International Journal Dental and Medical Sciences Research
Volume 2, Issue 6, pp: 128-135 www.ijdmsrjournal.com ISSN: 2582-6018

Zinc and Magnesium Level and Its Association with Glycated Hemoglobin in Type2 Dm

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Date of Submission: 10-11-2020 Date of Acceptance: 24-11-2020

ABSTRACT: INTRODUCTION: 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 level & its association with glycated hemoglobin (HbA1c) in Type 2 DM and healthy controls. **MATERIALS AND METHODS:** 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 HPLC method in D10 analyzer . Zinc and magnesium was analyzed by AAS in PerkinElmer 300 AA and colorimetric kit method .statistical analysis include student 't'test and Pearson's correlation to see the association between serum magnesium and zinc with HbA1c. **RESULT:** 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, P value is 0.714. Negative correlation 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. **CONCLUSION**: Magnesium supplementation to the patients will improve glycemic status and prevent the complication and progression of the disease. Serum zinc and magnesium level is used as a screening procedure in detecting the complication of diabetes mellitus.

KEY WORDS: Diabetes mellitus, Zinc,Magnesium, Glycated Hemoglobin.

I. INTRODUCTION

'Diabetes mellitus is a chronic disorder of various metabolism involving carbohydrate, fat and protein. It is associated with many causes which end in chronic hyperglycemia. The cause may be due to insufficient insulin secretion, or 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 among diabetes and micro nutrients like magnesium, vanadium, manganese, zinc and selenium [2]. A mechanism which is accepted explains, that enhancement of insulin action at the receptor level occurs by these micro nutrients [3]. They act as cofactors or part of the enzyme system, needed for the citric acid cycle in the carbohydrate metabolism. These minerals behave as antioxidants and prevent lipid per oxidation. 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

International Journal Dental and Medical Sciences Research
Volume 2, Issue 6, pp: 128-135 www.ijdmsrjournal.com ISSN: 2582-6018

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 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 cation 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 macro mineral 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 immune system. Development of B lymphocytes, T-Helper 1(Th1) cytokine production and NK cell Th1 production of antibodies, and cytolytic activity are affected mostly [6] Neutrophil, macrophage functions are adversely affected by zinc deficiency. Apoptosis of lymphocytes are initiated due to zinc deficiency. Zinc also acts as an antioxidant and thus can play a prime role in stabilization of cell membranes [6].

Constantly elevated blood sugar level 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, evaluation of zinc and magnesium level and its association with glycated hemoglobin was decided to be studied.

II. AIMS AND OBJECTIVES:

To assess the level of zinc and Magnesium and its levels are compared with Glycated Hemoglobin in type2 DM patient and in normal subjects. The secondary objective of the study is Improvement in Zinc and Magnesium level in diabetic patients will have a better glycemic control which in turn will prevent the complication and progression of the disease.

III. 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

STUDY POPULATION

CASES

50 patients of known type2 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.

CONTROLS

Control group comprises 50 normal subjects.

REFERENCE RANGE FOR ZINC AND MAGNESIUM

Serum Zinc – 80 to 120 µg/ dl (12 to 18 µmol/L)
Serum Magnesium – 1.7 to 2.4 mg/dl (0.66 to 1.07 mmol/L)

INCLUSION CRITERIA

Individual 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.

The study was approved by the Institutional Ethical Committee of the Govt. Kilpauk Medical College, Chennai. After giving full explanation of the study a 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. 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.

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IV. 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 the 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= 50 Mean ±SD	P Value	Statistical Significance
Fasting blood glucose(mg/dl	90.01±16.67	179.12±73.0	< 0.001	HS

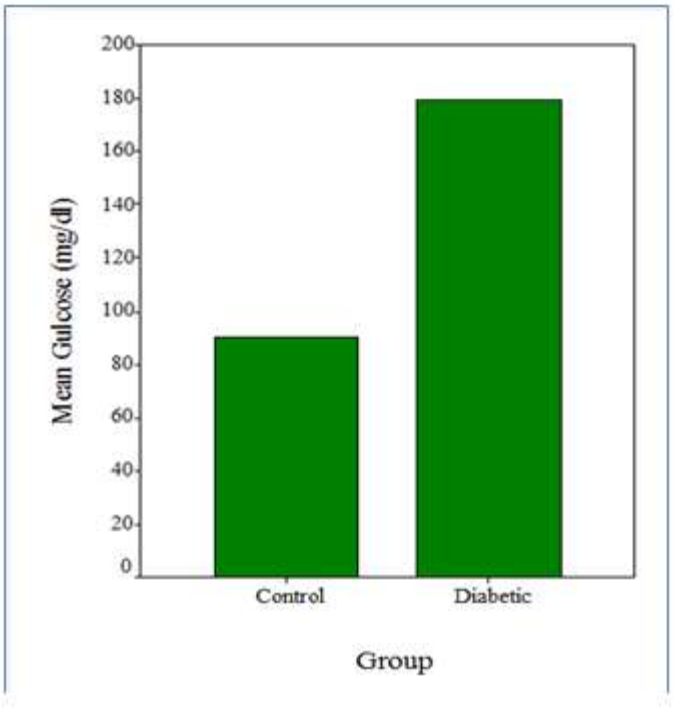

TABLE-2: SHOWS THE MEAN AND STANDARD DEVIATION OF SERUM UREA OF GROUPI CONTROLS AND GROUP II DIABETIC PATIENTS

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 groupI controls and the groupII diabetic patients.

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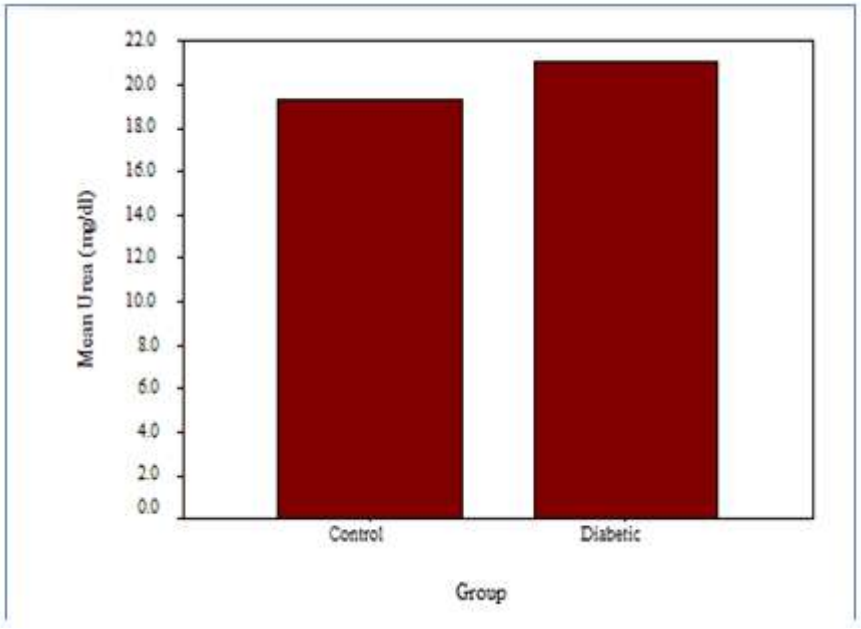
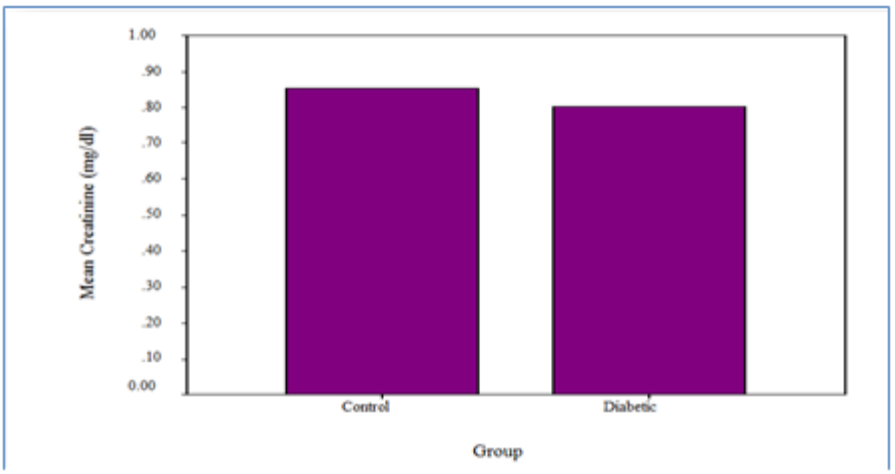


TABLE-3: SHOWS THE MEAN AND STANDARD DEVIATION OF SERUM CREATININE VALUES BETWEEN GROUPI CONTROLS AND GROUPII DIABETIC PATIENTS

variable	GroupI (controls) N=50 Mean±SD	GroupII 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.

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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 the Group II controls.

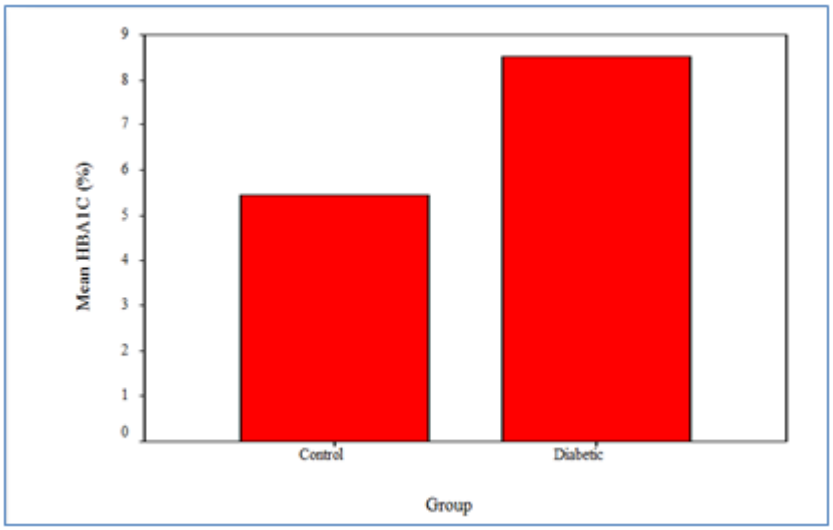

TABLE-5: SHOWS THE MEAN, STANDARD DEVIATION AND P VALUE OF SERUM MAGNESIUM IN GROUP I CONTROLS AND GROUP II DIABETIC PATIENTS.

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

From 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).

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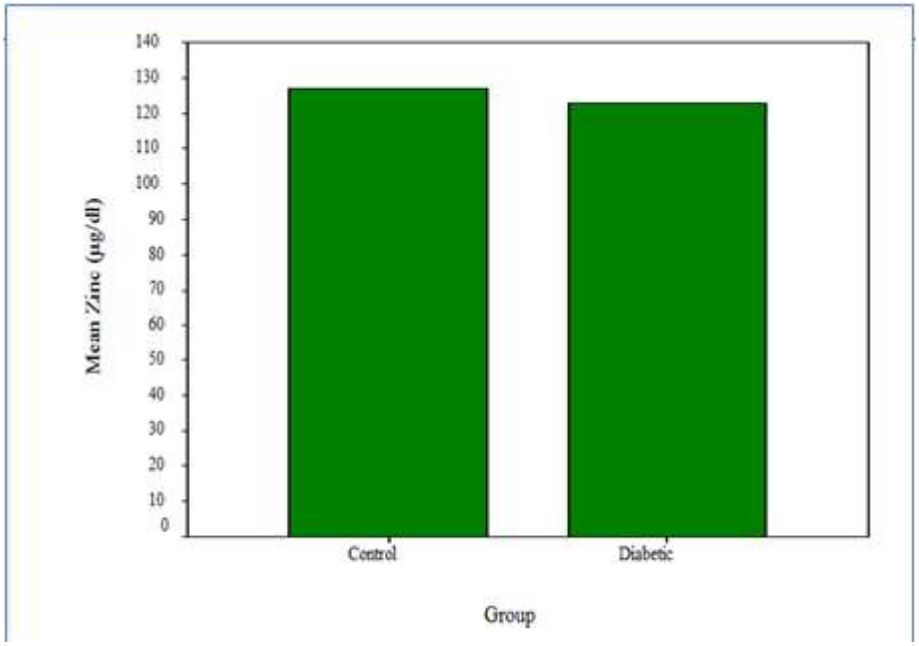

TABLE-7: SHOWS THE CORRELATION OF SERUM MAGNESIUM AND SERUM ZINC LEVELS WITH HBA1C IN DIABETIC SUBJECTS

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.

V. DISCUSSION

This study was done to find an association between trace elements (zinc and Magnesium) and type2 DM. Zinc and magnesium plays an important role in various metabolic processes of our body. So in this study the trace elements like serum magnesium and serum zinc levels were measured and its association with glycated hemoglobin was compared between type 2 diabetic patients and healthy non diabetic controls. Zinc act as a cofactor for insulin. But its mechanism in carbohydrate metabolism is not yet known. In this study, S. Zinc levels between type2 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 Niewoehner et al. [6]. There are various other studies that show relationship between DM and serum Zinc levels. These differences are partly due to heterogeneity in patient selection and study design.The cause for higher level of serum zinc concentration in diabetic patients is due to the presence of vascular complications according to Rusu et al. [9]. They showed that the 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 pathogenesis of diabetes and its complication. 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 when they 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 type2 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 increase in zinc levels [12]. Our study did not include the diabetic patients who were receiving Insulin.Fasting glucose, 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 for

hypomagnesemia. In this study, serum magnesium levels in type 2 DM was significantly lower than that of control group (P value < 0.001) and it is negatively correlated with HbA1C.
Zinc and magnesium plays 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], they 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 level has been shown in NIDDM patients [15, 16].
The cause for hypomagnesemia in type2 DM is not clear. May be due to

- Indirect hormonal effects
- Osmotic dieresis [9]
- Impaired absorption of magnesium
- Increased urinary losses.

Magnesium has an important role in improving insulin resistance. Decrease in magnesium level in type2 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 type2 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 the 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 increase in HbA1c level. The altered metabolism of these minerals may be the cause for progression of type 2 DM and its complications [22].

VI. 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 control. No correlation between zinc and glycated hemoglobin. Hypomagnesemia is common among type 2 diabetic patients. So reduced magnesium level in diabetic patients decreases the insulin sensitivity and increases the risk of complications.

Since zinc acts as an antioxidant, only altered zinc metabolism in diabetic patients were more prone for lipid peroxidation and the 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 the serum zinc and serum magnesium should be a part of the screening procedure in detecting the complications for type2 DM. So supplementation of zinc and magnesium in type 2DM patients and strict glycemic control can prevent the complications to some extent

REFERENCES

[1]. Murray, R.K., Granner, D., Mayes, P., Rodwell, V. (2000). Harper's Biochemistry (25 th International Edition) Appleton and Lange, USA.
[2]. Vincent, J.B. (2000). Quest for the molecular mechanisms of chromium action and its relationship to diabetes. Nutr. Rev, 58: 67-72.
[3]. Monika, K., Waltr., Michael, B. (2003). Zimmermann, Giatgen A. Spinas, Richard F. Hurrell
[4]. Low plasma magnesium in type 2 diabetes. Swiss Med Wkly, 133:289-92
[5]. Kruse-Jarres, J.D., Rukguaer, M. (2000). Trace Elements in Diabetes Mellitus.Peculiarities and Clinical Validy of determinations of red blood cells. J Trace Elem. Med. Biol, 14: 21-27.
[6]. Chausmer, A.B.(1998). Zinc, insulin and diabetes. J am college of nutr, 17(2): 109 – 15
[7]. Niewoehner, C.B., Allen, J.l., Boosalis, M., Levine, A.S., Morley, J.E. (1986). Role of zinc supplementation in type II diabetes mellitus. Am J Med, 81; 63-68,
[8]. Wild, S., Roglic, G., Green, A., Sicree, R., King,
[9]. H. (2004). "Global prevalence of diabetes:

Estimates for the year 2000 and projections for 2030". Diabetes Care, 27(5): 1047–53.

[10]. Zargar, A.H., Shah, N.A., Masoodi, S.R., Laway, B.A., Dar, F.A., Khan, A.R. (1998). Wani AI. Copper, zinc, and magnesium levels in non-insulin dependent diabetes mellitus. Postgrad Med J, 74: 665-668

[11]. Rusu, M.L., Marutoiu, C., Rusu, L.D., Marutoiu, O.F., Hotoleanu, C., Poanta, L.(2005). Testing of Magnesium, Zinc and Copper Blood Levels in Diabetes Mellitus Patients. Acta Universitatis Cibiniensis Seria F Chemia, 8: 61-63.

[12]. Kinlaw, W.B., Levine, A.S., Morely, J.E., Silvis, S.E., Mcclain, C.J. (1991). Abnormal zinc metabolism in type 2 Diabetes mellitus Am J Med 1983; 75: 273-

[13]. 7 disorders. Diabetes Care, 18:129-34.

[14]. Schlienger, J.L., Grunenberger, F., Maier, E.A., Simon, C., Chabrier, G., Leroy, M.I. (1988). Disorders of plasma trace elements in diabetes, relation to blood glucose equilibrium. Presse Med,17: 1076-9.

[15]. Roth, H.P., Kirchgessner, M. (1981). Zinc and insulin metabolism. Biol Trace Elem Res, 1981;3:13-32.

[16]. Fujimoto, S. (1987). Studies on the relationship between bloods trace metal concentration and the clinical status of patients with cerebrovascular disease, gastric cancer and diabetes mellitus. Hokoido Igaku Zasshi, 62:913-32.

[17]. Kim, D.J., Xun, P., Liu, K., Loria, C., Yokota, K., Jacobs, Dr. Jr. (2010). Magnesium intake in relation to systemic inflammation, insulin resistance, and the incidence of diabetes. Diabetes Care, 33:2604-10.

[18]. De-Valk, H.W. (1992). Hypomagnesemia and type-2 (non-insulin dependent) diabetes mellitus (letter). Diabetologia, 35: 904-5.

[19]. Resnick, L.M., Altru, B.T., Gupta, R.K., Laragh, J.H., Alderman, M.H., Altm, B.M. (1993). Intracellular and extracellular magnesium depletion in type-2 (non-insulin dependent) diabetes mellitus. Diabetologia , 36:767-70.

[20]. Mishra, S., Padmanaban, P., Deepti, G.N., Sarkar, G., Sumathi, S., Toora, B.D.(2012). Serum Magnesium and Dyslipidemia in Type-2 Diabetes Mellitus. Biomedical Research, 23: 295-306.

[21]. Nadler, J.L., Malayan, S., Luong, H. (1992). Intracellular free magnesium deficiency plays a key role in increased platelet reactivity in type II diabetes mellitus. Diabetes Care, 15: 835– 841. 23.

[22]. Altura, B.M., Altura, B.T.(1985). New perspectives on the role of magnesium in the pathophysiology of the cardiovascular system: clinical aspects. Magnesium, 4: 226-244.

[23]. Pujar, S., Pujar, B.L.L., Ganiger, A., Hiremath, K., Mannangi, N., Mahanthesh.(20140. Correlation of serum zinc, magnesium and copper with HbA1c in type 2 diabetes mellitus patients among Bagalkot population-A case control Study. Medica Innovatica, 3(2):4-9.

[24]. Viktorinova, A., Toserova, E., Krizko, M., Durackova, Z. (2009). Altered metabolism of copper, zinc, and magnesium is associated with increased levels of glycated hemoglobin in patients with diabetes mellitus. Metabolism, 58: 1477-1482.

[25]. Mohanty, S.S., Pinnelli, V.S., Murgod, R., Raghavendra, D.S.(2013). Evaluation of serum copper, magnesium and glycated hemoglobin in type 2 diabetes mellitus. Asian J Pharm Clin Res, 6(2): 188-190.