North Clin Istanb 2025;12(2):239–243
doi: 10.14744/nci.2024.75725

Original Article INTERNAL MEDICINE

Relationship between serum magnesium levels and glycemic control and insulin resistance

Osman Erinc, Soner Yesilyurt

Department of Internal Medicine, Taksim Training and Research Hospital, Istanbul, Turkiye

ABSTRACT

OBJECTIVE: The role of magnesium in glucose homeostasis, its effects on glycemic control and the causal relationship between them have been the subject of many studies. In this direction, in our study, we aimed to investigate the relationship between serum magnesium (Mg) levels and hemoglobin A1c (HbA1c) and insulin resistance.

METHODS: Based on their HbA1c levels, 305 participants were split into 3 groups: 121 were in the control group, 85 were in the prediabetes group, and 99 were in the diabetes group. Serum magnesium levels were measured in these three groups. The correlation between Mg and fasting plasma glucose, fasting insulin and homeostasis model assessment of insulin resistance (HOMA-IR) was also investigated. In addition, patients' demographic data, blood pressure, smoking habits and basic biochemical data were also included in the analysis.

RESULTS: There was a significant statistical difference in terms of serum magnesium levels among all the groups ($p<0.001$). A strong negative correlation was found between serum magnesium levels and HbA1c ($r=-0.316$, $p<0.001$). There was also a weak negative relationship between Mg and serum fasting glucose, insulin, and HOMA-IR ($r=-0.167$ $p=0.004$, $r=-0.167$ $p=0.003$, and $r=-0.198$ $p=0.001$, respectively).

CONCLUSION: We observed a statistically significant negative correlation between serum magnesium levels and HbA1c in our study. According to this finding, it would be useful to assess magnesium levels in patients with high HbA1c levels. However, due to conflicting results among studies investigating the relationship between magnesium, glycemic control and insulin sensitivity with increasing interest, more comprehensive, prospective studies with longer follow-up periods are needed.

Keywords: Diabetes mellitus; glycemic control; hemoglobin A1c; insulin resistance; magnesium.

Cite this article as: *Erinc O, Yesilyurt S. Relationship between serum magnesium levels and glycemic control and insulin resistance. North Clin Istanb 2025;12(2):239–243.*

Diabetes Mellitus (DM), which is predicted to affect 1.3 billion people worldwide in 2050, is a global health problem that requires early diagnosis and treatment due to the morbidities and high mortality rates it causes [1]. The critical goal in preventing microvascular and macrovascular complications of diabetes is to ensure blood sugar regulation. For this purpose, many clinical studies are carried out examining the pathophysiological basis of the disease.

Magnesium (Mg), one of the most common cations, has an important function in several biochemical reactions, including glucose homeostasis, phosphorylation of proteins, nucleic acid, and protein synthesis. It functions as a cofactor for a number of enzymes that participate in energy metabolism, transport of glucose throughout membranes, gluconeogenesis, insulin secretion, and connection with receptors in pancreatic cells and target tissues [2–4]. With a decrease in Mg levels,

Received: January 04, 2024 *Revised:* January 29, 2024 *Accepted:* February 12, 2024 *Online:* April 25, 2025

Correspondence: Osman ERINC, MD. Taksim Egitim ve Arastirma Hastanesi, Ic Hastaliklari Klinigi, Istanbul, Turkiye.
Tel: +90 553 239 90 98 e-mail: doctorerinc@gmail.com

Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

tyrosine kinase activity at the insulin receptor decreases and intracellular calcium levels increase, resulting in impaired insulin signaling. Also, Mg deficiency is linked with insulin resistance, dysfunction in pancreatic beta-cells, and hence insulin secretion [5, 6]. Patients with DM have lower amounts of intracellular free Mg^{2+} compared to patients without diabetes [7]. In light of all these findings, maintaining normal glucose metabolism requires the essential regulation of intra-extracellular magnesium levels [8–10].

The influence of Mg on carbohydrate metabolism pathways, particularly the impact of magnesium deficiency on glycemic control and insulin sensitivity, has been extensively investigated in clinical studies, and this interest persists. Our study aims to scrutinize the relationship between serum Mg levels and hemoglobin A1c (HbA1c) and assess their association with insulin resistance.

MATERIALS AND METHODS

Patients and Study Design

In this retrospective study, the diabetic group comprised individuals with HbA1c levels ≥6.5%, the control group consisted of individuals with HbA1c levels below 5.7%, and the prediabetes group included participants with HbA1c levels between 5.7% and 6.4%. Participants were exclusively sourced from our hospital's internal medicine outpatient clinic who were admitted between August 2022 and August 2023 and aged from 18 to 75 years. Their demographic, anthropometric, and laboratory data were obtained from the medical records of the hospital, ensuring a comprehensive representation of the study population.

Exclusion Criteria

To maintain the study's focus and eliminate potential confounding factors, certain exclusion criteria were applied. Participants whose laboratory data could not be accessed completely were excluded from the study. Also, the patients with chronic renal, hepatic, hematological, or oncological diseases were excluded from participation. Additionally, individuals currently using medications that could impact serum magnesium, calcium, and phosphorus levels were not included in the study. These strict inclusion and exclusion criteria aimed to enhance the study's internal validity by ensuring a homogeneous study population with a specific focus on the association among serum Mg, HbA1c, and insulin resistance.

Highlight key points

- A statistically significant negative correlation was found between serum magnesium levels and HbA1c, indicating that lower magnesium levels are associated with poorer glycemic control.
- Weak inverse correlations were observed between serum magnesium and fasting glucose, insulin, and HOMA-IR values.
- Serum magnesium levels significantly differed among control, prediabetes, and diabetes groups, reinforcing its potential role in glucose metabolism.

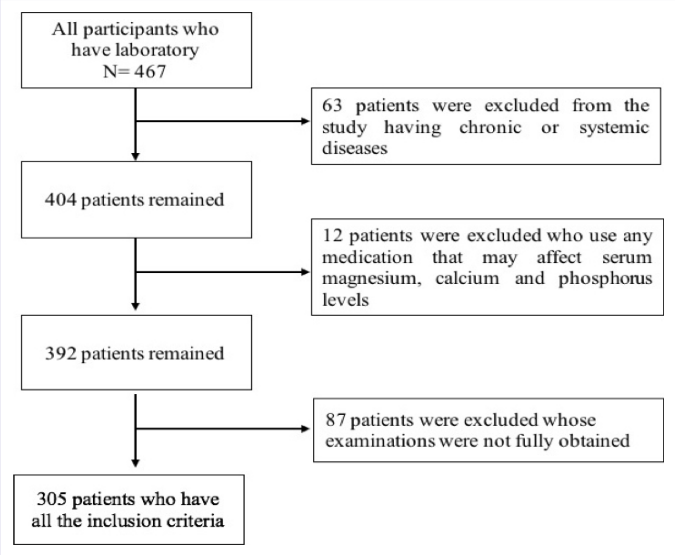

FIGURE 1. The determination of all participants.

The determination of all participants was summarized in Figure 1.

Laboratory Analyses and Other Measurements

HbA1c values were calculated using ADAMS HV8380V, while biochemical tests were made with Roche Cobas c501. Blood pressure (BP) measurement was obtained using a manual BP cuff (Omron, Kyoto, Japan). BMI was calculated as BMI=weight (kg)/height (m^2).

Primary Objective

The primary objective of this retrospective study was to assess the relationship between serum Mg and HbA1c levels. The study aimed to investigate whether variations in serum magnesium levels correlate with HbA1c levels, providing insights into the potential role of magnesium in glycemic control among diabetic individuals.

Table 1. Demographic and clinical characteristics of groups scale scores

	Control (n=121)	Prediabetes (n=85)	Diabetes (n=99)	p
Age, years	35 (25–46)	48 (39–58)	51 (44–61)	<0.001
Gender				0.019
Female, (%)	52.9	61.2	57.6	
Male, (%)	47.1	38.8	42.4	
BMI, kg/m^2	24.8 (22.3–29)	30.3 (27.2–33.3)	30.3 (27–34.3)	<0.001
Smoking status, % no-smoker/current/ex	72.7/25.6/1.7	67.1/29.4/3.5	69.7/20.2/9.1	0.381
Hypertension				
Systolic BP, mmHg	120 (109–131)	126 (118–135)	130 (120–148)	<0.001
Diastolic BP, mmHg	76 (69–82)	80 (70–85)	85 (80–94)	<0.001

BMI: Body Mass Index; BP: Blood pressure.

Secondary Objective

The secondary objective was to evaluate the association between serum magnesium and insulin resistance in the same cohort of individuals with type 2 DM. The study sought to explore whether there is a correlation between magnesium levels and insulin resistance, as measured by parameters such as fasting plasma glucose, insulin levels, and the homeostatic model assessment of insulin resistance (HOMA-IR). This secondary analysis aimed to contribute additional insights into the broader metabolic implications of magnesium levels in individuals with type 2 DM.

Ethics

Approval of the study was received from the Ethics Committee of Gaziosmanpasa Training and Research Hospital (decision number 147, dated 08.11.2023). Every procedure was completed in compliance with the Helsinki Declaration.

Statistical Analysis

Given the retrospective structure of this study, it is important to point out that a formal power analysis was not deemed appropriate during the study design phase. Retrospective analyses often lack the prospective planning necessary for a priori power calculations. The statistical software SPSS 26.0 version (Chicago, IL, IBM Corp.) was used for all of the analysis. The Kolmogorov-Smirnov test determined the distributions of variables. The distribution of parameters was non-parametric. Categorical parameters were indicated as percentages. We used the Kruskal-Wallis to assess significance among study groups. Also, the correlation between serum magnesium and HbA1c levels and other related laboratory parameters was determined with the Spearman test. The statistical significance cut-off value was deemed to be $p<0.05$.

RESULTS

The comprehensive characterization of study participants is delineated in Table 1, where a predominance of female subjects is evident, constituting 56.7% of the cohort. The median age of participants was 46 years, with an interquartile range of 33 to 56 years. Pertinent clinical attributes, encompassing body mass index, smoking status (categorized as no-smoker/current/ex-smoker), and blood pressure measurements, are detailed in Table 1 to elucidate the demographic heterogeneity within the study population.

Table 2 unveils compelling statistical disparities in serum magnesium levels across the delineated groups, reaching a significance level of $p<0.001$. Concurrently, discernible differentials in fasting plasma glucose, insulin, and HOMA-IR were observed among these groups, attaining statistical significance with p-values less than 0.001 for all three parameters. It is noteworthy that while lipid parameters displayed variations, they did not attain statistical significance among the defined groups.

Concurrently, correlation analysis, as outlined in Table 3, unearthed a robust negative correlation ($r=-0.316$, $p<0.001$) between serum magnesium levels and HbA1c. Notably, a nuanced, albeit weak, negative relationship

Table 2. Comparison of laboratory data between the groups

	Control (n=121)	Prediabetes (n=85)	Diabetes (n=99)	p
Magnesium, mg/dL	1.96 (1.81–2.15)	1.83 (1.53–2.03)	1.7 (1.49–1.93)	<0.001
HbA1c, %	5.2 (5.1–5.4)	5.8 (5.7–6)	7,5 (6.7–8.6)	<0.001
Glucose, mg/dL	91 (87–95)	101 (92–108)	104 (95–123)	<0.001
Insulin, mU/L	8 (5.85–15)	16 (10–28.1)	15.4 (10–30.1)	<0.001
HOMA-IR	1.87 (1.34–3.17)	3.95 (2.39–6.95)	4.9 (2.72–8.42)	<0.001
Vitamin D, µg/L	14.2 (9.72–18.85)	14 (8.84–19.1)	13.5 (9.23–19.5)	0.947
Total cholesterol, mg/dL	187 (162–212)	208 (180–239)	206 (180–227)	<0.001
LDL, mg/dL	111 (92–129)	126 (105–156)	120 (104–147)	0.001
Triglyceride, mg/dL	90 (66–130)	124 (93–170)	141 (100–196)	<0.001
HDL, mg/dL	55 (45–64)	50 (44–61)	48 (41–56)	0.02
Creatinine, mg/dL	0.72 (0.64–0.87)	0.77 (0.66–0.87)	0.75 (0.68–0.88)	0.157
Calcium, mg/dL	9.52 (9.28–9.83)	9.6 (9.3–9.79)	9.53 (9.34–9.74)	0.941
Potassium, mmol/L	4.5 (4.3–4.72)	4.6 (4.37–4.81)	4.53 (4.34–4.81)	0.194
Hemoglobin, g/dL	13.6 (12.6–15.1)	13.6 (12.2–14.75)	13.6 (12.9–14.6)	0.587

HbA1c: HemoglobinA1c; HOMA-IR: Homeostatic model assessment-insulin resistance; LDL: Low density lipoprotein; HDL: High density lipoprotein.

Table 3. Correlation analysis between serum magnesium levels, HbA1c and other relevant parameters

	HbA1c	Glucose	Insulin	HOMA-IR	BMI
Magnesium					
r	-0.316	-0.167	-0.167	-0.198	-0.034
p	<0.001	0.004	0.003	0.001	0.554

HbA1c: HemoglobinA1c; HOMA-IR: Homeostatic model assessment-insulin resistance; BMI: Body mass index.

was discerned between serum magnesium and fasting plasma glucose, fasting insulin, and HOMA-IR. This nuanced exploration of correlations contributes to our understanding of the intricate interplay between serum magnesium levels and key metabolic parameters in individuals with Type 2 Diabetes Mellitus.

DISCUSSION

Investigating the relationship between serum magnesium and HbA1c levels and insulin resistance was the objective of our study. A significant difference was obtained among the groups in terms of Mg and HbA1c. Also, while a reverse correlation was detected between magnesium and HbA1c levels among all 3 groups, there was a weak inverse association between serum Mg and glucose, insulin and HOMA-IR.

Numerous prior studies have demonstrated a strong correlation between serum magnesium levels and glycemic control [11–13]. In a study by Galli-Tsinopoulou et al. [14] with 138 patients, an inverse correlation was found across Mg and HbA1c. Another study conducted by Kumar et al. [15] revealed that Mg deficiency is linked to a higher risk of inadequate glycemic control. In parallel with these studies, we found that patients with poor glycemic control had lower serum magnesium levels.

These results we found are supported by the findings obtained in many studies investigating the functions of magnesium in glucose homeostasis. According to Wan Nik et al.'s [16] review study from 2023 and numerous other studies, magnesium in the Mg-ATP structure regulates the glucokinase effect, and pancreatic insulin secretion decreases as a result of a reduction in glucokinase enzyme activity in magnesium deficiency. Additionally, magnesium affects insulin sensitivity, signaling, phosphorylation of receptor tyrosine kinase and many other kinases involved in glucose metabolism [2, 17].

On the other hand, numerous research demonstrate that serum magnesium replacement has no impact on glycemic control and insulin sensitivity [18, 19]. A random-

ized controlled study conducted by Drenthen et al. [20] in November 2023 showed that oral magnesium treatment did not provide improvement in glycemic control or insulin resistance in hypomagnesemic diabetic patients. In a prospective study with normomagnesemic diabetic patients, Navarrete-Cortes et al. [21] found no significant change in HbA1c, fasting glucose, insulin, or HOMA-IR values after magnesium treatment. Although the effect of magnesium treatment was not evaluated because of our study's retrospective design, in parallel with the above-mentioned studies, a strong correlation was not detected between insulin sensitivity and magnesium levels.

Conclusion

In conclusion, our study adds valuable insights to the current understanding of the interplay between serum magnesium levels and glycemic control. Yet, the conflicting nature of existing literature highlights the intricacies of this relationship, emphasizing the imperative for larger, well-designed prospective studies to provide a more nuanced comprehension of magnesium's role in metabolic regulation among individuals with Type 2 DM.

Ethics Committee Approval: The Gaziosmanpasa Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 08.11.2023, number: 147).

Authorship Contributions: Concept – OE; Design – OE; Supervision – OE, SY; Fundings – OE; Materials – OE, SY; Data collection and/or processing – OE, SY; Analysis and/or interpretation – OE; Literature review – OE; Writing – OE; Critical review – OE, SY.

Conflict of Interest: No conflict of interest was declared by the authors.

Use of AI for Writing Assistance: The authors declared that artificial intelligence supported technologies were not used in our study.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

REFERENCES

1. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 2023;402:203-34. Erratum in: Lancet 2023;402:1132. Erratum in: Lancet 2025;405:202.
2. Morais JBS, Severo JS, de Alencar GRR, de Oliveira ARS, Cruz KJC, Marreiro DDN, et al. Effect of magnesium supplementation on insulin resistance in humans: a systematic review. Nutrition 2017;38:54-60. [CrossRef]
3. Alghobashy AA, Alkholy UM, Talat MA, Abdalmonem N, Zaki A, Ahmed IA, et al. Trace elements and oxidative stress in children with type 1 diabetes mellitus. Diabetes Metab Syndr Obes 2018;11:85-92. [CrossRef]
4. Jahnen-Dechent W, Ketteler M. Magnesium basics. Clin Kidney J 2012;5 Suppl 1:i3-14. [CrossRef]
5. Barbagallo M, Dominguez LJ. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. Arch Biochem Biophys 2007;458:40-7. [CrossRef]
6. Gunther T. The biochemical function of Mg^{2}+ in insulin secretion, insulin signal transduction and insulin resistance. Magnes Res 2010;23:5-18. [CrossRef]
7. Barbagallo M, Dominguez LJ. Magnesium and type 2 diabetes. World J Diabetes 2015;6:1152-7. [CrossRef]
8. Kostov K. Effects of magnesium deficiency on mechanisms of insulin resistance in type 2 diabetes: focusing on the processes of insulin secretion and signaling. Int J Mol Sci 2019;20:1351. [CrossRef]
9. Barbagallo M, Veronese N, Dominguez LJ. Magnesium-An ion with multiple invaluable actions, often insufficiently supplied: from in vitro to clinical research. Nutrients 2023;15:3135. [CrossRef]
10. Mooren FC. Magnesium and disturbances in carbohydrate metabolism. Diabetes Obes Metab 2015;17:813-23. [CrossRef]
11. Oost LJ, van Heck JIP, Tack CJ, de Baaij JHF. The association between hypomagnesemia and poor glycemic control in type 1 diabetes is limited to insulin resistant individuals. Sci Rep 2022;12:6433. [CrossRef]
12. Asbaghi O, Moradi S, Kashkooli S, Zobeiri M, Nezamoleslami S, Hojjati Kermani MA, et al. The effects of oral magnesium supplementation on glycaemic control in patients with type 2 diabetes: a systematic review and dose-response meta-analysis of controlled clinical trials. Br J Nutr 2022;128:2363-72. [CrossRef]
13. El Derawi WA, Naser IA, Taleb MH, Abutair AS. The effects of oral magnesium supplementation on glycemic response among type 2 diabetes patients. Nutrients 2018;11:44. [CrossRef]
14. Galli-Tsinopoulou A, Maggana I, Kyrgios I, Mouzaki K, Grammatikopoulou MG, Stylianou C, et al. Association between magnesium concentration and HbA1c in children and adolescents with type 1 diabetes mellitus. J Diabetes 2014;6:369-77. [CrossRef]
15. Kumar P, Bhargava S, Agarwal PK, Garg A, Khosla A. Association of serum magnesium with type 2 diabetes mellitus and diabetic retinopathy. J Family Med Prim Care 2019;8:1671-7. [CrossRef]
16. Wan Nik WNFH, Zulkeflee HA, Ab Rahim SN, Tuan Ismail TS. Association of vitamin D and magnesium with insulin sensitivity and their influence on glycemic control. World J Diabetes 2023;14:26-34. [CrossRef]
17. de Sousa Melo SR, Dos Santos LR, da Cunha Soares T, Cardoso BEP, da Silva Dias TM, Morais JBS, et al. Participation of magnesium in the secretion and signaling pathways of ınsulin: an updated review. Biol Trace Elem Res 2022;200:3545-53. [CrossRef]
18. Saeed H, Haj S, Qasim B. Estimation of magnesium level in type 2 diabetes mellitus and its correlation with HbA1c level. Endocrinol Diabetes Metab 2018;2:e00048. [CrossRef]
19. de Valk HW, Verkaaik R, van Rijn HJ, Geerdink RA, Struyvenberg A. Oral magnesium supplementation in insulin-requiring Type 2 diabetic patients. Diabet Med 1998;15:503-7. [CrossRef]
20. Drenthen LCA, de Baaij JHF, Rodwell L, van Herwaarden AE, Tack CJ, de Galan BE. Oral magnesium supplementation does not affect insulin sensitivity in people with insulin-treated type 2 diabetes and a low serum magnesium: a randomised controlled trial. Diabetologia 2024;67:52-61. [CrossRef]
21. Navarrete-Cortes A, Ble-Castillo JL, Guerrero-Romero F, Cordova-Uscanga R, Juárez-Rojop IE, Aguilar-Mariscal H, et al. No effect of magnesium supplementation on metabolic control and insulin sensitivity in type 2 diabetic patients with normomagnesemia. Magnes Res 2014;27:48-56. [CrossRef]