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Original Research Article

A Correlational Study of Serum Magnesium Level with Microalbuminuria in Type 2 Diabetes Mellitus Patients

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Abstract

Objectives: This study was to evaluate the correlation between serum magnesium level with microalbuminuria in type 2 diabetes mellitus patients. **Methods:** Under aseptic conditions, 5 mL blood was collected from ante-cubital vein for Serum Magnesium and random sample of urine was collected in sterile container for urine microalbumin. Magnesium was assayed by using photometric methods. Urine MA analysis was done by using Nephlometric method for the detection of albumin in urine. **Results:** when we compared the mean ± S.D. of U. microalbumin between cases and control, then p value was found to be less than 0.001. which is extremely statistically significant differences. But, when we performed correlation between mean ± S.D. of S. magnesium and urine microalbumin, r value was found to be -0.35 and p value was found to be greater than 0.05. which is not statistically significant. **Conclusions:** This study concluded that type 2 diabetes mellitus patients had significantly lowered serum magnesium levels. Serum magnesium and urine microalbumin was negatively correlated with each other in type 2 diabetes mellitus patients. And it was not statistically significant.

Key words: Type 2 diabetes mellitus, Serum magnesium level, Microalbuminuria

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending upon the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems, leading to microvascular and macrovascular complications [1].

Magnesium (Mg) is the fourth most abundant cation in the human body and plays a key role in many fundamental biological processes including metabolism and DNA synthesis. Mg deficiency has been shown to cause endothelial cell dysfunction, inflammation, and oxidative stress, which are major contributors to atherosclerosis[2]. Mg and Type 2 Diabetes mellitus (DM) have a close relationship. Approximately one-third of subjects with Type 2 DM have hypomagnesemia mainly caused by enhanced renal excretion [3]. Mg

deficiency is associated with poor glycemic control and Mg supplementation improves insulin sensitivity.

Microalbuminuria was first reported in diabetic patients by Viberti et al. in 1982 [4]. It has been shown to be associated with increased risk of cardiovascular morbidity and mortality in diabetic patients [5]. Furthermore, the presence of microalbuminuria is generally associated with a poorer glycometabolic control and a higher prevalence of chronic complications including diabetic retinopathy, peripheral vascular disease, and diabetic neuropathy [6]. The association between microalbuminuria and Mg depletion is a controversial issue. A previous report showed that high doses of Mg reduce microalbuminuria in traumatic critically ill patients at 36 hour, after infusion [7]. Conversely, there were no significant differences between patients with hypomagnesemia and normal subjects with respect to microalbuminuria [8]. Objectives of this study was to evaluate the correlation between serum magnesium level with micralbuminurea in various age group of type 2 diabetes mellitus patients.

Material & Methods

A total of 120 subjects were enrolled in this study. Among them, 60 subjects had type 2 diabetes mellitus and 60 subjects were normal as control. This study was conducted during a period from January 2021 to September 2021 in Department of Biochemistry with the collaboration of department of Medicine in Katihar Medical College and Hospital, Katihar, Bihar. All the subjects signed an informed consent approved by institutional ethical committee of Katihar Medical College, Katihar, India was sought.

The individuals of the control group were selected in such a way that the total number of controls and cases in each age and sex group were the same. History was taken for smoking, alcohol use, chronic diseases history, and medications for antidiabetics & anti-hypertensives were obtained by a standard interview questionnaire.

Inclusion Criteria: The cases included in the study were known type 2 DM patients attending the outpatient clinic in the department of Medicine.

Exclusion Criteria: Renal failure patients, Type I DM patients, chronic alcohol consumption, acute pancreatitis, Patients on loop/thiazide diuretics or Magnesium supplement/Magnesium containing antacids, were excluded from the study.

Procedures: Under aseptic conditions, 5 mL blood was collected from ante-cubital vein for Serum Magnesium and random sample of urine was collected in sterile container for urine microalbumin. Magnesium was assayed by using Photometric method, its normal range was taken as 1.7–2.4 mg/dL. The normal reference range as provided in the kit had been used for the purpose of estimation. Urine MA analysis was done by using Nephlometric method for the detection of albumin in urine.

Normal urinary albumin concentration (UAC) was defined as < 20 mg/L. Microalbuminuria was defined in the range of 20-200 mg/L as defined by various standard literatures.

Statistical Analysis

Data was analysed by using SPSS version 21 software. Mean and standard deviations were observed. P value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Observations

A total of 120 subjects (60: cases and 60: control) were included in this study. 42 subjects were male in each group and 18 subjects were females in each group (case and control).

Table 1: Gender wise distributions

Gender	Cases	Controls
Male	42	42
Female	18	18
Total	60	60

In this present study, majorities of the patients 61(50.83%) were belonged in age group of 46-60 years**.**

Table 2: Age wise distributions of patients

Age group (years)	No. of patients
15-30	12(16.67%)
31-45	23(34.16%)
46-60	61(50.83%)
>60	24(20%)
Total	120(100%)

Table 3: serum Mg level in control and cases

Gender	S. Mg in controls(mg/dl)	S. Mg in cases(mg/dl)
Males	1.97 ± 0.18	1.58 ± 0.18
Females	1.95 ± 0.18	1.69 ± 0.14

Mean serum magnesium level of males and females in control group had 1.97 ± 0.18 and 1.95 ± 0.18 respectively. Similarly, mean serum magnesium levels in case group patients of males and females had 1.58 ± 0.18 and 1.69 ± 0.14 respectively.

Table 4: Distribution of cases with Normoalbuminuria and Microalbuminuria

Urine microalbumin level (mg/l)	No. of cases	% of cases
Normoalbuminurea	38	63.33%
Microalbuminurea	22	36.67%
	60	

In this present study, in case group, normoalbuminurea and microalbuminuria were seen in 38(63.33%) and 22(36.67%) patients respectively.

Greater mean serum magnesium levels (1.67 ± 0.18) in cases of normoalbuminurea patients was seen in 51-55 age group patients. And greater mean serum magnesium levels (1.90 ± 0.16) was seen in 46-50 years age group patients of microalbuminurea. When compared mean ± S.D. deviations of serum magnesium levels in cases of normoalbuminurea with microalbuminuria. P value was found to be greater than 0.05. Hence, it was not significant.

Table 5: mean S. magnesium in cases with normoalbuminurea and microalbuminuria

Age group(years)	Mean serum Magnesium in cases with normoalbuminurea(mg/dl)	Mean serum Magnesium in cases with microalbuminuria(mg/dl)
40-45	1.72 ± 0.18	1.01 ± 0.05
46-50	1.65 ± 0.19	1.90 ± 0.16
51-55	1.67 ± 0.18	1.84 ± 2.00
56-60	1.66 ± 0.00	1.73 ± 0.18
>60	1.53 ± 0.00	1.85 ± 0.16
Mean	1.74 ± 0.19	1.73 ± 0.18
p-value	>0.05	

In this present study, when we compared the mean ± S.D. of U. microalbumin between cases and control, then p value was found to be less than 0.001. which is extremely statistically significant differences.

Table 6: comparison of U. microalbumin between cases and controls

U. Microalbumin	No. of observed cases	Mean ± S.D. (mg/L)	P-value
Controls	60	11.84 ± 3.74	<0.001
Cases	60	23.03 ± 8.21	

When correlation was performed between mean ± S.D. of S. magnesium and urine microalbumin, r value was found to be -0.35 and p value was found to be greater than 0.05. which is not statistically significant differences.

Table 7: Correlation between S.Magnesium (mg/dL) and urine micro albumin (mg/L).

Compared variable	No. of observed cases	Mean ± S.D	r-value	p-value
S. Magnesium	60	1.82 ± 0.17	-0.35	>0.05
U. Microalbumin	60	23.92 ± 8.23		

Discussions

Studies have shown that low serum magnesium levels and microalbuminuria are associated with type 2 diabetes mellitus patients, which are the known predictors of risk for cardiovascular disease. This is due to decrease in the insulin sensitivity, increasing angiotensin II activity and increasing platelet aggregation. The aim of this study was to correlate serum magnesium levels with glycemic control, risk for cardiovascular and renal involvement in clinically uncomplicated type 2 diabetes mellitus patients.

Magnesium, the second most abundant divalent cation in the intracellular fluid, serves as a cofactor for about 250 cellular enzymes which are involved in energy metabolism. It also plays an important role in protein and nucleic acid synthesis within the cell [9]. The serum magnesium concentration is about 0.3% of total body magnesium [10]. So serum magnesium concentration is an insensitive but specific indicator of low magnesium status [10].

In this present study, a total 0f 120 subjects (60: cases and 60: control) were included in this study.

Majorities of subjects 42(70%) were males. Most of the patients 61(50.83%) were belonged in age group of 46-60 years**.**

This study supports to the studies done by Arpaci, et al., and Dasgupta, et al., where only 42.1% and 38% of subjects were females [11,12].

The kidney is the organ that most closely regulates magnesium homeostasis. About 80% of the total plasma magnesium is filtered through the glomerular membrane

(ionized and complex fractions). The major sites of magnesium reabsorption in the nephron are the proximal tubule (5-15%), the thick ascending limb of the loop of Henle (70-80%) and the distal convoluted tubule (5-10%). Experimental researches have shown that patients with diabetes have a low concentration of plasma magnesium level significantly low ionized magnesium [13]. In a study by Corsonello, et al., type 2 diabetic patients with microalbuminuria or clinical proteinuria had significantly low ionized magnesium [13].

The intracellular depletion of myo-inositol due to disruption of its paracellular transport mechanisms is a major factor in the development of diabetes complications in magnesium deficiency [14]. Therefore, magnesium deficiency has specific pathogenic significance in diabetic nephropathy. Magnesium chloride supplementation lowers HbA1c, improves the Insulin sensitivity in type 2 diabetics and higher magnesium intake is associated with lower risk of diabetes in the general population [15,16].

In this present study, mean serum magnesium level of males and females in control group had 1.97 ± 0.18 and 1.95 ± 0.18 respectively. Similarly, mean serum magnesium levels in case group patients of males and females had 1.58 ± 0.18 and 1.69 ± 0.14 respectively.

When compared mean ± S.D. deviations of serum magnesium levels in cases of normoalbuminurea (1.74 ± 0.19) with microalbuminuria (1.73 ± 0.18). P value was found to be greater than 0.05. Hence, it was not significant differences. But, when we compared the mean ± S.D. of U. microalbumin between cases(23.03 ± 8.21) and control (11.84 ± 3.74), then p value was found to be less than 0.001. which is extremely statistically significant.

Insulin resistance probably explains the relation between diabetic nephropathy and hypomagnesemia; magnesium deficiency reduces tyrosine kinase activity, post-receptor activity, and insulin-dependent glucose uptake, thereby leading to insulin resistance. In addition, increased intracellular calcium in magnesium deficiency interrupts skeletal muscle and adipocyte response to Insulin. On the other hand, Insulin deficiency and resistance lead to reduced tubular reabsorption of magnesium and ensuing hypomagnesemia favor the onset and progression of diabetic microangiopathy, via a reduction in activity of Na+/K+ ATPase pump. A Recent study by Yusuke, et al., concluded that hypomagnesemia independently predicts the progression to end stage renal disease in patients with advanced nephropathy [17].

In a study by Alan R. Dyer et al [18] it was suggested that both albumin concentration (UAC) and ACR appear to be a rational alternative to 24-hour albumin excretion on the basis of their relative positives and negatives. They suggested that UAC is a viable alternative to 24-hour albumin excretion for epidemiologic studies in which body size and weight measurements are not readily available or the additional expense incurred for measurement of creatinine is taken into account. In the present study evaluation of S. Magnesium status in type 2 DM patients showed a significant decrease in its level in cases as compared to controls. This is consistent with studies of Razeena KC et al [19] and Vijaylakshmi S et al [20].

Also Xu B et al [21] has reported a prevalence of microalbuminuria in somewhat lower range of 11.37%. Further, a study conducted by Corsonello et al [22] demonstrated that diabetic patients with microalbuminuria or overt Proteinuria showed a significant decrease in serum Mg compared with normoalbuminuric group. However some studies such as Zargar et al [23] and Sales et al [24] were in discordance with our results and they have reported that no association is present between S.Mg & Microalbuminuria in diabetic patients (Type 1 & 2) According to F. Guerrero-Romero et al [25] the reasons for the

variation in different studies may be due to different geographical locations along with change in dietary habits leading to differences in magnesium intake in the study population Since magnesium is a mild, natural calcium antagonist, intracellular accumulation of calcium occurs in deficient subjects. This increased intracellular calcium may alter the cells responsiveness to insulin, leading to development of insulin resistance [26]. Therefore, an amplification of insulin resistance may be a possible mechanism that connects Serum magnesium to microalbuminuria. In addition, in another study by Barbagallo M et al, [26] it was found that hypomagnesemia can also be caused due to impaired tubular absorption of magnesium in diabetic patients with insulin deficiency or resistance. Therefore, a hypomagnesaemic and insulin resistant state can increase the risk of Microalbuminuria [27]. Anastasia A. Zheltova et al [28] found a strong link between oxidative stress and hypomagnesemia but no conclusive evidence about the mechanism causing oxidative stress in magnesium deficiency has been ascertained. Various studies exist which show associations between hypomagnesemia and complications of Type 2 DM such as neuropathy, retinopathy, foot ulcers, and albuminuria [29]. In our study, we found an inverse correlation (r=–0.32) between serum Mg levels and urine microalbumin which was consistent with many studies by other authors, but our result ($P > 0.05$) were statistically insignificant. A somewhat similar findings were observed in a study conducted by Rao et al [30] who reported only 6% of cases in their study with hypomagnesemia and the urine microalbumin (SUACR) when compared in microalbuminuria with hypomagnesemia group and microalbuminuria with normomagnesemia group, they didn't find any significance of levels of urine microalbumin in the groups. They surmised that these results may be due to small number of cases and reduced detection of hypomagnesemia in their cases. Rooney et al [31] in their study measured Total serum magnesium and ionised magnesium in healthy subjects before and after supplementation of oral magnesium and for 10 weeks resulted in increased concentrations of ionised Mg but was not statistically significant.

Conclusions

This study concluded that type 2 diabetes mellitus patients had significantly lowered serum magnesium levels. Serum magnesium and urine microalbumin was negatively correlated with each other in type 2 diabetes mellitus patients. And it was not statistically significant.

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