National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Serum magnesium levels in type 2 diabetes with metabolic syndrome

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Received: May 17, 2016; **Accepted:** June 07, 2016

ABSTRACT

Background: Diabetes is a serious illness with multiple complications and premature mortality. Type 2 diabetes is the predominant form of diabetes worldwide, and it accounts for 90% of cases globally. Large majority with Type 2 diabetes have the metabolic syndrome (MS). MS is a widely prevalent disorder, and it is associated with increased risk for the development of cardiovascular disease, cerebrovascular disease, and renal disease. **Aims and Objectives:** The present study was conducted to find out the relationship between serum magnesium levels and MS. **Materials and Methods:** The study was conducted in 135 diabetic patients. They were divided into 2 groups. 90 Type 2 diabetic patients with MS and 45 Type 2 diabetic patients without MS. 45 normal healthy adults were included in the control group. **Results:** The study showed that mean serum magnesium levels were significantly lower in patients with MS when compared with that of healthy adults. Correlation analysis revealed a significant negative correlation between serum magnesium levels and fasting blood sugar, systolic blood pressure (BP), diastolic BP, triglyceride levels, and a positive correlation between serum magnesium and high-density lipoprotein levels. **Conclusion:** MS is highly prevalent in our population. Low serum magnesium levels play an important role in the pathogenesis of MS. Studies have shown that magnesium intake is inversely associated with incident MS and its components. Hence, magnesium supplementation in young adults can prevent the development of MS and thereby the complications related to it.

KEY WORDS: Magnesium; Metabolic Syndrome; Type 2 Diabetes

INTRODUCTION

Diabetes mellitus is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia with disturbance of carbohydrate metabolism resulting from defect in insulin secretion, insulin action, or both.[1] India is one among the leading countries having the largest number of diabetic subjects in the world. Pronounced changes in the human environment, behavior, and lifestyle has led to an alarming increase in the prevalence of diabetes in the past two decades.

Type 2 diabetes is the predominant form of diabetes worldwide accounting over 90% of cases globally.[2] Large majority of patients with type 2 diabetes have the metabolic syndrome (MS). The MS, or the insulin resistance syndrome, or syndrome X are terms used to describe a constellation of metabolic derangements that includes type 2 diabetes, hypertension, dyslipidemia (low high-density lipoprotein [HDL] and elevated triglycerides [TG]), central or visceral obesity.[3] MS is emerging as one of the major medical and public health problems worldwide.

Changes in lifestyle, increased dietary intake of carbohydrates and saturated fats, reduced intake of fiber, and increased body mass index have led to an increased risk for the development of MS. Approximately 20-30% of the population in

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Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2016.6.0615307062016	

industrialized countries has MS.[4] Asian Indians have a greater prevalence of this syndrome. Genetics and the environment both play important roles in the development of MS. Genetic factors influence each component of the syndrome and the syndrome itself. Environmental issues such as low physical activity, sedentary lifestyle, and progressive weight gain also contribute significantly to the risk of developing the MS.[4]

Each component of the MS is an established cardiovascular risk factor, and the presence of multiple components greatly increases the risk for the development of cardiovascular disease. Besides cardiovascular disease, individuals with MS are susceptible to other conditions such as polycystic ovary syndrome, fatty liver, cholesterol gallstones, asthma, sleep disturbances, and some forms of cancer.[5]

Dyslipidemia of MS is characterized by raised serum TG, lowered concentrations of HDL cholesterol, and small low-density lipoprotein (LDL) particles.[1] These lipid abnormalities have been called atherogenic dyslipidemia because each component of atherogenic dyslipidemia appears to promote atherosclerosis independently.

Patients with MS are found to have increased blood levels of apolipoprotein B, uric acid, pro-inflammatory cytokines, and increase in blood viscosity.[1] They also have increased levels of prothrombotic factors (plasma plasminogen activator inhibitor-1, fibrinogen, and certain coagulation factors). The combination of these coagulation factors gives rise to a prothrombotic state, which predisposes to coronary heart disease.[6] Adiponectin levels were found to be low in people with MS. Adiponectin is a protein which inhibits the expression of gluconeogenic enzymes and the rate of glucose production in the liver. In muscle, adiponectin increases glucose transport and enhances fatty acid oxidation. Thus, it helps to reduce blood sugar levels.[1]

Mg is a bivalent cation, which has very important roles in body metabolism. Magnesium is a cofactor for hundreds of enzymes, particularly those involved in the transfer, storage, and use of energy.[7] It is part of many enzymes, which play important roles in carbohydrate, protein, and fat metabolism.

Magnesium balance is regulated by the interaction between intake through the diet, its absorption, and renal excretion. Its deficiency provokes biochemical and symptomatic alterations in the body.

Magnesium plays a fundamental role in carbohydrate metabolism by stimulating glucose uptake in the insulin-sensitive tissues such as the adipose tissue and skeletal muscle. It influences blood pressure (BP) by modulating the vascular tone. Mg acts as a natural physiologic calcium channel blocker thereby decreasing the vasoconstrictor actions of calcium.[8]

In cholesterol biosynthesis, magnesium inhibits the conversion of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) to mevalonate by HMG-CoA reductase which is the rate limiting step. It is also necessary for the activity of lecithin cholesterol acyl transferase (LCAT) and lipoprotein lipase (LPL), which help to lower LDL cholesterol and TG and to raise the levels of HDL cholesterol.[9]

The present study was done to find out the serum magnesium levels in MS patients and to find out its relation with different components of the syndrome.

MATERIALS AND METHODS

The study was conducted in a total of 180 subjects in the age group 45-65 years. Of this, 45 were included in the control group. The rest 135 were diabetic patients admitted to medical wards of Medical College Hospital, Kozhikode. The study was done after obtaining approval from the Institutional Ethics Committee.

The study population was divided into two groups.
Group 1: Consisted of 90 type 2 diabetic patients with MS.
Group 2: Consisted of 45 type 2 diabetic patients without MS.

Patients were grouped into those having MS and those not having MS based on the diagnostic criteria suggested by the US National Cholesterol Education Program – Adult Treatment Panel III (NCEP ATP-III).[1] According to the US NCEP ATP-III, MS is diagnosed by the presence of any 3 of the following criteria:

- Elevated values of waist circumference >102 cm in males and >88 cm in females
- BP ≥130 mm systolic or ≥85 mm diastolic (SBP or DBP)
- Fasting blood sugar (FBS) ≥100 mg/dL
- TG ≥150 mg/dL
- Reduced levels of HDL <40 mg/dL in males and <50 mg/dL in females.

In the present study, patients having diabetes and any two or more of the above criteria were grouped as diabetics with MS and those having diabetes and none of the above criteria were grouped as diabetics without MS. The control group consisted of 45 normal healthy adults who were the bystanders from various wards. They had no history of diabetes. Patients with renal failure, malignancies, psychiatric problems, alcoholics, and smokers were excluded from the study.

Waist circumference was measured in centimeters using a tape kept midway between lower costal margin and the upper border of iliac crest.

BP was recorded in the sitting position.

Blood samples were collected after 8-12 h of FBS, serum lipid profile, and serum magnesium were estimated. The various tests with blood samples were done in clinical biochemistry laboratory of Medical College Hospital.

Colorimetric end point method with xylidyl blue was used for the quantitative determination of magnesium. In alkaline solution, magnesium forms a colored complex with xylidyl blue which is determined photometrically. The color is proportional to the magnesium concentration up to 5 mg/dl.

Statistical Analysis

The present study is designed as a case-control study. Data were analyzed using Statistical Package for Social Sciences. Mean differences between the groups were analyzed using ANOVA (Analysis Of Variance). The correlation coefficient used to denote association between two continuously measured variables is the Pearson's correlation coefficient. Correlation coefficient "*r*" tends to lie between +1.0 and −1.0. If '*r*' is near +1.0, it indicates a strong positive association. A value near −1.0 indicates a strong negative association. A correlation coefficient of zero denotes absolutely no correlation. The nearer the coefficient is to zero; the poorer is the correlation. All correlations were considered to be significant if $P \leq 0.05$.

RESULTS

Observations of the present study were recorded in Tables 1-3 and Figures 1-5.

DISCUSSION

Magnesium is the second most abundant cation (after potassium) present in living. It is directly involved in numerous important biochemical reactions. It is also involved in hormone receptor binding, gating of calcium channels, transmembrane ion flux, and control of vascular tone and cardiac excitability.[7]

The present study was conducted to find out the relationship between magnesium and the components of MS. Our study showed that mean serum magnesium levels were significantly lower in patients with MS when compared with that of healthy adults (Table 2 and Figure 1). Similar results were observed by Guerrero-Romero and Rodríguez-Morán[10] and Evangelopoulos et al.[11] Low magnesium levels have been implicated as an important pathogenic factor in most of the disorders of MS.[12] Low magnesium levels promote endothelial cell dysfunction. Endothelial dysfunction forms the basis of development of several components of MS including hypertension, blood lipid disorders, and thrombosis.[13]

The present study also showed a significant decrease in the serum magnesium levels in type 2 diabetic patients without MS when compared with those of normal controls (Table 2 and Figure 2). Similar findings were observed in studies by Chambers et al.[14] and Seyoum et al.[15] Low levels of Mg increase the microviscosity of the plasma membrane and this, in turn, impairs the interaction of insulin with its receptor.[14] Low dietary intake of Mg and increased loss of Mg in urine are the main causes of Mg deficit in diabetic subjects.

Correlation analysis revealed a significant negative correlation between serum magnesium levels and fasting blood sugar (Figure 4). The studies done by Rosolova et al.[16] indicated that insulin-mediated glucose disposal was decreased in subjects with low plasma magnesium concentration. A poor intracellular Mg concentration, result

Table 1: Mean levels of FBS, SBP, DBP, HDL, TG, and waist circumference in the study groups

Parameters	Control	DM without MS	DM with MS
FBS (mg/dL)	88±5.96	165.44±38.31	180.51±78.07
SBP (mm of Hg)	121.2±5.53	123.78±4.16	138.22±20.01
DBP (mm of Hg)	79.56±4.09	81.2±2.68	88.47±8.62
HDL (mg/dL)	55.16±4.65	51.51±3.26	42.6±6.70
TG (mg/dL)	117.3±15.81	120.53±15.8	165.61±59.30
Waist circumference (cm)	82.49±5.17	83.44±5.04	91.28±7.41

FBS: Fasting blood sugar, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL: High-density lipoprotein, TG: Triglycerides, DM: Diabetes mellitus, MS: Metabolic syndrome

Table 2: Comparison of serum magnesium levels in type 2 diabetic patients with MS and in control group

	Serum magnesium mg/dL	
	Control	DM with MS
Mean±SD	2.424±0.246	1.897±0.247

n=135, *P*=0.001. SD: Standard deviation, DM: Diabetes mellitus, MS: Metabolic syndrome

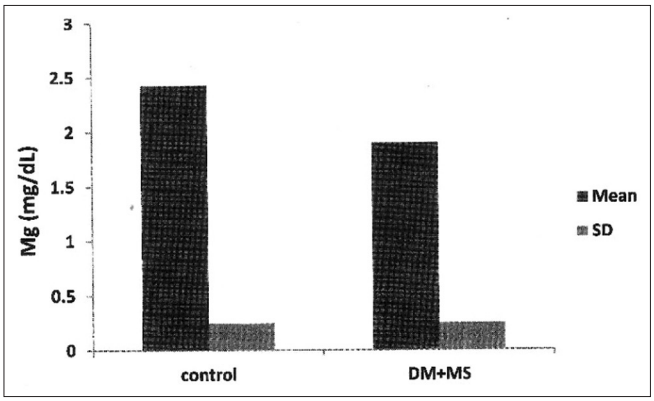

Figure 1: Comparison of serum magnesium levels in type 2 diabetic patients with metabolic syndrome and in control group

in a defective tyrosine-kinase activity at the insulin receptor level.[17] Impaired response of the tyrosine kinase to insulin stimulation is one of the potent mechanisms causing insulin resistance in type 2 diabetes. The study also showed that the serum magnesium levels in diabetic patients with MS were lower when compared with serum magnesium levels of diabetic patients without MS (Table 4 and Figure 2).

A negative correlation was noted between serum magnesium levels and SBP as well as SBP, both of which were statistically significant (Figures 4 and 5). Guerrero-Romero and Rodríguez-Morán[10] and Lima Mde et al.[18] also obtained similar negative correlation.

Mg acts as modulator of contraction of smooth muscle of vessel wall. Magnesium stimulates the production of vasodilator substances such as prostacyclin and nitric oxide and decreases the production of endothelial-derived vasoconstrictors such as endothelin-1.[19] Magnesium deficiency also causes increased sympathetic nervous system activity thereby leading to elevated BP.[12]

Our study also showed a significant negative correlation between serum magnesium levels and TG levels and a positive correlation between serum magnesium and HDL levels (Figures 6 and 7). These findings were consistent with the results obtained by Guerrero-Romero and Rodríguez-Morán[13] and Nozue et al.[20]

Table 3: Comparison of serum magnesium levels in type 2 diabetic patients without metabolic syndrome and in control group

	Serum magnesium mg/dL	
	Control	**DM without MS**
Mean±SD	2.424±0.246	2.053±0.196

n=90, *P*=0.001. SD: Standard deviation, DM: Diabetes mellitus, MS: Metabolic syndrome

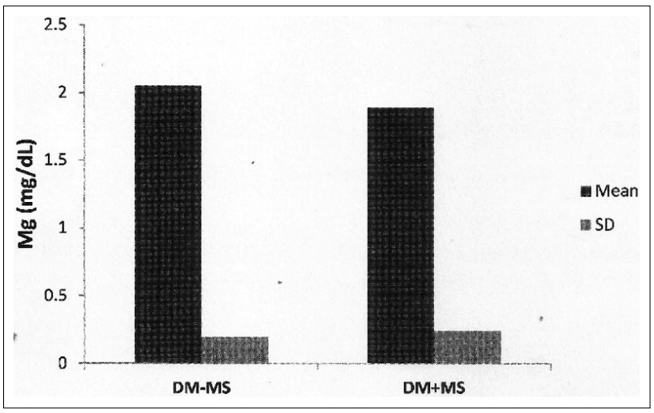

Figure 2: Comparison of serum magnesium levels in type 2 diabetic patients with and without metabolic syndrome

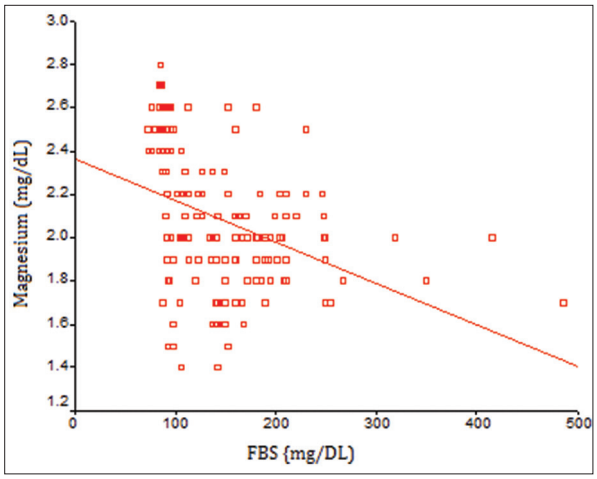

Figure 3: Scatter plot showing correlation between serum magnesium and fasting blood sugar in the study groups [Negative correlation; Correlation coefficient r = - 0.4; *p* = 0.001 (Significant)]

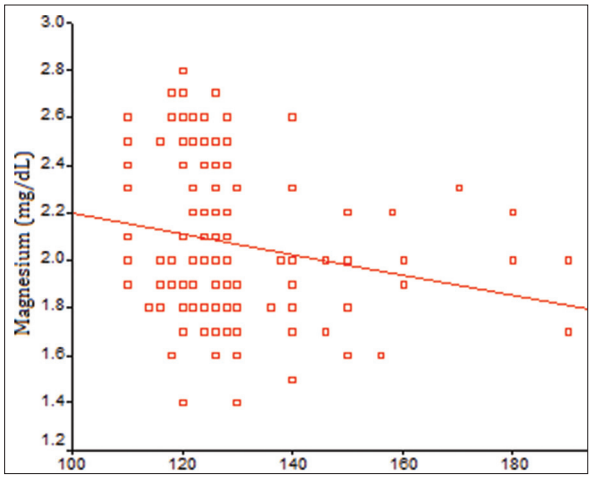

Figure 4: Scatter plot showing correlation between serum magnesium and systolic blood pressure in the study groups [Negative correlation; Correlation coefficient r = - 0.2; *p* = 0.001 (Significant)]

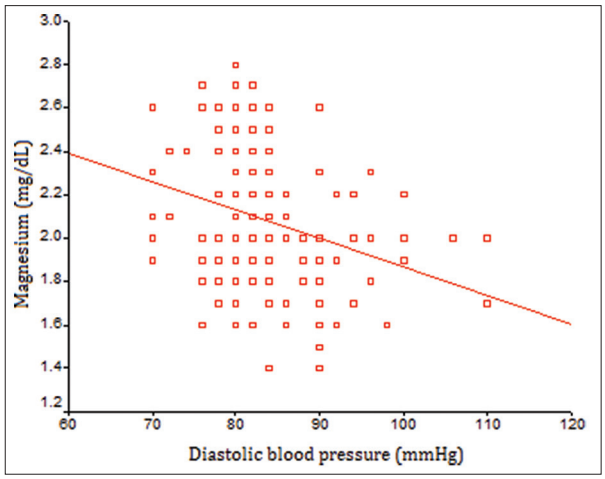

Figure 5: Scatter plot showing correlation between serum magnesium and diastolic blood pressure in the study groups [Negative correlation; Correlation coefficient r = - 0.3; *p* = 0.002 (Significant)]

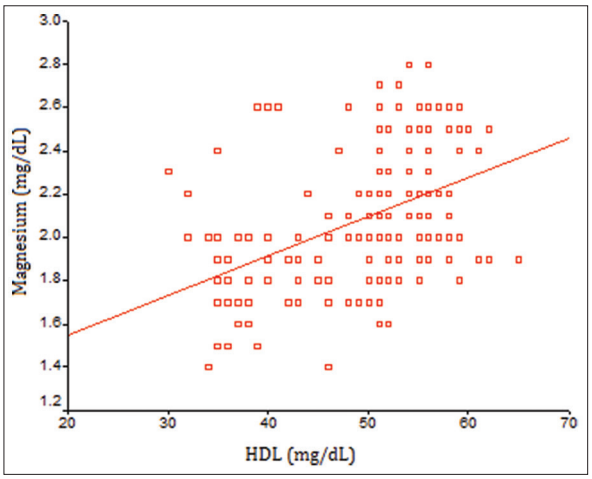

Figure 6: Scatter plot showing correlation between serum magnesium and HDL in the study groups [Positive correlation; Correlation coefficient r = 0.45; p = 0.001 (Significant)]

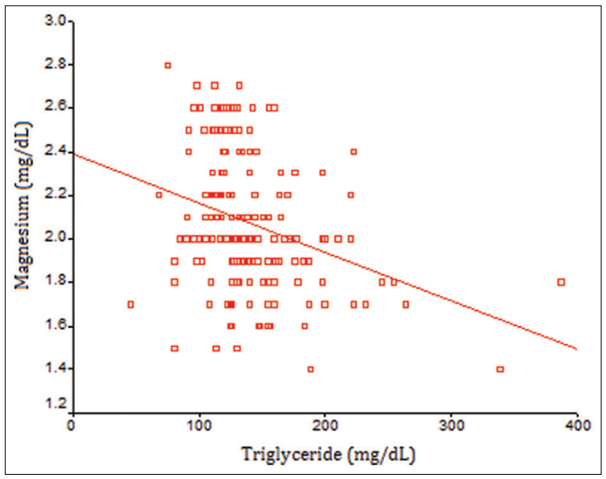

Figure 7: Scatter plot showing correlation between serum magnesium and Triglyceride in the study groups [Negative correlation; Correlation coefficient r = - 0.3; p = 0.001 (Significant)]

Magnesium deficiency produces hypertriglyceridemia and low levels of HDL by modulating the actions of enzymes involved in cholesterol metabolism. Low Mg levels diminish the activity of lecithin cholesterol acetyltransferase and LPL and increase the activity of HMG-CoA reductase. Impaired LCAT activity can reduce the formation of HDL and impair transport and disposal of TG.[9]

Hypomagnesemia is highly prevalent both in diabetic patients and in patients with MS. As hypomagnesemia is involved in the pathogenesis of risk factors contributing to coronary heart disease correction of Mg deficiency is of great importance in MS patients.

Clinical trials have shown that high intake of Mg produces significant improvements in blood sugar levels, lipid status, and hypertension.[21] Dietary magnesium intake and supplementation are inversely associated with the risk for MS and its components.[13] Correction of magnesium levels by magnesium supplementation helps to prevent the development of complications and thus reduce the morbidity and mortality in these patients.

Hence, the current study emphasizes the need for early magnesium supplementation in diabetic patients and in patients with MS to improve their glycemic control and to prevent the complications related to them.

CONCLUSION

MS is highly prevalent in our population. Low serum magnesium levels play an important role in the pathogenesis of MS. Studies have shown that magnesium intake is inversely associated with incident MS and its components. Hence, magnesium supplementation in young adults can prevent the development of MS and thereby the complications related to it.

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How to cite this article: Razeena KC, Maliekkal J, Nair G. Serum magnesium levels in type 2 diabetes with metabolic syndrome. Natl J Physiol Pharm Pharmacol 2016;6(6):520-525.

Source of Support: Nil, **Conflict of Interest:** None declared.