Diabetes, Metabolic Syndrome and Obesity

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Association Between Serum Magnesium Levels and Glycemic Control in Type 2 Diabetes

Beibei Luo[1], Baolong Pan[2], Guancheng Zhao[1], Jiefen Li[1], Li Sun[1]

[1]Clinical Laboratory, People's Hospital of Yuxi City, the Sixth Affiliated Hospital of Kunming Medical University, Yuxi City, Yunnan Province, 653100, People's Republic of China; [2]Physical Examination Center, People's Hospital of Yuxi City, the Sixth Affiliated Hospital of Kunming Medical University, Yuxi City, Yunnan Province, 653100, People's Republic of China

Correspondence: Baolong Pan, Physical Examination Center, People's Hospital of Yuxi City, the Sixth Affiliated Hospital of Kunming Medical University, 21 Nieer Road, Yuxi City, Yunnan Province, 653100, People's Republic of China, Email pbl1210@126.com

Introduction: Serum magnesium is a crucial mineral within the human body. It is imperative for diabetic patients to maintain optimal serum magnesium levels. We focus on the relationship between glycemic control and serum magnesium in type 2 diabetes mellitus (T2DM).

Methods: The retrospective, observational, cross-sectional study comprised 1694 patients recruited from the People's Hospital of Yuxi. Fasting blood samples were collected for analysis, accompanied by the recording of participants' demographic characteristics. Patients were categorized into two groups based on whether their glycosylated hemoglobin (HbA1c) levels < 7%. A *t*-test was employed to identify significant differences between the two groups. Correlation coefficients were calculated using Pearson's method. A Logistic regression analysis was conducted to assess the association between variables and glycemic control. A linear regression analysis was performed to assess the relationship between serum magnesium levels and HbA1c.

Results: Patients with poor glycemic control exhibited elevated age, low-density lipoprotein (LDL-C), fasting plasma glucose (FPG), and homeostasis model assessment (HOMA-IR) compared to those with good glycemic control ($P < 0.001$). Additionally, total cholesterol (TC) levels were significantly higher in patients with poor glycemic control. Conversely, high-density lipoprotein (HDL-C) and serum magnesium levels were lower in patients with poor glycemic control. Serum magnesium levels exhibited negative correlations with HOMA-IR ($r = -0.05$, $P < 0.05$), HbA1c ($r = -0.29$, $P < 0.05$), and FPG ($r = -0.20$, $P < 0.05$). Moreover, serum magnesium was significantly associated with reduced odds of glycemic control (OR = 0.0005, 95% CI 0.0001–0.0027, $P < 0.001$).

Conclusion: The serum magnesium level in patients with T2DM is closely associated with glycemic control.

Keywords: serum magnesium, glycaemic control, diabetes

Introduction

The prevalence of type 2 diabetes mellitus (T2DM) has emerged as a significant public health concern in China over recent decades.[1] Data from the International Diabetes Federation (IDF) reveals that China holds the world's highest number of adult diabetic patients, totaling 140 million.[2] Concurrently, the market for drugs treating type 2 diabetes in China demonstrates a consistent upward trajectory. This trend reflects the growing awareness of diabetes, leading to an increase in patients seeking treatment. However, despite treatment, achieving optimal blood sugar control rates remains suboptimal.[3] The American Diabetes Association (ADA) recommends a target glycosylated hemoglobin (HbA1c) level below 7% for diabetic patients lacking complications or previous hypoglycemic episodes.[4]

Serum magnesium is a vital mineral within the human body.[5] Maintaining an appropriate serum magnesium level is crucial for diabetic patients, as it plays a significant role in glucose and insulin metabolism.[6] Researches[7,8] indicate that low serum magnesium levels may contribute to insulin resistance and increase the risk of diabetes.

There is a recognized relationship between serum magnesium levels and T2DM. However, the majority of studies primarily examine dietary magnesium intake rather than serum magnesium levels, and their focus lies on its association with T2DM. Therefore, through examining the relationship between serum magnesium levels and fasting plasma glucose

Received: 31 May 2024
Accepted: 25 July 2024
Published: 26 July 2024

© 2024 Luo et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v3.0) License (http://creativecommons.org/licenses/by-nc/3.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

(FPG), HbA1c, body mass index (BMI), and visceral fat area (VFA) in individuals with T2DM, we can further understand the relationship between serum magnesium and glycemic control, as well as elucidate the impact of obesity on glycemic control.

Methods

Study Design and Participants

This retrospective, observational, cross-sectional study conducted at the People's Hospital of Yuxi, Yunnan Province. The study data were collected from patients admitted to the Metabolic Management Center (MMC) between March 2018 and September 2023. This study received approval from the ethics committee of the Sixth Affiliated Hospital of Kunming Medical University (Approval No. 2024kmykdx6f003), adhering to the principles outlined in the Declaration of Helsinki. This retrospective analysis did not involve the collection of personal information from patients. Given that the exemption of informed consent would not adversely affect the rights or welfare of the subjects, we obtained approval for this exemption from the Ethics Committee.

The study included patients diagnosed with T2DM and a recorded serum magnesium level in their electronic medical records. Baseline information regarding patients' lifestyle habits, dietary habits, demographics, and medications upon discharge was documented. Additionally, a series of laboratory tests were performed. The study excluded participants with prior diagnoses of type 1 diabetes and Other patients with non-T2DM, such as hyperthyroidism as determined by either medical records or the primary care physician's diagnosis at baseline. Participants with missing data in laboratory tests or disease history were excluded. Finally, a total of 1694 patients were analyzed.

Measurements

Participants' body weight and height were measured with them barefoot and wearing light clothing, and recorded to the nearest 0.1 kg and 0.1 cm, respectively. BMI was calculated using the formula weight (kg) divided by the square of height (m). Systolic and diastolic blood pressures (SBP/DBP) were measured twice using mercury sphygmomanometers following a 10-minute rest, and the average of the readings was recorded.

Blood samples were obtained via venipuncture after fasting. The serum samples were allowed to clot and then centrifuged at 5000 rpm for 10 minutes. FPG levels were determined using the hexokinase method. HbA1c levels were measured using high-performance liquid chromatography. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL-C), and low-density lipoprotein (LDL-C) levels were measured using enzymatic methods. Plasma insulin concentration was assessed using a chemiluminescence-based assay. The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated using the formula: fasting insulin × fasting glucose/22.5.[9] Serum magnesium concentrations were determined using the colorimetric method. VFA was measured in cm^2 using the DUALSCAN device.

Definitions

Patients were categorized into two groups based on their HbA1c levels: good glycemic control (HbA1c < 7%) and poor glycemic control (HbA1c ≥ 7%).[4] BMI categories were defined as follows: normal (18.5 ≤ BMI < 24), overweight (24 ≤ BMI < 28), and obese (BMI ≥ 28) according to the China Working Group on Obesity guidelines.[10] Visceral obesity was defined as VFA of 100 cm^2 or greater.[11]

Statistical Analysis

Data are presented as mean ± standard deviation (SD). Chi-square tests were employed to compare categorical variables, presenting results as percentages. Correlation analysis was utilized to assess associations between variables. Pearson's correlation coefficients were calculated to measure the strength and direction of relationships between variables. Additionally, a correlation matrix diagram was generated. Logistic regression analysis was conducted to assess the association between variables and the quality of glycemic control. Linear regression analysis was performed to evaluate

the relationship between serum magnesium levels and HbA1c. $P < 0.05$ was considered significant. All the analyses were performed with the statistical software packages R (http://www.R-project.org, The R Foundation).

Results

Baseline Characteristics

The retrospective study comprised 1694 patients, with a male-to-female ratio of 63.8% to 36.2% and a mean age of 54.3 ± 11.1 years. Of these, 247 patients exhibited good glycemic control, while 1447 patients had poor glycemic control. Patients with poor glycemic control exhibited higher age, LDL-C, FPG, and HOMA-IR levels compared to those with good glycemic control ($P < 0.001$). Additionally, TC levels were significantly higher in patients with poor glycemic control. Conversely, HDL-C and serum magnesium levels were lower in patients with poor glycemic control. Interestingly, no significant differences were observed in BMI and VFA between the two groups. However, when grouped according to their respective standards, significant differences were observed ($P < 0.05$) (Table 1).

Association of Serum Magnesium Levels with Glycaemic Control

In the correlation matrix diagram, the correlation matrix revealed negative correlations between serum magnesium levels and HOMA-IR ($r = -0.05$, $P < 0.05$), HbA1c ($r = -0.29$, $P < 0.05$), and FPG ($r = -0.20$, $P < 0.05$) (Figure 1). A linear regression curve was used to estimate the correlation between serum magnesium levels and HbA1c, revealing that serum

Table 1 Comparison of Basic Characteristics

Variables	Total (n = 1694)	HbA1c <7.0% (n = 247)	HbA1c ≥7.0% (n = 1447)	P
Gender, n (%)				0.433
Male	1080 (63.8)	152 (61.5)	928 (64.1)	
Female	614 (36.2)	95 (38.5)	519 (35.9)	
Age (years)	54.3 ± 11.1	56.7 ± 10.0	53.9 ± 11.2	< 0.001
SBP (mmHg)	122.9 ± 16.9	123.5 ± 16.9	122.8 ± 16.9	0.524
DBP (mmHg)	71.9 ± 10.9	70.8 ± 10.4	72.0 ± 10.9	0.11
BMI (kg/m^2)	25.6 ± 7.8	24.9 ± 3.2	25.8 ± 8.3	0.095
VFA (cm^2)	92.4 ± 116.5	82.1 ± 35.1	94.2 ± 125.1	0.13
TC (mmol/L)	4.4 ± 1.1	4.2 ± 1.0	4.4 ± 1.2	0.008
TG (mmol/L)	2.5 ± 2.6	2.3 ± 2.0	2.6 ± 2.7	0.121
HDL-C (mmol/L)	1.1 ± 0.3	1.2 ± 0.3	1.1 ± 0.3	< 0.001
LDL-C (mmol/L)	2.5 ± 0.9	2.3 ± 0.7	2.5 ± 0.9	< 0.001
Mg^{2+} (mmol/L)	0.8 ± 0.1	0.9 ± 0.1	0.8 ± 0.1	< 0.001
HbA1c (%)	9.4 ± 2.4	6.3 ± 0.4	10.0 ± 2.2	< 0.001
FPG (mmol/L)	9.3 ± 3.5	6.4 ± 1.8	9.8 ± 3.5	< 0.001
Insulin	10.6 ± 7.7	11.1 ± 6.1	10.5 ± 8.0	0.305
HOMA-IR	4.3 ± 3.4	3.2 ± 2.1	4.5 ± 3.6	< 0.001
BMI, n (%)				0.043
Normal weight	576 (34.0)	96 (38.9)	480 (33.2)	
Over weight	787 (46.5)	116 (47)	671 (46.4)	
Obesity	331 (19.5)	35 (14.2)	296 (20.5)	
VFA, n (%)				0.031
<100 cm^2	1062 (62.7)	170 (68.8)	892 (61.6)	
≥100 cm^2	632 (37.3)	77 (31.2)	555 (38.4)	
Mg^{2+}, n (%)				< 0.001
<=0.75mmol/L	404 (23.8)	28 (11.3)	376 (26)	
>0.75mmol/L	1290 (76.2)	219 (88.7)	1071 (74)	

Note: $P < 0.05$ was considered significant.

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; VFA, visceral fat area; TC, Total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein; LDL-C, low-density lipoprotein; Mg^{2+}, serum magnesium; FPG, fasting plasma glucose; HOMA-IR, insulin resistance measured by the homeostasis model assessment; VFA, visceral fat area.

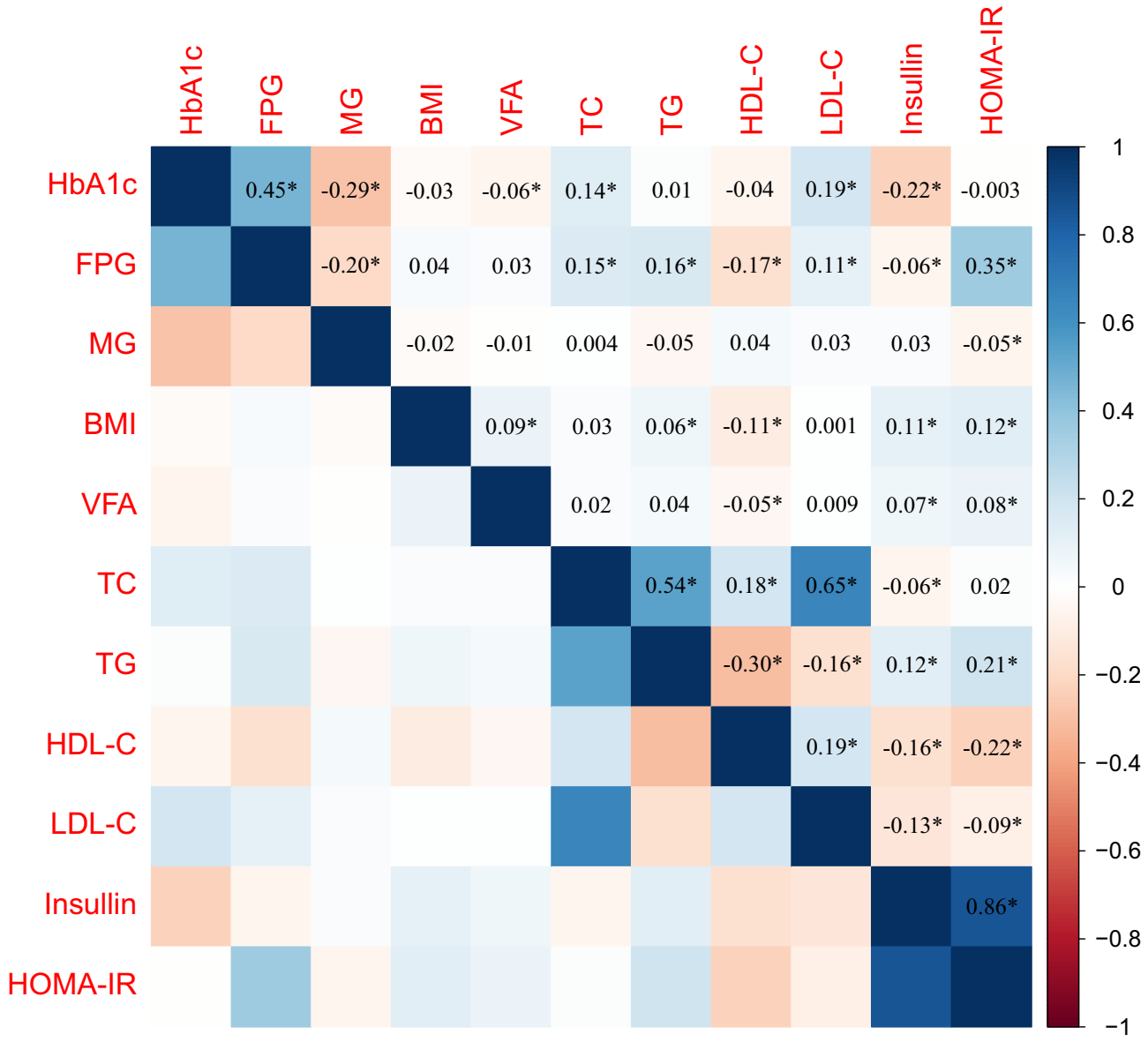

Figure 1 Correlation coefficients between the varies. *P values <0.05.

magnesium levels decrease with increasing HbA1c (Figure 2). A logistic regression analysis was conducted to estimate the independent contribution of variables to the risk of poor glycemic control. The analysis revealed a significant association between serum magnesium levels and reduced odds of glycemic control (OR = 0.0005, 95% CI 0.0001–0.0027, P < 0.001). Additionally, age, BMI, TC, TG, HDL-C, LDL-C, FPG, and VFA demonstrated associations with glycaemic control (P < 0.05) (Table 2).

Discussion

In this study, we found a correlation between serum magnesium levels and glycemic control, indicating that serum magnesium levels decrease with increasing HbA1c. Furthermore, correlation analysis indicated associations between magnesium levels and FPG, as well as HbA1c, but not with BMI and VFA. This suggests that to enhance magnesium levels and decrease the occurrence of hypomagnesemia, emphasis should be on glycemic control rather than weight loss.

Magnesium homeostasis is tightly regulated and depends on the balance between intestinal absorption and renal excretion.[12] Additionally, when serum magnesium concentration decreases, magnesium stored in bones can be released

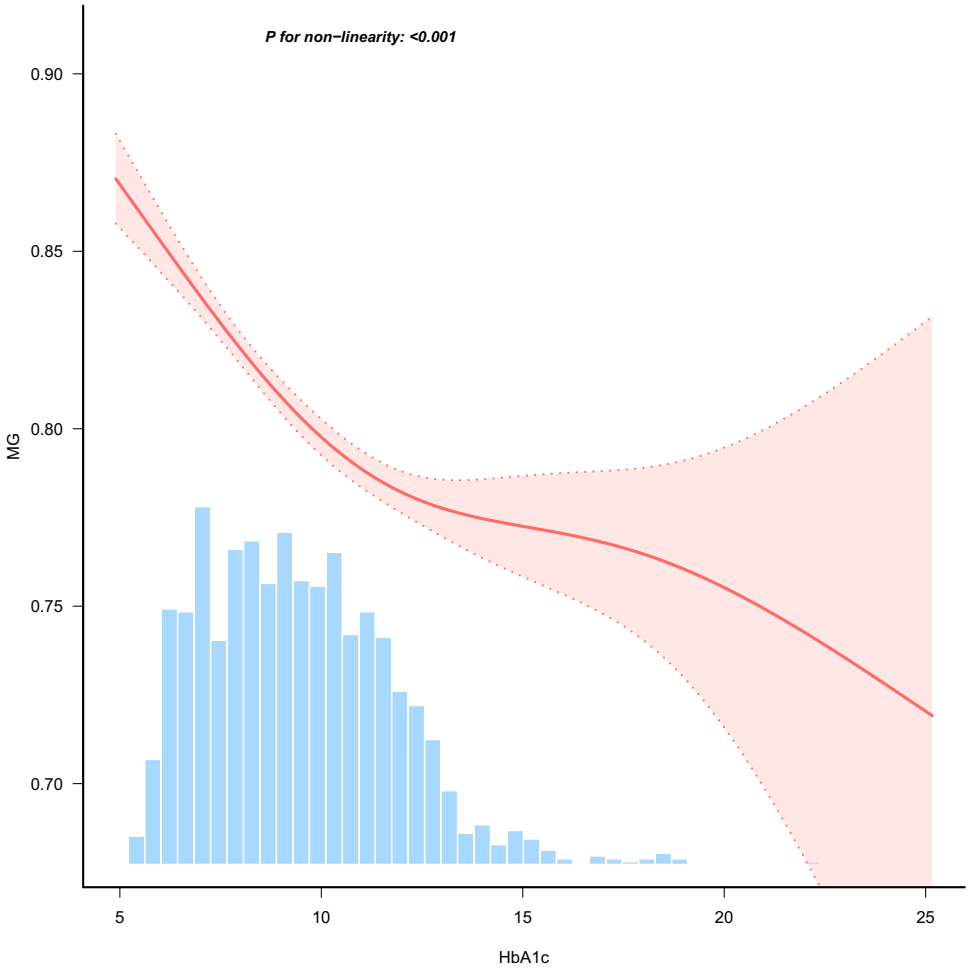

Figure 2 Association between HbA1c and serum magnesium.

into the blood to compensate for the deficiency.[13] The mechanisms underlying the association between T2DM and low serum magnesium levels remain incompletely understood. Gender has little direct influence on serum magnesium level, and the results of this study also prove this statement. With the increase of age, the absorption and utilization ability of magnesium may gradually decline, and at the same time, due to the weakening of metabolic function, blood sugar control may be more difficult. Some studies[14,15] suggested that hyperglycemia in T2DM increases the glomerular filtration rate, leading to inadequate magnesium reabsorption in renal tubules, resulting in elevated urinary magnesium excretion and decreased serum magnesium concentration. Furthermore, a study[16] in pre-diabetes indicated that increased renal magnesium consumption due to uncontrolled diabetes may contribute to low serum magnesium levels. Moreover, it has been suggested that insulin resistance may disrupt the absorption and utilization of magnesium ions, contributing to low serum magnesium levels. This is because the primary site of magnesium absorption is the small intestine.[17] Insulin resistance may induce inflammation and oxidative stress,[18] damaging the mucosa of the small intestine and impairing its absorption function.[19] Thus, while magnesium excretion was not directly measured in this study, the elevated urinary magnesium loss may account for the observed low serum magnesium concentration in T2DM patients with poor glycemic control.

Our study revealed no correlation between BMI, VFA, and serum magnesium levels. While many studies[20] have linked glucose levels with obesity, it is important to note that obesity can contribute to hyperglycemia to some extent. However, it has been observed that low magnesium levels in obese individuals are associated with diabetes and glycemic control, rather than obesity itself.[21] Similarly, Li et al demonstrated that there was no difference in BMI among magnesium quintiles.[9] Additionally, some studies[16] have demonstrated that the impact of serum magnesium on the

Table 2 Logistic Regression Analysis for Whether Glycaemic Control is Well

Variable	OR_95CI	P
Gender		
Male	Ref.	Ref.
Female	0.89 (0.68~1.18)	0.433
Age (years)	0.98 (0.96~0.99)	<0.001
TC (mmol/L)	1.2 (1.05~1.37)	0.008
HDL-C (mmol/L)	0.36 (0.23~0.57)	<0.001
LDL-C (mmol/L)	1.35 (1.15~1.59)	<0.001
Mg^{2+} (mmol/L)	0.0005 (0.0001~0.0027)	<0.001
FPG (mmol/L)	1.92 (1.75~2.1)	<0.001
HOMA-IR	1.21 (1.13~1.29)	<0.001
BMI		
Normal weight	Ref.	Ref.
Over weight	1.16 (0.86~1.55)	0.332
Obesity	1.69 (1.12~2.56)	0.013
VFA		
<100 cm^2	Ref.	Ref.
≥100 cm^2	1.37 (1.03~1.83)	0.031
Mg^{2+}		
<=0.75mmol/L	Ref.	Ref.
>0.75mmol/L	0.36 (0.24~0.55)	<0.001

Note: P < 0.05 was considered significant.
Abbreviations: TC, Total cholesterol; HDL-C, high density lipoprotein; LDL-C, low-density lipoprotein; Mg^{2+}, serum magnesium; FPG, fasting plasma glucose; HOMA-IR, insulin resistance measured by the homeostasis model assessment; BMI, body mass index; VFA, visceral fat area.

risk of pre-diabetes and diabetes is partially mediated by insulin resistance. Therefore, while weight loss is crucial for improving the overall health of patients with T2DM, controlling glucose levels may be the primary consideration in preventing hypomagnesemia. In general, maintaining good glycemic control is crucial for patients with T2DM. This can help prevent hypomagnesemia, as well as slow the progression of the disease and improve quality of life.

Several potential limitations need consideration when evaluating our study results. First, we did not assess daily magnesium intake. This limitation arises from the retrospective nature of our research, making it impractical to effectively follow up with every patient. This study relies on previously collected case information, which in some instances is incomplete, particularly concerning drug use, lifestyle, and comorbidities. Therefore, in future research, we will enhance the collection of participants' personal information and expand the sample size. Additionally, the imbalance in the number of subjects with good and poor glycemic control, stemming from the majority seeking hospitalization due to poor glycemic control, limited our ability to achieve parity between the groups. Lastly, we did not analyze the relationship between serum magnesium and insulin resistance as in other studies, primarily due to the absence of non-diabetic individuals as controls, despite calculating HOMA-IR. However, investigating this relationship will be a focus of our future research.

Conclusion

In patients with T2DM, serum magnesium levels are closely associated with glycemic control. Prioritizing glycemic control over weight loss is essential for reducing the incidence of hypomagnesemia.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Yuan J, Li F, Shen X, et al. Genetic and pharmacological inhibition of GCN2 ameliorates hyperglycemia and insulin resistance in type 2 diabetic mice. *Antioxidants*. 2022;11(8). doi:10.3390/antiox11081584
2. Li X, Sun M, Yang Y, et al. Predictive effect of triglyceride glucose-related parameters, obesity indices, and lipid ratios for diabetes in a Chinese population: a prospective cohort study. *Front Endocrinol*. 2022;13:862919. doi:10.3389/fendo.2022.862919
3. Hu C, Lin L, Zhu Y, et al. Association between age at diagnosis of type 2 diabetes and cardiovascular diseases: a nationwide, population-based, cohort study. *Front Endocrinol*. 2021;12:717069. doi:10.3389/fendo.2021.717069
4. Michno A, Grużewska K, Ronowska A, et al. Resveratrol inhibits metabolism and affects blood platelet function in type 2 diabetes. *Nutrients*. 2022;14(8). doi:10.3390/nu14081633
5. Chen H, Chen X, Wang B, et al. Double network composite scaffolds based on oxidized dextran/gelatin hydrogel and magnesium calcium phosphate cement. *Colloids Surf A*. 2023;677:132307. doi:10.1016/j.colsurfa.2023.132307
6. Yang J, Zhang H, Cao Y, et al. The association of dietary magnesium and prediabetes in childbearing Chinese women: results from China Nutrition and Health Surveillance (2015–2017). *Nutrients*. 2022;14(21). doi:10.3390/nu14214580
7. Li W, Jiao Y, Wang L, et al. Association of serum magnesium with insulin resistance and type 2 diabetes among adults in China. *Nutrients*. 2022;14(9). doi:10.3390/nu14091799
8. Ng HY, Kuo WH, Tain YL, et al. Effect of dapagliflozin and magnesium supplementation on renal magnesium handling and magnesium homeostasis in metabolic syndrome. *Nutrients*. 2021;13(11). doi:10.3390/nu13114088
9. Balasubramanian P, Schaar AE, Gustafson GE, et al. Adiponectin receptor agonist AdipoRon improves skeletal muscle function in aged mice. *Elife*. 2022;11. doi:10.7554/eLife.71282
10. Yang Y, Piao W, Huang K, et al. Dietary pattern associated with the risk of hyperuricemia in Chinese elderly: result from China Nutrition and Health Surveillance 2015–2017. *Nutrients*. 2022;14(4). doi:10.3390/nu14040844
11. Luo B, Xu W, Feng L, et al. Association between visceral fat area and glycated hemoglobin in type 2 diabetics: a retrospective study. *DMSO*. 2023;16:3295–3301. doi:10.2147/DMSO.S425166
12. Zocchi M, Béchet D, Mazur A, et al. Magnesium influences membrane fusion during myogenesis by modulating oxidative stress in C2C12 myoblasts. *Nutrients*. 2021;13(4). doi:10.3390/nu13041049
13. Pouroutzidou GK, Liverani L, Theocharidou A, et al. Synthesis and characterization of mesoporous Mg- and Sr-doped nanoparticles for moxifloxacin drug delivery in promising tissue engineering applications. *Int J Mol Sci*. 2021;22(2). doi:10.3390/ijms22020577
14. Dong Y, Chen L, Gutin B, et al. Magnesium intake, C -reactive protein, and muscle mass in adolescents. *Nutrients*. 2022;14(14). doi:10.3390/nu14142882
15. Lian H, Wu H, Ning J, et al. The risk threshold for hemoglobin A1c associated with albuminuria: a population-based study in China. *Front Endocrinol*. 2021;12:673976. doi:10.3389/fendo.2021.673976
16. Kieboom BCT, Ligthart S, Dehghan A, et al. Serum magnesium and the risk of prediabetes: a population-based cohort study. *Diabetologia*. 2017;60(5):843–853. doi:10.1007/s00125-017-4224-4
17. Liu Y, Han R, Wang J, et al. Magnesium sensing regulates intestinal colonization of enterohemorrhagic Escherichia coli O157:H7. *mBio*. 2020;11(6). doi:10.1128/mBio.02470-20
18. Johny E, Jala A, Nath B, et al. Vitamin D supplementation modulates platelet-mediated inflammation in subjects with type 2 diabetes: a randomized, double-blind, placebo-controlled trial. *Front Immunol*. 2022;13:869591. doi:10.3389/fimmu.2022.869591
19. Ji Y, He Y, Yang Y, et al. Hydroxyproline alleviates 4-hydroxy-2-nonenal-induced DNA damage and apoptosis in porcine intestinal epithelial cells. *Anim Nutr*. 2022;9:7–15. doi:10.1016/j.aninu.2021.08.003
20. Zhu BL, Hu AY, Huang GQ, et al. Association between obesity and post-stroke anxiety in patients with acute ischemic stroke. *Front Nutr*. 2021;8:749958. doi:10.3389/fnut.2021.749958
21. Lecube A, Baena-Fustegueras JA, Fort JM, Pelegri D, Hernandez C, Simo R. Diabetes is the main factor accounting for hypomagnesemia in obese subjects. *PLoS One*. 2012;7(1):e30599. doi:10.1371/journal.pone.0030599

Diabetes, Metabolic Syndrome and Obesity Dovepress

Publish your work in this journal

Diabetes, Metabolic Syndrome and Obesity is an international, peer-reviewed open-access journal committed to the rapid publication of the latest laboratory and clinical findings in the fields of diabetes, metabolic syndrome and obesity research. Original research, review, case reports, hypothesis formation, expert opinion and commentaries are all considered for publication. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/diabetes-metabolic-syndrome-and-obesity-journal