Original Article

Magnesium Levels In Type 2 Diabetic Patients And Its Correlation With Blood Glycaemia And Inflammation

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Abstract

Background: Magnesium (Mg) deficiency is a common problem in diabetic patients. Deficiency of Mg may increase the incidence of diabetes mellitus (DM) and occurrence of diabetic complications. Our study aimed to evaluate Mg levels in type 2 diabetic patients and its correlation with blood glycaemia and inflammation. **Patients and methods:** In this cross sectional study 80 diabetic patients were evaluated. Total Mg, ionized Mg, fasting blood glucose, HBA1C and C- reactive protein (CRP) were estimated in all studied patients. **Results:** There was statistically significant negative correlation between total serum Mg and FBS among studied T2DM patients. There was no statistically significant negative correlation between total serum Mg and HBA1C among studied T2DM patients. There was no statistically significant negative correlation between total serum Mg and CRP among studied T2DM patients. There was statistically significant association between total and ionized Mg levels. Among studied T2DM patients there was statistically significant negative correlation between ionized Mg and FBS and there was statistically significant positive correlation between ionized Mg and total serum Mg. **Conclusion:** Hypomagnesaemia was found to be associated with poor glycemic control and inflammation.

Keywords: Magnesium levels; blood glycaemia; inflammation; correlation

INTRODUCTION

Diabetes mellitus (DM) is a chronic, non-communicable disease with high morbidity and mortality due to chronic deterioration of insulin-producing cells **(1)**. DM is closely related to the disruption of the body's energy balance, which includes a sedentary life together with a high caloric intake that induces obesity **(2)**. The presence of complications in DM has devastating implications, leading to deterioration in the quality of life for those who suffer from the disease **(3)**.

Magnesium (Mg) has a critical role in the actions of important enzymes and is the fourth most abundant cation in the human body **(4)**. It is claimed that there is an inverse relationship between Mg intake and incidence of diabetes mellitus (DM)**(5)**.

Intracellular free Mg levels are consistently reduced in subjects with T2DM, when compared with nondiabetic subjects. Although the mechanism has not been fully elucidated, an alteration in the mechanism(s) of the Mg uptake in the cells, and/or a deficit of ATP, may help to understand the cellular Mg deficit observed in T2DM **(5)**.

Patients are considered frankly hypomagnesemic with serum Mg concentrations ≤ 0.61 mmol/L or 1.5 mg/dL. Mg concentrations ≤ 0.75 mmol/L or 1.8 mg/dL may be considered as preclinical hypomagnesemia. Mg deficiency can be present without hypomagnesemia. However, hypomagnesemia, when present, is usually indicative of an important systemic Mg deficit. A depletion in intracellular and/or ionized plasma Mg can be found in individuals with normal total serum Mg **(6)**.

During the last few years, the role of CRP in inflammatory states has been reported. The CRP is a protein of an acute phase secreted by the liver as well as by other tissues in response to any inflammatory condition **(7)**.

This study aimed to evaluate Mg levels in type 2 diabetic patients and its correlation with blood glycaemia and inflammation.

PATIENT AND METHOD:

In this cross section study, a total of 80 patients with type 2 diabetes mellitus who were recorded in diabetes outpatient clinic of

our hospital, were included.

Ethical Consideration:

An approval of the study was obtained from Cairo University Academic and Ethical Committee. Written informed consent of all the participants was obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Exclusion criteria were: patients on drugs that affect Mg levels (diuretics, aminoglycosides, amphotericin B, etc), malabsorption or diarrhea, alcohol consumption, vitamin or mineral supplements in recent past, pregnancy, lactation or sepsis.

All measurements and indicators were assessed. Blood samples were collected into centrifuge tubes. Blood was allowed to clot at room temperature for about 1 h and then centrifuged at 3000 rpm for 10 min. The serum was carefully separated into storage tubes and frozen at −20 °C prior to analysis for biochemical tests. Total Mg, ionized Mg, fasting blood glucose, HBA1C and CRP were estimated in all studied patients.

Fasting glucose was measured in fluoridated sera by glucose oxidase/peroxidase method. Glycated hemoglobin (HbA1c) was measured on EDTA blood using Nyco card reader.

Statistical analysis

Using SPSS 18.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics for numeric variables as mean ± standard deviation and median and categorical structure of data was expressed as numbers and percentages. Categorical differences were examined between groups, in terms of structure variables with the Chi-square test. One-way ANOVA test was used for comparison of the normal and low magnesium group. Quantitative variables with normal distribution were compared between two groups using parametric tests, otherwise the Mann-Whitney U test was used. The relationship between two numerical variables was examined using Spearman's correlation analysis. Results were evaluated in 95% confidence interval, and p value of <0.05 was considered as significant.

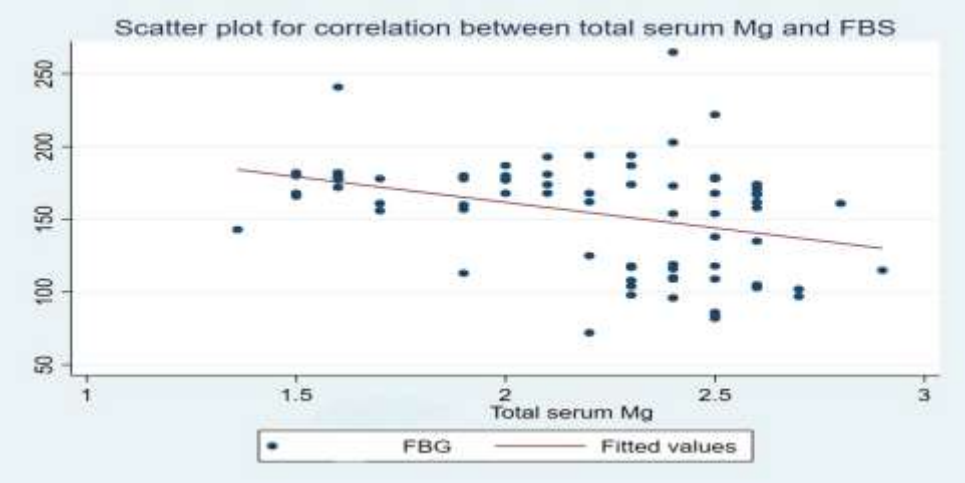
RESULTS

Prevalence of hypomagnesemia among the studied patients with T2DM showed 53.75 % had normomagnesemia and 46.25% had hypomagnesemia for total serum Mg. The estimated ionized showed 20% of diabetic patients had normomagnesemia and 80 % had hypomagnesemia (Table 1). There was statistically significant negative correlation between total serum Mg and FBS among studied T2DM patients (Figure 1).There was no statistically significant negative correlation between total serum Mg and HBA1C among studied T2DM patients (Figure 2).There was no statistically significant negative correlation between total serum Mg and CRP among studied T2DM patients (Figure 3).There was statistically significant association between total and ionized Mg levels (Table 2). Among studied T2DM patients there was statistically significant negative correlation between ionized Mg and FBS and there was statistically significant positive correlation between ionized Mg and total serum Mg (Table 3).

Table (1): Prevalence of hypomagnesemia in patients with T2DM

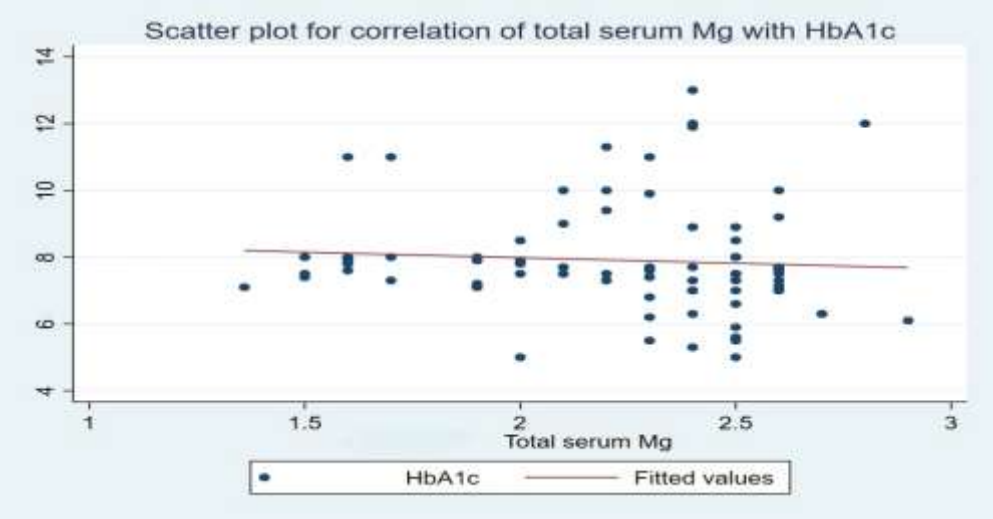
	Control group (n=40) No (%)	%
Total serum Mg		
Normomagnesemia	**43**	**75**
Hypomagnesemia	**37**	**25**
Ionized Mg		

Normomagnesemia	**20**
Hypomagnesemia	**60**



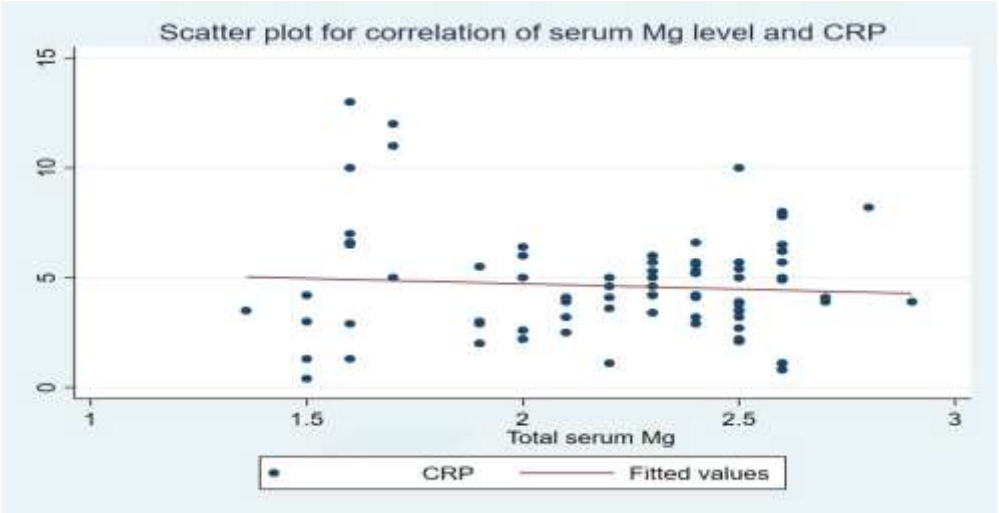
r=-0.3, P=0.001, FBS: fasting blood sugar, Mg: magnesium, *p value is considered significant if <0.05

Figure (1): Correlation between total serum Mg (md/dl) and FBS (mg/dl) among studied T2DM patients



r=-0.007, P=0.5, HBA1C: hemoglobin A1C, Mg: magnesium, *p value is considered significant if <0.05

Figure (2): Correlation between total serum Mg (mg/dl) and HBA1C (%) among studied T2DM patients



r=- 0.07, P=0.5, CRP: C-reactive protein, Mg: magnesium, *p value is considered significant if <0.05

Figure (3): Correlation between total serum Mg (mg/dl) and CRP (mg/l) level among studied T2DM patients

Table (2): Association between total and ionized Mg

	Total serum Mg			
	Normomagnesemia (N=43) No. (%)	**Hypomagnesemia (N=37) No. (%)**	**X^2**	**P-value**
Ionized Mg				
			18.2	<0.001
Normomagnesemia	19 (44.2)	1 (2.7)		
Hypomagnesemia	24 (55.8)	36 (97.3)		

Mg: magnesium

Table (3): Correlation between ionized Mg and and glycemic control, level of CRP and total Mg after intervention among studied T2DM patients

Variables	**Ionized Mg (mg/dl)**	
	r	**P value**
FBS (mg/dl)	**-0.4**	**0.001**
HBA1C (%)	**-0.09**	**0.4**
CRP (mg/l)	**-0.08**	**0.5**
Total serum Mg (mg/dl)	**0.9**	**<0.001**

FBS: fasting blood sugar, HBA1C: hemoglobin A1C, CRP: C-reactive protein, Mg: magnesium, r: Pearson correlation, *p value is considered significant if <0.05

DISCUSSION:

Diabetes mellitus is the most common disorder among endocrine disorders that are associated with hypomagnesemia. So far many studies have shown that Mg levels are lower in diabetic patients **(8,9)**.

According to CARDIA Study (Coronary Artery Risk Development in young Adults) there was an inverse relationship between Mg intake and the incidence of diabetes **(9)**.

The present study included 80 diabetic patient for evaluate Mg levels in type 2 diabetic patients and its correlation with blood glycaemia and inflammation.

In our study, 53.75 % had normomagnesemia and 46.25% had hypomagnesemia for total serum Mg. The estimated ionized showed 20% of diabetic patients had normomagnesemia and 80 % had hypomagnesemia.

The incidence of hypomagnesemia in diabetic patients varies between 11 and 47.7% **(10-12)**. hypomagnesemia in newly diagnosed diabetes is 10.5-fold and in patients with previously diagnosed diabetes is 8.5-fold more common **(13)**.

In our study, there was statistically significant negative correlation between total serum Mg and FBS among studied T2DM patients.

This agree with previous studies revealed a significant negative correlation between Mg and fasting plasma glucose **(9,14).**

Mg depletion may cause poor glycemic control in diabetic patients **(15-17)**. Furthermore, poor glycemic control in diabetic patients is a well-known risk factor for Mg depletion.

On the other hand, in other studies a significant reduction in serum Mg level in diabetic cases were reported **(18,19)**.

In our study, there was no statistically significant negative correlation between total serum Mg and HBA1C among studied T2DM patients.

However, **Pickup et al. (20)** showed a negative correlation between serum Mg and glycosylated hemoglobin (HbA1c) levels was noted. Similarly, a significant negative correlation between Mg and HbA1c **(17)**.

Arpaci et al. (13) found a negative correlation between serum Mg level and HbA1c level. Also, **Mahalle et al. (21)** have found that diabetes was inversely related with serum Mg levels.

There was a statistically significant negative correlation between ionized Mg and FBS and there was statistically significant positive correlation between ionized Mg and total serum Mg.

Many hypotheses for hypomagnesaemia among diabetic patients reported. In patients with Mg deficiency, intracellular calcium is increased. Increased calcium may interrupt response of skelatal muscles and adipocytes to insulin and lead to insulin resistance **(22)**. Intracellular Mg plays a role in regulating insulin action, insulin-dependent glucose uptake, and vascular tone. Deficiency of Mg can reduce tyrosine-kinase activity, postreceptorial activity and eventually it may contribute to the development of insulin resistance **(23,24).**

According to other hypotheses, oxidative stress is important in complications of diabetes[2]. The antioxidative capacity of Mg have also been reported **(25)**. Another hypothesis is that by influencing the activity of Na^+/K^+-ATPase reduction of Mg favors the onset **(26)**.

Therefore, poor glycemic control, and high CRP were the significant predictors of low serum magnesium in diabetic patients.

Besides their regular anti-diabetic treatment, clinicians should also consider dietary supplementation of magnesium to prevent further complications of diabetes in these patients **(27)**.

CONCLUSION:

Strong correlation between hypomagnesaemia and inflammation and glycemic control in patient with type 2 diabetes mellitus suggests that hypomagnesaemia plays an important role in the pathogenesis of diabetes.

REFERENCES:

1- Heydari, I., Radi, V., Razmjou, S., & Amiri, A. (2010). Chronic complications of diabetes mellitus in newly diagnosed patients. International Journal of Diabetes Mellitus, 2(1), 61-63.
2- Zein, C. O., Levy, C., Basu, A., & Zein, N. N. (2005). Chronic hepatitis C and type II diabetes mellitus: a prospective cross-sectional study. Official journal of the American College of Gastroenterology| ACG, 100(1), 48-55.
3- Lotfy, M., Adeghate, J., Kalasz, H., Singh, J., & Adeghate, E. (2017). Chronic complications of diabetes mellitus: a mini review. Current diabetes reviews, 13(1), 3-10.
4- Mather, H., & Levin, G. (1979). Magnesium status in diabetes. The Lancet, 313(8122), 924.
5- Schnack, C. H., Bauer, I., Pregant, P., Hopmeier, P., & Schernthaner, G. (1992). Hypomagnesaemia in type 2 (non-insulin-dependent) diabetes mellitus is not corrected by improvement of long-term metabolic control. Diabetologia, 35, 77-79.
6- Salhi, H., & El Ouahabi, H. (2021). Magnesium status in patients with Type 2 diabetes (about 170 cases). Annals of African Medicine, 20(1), 64.

7- Zghoul, N., Alam-Eldin, N., Mak, I. T., Silver, B., & Weglicki, W. B. (2018). Hypomagnesemia in diabetes patients: comparison of serum and intracellular measurement of responses to magnesium supplementation and its role in inflammation. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 389-400.
8- Del Gobbo, L. C., Song, Y., Poirier, P., Dewailly, E., Elin, R. J., & Egeland, G. M. (2012). Low serum magnesium concentrations are associated with a high prevalence of premature ventricular complexes in obese adults with type 2 diabetes. Cardiovascular diabetology, 11(1), 1-8.
9- Ramadass, S., Basu, S., & Srinivasan, A. R. (2015). SERUM magnesium levels as an indicator of status of Diabetes Mellitus type 2. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 9(1), 42-45.
10- Ma, J., Folsom, A. R., Melnick, S. L., Eckfeldt, J. H., Sharrett, A. R., Nabulsi, A. A., ... & Metcalf, P. A. (1995). Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: the ARIC study. Journal of clinical epidemiology, 48(7), 927-940.
11- Hashizume, N., & Mori, M. (1990). An analysis of hypermagnesemia and hypomagnesemia. Japanese journal of medicine, 29(4), 368-372.
12- Guerrero-Romero, F., Tamez-Perez, H. E., Gonzalez-Gonzalez, G. E., Salinas-Martinez, A. M., Montes-Villarreal, J., Trevino-Ortiz, J. H., & Rodriguez-Moran, M. (2004). Oral magnesium supplementation improves insulin sensitivity in non-diabetic subjects with insulin resistance. A double-blind placebo-controlled randomized trial. Diabetes & metabolism, 30(3), 253-258.
13- Arpaci, D., Tocoglu, A. G., Ergenc, H., Korkmaz, S., Ucar, A., & Tamer, A. (2015). Associations of serum Magnesium levels with diabetes mellitus and diabetic complications. Hippokratia, 19(2), 153.
14- Pham, P. C. T., Pham, P. M. T., Pham, S. V., Miller, J. M., & Pham, P. T. T. (2007). Hypomagnesemia in patients with type 2 diabetes. Clinical journal of the American Society of Nephrology, 2(2), 366-373.
15- Dasgupta, A., Sarma, D., & Saikia, U. K. (2012). Hypomagnesemia in type 2 diabetes mellitus. Indian journal of endocrinology and metabolism, 16(6), 1000-1003.
16- Simmons, D., Joshi, S., & Shaw, J. (2010). Hypomagnesaemia is associated with diabetes: Not pre-diabetes, obesity or the metabolic syndrome. Diabetes research and clinical practice, 87(2), 261-266.
17- Xu J, Xu W, Yao H, Sun W, Zhou Q, Cai L. Associations of serum and urinary magnesium with the pre-diabetes, diabetes and diabetic complications in the Chinese Northeast population. PLoS One. 2013;8:e56750.
18- Corsonello A, Ientile R, Buemi M, Cucinotta D, Mauro VN, Macaione S, et al. Serum ionized magnesium levels in type 2 diabetic patients with microalbuminuria or clinical proteinuria. Am J Nephrol. 2000;20:187–192.
19- Kim DJ, Xun P, Liu K, Loria C, Yokota K, Jacobs DR, Jr, et al. Magnesium intake in relation to systemic inflammation, insulin resistance, and the incidence of diabetes. Diabetes Care. 2010;33:2604–2610.
20- Pickup JC, Chusney GD, Crook MA, Viberti GC. Hypomagnesaemia in IDDM patients with microalbuminuria and clinical proteinuria. Diabetologia. 1994;37:639.
21- Mahalle, N., Naik, S. S., & Kulkarni, M. V. (2012). Is hypomagnesaemia a coronary risk factor among Indians with coronary artery disease?. Journal of cardiovascular disease research, 3(4), 280-286.
22- Nadler, J. L., Malayan, S., Luong, H., Shaw, S., Natarajan, R. D., & Rude, R. K. (1992). Intracellular free magnesium deficiency plays a key role in increased platelet reactivity in type II diabetes mellitus. Diabetes care, 15(7), 835-841.
23- Takaya, J., Higashino, H., & Kobayashi, Y. (2004). Intracellular magnesium and insulin resistance. Magnesium research, 17(2), 126-136.
24- Barbagallo, M., & Dominguez, L. J. (2007). Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. Archives of biochemistry and biophysics, 458(1), 40-47.
25- Resnick, L. M., Altura, B. T., Gupta, R. K., Laragh, J. H., Alderman, M. H., & Altura, B. M. (1993). Intracellular and extracellular magnesium depletion in type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia, 36, 767-770.
26- Barbagallo, M., Di Bella, G., Brucato, V., D'Angelo, D., Damiani, P., Monteverde, A., ... & Dominguez, L. J. (2014). Serum ionized magnesium in diabetic older persons. Metabolism, 63(4), 502-509.
27- Behrouz, V., Dastkhosh, A., & Sohrab, G. (2020). Overview of dietary supplements on patients with type 2 diabetes. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 14(4), 325-334.