

The Study of Relationship between Serum Magnesium and Glycated Hemoglobin in Clinically Uncomplicated Type 2 Diabetes Mellitus Patients

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ABSTRACT

Background: Studies have shown that low serum magnesium levels and microalbuminuria are associated with type 2 diabetes mellitus patients, which are the known predictors of risk for cardiovascular disease. The chief objective of this study is to evaluate the relationship between serum magnesium level with glycated hemoglobin and urine albumin levels in clinically uncomplicated type 2 diabetes mellitus patients.

Methodology: During this study, 35 were type 2 diabetes mellitus patients and 20 normal healthy subjects were age and sex matched, were evaluated for serum magnesium, urine albumin, glycated hemoglobin, fasting blood sugar, blood urea and serum creatinine levels.

Results: In 37% of the diabetic patients, magnesium concentrations were below the normal reference value. Microalbuminuria was seen in 60% of the diabetic cases. Serum magnesium level was correlated with glycemic control, as measured by HbA1c.

Conclusion: The findings of this study indicate that lower serum magnesium concentrations and microalbuminuria are common in type 2 diabetics. Low serum magnesium level was attributed to poor glycemic control in diabetics. Serum magnesium levels did not correlate with microalbuminuria among diabetics.

Keywords: Glycated hemoglobin, Microalbuminuria, Serum magnesium, Type 2 diabetes mellitus.

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INTRODUCTION

Studies have shown that low serum magnesium levels and microalbuminuria are associated with type 2 diabetes mellitus patients, which are the known predictors of risk for cardiovascular disease. This is due to decrease in the insulin sensitivity, increasing angiotensin II activity and increasing platelet aggregation. The aim of this study was to correlate serum magnesium levels with glycemic control, risk for cardiovascular and renal involvement in clinically uncomplicated type 2 diabetes mellitus patients. The objective of this study was to screen clinically uncomplicated type 2 diabetes mellitus patients for microalbuminuria and to study the correlation between serum magnesium, with the glycated hemoglobin levels and microalbuminuria in these patients.

Magnesium, the second most abundant divalent cation in the intracellular fluid, serves as a cofactor for about 250 cellular enzymes which are involved in energy metabolism. It also plays an important role in protein and nucleic acid synthesis within the cell.¹ The serum magnesium concentration is about 0.3% of total body magnesium.² So serum magnesium concentration is an insensitive but specific indicator of low magnesium status.²

Plasma magnesium is regulated within a narrow range of 1.7 to 2.4 mg/dl. Kidney is the primary regulator of magnesium balance. Renal magnesium handling is by filtration and reabsorption, even though magnesium secretion has been suggested.³ Over a 24 hours period 3500 mg of magnesium is filtered by the kidney and only 3 to 4% of this amount is excreted into the urine.⁴

The thick ascending limb of the loop of Henle (50–60%) is the principal site of renal handling of magnesium excretion.⁵

Magnesium deficiency may be due to, its decreased uptake and intestinal absorption, mobilization of bone magnesium, urinary leakage and insulin resistance. Magnesium in aging largely results from various pathologies like diabetes and treatment with hypermagnesuric diuretics in elderly persons. Osmotic diuresis caused due to glucosuria in diabetes mellitus results in urinary

loss of magnesium. Among the endocrine and metabolic disorders associated with magnesium deficiency diabetes mellitus is the most common.⁶

Recent studies show that low intracellular free magnesium levels induced by diet or in diabetes mellitus are associated with an increase in platelet aggregation, that can be reversed by supplementing with magnesium.⁷

Literatures have shown the presence of hypomagnesemia in nearly 25% of the diabetic patients.⁸ In the healthy subjects, insulin has shown to stimulate erythrocyte magnesium uptake.⁹ Studies have shown that insulin regulates the intracellular magnesium concentration by stimulating the plasma membrane ATPase pump.¹⁰ The intracellular magnesium deficiency may be due to the insulin resistance. Previous studies⁴ have indicated that insulin mediated glucose uptake is decreased in nondiabetic subjects having a low plasma magnesium concentration, than the subjects with a high magnesium concentration.

Cellular magnesium deficiency alters the activity of membrane bound sodium-potassium ATPase which is involved in maintenance of gradients of sodium, potassium and glucose transport. Low levels of magnesium can reduce secretion of insulin by the pancreas. Some evidence suggests that magnesium may play a role in insulin mediated glucose uptake.^{11,12} Therefore, intracellular free magnesium depletion may be an important link between insulin resistance, hypertension and accelerated cardiovascular disease.⁷

Microalbuminuria is abnormally elevated urine albumin levels, that cannot be detected with the use of a urine analysis dipstick. When albumin is excreted at the rate of about 20 to 200 mg/minute or 30 to 300 mg/24 hours, it is called as microalbuminuria.¹³ Microalbuminuria predicts diabetic nephropathy and an elevated risk of cardiovascular disease. Microalbuminuria is known to be an independent risk marker for early mortality in patients with noninsulin dependent diabetes mellitus.^{14,15} Microalbuminuria is generally associated with decreased glucose uptake, more prevalence of diabetic retinopathy, peripheral vascular disease, hypertension and diabetic neuropathy.¹⁶ Microalbuminuria is an independent risk factor for cardiovascular disease and death in hypertensive patients.¹⁷ Significant reduction in plasma magnesium levels has been found in type 2 diabetic patients with microalbuminuria.

METHODOLOGY

This is a comparative study in which clinically normal and biochemically proven cases of type 2 diabetes mellitus patients were included.

A total of 55 subjects were selected for this study. In this group, 35 were type 2 diabetes mellitus

patients and 20 were controls. The diabetic cases were grouped into having hypomagnesemia and not having hypomagnesemia. The normal serum magnesium level is 1.3 to 2.5 meq/l. The levels below this are considered as hypomagnesemia (Table 1).

Exclusion Criteria

Type 2 diabetes mellitus patients with clinical complications like neuropathy, nephropathy, retinopathy, chronic alcoholism, smoking and vascular complications, subjects having urinary tract infection, congestive heart failure and pregnant women.

Control group included age and sex matched normal healthy volunteers.

Screening was done for controls and type 2 diabetes mellitus patients by taking history, performing clinical examination and analyzing proteinuria using standard urinary analysis dipstick, which measures urinary protein greater than 30 mg/dl or 300 mg/24 hours after taking informed consent. The cases with urinary protein more than 300 mg/24 hours and controls with urinary protein more than 30 mg/24 hours were excluded.

Five milliliter of fasting blood from each group was collected under strict aseptic precautions. Fluoride tube sample was used for blood glucose estimation and ethylenediaminetetraacetic acid (EDTA) sample for glycated hemoglobin estimation. Serum was analyzed for magnesium, urea and creatinine levels.

RESULTS

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) software. Pearson's correlation coefficient, independent t-test for comparing the difference in mean values between different groups was used. p-value less than 0.05 was taken as statistically significant.

In diabetics without hypomagnesemia, 17 of them had a duration history of less than 5 years and the rest of them had duration history of 5 to 12 years. In diabetics with hypomagnesemia, eight of them had duration history of less than 5 years and the remaining had duration from 5 to 12 years as mentioned in Table 2.

The controls included 16 males and four females.

Among 22 diabetics without hypomagnesemia, 14 were males and eight were females. Among 13 diabetics with hypomagnesemia, 12 were males and one female (Table 3).

Table 1: Distribution of cases and controls

Sl. no.	Groups	Number
1.	Control	20
2.	Diabetes without hypomagnesemia	22
3.	Diabetes with hypomagnesemia	13

The low serum magnesium levels seemed to be more predominant among diabetic males when compared with the females (Table 4).

The microalbuminuria seemed to be predominant in the diabetic females when compared to diabetic males (Table 5).

The mean and p-values of all the parameters were measured against different groups (Tables 6 and 7).

The diabetic group without hypomagnesemia and the diabetics with hypomagnesemia, when compared

with the controls showed, lower levels of magnesium and higher levels of glycated hemoglobin and fasting blood sugar which was statistically significant. There was no statistically significant variation in blood urea and creatinine level.

The diabetic group with hypomagnesemia in comparison to the diabetic group without hypomagnesemia showed lower levels of serum magnesium with p-value of < 0.001, which was statistically significant.

The diabetic group with hypomagnesemia in comparison to the diabetic group without hypomagnesemia showed higher levels of glycated hemoglobin with p-value of < 0.05 which was statistically significant. It was observed that, serum magnesium levels are lower among diabetics and coincides with the glycated hemoglobin levels rather than fasting blood sugar levels.

Microalbuminuria, magnesium levels among diabetics with hypomagnesemia and diabetic group without hypomagnesemia did not show any significant correlation.

Table 2: Distribution of cases as per duration of diabetes

Duration of type-2 diabetes mellitus	Diabetes without hypomagnesemia (No. of subjects)	Diabetes with hypomagnesemia (No. of subjects)
Less than 5 years	17	8
5-12 years	5	5
Total no. of subjects	22	13

Table 3: Basic characteristics of cases and controls

Characteristics	Control	Diabetes without hypomagnesemia	Diabetes without hypomagnesemia
Age (mean)	44.8	50.04	50.61
Sex ratio (M:F)	4:1	7:4	12:1
Diabetes duration in years (mean \pm SD)	—	43 \pm 2.2	5.1 \pm 3

Table 4: Hypomagnesemia among male and female diabetics

Sex	Number among total diabetics	Number among diabetics with hypomagnesemia
Male	26	12
Female	9	1

Table 5: Urine microalbumin among cases and controls

Sex	Number	Microalbuminuria (mg/dl)
Male	26	118.23
Female	9	141.33

Table 6: Magnesium, glycemic and renal parameters among cases and controls

Sl. no.	Group	No.	Mg	GHB	FBS	Micro	Urea	Creat
1.	Control	20	2.46 \pm 0.23	5.60 \pm 0.38	88.6 \pm 15.14	—	22.6 \pm 8.02	1.03 \pm 0.23
2.	Diabetes without hypomagnesemia	22	1.80 \pm 0.34	7.06 \pm 0.92	127.1 \pm 49.87	91.26 \pm 109.68	25.7 \pm 9.1	0.95 \pm 0.30
3.	Diabetes with hypomagnesemia	13	1.12 \pm 0.10	8.11 \pm 1.21	121.4 \pm 30.63	158.3 \pm 107.34	23.4 \pm 8.30	0.88 \pm 0.31

Mg: Magnesium; GHB: Glycated hemoglobin; FBS: Fasting blood sugar; Micro: Microalbuminuria; Creat: Creatinine

Table 7: Statistical comparison of magnesium, glycemic and renal parameters between cases and controls

Group	Mg	GHB	FBS	Micro	Urea	Creat
Control vs diabetes without hypomagnesemia	< 0.001	< 0.001	0.002	0.001	0.260	0.434
Control vs diabetes with hypomagnesemia	< 0.001	< 0.001	< 0.001	< 0.001	0.787	0.118
Diabetes without hypomagnesemia vs diabetes with hypomagnesemia	< 0.001	0.006	0.710	0.086	0.470	0.431

Mg: Magnesium; GHB: Glycated hemoglobin; FBS: Fasting blood sugar; Micro: Microalbuminuria; Creat: Creatinine

handling in diabetic individuals.¹⁷ In diabetes, there is a direct relationship between serum magnesium level and cellular glucose disposal which is independent of insulin secretion. This change in glucose disposal has been shown to be related to increased sensitivity of the tissues to insulin in presence of adequate magnesium levels.⁷ Increased urinary magnesium excretion due to hyperglycemia and osmotic diuresis may contribute to hypomagnesemia in the diabetic patients.

CONCLUSION

Low serum magnesium levels were observed among 37% of type 2 diabetes mellitus patients. Microalbuminuria was present in 60% of type 2 diabetes mellitus patients. Low serum magnesium levels correlated with poor glycemic control as revealed by glycated hemoglobin levels among type 2 diabetics. There was no correlation between low serum magnesium level and microalbuminuria among type 2 diabetics.

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