ORIGINAL RESEARCH PAPER

General Medicine

STUDY OF PREVALENCE OF HYPOMAGNESEMIA IN PATIENTS WITH TYPE II DIABETES MELLITUS.

KEY WORDS: Diabetes mellitus, HbA1c (glycosylated hemoglobin),

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ABSTRACT

Introduction: Diabetes mellitus is a common metabolic disorder. Prevalence of diabetes is increasing globally and it is one of the major health problems of the 21st century. The disturbance in Serum Magnesium (S. Mg) has been reported among patients with type II diabetes mellitus. Hypomagnesemia has negative impact on glucose homeostasis and insulin sensitivity in patients with type II diabetes mellitus. **Aim:** This study was undertaken to know the prevalence of hypomagnesemia in patients with type II diabetes mellitus and its relation with glycated hemoglobin (HbA1c). The study was conducted on 200 patients with type II diabetes and 100 healthy controls at Pacific Institute of Medical Sciences, Umarda, Udaipur, Rajasthan. **Results:** Out of 200 diabetic patients, 115 (57%) had hypomagnesemia. We observed mean S. Mg (1.7 mg) significantly low in diabetic patients compared with controls (2.1 mg). We also found HbA1c was high (9%) in hypomagnesemia patients. We found that diabetic hypomagnesemia patients had high mean fasting blood glucose (242.6 mg%) and postprandial blood sugar (313 mg%) than controls.

INRODUCTION

Diabetes mellitus is a group of metabolic disorders accompanied by chronic hyperglycemia due to absolute or relative deficiency of insulin either due to secretion or action leading to disturbances in carbohydrate, protein, and fat metabolism. Diabetes mellitus is the major health problem of the 21st century. Rapid increase in number of diabetics has made the World Health Organization to declare India as the global capital of diabetes. Diabetes mellitus is increasing faster in Asian countries than in other regions. The present trend indicates that more than 60% of the world diabetic population will be in Asia. An increased prevalence of impaired fasting glucose was seen since 2000, more among the younger population <50 years of age. This is also an indicator of further increase in prevalence of diabetes, with a risk of approximately 50% conversion to diabetes over 10 years. The important risk factors for diabetes are urbanization, a racial predisposition, genetic risk, aging, obesity, and insulin resistance1. Among intracellular ions, magnesium has a major role in tyrosine kinase activity at the insulin receptor level and also at the post-insulin receptor level of action of insulin. Magnesium also has a major role in carbohydrate metabolism; it acts mainly as a cofactor for glucose transportation across cell membranes, glucose oxidation, and in the release of insulin. Magnesium participates at various levels of insulin functions like secretion, binding, and insulin activity. Hence, deficiency of magnesium may lead to disturbances in glucose metabolism and at various levels of insulin secretion and its function in carbohydrate metabolism2. Intracellular magnesium plays a key role in regulating insulin action, insulin-mediated glucose uptake, and vascular tone. Reduced intracellular magnesium concentration leads to decreased tyrosine kinase activity, post receptor impairment in insulin action, and worsening of insulin resistance in diabetic patients3. Clinically, hypomagnesemia is defined as serum magnesium (S.Mg) levels <1.8 mg/dL. The persistent hypomagnesemia leads to hyperglycemia and insulin resistance. Hypomagnesemia can be both a consequence and a cause for diabetic complications. The concept of magnesium deficiency in the pathogenesis of diabetic complications is still innovative. There is very less information about the core effect of hypomagnesemia in relation to the vascular complications in diabetes, which in turn occurs mainly due to various metabolic effect of chronic hyperglycemia. The present study was conducted at Pacific Institute of Medical Sciences, Umarda, Udaipur, Rajasthan. The study was conducted to know the frequency of hypomagnesemia in type II diabetes mellitus patients and its relation with glycated hemoglobin (HbA1c)

MATERIALS AND METHODS

This is a comparative case–control study, done at a tertiary care hospital. We recruited 200 diabetic patients from medical wards and outpatient department at Pacific Institute of Medical Sciences, Umarda, Udaipur, Rajasthan.

Inclusion criteria

Patients with age above 30 years, diagnosed for diabetes mellitus for more than 3 years. One hundred healthy subjects with no history of diabetes were taken as controls.

Exclusion criteria

Alcoholic patients, patients with diarrhea and vomiting, and patients who were using diuretics, antibiotics like aminoglycosides, amphotericin B, pentamidine, cisplatin, tacrolimus, cyclosporine, and proton-pump inhibitors.

Consent

A written informed consent was taken from all participants of the study. Institutional Ethical Committee clearance was obtained before study. About 4 mL of venous blood sample was drawn for the assessment of fasting blood glucose (FBS), HbA1c, and S. Mg level, and 2 mL of venous blood sample was

taken 2 hours after breakfast for postprandial blood sugar (PPBS) level from all participants. The S. Mg level was estimated by calmagite dye method. In our laboratory, S. Mg level of 1.8 to 2.5 mg was considered normal reference value. Serum magnesium levels less than 1.8 mg/dL are considered as hypomagnesemia and were included in the study. The HbA1c levels were done by calorimetric method.

Statistical Methods

We have used descriptive and inferential statistical tools for analyzing the data.We have used frequency and percentages, analysis of variance, Student's t-test, and Chi-square/Fisher exact test as statistical methods. We have considered a p-value of 0.05 as statistically significant.

RESULTS AND OBSERVATIONS

We conducted a comparative case–control study on 200 type II diabetic patients and 100 nondiabetic healthy controls.

In the study, the maximum number of diabetic patients was in the age group of 51 to 60 years (38%), followed by 42 to 50 years (26%), 61 to 70 years (23%), whereas maximum number of controls was between 41 to 50 years (30%) and 51 to 60 years (30%). Among cases, 55% were females and in controls 40% were females. The mean FBS in diabetic patients was 210 mg/dL and in controls 101.4 mg/dL (significant $p < 0.001$, Student's t-test, Table 1).

The mean PPBS in the study group was 277.3mg/dL and in control group 144.2 mg/dL (significant $p < 0.001$, Table 2). We also observed about 106 (53%) diabetic patients had HbA1c of more than 9% (Graph 1). The study group showed diabetic retinopathy in 77 (38%) patients (Graph 2). Hypomagnesemia (<1.8 mg/dL) was observed in 57.7% of patients with diabetes mellitus and 18% of control population (Table 3). The mean S. Mg in study patients was 1.7 mg/dL and in controls was 2.1 mg/ dL ($p < 0.001$ significant). Majority (75.5%) of patients with hypomagnesemia had HbA1c level above 9% (Table 4, Graph 3).

We also observed the mean FBS and PPBS in these patients were also high. It was observed that hypomagnesemia was less prevalent in patients with HbA1c less than 9%. Hypomagnesemia was more prevalent in patients with duration of diabetes mellitus more than 6 years (Table 5).

Table 1: Fasting blood glucose (mg/dL) distribution In patients studied

FBS (mg/dL)	Test group	Control group	Total
<125	33 (16.5%)	100 (100%)	133 (44.3%)
125–140	10 (5%)	0 (0%)	10 (3.3%)
>140	157 (78.5%)	0 (0%)	157 (52.3%)
Total	200 (100%)	100 (100%)	300 (100%)
Mean ± SD	210.93 ± 79.00	101.42 ± 8.85	174.43 ± 82.79

Table 2: Postprandial blood sugar (mg/dL) distribution in patients studied

PPBS (mg/dL)	Test group	Control group	Total
<140	7 (3.5%)	36 (36%)	43 (14.3%)
140–200	35 (17.5%)	64 (64%)	99 (33%)
>200	158 (79%)	0 (0%)	158 (52.7%)
Total	200 (100%)	100 (100%)	300 (100%)
Mean ± SD	277.30 ± 83.56	144.76 ± 21.65	233.12 ± 93.38

Table 3: Serum magnesium levels in patients studied

S. Mg	Test group	Control group	Total
<1.0	0 (0%)	0 (0%)	0 (0%)
1.0–1.8	115 (57.5%)	18 (18%)	133 (44.3%)
1.8–2.5	77 (38.5%)	75 (75%)	152 (50.7%)
>2.5	8 (4%)	7 (7%)	15 (5%)
Total	200 (100%)	100 (100%)	300 (100%)
Mean ± SD	1.84 ± 0.44	2.05 ± 0.31	1.91 ± 0.42

(**p < 0.001; Significant, Student's t-test; SD: Standard deviation)

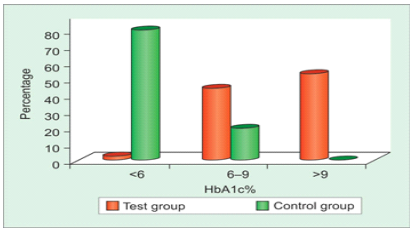
Table 4: Correlation of S. Mg levels in relation to HbA1c in patients studied

S. Mg.	</=6	6-9	>9	Total	p-value
Test group					
<1.0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<0.001
1.0–1.8	2 (33.3%)	33 (37.5%)	80 (75.5%)	115 (57.5%)	
1.8–2.5	4 (66.7%)	48 (54.5%)	25 (23.6%)	77 (38.5%)	
>2.5	0 (0%)	7 (8%)	1 (0.9%)	8 (4%)	
Total	6 (100%)	88 (100%)	106 (100%)	200 (100%)	
Control group					
<1.0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.286
1.0–1.8	18 (19.1%)	0 (0%)	0 (0%)	18 (18%)	
1.8–2.5	70 (74.5%)	5 (83.3%)	0 (0%)	75 (75%)	
>2.5	6 (6.4%)	1 (16.7%)	0 (0%)	7 (7%)	
Total	94 (100%)	6 (100%)	0 (0%)	100 (100%)	

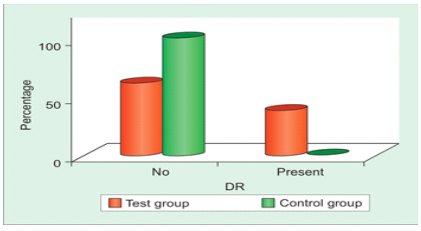
HbA1c **significant

Table 5: Comparison of clinical variables in relation to levels of HbA1c of patients studied

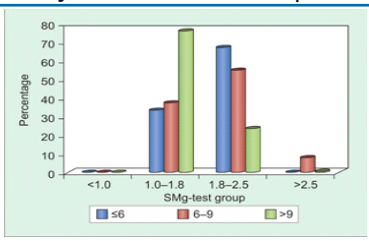
Variables	≤6	6–9	>9	Total	p-value
Age (years)	52.17 ± 11.34	54.02 ± 8.99	55.46 ± 10.07	54.73 ± 9.63	0.472
FBS (mg/dL)	134.33 ± 60.70	178.02 ± 64.82	242.58 ± 76.93	210.93 ± 79	<0.001 **
PPBS (mg/dL)	193.17 ± 90.90	239.89 ± 68.56	313.11 ± 77.94	277.30 ± 83.56	<0.001 **
S. Mg	1.98 ± 0.16	2.01 ± 0.50	1.70 ± 0.35	1.84 ± 0.44	<0.001 **
Duration	2.37 ± 1.92	5.08 ± 2.69	6.96 ± 3.67	5.99 ± 3.41	<0.001 **



Graph 1: Percentage distribution of HbA1c in patients studied



Graph 2: Diabetic retinopathy (DR) distribution in



Graph 3: Relation between S. Mg and HbA1c

DISCUSSION

Among the endocrine and metabolic disorders, diabetes mellitus has more prevalence of hypomagnesemia of around 25 to 39%[4]. Magnesium deficiency has been now implicated as a novel factor in the pathogenesis of many diabetic complications. Hypomagnesemia can be both a consequence and a cause of diabetic complications[8]. The factors responsible for magnesium deficiency in patients with diabetes mellitus are osmotic diuresis and reduced renal tubular absorption of magnesium; insensitivity to insulin in turn affects the intracellular magnesium transport and thereby increased loss of extracellular magnesium and frequent use of diuretics can also lead to magnesium loss[6,7]. Earlier studies have found associations between magnesium deficiency and insulin resistance, carbohydrate intolerance, dyslipidemia, and hypertension.[8,9]

In the present study, hypomagnesemia was observed in 57.7% of patients with type II diabetes mellitus; similar results were found by Shaikh et al[2] and Pham et al, who found hypomagnesemia in 55 and 47% of type II diabetic patients respectively[3,10]. In our study, hypomagnesemia was associated with raised HbA1c levels in 75.5% of patients and it is consistent with other studies done by Shaikh and Viktorinova et al[11,12]. We have observed that patients with high blood sugars and high glycemic index have increased prevalence of hypomagnesemia and increased prevalence of diabetic retinopathy. In diabetes, it is observed that inadequate metabolic control can affect the concentration of magnesium, developing hypomagnesemia, which has direct relation with micro- and macrovascular complications like cardiovascular disease, retinopathy, and neuropathy[13].

CONCLUSION

In our study, we have found hypomagnesemia is associated with chronic hyperglycemia. Almost all microvascular complications of diabetes mellitus are related to the extent and span of exposure to hyperglycemia. The benefits of having good glycemic control in preventing chronic diabetic complications are a well-known concept. There are many studies probing into the issue of intensive blood glucose control in Type 2 diabetics. Role of Other factors contributing to good glycemic control, like blood pressure control, lipid lowering therapy have also been under intense investigation. In this background, the concept of hypomagnesemia is still innovative for clinicians. Hence, physicians must learn to overcome clinical inertia in considering all the factors contributing to chronic hyperglycemia and treating them. We also need further studies on hypomagnesemia in type II diabetes and the effect of magnesium supplementation.

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