



STUDY OF SERUM MAGNESIUM AND ITS ASSOCIATION WITH GLYCEMIC CONTROL IN TYPE II DIABETES MELLITUS

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ABSTRACT

Background: During pre-insulin era diabetes was considered to be endless suffering which was relieved only by death. Diabetes mellitus is a chronic disorder that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Recently there has been an increasing interest regarding the important role played magnesium in various cell processes in the body.

Objectives: The present study was therefore undertaken to compare the levels of serum Magnesium in diabetic patients and healthy controls and to correlate levels of magnesium with HBA_{1c} value.

Material & Methods: Serum magnesium levels and HBA_{1c} values were estimated in 100 type II diabetes mellitus patients and 100 healthy controls.

Results: Mean serum magnesium level was found to be significantly lower in type II diabetes mellitus patients compared to controls. We further observed a significant negative correlation between serum magnesium and HBA_{1c} value.

KEYWORDS : Type II Diabetes mellitus, Insulin, Hypomagnesemia, HBA_{1c}

INTRODUCTION:

Diabetes mellitus is a chronic disorder that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.¹ Among the two types, type II Diabetes mellitus is characterized by insulin resistance or relative insulin deficiency and is more common. Out of total diabetic people around the world 90% are with type II diabetes mellitus.² Prevalence of diabetes mellitus is raising at alarming rate all over the world. Diabetes is predicted to become the seventh leading cause of death in the world by the year 2030.³ Estimated global healthcare expenditures were about 376 billion US Dollars in 2010. By 2030, this number is projected to exceed some 49.0 billion US Dollars.⁴

Recently there has been an increasing interest regarding the important role played magnesium in various cell processes in the body. Many researchers have observed direct associations of trace elements like magnesium with diabetes.⁵ Diabetes mellitus is probably the most common disease which is associated with magnesium depletion in intracellular and extracellular compartments.⁶ Researchers have observed association of hypomagnesaemia with poor glycemic control.^{7,8} Therefore the present study was carried out to gauge the changes in serum magnesium levels in type II diabetes mellitus patients.

MATERIAL & METHODS:

The existing study was carried out in a tertiary care medical teaching hospital over a period of one year in department of Biochemistry after approval taken from the ethics committee of the institution.

Study design: Hospital based cross sectional study with comparison groups.

Sample size calculation: From the study of Ankush RD et al⁹ Biochemical parameter of serum magnesium

- SD₁ in type II diabetes cases= 39.44
- SD₂ in controls= 5.06
- Difference in means of serum magnesium in two groups= 1.8
- α error = 5%
- β error = 0.10
- Power = 90%
- Minimum sample size needed in each arm = 50

Sample size calculated using Power and sample size version 3.0

software

Selection of Study population: 100 patients were chosen from those patients be present in the OPD of Medicine department and those who were hospitalised in wards. 100 healthy age matched and gender matched volunteers were taken as controls.

Inclusion criteria:

1. Patients and healthy age and sex matched controls willing to enter the study in the age group 30 to 59 years
2. All type II diabetes mellitus patients regardless of glycemic control
3. All type II diabetes mellitus patients regardless of treatment

Exclusion criteria:

1. Study subjects less than 30 years and more than 59 years
2. Patients with type I diabetes mellitus
3. Gestational diabetes mellitus
4. Pancreatitis
5. Pregnant and lactating women
6. Patients with renal failure, acute myocardial infarction, chronic diarrhoea
7. Patients on diuretics, aminoglycosides, vitamins and minerals supplementation

Sample collection: 4 ml venous blood from antecubital vein was drawn after taking all the aseptic precautions. 1 ml sample was transferred to Fluoride bulb which was used for estimation of blood sugar. 2 ml blood was transferred to EDTA bulb and after centrifugation; plasma separated from it was used for estimation of Glycated haemoglobin. 1 ml sample was transferred to plain bulb from that serum was separated by centrifugation after coagulation which was used for estimation of serum magnesium. All the samples were estimated on the same day. Haemolysed samples were discarded.

Method of estimation:-

| PARAMETER | METHOD OF ESTIMATION | EQUIPMENT |
|--------------------------|---|--------------------------|
| Plasma glucose | Enzymatic GOD-POD method ¹⁰ | Erba XL-300 Autoanalyser |
| Glycosylated haemoglobin | Ion exchange resin method ¹¹ | Erba XL-300 Autoanalyser |
| Serum magnesium | Calmagite Kit method ¹² | Erba XL-300 Autoanalyser |

Statistical analysis:

- All the demographic and biochemical parameters were expressed as Mean±SD
- Unpaired t test was used for comparison between cases and controls
- Pearson's correlation coefficient was calculated to assess the correlation
- p value<0.05 was considered statistically significant and p<0.001 was considered as highly significant
- Software GRAPH PAD Prism version 6.0 was used for analysis

RESULTS:

TABLE No: 1

Table showing age wise distribution of study subjects

| Age in years | Cases | | Controls | | p Value |
|-----------------|--------------------|------------|--------------------|------------|--------------|
| | n | % | n | % | |
| 30 to 40 | 14 | 14 | 15 | 15 | |
| 41 to 50 | 42 | 42 | 43 | 43 | |
| 51 to 59 | 44 | 44 | 42 | 42 | |
| Total | 100 | 100 | 100 | 100 | |
| Mean Age | 49.52 ± 9.1 | | 48.23 ± 9.3 | | 0.826 |

The above table shows age distribution in cases and controls. There was no statistical difference between the mean age of cases and controls. (p value=0.826)

TABLE No: 2

Table showing values of fasting plasma glucose and HbA1C in cases & controls

| Parameter | Cases (n=100) | | Controls (n=100) | | p Value |
|-------------------------------|---------------|-------|------------------|-------|----------|
| | Mean | SD | Mean | SD | |
| Fasting blood glucose (mg/dL) | 177.2 | 55.10 | 94.66 | 10.15 | p=0.0001 |
| HbA1C (%) | 8.38 | 1.6 | 4.89 | 0.37 | p=0.0001 |

p<0.001= highly significant

Above table shows the comparison of mean fasting plasma glucose levels and glycated haemoglobin in between type II diabetes mellitus cases and healthy controls. Both the values are significantly higher in cases compared to controls.

TABLE No: 3

Table showing comparison of mean serum magnesium in cases & controls

| Parameter | Cases (n=100) | | Controls (n=100) | | p Value |
|-------------------------|---------------|------|------------------|------|----------|
| | Mean | SD | Mean | SD | |
| Serum Magnesium (mg/dL) | 1.29 | 0.23 | 2.09 | 0.28 | p=0.0001 |

p<0.001= highly significant

Table No 3 shows the comparison of mean serum magnesium values between patients of type II diabetes mellitus and healthy controls. On comparison it was found that mean serum magnesium levels were decreased statistically highly significantly in diabetic cases compared to controls.

TABLE No: 5

Table showing correlation between mean serum magnesium and HbA1C in type II diabetes mellitus patients

| Parameter | HbA1C |
|-----------------|-------------------------|
| Serum Magnesium | r= -0.5708 p= 0.0001 |

The above table shows statistically significant negative correlation between the mean serum magnesium and HbA_{1c} in type II diabetes patients.

DISCUSSION-

The present study was conducted in a tertiary care teaching medical institution with the prime objective to evaluate the alterations in serum magnesium levels of patients with type II diabetes mellitus and to deduce the correlation between glycemic control and serum magnesium. We estimated serum magnesium and HbA_{1c} levels in 100 type II diabetes mellitus patients and 100 age and sex matched healthy controls.

The results of the study indicated that mean plasma glucose and HbA_{1c} were elevated statistically highly significantly in type II diabetic cases as compared to healthy controls while serum levels of magnesium were decreased statistically highly significantly in type II diabetic cases when compared to healthy controls. As observed from Pearson's correlation coefficient, a substantial negative association was observed between mean serum magnesium and glycated haemoglobin. The results of our study corroborated fine with the studies conducted by Paolisso G et al⁶, Dasgupta A et al⁷, Ankush RD et al⁹, Meludu SC et al¹³ and Chinyere NAC et al¹⁴.

The reasons of reduced magnesium levels in diabetes are not that clear. One of the reason might be higher urinary loss or impaired absorption of magnesium in diabetic patients.⁸ A specific tubular defect in thick ascending loop of Henle has been postulated behind decreased renal absorption of magnesium.^{15,16} Other reason could be due to depletion of magnesium caused by osmotic diuresis and by indirect hormonal effects.¹⁷ Intracellular magnesium is crucial for normal energy metabolism a cofactor for ATP and various other enzymes. Hence magnesium deficiency may cause global clinical effects.¹⁸ Magnesium is also important for insulin secretion, insulin receptor interaction, post receptor events and normal carbohydrate utilisation. Magnesium deficiency causes problems in these events and lead to insulin resistance.¹⁹ Hypomagnesaemia leads to further progression of diabetes and diabetes further aggravates hypomagnesaemia.¹⁸ Hence it is recommended that diabetic patients shall take magnesium rich food to maintain its normal level in the body.²⁰ The inverse relationship between hypomagnesaemia and glycemic control found in our study was also found in studies conducted by Kareem I et al²¹ Seedahmed T et al²². In view of support to previous hypothesis, present study offers valuable information towards a better understanding of degree and type of magnesium related abnormalities and their correlation with glycemic status.

CONCLUSION:

Significant reduction in serum magnesium levels suggest that diabetic state may interfere in the maintenance of normal magnesium concentrations and can trigger hypomagnesaemia easily, mainly in patients with poor glycemic control. Impaired magnesium metabolism may have a contributory role in the progression of diabetes and later development of secondary complications. Hence it can be concluded that early detection and treatment of hypomagnesaemia may have an affirmative influence on glycemic status and treatment of type II diabetes mellitus.

References:

1. World Health Organization. Fact sheet No. 312: What is Diabetes? [Internet]. Available from: www.who.int/mediacentre/factsheets/fs312/en/.
2. International Diabetes Federation. Diabetes Atlas. 4th ed. Brussels; 2009. Available from: www.diabetesatlas.org
3. Ten Facts About Diabetes. World Health Organisation. Available from: www.who.int/features/factfiles/diabetes/facts/en.
4. International Diabetes Federation. Diabetes Atlas. 4th ed. The economic impact of Diabetes. Available from: www.diabetesatlas.org/content/economic-impactofdiabetes.
5. Nourmohammadi I, Shalmani I, Shaabani M, Gohari L. Zinc, Copper, Chromium, Magnese and Magnesium levels in serum & hair of Insulin dependant Diabetics. Arch Iran med. 2000; 17:286-310.
6. Paolisso G, Barbagallo M. Hypertension, Diabetes mellitus and Insulin Resistance: The role of Intracellular Magnesium. Am J Hypertens. 1997; 10(3):346-55.
7. Dasgupta A, Sarma D, Saikia UK. Hypomagnesaemia in type 2 diabetes mellitus. Indian J Endocrinol Metab. 2012 Nov; 16(6):1000-3.
8. Pham PC, Pham PM, Pham SV, Miller JM, Pham PT. Hypomagnesaemia in patients with type 2 diabetes. Clin J Am Soc Nephrol. 2007 Mar; 2(2):366-73.
9. Ankush RD, Suryakar AN, Ankush NR. Hypomagnesaemia In Type-2 Diabetes Mellitus Patients: A Study On The Status Of Oxidative And Nitrosative Stress. Ind J Clin Biochem. 2009; 24(2):184-9.

10. Glucose Reagent Set [Kit insert]. Accurex Biomedical Pvt Ltd.
11. Glycosylated haemoglobin ion exchange resin method [kit insert]. Labcare diagnostic Pvt.Ltd.
12. Magnesium Calmagite Kit [Kit insert]. Crest Biosystems. A division of Coral Clinical Systems Goa.
13. Meludu SC, Adeniyi FAA. Effect of magnesium supplementation on plasma glucose in patients with diabetes mellitus. *African J Biomed Res.* 2001;4:111-3.
14. Chinyere NAC, Opara UCA, Henrieta EM, Nathaniel UI. Serum and urine levels of chromium and magnesium in type 2 diabetics in Calabar, Nigeria. *Mal J Nutr.* 2005; 11(2):133-42.
15. Cole D, Quamme G. Inherited disorders of renal magnesium handling. *J Am Soc Nephrol.* 2000; 11(10):1937-47.
16. Antin S, Kashinkunti M, Kataria AV, Dhananjaya M, Alevoor S. A cross sectional study of fasting serum magnesium levels in patients with type 2 Diabetes mellitus and its relation to Diabetic complications. *Sch J Appl Med Sci.* 2014; 2(2A):502-6.
17. Rusu ML, Marunoiu C, Rusu LD, Marunoiu OF, Honoleanu C, Poanta L. Testing of magnesium, zinc and copper blood levels in diabetes mellitus patients. *Acta Univ Cibiniensis Ser F Chem.* 2005;8:61-3.
18. Richard F, Kronenberg HM. Hormones and disorders of mineral metabolism. In: Kronenberg HM, editor. *Williams textbook of Endocrinology.* 11th ed. 2012. p1203-68.
19. Badyal A, Sodhi K, Pandey R. Serum magnesium levels: A key issue for Diabetes mellitus. *J K Sci.* 2011 Sep; 13(3):132-4.
20. Mishra S, Padmanaban P, Deepti GN, Sumathi S, Toora BD. Serum magnesium and dyslipidemia in type-2 diabetes mellitus. *Biomed Res.* 2012; 23(2):295-300.
21. Kareem I, Jaweed SA, Bardapurkar JS, Patil VP. Study of magnesium, glycosylated haemoglobin and lipid profile in diabetic retinopathy. *Indian J Clin Biochem.* 2004 Jul; 19(2):124-7.
22. Seedahmed T, Ahmed S. Correlation between the plasma magnesium levels and glycated haemoglobin in Sudanese patients with type 2 Diabetes mellitus in Khartoum State. *Adv Diabetes Metab.* 2013; 1(1):1-5.