ORIGINAL ARTICLE

Relation of Low Serum Magnesium Level with Type 2 Diabetes Mellitus in Eastern India

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Abstract

Background: Odisha, a state in eastern India is swiftly becoming one among the diabetes hotspots in the country. Magnesium deficiency is implicated in poor glycemic status and various complications of diabetes. However, prevalence of hypomagnesemia is wide-ranging and its association with micro-vascular complications is contradictory. **Purpose:** To estimate the prevalence of hypomagnesemia in type 2 diabetes and determine its association with microvascular complications and glycemic status. **Methods:** A cross-sectional study was conducted on 165 type 2 diabetic patients. HbA1c was measured by HPLC method and serum Mg2+ was measured by colorimetric method. Serum Mg2+ level of <1.7mg/dl was defined as hypomagnesemia. **Results:** Hypomagnesemia was found in 12.1% (n=20) of patients. Retinopathy and microalbuminuria were found as 40% vs. 35.8 % and 30% vs. 20% between hypomagnesemia and normomagnesemia groups, respectively. Patients with poor glycemic control were more susceptible to have hypomagnesemia (16.5% vs. 3.5%) (OR: 5.314, 95% CI: 1.193-23.915, p=0.016). Moreover, HbA1c had significant inverse relation with serum Mg2+ (r= -0.3, p<0.001). **Conclusion:** Strict glycemic control or increased dietary intake of magnesium may decline the incidence of hypomagnesemia in diabetic patients.

Key Words

Glycemic Status, Hypomagnesemia, Microvascular Complications, HbA1c

Introduction

According to 'India State-Level Disease Burden Initiative Diabetes Collaborators', the prevalence rate of diabetes in adults has increased from 5.5% in the year 1990 to 7.7% in 2016, with rising prevalence in every state of India. [1] Odisha as a State among diabetes hotspots in the country has the prevalence rate increased from 4.5% in 1990 to 6.0 -7.4% in 2016. [1] Currently, the prevalence rate of diabetes in India is 10.4% and projected to be 12.2% by the year 2030. [2] Diabetes is the most common endocrine disorder associated with hypomagnesemia and 90-95% of all cases are type 2 diabetes. [3]

Magnesium is essential for life. As an important cofactor, it involves in hundreds of enzymatic reactions and biologic processes that require ATP; rendering it critical for normal cell function, DNA synthesis and energy metabolism. It also plays a major role in carbohydrate and insulin metabolism. Chlorophyll containing green leafy vegetables are rich in magnesium. Seeds, beans, peas, nuts, whole grains and fruits are also good sources whereas meat and fish have intermediate values.[4,5] Serum magnesium level varies between 1.7 and 2.5mg/dl (0.7-1.05mmol/L) in health. [6]

Persistent glycosuria with osmotic diuresis and low dietary intake are the principal factors for hypomagnesemia in diabetic patients. Various studies have reported the prevalence of hypomagnesemia in diabetes between 9.6

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and 48%. [7-9] The wide variation in prevalence of hypomagnesemia can be attributed to the changing pattern of dietary habits besides different study designs and methods. Furthermore, the reported association of hypomagnesemia with microvascular complications is contradictory as some studies showed the positive association while others negated it. [8,10-13] Present study was aimed to estimate the prevalence of hypomagnesemia in type 2 diabetic patients and to determine its association with microvascular complications and glycemic status.

Material & Methods

This cross-sectional analytical study was carried out over a period of one year in a tertiary care teaching hospital, in Bhubaneswar, Odisha after getting approval from the Institution's Ethical Committee. Type 2 diabetic patients aged above 18 years; attending the outpatient department and admitting to the medicine wards during November 2018 to October 2019 were included in the study. Patients with sepsis, metabolic acidosis, chronic renal failure, diabetics with history of myocardial infarction in last six months, chronic alcoholism, chronic diarrhea, patients on magnesium containing supplements, diuretics, nephrotoxic and anti-epileptic drugs, subjects with pregnancy and lactation were excluded from the study.

Sample size was estimated at confidence level of 95% with absolute precision of 5% on either side of true value. The expected proportion was considered as 11% from the previous study. [8] Therefore, using the formula $[z^2_{1-\alpha} \, p \, (1-p) \, / \, d^2]$ the minimum sample size required for the study was calculated as 151. Each participant was explained about the study procedures and a written informed consent was obtained prior to the beginning of the study. Thus, a total of 165 subjects were included in the study.

Detailed history and thorough clinical examination was done in all patients. Demographic data, all clinical details including complications and biochemical parameters were recorded in a structured format. Diabetic retinopathy and nephropathy were considered as microvascular complications in the present study. All patients were referred to the department of ophthalmology for opthalmoscopic examination and detection of diabetic retinopathy by an ophthalmologist. Urine albumin-to-creatinine level was measured on morning spot sample by immuno-turbidimetric assay. Microalbuminuria and macroaluminuria were defined as urinary albumin-to-creatinine level of 30-300 mg/g Cr (creatinine) and >300mg/g Cr, respectively (14). Blood sample was taken in the morning after overnight fasting. Blood sugar was measured by hexokinase method. Glycosylated hemoglobin (HbA1c) was measured by high performance liquid chromatography (HPLC) method. HbA1c of < 7% was referred to as good glycemic control. [15] Serum magnesium was estimated by colorimetric method with chlorophosphonazo III by automated analyzer (Cobas Integra 400 plus). Low serum magnesium (hypomagnesemia) was defined as serum magnesium level of <1.7mg/dl. [6, 16]

All the data were analyzed by using statistical package SPSS, version 20.0. Data were first analyzed for normal distribution by Kolmogorov- Simrinov test and Histogram. Numbers and percentages were used for categorical variables and mean with standard deviation, median and range for continuous variables. Based on serum Mg2+ levels, participants were divided into hypomagnesemia and normomagnesemia groups. Chi-Square and Fisher's Exact tests for categorical variables and Independent't' and Mann-Whitney U tests for continuous variables were used for comparison between the two groups. Hypomagnesemia was also compared between patients with HbA1c of < 7% and HbA1c of ≥7%. Pearson test and Spearman test were used to correlate serum Mg2+ with other continuous variables. Two-tailed p-value of <0.05 was considered as statistically significant.

Results

Mean age of the participants was 58.13 ±12.39 years and 46.1% were female. The median duration of diabetes in the participants was 7years and mean HbA1c was 8.55 ±2.67 %. Other characteristics of the participants are described in *Table1*. On comparison between hypomagnesemia and normomagnesemia groups, mean HbA1c was found significantly higher in patients with hypomagnesemia (11.6 ±4.07% vs. 8.1 ±2.11%, p=0.0001). Comparison of retinopathy, microalbuminuria and macroalbuminuria are depicted in *Table2*. Further, 16.5% of diabetic patients with poor glycemic control (HbA1c ≥7%) were having hypomagnesemia as compared to 3.5% with good glycemic status, which was statistically significant (OR: 5.314, 95% CI: 1.193-23.915, p=0.016) (*Table3*). On correlation of serum Mg2+ levels with continuous variables, only HbA1c had inversely related with serum Mg2+ with statistical significance (r = -0.306, p=0.0001) (*Fig 1*). Correlation with age, BMI, blood pressure, duration of diabetes, and lipid profile were not significant (*Table 4*).

Discussion

Present study observed the prevalence rate of hypomagnesemia as 12.1% among type 2 diabetics. Another study in eastern India by Dasgupta *et al.*, too observed the similar prevalence rate. [8] Consumption of diet mainly consists of green vegetables, fish and brown

Table1. Baseline characteristics of the participants (n=165)

Parameters	Mean ± SD	% (number)	Median (Range)
Female sex		46.1 (76)	
Age (Years)	58.13 ± 12.39		
BMI (Kg/m^2)	25.70 ± 3.15		
Duration of DM (Years)	7.52 ± 5.11		7.0 (29.5)
Hypertension		41.2 (68)	
Systolic BP (mmHg)	136.33 ± 18.68		
Diastolic BP (mmHg)	81.64 ± 9.52		
HbA1c (%)	8.55 ± 2.67		
FBS (mg/dl)	175.63 ± 64.81		
Triglyceride (mg/dl)			140 (963)
Total Cholesterol (mg/dl)	155.04 ± 47.09		
LDL-C (mg/dl)	82.30 ± 36.80		67.0 (159)
HDL-C (mg/dl)			38.0 (90.7)
Serum Mg^{2+} (mg/dl)	2.0 ± 0.31		
Retinopathy		36.4 (60)	
Microalbuminuria		21.2 (35)	
Macroalbuminria		35.2 (58)	
Hypomagnesemia		12.1 (20)	

Table 2. Comparison of Clinical Parameters across Hypomagnesemia and Normomagnesemia groups

Parameters	Hypomagnesemia (n=20)	Normomagnesemia (n=145)	'P' Value
Female sex % (n)	45 (n=9)	46.2 (n=67)	0.919 [*]
Mean Age (in years)	57.40 ±14.55	58.23 ±12.11	0.779 [#]
Mean BMI (in Kg/m^2)	25.32 ±2.96	25.75 ±3.18	0.561 [#]
Median Duration of DM (in years)	8.0	7.0	0.817 [##]
Mean HbA1c (in %)	11.6 ±4.07	8.13 ±2.11	0.0001 [#]
Mean FBS (in mg/dl)	205.10 ±61.78	171.56 ±64.37	0.030 [#]
HTN % (n)	40 (n=8)	41 (n=60)	0.906 [*]
Mean S. Mg^{2+} (in mg/dl)	1.47 ±0.22	2.08 ±0.24	0.0001 [#]
Retinopathy % (n)	40 (n=8)	35.86 (n=52)	0.718 [*]
Microalbuminuria % (n)	30 (n=6)	20 (n=29)	0.187 [**]
Macroalbuminuria % (n)	45 (n=9)	33.79 (n=49)	0.730 [**]
Chi-Square test; Fisher's Exact test; [#] Independent't' test; [##] Mann-Whitney U test			

rice may be responsible for lower prevalence rate in this part of the country.
Hypomagnesemia can cause defect in tyrosine kinase activity, post receptor insulin inaction and impaired cellular glucose transport eventuating insulin resistant and poor glycemic state. [6,17] Our study found significantly higher HbA1c level in hypomagnesemia patients as compared to patients with normal magnesium levels (p<0.001). Other studies on Indian population, Dasgupta et al. [8] and Kumar et al. [10] also reported analogous results. Present study further observed that those with poor glycemic control are more susceptible for magnesium deficit than diabetics with good glycemic control (OR: 5.314, p=0.016). In fact, hypomagnesemia can be both the cause and consequence of hyperglycemia. Insulin deficiency or resistance impairs the intracellular transport and reduces the tubular reabsorption promoting increased urinary loss of Mg2+; besides osmotic diuresis and oxidative stress causing hypomagnesemia. [3,6] In addition, significant inverse correlation between serum Mg2+ and HbA1c

Table 3. Hypomagnesemia with Glycemic Status of the Participants (n=165)

Glycemic status (n=165)	Hypomagnesemia (n=20)	'P' value 0.016 [*]
HbA1c <7% (n=56)	3.5% (n=2)	OR: 5.341[£]; 95% CI
HbA1c ≥7% (n=109)	16.5% (n=18)	1.193 - 23.915

* Chi-square test; £ Mantel-Haenszel Odds ratio; CI: Confidence Interval

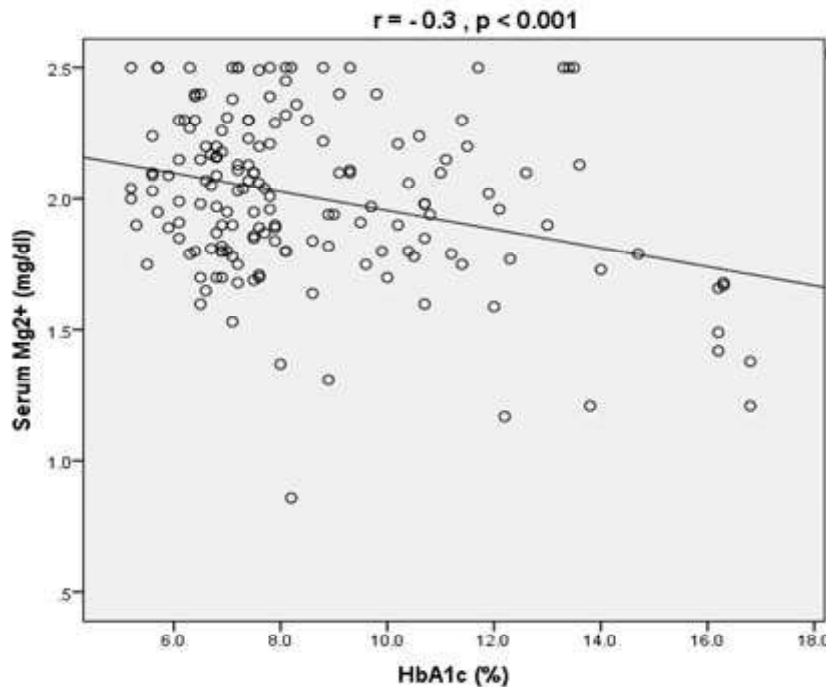*Fig1. Scatter Plot Showing Inverse Correlation Between Serum Mg2+ and HbA1c*

Table 4. Correlation of Serum Magnesium with Other Continuous Variables

Poportions	Correlation coefficient ('r')	'P' Value
Age	0.109	0.164 [¥]
Duration of DM	-0.113	0.148 [©]
BMI	0.067	0.396 [¥]
FBS	-0.079	0.314 [¥]
Systolic BP	-0.059	0.450 [¥]
Diastolic BP	-0.135	0.085 [¥]
Triglyceride	-0.036	0.651 [©]
Total Cholesterol	-0.117	0.134 [¥]
LDL-C	-0.075	0.350 [¥]
HDL-C	0.023	0.772 [©]

¥ Pearson test; © Spearman test

level is found in our diabetic cohorts ($r = -0.3$, $p<0.001$). Simillar observations have been reported by Lu J *et al.* ($r= -0.21$, $p<0.001$) and Lecube *et al.* ($r= -0.38$, $p=0.01$) in their respective studies. [9,14] Further, a recent meta-analytical study concluded that dietary intake of magnesium reduces the risk of type 2 diabetes with a statistically significant linear

dose-response relationship. [18]

In India alone, diabetes had contributed to 42.6% of all cause mortality and 2.2% of total disability adjusted life years (DALY) as on 2016. [1] However, the association of hypomagnesemia with microvasccular complications is controversial. Present study did not find statistically significant relation with retinopathy or nephropathy. Although, microalbuminuria and macroalbuminuria were increasingly associated with hypomagnesemia patients (30% vs. 20% and 45% vs. 33.79%, respectively), it was statistically not significant; probably due to a smaller sample size and relatively lower prevalence of hypomagnesemia in the study group. Nevertheless, previous studies [8,11,13] also reported no significant relations which support our observations.

However, this is a hospital-based study and study population may not be the true representative of the target population. Therefore, population-based studies with larger sample size are recommended for generalization of the findings of present study.

Conclusion

Prevalence of hypomagnesemia was relatively lower in the diabetic cohort of present study. Hypomagnesemia was significantly associated with diabetic patients with poor glycemic status and glycosylated hemoglobin was inversely related with serum magnesium. Therefore, strict glycemic control or increased dietary intake of magnesium may decline the incidence of hypomagnesemia in diabetic patients.

Financial Support and Sponsorship

Nil.

Conflicts of Interest

There are no conflicts of interest.

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