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A Study On Zinc And Magnesium Level And Its Association With Glycated Hemoglobin In Type II DM.

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ABSTRACT

Diabetes Mellitus is a major health problem worldwide. DM is characterized by chronic hyperglycemia. Causes include environmental and genetic. A relationship has been noted between trace elements and DM. The study was to estimate the serum zinc & magnesium levels & their association with glycated hemoglobin (HbA1c) in Type 2 DM and healthy controls. A comparative cross-sectional Study included 50 Type 2 DM cases and 50 healthy controls without any complications. Fasting venous sample was analyzed for serum glucose, zinc, magnesium, and glycated hemoglobin.HbA1c was estimated by the HPLC method in the D10 analyzer. Zinc and magnesium were analyzed by AAS in PerkinElmer 300 AA and colorimetric kit method Statistical analysis included student's t-test and Pearson's correlation to see the association between serum magnesium and zinc with HbA1c. Significant decrease in magnesium level in cases when compared to controls (1.56±0.46, 2.0±0.56) ($p<0.001$). HbA1c was significantly high in cases when compared to controls (8.52±2.14, 5.44±0.40) ($p< 0.001$). No significance in zinc level between cases and controls, the P value is 0.714. A negative correlation was seen between S. Magnesium and HbA1c r = -0.56. No correlation between S. Zinc and HbA1c r= 0.047. We conclude that serum Magnesium levels are only altered in type 2 DM and not serum zinc levels because we have not included the diabetic complication patients. Magnesium supplementation to the patients will improve glycemic status and prevent complications and progression of the disease. Serum zinc and magnesium levels are used as a screening procedure in detecting the complications of diabetes mellitus.

Keywords: Diabetes mellitus, Zinc, Magnesium, Glycated Hemoglobin.

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INTRODUCTION

Diabetes mellitus is a chronic disorder of various metabolisms involving carbohydrates, fat, and protein. It is associated with many causes which end in chronic hyperglycemia. The cause may be due to insufficient insulin secretion, insulin action, or both [1]. These may end in long term complications, and failure of multiple organ systems. Death is due to acute metabolic complications. The chronic disease will lead to irreversible physiological and anatomical changes in various tissues in the body, but mainly in the vascular system. A correlation was noticed between diabetes and micronutrients like magnesium, vanadium, manganese, zinc, and selenium [2]. A mechanism that is accepted explains, that enhancement of insulin action at the receptor level occurs by these micronutrients [3]. They act as cofactors or part of the enzyme system, needed for the citric acid cycle in carbohydrate metabolism. These minerals behave as antioxidants and prevent lipid peroxidation. It also stimulates the biological action of insulin [4]. The main complication of type 2 DM is an elevated blood glucose level. The action of zinc is based on its enzymatic affinity and its metalloenzyme complex [4] which is needed for the secretion and sorting of insulin .zinc enhances the structural integrity of biological receptors of insulin. The central role of zinc is in cell division and protein synthesis. It is mainly needed for the growth of infants and adolescents. In pregnant women, it is needed for the growth of the fetus. The deficiency in this group is due to poor intake of food which is rich in zinc. Magnesium has an essential role in carbohydrate metabolism. Hypomagnesaemia causes altered phosphorylations in the citric acid cycle. So mineral deficiency may lead to a disease condition or it may be either way [5]. Magnesium is one of the important intracellular cations in the body. It acts as a cofactor for enzymatic reactions involved in carbohydrate metabolism, nucleic acid, and protein synthesis [6]. Magnesium is one of the essential minerals and is associated with glucose intolerance, insulin release, and insulin resistance in experimental animals and humans. Hypomagnesaemia is a more common finding in diabetes patients. Clinically, zinc deficiency shows growth retardation, delayed sexual and bone maturation, skin patches, diarrhea, alopecia, decreased appetite, more vulnerability to infections due to defects in the immune system, and changes in behavior. Mild zinc deficiency is implicated in diseases, like, HIV/AIDS, diabetes, alcoholism, cirrhosis, and inflammatory bowel disease, zinc is linked with several aspects of the immune system. Development of B lymphocytes, T-Helper 1(Th1) cytokine production NK cell Th1 production of antibodies, and cytolytic activity are affected mostly [6] Neutrophil and macrophage functions are adversely affected by zinc deficiency. Apoptosis of lymphocytes is initiated due to zinc deficiency. Zinc also acts as an antioxidant and thus can play a prime role in the stabilization of cell membranes [6]. Constantly elevated blood sugar levels will lead to glycosylation of the proteins primarily hemoglobin. Hemoglobin glycation, measured by percentage of glycated hemoglobin (HbA1c) was done 30 years ago to estimate the degree of chronic hyperglycemia in diabetic patients. The results reflect the average glucose levels over the preceding three months. In Diabetics, an elevation of HbA1c of 1 percent increase will lead to 30% in mortality associated with cardiovascular events [7]. So in this study, the evaluation of zinc and magnesium levels and their association with glycated hemoglobin was decided to be studied.

MATERIALS AND METHODS

This research was conducted during the period January 2016 – June 2016 as a comparative cross-sectional study in the Department of Diabetology and Department of Biochemistry in Govt. Kilpauk Medical College Hospital, Chennai. 50 patients of known type 2 DM for ≥ 5 years without any complication will be selected as cases from the OPD of the Department of Diabetology, at Govt. Kilpauk Medical College Hospital, Chennai. The control group comprises 50 normal subjects.

Inclusion Criteria

Individuals between 35 to 60 years with both sexes and they are divided into 2 groups

- Group 1-Age and sex-matched Controls (Normal subjects)
- Group 2- patient with type2 DM for ≥ 5 years

Exclusion Criteria

- Patient taking any kind of trace element.
- Hemolysed and jaundiced sample
- Liver and kidney diseases.

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The study was approved by the Institutional Ethical Committee of the Govt. Kilpauk Medical College, Chennai. After giving a full explanation of the study written informed consent was obtained from every participant.

Sample Collection

5 ml of fasting venous blood sample is drawn from the antecubital vein of the patient in a plain test tube after fulfilling the selection criteria. The serum is separated by centrifugation at 3000 RPM for 10 minutes after 30 minutes of collection. Separated serum is stored at -20◦ C for further analysis.

RESULTS

In this study, a total of 100 subjects were enrolled. Out of which 50 were diabetic cases and the rest 50 were controls. They are divided into two groups. Group I includes normal subjects as controls and group II includes diabetic cases. Serum glucose, S. urea, S. Creatinine, HbA1C, S. magnesium, and S. zinc levels were measured in fasting samples of both groups

Table 1: Shows The Mean And Standard Deviation Of Fasting Blood Glucose Levels Between Group I Controls And Group II Diabetic Patients

Variable	GroupI (controls) N=50 Mean ±SD	Group II (diabetic pts)N= 50Mean ±SD	P Value	Statistical Significance
Fasting blood glucose (mg/dl)	90.01±16.67	179.12±73.0	< 0.001	HS

Table 2: Shows The Mean And Standard Deviation Of Serum Urea Of Group-I- -I Controls And Group-II Diabetic Patients

variable	GroupI (controls) N= 50(mean ±SD)	Group II(diabetic pts) N= 50 Mean± SD	P value	Statistical Significance
S. urea (mg/dl)	19.36±5.18	21.0±6.69	0.165	NS

NS – not significant

From the above p-value (0.165), it is known that there is no statistical significance in urea values between the group-I controls and the group-II diabetic patients.

Table 3: Shows The Mean And Standard Deviation Of Serum Creatinine Values Between Group I Controls And Group II Diabetic Patients

variable	Group I (controls) N=50 Mean±SD	Group II Diabetic pts N=50 Mean±SD	P value	Statistical significance
S.creatinine mg/dl	0.85± 0.17	0.80±0.19	0.161	NS

NS = not significant from the p-value (0.16) It is known that there is no statistical significance in the creatinine values between group I controls and group II patients.

Table-4: Shows The Mean And Standard Deviation Of Hba1c Values In Group I Controls And Group II Diabetic Patients

variable	groupI (controls) N= 50 Mean±SD	GroupII (diabetic pts) N=50 Mean±SD	P value	Statistical significance
HbA1C %	5.44±0.40	8.52±2.14	< 0.001	HS

HS – highly significant From the table, it is known that the HbA1C value was significantly elevated in Group II diabetic patients than in the Group II controls.

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Table 5: Shows The Mean, Standard Deviation, And P Value Of Serum Magnesium In Group I Controls And Group II Diabetic Patients.

Variable	GroupI (controls) N=50 Mean±SD	Group II (diabetic pts) N=50 Mean± SD	P value	Statistical significance
S.Magnesium mg/dl	2.0±0.56	1.56±0.46	< 0.001	HS

HS – highly significant in the above table it is known that the serum Magnesium level was significantly lower in group II diabetic patients when compared to group I controls.

Table 6: Shows The Mean, Standard Deviation, And P Value Of Serum Zinc Levels In Group I Controls And Group II Diabetic Patients

variable	Group I(controls) N= 50 Mean± SD	Group II (diabetic pts) N= 50 Mean ±SD	P value	Statistical significance
S. Zinc (µg/dl)	126.84 ± 58.93	122.84±49.61	0.714	NS

NS – not significant From the above table it is known that the serum zinc levels were decreased in Group II diabetic patients when compared to Group II controls but, it was not statistically significant (P value > 0.05).

Table 7: Shows The Correlation Of Serum Magnesium And Serum Zinc Levels With Hba1c In Diabetic Subjects

Correlation between	Pearson's correlation Coefficient (r)	P value	Statistical Significance
Serum magnesium and HbA1C	-0.56	< 0.01	Highly significant negative correlation
Serum zinc and HbA1C	0.047	>0.05	Not significant, No correlation.

DISCUSSION

This study was done to find an association between trace elements (zinc and Magnesium) and type 2 DM. Zinc and magnesium play an important role in various metabolic processes of our body. So in this study, trace elements like serum magnesium and serum zinc levels were measured and their association with glycated hemoglobin was compared between type 2 diabetic patients and healthy non-diabetic controls. Zinc acts as a cofactor for insulin. However, its mechanism in carbohydrate metabolism is not yet known. In this study, S. Zinc levels between type DM and controls were not significant since the P value is >0.05 which is consistent with the findings of studies by Zargar *et al*. in Kashmir [8] and Rusu *et al*. in seria [9]. In our study zinc concentrations were similar in diabetic patients and controls. This is consistent with the study by Niewoehner *et al*. [6]. Various other studies show the relationship between DM and serum Zinc levels. These differences are partly due to heterogeneity in patient selection and study design. The cause for higher levels of serum zinc concentration in diabetic patients is due to the presence of vascular complications according to Rusu *et al*. [9]. They showed that zinc levels have a moderate but constant increase with obliterative arteriopathy, retinopathy, or nephropathy in diabetic patients [9]. So the abnormality in zinc metabolism is proposed to play a role in the pathogenesis of diabetes and its complications. According to Kinlaw WB *et al*. [10], serum zinc concentrations were decreased in type 2 DM patients and this decrease was due to excessive urinary losses, but this loss was found to be greater in patients who had proteinuria. In our study, we excluded the nephropathy patients. In our study, we excluded the patients who are all having diabetic complications. In another study, Schlienger JL *et al*. [11], found that serum zinc concentrations were reduced in patients with type 2 DM and there was no association between zinc and glycated hemoglobin. Control of diabetes did not influence the zinc concentration. Patients who were previously treated with Insulin showed an increase in zinc levels [12]. Our study did not include the diabetic patients who were receiving Insulin. Fasting glucose and glycated

hemoglobin were significantly elevated in type 2 DM patients as compared to healthy controls (P < 0.001) whereas serum magnesium levels were decreased significantly in DM patients (P < 0.001)[13].DM is one of the causes of hypomagnesemia. In this study, serum magnesium levels in type 2 DM were significantly lower than that of the control group (P value < 0.001), and it is negatively correlated with HbA1C. Zinc and magnesium play an important role in various metabolic processes of our body. Various other studies showed that serum magnesium levels are lower in type 1 and type2 DM compared with control normal subjects. Kim DJ *et al*. [14], observed the negative correlations between magnesium and HbA1C, fasting blood glucose, and HOMA – IR (homeostatic model assessment of Insulin resistance) and this is consistent with our study. Reduced plasma magnesium levels have been shown in NIDDM patients [15, 16]. Magnesium has an important role in improving insulin resistance. The decrease in magnesium levels in type 2 DM patients is mainly due to poor metabolic control or is due to chronic complications according to clinical and epidemiological studies. The mechanism for magnesium deficiency in diabetic patients has not been clarified, mainly about the effect on insulin resistance and its complications. Decreased insulin sensitivity due to magnesium deficiency causes alteration of the insulin receptor-mediated tyrosine kinase in type 2 DM patients [17]. The decreased magnesium level in type 2 DM patients causes increased vascular and adrenal responses to angiotensin II mediated thromboxane A2 release and increased platelet activity which leads to multiple organ damage from free radical production [18, 19]Our finding of serum magnesium levels and its correlation with HbA1C was similar to the findings of Pujar S *et al*. [20]. The study of Viktorinova *et al*. [21] showed the negative correlation between serum magnesium and HbA1C in diabetic patients is in agreement with our study. The altered metabolism of zinc and magnesium in diabetic patients was most probably related to hyperglycemia as indicated by an increase in HbA1c level. The altered metabolism of these minerals may be the cause of the progression of type 2 DM and its complications [22].

CONCLUSION

In our study, serum magnesium levels are decreased and there is a negative correlation in the serum levels of magnesium with HbA1c in diabetic patients. Serum zinc levels were similar in diabetic patients and controls. No correlation between zinc and glycated hemoglobin. Hypomagnesemia is common among type 2 diabetic patients. So reduced magnesium level in diabetic patients decreases insulin sensitivity and increase the risk of complications. Since zinc acts as an antioxidant, only altered zinc metabolism in diabetic patients were more prone to lipid peroxidation and complications such as retinopathy, nephropathy, and peripheral neuropathy. Here the zinc metabolism is not altered. Improvement in glycemic control is possible with trace element therapy. Poor glycemic control and its association with type 2 DM patients suggest that serum zinc and serum magnesium should be a part of the screening procedure in detecting the complications of type 2 DM. So supplementation of zinc and magnesium in type 2DM patients and strict glycemic control can prevent the complications to some extent

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