Study of Plasma Glycemic Levels and Serum Magnesium Levels in Diabetes Mellitus (DM) and Non-Diabetic Healthy Controls: A Comparative Study

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ABSTRACT

Introduction: Patients of DM are known to have low levels of serum magnesium levels as compared to non-diabetics. There is a link between the low magnesium levels and poor glycemic controls and subsequently leading to complications in diabetic patients. The aim of this study was to assess the serum magnesium levels in relation to glycemic status in diabetic patients as compared to non-diabetics.

Material and Methods: 172 cases of previously diagnosed DM were taken along with the age and sex matched controls who were healthy and non-diabetic and their blood samples were analyzed for magnesium and blood sugar fasting and post prandial.

Results: In our study we have found that there is a significant hypomagnesemia in diabetic cases as compared to non-diabetic controls which is in accordance with other studies. There also exists a negative correlation between mean serum magnesium levels (2.08 ± 0.4 mg/dL) and mean fasting plasma sugar (FBS) (159.72 ± 71.60 mg/dL) and mean post prandial sugar (PPS) (222.76 ± 100.86 mg/dL) levels. No significant variation as per age and sex in serum magnesium levels amongst diabetic subjects have been found in our study.

Conclusion: Hypomagnesemia is common in diabetics as has been found in our study also, and it helps in regulation of glycemic levels and in turn also affects magnesium levels. Considering estimation of magnesium as a routine laboratory work up protocol in the management of diabetes may prevent various complications due to hypomagnesemia with early therapeutic intervention.

Keywords: Hypomagnesemia, Poor Glycemic Control, FBS, PPS, Diabetic Complications

INTRODUCTION

DM is a complex endocrine disorder caused by inherited and/or acquired deficiency of insulin production or by insulin resistance, leading to abnormally high levels of glucose in the blood, which in turn can damage various organ systems. Approximately 422 million people have diabetes mellitus worldwide as per World Health organization (WHO) factsheet and there is likelihood of this number being doubled up by the year 2045 which is a cause of much concern. About 43% deaths occurs due to high blood glucose levels at age less than 70 years amongst diabetics.[1] The majority of population being affected is in developing countries like India are people in their most productive age group from 45-64 years as compared to developed countries where people aged 65 years and above are affected. The main reason behind such rise in the number of cases is population growth, ageing, unhealthy diets and sedentary lifestyles.

Magnesium is one of the known abundant intracellular elements in the human body. Its role has been found significant in various biologic reactions, one of which is glucose metabolism as it has been associated with various enzymes as cofactor. It plays an important role in the modulating insulin secretion and its action in the target tissues via receptors of this hormone and glucose homeostasis.[2]

DM induces metabolic changes related to high levels of serum glucose. The main pathophysiology involves destruction of beta cells of pancreas and insulin resistance with relative insulin deficiency to predominantly insulin secretion defect with insulin resistance.[3] Hypomagnesemia in DM, has been reported to reduce tyrosine kinase activity and receptor signaling by causing disruption.[4] In diabetes the various causes that can cause hypomagnesemia are mentioned in Table 1.[5]

Low levels of magnesium in both intracellular and extracellular compartments interferes with enzymatic reactions involved in the production of adenosine triphosphate, thus modifying the cascade of enzymes involved in carbohydrate metabolism, triggering DM and its complications.[6] Hypomagnesemia is common in DM, is very commonly underdiagnosed and has been implicated in carbohydrate intolerance, hyperglycemia, insulin resistance and hyperlipidemia.[7]

Hence low serum levels of magnesium can be responsible for onset or worsening of DM and even DM can induce hypomagnesemia.[8] Several studies have been conducted in past which have revealed significant low magnesium levels in DM as compared to non-diabetic healthy controls. This inverse relationship of magnesium intake with DM can be

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due to systemic inflammation and insulin resistance.[9]

Low levels of magnesium in DM have been found and reported worldwide, however limited significant data had been reported in our country based on the fasting and post prandial glycemic levels in DM and non-diabetic healthy controls.[10] Keeping this framework as the basis of the study, we decided to study the plasma glycemic levels and serum magnesium levels in DM and non-diabetic healthy adult.

MATERIAL AND METHODS

Study design and patient selection

The study was designed as a hospital based, cross sectional, comparative study for assessment of serum magnesium levels between non-diabetic healthy controls and DM patients visiting the medical or endocrine outpatient department at tertiary care hospital in western India.

A total of 172 diabetic cases and 100 non-diabetic healthy controls were recruited for the study. Subjects between age of 22 to 85 years, who were not having any complications in the form of renal failure, hepatic failure, cardiac failure and thyroid disorders and not having any comorbidity like hypertension were recruited for the study after informed consent. Pregnant and lactating females, patients with known magnesium deficiency on supplementation and malignancy were excluded from the study.

5 ml of blood was collected, after overnight fasting of 10 hours in two vacuum evacuated tubes, one with additives EDTA and Sodium fluoride for estimating plasma glucose and other tube free from trace element. FBS was estimated using Hexokinase method[11] and Serum magnesium levels were estimated using complexometric photometric method[12] based on bichromatic end point technique on the Siemens fully automated Dimension EXL 200 clinical chemistry system in National Accreditation Board for testing and calibration Laboratories (NABL) certified laboratory with all the Quality control procedures in place.

Two study groups were made based on glycemic levels, Group 1 with age ≤ 45 years and Group 2 with age > 45 years and the magnesium levels were compared.

S. No	Causes of Hypomagnesemia in diabetic patients
1.	Diet tend to be low in magnesium
2.	Renal excretion of magnesium is high
3.	Insulin deficiency and/or resistance
4	Use of diuretics promotes magnesium wasting
5.	Decrease absorption from intestine

Table-1: Major causes of Hypomagnesemia in DM Patients

Magnesium Levels	Diabetic	Non-diabetic control	P value
Hypomagnesemia <1.8 mg/dL	34	4	0.009 Significant
Normomagnesemia (1.8-2.4 mg/dL)	113	52	

Table-2: Showing number of cases of hypomagnesemia in diabetic and non-diabetic controls

STATISTICAL ANALYSIS

The collected data were tabulated, and statistically analysed using SPSS program (Statistical Package for Social Sciences) 20.2 software.

Descriptive statistics were done for numerical data by mean and standard deviation. Analytical analysis was done for quantitative variables using t-test in cases of two groups with parametric data, while correlations were done using Spearman Correlation for non- parametric data. Analytical analyses were done for qualitative data using Fisher's exact test for less than 5 variable.

RESULTS

Among the study group significant hypomagnesemia was found amongst with mean age of 54.04 ± 12.12 years as compared to healthy controls with mean age of 54.05 ± 11.49 years with mean magnesium levels of 1.55 ± 0.16 mg/dL.

Hypomagnesemia was found in 34 cases amongst 172 diabetic subjects as compared to 04 cases amongst 100 controls. There is a significant difference in the number of hypomagnesemia cases amongst diabetic and non-diabetic controls as seen in Table 2.

There is a negative correlation between FBS and PPS levels and magnesium levels, which means that higher the FBS and PPS values lesser will be magnesium levels in diabetic subjects as seen in Table 3 and represented via scatter plot in Figure 1 and 2.

There is no significant variation of magnesium levels as per age and sex distribution amongst diabetic subjects as seen in

	Mean Serum magnesium (2.08±0.4 mg/dl)	Correlation Coefficient (r)	P Value
FBS (Mean±SD in mg/dL)	159.72±71.60	-0.03	<.0001
PPS (Mean±SD in mg/dL)	222.76±100.86	-0.09	<0.001

Table-3: Showing correlation of mean fasting blood sugar and post prandial blood sugar with mean serum magnesium Values in diabetic subjects.

	Male	Female	P value
Hypomagnesemia (<1.8mg/dL)	19	15	0.33 Not significant
Normomagnesemia (1.8-2.4mg/dL)	52	61	

Table-4: showing magnesium levels in diabetic subjects amongst males and females

	Group 1 Age ≤ 45years	Group 2 Age > 45 years	P value
Hypomagnesemia (<1.8mg/dL)	9	25	0.82 Not significant
Normomagnesemia (1.8-2.4mg/dL)	27	86	

Table-5: Showing magnesium levels in diabetic group amongst two age groups

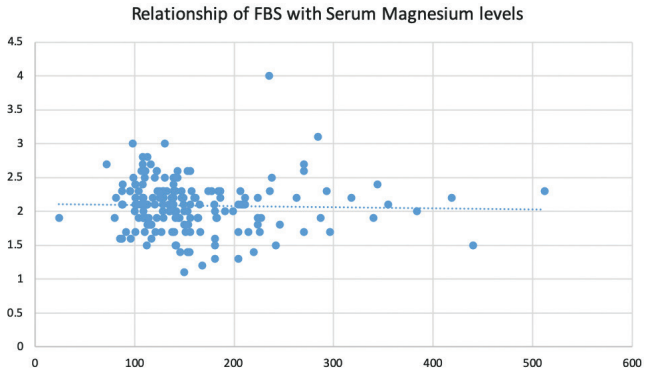

Figure-1: Scatter plot 1

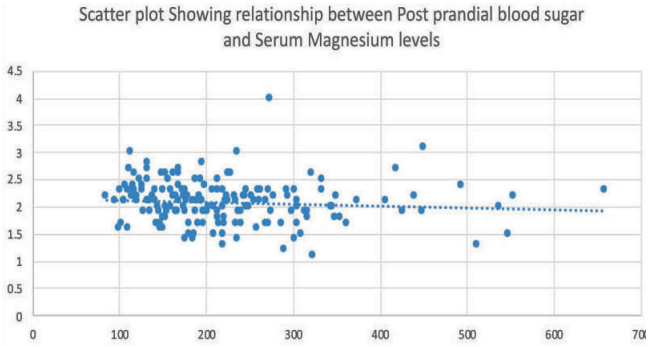

Figure-2: Scatter plot 2

the Table 4 and 5. Amongst the study group a greater number of males were found to have hypomagnesemia as compared to females. Similarly, a greater number of diabetic study group 2 with age > 45 years were found to have hypomagnesaemia as compared to group 1 with age ≤ 45years.

DISCUSSION

In this study we found that mean values of FBS (168.76 ± 70.41 mg/dL) and PPS (239.02 ± 98.85 mg/dL) and serum magnesium (1.55 ± 0.16 mg/dL) levels that were significant with 19% prevalence of hypomagnesemia amongst diabetics in our study which is contrary to study by Kareem et al[13] that has a prevalence of 74.3%. Results were slightly lesser than our study in another study from eastern India[14] that has documented 11% prevalence of hypomagnesemia amongst 150 diabetic patients.

Also, there was a weak negative correlation between magnesium and FBS and PPS levels in diabetics which is consistent with study of MA J, Aaron R et al.[15] The reasons for lower magnesium levels are not clear but that may include lower dietary intake, decreased absorption from intestine, increased loss of urinary magnesium along with glucose or due to reduced magnesium uptake by cells as compared to non-diabetic healthy individuals.[16] A significant number of prospective cohort studies and meta-analyses have suggested that magnesium intake reduces the risk of diabetes but the results still remains inconsistent and more studies are required to establish the same.

Hypomagnesemia is not uncommon in patients with diabetes mellitus, it has effect on the regulation of glycemic control as well as occurrence of diabetic related complications like nephropathy, retinopathy and foot ulcers.[14]

Our study revealed that mean serum magnesium in diabetic study group was lower (1.55 ± 0.16 mg/dL) when compared to control group (2.41 ± 0.40 mg/dL).These results are in accordance with the study by Nazar S. Haddad, Salah Zuhair et al[17], Badyal et al[18] and Chambers et al[19]

A close monitoring of the patients with a multi-dimensional approach involving thorough investigation panel and treatment protocol is required. Serum magnesium levels are not investigated in routine clinical practice despite as a part of management of diabetes knowing its evident significance with the glycemic levels. Similarly, even though hypomagnesaemia has been reported to occur at an increased frequency among patients with DM, it is often not given importance and hence overlooked and not considered for treatment.[20] Based on the results of our study, it is therefore recommended to include serum magnesium in the routine electrolyte panel for the better management of DM to prevent complications like diabetic nephropathy[21] and retinopathy. Inclusion of magnesium supplementation as a part of therapeutic management may prevent the associated complications and more studies may be undertaken to establish the fact for better management of diabetic patients.

CONCLUSION

Hypomagnesemia is a common analyte disorder in DM which has been found significant in our study also. Low serum magnesium levels are associated with high fasting and post prandial glycaemic levels and it is a cause as well as effect for an increased risk of diabetes complications. Inclusion of serum magnesium as a routine laboratory analyte panel in diabetics may detect early hypomagnesemia and the complications associated with the same may be prevented by early intervention with oral magnesium supplementation as a therapeutic measure, such a potential role of magnesium supplementation in preventing development of diabetic complications warrants future randomised controlled trials.

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