

Fasting Serum Magnesium Level and its Association with Type 2 Diabetes Mellitus and its Chronic Complications

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ABSTRACT

Introduction

Diabetes mellitus is one of the most common metabolic disorders. Hypomagnesemia is a common feature in patients with type 2 diabetes mellitus (T2DM). This study aims to assess the serum magnesium level and its association with chronic complications in patients with T2DM.

Methods

A total of 173 T2DM patients at Tribhuvan University Teaching Hospital were evaluated from July 2016 to August 2017. Patients were investigated for fasting serum magnesium level, fasting plasma glucose (FPG), postprandial plasma glucose (PPG), Glycosylated haemoglobin (HbA1c) and also target organ evaluation for diabetes. Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 20.

Results

Hypomagnesemia was found in 86 patients out of the 173 enrolled patients. Observations revealed significant association between hypomagnesemia and various microvascular complications viz. retinopathy ($p=0.001$), neuropathy ($p<0.001$) and nephropathy ($p<0.001$). There was also a significant association between hypomagnesemia and FPG ($p=0.008$) and HbA1c ($p=0.009$). The overall prevalence of hypomagnesemia among T2DM patients was 49.7% and the prevalence of hypomagnesemia was significantly higher (74%) among diabetic patients with microvascular complications ($p=0.001$) compared to diabetics with no microvascular complications.

Conclusion

There was a high prevalence of hypomagnesemia among T2DM patients. A significant association was seen between hypomagnesemia and various microvascular complications like retinopathy, neuropathy and nephropathy. Routine surveillance and timely treatment of hypomagnesemia is advisable for patients with T2DM.

Keywords

Diabetic retinopathy; glycosylated haemoglobin; hypomagnesemia; type 2 diabetes mellitus

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INTRODUCTION

Diabetes is a metabolic disease causing hyperglycemia that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.¹ Between 2010 and 2030, developing countries will have 69% increase in numbers of adults with diabetes while developed countries will have 20% increase.²

Hypomagnesemia is a common feature in patients with type 2 diabetes mellitus (T2DM) with prevalence ranging from 14% to 48%.³ Diabetic complications and rapid disease progression in hypomagnesemia are due to inhibition of glucose transporter type four translocation, reduced pancreatic β -cell activity, increased insulin resistance, altered lipid metabolism, induced oxidative stress and impaired antioxidant system of endothelial cells.⁴

This study aimed to assess the serum magnesium level in patients with T2DM and its association with chronic complications of diabetes mellitus.

METHODS

This descriptive cross-sectional study was performed in the medical ward and Outpatient Department of Tribhuvan University Teaching Hospital from July 2016 to August 2017. Ethical approval was taken from the Institutional Review Committee (IRC) of the Institute of Medicine, and informed written consent was obtained from all enrolled patients.

The inclusion criteria of the study were: i) patients with a diagnosis of T2DM as per ADA criteria,¹ ii) Patients with treatment with dietary restrictions and / or oral hypoglycemic agents (OHA) and / or insulin for at least 6 months. The exclusion criteria were the patients with: i) Gastrointestinal disorders (chronic diarrhea, Gastrointestinal fistula and malabsorption), ii) Impaired renal function (chronic renal disease), iii) Alcoholic pancreatitis, iv) Diuretic therapy, v) Drug (magnesium containing antacids).

Sample size was calculated using the formula, $n = (Z^2 \cdot P \cdot Q) / L^2$, where, Z is the value at 95% confidence level (i.e. 1.96), P is the prevalence of diabetes mellitus (25%),⁵ Q is the probability of non-occurrence of p (i.e. 1-P) and L is the estimated error (7% or 0.07). This gives the sample size of 172.

Serum Magnesium (Mg) was measured by automated analyzer Biotechnica Instruments S.P.A via Licenza, 18 00156 Rome, Italy, model BT3500 in the fasting state. The normal level of serum magnesium is within the range as 1.7-2.1 mg/dL. Laboratory parameters included HbA1c, Fasting Plasma Glucose (FPG), and two hour PPG.

Common diabetes related complications were searched which included macro-vascular

complications like coronary artery disease (CAD), and microvascular complications like diabetic retinopathy, diabetic neuropathy, and diabetic nephropathy. Sensory and motor neuropathy was diagnosed based on history and clinical examination. Autonomic symptoms were assessed with blood pressure and resting heart rate.⁶

Presence of albumin in the urine (microalbuminuria), the earliest sign of diabetic nephropathy, is defined as the mean urine albumin concentration of 30-300 mg/mL detected by nephelometry. Macroalbuminuria is defined as urine albumin >300 mg/dL.⁷

Diabetic retinopathy was classified based on funduscopy after dilation of eye as performed by ophthalmologists. A 12-lead electrocardiogram and echocardiography was done to note the presence of ischemia or infarction to indicate CAD.⁷

The data was recorded in Excel and analyzed using SPSS version 20. A descriptive analysis was done using mean, frequency, percentage and standard deviation. Chi square Test for categorical variables and Man-Whitney U test were used for non-normally distributed variables to test the level of significance.

RESULTS

Among the 173 patients (mean age 54.78 ± 14.46 years), 89 (50.9%) were male and 85 (49.1%) were female. The mean duration of diabetes among diabetic patients was 7.5 ± 6.6 years. Average BMI of the participants was 24.56 ± 4.1 kg/m² (Table 1).

Mean age, duration of T2DM and smoking habits were higher in those with hypomagnesemia. The prevalence of hypomagnesemia was almost half (49.7%) among the study participants. BMI and gender characteristics were almost similar in both groups as shown in table 2.

The mean Fasting Plasma Glucose (FPG), Postprandial Plasma Glucose (PPG) and HbA1c were higher in participants with hypomagnesemia. FPG and HbA1c were found statistically significant ($P < 0.05$). The participants with hypomagnesemia

Table 1. Characteristics of participants of Type 2 diabetes

Variable	Values
Age (years)*	54.78 ± 14.46
Male †	88 (50.9)
Female †	85 (49.1)
Duration of diabetes (years)*	7.5 ± 6.6
BMI (kg/m ²)*	24.56 ± 4.1
Smoker †	55 (31.8)
Non-smoker †	118 (68.2)

*data presented as mean $\pm$ SD ; † data presented as number (%)

Table 2. Distribution of serum magnesium level with characteristics of participants

Variable	Hypomagnesemia (n=86)	Normomagnesemia (n=87)
Age (years)*	56.17±14.21	53.41±14.46
Male †	45(52.4)	43(47.6%)
Female †	41(47.7)	44(52.3%)
Duration of diabetes (years)*	8.47±7.30	5.50±5.65
BMI (kg/m ²)*	24.29±3.91	24.84±4.27
Smoker †	32 (37.2)	23 (26.4)
Non-smoker †	54 (62.8)	64 (73.6)

* data presented as mean ± SD ; † data presented as number(%)

Table 3. Association of serum magnesium level with different parameters and duration of diabetes

Parameters	Hypomagnesemia (n=86)	Normomagnesemia (n=87)	Mann-Whitney U	p-value
Fasting Plasma Glucose (mg/dl)	204.74±94.66	173.76±77.58	2868.5	0.008
Postprandial Plasma Glucose (mg/dl)	288.42±105.91	258.31±89.19	3165	0.08
HbA1C %	9.66±2.66	8.75±2.67	2881.5	0.009
Duration of diabetes	8.48 ± 7.30	6.50 ± 5.65	3304.5	0.184

Table 4. Association of serum magnesium level with microvascular complications and coronary artery disease

Microvascular complications		Hypomagnesemia n (%)	Normomagnesemia n (%)	OR (95% C.I.)	p-value
Retinopathy	Present	50 (58.13%)	28 (32.18%)	2.92 (0.184-0.636)	0.001
	Absent	36 (41.86%)	59 (67.81%)		
Neuropathy	Present	53 (61.62%)	25 (28.73%)	3.98 (2.109-7.524)	<0.001
	Absent	33 (38.37%)	62 (71.26%)		
Nephropathy	Present	56 (65.11%)	40 (45.97%)	2.193 (1.19-4.04)	<0.001
	Absent	30 (34.88%)	47 (54.02%)		
Coronary artery disease	Present	13 (15.11%)	19 (21.83%)	1.6 (0.720-3.419)	0.25
	Absent	73 (84.88%)	68 (78.16%)		
Triopathy	Present	74 (86.04%)	55 (63.22%)	0.279(0.132-0.590)	0.001
	Absent	12 (13.96)	32 (36.78%)		

had higher duration of diabetes but were statistically insignificant (Table 3).

Diabetic retinopathy, neuropathy and nephropathy were higher in the participants with hypomagnesemia and were statistically significant ($P < 0.05$). CAD was lesser in those with hypomagnesemia but was

not statistically significant. Among 129 patients with triopathy (retinopathy, nephropathy and neuropathy), 74 had hypomagnesemia which was statistically significant with $p=0.001$ (Table 4). All the microvascular complications were more common in those with longer duration of diabetes ($P < 0.05$) as shown in Table 5.

Table 4. Association of serum magnesium level with microvascular complications and coronary artery disease

Microvascular complications		Duration of diabetes years (mean ± SD)	OR (95% C.I.)	p-value
Retinopathy	Present	10.56 ± 6.67	1713.5	<0.001
	Absent	4.96 ± 5.33		
Neuropathy	Present	9.93 ± 6.92	2230.5	<0.001
	Absent	5.47 ± 5.56		
Nephropathy	Present	8.68 ± 7.21	2929.5	0.019
	Absent	5.99 ± 5.37		

DISCUSSION

Our study showed the prevalence of hypomagnesemia among Nepalese Type 2 diabetic patients to be 49.7% (87/173) which is similar to that reported in a study done in western Nepal by Pokharel et al. in 2015.⁸ The higher prevalence of hypomagnesemia in our part of the world could be attributed to the poor nutritional status and delay in the diagnosis of diabetes for several years due to poor awareness. Also the negative association of FPG and HbA1c with hypomagnesemia found in our study corroborates the findings by Wahid et al. and Arpaci et al.^{9,10} PPG was also higher in patients with hypomagnesemia, however the result was not statistically significant. Similar study conducted by Halder et al. showed negative correlation with magnesium level but was statistically significant.¹¹ In this study, level of serum magnesium decreased with increase in duration of diabetes but was not statistically significant and the finding is supported by some similar studies.^{11–13}

All the microvascular complications of T2DM increased with decrease in serum magnesium level ($P < 0.05$) just like the findings by Premraj et al and Lu et al.^{12,13} Though statistically not significant, the odds of CAD in the study patients decreased with the decrease in serum magnesium level like in the Indian study by Dasgupta et al but unlike the findings by Keiboom et al.^{14,15} This could be due to the presence of confounders like smoking, hypertension and dyslipidemia. In our study, all the microvascular complications were significantly associated with the duration of diabetes just like the findings in studies done elsewhere.^{16,17,18,19}

The mechanisms whereby hypomagnesemia may induce or worsen existing diabetes are not well understood. Nonetheless, it has been suggested that hypomagnesemia may induce altered cellular glucose transport, reduced pancreatic insulin secretion, defective postreceptor insulin signaling, and/or altered insulin–insulin receptor interactions.^{20,21} Decreased magnesium levels may result from the diabetic state since renal glycosuria that accompanies it is believed to impair renal tubular reabsorption of magnesium from the glomerular filtrate. Low dietary intake of Magnesium has also been attributed to the development of metabolic syndrome and T2DM.²¹

Low circulating magnesium levels have been related to elevated blood pressure, dyslipidemia, increased inflammatory burden, oxidative stress, carotid wall thickness as well as to increased platelet reactivity in T2DM all of which can contribute to the development of microvascular and macrovascular complications of DM.^{22,23,24} Thus dietary magnesium supplementation is advisable to prevent or treat hypomagnesemia and these multiple complications of metabolic syndrome and T2DM.

This study also has limitations as it was purely hospital based study and did not measure the serum ionized and intracellular magnesium levels that could have better represented the biochemical functions of magnesium in the body. Moreover, we also could not study the influence of diet and dietary supplements on serum magnesium as the quantization of daily intake of magnesium was not feasible during this study.

CONCLUSION

The high prevalence (~ 50%) of hypomagnesemia among Nepalese patients with T2DM and its significant association with microvascular complications found in our study suggest that magnesium levels should be routinely checked in these patients and hypomagnesemia should be treated whenever possible.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

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