Original Article

# Role of magnesium in glycemic control

Kapila B Gaikwad[1*], S M Sonune[2], Milind Vyawhare[3]

{[1]Assistant Professor, [2]Professor and HOD, Department of Biochemistry} {[3]Associate Professor, Department of Medicine}
Government Medical College and Super Speciality Hospital, Nagpur, Maharashtra, INDIA.
**Email:** drkapila27@gmail.com

## Abstract

**Background:** The WHO theme for 2014 was 'Healthy living and diabetes'. The burden of diabetes is increasing globally, particularly in developing countries and the causes are complex. Optimal glycemic control is fundamental to the management of diabetes. Magnesium is needed for more than 300 biochemical reactions in the body. It is involved in energy metabolism and protein synthesis Magnesium is a necessary cofactor for several enzymes that play an important role in glucose metabolism. Magnesium is essential for insulin secretion, insulin receptor interaction and normal carbohydrate utilization (by Mg dependent enzymes). A compromise in these functions leads to insulin resistance in hypomagnesaemia. With this background, this study is carried out to evaluate the role of magnesium in maintaining glycemic control. **Aims and Objectives:** To evaluate the role of magnesium in glycemic control in diabetes mellitus. **Materials and Methods:** 90 patients of age group 25-80 yrs with Diabetes mellitus type 2 with and without complications were included in the study. Their fasting, post meal blood glucose, glycosylated hemoglobin and serum magnesium were estimated. **Results:** The study showed lower levels of magnesium in diabetic patients without complications and more less in diabetic with complications as compared to control. HbA1C levels were high in diabetic complications as compared to well controlled diabetic. Serum magnesium levels had negative correlation with HbA1c. Magnesium is a cofactor for several enzymes involved in carbohydrate metabolism. It is involved at various stages of insulin secretion, binding and activity. Serum magnesium levels were reduced in diabetic compared to control group. Hypomagnesemia was more in diabetic with complications than diabetic without complications. Glycosylated hemoglobin is a measure of glycemic control. The study shows correlation between magnesium and glycated hemoglobin. **Conclusion:** Hypomagnesemia is associated with Diabetic complications and thus glycemic control.
**Keywords:** Magnesium, glycosylated hemoglobin, glycemic control.

[*]**Address for Correspondence:**
Dr. Kapila B Gaikwad, Assistant Professor, Department of Biochemistry, Government Medical College and Superspeciality Hospital, Nagpur, Maharashtra, INDIA.
**Email:** drkapila27@gmail.com
Received Date: 20/11/2016 Revised Date: 12/12/2016 Accepted Date: 03/01/2017

| Access this article online | |
|---|---|
| Quick Response Code: | Website: www.statperson.com |
| | DOI: 08 January 2017 |

## INTRODUCTION

The WHO theme for 2014 was 'Healthy living and diabetes'. The burden of diabetes is increasing globally, particularly in developing countries and the causes are complex. Optimal glycemic control is fundamental to the management of diabetes. In epidemiological analyses, glycosylated hemoglobin levels >7.0% are associated with a significantly increased risk of both microvascular and macrovascular complications, regardless of underlying treatment.[1] Glycemic control is a medical term referring to the typical levels of blood sugar (glucose) in a person with diabetes mellitus. Magnesium is needed for more than 300 biochemical reactions in the body. It is involved in energy metabolism and protein synthesis.[2] Studies have shown that magnesium levels are lower in patients with diabetes compared with non diabetic controls.[3-4] Magnesium is a necessary cofactor for several enzymes that play an important role in glucose metabolism. Magnesium is essential for insulin secretion, insulin receptor interaction and normal carbohydrate utilization (by Mg dependent enzymes).[3] A compromise in these functions leads to insulin resistance in hypomagnesaemia Thus, reduction of magnesium in the cells strengthens insulin resistance leading to poor glycemic control.[5] With this background, this study is carried out to evaluate the role of magnesium in maintaining glycemic control.

How to cite this article: Kapila B Gaikwad, S M Sonune, Milind Vyawhare. Role of magnesium in glycemic control. *International Journal of Recent Trends in Science and Technology.* January 2017; 21(3): 256-259. http://www.statperson.com (accessed 20 January 2017).

## MATERIAL AND METHODS

This prospective study was carried out at for a period of 1 year i.e. from April 2015 to March 2016. The study population comprised of 90 patients of age group 25-80 yrs with Diabetes mellitus type 2 with and without complications which were included in the study. Persons on magnesium supplements, on antacids containing magnesium, chronic renal failure due to factors other than diabetic mellitus, on loop diuretics were excluded from the study. Type-2 DM patients were diagnosed on the basis of biochemical investigations as per WHO criteria. Blood samples were collected in sugar bulb from healthy persons as well as from Diabetic patients attending O.P.D. of our hospital with prior written consent. Plasma was separated for glucose estimation. Samples were collected from known diabetic patients in EDTA and plain bulb. Group I included normal control, group II included diabetic without complications and group III included diabetic with complications.

| | | |
|---|---|---|
| 1 | Fasting glucose | GOD-POD method [6] |
| 2 | Post-meal glucose | GOD-POD method |
| 3 | Glycosylated Hemoglobin | Turbidimetric method[7,8] |
| 4 | Serum Magnesium | Xylidyl Blue method[9] |

Above parameters were analyzed on Erba XL 300 autoanalyzer.

**GOD-POD Method**

Glucose oxidase (GOD) catalyses the oxidation of glucose to gluconate. The formed hydrogen peroxide (H2O2) is detected by a chromogenic oxygen acceptor, phenol, 4- Aminophenazone (4-AP) in the presence of peroxidase (POD):

β-D-Glucose + $O_2$ + $H_2O$ GOD Gluconate +$H_2O_2$

$H_2O_2$ + Phenol + (4-AP) POD Red Quinone dye + $H_2O$

The intensity of the color formed is proportional to the glucose concentration in the serum.

**Glycosylated Hemoglobin-Turbidimetric Method**

HbA1c Turbitest AA is a turbidimetric inhibition immunoassay to determine hemoglobin concentration A1c (HbA1c) as a percentage of a total hemoglobin in human whole blood (%HbA1c). Consequently, the hemoglobin contained in red blood cells is released by hemolysis of the sample. This method uses the Reactive Hemolizante (Hemolyzing Reagent) containing a detergent (tetradecyltrimethylammonium. bromide - TTAB) to specifically lysate red blood cells. HbA1c and Hb levels in the sample are determined from the obtained hemolysate by two independent reactions. HbA1c During the first stage of the reaction, the HbA1c in the sample reacts with the anti-HbA1c specific antibody (Reagent A1) to form soluble antigen-antibody complexes. Since the specific. HbA1c antibody site is present only once on the HbA1c, complex formation does not take place. Then, the polyhapten is added (Reagent A2). The polyhapten has numerous epitopes per molecule and reacts with the specific antibody excess from the first reaction, producing insoluble immunocomplexes which can be measured turbidimetrically at 340 nm. Therefore, the greater the HbA1c content in the sample, the lesser is the insoluble immunocomplex formation and the lesser the obtained turbidimetric signal. Hb liberated hemoglobin in the hemolyzed sample is converted to a derivate that can be spectrophotometrically measured.

**Serum Magnesium-Xylidyl Blue method**

This Magnesium procedure utilizes a direct method in which magnesium forms a colored complex with xylidyl blue in a strongly basic solution, where calcium interference is eliminated by glycoletherdiamine-N,N,N`, N`-tetraacetic acid (GEDTA).3,4,5 The color produced is measured bichromatically at 520/800 nm and is proportional to the magnesium concentration.

$$Mg^{2+} + \text{xylidyl blue} \xrightarrow{\text{pH 11.4}} \text{Purple complex}$$

**Statistical analysis**

Statistical analysis was done by applying Turkey post hoc test. The data was expressed as mean ± standard error.

## RESULTS

**Table 1:** Comparison of Mean Fasting Blood Sugar level in all groups

| Sr. No. | Variable | Group I | Group II | Group III | F Ratio | 'p' value | Significance |
|---|---|---|---|---|---|---|---|
| 1 | Fasting Blood Sugar Level | 90.27 ± 9.89 | 150.97 ± 18.67 | 249.67 ± 53.03 | 176.75 | < 0.0001 | Significant |

**Table 2:** Comparison of Mean Fasting Blood Sugar level in all groups (After Applying Tukey's Post hoc test)

| Sr. No. | Mean Fasting Blood Sugar level | 'p' value | Significance |
|---|---|---|---|
| 1 | Group I vs Group II | < 0.01 | Significant |
| 2 | Group I vs Group III | < 0.01 | Significant |
| 3 | Group II vs group II | < 0.01 | Significant |

**Table 3:** Comparison of Mean Postmeal Blood Sugar level in all groups

| Sr. No. | Variable | Group I | Group II | Group III | F Ratio | 'p' value | Significance |
|---|---|---|---|---|---|---|---|
| 1 | Postmeal Blood Sugar Level | 115.4 ± 11.53 | 181.3 ± 16.37 | 272 ± 33.13 | 371.26 | < 0.0001 | Significant |

**Table 4:** Comparison of Mean Postmeal Blood Sugar level in all groups (After Applying Tukey's Post hoc test)

| Sr. No. | Mean Postmeal Blood Sugar level | 'p' value | Significance |
|---|---|---|---|
| 1 | Group I vs Group II | < 0.01 | Significant |
| 2 | Group I vs Group III | < 0.01 | Significant |
| 3 | Group II vs group II | < 0.01 | Significant |

**Table 5:** Comparison of Mean magnesium level in all groups

| Sr. No. | Variable | Group I | Group II | Group III | F Ratio | 'p' value | Significance |
|---|---|---|---|---|---|---|---|
| 1 | Magnesium Level | 1.95 ± 0.21 | 1.58 ± 0.08 | 1.37 ± 0.1 | 128.13 | < 0.0001 | Significant |

**Table 6:** Comparison of Mean Magnesium level in all groups (After Applying Tukey's Post hoc test)

| Sr. No. | Mean Magnesium level | 'p' value | Significance |
|---|---|---|---|
| 1 | Group I vs Group II | < 0.01 | Significant |
| 2 | Group I vs Group III | < 0.01 | Significant |
| 3 | Group II vs group II | < 0.01 | Significant |

**Table 7:** Comparison of Mean HbA1C level in all groups

| Sr. No. | Variable | Group I | Group II | Group III | F Ratio | 'p' value | Significance |
|---|---|---|---|---|---|---|---|
| 1 | HbA1C Level | 4.83 ± 0.5 | 7.77 ± 0.87 | 10.25 ± 0.72 | 432.69 | < 0.0001 | Significant |

**Table 8:** Comparison of Mean HbA1C level in all groups (After Applying Tukey's Post hoc test)

| Sr. No. | Mean HbA1C level | 'p' value | Significance |
|---|---|---|---|
| 1 | Group I vs Group II | < 0.01 | Significant |
| 2 | Group I vs Group III | < 0.01 | Significant |
| 3 | Group II vs group II | < 0.01 | Significant |

**Table 9:** Correlation between Magnesium level and HbA1C

| Sr. No. | Group | Correlation Coefficient | Interpretation | P value | Significance |
|---|---|---|---|---|---|
| 1 | Group I | -0.07 | Negative | <0.05 | Significant |
| 2 | Group II | 0.5 | Positive | <0.05 | Significant |
| 3 | Group III | 0.2 | Positive | <0.05 | Significant |

Group II and Group III showed hypomagnesemia as compared to Group I. Group III showed more hypomagnesemia as compared to Group II. There is negative correlation between magnesium and HbA1C. Study also showed positive correlation of HbA1C with fasting blood sugar.

## DISCUSSION

Magnesium is the fourth most abundant divalent intracellular cation in cells next to potassium.[10] ATP (adenosine triphosphate), the main source of energy in cells, must be bound to a magnesium ion in order to be biologically active. Magnesium plays a role in the stability of all polyphosphate compounds in the cells, including those associated with the synthesis of DNA and RNA. Magnesium is required for more than 300 different enzymes in our body, many of which are crucial for proper metabolic function.[11-13] Magnesium is keeping our metabolism as well oiled clock specifically in terms of insulin sensitivity and glucose regulation. Magnesium improves and helps correct insulin sensitivity, which is the fundamental defect that characterizes pre-diabetes, metabolic syndrome and even full blown diabetes and heart disease.[14-16] An intracellular enzyme called tyrosine kinase requires magnesium to allow insulin to exert its blood-sugar-lowering effects. Magnesium improves insulin sensitivity thus lowering insulin resistance. Magnesium and insulin need each other. Without magnesium, our pancreas won't secrete enough insulin–or the insulin it secretes won't be efficient enough–to control our blood glucose. Magnesium depletion may be due to increased magnesium excretion brought about by osmotic diuresis or there may be a specific tubular defect. The decrease in serum magnesium concentration is correlated with fasting blood glucose, glycosylated haemoglobin, and complications in diabetes. Magnesium depletion, via its effect on inositol transport, is of pathogenic significance in the development of diabetic complications.[17] Glycemic control is seen via, glycosylated hemoglobin. HbA1C is formed through the nonenzymatic binding of circulating glucose to

hemoglobin[18]. Higher levels of glucose in the blood contribute to more binding and consequent higher levels of HbA1C. It reflects average plasma glucose over the previous 8-10 weeks. Magnesium is negatively correlated with glycosylated hemoglobin. Thus, magnesium has a role in glycemic control as well as in insulin signaling.

## CONCLUSION

Hypomagnesemia is higher in diabetic with complications. Hypomagnesemia is more in patients with poor glycemic control i.e. HbA1C > 7%. The study shows magnesium has a role in glycemic control as well as in insulin signaling. Hypomagnesemia set the stage for deterioration of proper metabolic function that snowballs into more diabetic complications.

## REFERENCES


1. Imran SA, Rémi Rabasa-Lhoret, Ross S. Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Targets for Glycemic Control. Canadian Journal of Diabetes 2013; 37(supp 1): S31-S34
2. Khubchandani AS and Sanghani H. Study of Serum Magnesium and $HbA_{1c}$ in Diabetic Patients along with Changes in their Lipid Profiles. Indian Journal of Clinical Practice 2013; 23(11): 717-719.
3. Ramchandra Prabhu HD and Kunche S. Study of Serum Magnesium and HbA1c in Type 2 Diabetes Mellitus Patients. International Journal of Science and Research 2015; 4(6):2521-2524.
4. Wälti MK, Zimmermann MB, Spinas GA, Hurrell RF. Low Plasma Magnesium In Type 2 Diabetes. Swiss Medical Weekly 2003; 133:289–292.
5. Mohanty SS, Pinnelli VB, Murgod R, Raghavendra DS. Evaluation Of Serum Copper, Magnesium And Glycated Haemoglobin In Type 2 Diabetes Mellitus. Asian Journal of Pharmaceutical and Clinical Research 2011; 6(2):188-190.
6. Trinder, P. Determination Of Blood Glucose Using An Oxidase-Peroxidase System With A Non-Carcinogenic Chromogen. Journal of Clinical Pathology 1969; 22(2):158-161.
7. Jeppsson JO, Kobold U, Barr J, Finke An et to the. Approved IFCC reference method for the measurement of HbA1c in human blood.ClinChemLabMed 2002;40:78-89.
8. Hoezel W, Weykamp C et to the. IFCC Reference System for measurement or Hemoglobin A1c in human blood and the National Standardization Schemes in the United Stastes, Japan, and Sweden: To method-comparison Study. Clin Chem 2004; 50:1:166-74. Ceriello, To., et to the, Diabetologia 22, p 379.
9. Abernethy MH, Flower RT. Micellar Improvement of the Calmagite Complexiметric Measurement of Magnesium In Plasma. Clinical Chemistry 1982; 28(3):520-522.
10. Barbagallo M, Dominguez LJ. Magnesium Metabolism In Type 2 Diabetes Mellitus, Metabolic Syndrome And Insulin Resistance. Archives of Biochemistry and Biophysics 2007; 458:40–47.
11. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington (DC): National Academic Press, 1997.
12. Rude RK. Magnesium. In: Coates PM, Betz JM, Blackman MR, Cragg GM, Levine M, Moss J, White JD, eds. Encyclopedia of Dietary Supplements. 2nd ed. New York, NY: Informa Healthcare; 2010:527-37.
13. Rude RK. Magnesium. In: Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR, eds. Modern Nutrition in Health and Disease. 11th ed. Baltimore, Mass: Lippincott Williams and Wilkins; 2012:159-75.
14. Ma J, Folsom AR, Melnick SL, Eckfeldt JH, Sharrett AR, Nabulsi AA, Hutchinson RG, Metcalf PA. Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid wall thickness: the ARIC study. Journal of Clinical Epidemiology 1985; 48:927–940.
15. Rosolova H, Mayer O Jr, Reaven GM. Insulin-mediated glucose disposal is decreased in normal subjects with relatively low plasma magnesium concentrations. Metabolism 2000; 49:418–420.
16. Resnick LM, Gupta RK, Gruenspan H, Alderman MH, Laragh JH. Hypertension and peripheral insulin resistance: possible mediating role of intracellular free magnesium. American Journal of Hypertension 1990; 3:373–379.
17. Rodriguez-Moran M and Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: a randomized double-blind controlled trial. Diabetes Care 2003; 26(4): 1147-1152.
18. Mailankot M, Thomas T,Praveena P, Jacob J, Rajan J. Various Anticoagulants and Fluoride do not Affect HbA1C Level. Indian J Clin Biochem. 2012 Apr; 27(2): 209.


Source of Support: None Declared
Conflict of Interest: None Declared