



Hypomagnesaemia in Diabetes

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ABSTRACT

Background: Relationship between Diabetes Mellitus and minerals has been reported frequently. Recent studies have demonstrated reduced levels of serum magnesium in diabetes mellitus especially in poorly controlled patients. Clinically, there are significant data linking hypomagnesemia to various diabetic micro- and macrovascular complications. Therefore, Mg supplementation may provide a new therapeutic approach to reducing vascular disease in patients with diabetes.

Objective: To study the levels of serum magnesium in diabetic patients in a tertiary hospital in North Kerala.

Methodology: A hospital based cross sectional study was done in all diabetic patients attending the out-patient and in-patient facilities of Department of Internal Medicine at a tertiary hospital in North Kerala between January 1st and March 31st 2014. Results: In the study hypomagnesemia was seen in 15.7% of the participants. No significant difference was found in Serum Magnesium neither between genders (p 0.35) nor age (p 0.057). Serum magnesium levels was not seen to have any significant association with duration of diabetes or type of treatment. Significant relation could not be established with other complications associated with type 2 Diabetes Mellitus like hypertension and dyslipidemia. A significant negative correlation was seen between serum magnesium and Fasting blood sugar ($p < 0.001$) as well as HbA1c values ($p < 0.001$). In the present study it was observed that there was significant difference in the level of serum magnesium among controlled and uncontrolled diabetics (p 0.002).

Conclusion: Hypomagnesemia is common in diabetes and negatively correlated with fasting blood sugar but not related to duration or type of treatment taken.

Keywords: Hypomagnesaemia, Diabetes Mellitus.

INTRODUCTION

Relationship between Diabetes Mellitus and minerals has been reported frequently.^{1,2} Decreased levels of Zn and Mg are associated with increased values of HbA1c. These findings suggest that impaired metabolism of trace elements are involved in pathogenesis of diabetes by participation in oxidative stress.³

Recent studies have demonstrated reduced levels of serum magnesium in diabetes mellitus especially in poorly controlled patients.⁴ This reduction in magnesium level has been attributed to renal losses, decreased intestinal absorption and redistribution of Magnesium from plasma into blood cells caused by insulin effect.⁵ Hypermagnesuria results specifically from a reduction in tubular absorption of magnesium.⁶ Use of diuretics among patients with diabetes may also contribute to magnesiuria.⁷ Finally, the common use of antibiotics and antifungals such as aminoglycosides and amphotericin in patients with diabetes may also contribute to renal Mg wasting.⁸ Although many authors have suggested that diabetes per se may induce hypomagnesemia, others have reported that higher Mg intake may confer a lower risk for type 2 diabetes.⁹⁻¹¹

Hypomagnesemia, has been reported to occur in 13.5 to 47.7% of non-hospitalized patients with type 2 diabetes compared with 2.5 to 15% among their counterparts without diabetes.¹²⁻¹⁴ The wide range in the reported incidence of hypomagnesemia most likely reflects the difference in the definition of hypomagnesemia, techniques in Mg measurements and the heterogeneity of the selected patient cohort.

Type 2 diabetes is on track to become one of the major global health challenges of the 21st century. Primary prevention remains the major strategic approach. Clinically, there are significant data linking hypomagnesemia to various diabetic micro- and macrovascular complications. Hypomagnesemia has been demonstrated in patients with diabetic retinopathy, with lower magnesium levels predicting a greater risk of severe diabetic retinopathy.⁶ Magnesium depletion has been

associated with multiple cardiovascular implications like arrhythmogenesis, vasospasm and hypertension and platelet activity.⁵ Magnesium deficiency may have some effects on the development of diabetic vascular complications with other risk factors like systemic hypertension and dyslipidemia.⁶ As per some studies, changes in Magnesium levels can affect Insulin action which is mainly attributed to the changes in decreased activity of insulin tyrosine kinase.¹⁵ Long term hyperglycemia in patients with type 2 diabetes increases the risk of chronic complications such as nephropathy, which may exacerbate hypomagnesemia and aggravate the complications.¹⁶

Serum Mg concentration between 2.0 and 2.5 mg/dl in patients with diabetes, may be favorable. Although the correction of low serum Mg levels has never been proved to be protective against chronic diabetic complications, intervention is justified because hypomagnesemia has been linked to many adverse clinical outcomes. Therefore, Mg supplementation may provide a new therapeutic approach to reducing vascular disease in patients with diabetes.¹⁷ In addition, Mg supplementation is inexpensive and, with the exception of diarrhea, a relatively benign medication. Nonetheless, close observation must be given to those with renal insufficiency.

The present study is to evaluate serum magnesium levels in Diabetic patients in a tertiary hospital in North Kerala. The present study has particular relevance in Kerala since no study has been reported to determine the prevalence of hypomagnesemia among diabetics.

METHODOLOGY

A hospital based cross sectional study was done in all Diabetes Mellitus patients attending the out-patient and in-patient facilities of Department of Internal Medicine at a tertiary hospital in North Kerala between January 1st and March 31st 2014.

Inclusion Criteria: Already diagnosed diabetics on treatment even if at the time of inclusion they do not meet the glycaemic criteria for diagnosis;

Symptoms of Diabetes Mellitus plus a Random Blood glucose concentration ≥ 200 mg/dL; Fasting blood glucose ≥ 126 mg/dl and or 2 hour Post Prandial glucose ≥ 200 mg/dL.

Exclusion Criteria: Patients on Diuretic/ amphotericin/ Protein Pump Inhibitors therapy/ Iatrogenic magnesium administration

Data was collected using a pre-tested structured questionnaire and clinical examination findings were recorded. Relevant investigations including fasting blood sugar, glycated hemoglobin and serum magnesium were done. Hypomagnesemia was defined as a serum Mg concentration < 1.6 mg/dl. Glycated hemoglobin values 6-7 means good control, between 7-8 means diabetes under moderate control and values more than 8 indicates poor control. Descriptive analysis was done.

RESULTS

A total of 70 diabetic patients were studied during the study period. Half (51.4%) of the subjects were males. Table 1 shows the baseline characteristics of these 70 subjects.

The age of the study population ranged between 36 and 95 with a mean age of 55.93 years (+10.03). Three fourths (75%) are aged between 50 – 69 years. Very few (4.3%) had gone beyond high school education. Most (98.6%) were currently married and one person was widowed. Half of the diabetic subjects (54.3%) reported having used some type of tobacco products and 10% reported alcohol consumption. Twenty three (32.9%) subjects gave history of diabetes in their families. The duration of diabetes was found to be between 1 and 30 years with a mean duration of 9.71 years (+ 6.125). Thirty one subjects (44%) were diabetic for the past 10 years and another 35 (50%) for the past 10 – 20 years. Only 3 were diabetic for more than 20 years. No relation was seen between duration of diabetes and Serum Magnesium (p 0.736).

Except for 2 on dietary control alone, the remaining 68 were on some kind of medications. Table 2 depicts the treatment pattern followed by these subjects. Nearly three-fourths (72.86%)

were on oral hypoglycemic agents and a few (17.14%) were on both OHA and Insulin. No significant difference was seen in serum magnesium between the treatment modality the patient is taking (p 0.855). Table 3 shows the proportion of subjects having other comorbidities. A quarter (24.28%) had hypertension and 8.5% had history of coronary artery disease and peripheral vascular disease each.

Table 4 depicts the distribution of the study participants based on of Fasting blood sugar values, Serum magnesium levels and control based on HbA1c level. The table also gives the mean (\pm SD) of these variables. Most (82.9%) of the subjects had a fasting blood sugar value > 126 mg/dL. The blood sugar levels of majority (62.9%) were found to be under poor control based on HbA1c level. Hypomagnesemia (< 1.6 mg/l) was found in 15.7% (10) subjects.

The mean FBS level was found to be higher in the hypomagnesemic group when compared to the normomagnesemic group as shown in Table 5. This difference was found to be significant (p 0.003). A negative correlation was found between serum Magnesium and Fasting Blood Sugar ($r = -0.349$; p 0.003) ie as FBS value increases the S.Magnesium will decrease.

Similarly, the mean HbA1c value was higher in hypomagnesemic patients when compared to patients with normal magnesium levels (Table 5). The finding that patients with hypomagnesemia have poorly controlled diabetes has been found to be significant (p 0.002). A negative correlation was found between HbA1c and serum Magnesium (-0.296 ; p 0.013) ie as HbA1c increases the S.Magnesium will decrease.

No significant significant difference was found in Serum Magnesium levels between males (mean S.Mg 1.89 + 0.35) and females (mean S.Mg 1.82 + 0.281) [t 0.941; p 0.35].

Table 1: Baseline characteristics of study subjects

Baseline characteristics	Number	Percentage	
AGE	30 -39 years	5	7.1
	40 – 49 years	9	12.9
	50 – 59 years	33	47.1
	60 -69 years	20	28.6
	≥70 years	3	4.3
EDUCATIONAL QUALIFICATIONS	Illiterate	5	7.1
	Lower primary	9	12.9
	Upper primary	33	47.1
	High school	20	28.6
	Graduation	3	4.3
OCCUPATIONAL STATUS	Unemployed	5	7.1
	Unskilled	35	50
	Semiskilled	19	27.1
	Skilled	8	11.4
	Professional	3	4.3
TOTAL	70	100	

Table 2: Treatment pattern of the diabetic patients

Treatment pattern	Number	Percentage
OHA	51	72.86%
Insulin	5	7.14%
both Insulin and OHA	12	17.14%
dietary restriction	2	2.85%

Table 3: Co-morbidity profile

Comorbidity	Number	Percentage
Hypertension	17	24.28%
Renal Disease	2	2.86%
Peripheral Vascular D/S	6	8.57%
Cva	3	4.28%
Coronary Artery D/S	6	8.57%
Thyroid D/S	2	2.86%

Table 4: laboratory parameters

Variable	Number (%)	Mean (\pm SD)	Min.value	Max.value
Serum magnesium				
<1.6 mg/l	11 (15.7)	1.86 (\pm 0.32)	1	3
- 2.3 mg/l	53 (75.7)			
>2.3mg/l	6 (8.6)			
Fasting Blood Sugar				
80-110 (normal)	3 (4.3)	169.37 (\pm 48.77)	100	295
111-126 (impaired)	9 (12.9)			
>126 (hyperglycemic)	58 (82.8)			
HbA1c				
5.1-6 (normal)	2 (2.9)	8.74 (\pm 1.59)	5	13
6-7 (good control)	6 (8.6)			
7-8 (moderate control)	17 (24.3)			
>8 (poor control)	44 (62.9)			

Table 5: Fasting blood sugar/ HbA1c and status of serum magnesium

Serum magnesium status	Variable	Frequency	Mean	SD	't'	Significance
Hypomagnesemia	FBS	10	211.00	60.72	3.091	0.003
Normomagnesemia		60	162.43	43.32		
Hypomagnesemia	HbA1c	10	10.14	1.88	3.191	0.002
Normomagnesemia		60	8.51	1.43		

DISCUSSION

Hypomagnesemia is a common feature in patients with Type 2 Diabetes Mellitus. This study was designed to find out the serum magnesium levels and its influence on Type 2 diabetics and how it is associated with duration, treatment modalities and complication of the disease. The present study included 70 Diabetes Mellitus patients.

In this study hypomagnesemia was seen in 15.7% of the participants and this falls within the range seen in another study (13.5- 47.7%) among non-hospitalized patients with type 2 diabetes.¹²⁻¹⁴ The study conducted by AP Jain *et al*¹⁸ in 1986 had 32% diabetic subjects below 1.6mg/dl.

In the present study no significant difference was found in Serum Magnesium between males and females [t 0.941; p 0.35]. Independent studies have reported a higher incidence of hypomagnesemia in women compared with men, at a 2:1 ratio.¹⁹⁻²¹ In addition, men with diabetes may have higher ionized levels of Mg.²²

In the present study no significant correlation was observed between age of the cases and serum magnesium levels (Pearson correlation -0.207; p=0.057). Previous studies by Mishra S *et al*²³ and Nasri H *et al*²⁴ also noted significant negative correlation both in cases as well as in controls depicting as the age advances plasma magnesium level decreases.

In our study a significant negative correlation existed as for Fasting blood sugar and HbA1c values with serum magnesium (p<0.001). As the plasma fasting glucose levels and HbA1c increases the serum magnesium levels dropped. Sharma A *et al*⁵, Mishra S *et al*²³ and few other recent studies also established the same i.e. there is a negative correlation between fasting blood sugars and HbA1c with plasma magnesium.

In the present study no significant association with duration of diabetes and serum magnesium levels was observed which was statistically analyzed with ANOVA. It was noticed that as the duration of diabetes increases the serum magnesium values showed a low normal values. Sharma A *et al*⁵, Mishra S *et al*²³, Walti MK *et al*²⁰ also had similar

observations and came to a conclusion of an inverse correlation of duration of diabetes and serum magnesium.

There was no significant difference noted when analyzed serum magnesium levels between OAD and insulin treated patients with which was against the observation obtained by previous studies by Yajnik CS *et al*²⁵ and AP Jain *et al*.¹⁸

In the present study it was observed that there was significant difference in the level of serum magnesium among controlled and uncontrolled diabetics (p0.002). Observation made in recent studies by Sharma A *et al*, Mishra S *et al*²³ and Nasri H *et al*²⁴ proved the same. Earlier studies done by Nagase N *et al*²⁶ also had similar findings. Numerous studies have reported an inverse relationship between glycemic control and serum Mg levels²⁷⁻²⁹ similar to our findings in this study (-0.296; p 0.013).

Other associated complications of type 2 Diabetes Mellitus like hypertension and dyslipidemia was also analyzed with serum magnesium but could not establish significant correlation. But recent studies by Sharma A *et al*⁵, Mishra S *et al*²³, Nasri H *et al*²⁴ showed a significant inverse correlation of serum magnesium with lipids and hypertension.

CONCLUSION

In this study hypomagnesemia was seen in 15.7% of the participants. No significant difference was found in Serum Magnesium between the genders (p 0.35) nor between age of the cases and serum magnesium levels (p=0.057). In the present study no significant association with duration of diabetes and serum magnesium levels. There was no significant difference noted when analyzed serum magnesium levels between OAD and insulin treated patients. Other associated complications of type 2 Diabetes Mellitus like hypertension and dyslipidemia was also analyzed with serum magnesium but could not establish significant relation.

In our study a significant negative correlation existed as for Fasting blood sugar and HbA1c

values with serum magnesium ($p < 0.001$). In the present study it was observed that there was significant difference in the level of serum magnesium among controlled and uncontrolled diabetics ($p = 0.002$).

LIMITATIONS OF THE STUDY

Plasma magnesium is relatively an insensitive measurement of magnesium status of the body because major bulk of magnesium lies within the cell. Intra erythrocyte magnesium and urinary magnesium are not done in the present study due to lack of facility and financial burden.

There is no follow up in this study hence change in magnesium states with respect to improvement or worsening of diabetic state in the long run is not studied.

This study focuses on magnesium levels in type 2 Diabetes mellitus at a given point but not on therapeutically correcting hypomagnesemia or otherwise not correcting in the future course of the disease and its outcome.

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