MATERIALS AND METHODS

This study was conducted at SRM Medical College Hospital & Research centre medicine OP. Approval from institutional ethical committee and informed consent from the participants were obtained. Subjects were 50 type 2 diabetic persons with clinically diagnosed micro-vascular complications, retinopathy and nephropathy were recruited for the study. The control group were 50 types 2 DM without any complications. Subjects and controls were

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*A Author for Correspondence*
Table 1: Comparison of zinc levels in DM complications.
HbA1C was significantly high in study group when compared to control (9.5±2.5, 6.5±1.5) (p≤0.0001). Similar consistent findings were reported by Nathan et al (28), and Trivelli et al., (29).

Table 2: Comparison of HbA1c in DM complications.
HbA1c in patients without complications as control and with complications as study group. (P < 0.001 is significant).

Graph showing negative correlation between HbA1c and zinc.
between 40 - 65 age group and both the genders were included for the study. Patients with nephropathy, nutritional supplements and acute and chronic illness were excluded from the study. After overnight fasting blood samples were collected in sterile containers. Fasting plasma glucose was estimated by GOD - POD method. HbA1C was estimated using D10 analyser by HPLC method. Serum zinc was estimated using colorimetric kit method. Blood urea by enzymatic method and serum creatinine by alkaline picrate method. 

 statistical analysis was done using student’s test and Pearson correlation was found out by regression analysis. p value less than 0.05 is considered significant. 

**DISCUSSION**

The study of zinc levels focuses on essential role of trace elements in the pathogenesis of diabetic complications. Zinc and HbA1C are inversely related where with the increase in HbA1c levels there is decrease in zinc levels. In our study the serum levels of zinc was low in uncontrolled diabetes patients with micro-vascular complications which was in concordance with the other studies. Study by Rai et al showed that serum zinc concentration were lower in diabetics when compared to healthy controls and found a negative correlation with glycated proteins in the blood. Similar observations were reported by Al- Maroof in his studies. Studies by Tripathy found a negative correlation between HbA1C and zinc.

Marchesini et al explained hypozincemia seen in the diabetic population due to low gastrointestinal absorption and high urinary excretion of zinc in diabetic patients. Kinlaw et al also expressed similar results in their studies and explained that zinc absorption has been defect or reduced, by uncontrolled blood sugar (hyperglycemia) and it would lead to an elevation of HbA1C. We have observed decrease in zinc levels in patients with uncontrolled blood sugar and consistent with our study, Walter RM et al also reported similar results. A physical chemical relationship between insulin and zinc has been known for decades, it was clear that the addition of zinc to insulin would change the ternary structure of insulin and can reduce the immunological insulin activity due to changes in antigenic determinations of insulin.

Researchers from their studies showed that hyperglycemia interferes with active transport of Zinc back into the renal tubular cells leading to hyperzincemia. Zinc also increases insulin sensitivity by increasing the binding ability of insulin to its receptors.

**RESULTS**

There was significant decrease in serum concentrations of Zinc in study group when compared to control (50±12.5, 95 ± 20.42) (p<0.001). Similar observations were made by Kinlaw et al, and Zalewski et al, Williams et al, in their study Mc Nair et al, in their study reported a definite hypozincemia in 39.7% of patients and showed that there is inverse relationship between zinc and glycemic status, Garg et al and Williams et al also reported that hypozincemia is frequently associated with DM. Al Maroof observed significantly lower levels of zinc levels in diabetics than in healthy controls in his study. There was an inverse relation between HbA1C and levels of zinc in our study which implies that as blood glucose concentration is increased zinc values were decreased in patients with diabetic complication. The correlation of HbA1c and zinc was done using Pearsons correlation coefficient and is inversely related r= - 0.4, even though statistical significance was not found (p=0.8).

Studies by Tripathy et al., reported negative correlations between serum zinc and HbA1C. Zinc levels in blood are decreased with the increase in HbA1c in diabetics when compared to healthier. Routine parameters like urea and creatinine and lipid profile was also analysed in both the groups. There was increase in urea and creatinine levels in patients with complications compared to patients without complications even though significance was not found (p=0.07) Similarly triglycerides and LDL levels were higher in study group when compared to controls and showed statistical significance among patients in study group and control.(p<0.04) (p<0.05) respectively.

In conclusion, diabetics are more prone for deficiency of zinc as increased glycosylation in these persons could in

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turn cause increased oxidative damage due to increased production of free radicals. Diabetic complications are attributed to increased susceptibility to lipid peroxidation due to free radical damage. Strict glycemic control and zinc supplementations can prevent complications to some extent.

REFERENCES