Research Article

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Evaluation of calcium/magnesium ratio in patients with type 2 diabetes mellitus

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Abstract

Objectives: This study aimed to evaluate the calcium/magnesium (Ca/Mg) ratio in patients diagnosed with type 2 diabetes mellitus (T2DM).
Methods: This study is a retrospective cross-sectional study. Mg levels were determined by measuring the total serum Mg levels. Magnesium was measured by colorimetric method and HbA_{1c} was measured by turbidimetric inhibition immunoassay method. Subject were divided into two groups (<7 % and ≥7 %) based on HbA_{1c} levels. Also, subjects were divided into four groups (quartiles) based on serum Mg concentrations.
Results: A total of 891 (636F, 255M) patients diagnosed with T2DM were included in the study. The Mg increase in the group with good glycemic control was also remarkable. One of our most important findings is that as the Mg concentration increases, the fasting glucose, HbA_{1c}, and Ca/Mg rate decreased with increasing Mg concentration. In the ROC analysis performed between the poor and good glycemic control groups, we found the AUC was 0.672, 0.650, 0.611, and 0.578 for Ca/Mg ratio, Mg, K, and Ca, respectively.
Conclusions: While the Ca/Mg ratio and Ca levels were significantly higher, Mg levels were significantly lower among poor glycemic control than good glycemic control T2DM. The Ca/mg ratio and Mg are important parameters for T2DM patients, but more comprehensive studies are needed before they can monitor glycemic control.

Keywords: calcium:magnesium ratio; glycemic control; magnesium; receiver operating characteristic; type 2 diabetes mellitus.

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Introduction

Type 2 diabetes mellitus (T2DM) is a heterogeneous metabolic disorder characterized by chronic hyperglycemia, resulting in a deficiency in insulin secretion, insulin action, or both [1, 2]. β-cell dysfunction and insulin resistance are potential mechanisms in the development of T2DM. Insulin or receptor defects in target tissues lead to chronic hyperglycemia, increased oxidative stress, and proinflammatory cytokine production, impairing insulin signaling pathways, lipid metabolism, protein synthesis and cell differentiation. In addition, chronic hyperglycemia leads to dehydration, urinary excretion of glucose, and damage to the endothelium and many tissues [3–5]. Dietary habits, a sedentary lifestyle, and environmental and genetic factors play an important role in the development of T2DM [2, 6]. Type 2 diabetes mellitus and the obesity that often accompanies it increase the inflammatory burden. Studies suggest micronutrient deficiencies may contribute to body fat accumulation and chronic inflammation [7, 8]. A balanced diet with adequate nutrient content can reduce HbA_{1c} by 0.3–2 % in people with T2DM. Recent studies have confirmed the role of minerals in the synthesis, secretion, and action of insulin [9, 10]. Zinc, potassium (K), calcium (Ca), and magnesium (Mg) minerals are reported to be necessary for the regulation of glucose metabolism [11–15].

Magnesium is the most abundant cation in the intracellular fluid after potassium, and it is a mineral that has not been given enough scientific value. Mg, which plays a key role in many metabolic reactions, cannot be produced in the body and must be constantly taken from the outside through food [15–17]. As a cofactor for enzymes involved in glucose metabolism, Mg may play a protective role against diabetes depending on the effectiveness of insulin and its effects on glucose homeostasis. Mg ion is involved in the autophosphorylation of protein kinases in insulin signaling [13, 18, 19]. Furthermore, as the Mg levels decrease, tyrosine phosphorylation of insulin receptors is impaired, and insulin resistance sets in. Type 2 DM; is often associated with hypomagnesemia. The leading cause is increased urinary Mg excretion due to diabetic ketoacidosis and glycosuria [19–21]. Many studies have shown the beneficial effects of Mg in diabetes [15, 19, 20, 22, 23].

Calcium, the most abundant mineral in the human body, regulates of voltage-dependent channels required for insulin release in pancreatic cells [24]. Insulin secretion depends on Ca, but some studies have suggested that the high Ca intake may affect the absorption of Mg, which may predispose to some diseases [13, 25, 26]. Several extensive cohort studies have associated higher serum Ca levels with an increased risk of T2DM. Although the exact mechanism is unclear, it has been reported that the high intracellular Ca levels may lead to the development of T2DM in the long term by reducing insulin use and adipose tissue receptor activity [27, 28].

Magnesium is a Ca antagonist in membrane channels and intracellular regions [17, 29]. Only 1 % of body Mg is found in the extracellular space. This is the measurable amount, but it is challenging to detect Mg deficiency with the 1 % measurable amount [16, 17]. For this reason, current studies have compared their ratios with other laboratory parameters; rather than evaluating only the amounts of Mg and only Ca. In recent studies, the Mg/Ca ratio decrease has attracted attention. It has been reported that dietary Ca/Mg ratios in the USA increased to 2.3–2.9 in 1977 and 2.9–3.5 in 2007–8 [29]. A serum Ca/Mg ratio above 2:1 has been associated with an increased risk of metabolic, inflammatory, and cardiovascular diseases [30]. Some clinical or experimental studies also show that the effect of Mg on vascular calcification should be analyzed together with the Ca levels. The Mg/Ca ratio may be helpful in this context [30, 31]. The NHANES study reported that a higher intracellular Ca/Mg ratio causes insulin resistance and hypertension [26].

As T2DM is a chronic inflammatory disease, it has been associated with increased Ca/Mg ratio and hypomagnesemia [3, 32]. The laboratory's measuring methods of Mg give information about 1 % of total body Mg. Magnesium deficiency is, therefore, difficult to detect. Excess Ca reduces Mg absorption through antagonistic interaction. Due to the limitations of evaluating the measurable amount of Mg in T2DM patients, we hypothesized that the Ca/Mg ratio would be higher in the poor glycemic control group, taking advantage of the antagonistic effect of Mg with Ca. Based on this hypothesis and the data from existing studies, we aimed to evaluate the Ca/Mg ratio in patients with T2DM and compare the data we obtained in poor and good glycemic control groups. No study in the literature has compared T2DM patients by grouping them according to good and poor glycemic control groups and according to Mg quartiles and evaluated the Ca/Mg ratio comprehensively. Therefore, our study is original and will contribute to the literature.

Materials and methods

Study population

This study is a retrospective cross-sectional study. After ethics committee approval, patients diagnosed with T2DM at the Department of Internal Medicine, Van Training and Research Hospital, Health Sciences University, were retrospectively analyzed between 1 January 2012 and 1 January 2022. Patients' age, gender, biochemistry, and hemogram data were obtained retrospectively from the hospital's automated system and patient records. Participants were not randomly selected, and all participants who met the inclusion criteria between those dates were included in the study. The diagnosis of T2DM was made according to the American Diabetes Association guidelines [33]. A total of 891 patients with T2DM were included in the study.

Inclusion criteria:

1. Duration of T2DM for >3 months (those who are treated for diabetes by pill or subcutaneous injection)
2. Age >18 years (men, non-pregnant women)
3. Absence of additional disease diagnosis (metabolic or liver diseases, T1DM, hyperparathyroidism, cancer, etc.) other than T2DM in the system
4. Those with complete Ca, Mg and HbA_{1c} values in laboratory results

Exclusion criteria:

1. Those without a diagnosis of T2DM and having a duration of T2DM <3 months
2. Age <18 years man and woman
3. Pregnant women, having another additional disease diagnosis (metabolic or liver diseases, T1DM, hyperparathyroidism, cancer, etc.) in the system
4. Missing laboratory data for serum Ca, Mg, and HbA_{1c}.

Analytical methods

Mg levels were determined by measuring the total serum Mg levels. Magnesium was measured by the colorimetric method, and HbA_{1c} was measured by the turbidimetric inhibition immunoassay method. Roche Cobas c502 and Cobas c501 were used for Mg and HbA_{1c} measurements.

Groups and definition of cut-off points

We used standard international criteria to define "glycemic control" [34]. Subjects were divided into two groups based on HbA_{1c} levels:

Good glycemic control: HbA_{1c} levels <7 %

Poor glycemic control: HbA_{1c} levels ≥7 %

We wanted to group patients according to their magnesium levels, whether above or below the reference range of 1.7–2.55 mg/dL. Since very few of the participants had Mg levels below the reference range (7.86 %), to examine the association between demographics, clinical or laboratory measurements and Mg, subjects were divided into four groups (quartiles) [35] based on serum Mg concentrations as follows: quartile (Q)1, serum Mg <1.82 mg/dL; Q2, serum Mg between 1.82 and 1.94 mg/dL; Q3, serum Mg between 1.95 and 2.05 mg/dL; and Q4, serum Mg >2.06 mg/dL.

Statistical analysis

Statistical data were analyzed using the SPSS 27.0 package program (IBM SPSS, Chicago, IL, USA). Means ± standard deviations were used to summarise numerical data and numbers and percentages were used to summarise categorical data. The data are assumed to be normally distributed according to the central limit theorem. When comparing normally distributed numerical data with two independent groups, the independent groups t-test was used. One-way ANOVA test compared normally distributed numerical data with more than two groups. Post hoc Sheffe and Tamhane tests were used to determine which group the significance originated from in groups with a significant difference due to the one-way ANOVA test. Correlations between numerical variables were analyzed using Pearson's correlation coefficient. The discriminatory power of serum Ca/Mg ratio, Mg, K, and Ca levels was assessed by receiver operating characteristic (ROC) curves and the corresponding area under the ROC curve (AUC). The result of the ROC analysis was reported as the AUC. Data were analyzed at 5 % significance level and 95 % confidence level. The type-1 error level was accepted as 5 % for statistical significance.

Ethical approval

For this study, approval was obtained from the Van Training and Research Hospital and Clinical Research Ethics Committee, and research and publication ethics were followed in the article (No: 2022/05-02, Date: March,02,2022). Care was taken to ensure the study complies with the Declaration of Helsinki.

Results

A total of 891 (636F, 255M) patients diagnosed with T2DM were included in the study. The mean age of all patients was 46 ± 16.05 years. When we compared the male and female groups, we found a statistically significant difference between groups depending on the increase of age, HGB, RBC, AST, ALT, urea, creatinine, fasting glucose, HbA_{1c}, K, and Mg values in males. The HbA_{1c} levels were <7 % in 74.5 % of women and 69 % of men. The comparison of the patient's laboratory data according to gender is shown in Table 1.

27.04 % of all patients in the study had poor glycemic control (n=241). When we compared the laboratory parameters between the groups with poor and good glycemic control, age, HGB, RBC, WBC, neutrophil, lymphocyte, ALT, urea, creatinine, fasting glucose, HbA_{1c}, K, and Ca/Mg ratio values were found to be statistically significant between the groups, depending on their elevation in the group of patients with poor glycemic control. The increase in Mg in the group with good glycemic control was also notable. The comparison of the patient's laboratory data regarding glycemic control is shown in Table 2.

Table 1: Comparison of some laboratory parameters according to gender.

Laboratory findings	Female (n=636)	Male (n=255)	p-Value
Age	45.78 ± 16.13	48.49 ± 15.73	0.02[a]
HGB, g/dL	13.75 ± 1.43	16.04 ± 1.36	0.00[a]
PDW, fL	16.07 ± 0.65	16.18 ± 0.78	0.07
RBC (10^6/mm^3)	4.91 ± 0.41	5.45 ± 0.51	<0.001
WBC (10^3/mm^3)	7.46 ± 2.04	7.64 ± 2.16	0.24
PLT (10^3/mm^3)	276.99 ± 66.01	238.00 ± 57.06	<0.001
Neutrophil (10^3/mm^3)	4.58 ± 2.34	4.56 ± 1.74	0.88
Lymphocyte (10^3/mm^3)	2.35 ± 0.71	2.37 ± 0.75	0.68
AST, U/L	18.48 ± 7.48	21.39 ± 9.92	<0.001
ALT, U/L	17.24 ± 10.56	24.68 ± 17.97	<0.001
Urea, mg/dL	25.43 ± 11.83	31.42 ± 12.12	<0.001
Creatinine, mg/dL	0.69 ± 0.22	0.90 ± 0.23	<0.001
Fasting glucose, mg/dL	147.52 ± 60.90	158.76 ± 74.66	0.03[a]
HbA1c, %	6.77 ± 2.11	7.17 ± 2.61	0.03[a]
K, mmol/L	4.36 ± 0.42	4.44 ± 0.43	0.03[a]
Ca, mg/dL	9.43 ± 0.51	9.55 ± 1.31	0.05
Mg, mg/dL	1.93 ± 0.19	2.00 ± 0.47	<0.001
NLR	2.09 ± 1.20	2.08 ± 1.00	0.98
PLR	127.92 ± 54.68	109.32 ± 40.44	<0.001
Ca/Mg ratio	4.93 ± 0.57	4.86 ± 0.80	0.16

Statistics: independent samples test, data are expressed as mean ± standard deviation (X ± SD), [a]p<0.05.

In 7.86 % of the patients (n:70), the Mg levels were below the hospital system reference value (<1.7 mg/dL) specified in the hospital's system. Table 3 summarizes the results of comparisons of demographics and laboratory measurements between different serum Mg quartiles. There were 219, 223, 223, and 226 subjects in Q1, Q2, Q3, and Q4, respectively. There was a significant difference in age between the groups. The average age of the low magnesium group was higher. One of our most important findings was that the fasting glucose, HbA_{1c} and Ca/Mg ratio decreased in the groups with higher Mg concentrations (Table 3).

A significant, positive correlation was found between the serum HbA_{1c} levels and fasting glucose (r=0.996; p<0.01). There was a significant, positive and moderate correlation between age and HbA_{1c} (r=0.406; p<0.01), and fasting glucose levels (r=0.403; p<0.01). There was also a significant, positive, and low correlation between the Ca/Mg ratio and HbA_{1c} (r=0.240; p<0.01), and fasting glucose levels (r=0.235; p<0.01). There was also a significant, very low, and negative correlation between the Mg and HbA_{1c} (r=−0.150; p<0.01), fasting glucose (r=−0.148; p<0.01). There was no significant correlation between serum Mg levels and Ca levels (r=0.014; p>0.05).

ROC curves and AUC analyses were performed to investigate the predictive power of the Ca/Mg ratio, Ca, Mg, and K. In the ROC analysis performed between the poor and

Table 2: Comparison of the laboratory data between those with poor and good glycemic control.

Laboratory findings	Glycemic control		p-Value
	Poor (n=241) (162F/79M)	Good (n=650) (474F/176M)	
Age	57,87 ± 12.06	42.36 ± 15.31	<0.001
HGB, g/dL	14.69 ± 1.65	14.20 ± 1.77	0.03[a]
PDW, fL	16.08 ± 0.79	16.10 ± 0.65	0.59
RBC (10^6/mm^3)	5.37 ± 0.50	5.00 ± 0.49	<0.001
WBC (10^3/mm^3)	8.16 ± 2.30	7.27 ± 1.93	<0.001
PLT (10^3/mm^3)	265.14 ± 71.64	266.35 ± 63.64	0.80
Neutrophil (10^3/mm^3)	4.91 ± 1.76	4.45 ± 2.31	<0.001
Lymphocyte (10^3/mm^3)	2.56 ± 0.83	2.28 ± 0.66	<0.001
AST, U/L	18.98 ± 9.43	19.44 ± 7.91	0.46
ALT, U/L	22.56 ± 14.96	18.19 ± 22.56	<0.001
Urea, mg/dL	31.92 ± 17.29	25.66 ± 9.69	<0.001
Creatinine, mg/dL	0.90 ± 0.31	0.73 ± 0.21	<0.001
Fasting glucose, mg/dL	235.56 ± 71.99	119.29 ± 16.31	<0.001
HbA1c, %	9.85 ± 2.49	5.78 ± 0.55	<0.001
K, mmol/L	4.49 ± 0.35	4.26 ± 0.44	<0.001
Ca, mg/dL	9.59 ± 1.01	9.42 ± 0.74	<0.001
Mg, mg/dL	1.87 ± 0.20	1.98 ± 0.32	<0.001
NLR	3.50 ± 0.52	2.09 ± 1.21	0.73
PLR	113.73 ± 125.76	125.76 ± 49.34	<0.001
Ca/Mg ratio	5.17 ± 0.80	4.81 ± 0.55	<0.001

Statistics: independent samples test, data are expressed as mean ± standard deviation (X ± SD), [a]p<0.05.

good glycemic control groups, we found that the AUC were 0.672 (p<0.01, confidence interval (CI)=0.631–0.712), 0.650 (p<0.01, CI=0.609–0.691), 0.611 (p<0.01, CI=0.569–0.654), and 0.578 (p<0.01, CI=0.536–0.621) for Ca/Mg ratio, Mg, K, and Ca, respectively. As Mg was high in the group with good glycemic control, we could not show the ROC curve on the same figure with other parameters (Figures 1 and 2).

Discussion

This study shows that low serum Mg levels and high Ca/Mg ratio are associated with an increased risk of poor glycemic control in patients with T2DM. Diabetes mellitus is a public health problem with a rapidly increasing number of cases. It occurs more frequently in women than men. Consistent with the studies in the literature [2, 36], 71.38 % of the patients in our study were female. When we compared the male and female groups, the mean age, HGB, AST, ALT, HBA_{1c}, urea, creatinine, and K were higher in males than in females. As 74.5 % of women had HbA_{1c} <7 %, we found better glycemic control in women than in men. In a study by Jeon et al. in 2013, it was reported that 52.3 % of patients with HbA_{1c} levels <6.5 were women [37]. In addition, in line with studies in the literature [38, 39], we believe that age and high HbA_{1c} levels

Table 3: Association of demographic and laboratory data with serum Mg concentration.

Laboratory findings	Q1 (n=219)	Q2 (n=223)	Q3 (n=223)	Q4 (n=226)	p-Value
Age	50.45 ± 16.03[a,b]	47.32 ± 15.36	44.36 ± 15.88[a]	44.20 ± 16.21[b]	<0.001
HGB, g/dL	13.96 ± 1.83[a,b,c]	14.46 ± 1.57[a]	14.55 ± 1.73[b]	14.64 ± 1.78[c]	<0.001
PDW, fL	15.93 ± 1.10[a,b]	16.18 ± 0.36[a]	16.12 ± 0.67	16.15 ± 0.35[b]	<0.001[a]
RBC (10^6/mm^3)	5.03 ± 0.52	5.07 ± 0.47	5.08 ± 0.54	5.09 ± 0.48	0.61
WBC (10^3/mm^3)	7.63 ± 2.14	7.64 ± 2.15	7.37 ± 1.73	7.40 ± 2.22	0.36
PLT (10^3/mm^3)	266.16 ± 63.24	266.30 ± 65.77	262.82 ± 71.14	268.77 ± 63.27	0.82
Neutrophil (10^3/mm^3)	4.57 ± 1.65	4.64 ± 1.73	4.65 ± 3.20	5.45 ± 1.78	0.76
Lymphocyte(10^3/mm)	2.39 ± 0.79	2.41 ± 0.75	2.30 ± 0.69	2.33 ± 0.05	0.34
AST, U/L	18.95 ± 10.09	19.13 ± 7.71	19.66 ± 8.21	19.52 ± 7.18	0.79
ALT, U/L	20.13 ± 14.47	19.46 ± 13.68	19.81 ± 15.09	18.12 ± 10.45	0.41
Urea, mg/dL	27.73 ± 10.28	26.14 ± 9.81	26.99 ± 11.34	27.75 ± 15.98	0.50
Creatinine, mg/dL	0.73 ± 0.25	0.74 ± 0.25	0.78 ± 0.28	0.76 ± 0.19	0.12
Fasting glucose	175.35 ± 80.26[a,b,c]	153.32 ± 67.23[a,d]	143.09 ±57.51[b]	131.91 ± 43.44[c,d]	<0.001
HbA1c, %	7.57 ± 2.80[a,b,c]	6.97 ± 2.33[a,d]	6.61 ± 1.99[b]	6.22 ± 1.51[c,d]	<0.001
K, mmol/L	4.40 ± 0.36	4.36 ± 0.34	4.39 ± 0.61	4.41 ± 0.34	0.62
Ca, mg/dL	9.48 ± 1.07	9.38 ± 0.52	9.48 ± 0.41	9.52 ± 1.06	0.31
NLR	2.07 ± 0.96	2.08 ± 0.99	2.18 ± 1.56	2.06 ± 0.96	0.56
PLR	121.34 ± 45.62	119 ± 45.51	124.53 ± 59.79	124.91 ± 3.77	0.60
Ca/Mg ratio	5.58 ± 0.71[a,b,c]	4.91 ± 0.28[a,d,e]	4.73 ± 0.21[b,d,f]	4.37 ± 0.53[c,e,f]	<0.001

Statistics: One-Way ANOVA, Quartile (Q)1, serum Mg <1.82 mg/dL; Q2, serum Mg between 1.82 and 1.94 mg/dL; Q3, serum Mg between 1.95 and 2.05 mg/dL; and Q4, serum Mg >2.06 mg/dL; a, b, c, d, e, f: differences between pairs are indicated by the same letters; data are expressed as mean ± standard deviation (X ± SD) [a]p<0.05.

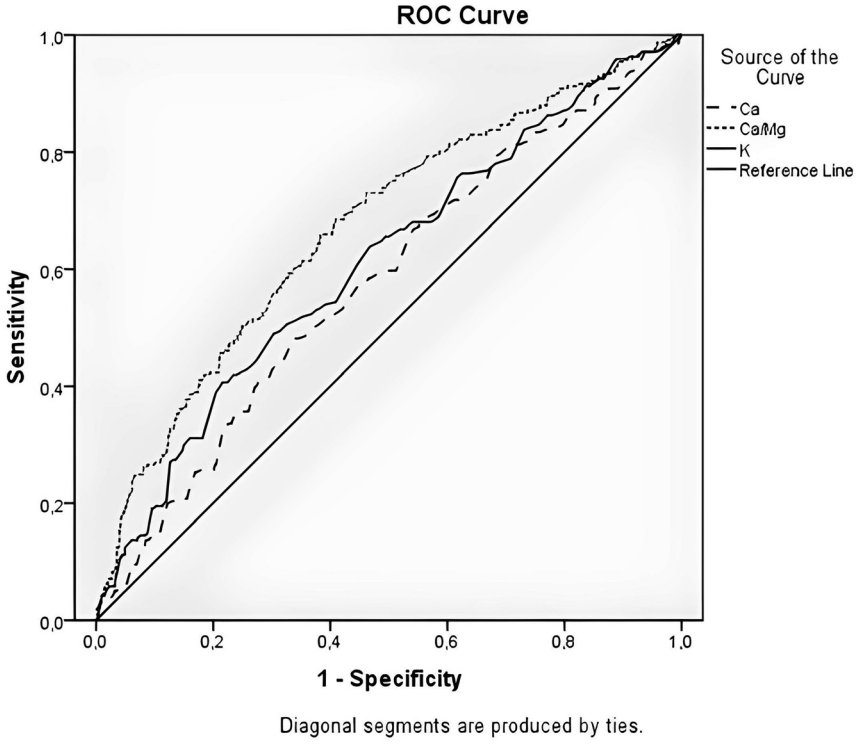

Figure 1: The ROC analysis for Ca/Mg ratio, K and Ca (AUC: 0.672, 0.611, 0.578, respectively).

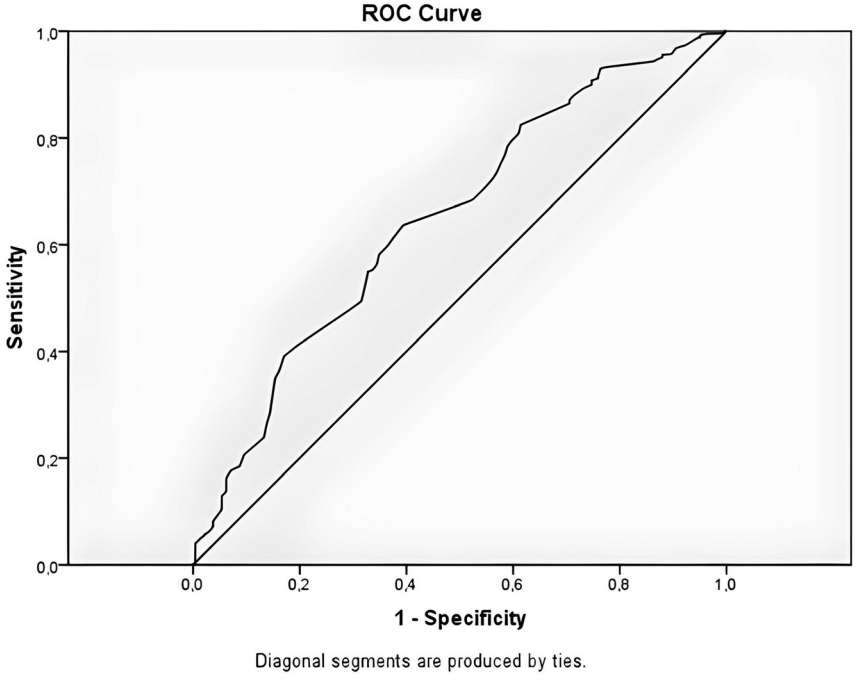

Figure 2: The ROC analysis for Mg (AUC: 0.650).

affect hepatorenal function in men. Glucose tolerance in T2DM is likely to increase with age [9]. Our study found that the mean age of the group with poor glycemic control group was statistically significantly higher than that of good glycemic control.

Type 2 DM is an inflammatory disease, and many studies in the literature show that WBC, neutrophils, lymphocytes, NLR, and PLR increase in inflammatory diseases. Among the parameters we analyzed, we found that WBC, neutrophils, lymphocytes, and PLR were significantly higher in the poor

glycemic control group, in line with the literature [40, 41]. NLR was also higher in the poor glycemic control group, but the difference was not statistically significant.

Hyperkalemia and hyperuricemia are higher in T2DM than in the normal population [42]. A decrease in Mg levels reduces ATP activity. The decrease in ATP activity slows down the function of ATP-dependent potassium channels in the kidney and reduces the potassium-holding capacity of the cell. Most people with Mg deficiency also have potassium deficiency [16, 43]. In our study, we found that Mg levels were significantly lower and potassium levels were significantly higher in the group with poor glycemic control. Reasons for the high level of K in the group with poor glycemic control include potassium leakage from the cell due to insulin deficiency, use of drugs that affect K excretion, decreased K expression due to decreased glomerular filtration rate, and a diet rich in K can be counted [42]. One of the most important organs damaged in people with diabetes is the kidney. Two studies conducted in 2014 and 2018 in diabetic and nondiabetic people found that urea and creatinine levels were significantly higher in the diabetic group than in the nondiabetic group [44, 45]. Another study conducted in 2018 compared groups with good (n: 29) and poor (n: 26) glycemic control. It was reported that there was no significant difference in urea and creatinine levels between the groups [46]. In our study, the urea, creatinine, and K levels were significantly higher in the poor glycemic control group than in the good glycemic control. It is an obvious fact that good glycemic control improves renal function. We think the differences between the studies are due to the different numbers of patients and the lack of information about the patient's kidney function.

Calcium, one of the most abundant minerals in the human body, plays a role in insulin secretion. However, there are also studies suggesting that excessive increases in Ca levels may be a risk factor for T2DM [27, 28, 47]. In their study of 197 patients with T2DM, Huang et al., found that high or low Ca intake in elderly patients with T2DM increased the risk of cardiovascular disease [25]. Another study conducted in 2021 emphasized that high Ca levels and low Mg levels are independent risk factors for diabetic retinopathy [48]. In support of these studies, we found that Ca levels were significantly higher in the poor glycemic control group compared to the good glycemic control group in our study.

Magnesium is an essential mineral. Especially T2DM, in particular, is often associated with hypomagnesemia [16, 21, 49]. A cohort study of 17.592 individuals without diabetes or any chronic disease evaluated the relationship between dietary Mg intake and the risk of developing diabetes. In this study, 459 cases of diabetes were observed after 5 years of follow-up, and it was concluded that dietary Mg intake reduced the risk of diabetes [23]. In a study conducted in Hawaii with 75.512 participants aged 45–75 years, 8.587 diabetes cases of diabetes were seen after 14 years of follow-up. The study concluded that high magnesium levels reduce the risk of diabetes [22]. In another study of 189 patients with T2DM [50], fasting glucose and HbA_{1c} levels were found to be significantly higher in the hypomagnesemic group (n: 64) than in the normomagnesemic group (n: 125). A weak negative correlation was found between serum Mg levels and HbA_{1c}, glucose, and proteinuria levels ($r=-0.187$, $p=0.011$; $r=-0.152$, $p=0.039$; $r=-0.149$, $p=0.044$, respectively).

Magnesium acts as a Ca antagonist in membrane channels and intracellular regions. Low Mg is associated with high Ca [51]. One study, reported that the prevalence of hypomagnesemia and osteoporosis was higher in patients with chronic kidney disease and diabetes [52]. A study conducted with 102 patients with T2DM reported that potassium and Mg intake was inversely related to HbA_{1c} [13]. Galli-Tsinopoulou A. et al. found in their study of 138 patients with T1DM that Mg was low in the group with a poor glycemic control group. In addition, when they compared Mg by dividing it into 4 quarts, they found, in parallel with the results of our study, that the HbA_{1c} level decreased as the Mg level increased in the patients [35]. In a way that supports the information in the literature, in our study, we found that the Mg levels were significantly lower and Ca levels were significantly higher in the group with poor glycemic control. In the grouping where we divided the patients into 4 quarters according to their Mg levels, we found that fasting glucose and HbA_{1c} decreased as the Mg levels increased. This result is one of the best results of our study.

Recently, the increase in the amount of Ca and the decrease in the amount of Mg in dietary components have made it more important to evaluate the Ca/Mg ratio rather than evaluating the amount of Ca and Mg amounts separately [29]. The 2005 study by Soltani et al. in diabetic mice concluded that chronic administration of Mg reduces plasma glucose in the first 24 h and that Mg could improve the structure of the diabetic pancreas. The study reported that when diabetes was induced in rats, Mg levels decreased and the Ca/Mg ratio increased in rats [53]. A study conducted in 2020 reported that a high Ca/Mg ratio is associated with an increased risk of T2DM in the population [14]. In their 2014 study, Huang et al. emphasized that a Ca/Mg ratio between 2.0 and 2.5 and adequate Mg intake in elderly patients with diabetes are important for reducing the risk of cardiovascular disease [25]. The results of our study support the data in the literature. This study found that the Ca/Mg ratio was significantly higher in the poor glycemic control group than in the good glycemic control group. Furthermore, In the ROC analysis for Ca/Mg ratio, Ca, Mg, and K between the poor and

good glycemic control groups, we found the highest AUC value (0.672) for the Ca/Mg ratio.

Study limitations

The retrospective of this study is the main limitation. Our study's lack of a control group is also a major limitation. Our study obtained information about T2DM and other chronic diseases from the hospital's automation system. Patients receiving T2DM treatment by pill or subcutaneous injections were included, but there was no data on whether they were taking other medications. There is insufficient information on patients' diet, whether they use additional supplements such as Ca-Mg, their medication status, the insulin dose, and how many years ago they were diagnosed with T2DM.

Implications and conclusions

Type 2 DM is associated with low Mg. However, in addition to the decrease in Mg levels in T2DM, the increase in the Ca/Mg ratio is also interesting. The results of our study are compatible with the studies in the literature. However, no other study in the literature that shows the Ca/Mg ratio in T2DM patients. As a result, in our study, while the Ca/Mg ratio and Ca levels were significantly higher, Mg levels were significantly lower among poor glycemic control than among good glycemic control T2DM patients. Another robust study findings is reduced fasting glucose, HbA_{1c}, and Ca/Mg ratio in the high Mg levels groups. The Ca/mg ratio and Mg are important parameters for T2DM patients, but more comprehensive studies are needed before they can be used to monitor glycemic control.

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