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Original Article

Correlation Between Magnesium and HbA1C in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Magnesium (Mg) is most abundant electrolyte with unlimited physiologic importance in the body, playing a vital role in many fundamental processes. Cellular magnesium is an essential cofactor for various enzymes involved in glucose transport, insulin release and glucose oxidation. Mg has potential role in improving insulin sensitivity and preventing diabetes and its complications. Hypomagnesemia promotes to the initiation and progression of Diabetes Mellitus (DM) and its macrovascular and microvascular complications. The aim of this study was to evaluate the correlation of magnesium with HbA_1C in T2DM.

Material and Methods: This cross sectional study conducted at Tribhuvan University Teaching Hospital, included 85 diagnosed with type 2 diabetes mellitus visiting Medicine OPD and 85 apparently healthy controls. Clinical and anthropometric characteristics were documented using clinical proforma. The fasting blood samples were collected for estimating serum glucose, HbA_1C and magnesium.

Results: The mean values of BMI, FBG, HbA_1C were found to be significantly elevated in T2DM, but that of Mg were higher in healthy controls ($p<0.05$). The prevalence of hypomagnesemia in T2DM was found to be 32.94%. The Serum magnesium levels were moderate negatively correlated ($r = -0.544$, $P<0.001$) with HbA_1C.

Conclusions: Patient with Type 2 Diabetes Mellitus showed significantly low magnesium levels compared to heathy controls as well as uncontrolled HbA_1C levels also showed significantly low magnesium level than controlled HbA_1C level. There was significant inverse correlation between serum Mg level and HbA_1C level in patients with T2DM. So if serum magnesium values are made to rise, HbA_1C values will fall.

Key words: HbA_1C; Magnesium; Type 2 Diabetes Mellitus

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INTRODUCTION

Magnesium is fourth most abundant cation in the human body and second most abundant intracellular cation that serves as a co-factor for all enzymatic reactions which requires ATP. Besides that, it is an essential enzyme activator for cell permeability and neuromuscular excitability, mitochondrial function, a perilous element in cellular proliferation and apoptosis, and an important factor in both humoral and cellular immune reactions.[1] Cellular magnesium is an essential cofactor for various enzymes involved in glucose transport, insulin release, glucose oxidation, and is and adenylate cyclase enzymes.[2] It plays vital role as second messenger for insulin action; on the other hand, insulin itself is an important regulatory factor of intracellular magnesium accumulation.[3]

Type 2 Diabetes Mellitus (T2DM), the foremost prevalent category, is caused by a combination of resistance to insulin action and inadequate compensatory insulin secretory response. The prevalence of DM in Nepal in 2016 was 9.1% in total where males were 10.5% and females were 7.9%.[4] There 451 million (age 18–99 years) people affected by diabetes worldwide and expected to extend to 693 million by 2045.[5]

Glycosylation of hemoglobin (Hb) occur under physiological conditions where a reaction between glucose and N-terminal valine of Beta chain of Hb molecules to form Glycosylated Haemoglobin (HbA1 c) and their levels relate well with glycemic levels over the previous six to ten weeks..[6] The American Diabetes Association (ADA), International Diabetes Association (IDF) and also the European Association for the Study of Diabetes (EASD) recommend the use of HbA_1Cassay in the diagnosis of T1DM and T2DM.[7] HbA_1C shows a promising tactic to monitor diabetic patient and also provides information regarding the pathogenesis of secondary consequence of Diabetes Mellitus (DM).[8]

The worldwide prevalence of hypomagnesemia among type 2 DM is ranged between 14 and 48%.[9] Mg has prospective role in improving insulin sensitivity and preventing diabetes and its complications. Hypomagnesaemia may be a cause or a consequence of diabetic complications.[2] There is limited study on magnesium in Diabetes Mellitus. The correlation of magnesium level with HbA1c might be helpful in understanding their relationship in diabetic patients.

MATERIAL AND METHODS

This cross sectional study conducted in Department of Biochemistry, Tribhuvan University Teaching Hospital, Kathmandu, included 85 diagnosed with ttype 2 diabetes mellitus visiting Medicine OPD and 85 apparently healthy controls from November 2021 to April 2022 after obtaining Institutional Review Committee (IRC) approval. Whereas, patients taking magnesium supplementation and loop diuretic, history of alcohol abuse, critically ill patients (renal and hepatic disease, malignancy), Gestational Diabetes Mellitus, patients refusing to give informed consent were excluded for the study.

Those Non diabetes mellitus individual who has no general complain of health, not on any medication and who had given written consent were enrolled as controls.

Anthropometry measurements: Standardized stadiometer and scale were employed for measuring the height and weight respectively. The circumference midpoint between the lowest rib and the iliac crest was detailed as WC. Measurements were carried out with a standardized tape measure, and were rounded off to the nearest centimeter (cm).

Laboratory analysis: Fasting blood was sampled, after an overnight fast (8 -12 hours) and serum samples were separated for analysis. Measurement of Fasting Glucose and Serum Magnesium were done by using fully automatic biochemistry analyzers (BT 1500 chemistry analyzer). EDTA samples were analyzed for HBA_1C by using Hb-vario HPLC analyzer. All laboratory analysis was performed maintaining the laboratory standard operating procedures.

Statistical analyses were done by SPSS 20.0version (Statistical Package for Social Science for windows version). Results are presented as means (±standard deviation (SD)). The significance of differences between means was assessed using Student's t test for data sets. Relationships between quantitative variables were analyzed using Pearson's correlation coefficient. Results were considered as statistically significant or non-significant (NS) for $p < 0.05$ or $p > 0.05$, respectively.

RESULTS

Demographic distribution of study population

In this study 85 T2DM patient with mean age of 53.86 ± 10.68 years as cases and 85 apparently healthy participants with mean age of 54.19 ± 11.57 years as control were recruited. Among 85 T2DM patients, 59 were uncontrolled and 26 were controlled diabetics. The distribution of Mg level in both cases and controls was shown in figure 1.

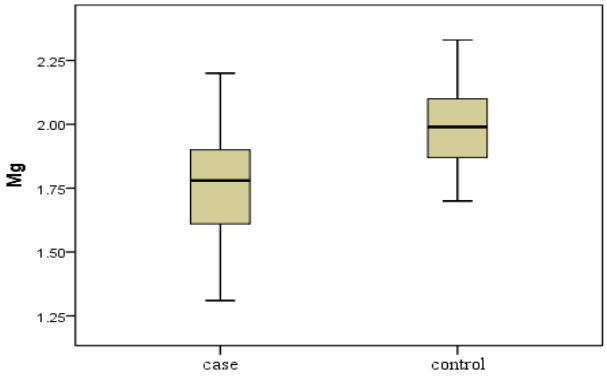

Figure 1: Box plot showing the distribution of magnesium among the studied groups.

Anthropometric and Biochemical characteristic of T2DM and controls

While comparing the anthropometric and biochemical data between cases and controls, the mean values of BMI, FBG,

HbA_1C were found to be significantly elevated in T2DM, but that of Mg were higher in healthy controls. The mean values of various Variables (with S.D), cases and controls, along with their corresponding p value shown in table 1. Patients were divided into two groups according to HbA_1C levels; controlled with $HbA_1C \leq 7\%$ and uncontrolled with $HbA_1C > 7\%$. The comparison between uncontrolled and controlled diabetic shown in table 2.

Table 1: Biochemical characteristic of cases and controls.

Variables	Cases (Mean ± S.D) N=85	Controls (Mean ± S.D) N=85	p value
Age(yrs)	53.86 ± 10.67	54.19 ± 11.57	0.812
BMI (kg/m2)	24.92 ± 2.67	23.65 ± 1.77	<0.001
FBG (mg/dL)	151.21 ± 53.92	93.68 ± 11.88	<0.001
HbA1C (%)	8.40 ± 2.0	5.50 ± 0.64	<0.001
Mg (mg/dL)	1.75 ± 0.20	2.0 ± 0.15	0.012

Table 2: Comparison between uncontrolled and controlled diabetic

Variables	Uncontrolled DM (Mean ± S.D) n=59	Controlled DM (Mean ± S.D) n=26	p value
Age(yrs)	53.41 ± 10.12	54.88± 12.00	0.204
BMI (kg/m2)	25.27± 2.46	24.11 ± 3.01	0.342
FBG (mg/dL)	164.88 ± 58.41	120.19 ± 20.26	0.003
HbA1C (%)	9.24 ± 1.84	6.49 ± 0.52	<0.001
Mg (mg/dL)	1.70 ± 0.20	1.86 ± 0.14	0.026

Amnog 85 T2DM patients, 28 (32.94%) patients were found to have hypomagnesemia, however 57 (67.06%) patients were found to have normal magnesium level. Serum magnesium levels were moderate negatively (r = -0.544, P<0.001) correlated with HbA_1C (fig. 2)

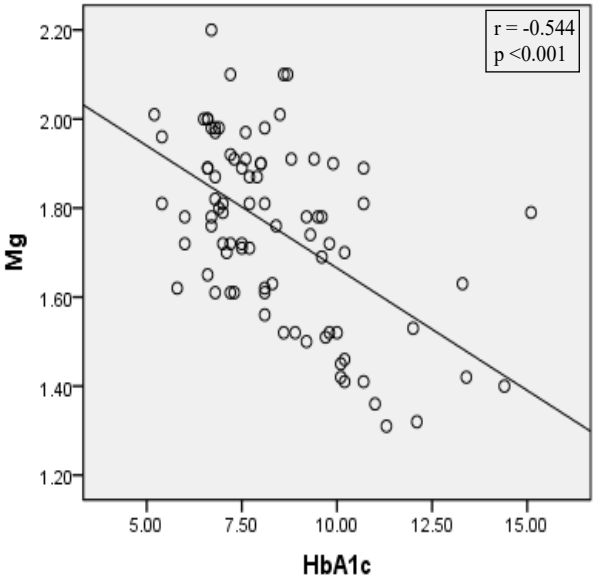

Figure 2: Correlation of serum magnesium level with HbA_1C in type 2 diabetes patients

DISCUSSION

In this study the serum magnesium levels in type 2 diabetic patients were significantly lower than in apparently healthy subjects (P <0.05). These results were in agreement with previous studies which reported low serum magnesium levels in type 2 diabetes.[10-12]. The worldwide prevalence of hypomagnesemia among type 2 DM is ranged between 14 and 48%.[9]Similar to that 32.94% diabetes mellitus patients were presented with hypomagnesemia in this study. In contrast to present study results Naila M et al[13] reported insignificant difference in serum magnesium level in type 2 diabetic patients when compared to healthy controls. Among diabetic patient, uncontrolled individual had significantly lower magnesium in compared to control diabetic individuals with similar to others study.[14, 15]

Magnesium is one in all the foremost common micronutrients deficient in diabetes[9] The exact mechanism for hypomagnesemia in type 2 DM is not clear but possible explanation includes poor dietary intake, poor gastrointestinal absorption, altered insulin metabolism and enhanced renal Mg excretion.[1] Reduced intracellular Mg concentrations lead to a defective tyrosine kinase activity and deterioration of insulin resistance in diabetic patients.[16] Nadler et al have informed that even in nondiabetic individuals insulin sensitivity decreases after induction of magnesium deficiency.[17]

Hypomagnesemia has been shown in patients with diabetic retinopathy, with lower magnesium levels predicting a greater risk of severe diabetic retinopathy.[18, 19] Hypomagnesemia may be a contributing factor for the long term complications, particularly peripheral neuropathy[20] and ischemic heart disease [17].

In this study, on the correlation analysis, magnesium showed the negative correlation with HbA_1C in T2DM.The findings were consistent with S.Ramadas et al[21], Sharma A et al[22], Siddiqui MU et al[23] de Lordes et al[20] and Reddy S B [15]. Similarly, Palathingal J et al showed a directly proportional increase of the HbA1C values in an order of non-diabetic, newly diagnosed diabetic, and established diabetic subjects while the magnesium levels showed inversely proportional to the HbA1c values.[24] Our results were in contrast to that reported by Saeed H et al who founded that nonsignificant correlation between serum Mg level and HbA_1Cin type 2 diabetes mellitus.[25]

Limitation

- The study would not show the relation of magnesium with different complication of diabetes mellitus and duration of disease.
- The study would not demonstrate the serum magnesium levels in patients on insulin treatment and on oral hypoglycemic agents and their comparison.

CONCLUSIONS

Patient with Type 2 Diabetes Mellitus showed significantly low magnesium levels compared to heathy controls as well as uncontrolled HbA1C levels also showed significantly low magnesium level than controlled HbA1C level. There was

significant inverse correlation between serum Mg level and HbA1c level in patients with T2DM. So if serum magnesium values are made to rise, HbA1c values may fall.

Recommendation: This study recommend to measure serum Mg routinely in Type 2 Diabetes Mellitus and patients who need supplementation should be considered. Hypomagnesemia in diabetics can also predict the inadequate glycemic control. Thus, from the observations from the current study, it is marked that serum magnesium plays a role in glycemic control. Further examination on the low magnesium diabetic with supplementation responsive is important to do adjustments of clinical management of diabetes.

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