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Correlation of Magnesium Serum Level with Glycosylated Hemoglobin in Patients with Type 2 Diabetes

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Abstract

Diabetes is a chronic, long-term metabolic complication commonly associated with high blood sugar, insulin resistance, and decreased insulin secretion, and is the third most common chronic disease in the world. According to the World Health Organization, diabetes is on the rise. Magnesium plays a vital role in carbohydrate metabolism, and changes in its status are often discussed as either the cause or outcome of diabetes. This study aimed to investigate the association between serum magnesium levels and glycosylated hemoglobin in patients with type 2 diabetes.
In this descriptive-analytical study, patients with type 2 diabetes referred to Valiasr Hospital Diabetes Clinic in Birjand in 2021 were examined. To assess fasting blood sugar (FBS), mean serum levels of magnesium, and HbA1c, 7.5 cc of blood were drawn from fasting diabetic patients at 8 A.M. The data were collected, entered into SPSS software version 22, and analyzed with a 95% confidence interval.
The mean age of the studied patients was 58.96 ± 10.48 years, with the majority being women (56.7%). The mean serum levels of FBS, HbA1C, and Mg^{2+} were 148.59 ± 45.43 mg/dl, 8.53 ± 1.35%, and 1.94± 0.22 mg/dl, respectively. The mean serum magnesium levels did not differ significantly regarding glycosylated hemoglobin and fasting blood sugar ($P > 0.05$). There was no significant relationship found between serum levels of glycosylated hemoglobin and magnesium.

Keywords: Diabetes, magnesium, glycosylated hemoglobin, blood sugar

Introduction

Diabetes is a chronic metabolic complication associated with high blood sugar, insulin resistance, and reduced insulin secretion, the third most prevalent non-infectious disease in the world after cardiovascular diseases and cancer (1, 2).

The prevalence of diabetes is increasing in developed and developing countries. According to the World Health Organization (WHO), the number of diabetics has increased from 108 million in 1980 to 422 million in 2014. The global prevalence of diabetes in adults (over 18 years) has increased from 4.7% in 1980 to 8.5% in 2014 (3, 4).

The prevalence of diabetes in Iran is also not favorable. The World Health Organization report shows that the prevalence of diabetes in 2016 was 10.3%. In that year, diabetes directly accounted for 8,580 deaths, while high blood sugar was associated with 28,170 deaths, representing 2% of all-cause mortality across all age groups. (5). According to the International Diabetes Federation, the prevalence of diabetes in the elderly population (20-70 years) in 2019 was 9.4% (5,387,200 people with diabetes in 53,188,400 adults), and it is predicted that the number of patients will reach 7,651,700 in 2030 and 9,889,300 in 2045. The number of people with glucose tolerance disorder was 4,323,100 in 2019 (6).

The cause of these chronic complications in diabetic patients has not been precisely determined. However, some studies have stated that the leading cause may be the random attachment of glucose to a group of crucial proteins (glycosylation) in the body. Sugar binding to protein is a non-enzymatic process that occurs in small amounts in healthy people (7-9).

Magnesium is required for hundreds of physiological processes, including glucose and insulin metabolism, but dietary magnesium intake has been inadequate in the general population in both the USA and worldwide (10). Mg2+ is involved in more than 300 enzymatic reactions and numerous physiological processes by acting as a cofactor for many enzymes, such as energy metabolism, glucose transport across the cell membrane, hepatic gluconeogenesis, pancreatic functions, insulin secretion, and action in pancreatic cells and target tissues through interaction with receptors of this hormone. On this basis, intracellular magnesium (Mg2+) balance is vital for adequate carbohydrate metabolism. There is evidence to suggest that dietary magnesium intake may have potential benefits in preventing metabolic syndrome and its components, as well as Type 2 diabetes (11).

In two double-blind, placebo-controlled randomized trials, oral magnesium supplementation at various doses reduced insulin resistance, a central feature of metabolic syndrome (12).

Magnesium deficiency has been claimed to be expected in diabetic patients, and there is an inverse relationship between magnesium intake and the incidence of type 2 diabetes. Hypomagnesemia (1.4-2.6) is associated with poor control of type 2 diabetes, and serum magnesium levels decrease exponentially during the disease (13-16).

Considering the importance of magnesium and the potential relevance between magnesium and type 2 diabetes, we decided to determine the magnesium serum levels and glycosylated hemoglobin in patients with type 2 diabetes.

Material and Methods

Patients

This study was conducted on 120 patients with type 2 diabetes mellitus, as defined by the diagnostic criteria of the American Diabetes Association (Table 1). They referred to the Diabetes Clinic of Birjand, Iran. Inclusion criteria include informed consent, not taking magnesium supplements before the study, taking the same diabetes medications in advance, and the patient's glycosylated hemoglobin A1C (HbA1C) percentage of 7% or above.

Table 1. Diagnostic criteria of diabetes mellitus according to the American Diabetes Association (17)

Patient with symptoms plus at least one of the following criteria
Random venous blood glucose concentration≥ 11.1 mmol/l
Fasting plasma glucose ≥ 7.0 mmol/l (whole blood ≥ 6.1 mmol/l)
Two-hour plasma glucose ≥ 11.1 mmol/l during an oral glucose tolerance test (OGTT)

Sample size and sampling method

The sample size was 120 patients, calculated with the following formula based on the study of Besharat et al. (18). Considering the mean and standard deviation of magnesium level 1.63 ± 0.96, with a confidence level of 95%.

N=Z (1-α/2)2S2/D2
Z (1-α/2) =1.96 S=0.96 D =0.17
N=3.84*0.92/0.028 N=120

Measurement

7.5 cc of venous blood samples were taken from the patients at 8 A.M. after 12 hours of fasting, based on the principles and standards of sampling by an experienced laboratory expert. Three cc of blood were drained into the CBC tube, and the other 4.5 cc into the clot vacuum tube, then the serum was separated by centrifugation at 3000 rpm for 10 minutes. The patient's demographic information was also gathered in a checklist based on the study's objectives, including age, sex, serum magnesium level, fasting blood sugar (FBS), and HbA1C.

Serum fasting blood glucose level was measured by the COBAS6000 device [hexokinase with enzymatic reference methods, (Roche Diagnostics GmbH, Mannheim, Germany)] serum magnesium level was measured with [Colorimetric endpoint methods with ksilidil blue (Roche Diagnostics GmbH, Mannheim, Germany)], HbA1c [HPLC-high performance liquid chromatography- Tosoh, G8 device (Tosoh bioscience, TOKYO, Japan)]

In this study, the basic information of patients, including age, duration of T2DM, height, weight, and body mass index (BMI), was recorded by the researcher through interviews and observation.

The patients' height and weight were measured using a shoeless weight-height digital scale made by Seca (Seca GmbH, Hamburg, Germany) with an accuracy of 100 grams.

Statistical Methods

Statistical analysis was done using SPSS software version 2022 (SPSS Inc., Chicago, IL, USA). Descriptive statistics used for numeric variables, including mean ± standard deviation, median (minimum-maximum), and the categorical structure of data, were expressed as numbers and percentages. The Chi-square test examined structural variables.

Quantitative variables with normal distribution were examined using the Kolmogorov-Smirnov test, whereas the Mann-Whitney test was performed for variables with abnormal distribution (BMI, fasting blood sugar, HbA1C, and Mg^{2+}). Results were evaluated in a 95% confidence interval, and a p-value of <0.05 was considered significant. Spearman's correlation analysis also investigated the relationship between not-normally distributed variables.

Consent and ethical approval

Written informed consent was taken from the patients, and the participants' information was kept private during the procedure. This study was designed and conducted after receiving approval from the Research Council and the Ethics Committee of Birjand University of Medical Sciences, under approval number Ir.bums.REC.1399.028.

Results

This study was conducted on 120 patients with diabetes referred to our outpatient diabetes clinic.

Among these patients, 52 (43.3%) were men, and 68 (56.7%) were women. The mean age was 58.96 ± 10.48 years, and the mean duration of diabetes was 7.42 ± 5.06 years. Mean BMI was 26.72 ± 2.99 kg/m^2

The mean HbA1c was 8.53 ± 1.35 % (range 7.0-14.41). The mean serum Mg^{2+} level was 1.94 ± 0.22 mg/dl (range 1.5-2.6). The mean FBS level was 148.59 ± 45.43 mg/dl (range 59-328)

Based on our findings, the age distribution and BMI level of patients studied in this study are expressed in the following table. Accordingly, the age group of 50-60 and 60-70 years was the most common, and patients with a BMI of 25 to 30 (overweight) had the highest distribution. Moreover, the diabetes duration of most of the patients was less than ten years (Table 2).

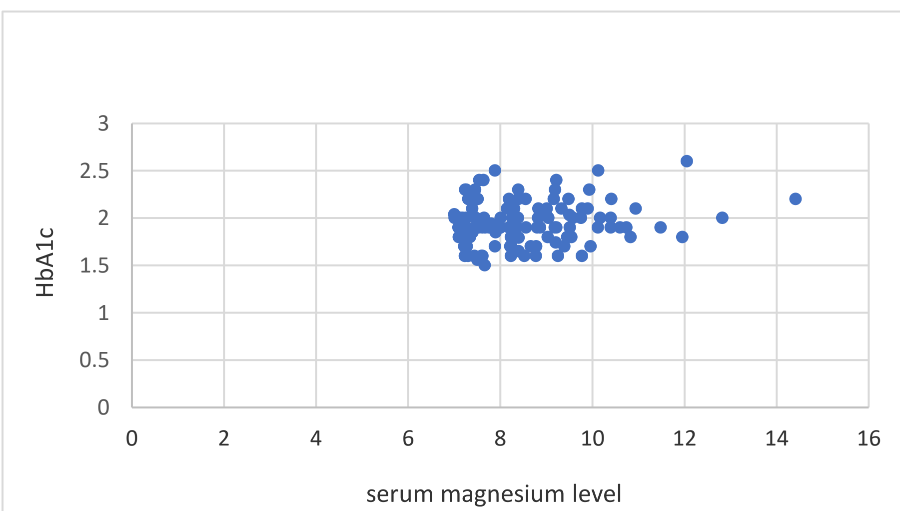
Table 2. Distribution of age group and BMI in diabetic patients

Parameters	Groups	Distribution (Number/percentage)
Age group (year)	≤50	24 (20.0%)
	50-60	38 (31.7%)
	60-70	38 (31.7%)
	≥70	20 (16.7%)
BMI (Kg/m^2)	underweight	0 (0%)
	normal	40 (33.3%)
	overweight	60 (50.0%)
	obese	20 (16.7%)
Diabetes duration	≤10 years old	86 (71.7%)
	≥10 years old	34 (28.3%)

Based on the results of our study, the serum levels of FBS, HbA1c, and Mg2+ were not significantly different between men and women (P> 0.05). Also, the mean of the mentioned factors in patients was not significantly associated with the duration of diabetes (P> 0.05) (Table 2).

There was no significant relationship between the mean serum level of FBS with Mg and HbA1C with Mg2+ (P> 0.05) (Chart 1).

Chart 1. Correlation between serum magnesium levels and glycosylated hemoglobin in patients participating in the study



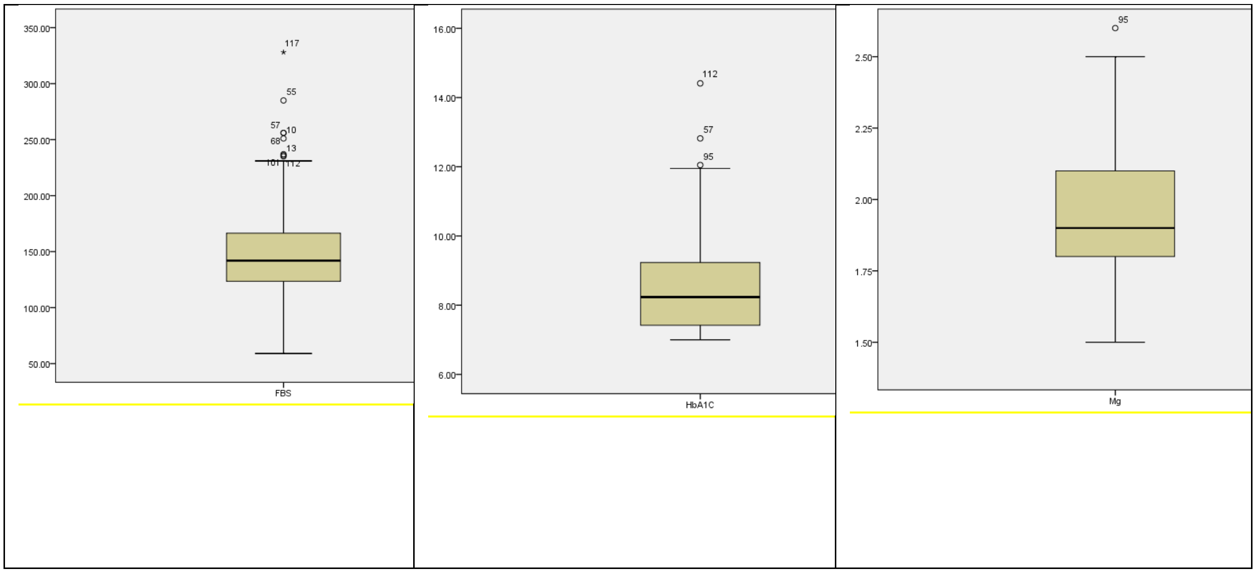


Fig 2. FBS, HbA1C, and magnesium graphs

Discussion

Today, due to the increasing burden of non-communicable diseases, especially diabetes, in developing countries, prevention and proper control to prevent its complications are of great importance (19). On the other hand, due to the essential and undeniable role of magnesium in this disease, our aim in this study was to correlate serum magnesium levels with glycosylated hemoglobin in patients with type 2 diabetes

In our study, the majority of patients were women. Because women care more about their health and have more available time. Therefore, they refer to medical centers for diagnosis, treatment, and disease control more frequently than men; hence, most of the patients studied in this study are women.

In the present study, most of the patients were overweight, which was consistent with the study of Besharat et al. (18).

In our study, the patients' mean serum levels of magnesium and HbA1c were 1.94 mg/dl and 8.53%, respectively. In the present study, the mean serum magnesium level was lower than the normal range of healthy individuals. In the study by Shahdadi et al., it was stated that the mean serum levels of magnesium and HbA1C were 1.89 ± 0.22 mg/dl and 8.51± 1.35%, respectively, which was in line with our study (20).

In the study conducted by Besharat, there was no significant difference between the duration of the disease and serum magnesium levels in the patients (P> 0.05) (18), which was consistent with our study.

Regarding the study of Garber et al., there was no significant relationship between the serum level of magnesium and HbA1C in diabetic patients (21). Conversely, a meta-analysis by Ebrahimi et al. demonstrated that magnesium deficiency plays a significant role in the progression of prediabetes (14).

In another study conducted by Butrabi et al. (22) in Yazd (2013) and Saeed et al. (13), it was stated that there is no significant correlation between the serum magnesium level and fasting blood sugar or glycosylated hemoglobin in patients, which is similar to the study conducted by Wälti et al. (23).

A study conducted by Pokharel and colleagues in Nepal in 2017 stated that there is an inverse relationship between glycosylated hemoglobin and magnesium. Among the causes of this inconsistency with our study, we can mention the difference in diet and lifestyle of the two countries and the decrease in renal function of the studied patients. (24).

In the study carried out by Shahdad et al., the mean magnesium level in patients with type 2 diabetes was 1.76 ± 0.43 mg/dL, and the mean HbA1c level in these patients was 8.51 ± 1.60%. A statistically significant correlation was found between magnesium levels and glycated hemoglobin (HbA1c) ($p = 0.01$) (22), which was not consistent with our study.

According to the results of this study and other literature, further studies should be conducted to investigate the role and relationship between serum magnesium levels, urine levels of this parameter, blood sugar, and glycosylated hemoglobin in diabetic patients. Moreover, considering that our study was descriptive-analytical, it is suggested that subsequent studies be conducted as case-control or cohort studies. One limitation of this study is that all patients included were individuals who sought care at the hospital, and therefore, the findings may not be generalizable to the entire population. Additionally, the HbA1c levels of the patients were predominantly above 7, which may limit the applicability of the results to patients with better glycemic control.

Conclusion

Based on the results of the present study, no significant relationship was found between serum magnesium levels, glycosylated hemoglobin, and fasting blood sugar in the patients. Further studies are needed.

Conflict of Interests

The authors declare no conflict of interest.

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