



**ORIGINAL RESEARCH PAPER**

**Medicine**

**A Study of Serum Ionized Magnesium Levels In Relation To Metabolic Syndrome In Type 2 Diabetic Patients**

**KEY WORDS:** Diabetic retinopathy, Glycosylated haemoglobin, Hypomagnesemia, Type 2 DM

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**ABSTRACT**

Hypomagnesemia has been proposed as a novel factor implicated in the pathogenesis of poor glycemic control and diabetic complications. Aim of the present study is to study serum magnesium level in patients with type 2 DM and to find the correlation between serum magnesium levels, HbA1c and diabetic complications. 200 patients with Type 2 DM (100 males and 100 females) who were diagnosed on the basis of ADA criteria or taking treatment for Diabetes were included in the study. All patients underwent tests for serum magnesium level, fasting blood sugar, postprandial blood sugar, HbA1c and also target organ evaluation for Diabetes. A detailed history and examination was also done. There was significant difference in the prevalence of hypomagnesemia (34% versus 6%) and serum magnesium levels (1.59±0.187 versus 1.78±0.126, p < 0.0001) between diabetics and control group. FBS (172.17±30.55 versus 137.06±37.76, p < 0.0001), PPBS (243±61.21 versus 195.84±59.1, p = 0.0003) and HbA1C (8.42±1.292 versus 7.04±0.956, p < 0.0001) were significantly higher in hypomagnesemic diabetics as compared to normomagnesemic diabetics. Significant proportion of hypomagnesemic diabetics were suffering from retinopathy as compared to normomagnesemic diabetics (47.06% versus 19.70%, p = 0.0042). Diabetic nephropathy, neuropathy, hypertension and IHD were also higher in hypomagnesemic diabetics as compared to normomagnesemic diabetics, but insignificant.

**Conclusions:** Prevalence of hypomagnesemia in Type 2 diabetics was 34%. Diabetics with hypomagnesemia had poor glycemic control. Hypomagnesemia was significantly associated with diabetic retinopathy.

**INTRODUCTION**

Incidence of diabetes is increasing worldwide due to population ageing and growth, obesity, unhealthy diets and sedentary life style. Microvascular and macrovascular complications of diabetes increase as a function of the duration of hyperglycemia. So, a reduction of chronic hyperglycemia prevents or delays these complications. Magnesium is an essential element and has a fundamental role in carbohydrate metabolism in general and in the insulin action in particular. Magnesium is a cofactor in both glucose transport mechanism of the cell membranes and for various intracellular enzymes involved in carbohydrate oxidation. Magnesium is involved in multiple levels in insulin secretion, binding and activity. Cellular magnesium deficiency can alter the activity of the membrane bound Na+K+ ATPase, which is involved in the maintenance of gradients of sodium and potassium and in glucose transport. The concentrations of magnesium in serum of healthy people are remarkably constant, whereas 25-39% of diabetics have low concentrations of serum magnesium. Hypomagnesemia in diabetics can be due to: osmotic renal losses from glycosuria, decreased intestinal magnesium absorption and redistribution of magnesium from plasma to red blood cells caused by insulin effect. Mc Nair P et al indicated that the net tubular reabsorption (in the thick ascending loop of Henle or more distally) of magnesium is decreased in diabetic patients in presence of hyperglycemia, leading to hypermagnesuria and hypomagnesemia. Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes as well as on the evolution of complications such as retinopathy, arterial atherosclerosis and nephropathy. Moreover, low serum magnesium is a strong, independent predictor of development of type 2 diabetes. In the atherosclerosis risk in communities (ARIC) Study, a dose response inverse relation between serum magnesium concentrations and the incidence of type 2 diabetes was observed amongst white participants. Several subsequent large prospective cohort studies have reported a statistically significant reduction in risk of type 2 diabetes associated with increased magnesium intake. In humans, several experimental metabolic studies have suggested that magnesium supplementation has beneficial effects on glucose metabolism, insulin action and/or insulin sensitivity. In addition, cross-sectional studies have found an inverse association between magnesium intake and fasting insulin concentrations, a good marker of insulin

resistance. High concentration of glucose can increase the glycation of hemoglobin, forming glycosylated hemoglobin (HbA1c). It is a simple and economical way for assessment of long term glycemic control (6-8 weeks). American Diabetes Association recommends twice per year measurements for patients who are meeting treatment goals and quarterly measurements for those whose therapy has changed or who are not meeting treatment goals. The present study was undertaken with an aim to estimate prevalence of hypomagnesemia in patients with type 2 Diabetes mellitus and to correlate the serum magnesium concentrations with glycosylated hemoglobin (glycemic control), and with microvascular and macrovascular complications of diabetes.

**MATERIAL AND METHOD**

The subjects were selected from the cases presenting with diabetes mellitus in the OPD and ward of department of medicine, RIMS, RAIPUR, CG. The study population consisted of 200 Diabetic (type 2) and 100 non-diabetic subjects. All the patients in the diabetic group were confirmed diabetics as per ADA criteria or were receiving treatment for diabetes mellitus. A detailed history was taken and examination done. Age- and sex-matched healthy volunteers without a history of diabetes were considered to be control subjects. All subjects were informed about the objectives of the study and an informed written consent was taken. The study excluded patients with diabetes mellitus other than type 2, critically ill patients (patients with significant hepatic and renal disease, haematological malignancy, chronic kidney disease, acute cerebrovascular accidents, acute myocardial infarction etc.), pregnant women with diabetes mellitus, patients receiving magnesium supplements or magnesium containing antacids, patients on diuretics, patients with history of alcohol abuse, malabsorption or chronic diarrhea, patients refusing to give informed consent for the study. Blood samples were collected from all the 300 subjects. They were kept on overnight fast at least for 8 hrs before blood collection. 5 ml of venous blood was taken in dry disposable syringe under aseptic conditions in sterile, dry vial for biochemical analysis. Calmagite dye method was used for quantitative estimation of serum magnesium. FBS, PPBS, HbA1c, cholesterol, triglycerides, HDL, LDL, VLDL, blood urea, serum creatinine, SGOT and SGPT, were determined on semi-automated clinical chemistry analyzer. The results were expressed as mean±SD of each variable. Student t test is used to compare parametric data.

Chisquare test used to compare groups wherever applicable. P value of <0.05 has been considered significant.

## DISCUSSION

In our study, serum magnesium concentrations were below the reference range in 34% patients with type2 diabetes (case group) and in 6% of control group. This confirms to the reported prevalence of low plasma magnesium status in type-2 diabetics in several studies, which ranged from 25 to 39%. 4-6 Walti MK et al, reported a prevalence of hypomagnesemia in type 2 diabetics as 37.6% versus 10.9% in nondiabetic controls in a study conducted in Zurich, Switzerland. The reasons for the high prevalence of magnesium deficiency in diabetes are not clear, but may include increased urinary loss, lower dietary intake, or impaired absorption of magnesium compared to healthy individuals. Recently a specific tubular defect in magnesium reabsorption in thick ascending loop of Henle is postulated. This defect results in reduction in tubular reabsorption of magnesium and consequently hypomagnesemia. Increased urinary magnesium excretion due to hyperglycemia and osmotic diuresis may contribute to hypomagnesemia in diabetes. Insulin treatment has been shown to correct renal magnesium loss in diabetics. Our results confirm to the recent reports that have not shown any significant associations between sex, age, duration of diabetes and in the present study, serum magnesium concentrations were below the reference range in 34% patients with type2 diabetes (case group) and in 6% of control group. This confirms to the reported prevalence of low plasma magnesium status in type-2 diabetics in several studies, which ranged from 25 to 39%. 4-6 Walti MK et al, reported a prevalence of hypomagnesemia in type 2 diabetics as 37.6% versus 10.9% in nondiabetic controls in a study conducted in Zurich, Switzerland. The reasons for the high prevalence of magnesium deficiency in diabetes are not clear, but may include increased urinary loss, lower dietary intake, or impaired absorption of magnesium compared to healthy individuals. Recently a specific tubular defect in magnesium reabsorption in thick ascending loop of Henle is postulated. This defect results in reduction in tubular reabsorption of magnesium and consequently hypomagnesemia. Increased urinary magnesium excretion due to hyperglycemia and osmotic diuresis may contribute to hypomagnnd obesity with serum magnesium levels. Walti MK et al and present study reported that diabetes treatment (insulin or OHA) did not significantly predict hypomagnesemia. Serum levels of magnesium have been found by several investigators to correlate inversely with fasting blood glucose concentration, post prandial blood glucose and the percentage of HbA1C. The present study also revealed that patients with low serum magnesium levels had poor glycemic control. There was statistically significant association between low serum magnesium levels and higher FBS, PPBS and HbA1C%. Hypomagnesemia is reported to be both a cause and result of poor glycemic control. In addition, magnesium deficiency has been shown to promote insulin resistance in multiple studies. Nadler et al. have reported that insulin sensitivity decreases even in nondiabetic individuals after induction of magnesium deficiency. Conversely, hyperglycemia and osmotic diuresis may lead to increased urinary magnesium excretion and hypomagnesemia in diabetics. Atherosclerosis risk in communities study, a cohort of 15,792 subjects were studied over 7 years and an increasing relative risk of coronary artery disease with decreasing serum magnesium was reported. However, in present study no significant relationship was found between hypomagnesemia and hypertension/IHD/lipid profile. Hypomagnesemia has been reported in patients with diabetic retinopathy, with lower magnesium levels predicting a greater risk of severe diabetic retinopathy. In our study there was a significant difference in prevalence of retinopathy between hypomagneseemic and normomagneseemic diabetics (47.06% versus 19.70%; P =0.0042). Grafton et al. have proposed the inositol transport theory to explain this association, but the exact reason remains obscure. With reference to other diabetic microangiopathies, no significant association was found between prevalence of hypomagnesemia and diabetic neuropathy or diabetic nephropathy. Corsonello et al demonstrated significantly lower serum magnesium in type 2 diabetics with nephropathy compared

to a normoalbuminuric group. Pham PC et al demonstrated that lower (Mg<sup>2+</sup>) is associated with a faster renal function deterioration rate in type2DM patients. Present study also found higher prevalence of diabetic nephropathy in hypomagneseemic diabetics compared to in normomagneseemic diabetics (20.59% versus 15.15%), but difference was statistically insignificant.

## RESULT

Prevalence rate of hypomagnesemia was 34% in the study group. There was significant difference in respect to serum magnesium levels between the cases and controls, with low value in the case group. Diabetic patients with hypomagnesemia did not differ from normomagneseemic diabetics in terms of age, sex, duration of diabetes and BMI. However, diabetic patients with hypomagnesemia had higher values of fasting plasma glucose, post prandial plasma glucose and HbA1c in comparison with the diabetic patients with normomagneseemia. Significantly higher proportion of diabetic patients with hypomagnesemia have found to be suffering from retinopathy as compared to normomagneseemic diabetics

## CONCLUSION

In our study, the prevalence of hypomagnesemia in type 2 diabetics is 34%. Hypomagnesemia is significantly associated with poor glycemic control. Hypomagnesemia is significantly associated with diabetic retinopathy. Hence, diabetic patients with hypomagnesemia must undergo frequent ophthalmic check-ups to rule out retinopathy. Thus according to our study Hypomagnesemia in diabetics can predict the poor glycemic control and diabetic Retinopathy.

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