Research Article

Magnesium status in a population of type 2 diabetes mellitus in Morocco

Abstract

Background: Type 2 diabetes mellitus (T2DM) contributes to 90% cases of diabetes–the ninth leading cause of death. Magnesium (Mg) levels have been found consistently low in the patients with T2DM around the world.

Objective: The objective of our work was to assess the Mg status in the patients with T2DM.

Material and methods: A descriptive prospective study including 103 patients with type 2 diabetes mellitus (T2DM) was carried out at Avicenna Military Hospital in Marrakesh over a period of four months (October 2019 - January 2020). The patients with T2DM and age above 35years with no history of Mg supplementation, cancer or autoimmune disease were included in the study. Blood samples were analyzed for fasting glucose, lipid profile, HbA1c, and serum magnesium. The data were analyzed by SPSS version 16, Pearson correlation was performed to establish the relationship between Mg and metabolic variables in T2DM patients.

Results: The study included 103 T2DM patients with 56 (54.4%) males and 47 (45.6%) females. Prevalence of hypomagnesemia was 14.56%. Mean age of the patients and duration of diabetes were 59±9 years and 9±4years, respectively. Most common antecedent conditions were dyslipidemia (43.7%), hypertension (42.7%), and retinopathy (25.2%). Hypomagnesemia was significantly associated with HbA1c (P=0.003) and arterial hypertension (P=0.002). Magnesium had negative linear relationship with increased fasting blood sugar and HbA1c.

Conclusion: In Morocco, the prevalence of hypomagnesemia in T2DM patient is low, but it has negative linear relationship with fasting blood sugar and HbA1c.

Keywords: hypomagnesemia, type 2 of diabetes mellitus, Morocco, insulin resistance

W Quiddi,[1] M Tarmidi,[1] A Mansouri,[3,4] M Amine,[3,4] H Baizri,[2] A Boukhira,[1] S Chellak[1]

[1]Clinical Biochemistry and Toxicology Department, Avicenne Military Hospital- FMPM-Cadi Ayyad University- Marrakesh, Morocco
[2]Endocrinology Department, Avicenne Military Hospital-FMPM-Cadi Ayyad University-Marrakesh, Morocco
[3]Clinical Research Department, Mohammed VI University Hospital, Morocco
[4]Community Medicine and Public Health Department, Bioscience et Health Research Lab, School of Medicine, Cadi Ayyad University, Morocco

Correspondence: Dr. Wafa Quiddi, Clinical Biochemistry and Toxicology Department, Avicenne Military Hospital-FMPM- Cadi Ayyad University- Marrakesh, Morocco, Tel +212687946777, Email wafaquiddi@gmail.com

Introduction

Diabetes is a serious and rising global issue, ranking it as the ninth leading cause of death around the globe.[1] Type 2 diabetes mellitus (T2DM) is a multi-factorial, chronic, metabolic disorder characterized by persistent hyperglycemia.[2] Approximately, 462 million people are suffering from T2DM all over the word, imposing a significant impact on human life and healthcare facilities.[3] Globally, T2DM contributes to 90% of all diabetes cases.[1] In the year 2016, the World Health Organization (WHO) reported total population of Morocco as 34378000 with overall prevalence of diabetes mellitus as 12.4% and 24,020 deaths attributable to diabetes.[4] Therefore, diabetes accounts for major mortality and morbidity in Morocco.

Minerals are inorganic micronutrients which play variety of roles in numerous metabolic pathways in the human. Therefore, deficiency of these minerals is linked to certain medical conditions including diabetes, cardiovascular disorders, aging, and kidney problems.[5] Magnesium (Mg) is one of the important minerals, ranking at fourth in its abundance in the world after calcium (Ca), sodium (Na) and potassium (K).[6] The importance of Mg can be recognized by the fact that it works as a cofactor for more than 300 enzymes involved in fundamental reactions occurring in numerous essential anabolic and catabolic processes like ATP generation, glycemic control, signal transduction, DNA replication and repair, and blood pressure maintenance.[7,8]

Magnesium has been reported to be low in metabolic disorders, especially in the patients with T2DM.[9] In this context, the deficiency of Mg is associated with insulin resistance, poor glycemic control, carbohydrate intolerance, lipid disorder and diabetic complications.[10] Therefore, poor intracellular Mg concentration results in insulin resistance and higher Mg levelsenhance insulin sensitivity.[11] The exact role of Mg in the pathogenesis of insulin resistance and T2DM is yet to be elucidated. However, studies have demonstrated that hypomagnesemia leads to defective tyrosine kinase activity, impaired insulin receptor activity, and exacerbated insulin resistance in the patients with T2DM.[11,12] On the other hand, adequate Mg level enhances tyrosine kinase phosphorylation, resulting in increased insulin sensitivity and improved glycemic control.[11]

Hypomagnesemia has been reported to be 44% in non-critically ill patients with T2DM which, in turn, is associated with poor glycemic control and complications like diabetic retinopathy, neuropathy, coronary artery disease and ischemic stroke.[10] However, the role of Mg in diabetes is still controversial. Some studies have favored the beneficial effects of Mg supplements in diabetes in terms of glycemic control and insulin sensitivity while others have negated any significant effect of Mg in diabetes.[11] Therefore, further research is required to elucidate the detailed role of Mg in the patients with diabetes. Therefore, this study was designed to evaluate magnesium status in the diabetic patients in Morocco.

Materials and methods

A descriptive study including 103 patients with T2DM was carried out at Avicenne Military Hospital in Marrakech over a period of four

months (October 2019-January 2020). Inclusion criteria included all the patients with T2DM and age above 35years, attending the outpatient clinic of diabetes. Exclusion criteria included the diabetic patients who were on vitamin supplements containing magnesium, and those who were suffering from cancer or autoimmune diseases. An informed consent was obtained on a consent form every patient willing to be included in the study. An operating sheet was used to collect demographic data, personal history of patients, clinical characteristics and laboratory – related data. Blood samples were obtained from the patients, and were processed in the biochemistry laboratory of the military hospital. Blood samples were analyzed for fasting blood sugar, lipid profile, HbA1c, and serum magnesium. The Mg status was assessed by measuring the magnesemia by colorimetric method on Cobas® 6000. The reference value taken for Mg was 0.65–1.05mmol/L.

Categorical variables were described by the relative percentages in the relevant subject groups, differences in proportions were compared with the Chi-square test or Fisher's exact test. Continuous variables were described by the mean and standard deviation (SD). Pearson correlation was used to analyse the association betweenmagnesium and fasting and HbA1c. All analyses were carried out using the statistical program SPSS (SPSS Statistics 16.0; SPSS Inc, Chicago, IL, USA). Statistical significance was considered at $P<0.05$.

Results

A total of 103 patients were included in the study where 56 (54.4%) were males and 47 (45.6%) females. Mean age of the patients and duration of diabetes were 59±9years and 9±4years, respectively (Table 1). Oral anti-diabetic therapy (OAD), insulin therapy, and insulin plus OAD were recorded in 54.4%, 29.1%, and 16.5% patients, respectively. Most common antecedent conditions were dyslipidemia (43.7%), hypertension (42.7%), and retinopathy (25.2%) (Table 1).

Table 1 Demographic and clinical characteristics of the patients

Characteristics		Frequency (n)	Percent (%)
Gender	Female	47	45.6
	Male	56	54.4
Age in year (mean±SD)		59±09.0	
Duration of diabetes in year (mean±SD)		09±04.0	
Therapy	Oral anti-diabetics	56	54.4
	Insulin	30	29.1
	Insulin+ OAD	17	16.5
Antecedents	Dyslipidaemia	45	43.7
	Arterial hypertension	44	42.7
	Retinopathy	26	25.2
	Nephropathy	12	11.7
	Coronaryartery disease	10	9.7
	Neuropathy	8	7.8

Mean values for fasting blood sugar, HbA1c and serum magnesium were 9.38±3.73mmol/L, 8.11±2.01%, and 0.8±0.12mmol/L, respectively. Similarly, mean values for total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides were 4.34±1.02mmol/L, 1.20±0.25mmol/L, 2.41±0.84mmol/L, and 1.49±0.62mmol/L, respectively (Table 2).

Table 2 Biological parameters of the patients

Parameter	Mean	Standard deviation
Fasting blood sugar (mmol/l)	9.38	3.73
HbA1C (%)	8.11	2.01
Total cholesterol(mmol/l)	4.34	1.02
HDL Cholesterol(mmol/l)	1.2	0.25
LDL Cholesterol(mmol/l)	2.41	0.84
Triglycerides(mmol/l)	1.49	0.62
Serum magnesium (mmol/l)	0.8	0.12

Hypomagnesemia was recorded in 14.56% cases. Hypomagnesemia was significantly associated with HbA1c (P=0.003) and arterial hypertension (P=0.002; Table 3).However, age, gender, duration of diabetes, retinopathy, nephropathy, neuropathy, coronary artery disease, dyslipidemia, and alcohol did not show significant association with hypomagnesemia (P>0.05; Table 3).

Table 3 Characteristics of patients associated with hypomagnesemia

Characteristics		Hypomagnesemia		
		Yes	No	P value
		n (%)	n (%)	
Age	≤ 55years	05 (20.0)	20 (80.0)	0.279*
	>56years	10 (12.8)	68 (87.2)	
Gender	Female	08(17.0)	39 (83.0)	0.517
	Male	07 (12.5)	49 (87.5)	
Glycemic Control	≤ 7%	00 (00.0)	31 (100.0)	0.003*
	> 7%	15 (20.8)	57 (79.2)	
Duration of Diabetes	≤ 5years	01 (05.9)	16 (94.1)	0.242*
	<5years	14 (16.3)	72 (83.7)	
Antecedents	Arterial hypertension	12 (80.0)	32 (36.4)	0.002*
	Coronary artery disease	00 (00.0)	10 (11.4)	0.191*
	Retinopathy	05 (33.3)	21 (23.9)	0.313*
	Smoking	04 (26.7)	18 (20.5)	0.403*
	Nephropathy	01 (06.7)	11 (12.5)	0.448*
	Alcohol	01 (06.7)	08 (09.1)	0.612*
	Neuropathy	01 (06.7)	07 (08.0)	0.671*
	Dyslipidaemia	06 (40.0)	39 (44.3)	0.755

Pearson correlation showed that magnesium had negative linear relationship with fasting blood sugar higher (r= -0,37, p<0,001) and HbA1c (r= -0,41, p<0,001) (Figure 1) (Figure 2). It means higher the fasting blood sugar or HbA1c, the deeper the hypomagnesemia.
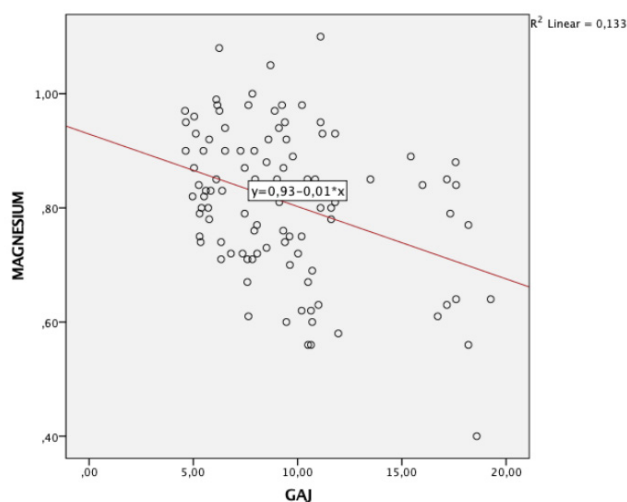
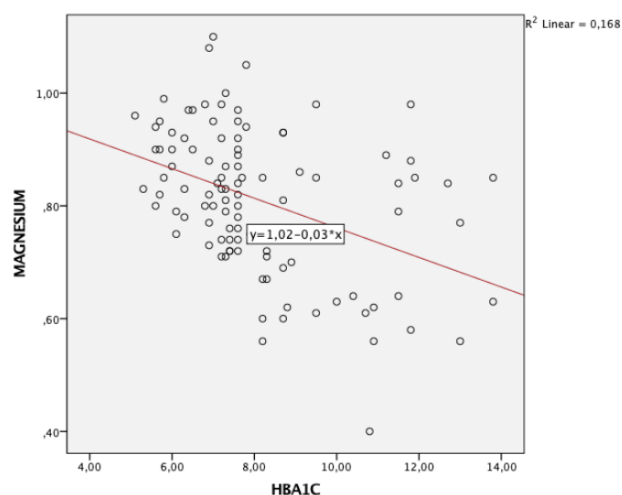**Figure 1** Association between magnesium level and fasting blood sugar.

Figure 2 Association between magnesium level and HbA1c.

Discussion

This cross sectional study was carried out to determine magnesium status in the patients with T2DM living in Morocco. The study revealed the prevalence of hypomagnesemia in 14.56% patients with T2DM presenting at Avicenne Military Hospital in Marrakech.The present study revealed significant association of hypomagnesemia with HbA1c and arterial hypertension. Although the prevalence of hypomagnesemia in T2DM patient was lower than the other regions of the world; however,negative linear relationship of hypomagnesemia with fasting blood sugar supports the positive role of Mg in the glycemic control in the patients with T2DM.

Hypomagnesemia has frequently been reported in the patients with T2DM and this prevalence of hypomagnesemia rises with the duration of diabetes.[13] The prevalence of hypomagnesemia ranges from 14 to 48% in the patients with T2DM as compared to 2.5 to 15% in healthy non-diabetic individuals.[14] Comparatively, the present study revealed only 14.56% prevalence of hypomagnesemia in the patients with T2DM which is lower than that reported in the other regions of the world. In Abbottabad Pakistan, Noor et al. reported hypomagnesemia in 33.89% patients with T2DM.[13] Similarly, in Karachi Pakistan, Hasan et al.[15] reported hypomagnesemia in 30% patients with T2DM.

In North India, Kumar et al.[10] carried out a cross sectional study including 250 patients with T2DM in order to determine the association or serum Mg with T2DM and diabetic retinopathy. They reported hypomagnesemia in 44% cases with poorly controlled fasting blood sugar, post-prandial blood sugar and HbA1c. They also demonstrated that hypomagnesemia is associated with poor glycemic control and increased risk of diabetic retinopathy.The varied prevalence of hypomagnesemia in T2DM patients may be attributed to various factors including poor dietary intake, impaired insulin metabolism, stressors, glomerular hyperfiltration and acid and electrolytes imbalance.[16]

The present study revealed negative linear relationship between magnesium level and HbA1c. This finding has already been reported in previous studies. Arpaci et al.[17] studied 673 diabetic patients in order to determine association among serum magnesium level, glycemic regulation and diabetic complications. They reported poor glycemic control in diabetic patients with depleted Mg level and weak negative correlation between Mg level and HbA1c. Similarly, Kumar et al.[10] reported significant association between hypomagnesemia and HbA1c level. Odusan et al.[18] studied the pattern of Mg in 125 T2DM patients in Nigeria. They reported HbA1c significantly high in the patients with hypomagnesemia. Similar to findings of the present study, Babikr et al.[19] studied 220 patients with T2DM and reported high significant negative relationship of Mg level with fasting blood sugar, HbA1c and metabolic index.

On the contrary, Saeed et al.[19] evaluated magnesium level and its correlation with HbA1c in Duhok Iraq, including 100 T2DM patients. They reported normal magnesium level in 95% patients and revealed no significant correlation of magnesium with HbA1c. Although numerous studies have reported negative linear relationship between magnesium level and HbA1c; however, further studies at large scale with large sample size are required to reach the final relationship between these two variables.

The present study also revealed significant association between hypomagnesemia and arterial blood pressure. It has been postulated that low Mg level in T2DM results in the activation of Na^+-Cl^- cotransporter and sodium re-absorption from kidneys, leading to elevated blood pressure.[14] Odusan et al.[18] also reported association between hypomagnesemia and hypertension.

The limitations of the present study include small sample size and involvement of only single center as the outcome variable may be affected by the large sample size from different multiple centers.[20]

Conclusion

In conclusion, the prevalence of hypomagnesemia is although low in Morocco; however, significant association of Mg level with fasting blood sugar and HbA1c indicates positive role of Mg in the glycemic control in T2DM.

This study is a useful addition to the literature on Mg and T2DM in Morocco, paving way for further research and subsequent development of improved management strategies for T2DM.

Acknowledgments

Conflicts of interest

The authors declare that they have no competing interests.

References

1. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat Rev Endocrinol*. 2018;14(2):88–98.

2. Galicia-Garcia U, Benito-Vicente A, Larrea-Sebal A, et al. Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci*. 2020;21(17):6275.

3. Khan MAB, Hashim MJ, King JK, et al. Epidemiology of type 2 diabetes – global burden of disease and forecasted trends. *J Epidemiol Glob Health*. 2020;10(1):107–111.

4. World Health Organization. 2016.

5. Heffernan SM, Horner K, De Vito G, et al. The role of mineral and trace element supplementation in exercise and athletic performance: a systematic review. *Nutrients*. 2019;11(3):696.

6. Schwalfenberg GK, Genius SJ. The importance of magnesium in clinical healthcare. *Scientifica (Cairo)*. 2017;2017:4179326.

7. Al Alawi AM, Majoni SW, Falhammar H. Magnesium and human health: perspectives and research directions. *Int J Endocrinol*. 2018;2018:9041694.

8. RalecC, Henry E, Lemor M, et al. Calcium-driven DNA synthesis by a high-fidelity DNA polymerase. *Nucleic Acids Res*. 2017;45(21):12425–12440.

9. Zhang Y, Li Q, Xin Y, et al. Association between serum magnesium and common complications of diabetes mellitus. *Technol Health Care*. 2018;26(Suppl 1):379–387.

10. Kumar P, Bhargava S, Agarwal PK, et al. Association of serum magnesium with type 2 diabetes mellitus and diabetic retinopathy. *J Family Med Prim Care*. 2019;8(5):1671–1677.

11. El Derawi WA, Naser IA, Taleb MH, et al. The effects of oral magnesium supplementation on glycemic response among type 2 diabetes patients. *Nutrients*. 2019;11(1):44.

12. Dasgupta A, Sarma D, Saikia UK. Hypomagnesemia in type 2 diabetes mellitus. *Indian J Endocrinol Metab*. 2012;16(6):1000–1003.

13. Noor MM, Nazir Q, Khan TM, et al. Association between low serum magnesium level and type 2 diabetes mellitus in Abbottabad. *J Ayub Med Coll Abbottabad*. 2019;31(2):226–229.

14. Gommers LMM, Hoenderop JGJ, Bindels RJM, et al. Hypomagnesemia in type 2 diabetes: a vicious circle? *Diabetes*. 2016;65(1):3–13.

15. Hasan M, Sultan S, Ashfaq S, et al. Hypomagnesemia in type ii diabetes mellitus patients; an experience from a tertiary care center. *Ann Pak Inst Med Sci*. 2017;13(2):146–150.

16. Pham PCT, Pham PMT, Pham SV, et al. Hypomagnesemia in patients with type 2 diabetes. *Clin J Am Soc Nephrol*. 2007;2(2):366–373.

17. Arpaci D, Tocoglu AG, Ergenc H, Korkmaz S, Ucar A, Tamer A. Associations of serum Magnesium levels with diabetes mellitus and diabetic complications. *Hippokratia*. 2015;19(2):153–157.

18. Odusan OO, Familoni OB, Odewabi AO, et al. Patterns and correlates of serum magnesium levels in subsets of type 2 diabetes mellitus patients in Nigeria. *Indian J Endocrinol Metab*. 2017;21(3):439–442.

19. Babikr WG, Shalayel MHF, Abdelraheem AHMK, et al. Impact of body mass index on hypomagnesemia and hypocalcemia in type 2 diabetic patients. *Biomed Pharmacol J*. 2016;9(3):933–940.

20. Saeed H, Haj S, Qasim B. Estimation of magnesium level in type 2 diabetes mellitus and its correlation with HbA1c level. *Endocrinol Diabetes Metab*. 2019;2(1):e00048.