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Research Article

Study of relation of serum magnesium level with glycemic control in diabetes mellitus

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ABSTRACT

Background: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. This study was done to evaluate the relation between serum magnesium and glycemic control in diabetics.
Methods: 50 patients of T2DM were included this study. Detailed history, physical examination and relevant systemic examination were performed and necessary laboratory tests FBS, PPBS, HbA1c, magnesium level were done
Results: The mean age (mean± SD) of the patients was 49.82±7.38 years with range 29-58 years and the median age was 51 years and Male 32 (64%), Female 18 (36%), M:F= 1.78:1. In this study, statistically significant correlation was found between level of magnesium and age (p=0.04). In present study no statistically significant association was found between level of magnesium and sex (p=0.738). In high magnesium level (≥1.7), mean BMI 25.08±2.82 whereas mean BMI 24.25±2.87 in low magnesium level (<1.7) and this difference was not statistically significant (p=0.308). Mean difference of FBS with magnesium level was statistically significant (p<0.001) and mean difference of PPBS with magnesium level was also statistically significant (p<0.001). It was also found that mean difference of HbA1c level with magnesium level was statistically significant (p<0.001).
Conclusions: This study clearly depicts that in diabetes mellitus serum magnesium levels had a positive correlation with glycemic control. Serum levels of magnesium have been found to correlate inversely with fasting blood glucose concentration, post prandial blood glucose concentration and the percentage of HbA1c. The study also establishes a positive correlation of magnesium with age.

Keywords: Type 2 diabetes mellitus, Fasting blood sugar, Post prandial blood sugar, Glycosylated hemoglobin (HbA1c), Magnesium, Body mass index

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. The worldwide prevalence of DM

has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013.

Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population. In 2013, the prevalence of diabetes in individuals from age 20–79 ranged from 23 to 37% in the 10 countries with the highest prevalence (Tuvalu, Federated States of Micronesia, Marshall Islands, Kiribati, Vanuatu, Cook Islands, Saudi Arabia, Nauru, Kuwait, and Qatar, in descending order of prevalence).

The countries with the greatest number of individuals with diabetes in 2013 are China (98.4 million), India (65.1 million), United States (24.4 million), Brazil (11.9 million), and the Russian Federation (10.9 million). Up to 80% of individuals with diabetes live in low-income or medium-income countries.[1]

Hypomagnesaemia has long been known to be associated with diabetes mellitus. Magnesium depletion is said to have a negative impact on glucose homeostasis and Insulin sensitivity. This association between diabetes mellitus and magnesium is said to have a wide range of impact on diabetic control and complications.[2,3]

Hypomagnesaemia is a common feature in patients with type 2 diabetes. Although diabetes can induce hypomagnesaemia, magnesium deficiency has also been proposed as a risk factor for type 2 diabetes. Magnesium is a necessary cofactor for several enzymes that play an important role in glucose metabolism. Animal studies have shown that magnesium deficiency has a negative effect on the post-receptor signaling of insulin. On the post-receptor signaling of insulin. Some short-term metabolic studies suggest that magnesium supplementation has a beneficial effect on insulin action and glucose metabolism.[4]

Hypomagnesaemia has long been known to be associated with diabetes mellitus. Low serum magnesium level has been reported in children with insulin dependent diabetes mellitus and through the entire spectrum of adult type1 and type 2 diabetes mellitus regardless of the type of therapy.[5]

Initially the cause of hypomagnesaemia was attributed to osmotic renal losses from glycosuria (2) decreased intestinal magnesium absorption and redistribution of magnesium from plasma into red blood cells caused by insulin effect. Recently a specific tubular magnesium defect in diabetes has been postulated. Hypermagnesuria results specifically from a reduction in tubular absorption of magnesium.[6] Magnesium is involved on multiple levels in insulin secretion, binding and activity. Cellular magnesium deficiency can alter of the membrane bound sodium potassium-adenosine triphospatase which is involved in the maintenance of gradients of sodium and potassium and in glucose transport.[7]

In diabetics there is a direct relationship between serum magnesium level and cellular glucose disposal that is independent of insulin secretion. This change in glucose disposal has been shown to be related to increased sensitivity of the tissues to insulin in the presence of adequate magnesium levels.[8]

Magnesium deficiency has been found to be associated with diabetic microvascular disease. Hypomagnesaemia has been demonstrated in patients with diabetic retinopathy, with lower magnesium levels predicting a greater risk of severe diabetic retinopathy.[9] Magnesium depletion has been associated with multiple cardiovascular implications: arrhythmogenesis, vasospasm, and hypertension and platelet activity.[10]

In elderly diabetics paolisso et al demonstrated that oral magnesium supplements given for 4 weeks resulted in lower fasting plasma glucose levels, increased plasma and erythrocyte magnesium levels and a slight but statistically significant increase in B-cell response to glucose and arginine.[11] In this study estimation of serum magnesium and HbA1c was carried out in patients of DM and the relation of serum magnesium level with glycemic control (evaluated by HbA1c) in diabetes mellitus studied.

METHODS

All patients of Type 2DM admitted in Medical Wards as well as attending outdoor who fulfilling inclusion and exclusion criteria are included to my study. This study was undertaken over a period of one and half year. 50 patients were included in this study. Valid consent was taken from all the patients who were included this study. Proper history from all patients was taken and relevant examination of all systems was done. I routinely send FBS, PPBS, HbA1c, magnesium level for all patients as well as other relevant investigations according to patients' profile. All data were then analyzed statistically.

Inclusion criteria

- Patient having diabetes mellitus.
- Age between 25-60.
- BMI between 17-30.
- Patient who is willing to participate in the study.

Exclusion criteria

- Not willing to participate in the study.
- Patients with chronic renal failure.
- Acute myocardial infarction in last 6 months.
- Patients on diuretics.
- Patients with history of alcohol, NSAIDS abuse.

- Patients receiving magnesium supplements or magnesium containing antacids & drugs like ethanol, diuretics (loop, thiazide and osmotic), cisplatin, cyclosporine, aminoglycosides, amphotericin B.
- Known case of malabsorption syndrome or histoy of chronic diarrhoea.

RESULTS

The mean age (mean±SD) of the patients was 49.82±7.38 years with range 29-58 years and the median age was 51 years. Higher proportion of patients 32 (64.0%) were in the age group <50 years and Male 32 (64%), Female 18 (36%) with M:F=1.78:1. In this study, statistically significant correlation was found between level of magnesium and age (p=0.04). But no statistically significant association was found between level of magnesium and sex (p=0.738).

Table 1: Mean level of magnesium according to HbA1c.

	Magnesium		
HbA1c	**<1.7**	**≥1.7**	**Total**
>7.9	24	2	26
Row %	92.3	7.7	100.0
Col %	82.8	9.5	52.0
≤7.9	5	19	24
Row %	20.8	79.2	100.0
Col %	17.2	90.5	48.0
Total	29	21	50
Row %	58.0	42.0	100.0
Col %	100.0	100.0	100.0

In high magnesium level (≥1.7) was found in mean age 46.62±8.49 years whereas mean age 52.14±5.53 years was associated with low magnesium level (<1.7) and this difference was statistically significant (p=0.007). In high magnesium level (≥1.7) was seen in mean BMI 25.08±2.82 whereas mean BMI 24.25±2.87 was associated with low magnesium level (<1.7) and this difference was not statistically significant (p=0.308).

Table 2: Mean level of magnesium according to FBS.

	Magnesium		
	<1.7	≥1.7	p-value
FBS	138.79±16.53	118.19±14.60	<0.001

Table 3: Mean level of magnesium according to PPBS.

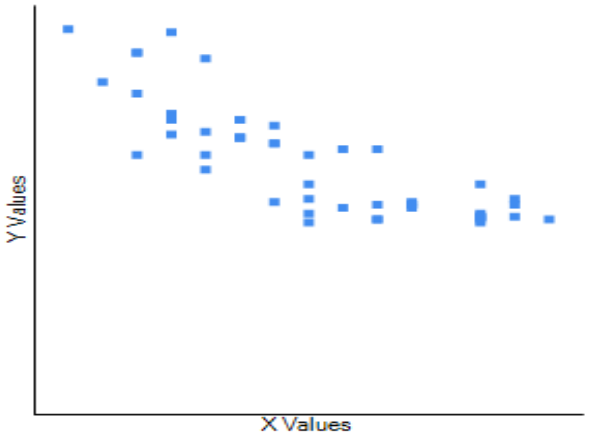
	Magnesium		
	<1.7	≥1.7	p-value
PPBS	186.07±22.97	161.00±17.17	<0.001

Association between HbA1c vs magnesium levels all patients (Table 1): It was seen from the study that statistically significant correlation was found between level of magnesium and HbA1c (p<0.0001). Mean of magnesium according to FBS (Table 2): It was seen that magnesium level <1.7 was associated in patients with FBS 138.79±16.53 whereas magnesium level ≥1.7 seen in patients with FBS 118.19±14.60. Mean difference of FBS level with magnesium level was statistically significant (p<0.001).

Table 4: Mean level of magnesium according to HbA1c.

	Magnesium		
	<1.7	≥1.7	p-value
HbA1c	9.80±1.75	7.20±0.70	<0.001

Mean of magnesium according to PPBS (Table 3): It was found that magnesium level <1.7 was associated in patients with PPBS 186.07±22.97 whereas magnesium level ≥1.7 found in patients with PPBS 161.00±17.17. Mean difference of PPBS level with magnesium level was statistically significant (p<0.001). Mean of magnesium according to HbA1c (Table 4): It was seen from the study that magnesium level <1.7 was associated in patients with HbA1C 9.80±1.75 whereas magnesium level ≥1.7 was seen in patients with HbA1C 7.20±0.70. It was found that mean difference of HbA1c level with magnesium level was statistically significant (p<0.001).



X value magnesium level; Y values HbA1c; The value of R is: -0.8302; The P-Value is < 0.00001; The result is significant at p < 0.05.

Figure 1: Pearson correlation coefficient test.

Pearson Correlation Coefficient test (Figure 1): The Pearson Correlation Coefficient test found that level of magnesium and HbA1c was statistically significant.

DISCUSSION

It was an Observational Cross sectional comparative hospital based study. The present study included 50 diabetic patients. In this study we focused to determine glycemic control by HbA1c (taking the limit as >6.5-8 as good control and >8 as poor control) and measures the level of serum magnesium (taking normal serum

magnesium level as 1.7-2.4 mg/dl.) in both the group of diabetics and try to relating the status of glycemic control with serum magnesium level. The mean age (mean±SD) of the patients was 49.82±7.38 years with range 29-58 years and the median age was 51 years with a mean BMI 25.08±2.82.

Diabetic patients were admitted to the hospital for various causes. The commonest in the present study was for various infections which accounted for 27% of patients. The next commonest cause for admission was cardiovascular disease which accounted for 16% of the admissions. Neurological problems accounted for 12% of admissions. Peripheral vascular disease accounted 12% of admissions. 6% of patients were admitted exclusively for poorly controlled diabetes. Serum magnesium levels, fasting blood glucose, post prandial blood glucose, HbA1c were determined in all these subjects.

The present study reveals:

- It was found that statistically significant correlation was found between level of magnesium and HbA1c ($p<0.0001$).
- It was found that mean difference of HbA1c level with magnesium level was statistically significant ($p<0.001$).
- The Pearson Correlation Coefficient test found that level of magnesium and HbA1c was statistically significant.
- Mean difference of FBS level& PPBS level with magnesium level was statistically significant ($p<0.001$).
- In high magnesium level (≥1.7), mean age 46.62±8.49 years whereas mean age 52.14±5.53 years in low magnesium level (<1.7) and this difference was statistically significant ($p=0.007$).
- The study has not shown any significant associations between sex, duration and BMI of diabetes with serum magnesium levels.

On establishing the relationship between magnesium levels and the state of control of diabetes, it was observed that in poorly controlled diabetic's serum magnesium levels were lower than that of well controlled diabetic. Serum levels of magnesium have been found by several investigators to correlate inversely with fasting blood glucose concentration and the percentage of HbA1c.[12,13]

Schlienger et al studied the influence of glycemic control (glycemic control evaluated by HbA1c) on various trace elements and reported significantly reduced plasma magnesium levels in patients with poor control of diabetes.[14]

Glycosylated hemoglobin (HbA1c) results from glycosylation of hemoglobin by a reaction between glucose and N-terminal valine of beta chain of Hb molecules. When plasma glucose is consistently elevated, there is an increased glycosylation of hemoglobin. HbA1c assays approximate with mean plasma glucose values over the previous 2 to 3 months. Higher percentages of HbA1c indicate poor glycemic control in the previous months. Hypomagnesaemia is reported to be both a cause and result of poor glycemic control. Magnesium is a cofactor in both glucose transporting mechanisms of cell membrane and various enzymes important in carbohydrate oxidation.[15] In addition; magnesium deficiency has been shown to promote insulin resistance in multiple studies.

Nadler et al have reported that insulin sensitivity decreases even in non-diabetic individuals after induction of magnesium deficiency. Likewise, elderly subjects were shown to have improved glucose tolerance when they received magnesium supplements.[16] Thus hypo-magnesaemia by itself results in poor glycemic control. Conversely, hyperglycemia and osmotic diuresis may lead to increased urinary magnesium excretion and hypomagnesaemia in diabetics. Present study reveals Sex, BMI and duration of diabetes were not the significant predictors of serum magnesium levels but statistically significant correlation was found between level of magnesium and age ($p=0.04$).

Yajnick et al reported that among diabetics plasma magnesium concentration was directly related to age and men had significantly higher concentrations than women.[12] The increasing magnesium levels with age were probably due to impaired renal function and the sample size, (87 diabetics, 30 non diabetics) was relatively small to confirm male preponderance. In present study, patients with impaired renal functions were excluded. Our results confirm to the recent reports that have not shown any significant associations between sex, and duration of diabetes with serum magnesium levels.[17,18]

Jain AP, et al study also establish positive correlation between magnesium levels with glycemic control in diabetics.[19] On establishing the relationship between magnesium levels and the state of control of diabetes, it was observed that in poorly controlled diabetic's serum and urinary magnesium levels were respectively lower and higher than that of fairly controlled diabetics.

So finally comparison of serum magnesium levels between well controlled and poorly controlled diabetics had a positive correlation with the present study which is supported by other above mentioned study also. However in the present study, the complications of diabetes in relation to hypomagnesaemia were not studied. Also magnesium supplementation and its effects towards magnesium levels or metabolic control were not done in this study which can be taken as limitations of the present study.

CONCLUSION

The present study clearly depicts that in diabetes mellitus serum magnesium levels had a positive correlation with

glycemic control. Serum levels of magnesium have been found to correlate inversely with fasting blood glucose concentration, post prandial blood glucose concentration and the percentage of HbA1c. The study also establishes a positive correlation of magnesium with age.

Present study also reveals Sex, BMI and duration of diabetes were not the significant predictors of serum magnesium levels. As the Levels of serum magnesium in poorly controlled diabetic patients were further lower than those in whom diabetes was under good control hence it is worthwhile estimating magnesium levels in the diabetes mellitus patients.

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