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Original Research Article

CORRELATION OF SERUM MAGNESIUM LEVEL WITH HbA1C IN TYPE 2 DIABETES MELLITUS: RURAL TERTIARY CARE STUDY

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Abstract

Introduction: The term, 'diabetes mellitus' describes a metabolic disorder of multiple aetiology, which is characterised by chronic hyperglycaemia, with disturbances of carbohydrate, fat and protein metabolism, which result from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long term damage, dysfunction and failure of various organs. A relationship was observed between diabetes mellitus and trace elements in many research studies. In many cases, an alteration in the metabolism of these minerals was demonstrated.[1–3] Hypomagnesemia has been associated with insulin resistance and related microvascular consequences due to its ability to trigger hyperglycemia. The latest therapeutic approaches may not be feasible to all. As a result, priority is given to preventive and primary care research.

Aim and objective: To study magnesium levels in patients with type 2 diabetes mellitus and its association with glycated haemoglobin (HbA1c) levels in patients with Type 2 Diabetes mellitus. This will help us to evaluate how glycaemic control in Diabetes can influence serum Magnesium levels.

Materials and Methods: It was a hospital-based cross-sectional study conducted in the Department of Medicine and Biochemistry at Dr. Rajendra Prasad Government Medical College and Hospital, Kangra (at Tanda). Ninety patients of either sex with type 2 diabetes mellitus fulfilling the inclusion and exclusion criteria were included. Study Period was one year (2020-2021) after approval from Institutional Ethics Committee (IEC). Recruitment of patients was done in Department of Medicine in diabetes mellitus OPD. For defining a case of T2DM, American Diabetes Association diagnostic criteria were used. Magnesium was measured by the xylidyl blue method. The other blood sample was transferred into an EDTA test tube which was used to estimate HbA1c level. Result: Participants were divided into groups based on their age. i.e., 41-50, 51-60, 61-70 and >71. In this study, the mean HbA1c level was 8.30±2.23%. HbA1c level was 6.5-8.5% in 42.2% patients, 32% of the patients' HbA1c level was ≥8.5% and 21.1% of patients HbA1C level was ≤6.5. In this study, the mean magnesium level was 1.80±0.24 mg/dl. 64.5% of the patients' magnesium level was ≥1.7 mg/dl while remaining 35.5% of the patients' magnesium level was ≤1.7 mg/dl. According to Pearson's correlation coefficient, inverse correlation was found between HbA1c levels and Serum magnesium levels.

Conclusion: Magnesium insufficiency has been linked to a higher incidence of diabetic due to poor glycaemic management in people with diabetes. Dietary supplements may be recommended to avoid such problems and maintain glycaemic control. Large-scale clinical research required.

Keywords: Diabetes mellitus, hyperglycemia, Hypomagnesaemia, and HbA1c.

Introduction

The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 366 million cases in 2011 and by 2030 this will have risen to 552 million. According to the International Diabetes Federation (IDF), there were an estimated 65.1 million cases of diabetes in India in 2013, which was more than double of the 2000 statistics. By 2030, DM is likely to afflict up to 79.4 million individuals in India.[4,5] Internationally, huge morbidity and socioeconomic impact has been observed due to the advancing burden of Type 2 Diabetes mellitus (T2DM).[6] Magnesium (Mg) being the fourth most abundant Cation and an established central electrolyte in the human body is instrumental in many fundamental biological processes.[6] It also has a crucial role to play in the phosphorylation reactions of glucose and its metabolism by activating various enzyme systems and helping insulin

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in its action.[6,7] It is claimed that there is an inverse relationship between Mg intake and glycaemic control.[8] Hypomagnesemia is associated with poor control of T2DM, and its deficiency occurs exponentially along the course of the disease.[9] Determination of HbA1c helps in monitoring the response to treatment in diabetic patients since it's free of day to day glucose variation and unaffected by recent physical activity and food intake.[10] The detection and correction of altered Mg status in diabetic patients is clinically appropriate, although many physicians tend to ignore Mg status. The increased risks to develop glucose intolerance and type 2 diabetes mellitus in subjects with dietary and/or serum Mg deficits have suggested potential benefits of Mg supplementation in persons who have type 2 diabetes or risk factors for diabetes. The use of Mg supplements has also been proposed as a potential tool for the prevention and the metabolic control of type 2 diabetes.[11,12] This study is a genuine endeavour to estimate the incidence of hypomagnesaemia in patients with Type 2 Diabetes Mellitus which will help us in better management of DM in future.

Objective The study is aimed at estimating serum magnesium concentration and glycated haemoglobin (HbA1c) levels in patients with T2DM. This will help us evaluate how glycaemic control in Diabetes can influence serum Magnesium levels.

Methodology: Study was a hospital-based and cross section, conducted in the Department of Medicine and Biochemistry at Dr. Rajendra Prasad Government Medical College and Hospital, Kangra (at Tanda) in 2020 to 2021.
Materials - Ninety patients of either sex with type 2 diabetes mellitus fulfilling the inclusion and exclusion criteria were included.

I**nclusion criteria** - T2DM patients of either sex with age more than 18 years were included.

Exclusion criteria - Critically ill patients, Patients with T2DM, with age less than 18 years of age, patients on drugs known to affect magnesium levels and patients taking supplements containing magnesium were excluded.

Method – Detailed history was taken from all patients regarding presenting complaints, symptoms of T2DM, its duration and complications, and current medications. Personal history was taken regarding alcohol, smoking, exercise, or any other addiction. Patients were thoroughly examined to look for signs of thyroid insufficiency. On clinical examination i.e. Measurement of blood pressure, Weight in kilogram by standard weighing machine, Height in centimeter with the help of stadiometer and BMI was calculated by standard equation. The equation used was as BMI=Weight (Kg)/[Height (Meter)]^2

Haematological and Biochemical investigations included: Hemoglobin, total leucocyte count, differential leucocyte count, platelet count, ESR, Fasting blood glucose (FBG). FBG was estimated by GOD/POD (glucose oxidase-peroxidase method). Serum urea, creatinine, Lipid profile: fasting serum total cholesterol, low density lipoprotein Cholesterol (LDL), high cholesterol (HDL), Triglycerides (TGL), Urine R/E and M/E and ECG in all leads. **Specific investigations**: Glycated haemoglobin (HbA1C - HPLC) and Serum magnesium was measured by the xylidyl blue method. Biological reference interval in serum was taken as 1.7–2.7 mg/dL.

STATISTICAL ANALYSIS: Data were entered into Microsoft® Excel 2007 and exported into SPSS v21.0 (IBM, USA) for statistical analysis. Categorical variables were expressed as frequency, percentages, and compared using Chi square test between the groups. Continuous variables were expressed as mean, standard deviation (SD), and compared using Student t-test between two groups or one-way analysis of variances (ANOVA) followed by Bonferroni's post hoc correction between more than two groups. P value <0.05 was considered statistically significant.

Results A cross sectional study consisting of 90 patients was undertaken to investigate the correlation of serum magnesium levels in T2DM. Description of the participants according to the gender and age group is depicted in Table 1. Participants were divided into groups based on their age. i.e., <40,41-50, 51-60, 61-70 and >70. The mean age was 58.93 ± 11.43. In this study male female ratio was 1:1, shown in Figure 1. In this study, there was no significant difference between magnesium level according to age and gender (P=0.053), (0.66) respectively. There was no significant difference between mean HbA1c of male and female patients (P=0.606). The normal range for serum magnesium level is 1.7 to 2.2 mg/dL. In this study, patients with FBS <130 mg/dl had a significantly higher levels of serum magnesium i.e 1.96 0 ± 0.24 compared with FBS ≥130 mg/dl 1.68 ± 0.17 and (P=<0.001). In this study, patients with RBS <180 mg/dl had a significantly higher levels of serum magnesium 1.93+ 0.22 compared with RBS ≥180 mg/dl magnesium is 1.66 ± 0.17 with (P=<0.001) shown in table 2 and 3 respectively. Prevalence of hypomagnesemia was observed among 32 (35.5%) study patients shown in table 4.

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Out of 32 (78%) type 2 diabetes mellitus patients had HbA1c >6.5%. Patients with HbA1c <6.5% had a significantly higher levels of serum magnesium compared with HbA1c 6.5-8.5 and >8.5% i.e., 2.060±0.25 and 1.60±0.13 respectively with (P=<0.001) shown in table 5 and Figure 2. The mean HbA1c levels was 8.30 ± 2.23%. Normal ranges for HbA1c in people without diabetes is about 4% to 5.9%. People with diabetes with poor glucose control have HbA1c levels above 7%.

Table 1: Age wise distribution of patients

Age group (years)	Frequency	Percentage
≤40	3	3.3
41-50	23	25.6
51-60	24	26.7
61-70	26	28.9
≥71	14	15.6
Mean age (Years)	58.93±11.43	

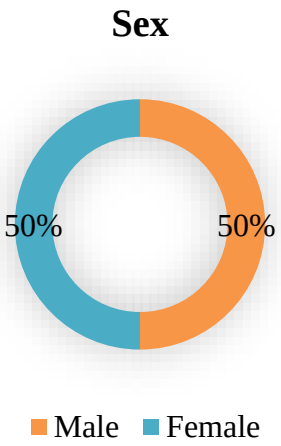

Figure 1: Gender wise distribution of patients

Table 2: Comparison of magnesium levels based on FBS

FBS	<130	≥130	P-value
Magnesium	1.96±0.24	1.68±0.17	<0.001

Figure 22).

Table 3: Comparison of magnesium levels based on RBS

RBS	≤180	≥180	P-value
Magnesium	1.93±0.22	1.66±0.17	<0.001

Table 4: Magnesium level

Magnesium	Frequency	Percentage
<1.7	32	35.5
≥1.7	58	64.5
Mean magnesium (mg/dl)	1.80±0.24	

Table 5: Comparison of magnesium levels based on HbA1c

HbA1C	<6.5	6.5-8.5	>8.5	P-value
Magnesium	2.06±0.25	1.85±0.15	1.60±0.13	<0.001

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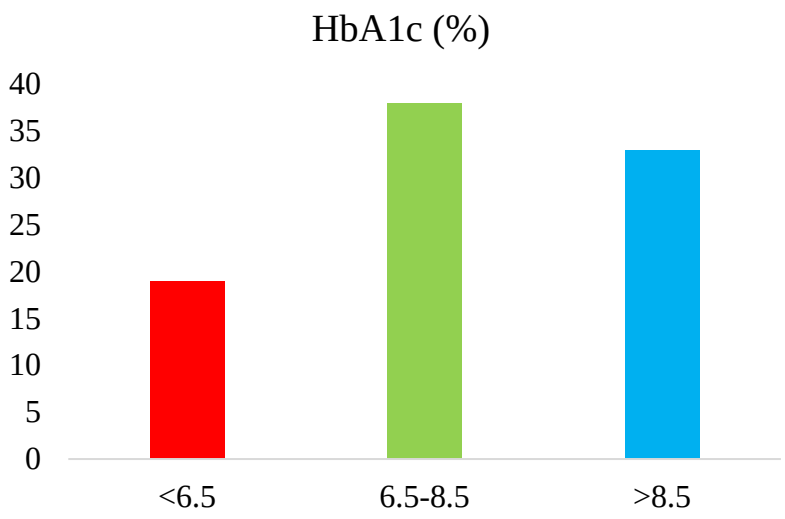

Figure 6: HbA1c

Discussion:

T2DM is a chronic condition caused by a complicated genetic environmental interplay, as well as additional risk factors like obesity and an inactive lifestyle.[13] Despite the use of latest diabetes management techniques, morbidity and mortality ratios remain high. Diet is commonly implicated in the development of type 2 diabetes and the comorbidities that come with it. Patients with Type 2 diabetes have been reported to have low magnesium levels repeatedly. Magnesium insufficiency appears to have a deleterious influence on glucose homeostasis and insulin resistance.[14] The present study was conducted on 90 patients to understand how hyperglycemia management affects blood magnesium levels in diabetic patients. The findings of this study provide a clear insight into the correlation of serum magnesium levels in Type 2 Diabetes mellitus. Hypomagnesaemia associated with raised HbA1c levels were present in 78% of the participants in the current study. The mean time since diagnosis was 6.69 ±5.21 years in our patients and there was no significant difference between magnesium level according to time since diagnosis (P=0.847) Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with T2DM. Magnesium is an essential mineral found in many foods, including whole grains, green leafy vegetables, coffee, legumes and nuts. Meanwhile, magnesium is an essential cofactor for multiple enzymes involved in glucose metabolism and is hypothesized to play a role in glucose homeostasis, insulin action and in the development of T2DM. Epidemiological studies have investigated the association of serum magnesium with prediabetes and T2DM, but the findings were inconsistent. On the other hand, recent studies indicated that increasing dietary magnesium intake may be associated with a reduced risk of T2DM and have a dose-response relationship. The present study was aimed to evaluate magnesium levels in patients with type 2 DM, and to evaluate its relation with glycemic index and complications of T2DM. In the present study, hypomagnesemia was observed in 35.5% of the patients. Mean serum magnesium levels were 1.80±0.24 mg/dl. Kumar et al evaluated association of serum magnesium with T2DM and diabetic retinopathy.[15] Out of 250 patients, 110 patients (44%) were found to have hypomagnesemia. Among various other studies, hypomagnesemia has been reported to occur in 13.5%–47.7% of non-hospitalized patients with type 2 diabetes.[9,16] The wide range in the reported prevalence of hypomagnesemia most likely reflects the difference in the definition of hypomagnesemia, techniques in Mg measurements, and the heterogeneity of the selected patient cohort. In the study by Naik et al, 37% of diabetic patients had low serum magnesium levels and 9% of non-diabetic controls had low serum magnesium levels. The mean serum magnesium level was 1.96 mg/dL and 2.375 mg/dL in diabetics and controls respectively. Nadler et al. in their study showed that an intracellular RBC Mg^{2+}concentration of diabetic patients was significantly reduced compared with values in non-diabetic control subjects.[17] Resnick and associates suggest that extracellular and intracellular magnesium deficiency is typical in chronic, stable, mild type 2 diabetes mellitus and may be a strong predisposing factor for the development of the excess cardiovascular morbidity associated with diabetes.[18] In our study, age of T2DM patients was not significantly associated with serum magnesium levels. In the study by Kumar et al, in group with hypomagnesemia, the mean age of patients were 55.8 ± 10.05 years and in group of T2DM patients with normal serum magnesium level were 56.81 ± 11.45 years. There was no significant difference observed between these two groups. It was also similar to the study conducted by Al-Osali et al. in Muscat, Oman, which concluded that diabetics have significantly lower total Mg levels with a difference of 0.12 mmol/L (P< 0.001) irrespective of age.[19]Arpaci et al also reported that age was not significantly associated with serum magnesium levels.[20] In our

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study, there was no significant difference between magnesium level according to sex (P=0.699). Khanna et al reported that among cases 56% males and 29% females were hypomagnesemic, males were more likely to have hypomagnesemia, with significant p value 0.002.[21] In our study, there was no significant difference between magnesium level according to time since diagnosis (P=0.847). Our findings are in concordance with Arpaci et al who reported no significant association between duration of T2DM and serum magnesium. On statistical analysis, it was found that there was no significant correlation between duration of diabetes and serum magnesium levels (p= 0.803).[22]

In our study, patients with HbA1c <6.5% had a significantly higher levels of serum magnesium compared with HbA1c 6.5-8.5 and >8.5% (P=<0.001). In the study by Arpaci et al, there was a weak negative correlation between serum Mg and HbA1c levels (r =-0.110, p =0.004).20 Kumar et al reported that HbA1C (P = 0.01) was poorly controlled in hypomagnesemia group. Le cube et al reported a negative correlation between HbA1c and serum magnesium levels.[23]

In this study, patients with FBS <130 mg/dl had a significantly higher levels of serum magnesium compared with FBS ≥130 mg/dl (P=<0.001). Le cube et al reported that T2DM patients showed lower serum magnesium levels [0.75±0.07 vs. 0.81±0.06 mmol/L; p<0.001] than non-diabetic patients. Forty-eight percent of diabetic subjects, but only 15% of non-diabetic subjects showed a serum magnesium concentration lower than 0.75 mmol/L. Significant negative correlations between magnesium and fasting plasma glucose was observed.[23] A study by Dasgupta et al on diabetes and hypomagnesemia found significant negative correlations between magnesium and fasting plasma glucose.[24] In another study by Rao and Shariff, the mean value of FBS, PPBS, and HbA1C was higher among the group with serum Mg <1.7 mg/dL.[25]

Although a large number of potential cohort research and meta-analyses have indicated that magnesium consumption lowers the incidence of diabetes, the findings are still mixed, and additional research is needed to confirm this. Patients must be closely monitored using a multi-dimensional technique that includes full investigation and plan of care. Despite its obvious connection with glycemic values, serum magnesium levels are not routinely tested in clinical settings as part of diabetes care. To avoid and eliminate consequences of T2DM, dietary recommendations for increased intake of key magnesium-rich food should be made at the time of diagnosis. According to the findings of our investigation, serum magnesium should be integrated as a routine electrolyte test for improved Type 2 diabetes mellitus treatment and to avoid diabetic related complications. Despite the fact that type 2 diabetes is a multifactorial disease, our findings suggest that improved magnesium consumption, together with changes in other type 2 diabetes risk variables, could be new way to avoid the condition. Being a cross sectional study, no follow-ups were conducted. Furthermore, in the present study magnesium test was limited to serum, a fairly minor category for magnesium that may not yield precise amounts. The limitations of this study were its small sample size. To establish the link between magnesium deficiency and type 2 diabetes, large-scale clinical research is required.

Conclusion:

In the current study, we aimed to understand the relation between serum magnesium levels and HbA1c in T2DM. The main implication for our research is that hypomagnesemia has been linked to a lack of glycemic regulation which can lead to diabetic complications. Early detection with oral magnesium supplementation as a therapeutic approach can avoid this.

Conflict of interest: Nil

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