Relation of serum magnesium level to microvascular complications and the components of metabolic syndrome in patients with type 2 diabetes mellitus

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Background and aim
Diabetes mellitus is associated with magnesium (Mg) depletion in intracellular and extracellular compartments. Hypomagnesemia has been suggested to be associated with macrovascular and microvascular complications of diabetes. The effect of the metabolic syndrome (MetS) has markedly increased. Recently, there is increasing evidence that dietary Mg intake and supplementation are inversely associated with the risk for MetS and its components.
The aim of this study is to evaluate the relation of Mg level to diabetes, its microvascular complications, and MetS components in Egyptian patients with type 2 diabetes mellitus.
Patients and methods
The study involved 90 patients older than 35 years who were divided into two groups: 70 patients with type 2 diabetes and 20 patients as control. Patients' group was subdivided into those with complications (neuropathy, retinopathy, and nephropathy) and those without complications. For every patient, history and clinical examination including blood pressure, waist circumference, testing for peripheral neuropathy, and fundus examination were done. Fasting blood sugar (FBS) and 2-h postprandial blood sugar (2-h PPBS), glycated hemoglobin (HbA1c), albumin/creatinine ratio, creatinine level, total cholesterol, high-density lipoprotein-cholesterol, triglycerides, and serum Mg were obtained.
Results
Serum Mg was significantly lower in diabetic patients than in control (P=0.007). Hypomagnesemia was detected in 56 (80%) patients and none of control. Mg was lower in patients with complications than in patients without; however, the difference was statistically insignificant. Statistically significant negative correlation between serum Mg with serum cholesterol, triglyceride, creatinine level, albumin/creatinine ratio, FBS, 2-h PPBS, and HbA1c was found.
Conclusion
Hypomagnesemia is prevalent in diabetic patients. It is associated with diabetic complications and poor glycemic control. High plasma triglycerides, total cholesterol, creatinine level, albuminuria, HbA1c, FBS, and 2-h PPBS are independent correlates of hypomagnesemia.

Keywords:
diabetic complications, glycemic control, hypomagnesemia

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Introduction

Magnesium (Mg) is one of the most abundant intracellular cations with an essential role in biological reactions, whose deficiency provokes biochemical and symptomatic alterations in humans [1].

Several evidences suggest that Mg depletion may play a role in the pathophysiology of diabetes mellitus (DM), hypertension, dyslipidemia, and insulin resistance [2].

The Atherosclerosis Risk in the Community study found a significant association between hypomagnesemia and the incidence of type 2 DM [3]. Mg depletion is frequent in diabetic patients, and the impairment of Mg homeostasis may relate to the onset and progression of diabetic complications [4], and Mg intake can delay the development and decrease the incidence of type 2 DM [5,6].

Furthermore, it has been suggested that reduced serum Mg could be the missing link to understand the epidemiological link between DM and metabolic syndrome (MetS) [7]. As patients with MetS are at high risk of DM, cardiovascular disease, and increased

cardiovascular and all causes mortality, the knowledge of the MetS underlying mechanisms may help to produce interventions aimed to slow the growing dangerous epidemic [8,9].

Aim

The aim of the study is to evaluate the relation of Mg level to diabetes, its microvascular complications, and the correlation between Mg level and components of MetS in a random sample of Egyptian patients with type 2 DM.

Patients and methods

In this cross-sectional case–control study, 90 patients older than 35 years were involved, and they were divided into two groups: 70 patients with type 2 diabetes for 5 years or more (24 men and 46 women) and 20 patients as control (seven men and 13 women). All patients were selected from the outpatient clinic of Endocrinology and Diabetes department, Kasr El Aini Cairo University Hospital, and control were volunteers. Patients with known renal disease or obstructive uropathy; patients known to have endocrinal cause for obesity, for example, hypothyroidism or Cushing's syndrome; and patients receiving antipsychotics, antiepileptic drugs, corticosteroids, diuretics, or any preparation containing Mg were excluded.

Ethical aspects

Research protocols were approved by the medical ethics committee of Kasr El Aini Medical School, Cairo University. A verbal consent was taken from all participants after the research protocols were explained carefully to them. Data were coded, and the participants' names or identity was concealed in data collection forms or during statistical analysis.

Procedure

Patients' group was subdivided into those with complications (neuropathy, retinopathy, and nephropathy) and those without complications. For every patient, history and clinical examination including blood pressure, waist circumference, testing for peripheral neuropathy, and fundus examination were done. Fasting blood sugar (FBS) and 2-h postprandial blood sugar (2-h PPBS), glycated hemoglobin (HbA1c), albumin/creatinine ratio, serum creatinine level, total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and serum Mg (using spectrophotometer) were done.

Statistical analysis

Data were analyzed using Microsoft Office 2003 (Excel) and statistical package for the social science (SPSS, version 16; SPSS Inc., Chicago, Illinois, USA). Parametric data were expressed as mean and SD, and nonparametric data were expressed as number and percentage of the total. Determining the relation between two studied parameters was done using correlation coefficient. *P* value less than 0.05 is considered significant.

Results

Serum Mg level was significantly lower in diabetic patients with and without complications compared with control (1.38±0.27 vs. 1.95±0.33, respectively, P=0.007).

Hypomagnesemia was detected in 56 (80%) patients and none of control.

In the current study, FBS and 2-h PPBS, HbA1c, creatinine level, urinary albumin/creatinine ratio, cholesterol, and triglyceride were significantly higher and HDL was lower in diabetic patients than in control.

Regarding microvascular complications, 21 (30%) patients had retinopathy, 21 (30%) patients had neuropath, and 49 (70%) patients had nephropathy. The prevalence of hypomagnesemia was high among patients with microvascular diabetic complications, as 20 (95.2%) of 21 patients with retinopathy, 16 (76.1%) of 21 patients with neuropathy, and 51 (98%) of 52 patients with nephropathy had hypomagnesemia. Mg level was lower in patients with complications than in patients without; however, the difference was statistically insignificant.

We used the IDF diagnostic criteria for MetS assessment, and accordingly, all our patients had MS (among the studied 46 female patients, 24 of them had four criteria of MS and 22 had all criteria of MS, and among the 24 male patients, six of them had all criteria of MS and 18 had three criteria) [10].

In diabetic patients, statistically significant negative correlation was found between serum Mg level with serum cholesterol, triglyceride, creatinine, albumin/creatinine ratio, FBS, 2-h PPBS, and HbA1c; however, there was no significant correlation between serum Mg level and HDL, age, systolic, diastolic blood pressure, or waist circumference (Tables 1–3 and Figs 1–5).

Table 1 Demographic and clinical data of the studied groups

Parameters	Groups		
	Control group (*n*=20)	Patient group (*n*=70)	*P* value
Age (year)	47.65±9.30	48.70±6.25	0.124
Sex (male/female)	7/13	24/46	0.341
SBP (mmHg)	127.00±5.23	145.93±14.48	0.0001**
DBP (mmHg)	79.75±5.50	87.50±8.71	0.0001**
Waist circumference (cm)	82.60±9.99	95.77±9.37	0.0001**

There was a statistically significant increase in the mean±SD of systolic, diastolic blood pressure, and waist circumference among the patients group when compared with control group. DBP, diastolic blood pressure; SBP, systolic blood pressure. **$P<0.01$.

Table 2 Laboratory data of the studied groups

Parameters	Groups		
	Control group (*n*=20)	Patient group (*n*=70)	*P* value
Mg (mg/dl)	1.95±0.33	1.38±0.27	0.007**
FBS (mg/dl)	82.70±5.98	179.01±21.73	0.0001**
PPBS (mg/dl)	130.00±5.85	310.47±38.48	0.0001**
HbA1c (%)	5.15±0.65	8.11±1.10	0.0001**
Creatinine level (mg/dl)	0.97±0.17	1.94±0.45	0.0001**
Alb/Cr ratio (mg/dl)	21.50±3.25	145.93±62.89	0.0001**
Cholesterol (mg/dl)	163.95±18.55	184.97±25.25	0.0001**
TG (mg/dl)	126.25±13.75	168.44±24.35	0.0001**
HDL (mg/dl)	70.75±10.21	33.39±9.19	0.0001**

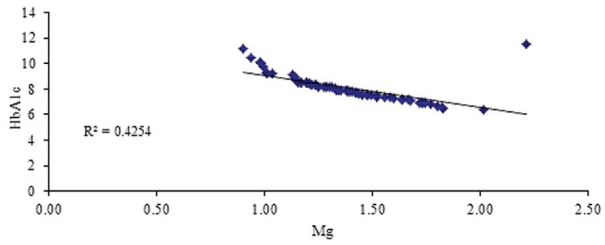
Serum Mg and HDL were significantly lower in diabetic patients compared with control, whereas FBS, PPBS, HbA1c, creatinine level, urinary Alb/Cr, cholesterol, and TG were significantly higher in diabetic patients than in control. Alb/Cr, albumin/creatinine ratio; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; Mg, magnesium; PPBS, postprandial blood sugar; TG, triglyceride. **$P<0.01$.

Table 3 Correlation between magnesium level and other studied parameters among diabetic patients

	Mg (mg/dl)	
	r Value	*P* value
Cholesterol (mg/dl)	–0.986	0.0001**
TG (mg/dl)	–0.932	0.0001**
HDL (mg/dl)	0.199	>0.05
Creatinine level (mg/dl)	–0.928	0.0001**
Alb/Cr (mg/dl)	–0.961	0.0001**
FBS (mg/dl)	–0.738	0.0001**
PPBS (mg/dl)	–0.862	0.0001**
HbA1c (%)	–0.569	0.0001**
Age (year)	0.307	>0.05
SBP (mmHg)	0.105	>0.05
DBP (mmHg)	0.173	>0.05
Waist circumference(cm)	–0.008	>0.05

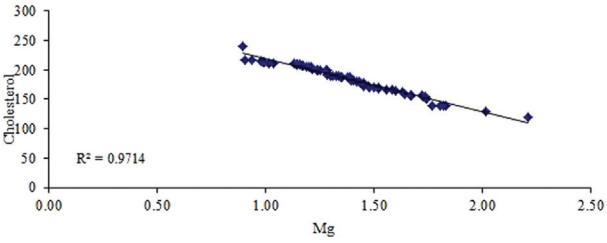
There was a statistically significant negative correlation between serum magnesium level and serum cholesterol, TG, creatinine level, Alb/Cr, FBS, PPBS, and HbA1c. Alb/Cr, albumin/creatinine ratio; DBP, diastolic blood pressure; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; Mg, magnesium; PPBS, postprandial blood sugar; SBP, systolic blood pressure; TG, triglyceride. **$P=0.0001$.

Figure 1



Correlation between serum magnesium (Mg) level and glycated hemoglobin (HbA1c).

Figure 2



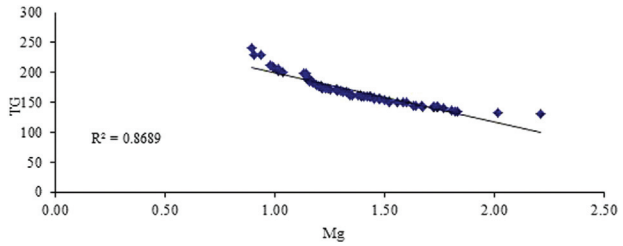
Correlation between serum magnesium (Mg) level and serum cholesterol level.

Discussion

In this study, we found that serum Mg level is significantly lower in diabetic patients than in control, and hypomagnesemia is more prevalent in diabetics as it was detected in 56 (80%) of patients of this study and none of the control.

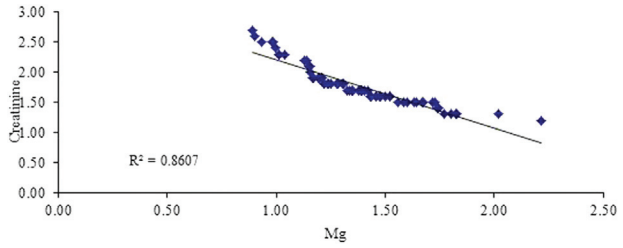
This is supported by many previous studies which have shown that mean plasma Mg levels are lower in patients with both type 1 and type 2 diabetes, prediabetes, and MetS compared with nondiabetic

Figure 3



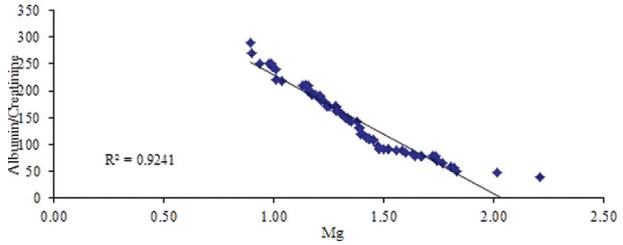
Correlation between serum magnesium (Mg) level and serum triglyceride (TG) level.

Figure 4



Correlation between serum magnesium (Mg) level and serum creatinine level.

Figure 5



Correlation between serum magnesium (Mg) level and urinary albumin/creatinine ratio.

control [11–14] and in patients with diabetic complications [15].

Our study showed statistically significant negative correlation between serum Mg level and FBS, 2-h PPBS, and HbA1c (*P*=0.0001), which is similar to the results of two studies that concluded that hypomagnesemia was associated with poor glycemic control [16,17].

Regarding Mg and lipid profile, our results showed statistically significant negative correlation between serum Mg and serum cholesterol and triglyceride, which agree with the results of some authors [13,18] but not others [19,20].

The prevalence of hypomagnesemia among patients with microvascular diabetic complications was high in the current study, as 20 (95.2%) of 21 patients with retinopathy, 16 (76.1%) of 21 patients with neuropathy, and 51 (98%) of 52 patients with nephropathy had hypomagnesemia.

Our study showed that serum Mg level was lower in patients with retinopathy than in those without retinopathy (1.35±0.27 vs. 1.42±0.27, respectively); however, the difference was not statistically significant (*P*=0.249), which is supported by two different studies which found that diabetic patients with retinopathy had significantly lower serum Mg than those without retinopathy [21,22].

Baig *et al.* [15] found similar results and suggested that hypomagnesemia may act through inhibition of prostacyclin receptor function producing an imbalance between prostacyclin and thromboxane effect which has marked atherogenic potential responsible for microvascular complications.

We found that serum Mg was lower in patients with neuropathy than patients without neuropathy (1.34±0.23 vs. 1.39±0.29, respectively); however, the difference was not statistically significant (*P*=0.478). This is supported by Dasgupta *et al.* [16] who found that hypomagnesemia in diabetes was associated with retinopathy, nephropathy, and foot ulcers as evidence of neuropathy and Xu *et al.* [23] who concluded that in patients with type 2 DM with diabetic complications, the decrease in serum Mg level and the increase in urinary Mg level were independent of the presence of either diabetic nephropathy, retinopathy, or peripheral neuropathy.

Additionally, low Mg level can be because of reduced intestinal absorption caused by diabetic autonomic neuropathy [24]. Studies have found that intracellular Mg levels are lower in patients with diabetic peripheral neuropathy with improvement in the nerve conduction following supplementation [25,26].

Our study showed a highly significant increase (26.35 ± 11.23) in serum creatinine level and albumin/creatinine ratio in patients with nephropathy compared with patients without nephropathy (1.91±0.30 vs. 1.41± 0.10, and 173.61±66.33 vs., respectively; *P*=0.001 and 0.041, respectively).

We found a statistically significant negative correlation between serum Mg level with serum creatinine level and albumin/creatinine ratio in spite of absence of significant difference between serum Mg levels in patients with and those without nephropathy. This is supported by Arpaci *et al.* [17], Corica *et al.* [27], and Corsonello *et al.* [28] who found that diabetic patients

with microalbuminuria or clinical proteinuria showed a significant decrease in serum ionized Mg compared with normoalbuminuria group.

In agreement with the current study results, Pham *et al.* [5,29] found that lower serum Mg levels are associated with more rapid decline of renal function in patients with type 2 DM and revealed in later study that serum Mg has significant negative correlation with estimated glomerular filtration rate. Other authors concluded that hypomagnesemia is a novel predictor of end-stage renal disease in patients with type 2 diabetic nephropathy [16] and found that serum Mg was inversely associated with microalbuminuria [17,30].

We found a highly significant increase in the mean±SD of systolic blood pressure, diastolic blood pressure, and waist circumference among the patient group when compared with that of the control group ($P<0.01$); however, there was no significant correlation between these parameters and serum Mg level. On the contrary, Corica *et al.* [27] found that waist circumference and high blood pressure are independently associated with low serum ionized Mg level.

Conclusion

Hypomagnesemia is prevalent in diabetic patients. It is associated with diabetic complications (retinopathy, neuropathy, and nephropathy) and poor glycemic control. High plasma triglycerides, total cholesterol, creatinine level, albuminuria, HbA1c, FBS, and 2-h PPBS are independent correlates of hypomagnesemia. Further studies are recommended to determine the effect of Mg supplementation on prevention of MetS, diabetes, and its complications.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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