Original Article

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Serum Magnesium Levels in Type 2 Diabetic Patients with Microalbuminuria and Normoalbuminuria

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Abstract

Background: Approximately, one-third of patients with Type 2 diabetes have hypomagnesemia mainly caused by enhanced renal excretion. Magnesium (Mg) deficiency is associated with the poor glycemic control, and Mg supplementation improves insulin sensitivity. Various studies have shown associations between hypomagnesemia and various complications of Type 2 diabetes, including neuropathy, retinopathy, foot ulcers, and albuminuria. In patients with diabetes mellitus who develop microalbuminuria, serum Mg was lower when compared with normoalbuminuric patients. Investigating for serum Mg levels and prompt correction may prevent further complications.

Objectives: The present study was done to know the status of serum Mg in microalbuminuric and normoalbuminuric Type 2 diabetic patients.

Materials and Methods: Nearly, 100 patients of Type 2 Diabetes mellitus attending K R Hospital OPD/inpatients were grouped into equal groups of 50 patients into microalbuminuria and normoalbuminuria. Fasting blood sugar (FBS), postprandial blood sugar (PPBS), HbA1C, renal function test, spot urine albumin creatinine ratio (SUACR), serum electrolytes including Mg levels were compared in both groups.

Results: About 6% of microalbuminuria had hypomagnesemia, and one patient had hypermagnesemia. FBS, PPBS, HbA1c, and SUACR were high and significant in microalbuminuria suggestive of poor glycemic control retinopathy was found to be higher in microalbuminuria group 26% when compared to normoalbuminuria 6%.

Interpretation and Conclusion: In our study, we found that low Mg levels were significantly associated with poor glycemic control and microalbuminuria levels were higher when compared to patients with normal Mg levels. Retinopathy was also significantly associated with hypomagnesemia. Therefore, screening for serum Mg levels in Type 2 diabetes and its correction may help in achieving better glycemic control, which can prevent further diabetic complications.

Key words: Albuminuria, Magnesium, Type 2 diabetes mellitus

INTRODUCTION

Magnesium (Mg) is the fourth most abundant cation in the human body and plays a key role in many fundamental biological processes including metabolism and DNA synthesis. Mg deficiency has been shown to cause endothelial cell dysfunction, inflammation, and oxidative stress, which are major contributors to atherosclerosis.[1] Mg and Type 2 Diabetes mellitus (DM) have a close relationship. Approximately one-third of subjects with Type 2 DM have hypomagnesemia mainly caused by enhanced renal excretion.[2] Mg deficiency is associated with poor glycemic control and Mg supplementation improves insulin sensitivity.[3]

There is substantial evidence of associations between hypomagnesemia and various complications of Type 2 DM such as neuropathy, retinopathy, foot ulcers, and

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albuminuria.[4] The serum Mg in Diabetes mellitus with microalbuminuria was lower when compared with normoalbuminuria subjects.[5-12]

Hence, this study was done to know the status of serum Mg in Type 2 DM subjects with microalbuminuria and normoalbuminuria and its relation to diabetic microvascular complications.

The aims and objectives of the study are:

1. To study the serum Mg levels in Type 2 DM with microalbuminuria and normoalbuminuria subjects.
2. To correlate microalbuminuria and serum Mg levels in diabetic nephropathy.

MATERIALS AND METHODS

The subjects of this study were Type 2 DM, attending to medical OPD/admitted to wards in K R Hospital, Mysore. A comparative study was done using a sample size of 100 Type 2 diabetic subjects using purposive sampling method, from December 2012 to August 2014. Exclusion criteria included hypertension, acute/chronic diarrhea, chronic alcohol consumption, acute pancreatitis, loop/thiazide diuretics, and other nephrotoxic drugs.

Method of Study

Data were collected using a pre-tested proforma meeting the objectives of the study. The cases for the study were selected in accordance with the above mentioned inclusion and exclusion criteria. The purpose of the study was explained to the patient, and informed consent was obtained. Cases with Type 2 DM (as per ADA 2012 Guidelines) were selected and categorized into microalbuminuria and normoalbuminuria based on spot urine protein creatinine ratio. The following investigations such as fasting blood sugar (FBS), postprandial blood sugar (PPBS), HbA1c, fundus examination of eye, urine routine, blood urea, and serum creatinine, electrolytes such as sodium, potassium, chloride, and Mg were also carried out.

Baseline characteristics of the study participants were expressed in percentage. Data were analyzed statistically using descriptive statistics, contingency coefficient analysis, and Student *t*-test. $P < 0.05$ was considered as statistically significant. IBM SPSS (Statistical Package for the Social Sciences) version 20 and Excel were used for data analysis.

RESULTS

About 100 subjects of Type 2, diabetes were grouped into microalbuminuria and normoalbuminuria based on spot urine albumin creatinine ratio (SUACR). Serum Mg levels were measured in both groups (Table 1).

The mean age (years) in microalbuminuria and normoalbuminuria were 53.06 ± 10.93 and 56.12 ± 11.754, respectively. About 66% were males and 34% were females in both groups. Mean FBS (mg/dL) in normoalbuminuria and microalbuminuria were 118.36 ± 40.43 and 164.82 ± 40.39 ($P < 0.01$), and mean PPBS (mg/dl) in microalbuminuria were 161.7 ± 49.43 and 226.52 ± 68.64, respectively ($P < 0.001$). The mean HbA1c (%) in normoalbuminuria and microalbuminuria were 6.37 ± 0.74 and 7.77 ± 1.62, respectively ($P < 0.01$) (Figure 1). The mean SUACR (mg/g) in normoalbuminuria and microalbuminuria were 20.66 ± 4.89 and 44.48 ± 12.64 ($P < 0.01$).

Of 50 microalbuminuria group 3 participants had hypomagnesemia (mean 2.09 ± 0.28 mg/dl) and 1 had hypermagnesemia (2.6 mg/dl). Mg levels were normal in normoalbuminuria group. Hypermagnesemia was seen in one subject of microalbuminuria group, where the serum Mg level was mildly elevated (2.6 mg/dl), and serum

Table 1: Characteristics of study group

Variables	Normoalbuminuria	Microalbuminuria
No. of subjects	50	50
Mean age (years)	56.12±11.754	53.06±10.93
Sex (%)	Male: 66 Female: 34	Male: 66 Female: 34
Mean FBS (mg/dl)	118.36±40.43	164.82±40.39 (*P*<0.01)
Mean PPBS (mg/dl)	161.7±49.43	226.52±68.64 (*P*<0.001)
HbA1c (%)	6.37±0.74	7.77±1.62 (*P*<0.01)
Hypomagnesemia	-	6%
Mean serum Mg levels (mg/dl)	2.086±0.21	2.09±0.28
Mean SUACR (mg/g)	20.66±4.89	44.48±12.64 (*P*<0.01)
Retinopathy (%)	6	26

FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, SUACR: Spot urine albumin creatinine ratio, Mg: Magnesium

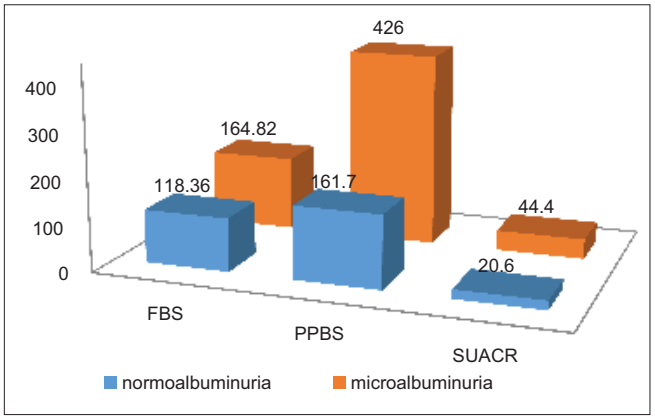

Figure 1: Comparison of normoalbuminuria and microalbuminuria

creatinine was also found to be elevated (1.5 mg/dl). On subsequent days of follow-up, serum creatinine had an increasing trend. USG abdomen suggested of acute on chronic kidney disease (CKD). Hence, it can be assumed that hypermagnesemia was seen due to CKD. The mean value of FBS, PPBS, and HbA1c is higher among the group with serum Mg < 1.7 mg/dl. The mean FBS of both the groups, i.e., serum Mg < 1.7 mg/dl and serum Mg 1.7-2.4 mg/dl is statistically different with *P*-value 0.047. The mean PPBS of both the groups serum Mg < 1.7 mg/dl and serum Mg 1.7-2.4 (mg/dl) is statistically different with *P*-value 0.044. The mean HbA1c of both the groups serum Mg < 1.7 mg/dl and serum Mg 1.7-2.4 (mg/dl) is statistically different with *P*-value 0.022 (Table 2 and Figure 2).

Retinopathy was found in 13 (26%) subjects of microalbuminuria group. The mean serum Mg (mg/dl) levels in microalbuminuria with retinopathy (1.94 ± 0.38) was lower than microalbuminuria without retinopathy (2.14 ± 0.16) (*P* = 0.0112).

Table 2: Microalbuminuria group

Variables	Microalbuminuria group	
	Serum Mg 1.7-2.4 mg/dl	Serum Mg<1.7 mg/dl
No. of subjects	46	3
Mean value		
FBS (mg/dl)	161.41±40.1	209.33±18.9
PPBS (mg/dl)	220.24±67.98	302.33±5.13
HbA1c (%)	7.57±1.52	9.7±1.04
SUACR (mg/g)	43.2±11.8	52.33±3.79
Serum Mg (mg/dl)	1.4±0.1	2.12±0.17

FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, SUACR: Spot urine albumin creatinine ratio, Mg: Magnesium

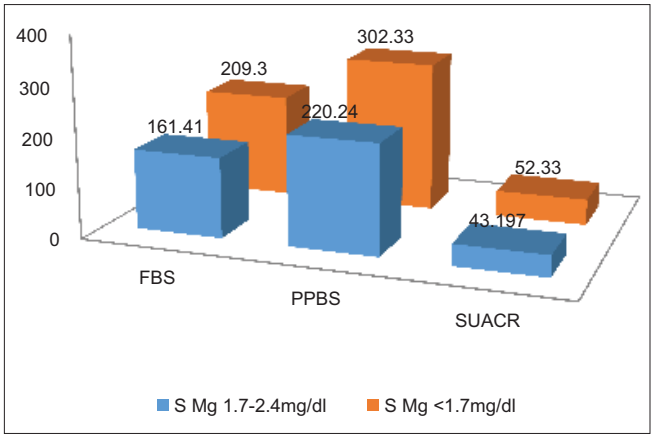

Figure 2: Comparison of fasting, postprandial blood sugar levels, and albuminuria in microalbuminuria with magnesium levels

DISCUSSION

Hypomagnesemia can be seen in Type 2 DM. It was found that Type 2 DM subjects with hypomagnesemia were more prone for complications. In this study, 100 subjects with Type 2 DM were grouped into microalbuminuria (50 subjects) and normoalbuminuria (50 subjects). Serum Mg levels were studied in both groups.

None of the subjects in normoalbuminuria group had hypomagnesium whereas in microalbuminuria group, 3 (6%) subjects had hypomagnesemia, and 1 (2%) patient had hypermagnesemia. In a study conducted by Dasgupta *et al.*, hypomagnesemia was seen in 11% of Type 2 DM subjects, 8.8% in normoalbuminuria, and 13.5% in microalbuminuria. In the present study, the mean serum Mg levels in normoalbuminuria and microalbuminuria were 2.086 ± 0.21(mg/dl) and 2.0 ± 0.24 (mg/dl), respectively. In a study conducted by Corsonello *et al.*, diabetic subjects with microalbuminuria or clinical proteinuria showed a significant decrease in serum ionized Mg with respect to normoalbuminuria group (normoalbuminuria: 0.45 ± 0. 02 mmol/l; microalbuminuria: 0.36 ± 0.05 mmol/l, *P* < 0.001; clinical proteinuria: 0.35 ± 0.04 mmol/l, *P* < 0.001).

The exact cause of hypomagnesemia is unknown, but an increased urinary loss of Mg may contribute to it. Some studies revealed that hyperglycemia contribute to hypomagnesemia by causing depression in the net tubular reabsorption of Mg.[13]

One of the potential pathophysiological mechanisms linking serum Mg to microalbuminuria is an amplification of insulin resistance. It was said that low serum Mg plays an important role in the pathogenesis of insulin resistance. Mg can function as a mild, natural calcium antagonist. Hence, the level of intracellular calcium is increased in Mg deficiency subjects. This increased intracellular calcium may compromise the insulin responsiveness of adipocytes and skeletal muscles leading to the development of insulin resistance.[13] Another study has also found that insulin deficiency or insulin resistance can affect the tubular absorption of Mg, leading to hypomagnesemia in DM subjects.[14] Finally, a vicious circle formed by mutual influence between insulin resistance and hypomagnesemia results in aggravation of insulin resistance which can increase the risk of microalbuminuria.[15]

Other hypothesis such as oxidative stress is becoming increasingly recognized as an important causative factor for microalbuminuria.[16] Mg has been reported to possess antioxidant property.[17] Hence, oxidative stress may be one of the mechanisms that underlie the association between low serum Mg and microalbuminuria. Study has also shown that Mg intake and serum Mg concentration were

inversely associated with systemic inflammation markers, which also play a crucial role in the pathogenesis of microalbuminuria.[18,19]

In the present study, microalbuminuria group had poor glycemic control. The mean FBS, PPBS, and HbA1c in microalbuminuria were 164.82 ± 40.9 mg/dl, 226.52 ± 68.64 mg/dl, and 7.77 ± 1.62 (%), respectively. In a study conducted by Prabhodh *et al.*, mean FBS, PPBS, and HbA1c were 184.42 ± 40.61 mg/dl, 270 ± 38.66 mg/dl, and 8.972 ± 1.82%.

In the present study, the mean FBS, PPBS, and HbA1C in microalbuminuria with hypomagnesemia group, when compared in subjects with microalbuminuria with normal Mg levels was statistically significant ($P < 0.01$). However, microalbuminuria levels in the above group were not significant. The explanation for nonsignificance of microalbumin levels, in the present study, could be due to low sample size and low incidence of hypomagnesemia.

In the present study, retinopathy was found to be higher in microalbuminuria group 26% (13 subjects) when compared to normoalbuminuria 6% (3 subjects). In a study conducted by Padmaja *et al.* (SN-DREAMS, report 12), retinopathy was seen in 31% and 14.1% of microalbuminuria and normoalbuminuria, respectively.

In the present study, the mean serum Mg levels in microalbuminuria with and without retinopathy are 1.94 ± 0.38 mg/dl and 2.14 ± 0.16 mg/dl, respectively ($P < 0.0112$). In study conducted by Dipankar *et al.*, mean Mg levels in microalbuminuria with and without retinopathy were 1.38 ± 0.39 and 2.02 ± 0.29 ($P < 0.001$).[20]

CONCLUSIONS

In the present study, hypomagnesemia was present in 6% of microalbuminuria group. These cases had poor glycemic control when compared with (1) normoalbuminuria group and (2) microalbuminuria group with normal Mg levels. The mean microalbuminuria levels in hypomagnesemia were higher when compared in subjects with normal Mg levels. Retinopathy was present in all hypomagnesemia subjects. Above findings suggest that hypomagnesemia in Type 2 DM are associated with poor glycemic status and microvascular complications.

Hypomagnesemia is related to the glycemic status of DM patient. In such subjects, diabetic complications are invariably present. Several studies have proved correction of hypomagnesemia in DM subjects achieved better glycemic control and reduced risk of complications. Hence, it is essential to investigate for serum Mg status in poorly controlled DM or with associated complications.

In the present study, low incidence of hypomagnesemia in microalbuminuria group may be due to low sample size. Further studies with large sample size are required to prove a definite role of hypomagnesemia in diabetic nephropathy and its correction to prevent progression to end-stage renal disease.

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