International Journal of Research in Medical Sciences
Surendra Naik N et al. Int J Res Med Sci. 2015 Mar;3(3):556-559
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: 10.5455/2320-6012.ijrms20150305

Research Article

The role of serum magnesium level in type 2 diabetes mellitus

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Received: 3 February 2015
Accepted: 13 February 2015

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ABSTRACT

Background: Diabetes mellitus is one of the most common metabolic disorder and leading cause of death and disability in the world. The incidence of diabetes is increasing globally and in India. Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes. Hypomagnesaemia can lead to development of complications in diabetes. Hence there is need for the study to explore the status of magnesium in type 2 diabetes. Objectives: To estimate and compare the serum magnesium levels in type 2 diabetes patients with age/sex matched non diabetic controls.
Methods: A case control study was done in randomly chosen 100 type 2 diabetic patients and 100 non diabetic age/sex matched controls. Estimation of serum magnesium was done by enzymatic end point method.
Results: 37% of diabetic patients had low serum magnesium levels (Mg^{2+} level ≤1.5 mg/dL) and 9 % of controls had low serum magnesium levels. The mean serum magnesium levels were 1.96 ± 0.54 mg/dL and 2.375 ± 0.449 mg/dL in diabetics and controls respectively (P value <0.0001 highly significant). Hypomagnesaemia (Mg^{2+} level ≤1.5 mg/dL) was correlating with retinopathy (P = 0.041 significant).
Conclusion: This study demonstrated that low serum Mg^{2+} status is common in type 2 diabetes mellitus patients when compared to non-diabetic controls. It may be prudent in clinical practice to periodically monitor plasma Mg^{2+} concentration in diabetic patients. If plasma Mg^{2+} is low, an intervention to increase dietary intake of magnesium may be beneficial to prevent the complications.

Keywords: Diabetes mellitus, Magnesium, Hypomagnesaemia, Enzymatic end point method

INTRODUCTION

Diabetes Mellitus (DM) is one of the most common metabolic disorder and leading cause of death and disability in the world. Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes. In 1997 WHO estimate of the prevalence of the diabetes in adults showed an expected rise of >120% from 135 million in 1995 to 300 million in 2025.[1]

Magnesium deficiency can lead to development of complications such as retinopathy, thrombosis and hypertension. Several studies have shown that high prevalence of low serum magnesium concentrations in Type 2 diabetes when compared to healthy controls.[2]

Marked decrease in plasma and erythrocyte magnesium level is associated with poor diabetic control and advanced retinopathy.[3] Preventing hypomagnesaemia in diabetes by supplementing magnesium may be helpful in

increasing insulin sensitivity and delaying the development of late diabetic complications.

Therefore, the aim of the study is to compare the serum magnesium concentrations in patients with type 2 diabetes and non-diabetic controls to prove hypomagnesaemia is present in Type 2 diabetes mellitus.

METHODS

A case control study was conducted in randomly chosen 100 type 2 diabetic patients attending diabetic clinic at B.L.D.E.A's Shri B.M. Patil medical college hospital and research centre, Bijapur and 100 non diabetic age and sex matched controls. Duration of the study was from December 2006 to June 2008. Each gave informed consent and the study was approved by ethical and research committee to use human subjects in the research study.

Inclusion and exclusion criteria for cases

Inclusion criteria: All cases of type 2 diabetes mellitus patients[4] aged between 30 to 70 years. Exclusion criteria: Patients with renal failure, patients who suffered acute myocardial infarction in last six months, patients on diuretics**,** patients with history of alcohol abuse, patients on magnesium supplements/magnesium containing antacids, mal absorption and chronic diarrhoea.

- Controls - Normal healthy age and sex matched individuals were included.

Method of sample collection

Informed consent was taken from patients and control subjects. Selected subject's blood samples were collected with all aseptic precautions. 5 ml of blood was collected from the median cubital vein. It was allowed to clot for 30 minutes in a clean dry test tube and was subjected to centrifugation for 20 minutes to separate the serum. The serum samples were stored at -80°C till they were analyzed.

Study design: Case control comparative study.

Sample size: 100 patients of type 2 diabetes mellitus and 100 non diabetic age/sex matched controls, aged between 30 years to 70 years.

Sample analysis

The separated serum was used to estimate magnesium levels by enzymatic end point photometric method in automated analyser.[5]

Estimation of serum Fasting Blood Sugar (FBS) and postprandial blood sugar (PPBS) by hexokinase method, HbA_{1C} by nephelometry, blood urea by urease method & serum creatinine by Jaffe's method and serum lipid profile by enzymatic method were also performed. The chemicals and reagents used for the procedures were of analytical grade.

Normal reference range of serum magnesium: 1.8 mg/dL - 2.9 mg/dL.

Serum magnesium levels ≤1.5 mg/dL were considered as low magnesium level in this study.

RESULTS

Statistical software: The statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and excel have been used to generate graphs, tables etc**.**

Statistical methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented as Mean ± SD (Min-Max) and results on categorical measurements are presented as Number (%). Significance is assessed at 5% level of significance.

Pearson correlation between study variables is performed to find the relationship. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures

+Suggestive significance (P value: 0.05 <P <0.10)

*Moderately significant (P value: 0.01 <P ≤0.05]

**Strongly significant (P value: P ≤0.01)

Maximum numbers of patients were in the age group of 51-60 i.e. about 47% of patients, followed by 26% between 41-50 years, 21% between 61-70 years and 6% patients between 30-40 years. Among controls maximum number in 51-60 years i.e. about 42% followed by 26% in 41-50 years, 22% in 61-70 years and 10% in 30-40 years age group which is shown in Table 1.

Table 1: Age incidence.

Age (years)	Total No. of diabetics	Controls
30-40	6	10
41-50	26	26
51-60	47	42
61-70	21	22

In diabetic group 51 patients were male and 49 females. In control group 58 were male and 42 were females. In this study out of 100 diabetic patients 37 patients had low magnesium levels (Mg^{2+} ≤ 1.5 mg/dL) and in controls

only 9 patients had low magnesium levels. This is shown in Table 2.

Table 2: Serum magnesium levels in type 2 DM patients and controls.

Serum magnesium levels (mg/dL)	Diabetic group	Control group	Test applied
≤1.5	37	9	$X^2 = 22.134$
≥1.6	63	91	P <0.0001 HS

HS - Highly significant

The serum magnesium levels in diabetic patients were 1.96 ± 0.54 mg/dL (Mean ± SD) and in non-diabetic controls 2.375 ± 0.449 mg/dL shown in Table 3.

Table 3: Mean serum magnesium level in type 2 DM patients and non-diabetic controls.

Variable	Particular	Control	Diabetic
Serum magnesium	Mean ± SD	2.375 ± 0.449	1.96 ± 0.54

Low magnesium levels were associated with retinopathy in patients of this study (P = 0.041 significant). This is shown in Table 4.

Table 4: Relation between serum magnesium levels and retinopathy.

Retinopathy	Mg^{2+} level (mg/dL)		Statistical test applied
	≤1.5	≥1.6	
Yes	10	07	$X^2 = 4.185$ P = 0.041*
No	27	56	
Total	37	63	

Table 5 shows that low magnesium levels were correlating with hypertension.

Table 5: Relation between serum magnesium levels and hypertension.

Hypertension	Mg^{2+} level (mg/dL)		Statistical test applied
	≤1.5	≥1.6	
Yes	18	16	$X^2 = 5.616$ P = 0.018**
No	19	47	
Total	37	63	

DISCUSSION

The present study included 100 type 2 diabetes mellitus patients and 100 non diabetic control subjects, their age were ranging from 30-70 years. In the diabetes group 51% of the patients were males and 49% were females. In controls 58% were males and 42% were females. Serum magnesium levels were determined in all these subjects. 37% of diabetic patients had low serum magnesium levels and 9% of non-diabetic controls had low serum magnesium levels. The mean serum magnesium level was 1.96 mg/dL and 2.375 mg/dL in diabetics and controls respectively. Similar results were found in a study done by Monika K et al.[6]

Nadler JL et al. in his study showed that an intracellular RBC Mg^{2+} concentration of diabetic patients was significantly reduced compared with values in non-diabetic control subjects.[2] The results of this study were similar to the study done by Nagase N et al.[7] and Sharma A et al.[8]

Magnesium is the major intracellular divalent cation. Normal concentrations of extracellular magnesium and calcium are crucial for normal neuromuscular activity. Intracellular magnesium forms a key complex with ATP and is an important cofactor for a wide range of enzymes, transporters and nucleic acids required for normal cellular function, replication and energy metabolism.[9]

Resnick and associates suggest that extracellular and intracellular magnesium deficiency is typical in chronic, stable, mild type 2 diabetes and may be a strong predisposing factor for the development of the excess cardiovascular morbidity associated with diabetes.[10]

Among its many actions, insulin stimulates the transport of magnesium from the extra-cellular to the intracellular compartment. Insulin resistance central to type 2 diabetes is associated with reduced intracellular magnesium and can be mitigated with magnesium. It has been demonstrated that insulin resistance in skeletal muscle can be reduced by magnesium administration. Reduced magnesium levels in diabetes are caused by several factors. The link between magnesium deficiency and the development of diabetes is strengthened by the observation that several treatments for type 2 diabetes appear to increase magnesium levels.[11-14]

Corica F et al. in their study showed that hypomagnesaemia is highly prevalent in diabetic patients. High plasma triglycerides, waist circumference and albuminuria are independent correlates of hypomagnesemia.[15]

Matthias B et al., in their prospective study showed that high cereal fiber and magnesium intakes may decrease diabetes risk.[16]

In the present study hypomagnesemia (Mg^{2+} level ≤1.5 mg/dL) was correlating with retinopathy (P = 0.041 significant) and hypertension (P = 0.018 significant).

De Valk HW in a study found that patients with severe retinopathy have a lower plasma magnesium level compared to patients without retinopathy and a prospective study has shown the plasma magnesium level to be inversely related to occurrence or progression of

retinopathy.[17] Garland HO in his study speculated on a potential link between the magnesium deficit in diabetes and several diabetic complications including cardiovascular problems and retionopathy.[18]

To conclude, in this study serum magnesium levels were lower in type 2 diabetic mellitus patients when compared with non-diabetic controls and hypomagnesaemia was correlating with retinopathy and hypertension. Because Mg^{2+} depletion reduces insulin sensitivity and may increase risk of secondary complications, it may be prudent in clinical practice to periodically monitor plasma Mg^{2+} concentrations in diabetic patients. If plasma Mg^{2+} is low, an intervention to increase dietary intake of magnesium may be beneficial.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics and research committee

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DOI: 10.5455/2320-6012.ijrms20150305
Cite this article as: Surendra Naik N, Lamani S, Devarmani SS. The role of serum magnesium level in type 2 diabetes mellitus. Int J Res Med Sci 2015;3:556-9.